Lessons from the ICU
Under the Auspices of the European Society of Intensive Care Medicine
Series Editors: Maurizio Cecconi · Daniel De Backer

František Duška
Mo Al-Haddad
Maurizio Cecconi *Editors*

Intensive Care Fundamentals

Practically Oriented Essential Knowledge for Newcomers to ICUs

Springer

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is a Book Series published by Springer under the auspices of the *European Society of Intensive Care Medicine* (ESICM). The aim of the Series is to provide focused and state-of-the-art reviews of central topics in Intensive Care. Ultimately, its mission is to transfer the latest knowledge to the bedside in order to improve patient outcomes. Accordingly, the ESICM has also developed *Lessons from the ICU* with the vision or providing the best resources for everyone working in Intensive Care. ***Lessons from the ICU***

Each volume presents a comprehensive review of topical issues in Intensive Care. The volumes are intended to cover the majority of aspects that intensive care professionals are likely to encounter in the course of their career. Books offer an excellent guide for residents who are new to the ICU, and for allied professionals, senior consultants as well as nurses and allied healthcare professionals.

The chapters are organized in a way that allows the reader to quickly familiarize or reacquaint themselves with the pathophysiological background before moving on to diagnosis and treatment. Each chapter includes a list of Take Home Messages, as well as practical examples that apply theoretical knowledge in real clinical scenarios. Each volume in the Series is edited by international Key Opinion Leaders in Intensive Care, and each chapter is written by experts in the field.

In summary, this Series represents a valuable contribution to fill the gap in the current Intensive Care literature by providing top-quality literature reviews that can be easily digested and used at the bedside to improve patient outcomes.

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How to Use This Book?

Intended Learning Outcomes

1. Describe the background and aims of intensive care fundamentals book
2. Explain how to use the book

The Origins of Intensive Care Fundamentals

Since its dawn in Blegdams Hospital in Copenhagen during the polio pandemic in 1952, ICM specialists have been helping individuals to survive critical illness. Nowadays, the development of many areas of healthcare is reliant on intensive care services, and the recent pandemic fostered further developments in this field. ICM is a multidisciplinary branch of medicine. There are different educational pathways to become an intensivist: in some countries (Spain, Switzerland, the UK), ICM is a primary specialty, whilst in most others ICM is a supra-specialty to different base specialties (anaesthesia, internal medicine, respiratory medicine, cardiology, neurology, nephrology, surgery, etc.). Invariably, these specialties include a degree of exposure to intensive care through specialised training pathways. In turn, there has been an increasing number of trainees who train and work in ICUs every year either at the start of the pathway to become an intensivist or as part of training in different specialties. The educational needs of these doctors-in-training are similar across Europe, but their training is different. Only a minority of hospitals use standardised induction courses tailored to the educational needs of doctors on their first placement in ICU.

The European Society of Intensive Care Medicine (ESICM) in close collaboration with national ICM societies contributes significantly to the advancement of knowledge in ICM. This was achieved by the promotion of the highest standards of multidisciplinary care of critically ill patients and their families through education, research, and professional development. The ESICM Academy and Master Classes offer the highest standard of education in ICM. The society also supervises summative assessment of ICM competences in the European Diploma in Intensive Care (EDIC) examination. Yet, a standardised induction course was missing in this rich educational landscape and ICF is an initiative aiming to fill this gap (see Fig. 1).

ICF is a standardised face-to-face course, which includes case-based scenarios, interactive workshops, and simulations that have been carefully prepared and standardised by ESICM expert to be delivered locally in local languages by ESICM-trained and certified faculty members. The format was chosen to allow enough flexibility to tailor the training according to local practices, SOPs, and customs, whilst on the other hand embedding the principles of current evidence-based practices in the standardised content. Before coming to the face-to-face course, trainees are required to refresh their basic knowledge, which is covered in this book.

ICF has been created based on intended learning outcomes, a priori defined using a Delphi method by ESICM Clinical Training Committee members, having in mind the needs of junior trainees during their first month of practice. ICF should by no means be mistaken as an advanced educational requirement for the European

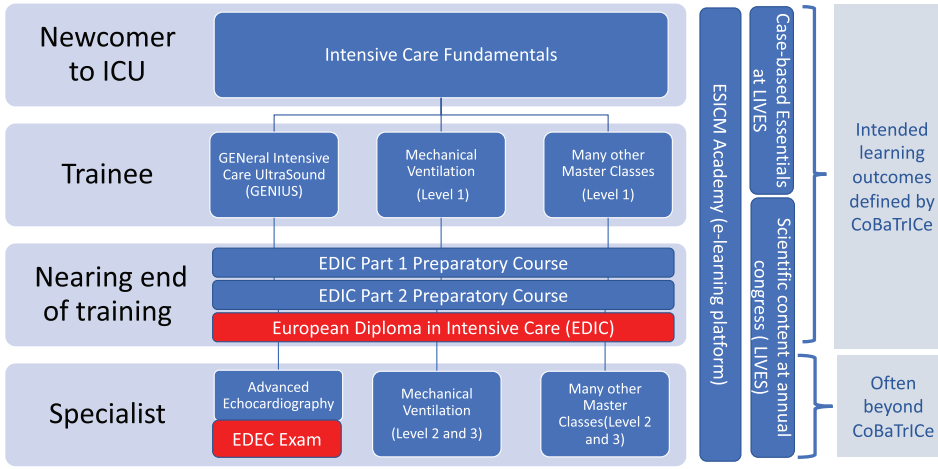

Fig. 1 Structure of educational content offered by ESICM for intensivists in different stages of training. ICF represent the induction for newcomers to intensive care. Note: *CoBaTrICE* Competency-Based Training in Intensive Care, ► https://www.esicm.org/education/cobatrice/; *EDEC* European Diploma in Echocardiography

Diploma in Intensive Care or national exams. The competencies that define an intensivist at the end of training, regardless of the pathway of the training, were defined by EU-funded Competency-Based Training programme in Intensive Care Medicine for Europe (CoBaTrICe) project, which has been recently updated. Rather, we consider ICF as the ideal start to the long training pathway in the fascinating field of intensive care.

How to Use This Book

We assume no previous exposure to intensive care, and we only rely on medical-student level knowledge of basic medical disciplines. Some readers may find basic physiology or pharmacology textbooks handy supplements when reading this book.

Most of the readers with previous experience in ICU might find some chapters too basic. In this case, we encourage you to go straight to the self-test at the webpage: ► https://academy.esicm.org/enrol/index.php?id=376 and verify that you have the required knowledge to make the most of the face-to-face course. Interested readers will find at the end of each chapter a list of suggested resources to enhance their knowledge in the respective field.

This book is intended to be read before the face-to-face course. After reading the book, please visit ► www.academy.esicm.org/icf/precourse to sit pre-course test, which is required for certification. Don't worry, there is no required pass mark at this stage. After completing the test, you can access the preparatory material for the face-to-face course, such as introductory vignettes to cases and simulation scenarios.

Note: If you have obtained this book without registering for ICF, you can still use the self-testing tools and some online supplementary materials after free registration at ► www.academy.esicm.org/icf.

Further Reading

- Common Training Framework in Intensive Care Medicine: ► https://www.uems.eu/__data/assets/pdf_file/0007/19753/Item-3.2.1-ETR-Training-requirements-in-ICM-final-26-sept-2014.pdf.
- Competency Based Training programme in Intensive Care Medicine for Europe (CoBaTrICe, 2022 updates): ► https://www.esicm.org/education/cobatrice/.

Intended Learning Outcomes

At the end of this course, the participant of ICF should be able to:

Outcomes 1: The Deteriorating Patient

- Demonstrate the identification of the acutely ill or deteriorating patient *(in a simulated setting)*.
- Identify life-threatening conditions in an effective and timely fashion using the ABCDE approach *(in a simulated setting)*.
- Demonstrate patient stabilisation and initial treatment for a critically ill patient *(in a simulated setting)*.
- Discuss the risks and possible pitfalls of transporting of the critically ill patient.
- Recognise and manage circulatory arrest and peri-arrest states *(in a simulated setting)*.
- Describe the patient at risk of difficult intubation and demonstrate an understanding of when to call for help.

Outcomes 2: Ward Round

- Demonstrate a routine daily reassessment of a patient in a structured manner (in a simulated setting).
- Adequately prescribe venous thromboembolic disease and stress ulcers prophylaxis.

Outcomes 3: Organ Support

3a. **Acute respiratory failure**

- Describe the indications and modalities of oxygen therapy, non-invasive ventilation methods, indicate intubation and invasive mechanical ventilation.
- Apply basic physiological principles of mechanical ventilation—volumes, pressures, compliance, etc. to the most common lung pathologies and basic modes of ventilation.
- Demonstrate the ability to initially set a ventilator and adapt ventilatory settings for the most common types of ventilation disorders, including obstructive pulmonary disease and ARDS (in a simulated setting/app).
- Select an adequate PEEP based on physiological values (in a simulated setting/app).
- Identify the most common types of ventilator interference.

- List the most common cause of sudden hypoxia in the tracheostomised patient.
- Discuss the management of the acutely hypoxic patient on mechanical ventilation in ICU.
- Describe the principles of weaning from mechanical ventilation, readiness testing, and the risk factors for weaning failure.

3b. **Shock and Haemodynamic monitoring**

- Describe basic cardiovascular physiology and its monitoring in the context of the most common pathologies in the ICU, including cardiac output and its measurement, left heart failure, and right heart failure.
- Demonstrate assessment of fluid responsiveness in the simulated haemodynamically unstable patient/case.
- Discuss the indications and use of vasopressor therapy.
- Describe the different aetiologies of shock, recognise the role of POCUS to help assess the causes of haemodynamic instability.

3c. **Sepsis and septic shock**

- Discuss the warning signs of life-threatening infection.
- Discuss the one-hour bundle of treatment.
- Describe the most common ICU acquired infections and propose an adequate initial antibiotic treatment.
- Identify the need for urgent source control in sepsis where appropriate in a simulated setting or case.
- Describe the basics of antibiotic stewardship.

3d. **Metabolic derangements**

- Interpret arterial blood gases.
- Describe a treatment plan for patients with life-threatening electrolyte and metabolic disturbances.
- Propose adequate management for patients with the most common mineral metabolism disorders, especially hyperkalaemia and hypernatraemia.
- Discuss the importance of fluid choice and balance in the critically ill patient.

3e. **Renal failure**

- Recognise patients indicated for urgent renal replacement therapy (in simulated patient/case).
- Describe common RRT modes and compare haemodialysis, haemofiltration, and haemodiafiltration.

3f. **Nutrition**

- Explain the benefits and risks of enteral and parenteral nutrition.

3g. **Treatment and prevention of delirium, sedation, and analgesia**

- Discuss the physical and psychosocial needs of hospitalised patients with regard to the prevention of delirium.
- Describe signs of hypo- and hyperactive delirium and potential treatments
- Safely prescribe sedation and analgesia in a simulated ICU setting or case, including adequate use of sedation holds.

Outcomes 4: Specific Pathologies in the ICU

4a. **Trauma and surgery**

- Discuss suitable options for perioperative pain management.
- Apply the principles of blood transfusion to a simulated patient with life-threatening haemorrhage/trauma.

- Diagnose and propose a treatment plan for the common coagulopathies in a simulated scenario or case.
- Discuss the management of haemorrhage in the setting of anticoagulant/anti-platelet agent use.

4b. **Neurological emergencies and basics of neurointensive care**

- Describe the pathophysiology of intracranial hypertension and its operative and non-operative management.
- Describe a treatment plan for patients with various neurological injuries (TBI and stroke).
- Plan neuroprotective strategies following cardiac arrest in a simulated patient or case.
- Discuss the immediate actions needed when the patient is showing signs of coning.
- Explain the meaning of neuroprotective measures in patients with brain injury.
- Discuss the initial management of seizures and status epilepticus.
- Describe the principles of post-resuscitation care prognostic assessment post-CPR.

4c. **Medical emergencies**

- Recognise life-threatening brady and tachyarrhythmias and provide treatment options in a simulated setting.

Outcomes 5: Non-Technical Aspects of Intensive Care

5a. **Ethics of intensive care, end-of-life aspects**

- Explain the limitations of intensive care, and the principles of withholding and withdrawing treatment, including potential organ donation.
- Describe a management and treatment plan for the patient at the end of life and adequately prescribe symptomatic therapy.

5b. **Crisis resource management and communication in crisis**

- Discuss the principles of communication in crisis and crisis resource management (leadership, membership, situational awareness) and relate them to their own experience and professional context.
- Communicate in a professional but effective and assertive manner in a simulated emergency.
- Demonstrate a succinct and structured handover in a simulated setting.

Outcomes 6: Equipment

- Troubleshoot common issues with equipment: monitoring, arterial line, central line, chest drain.

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Abbreviations

ARDS	Acute respiratory distress syndrome	ICU	Intensive Care Unit
		MAP	Mean arterial pressure
CARS	Compensatory Anti-inflammatory Response Syndrome	MODS	Multiple Organ Dysfunction Syndrome
CVC	Central venous catheter		
CVP	Central venous pressure	SOFA	Sequential Organ Failure Assessment

Key Concepts in Intensive Care Medicine

Contents

Identification and Initial Stabilization of Acutely Deteriorated Patients

Nicholas F. Parchim and Nathan D. Nielsen

Contents

F. Duška et al. (eds.), *Intensive Care Fundamentals*, Lessons from the ICU,
https://doi.org/10.1007/978-3-031-21991-7_1

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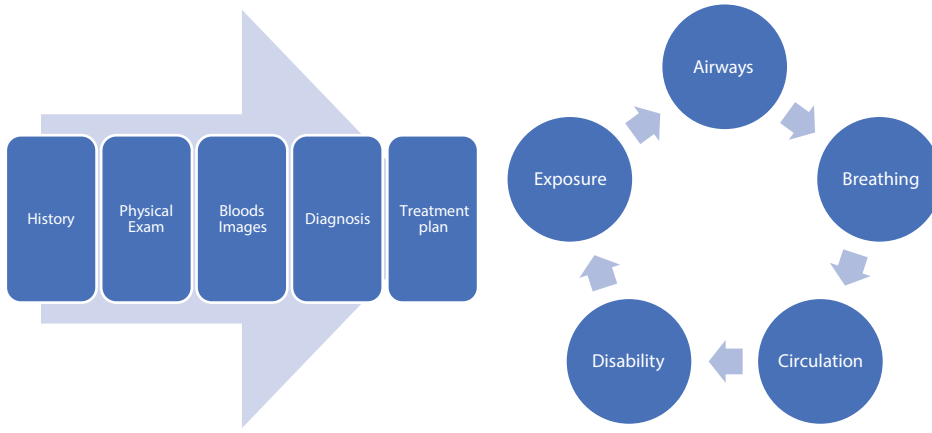
Intended Learning Outcomes

1. Demonstrate the identification of the acutely ill or deteriorating patient (in a simulated setting).
2. Identify life-threatening conditions in an effective and timely fashion using the ABCDE approach (in a simulated setting).
3. Stabilize and initiate treatment for a critically ill patient *(in a simulated setting)*.
4. Recognize and manage circulatory arrest and peri-arrest states (in a simulated setting).
5. Describe the patient at risk of difficult intubation.

» *Doc, come down quick please, they brought in a lady who seems peri-arrest to me.*

Triage of a critically ill patient can be difficult and overwhelming to a trainee or even to experienced intensivists, at times. Included with the patient presentation are a battery of vital signs, laboratory tests, ancillary information, and complicated medical history that can make initial evaluation confusing. Traditional approach in medicine is to obtain history and perform full physical examination. Based on these, form a differential diagnosis, which is narrowed by auxiliary test such as imaging or bloods and translates to treatment plan. Obviously, this linear approach is not applicable in emergency. In this section, we will attempt to provide algorithms which can form the basis of evaluation and triage of an ICU patient make them more easy to understand. The good news is, that the approach is very universal, so it does not matter if you have initially no idea what's wrong with your patients. Basically, the management of acutely deteriorated patients is based on repetitive evaluation of physiological functions with simultaneous treatments of the abnormalities. During each round, you mobilize more resources, which would allow you more sophisticated support of vital function. By doing so, you gain more information, including on the response to your treatment maneuvers, and also much valuable time. After you have dealt by immediately life-threatening abnormalities ("closest crocodile to the canoe"), you can take time to look around, gain more information and think about the next steps [1].



Comparison of linear (left) and ABCDE approach used in emergencies (right)

REMEMBER:
- Intensive care is always a team job. Call for help.
- Keep it simple and make it quick.

1.1 Remember Your ABCs…

Triage is a simplified method of rapid identification of life-threatening conditions, often employed during times of military medicine, which can also be applied to in-hospital patients. As early as the 1960s, a basic ABC algorithm was designed and implemented for those patients who presented with cardiac arrest. Over time, this algorithm has been adapted and changed for many applications, including trauma and medically critically ill patients. Now, all emergency departments use variations of the ABC algorithm to appropriately prioritize patients in order to sort them into groups in order to prevent deterioration of their clinical condition [2].

How Critically Ill Patients May Present:
- altered mental status
- altered respiratory patterns (noisy/stridulous breathing; rapid/shallow breathing)
- severe, intractable abdominal pain
- severe, intractable chest pain
- weakness/difficult ambulation
- seizure
- ingestion/exposure to drugs or environmental substances
- significant vital sign abnormalities

REMEMBER: Recognizing critical illness is neither trivial nor self-evident. More often than not it requires clinical experience, systematic approach and sometimes "a sixth sense: If in doubt, call for help!"

1.1.1 The ABCDEF Sequence for Triage

Each step in the algorithm is designed to be performed sequentially to avoid missing a crucial organ system which could potentially lead to a life-threatening complication. This algorithm has been designed to be applied within seconds-minutes during evaluation of a potentially unstable patient, with reevaluations performed during the assessment. If available, each organ system will be evaluated with examination and point-of-care testing to obtain the quickest information possible. If multiple team members are involved in the triage of a critically ill patient, the steps involved in triage can/should be performed simultaneously with closed-loop communication (i.e., commands with read-back confirmation, e.g., "Please obtain a point-of-care glucose measurement" "Glucose measurement obtained; the value is 6.2 mmol/L.")

Refer to Chap. 4 on non-technical skills and communication in a crisis page 51.

Briefly, the algorithm is listed below, but will be explained in more detail in the following section:

A: Airway Patency

- (Can the patient speak? Are they answering questions? Are they confused? Do you hear stridulous breathing or wheezing? Does the patient require cervical spine stabilization?)

B: Breathing

- (Quality of breathing; Normal respiratory rate? Rapid/shallow breathing?)

C: Circulation

- (Does the patient have a normal blood pressure? Do they appear cyanotic or flushed? Does the patient complain of chest pain?)

D: Disability

- (Do they appear confused? What is their level of consciousness? Check blood glucose, pupillary size, and responsiveness to light in all patients with altered consciousness)

E: Exposure

- (Does the patient have a history of exposure to environmental toxins? Do they require decontamination? Do they have heavy clothes or a helmet on which could limit your examination?)

F: Fever

- **(Is the patient experiencing hypo-/hyperthermia?)**

After having finished the first round of ABCDEF, your patient should have patent airways, be receiving oxygen, have blood pressure, heart rate and respiratory rate, and Glasgow coma scale checked. They have venous access secured. If you have not done so already, call for help now. Then come back to your sick patient and start ABCDEF again.

REMEMBER: All equipment you have is what is in the resus trolley. Make sure you get familiar with its content before you take on the bleep.

1.1.1.1 A: Airway

Securing the airways is usually the first step in the management of all patients. If the patients are able to vocalize (answers loudly), protective reflexes will also be present and the airways are OK. In others, rapidly assess the airway to examine for evidence of airway compromise including: noisy respirations, drooling/inability to clear secretions, swelling of lips/tongue/oropharynx that appears to block the airway, change in voice, vomiting with high risk of aspiration, exposure to fire/environmental chemicals, and trauma to the neck.

First step of airway management in unconscious patients is manually opening the airways by Head Tilt-Chin Lift and Jaw Thrust Maneuver, with reassessment of airway patency and breathing. If the patient is not breathing, start manual bag-mask ventilation.

Every healthcare professional working in intensive care should be capable of performing this basic airway maneuvers to prevent hypoxic cardiac arrest before help arrives.

More advanced airway management should be reserved to those who are adequately trained for it. Golden standard of airway protection in intensive care is endotracheal intubation. Securing the airways in an unstable patient is a delicate procedure, and it should be reserved for the most experienced team member. If possible, the patient and the team should be prepared for intubation when the airway trained person arrives.

If you are not airway trained, your role is to:

- Recognize the need for advanced airway management and call for help.
- Oxygenate: 15 L/min O_2 via non-rebreather mask or bag-mask manual ventilation.
- Get equipment ready (drugs, airway trolley).
- Secure i.v. access or two.
- Know and anticipate steps during routine and difficult airway algorithm and provide help and assistance. If you keep leading the team (acknowledge this clearly!), the airway operator can focus on the task.

ICU Intubation Checklist, predictors of difficult intubation, and Difficult Airway Society algorithm can be found in Useful Algorithms and Checklists (page 256).

What Can I Use in an Emergency?

- Head Tilt-Chin Lift and Jaw Thrust Maneuver
- Bag-mask ventilation with or without nasal trumpet/oral airway
- Suction—preferably rigid Yankauer[1]
- Laryngeal mask airway (LMA) if trained to do so

Note: ICU nightmare is an airway problem in tracheostomized patients. Be prepared to deal with this problem by carefully studying the algorithm (See Useful checklists and algorithms page 260) [3].

1.1.1.2 B: Breathing

Rapidly assess the quality of the patient's breathing—slow (Think of the effect of opioids!), shallow, agonal or quick, deep breathing. Pay special attention to abnormal lung sounds—wheezing, rhonchorous breaths—or the absence of breath sounds. Make note of any trauma to the patient's chest that could be responsible for the patient's current presentation.

Helpful Tools

- Stethoscope
- Pulse oximetry
- Waveform capnography (if intubated/tracheostomized)

1 Firm plastic suction tip with a large opening surrounded by a bulbous head. Named after Sidney Yankauer, American otorhinolaryngologist.

- Arterial or venous blood gas
- Upright CXR
- Pulmonary ultrasound—examine for lung sliding, effusion, or signs of pulmonary consolidation

What to Do in an Emergency?

- Give oxygen: 15 L/min of oxygen via non-rebreathing mask
- Noninvasive ventilation (i.e., high-flow nasal cannula; CPAP/BiPAP)
- Bag-valve-mask (BVM) with PEEP valve
- Surgical consultation for pneumothorax or placement of chest tube for hemothorax
- 14-gauge catheter for immediate pleural decompression in the setting of tension pneumothorax

1.1.1.3 C: Circulation

At first, feel patients central and peripheral pulse and check capillary refill time. This very simple examination only takes seconds and gives you very valuable information about heart rate (slow, normal, fast), rhythm (regular/irregular), and peripheral perfusion. Then, measure blood pressure, connect the monitor, and look at the EKG lead. Insert a peripheral venous catheter and start an infusion of crystalloid.

Tachycardia >90 bpm is abnormal and >150 bpm is usually symptomatic ("Fast, thus sick"). Bradycardia <50 bpm is abnormal and <30 bpm is usually symptomatic.

Assess for hypotension, which is relative given the patient's size, but usually MAP <65 mmHg is symptomatic. Pay attention to other signs of hemodynamic instability including skin changes (i.e., cyanosis, pallor, capillary refill), hives or swelling, confusion, pulseless extremities, signs of trauma and blood loss (i.e., rectal or oral bleeding, vomiting/diarrhea), and oliguria.

Helpful Tools (Point-of-Care Testing)

- ECG
- Bedside ultrasound exam—protocol depends on the context (e.g., RUSH in shock, FAST Focused assessment using sonography in trauma or POCUS in shock)—See Useful Checklists and Algorithms
- Continuous monitoring

What to Do in an Emergency?

- Establish large bore (14- or 16-gauge) bilateral IV access
- Take blood gas (Lactate? Potassium?)
- For shock, start with rapid fluid bolus (4 mL/kg of crystalloid and reassess). Shocked patients will always need arterial and central lines. If profound hypotension doesn't wait for the effects of fluids and give vasopressors:
  - No central line available: give ephedrine (10 mg boluses) or metaraminol (1 mg) and repeat as needed, in peri-arrest situations you can use 0.1 mg adrenalin boluses.
  - Central line available: start noradrenaline continuous infusion.
- For arrhythmias, refer to Useful Algorithms and Checklists page 263.
- Place Foley catheter.
- Think sepsis. Think blood loss (Do you need access to emergency blood?).

1.1.1.4 D: Disability

Your assessment should focus on neurologic disability as your primary target for this system. Examine for depressed or agitated consciousness indicating severe neuropsychiatric disability. Assess pupil size (i.e., dilated or constricted pupils) and symmetric reactivity to light or approach. Notice neck stiffness and other meningeal sign. Gross extremity strength or asymmetry is important. Examine the patient's ability to speak or make sensible answers to simple questions (i.e., "day/month/year?" "what season is it?" "who is the leader of the country?"). Examine for signs of seizure including stiffness, tonic/rhythmic jerking, and unresponsiveness.

REMEMBER: After initial examination, you should be able to narrow differential diagnoses of a patient with disordered consciousness into one of three groups: (1) with focal signs (CT is a priority as structural cause is likely), (2) meningeal signs (meningitis or subarachnoid hemorrhage), or (3) none of these (here extracranial causes are most likely).

How to Approach the Agitated Patient…

- Attempt calming them with voice and remove potential objects which may harm them.
  - Administer antipsychotics (e.g., haloperidol 2.5–5 mg i.v.) and/or short-acting benzodiazepines (e.g., midazolam in 2 mg i.v. boluses) with respiratory monitoring and 1:1 supervision.
  - Persistent agitation presents a significant danger to self/others. Make sure that enough staff is present to help restrain the patient. Sometimes the safest option in severest cases is to sedate and intubate.

How to Approach an Obtunded Patient

- Check a fingerstick glucose measurement first. Think of other extracranial causes (Hypercapnia/hypoxia? Is the patient receiving opioids or sedatives?).
- If GCS <9, consider intubation.
- If no clear extracranial cause, start with CT scan (If focal signs and native CT normal, ask for CT angiogram).
- If febrile and/or meningeal, take blood cultures and consider empiric antibiotics (e.g., ceftriaxone 2 g) and lumbar puncture.
- If CT demonstrates a new intracerebral bleed or epidural, subdural, SAH: control BP with systolic goal 140–160 mmHg, reverse any anticoagulant and perform a STAT neurosurgical consultation.
- If considering herniation of brainstem contents: administer 3% saline, elevate the head of the bed >30 degrees and consult neurosurgery STAT.

How to Approach a Patient with Epileptic Seizures

- Open airways, give oxygen, establish i.v. access.
- Give i.v. benzodiazepines (e.g., midazolam 0.15 mg/kg max 10 mg) and repeat in 5 min if still fitting.
- Give levetiracetam 40 mg/kg (max 3 g) or phenytoin 20 mg/kg over 30 min i.v.
- Get ready for rapid-sequence intubation.

1

1.1.1.5 E: Exposure

Examine areas not obtained by the four prior sections. You should remove the patients clothing and examine all areas of the skin, focusing on areas most commonly missed (i.e., back, buttocks, and genital areas). Focus will depend on the context, but you should not omit:

- Wounds (traumatic or surgical), drains/output.
- Check pulse on all extremities (asymmetry can be key cue to the diagnosis of diseases of aorta and major vessels).
- Consider and perform per rectum exam (always in suspected GI bleed or acute abdomen).
- Check all vascular access sites (Working and usable? How recent? Signs of infection?).

1.1.1.6 F: Fever

Some include checking body temperature into E, but we think it deserves its own letter. Temperature outside normal range can be an important diagnostic cue, but both extremes of temperature may present with altered mental status or agitation.

High Body Temperature

- *Fever* is a reaction of the body to infectious or other stimuli where thermoregulatory mechanisms are reset to higher temperatures. Usually, temperatures are in range 38.0–41.1 °C and are not on their dangerous.
- *Hyperthermia* results when bodily thermoregulatory mechanisms are disabled (anticholinergic/MAOI/cocaine/amphetamine toxicity, neuroleptic malignant syndrome, and thyroid storm), or overwhelmed (environmental exposure). Should be strongly considered if BT ≥ 41 °C and requires immediate physical cooling (See below).

Low Body Temperature (Hypothermia)

- *Core body temperature <36 °C* is abnormal. It can result from bioenergetic shutdown (sepsis, hypothyreosis, adrenal crisis) or environmental exposure (accidental hypothermia).
- *Signs and symptoms* are dependent on body temperature.
  - 33–35 °C: shivering + cold diuresis, mild confusion
  - 27–33 °C: progressive stupor, bradycardia, at risk of VF cardiac arrest
  - Below 27 °C: hypotension, coma, loss of brainstem reflexes, VF arrest, death

When and How to Manipulate Body Temperature?

- If bodily thermoregulatory mechanisms are intact, e.g., if alteration of bodily temperature is caused by infection, no intervention is urgently needed unless targeted temperature management (TTM) is indicated, such as after cardiac arrest or in patients after traumatic brain injuries.
- If thermoregulation is disordered (e.g., malignant hyperthermia) or overwhelmed (heat stroke or accidental hypothermia), intervene.
  - Initiate cooling or rewarming protocols: cooling/rewarming blankets, and use cooled or warmed IV fluids.
  - In severe cases, consider flushing stomach and/or urinary bladder with warm{cold normal saline, or using thermocirculating central venous catheters (i.e., CoolGuard©), RRT, or ECMO.

Note: Some special situation presenting with extremes of body temperature require specific treatment (e.g., dantrolene in malignant hyperthermia or hydrocortisone in Addisonian crisis).

Take Home Messages

- ABCDEF approach is a systematic way how to deal with acutely unstable patients without knowing the cause of deterioration
- ABCDEF aims identify and treat life-threatening conditions (quick killers) such an obstructed airway, tension pneumothorax, bleeding, or sepsis.
- Keep it simple and make it quick. Once you fix the physiology you can take time to gather more information, re-evaluate patient's response to your treatment and think about underlying cause.
- ABCDEF approach can be adopted to all environments—from out of hospital to deteriorated patients in ICU.
- Essential technical skills that need to be trained: Head Tilt-Chin Lift and Jaw Thrust Maneuver, bag-mask ventilation, peripheral vascular access.
- Typically, ABCDEF assessments are performed with many clinicians/nursing staff present, so it is imperative to use non-technical skills such as crisis resource management, role clarity in the team, and closed-loop communication, etc. These are covered in a separate chapter.
- In an unconscious patient, before you continue DEFG … Don't Ever Forget Glucose!

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ICU Routines and Bundles of Care

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Contents

F. Duška et al. (eds.), *Intensive Care Fundamentals*, Lessons from the ICU,
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Learning Goals

By the end of this chapter, you should be able to

- Demonstrate a routine daily reassessment of a patient in a structured manner (in a simulated setting).
- Effectively prescribe venous thromboembolic disease and stress ulcers prophylaxis.
- Describe the most common ICU acquired infections and propose an effective initial antibiotic treatment.
- Discuss the importance of fluid choice and balance in the critically ill patient.
- Discuss the benefits and risks of enteral and parenteral nutrition.
- Troubleshoot common issues with equipment: monitoring, arterial lines, central venous catheters, and chest drain.

2.1 ICU Ward Round and Daily Assessment ("Clerking") of ICU Patients

Each ICU has its own pace and daily routines. Stable patients' post-resuscitation receives medical and nursing care as per plan, which consists of the following components:

- *Causative treatment of the underlying disease* (e.g., antibiotics in severe community acquired infection). In general, causative treatment in the ICU does not differ from treatment in other settings. Often though, the initial ICU treatment functions to buy patients time to recovery, even in conditions for which there is no causative treatment.
- *Symptomatic and supportive treatment* (e.g., sedation and analgesia) to allow patients to bear ICU treatments in a dignified manner.
- *Support and replacement of failing organs, for example, mechanical ventilation, dialysis, cardiac pacemaker.* The ability to provide mechanical ventilation is often regarded as the hallmark of ICU.
- *Prevention of complications.* This is a crucial component of contemporary intensive care as outcomes of intensive care (not only survival, but also functional outcome) rely on the ability of the unit to prevent complications of treatment such as ventilator-associated pneumonia, pressure ulcers, thromboembolic events, delirium, or complications of immobility. Usually, effective prevention results from adherence to a range of measures called bundles of care. The level of adherence to these bundles as well as the incidence of complications are used as quality indicators of intensive care.

2.1.1 ICU Ward Round

To appropriately assess their patients and determine a management plan, intensivists should see all patients under their care at least twice daily in a structured bedside ward round. Often, first rounding is taking place in the morning where night staff hands over to the day team and general plans for the day are set. Then, the second "big" ward round usually aims to review what has to be done during the day and to discuss problems and plans in more detail as well as to provide the opportunity for bedside teaching. Although routines may vary, good practice is, that ward rounds are performed regularly (the same start time and location every day) and in a structured manner. They are usually led by the consultant intensivist in charge and include junior doctors, nurse in charge, and ideally also other allied healthcare professionals such as clinical pharmacists, physiotherapists, and dieticians. Bedside nurses participate in the discussion around the patients they look after. Clinical microbiologists are also essential in the daily assessment, but there might be separate rounds with them depending on the unit.

Productive ward rounds are uninterrupted and patient-centered. They give everyone the opportunity to speak up and discuss issues, and are conclusive for all team members, meaning the whole team agrees on the plan and the goals of care, and each team member knows what to do (e.g., nurses receive their physiological targets sets including thresholds to inform medical team, etc.). If the patients are conscious, they obviously must be involved, too. Ward rounds are usually not the place to discuss organizational or administrative issues, so it is recommended to start with a morning huddle to address these issues and to introduce new team members and delegate roles.

Junior doctors are usually expected to liaise with the bedside nurse and briefly present the patient and current issues and propose a plan. Therefore, before ward rounds, make sure you know your patients! Who are they? Why are they in ICU or remain there? What is the short-term and long-term plan? Is the patient or their family aware of the plan and is it in keeping with the patients' values? What are my concerns and questions?

In this chapter, we will discuss routine assessment of the critically ill patient including common practical issues and complications. Bundles of care are described in more detail separately.

2.1.2 Routine Daily Assessment of the Critically Ill Patient

Close monitoring and frequent clinical exams are necessary to tailor critical care treatment towards patients' needs and to become aware of life-threatening deterioration and react in a timely manner. Every patient should be examined in detail at least once daily ("daily clerking"). This is usually performed by staff doctors and consists of:

- *Checking patients notes:* Never omit this step even if the patient has been handed over to you in detail. Important information may be lost during multiple handovers.
- *Focused clinical exam from head to toe:* This includes assessment of the airway, breathing, cardiac function, and circulation as well as an abdominal and a focused

neurologic examination and a check of all line insertion sites. Often, it also includes a focused ultrasound examination (nowadays a natural extension of physical exam). A physical check of all infusion pumps and syringe drivers (What continuous drugs is the patients on and in what doses?), monitors as well as device screens and settings (ventilator, dialysis, ECMO, etc.) should be carried out, too.
- *Chart review:* Checking blood results, imaging, or other auxiliary exams.
- *Documentation:* Physical findings are noted. List of medication is carefully checked and updated—this requires a lot of focus and attention.
- *Communication:* Any issues, plans (globally set at ward rounds), or changes are always communicated with the bedside nurse or other relevant healthcare professionals.

There is a lot to be done, and it is easy to forget or overlook something important. Therefore, it may be useful to use a checklist (for example, see in Useful Checklists and Algorithms page 265) when going through this process.

2.1.3 ICU Equipment and Common Problems

Checking the equipment around the ICU patient is almost as important as examining the patient. It is mandatory to check that monitors are giving correct readings and the artifacts and inaccuracies are detected. Luckily, most of the technical issues are solved by experienced nurse staff at the bedside. Ask them, when not sure about the reliability of monitoring.

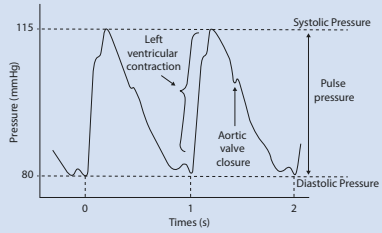
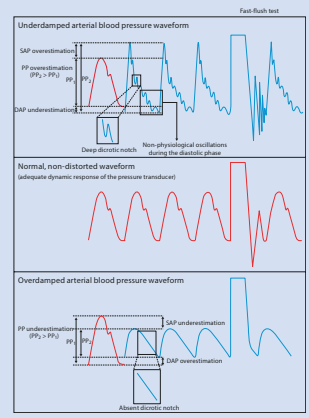
Minimum standard monitoring for critically ill patients include:
- ECG (3- or 5-lead, arrhythmia, and ST-segment analysis)
- non-invasive blood pressure measurement (NIBP)
- oxygen saturation (SpO_2) via pulse oximetry
- urine output

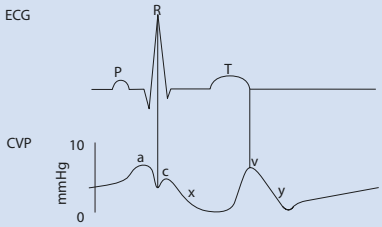
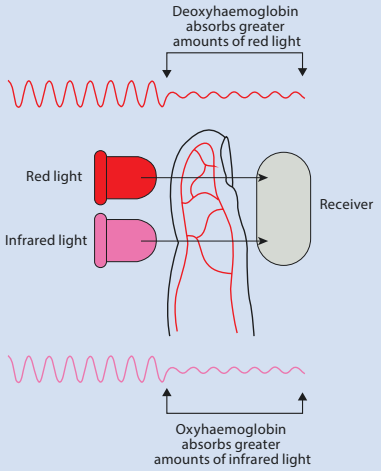
Often, ICU patients will also have invasive blood pressure measurement via an arterial line (IAP), a central venous catheter (CVC), a nasogastric tube, or other devices in place such as dialysis catheters, drains, end-tidal pCO_2 or semi-invasive cardiac output measurement tools, pacing wires, and ECMO catheters.

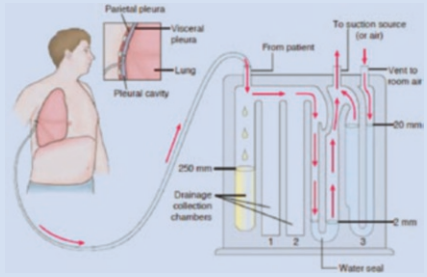
Common issues and pitfalls for frequently used ICU Equipment are summarized in the table.

Equipment	How does it work?	Issues and Pitfalls
Non-invasive blood pressure (NIBP)	Intermittent automated Oscillometer using a cuff (arm or leg) Displays systolic (SAP) and diastolic pressure (DAP) as well as mean arterial pressure (MAP) MAP is measured directly or calculated: MAP = DAP + 1/3 (SAP – DAP)	Cuff size too small → SAP over-estimated Cuff size too big → DAP under-estimated Optimal cuff size depends on arm circumference

2

Equipment	How does it work?	Issues and Pitfalls
Invasive arterial pressure (IAP)	Continuous invasive measurement of SAP, DAP, and MAP through arterial line Principle = hydraulic coupling = column of fluid directly connecting the arterial system to a pressure transducer Components: arterial catheter, fluid-filled tubing, transducer, pressurized flushing system, signal processor/amplifier Fast-flush test Underdamped arterial blood pressure waveform SAP overestimation PP overestimation (PP2 > PP1) DAP underestimation PP1 PP2 Deep dicrotic notch Non-physiological oscillations during the diastolic phase Normal, non-distorted waveform (adequate dynamic response of the pressure transducer) Overdamped arterial blood pressure waveform PP underestimation (PP2 > PP1) PP1 PP2 SAP underestimation DAP overestimation notch This picture is almost impossible to read. Consider changing graphical design.  Waveform and value may help with diagnosis of right heart failure/cor pulmonale, tricuspid regurgitation/stenosis, tamponade, constrictive pericarditis Impedance and harmonic resonance at the site of the vascular tree where IAP measurement is taken also determines waveform morphology	*Levelling* = transducer must be set at the appropriate level in relation to the patient (usually projection of the right atrium) to not introduce error due to adding hydrostatic pressure of the fluid column *Zeroing* = atmospheric pressure discounted from the pressure measurement, done by exposing transducer to atmospheric pressure, open stopcock of transducer to atmosphere → when transducer is used with a zero-line it has to be fluid filled *Over-/underdamping* = artifact of inappropriate dynamic response of the system, determined by damping coefficient that depends on internal radius and length of catheter/tubing → leads to misinterpretation of arterial waveform and values → assessed through visual check of IAP waveform and the "fast-flush test" (flushing the system with fluid at a pressure of 300mmHg generates high amplitude waves that fade depending on the damping coefficient of the system)  Saugel et al. Critical Care (2020) Reasons for underdamping: stiff tubing, defective transducer Reasons for overdamping: soft and long tubing, low infusion bag pressure, air bubbles, blot clots, lose/open connections, catheter kinking Important reference: Saugel et al. Critical Care (2020)

Equipment	How does it work?	Issues and Pitfalls
Central venous pressure (CVP)	Continuous or intermitted measurement of the pressure in the right atrium or superior vena cava through central venous line Represents the filling pressure of the right side of the heart Principle = hydraulic coupling = column of fluid directly connecting the central venous system to a pressure transducer  a = atrial contraction c = closing and bulging of the tricuspid valve x = atrial relaxation v = passive filling of atrium y = opening of the tricuspid valve	Measurement performed at end-expiration, ideally without fluids running Possible factors altering accuracy are placement, leveling, zeroing, system damping, and PEEP
Pulse oximetry	Principle = pulsatile blood absorbance of emitted infra-red or red light changes with the degree of oxygenation, detection via photodetector  Mildenhal et al., Journal of Paramedic Practice (2008)	Possible sources of error: – Lag time – Motion artifacts – Dys-hemoglobinemia – Anemia – Intravenous dyes – Low saturation (progressively inaccurate <80%) – Abnormal pulse or non-pulsatile flow (cardiopulmonary bypass) – Low cardiac output, hypothermia, vasoconstriction – Pigmented skin, nail polish

Equipment	How does it work?	Issues and Pitfalls
Chest drain system	For continuous drainage of fluids and/or air from the pleural space Principle = underwater seal for one-way drainage and prevention of outside air/fluid entering pleural space → drainage can be facilitated by hydrostatic pressure or additional suction (usually -20cmH_2O)  Morton PG, Essentials of Critical Care Nursing, 2012	Complications include: – Kinking and obstruction of the tubing – etrograde flow of fluid if collection chamber is raised above the level of the patient – Tension pneumothorax due to clamping or obstruction

2.2 Fluid Therapy in the Critically Ill Patients

2.2.1 Introduction

By the term "fluids" we mean intravenous crystalloid (or rarely colloid) solutions, which are among the most frequently administered intravenous drugs in critical care. According to the reason for administration, fluids can be divided into:

- resuscitation fluids, administered to correct intravascular volume deficit and increase preload
- replacement fluids, administered to correct losses of interstitial fluids or electrolytes
- maintenance fluids, administered to cover the needs of water and electrolytes, which cannot be given by enteral route
- creep fluids, administered as dilutant of other intravenous drugs (these average 800 mL/day)

Fluids should be considered as any other drug in ICU and given in the right time and in the right amount, based on understanding patients' physiology.

2.2.2 Physiology of Body Fluid Compartments in Acute Illness

Total body water oscillates between 50 and 70% of body mass, depending on age, sex, and fat to lean body mass ratio and, in ICU patients on the underlying disease (e.g., congestive heart failure vs. protracted diarrhea in the elderly) and previous fluid resuscitation. Body fluid is divided in two main compartments:

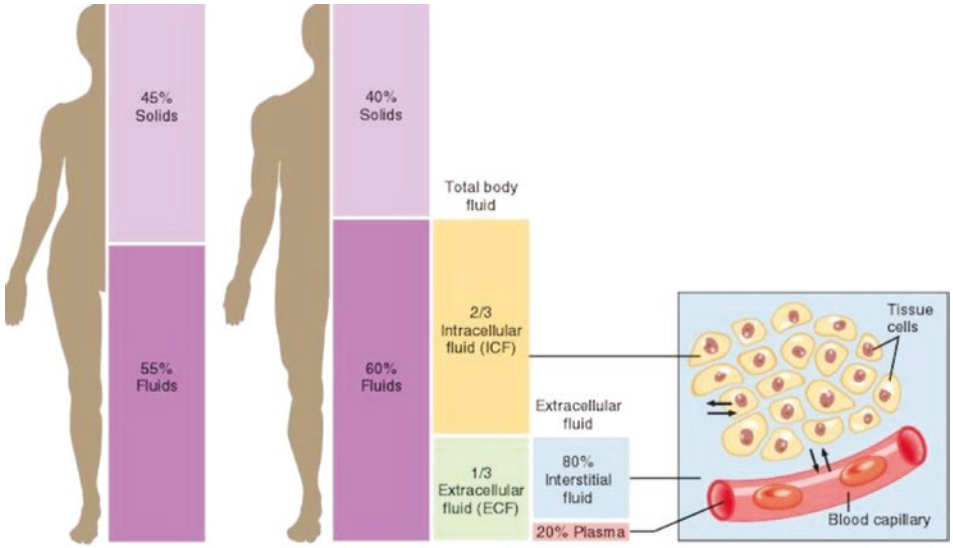
- Intracellular compartment.
- Extracellular compartment, further subdivided into intravascular (plasma) and extravascular (lymph, interstitial fluid).

Sometimes gland secretions and fluid in the lumen of gastrointestinal tract or body cavities (ascites, pleural fluid) are named as "third space." Losses into the third space can be very significant, i.e., in protracted obstructive ileus. Each compartment has different solute composition. Water movement between compartments is determined by osmotic and hydrostatic pressures through semipermeable membranes:

- The cell membranes mark the border between intracellular and extracellular space. Only water and small uncharged molecules (urea, ethanol) can cross, other transports (ions, glucose) are highly regulated.
- The endothelial glycocalyx marks the border between intravascular and extravascular (interstitial) space. It is normally permeable for water and small molecules such as ions and metabolites, but impermeable for proteins. Endothelium is disrupted during critical illness allowing even colloid solutions to leak into the extracellular space.

Note: Interstitial fluid can be almost endlessly expanded without raising hydrostatic pressure in this compartment. Together with disrupted endothelium this means that unlimited amount of infused fluid can accumulate in the interstitial space. Beneficial hemodynamic effects of fluid boluses are only short-lived, whilst the harm from the edema and worsened microcirculation remains.

Exogenous fluids can be iso-, hypo-, or hypertonic when compared to plasma. In theory, isotonic fluids target the extracellular compartment and distribute proportionally between intravascular (1/5 of infused volume) and extravascular (4/5 of infused volume) spaces. Hypotonic and glucose containing solutions reduce plasma osmolarity and load the intracellular space too. Colloids were designed to remain in the intravascular compartment and have more marked hemodynamic effects, but leaky endothelium and side effects (see below) limit the use of colloids in the critically ill.



2.2.3 Types and Characteristics of Intravenous Fluids

Crystalloids are solution of ions and small molecule metabolites in water.

i. **Unbalanced crystalloid solutions** such as normal saline contain high concentration of sodium chloride. High chloride concentrations induce renal afferent vasoconstriction and a decrease in renal blood flow and glomerular filtration rate. Administration of isotonic saline causes hyperchloremic acidosis.
ii. **Balanced crystalloid solutions** contain also other anions than chloride, such as metabolizable organic acid (lactate, acetate, gluconate). They are designed not to change patient's acid base status. See page 137 for detailed description of acid base effects of fluids.

Colloids: They contain macromolecules dissolved in crystalloid solution. They are not commonly used in critically ill patients.

iii. **Hydroxyethyl starch (HES):** It is associated with acute kidney injury and the need for renal replacement therapy in three large randomized clinical trials. Since 2013, they have not been recommended for the use in critically ill patients by the European Medicines Agency.
iv. **Gelatin:** It is a synthetic colloid with a relatively short plasma half-life. So far, there is no evidence of increased acute kidney injury or bleeding between gelatins and crystalloids and gelatins are still occasionally used as resuscitation fluids in some units.
v. **Albumin**: It is a plasma protein and the main determinant of plasma oncotic pressure. Endogenous albumin has antioxidant effects, serves as a transport protein, and may modulate inflammatory response. However, a large, randomized trial has shown no significant benefit of resuscitation with albumin over other types of fluid so its use in this indication is rare (perhaps with the exception of Italy). The administration of albumin in patients with acute decompensation of liver cirrhosis is well-established (Table 2.1).

Table 2.1 Normal plasma osmolarity ranges from 275 to 295 mOsm/kg of water and strong ion difference is 42 mEq/L

Solution	Na^+ (mEq/L)	K^+ (mEq/L)	Cl^- (mEq/L)	Glucose (mg/L)	Other anions (mEq/L)	Osmolarity (mOsm/L)	Strong ion difference (mEq/L)
Crystalloids							
Unbalanced							
• Glucose 5%	–	–	–	50	–	252	0
• Glucose-saline	30	–	30	40	–	282	0
• NaCl 0.9%	154	0	154	–	–	308	0
• NaCl 3%	510	0	510	–	–	1026	0
• NaCl 7.5%	1275	0	1275	–	–	2395	0
Balanced							
• Lactate Ringer	130	4	108	–	Lactate (27.6)	277	27.6
• Acetate Ringer	132	4	110	–	Acetate (29)	277	29
• Acetate gluconate (Plasma-lyte®)	140	5	98	–	Acetate (27) Gluconate (23)	294	50
• Acetate malate (Isofundin®)	145	4	127	–	Acetate (24) Malate (5)	304	29

2.2.4 Practical Guide to Fluid Use in ICU

Both inadequate and excessive use of fluids can be harmful for ICU patients. Lack of fluids typically worsen tissue hypoperfusion and in turn organ function, can cause sympathetic overactivation, arrhythmias. Excess of fluids lead to tissue edema, limb and abdominal compartment syndromes, electrolyte, and acid base abnormalities, dilutional coagulopathy, or acute hypothermia. Finding the right amount of fluid is the art of intensive care, and there is ongoing debate whether restrictive or liberal strategy is better. Evidence-based medicine has not yet brought the answers, either. As a general guide, "ROSE concept" can be used (see Fig. 2.1)—the principle being the liberal fluid strategy to preserve organ function early at resuscitation, whilst much more restrictive strategies later, aiming at negative fluid balance during the recovery phase.

The notorious "four D's" of antibiotic stewardship can also be used to guide fluid therapy.

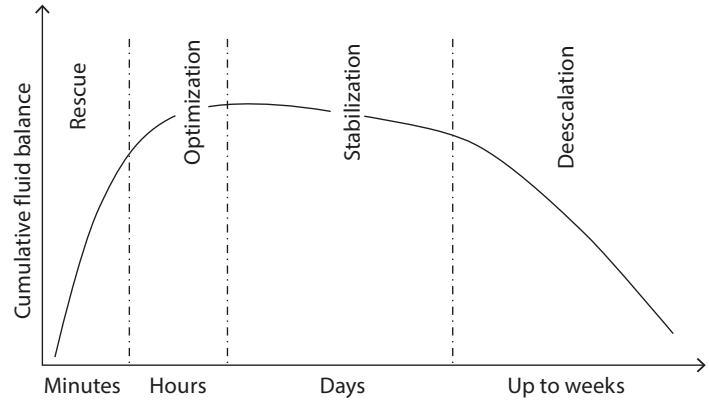


Fig. 2.1 ROSE concept of fluid administration

Drug: Different types of fluids are needed in different indications:

- Resuscitation: Current evidence favors crystalloids over colloids. Avoid excessive crystalloids in major hemorrhage and use blood products instead (see page 195).
- Replacement: Mimic the fluid that has been lost: blood when bleeding, saline in case of GI losses, isotonic replacement in case of burns.
- Maintenance: Deliver basic electrolytes and glucose for metabolic needs (water: 1 mL/kg/h; glucose 1 to 1.5 g/kg/day, sodium and potassium 1mmol/kg/day). Routinely administering maintenance fluids can have a significant overall contribution to fluid balance. The most physiological way to ensure free water intake is to mimic drinking by intermittent administration of tap water via NG tube.
- Creep fluids should be subtracted from maintenance fluids. Note that most of creep fluids is normal saline, so chloride content of maintenance fluids should be reduced even more (consider using high SID solutions such as PlasmaLyte for maintenance).

Dosing: Infusion rates should be dynamic according to the clinical situation.

Duration: Timing and administration rate are important.

De-escalation: Withdrawing of fluids when they are no longer required reduces the risk of fluid overload and derived complications. Fluid overload is consistently associated with worse patient-centred outcomes. The use of loop diuretics can decrease the net cumulative fluid balance and retrospective studies hint towards a benefit in survival. However, loop diuretics can lead to hemodynamic and electrolyte disturbances.

In practical terms, when seeing an ICU patient, before prescribing fluids try to answer the following questions:

- At what stage is the patient? Do I expect him/her to need more fluid (resuscitative phase) or be balanced or negative (during recovery)? Check fluid balance over last 24 h—is it in keeping with these expectations?
- Notes: What fluids is the patient already receiving and how much? What is the output (urine, NG, drains, other losses)?

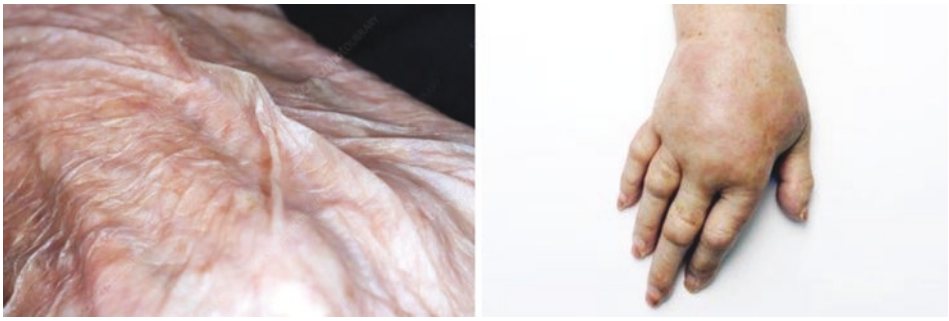


Fig. 2.2 Clinical signs of volume of interstitial fluid: too low on the left (skinfold in dehydration) and too high on the right (swollen hand of a critically ill patient).

- Physical exam plus ultrasound:
  - Intravascular volume status is assessed by (see Chap. 7 on shock and hemodynamic instability page 98) and signs of organ perfusion (urinary output, capillary refill time).
  - Interstitial compartment volume is assessed by skin turgor. In dehydration skin turgor is lost (Fig. 2.2) whilst if interstitial compartment is full, edema develops. There is usually pitting edema of all extremities and dependent parts of the body.
- Lab results: Elevated sodium and urea suggest a deficit of free water that may need to be replaced. Is the sodium chloride difference far from 34 and do I want to influence the acid base status to any direction? Does potassium need to be replaced?

Answering those questions should lead to a decision on which fluid and how much to prescribe using which route. In practice, there is usually one isotonic or slightly hypotonic balanced crystalloid in use as i.v. maintenance fluids (may or may not be prescribed) and enteral (NG) water. In severe metabolic alkalosis, normal saline can be used instead of balanced solution or 5% glucose in hypernatremia if NG water does not suffice to correct it.

2.3 Nutrition

Most critically ill patients lose the ability to eat and drink and their nutritional needs must be provided by means of artificial nutrition. At the same time, critical illness changes the way that metabolism adopts to starvation.

Normally, adaptation to fasting is achieved by lowering blood glucose to near 3 mmol/L, which suppresses secretion of insulin, which leads to hydrolysis of fat to free fatty acids. Free fatty acids are released to the bloodstream and converted in the liver to ketone bodies (acetoacetate and 3-hydroxybutyrate)—water soluble and a readily available energy source. The combination of low insulin levels with high ketones in the blood prevents most tissues and organs from using glucose as an energy source and glucose is saved to feed the brain. This is very crucial for the ability

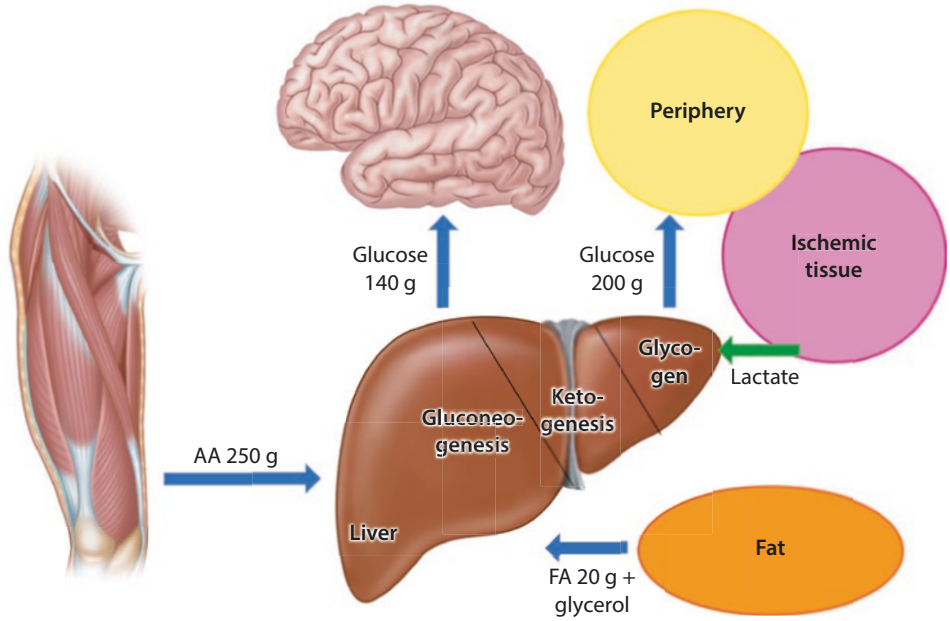


Fig. 2.3 Metabolism during critical illness (redraw)

to survive prolonged starvation. It is not the energy that limits survival (15 kg of fat provides 15,000 × 9 kcal, which is enough for over 67 days), but rather the reserves of body protein. After few days of starvation, the only source of glucose in the blood is gluconeogenesis from amino acids. In turn, minimizing glucose oxidation (by oxidizing fat instead) is key to minimizing protein catabolism. Indeed, providing energy substrates fully reverses all those changes and induces anabolism (Fig. 2.3).

In critical illness, there are significant changes to this adaptation to starvation. Counterregulatory hormones such as adrenal axis and systemic inflammation induce net protein breakdown and insulin resistance. Released amino acids are converted to glucose, which lead to an increase in blood glucose level. Insulin fails to control blood glucose levels and muscle catabolism. Mobilization of free fatty acids is limited by poor perfusion of adipose tissue, which further reduces the ability to control protein catabolism. Due to the stress response, energy expenditure increases above baseline (although not as much as previously thought). Importantly, unlike in normal fasting, providing energy substrates to the critically ill can only partially reverse the metabolic changes.

	Normal fasting	Critical illness
Glucose	Low (typically 3.3 mM)	High (above 6.1 mM)
Energy expenditure	Normal, later low	Higher
Fat mobilization and oxidation	Increased	Impaired
Reversible with refeeding	YES	NO
Protein catabolism	Low	High

► ***Clinical Examples***

Example 1: A 24-year-old fit and well woman had her planned morning arthroscopy postponed until late afternoon. She only drank a bit of water but has been starving for almost 24 h. During routine check, her blood glucose was 3.3 mmol/L. The doctor wisely did not respond to this by prescribing glucose infusion as she judged this to be a normal physiological response to fasting. A glucose infusion would interfere with the physiological regulation and its sudden interruption later could result in symptomatic hypoglycemia.

Example 2: A 36-year-old had a motorbike accident and was brought to hospital with multiple injuries. His blood glucose was 12.1 mmol/L despite having no history of diabetes. Hyperglycemia was a result of insulin resistance of critical illness. It persisted beyond the resuscitation phase, and he needed an intravenous insulin infusion for 4 days to control his blood glucose. ◄

Although long-term illness is not survivable without artificial nutrition and a calorie deficit is associated with poor outcomes, there is surprisingly little data from large scale randomized controlled trials in the field of nutrition clearly demonstrating benefit. Therefore, guidelines and recommendations are largely based on physiology, smaller studies, and expert opinions. In some units, nutrition is prescribed by dieticians, in others it is a task for the doctor.

2.3.1 Estimating the Needs: Nutritional Targets

Energy expenditure can be measured by indirect calorimetry (which calculates energy expenditure based on O_2 consumption and CO_2 production) and feeding should be individualized. In this case, hypocaloric (70% of measured expenditure) feeding is given during the acute phase and gradually increasing to 100%.

Nonetheless, in most units, indirect calorimetry is not available. There are plenty of equations to determine the recommended calorie intake, but perhaps best is to estimate the daily target, that should be gradually achieved over the first week of ICU stay is **25 kcal/kg per day and 1.3 g/kg per day of protein.** This is to be modified in extremes of body weight. Severely obese patients need relatively fewer calories and more protein. One of the ways is to use adjusted body weight (e.g., ► https://www.mdcalc.com/ideal-body-weight-adjusted-body-weight for calculations) or use ideal body weight and count 2.0–2.5 g protein/kg day.

2.3.2 Way of Delivery: Enteral vs Parenteral

Those few patients on ICU who can eat should be encouraged to do so and their intake should be carefully monitored by a dietician.

Most patients in ICU would be receiving **enteral nutrition**. This should be started in **all ICU patients (**if there are no contraindications) who are unlikely to resume full oral intake **within 48 h**. Most units use ready-made polymeric formulas that contain enough protein and usually 1.0, 1.5, or 2.0 kcal per mL, so correct dose can be easily calculated. Patients with impaired pancreatic secretions or short bowel may need

oligomeric formulas containing peptides instead of proteins. The preferred way of delivery is continuous administration into nasogastric tube. An alternative is feeding into a nasojejunal tube. Patients requiring long-term feeding can have a percutaneous endoscopic gastrostomy (PEG) or percutaneous jejunostomy (JEJ).

Contraindications to enteral feeding are relatively few. EN should be delayed, whenever:

- The intestine cannot be perfused with oxygenated blood, due to:
  - uncontrolled shock (only start low dose feed when vasopressor dose is stable and lactate is going down)
  - uncontrolled hypoxia and hypercapnia
  - overt bowel ischemia
- The intestine is under pressure in abdominal compartment syndrome (low dose feed can be started in controlled abdominal hypertension).
- The intestine is damaged
  - mechanical ileus
  - active upper GI bleed
  - intestinal perforation, anastomotic leak, or high output fistula without distal access

Common issues after starting enteral nutrition is high gastric output (above 500 mL after 6 h) or vomiting. Prokinetics (e.g., metoclopramide 10 mg every 8 h for max of 5 days) can be tried, together with pausing EN and restarting at half rate. If gastric feed intolerance persists, a nasojejunal tube should be inserted. A nasojejunal tube is inserted either endoscopically or blindly using special tubes (e.g., tiger tubes).

Parenteral nutrition is used if EN is contraindicated or fails. In well-nourished patients, it is possible to keep trying enteral feeding for up to 7 days, whilst in malnourished patients PN should be stated earlier. Nonetheless, there is no point in giving PN for 1 or 2 days, so the decision to start PN should be based on longer term outlook of each patient. Goals of feeding are identical and EN and PN can be combined if EN is only partially absorbed. The most common formulae are ready made all-in-one bags, containing proteins, glucose, and lipids. This is given continuously 16–24 h per day into a separate lumen of central venous catheter.

REMEMBER: The all-in-one bag does NOT contain all what is needed. Unlike enteral formulas, parenteral bags do not contain vitamins and trace elements, which must be added in form of 1 vial each of water-soluble vitamins, lipid soluble vitamins, and trace elements. Don't forget this when prescribing parenteral nutrition.

2.3.3 Special Formulas and Substrates

In previous years, a lot of research has been done on special formulas and additives such as omega-3-enriched formulas, antioxidants, glutamine dipeptides, and extra doses of vitamins. At present, there is no evidence for their routine use outside clinical research or special circumstances.

2.3.4 Blood Glucose Control

Currently, sliding scale insulin (i.e., continuous intravenous infusion of regular insulin with rate adjusted by a nurse according to regularly measured blood glucose level) is used in critically ill patients. Insulin is started if blood glucose is above 10 mmol/L and the dose is adjusted to a target of 6–8 mmol/L. These targets are a pragmatic compromise between tight glucose control, which risks hypoglycemia and increases mortality, and the harms from hyperglycemia (infections, osmotic diuresis, etc.). Experienced ICU nurses are usually very good at controlling blood glucose by sliding scale insulin.

REMEMBER: Patients without insulin secretion such as those with type 1 diabetes or after total pancreatectomy need continuous insulin delivery in the form of i.v. infusion at a minimum rate 0.5 IU/hour or long-acting s.c. insulin.

2.3.5 Common Issues with Feeding and What To Do

- "Nondefecation," unlike constipation, means no bowel movements for several days without other symptoms such as abdominal bloating, distension, or pain. Continue enteral feeding.
- Diarrhea is also very common in ICU. Review antibiotic treatment (consider stopping or de-escalating), stop prokinetics. Send out sample for C. dif. In some units, there are probiotics in use (not in pancreatitis, though!). If you strongly suspect EN, stop it for 1 day and reassess. If EN is to blame, restart at half dose, and consider using oligomeric formula instead.
- In pancreatitis, gastric feeding is an option, but it often fails due to mechanical pressure of swollen retroperitoneum onto gastric outlet. Therefore, NJ insertion is often necessary, PN nowadays very rarely.
- Patients with renal and liver failure should receive standard enteral nutrition as all other patients.
- To prevent refeeding syndrome, start feeding at half normal rate in patients with chronic alcoholic abuse and severely malnourished patients. Always give extra thiamine. Watch and replace potassium, magnesium, and phosphate.
- Enteral nutrition is possible in the prone position, but tolerance may be poor. Possible solution could be in giving higher doses of EN during the supine periods.

2.4 Venous Thromboembolism Prophylaxis

- Deep vein thrombosis (DVT) and pulmonary embolism (PE), collectively known as venous thromboembolism (VTE), are serious, potentially life-threatening conditions that occur frequently in ICU patients. Estimates suggest the incidence of VTE is 100 times greater in hospitalized patients compared to the general population, and higher still in ICU patients. Venous thromboembolism prophylaxis is a standard of care in the ICU and hospital wards and is usually continued until the

patient is fully ambulatory or discharged from hospital. For ICU patients—virtually all of whom are considered to be at high risk for VTE pharmacologic thromboprophylaxis should be used over mechanical methods or no prophylaxis. In general, low molecular weight heparins (LMWH) are the preferred agents. Mechanical methods are used in in combination with LMWH, or alone in ICU patients with high risk of bleeding. Indeed, ICU patients may develop DVT despite adequate prophylaxis. Subgroups of critically ill patients with a higher risk of thromboprophylaxis failure exist and include those on vasopressor therapy or patients with an increased BMI.

2.4.1 Low Molecular Weight Heparins

LMWH is considered the standard of care for VTE prophylaxis. Suggested prophylactic doses for ICU patients with a creatinine clearance >30 mL/min and no extremes in body weight are the following:

- ► Enoxaparin 40 mg subcutaneously (SQ) once daily
- ► Dalteparin 5000 units SQ once daily

The platelet count should be monitored regularly in all patients receiving LMWH to detect the development of heparin-induced thrombocytopenia (HIT). All LMWH are contraindicated in patients with HIT.

Special considerations: For extremes of body weight and in renal failure, the standard dose may not be appropriate. In complex cases, it is possible to guide dosing according to plasma aniXa activity, with target range of 0.2–0.4 IU/mL 3 to 4 h after the dose.

2.4.1.1 Contraindications to Pharmacological VTE prophylaxis

- VTE thromboprophylaxis is typically contraindicated in patients with active bleeding or recent intracranial hemorrhage, those in whom a surgical procedure is planned in the next 12 h (e.g., spinal neuroaxial anesthesia), patients who have a moderate or severe coagulopathy, and patients with a severe bleeding diathesis or thrombocytopenia (e.g., platelet count <50,000/μL or <100,000/μL plus additional risk factors for bleeding). Epistaxis and menstrual bleeding are *not* contraindications to pharmacologic thromboprophylaxis.
- LMWH should not be given 12 h before epidural catheter insertion or removal and the next dose should be given at least 3–4 h after this procedure.
- Most common ICU procedures (line insertions, intercostal drainage, etc.) can be safely performed regardless of LMWH dose timing.

2.4.1.2 Pharmacological Alternatives to LMWH

- **Unfractionated Heparin (UFH)** is an alternative in those with renal failure or in whom cost is an issue. It appears to be marginally inferior for VTE prevention and possess higher risk of HIT than LMWH and therefore its use is decreasing. Standard prophylactic dosing for UFH is 5000 units SQ 2–3 times daily. This dose does **not** need to be adjusted for patients with renal failure.

- **Fondaparinux** is an indirect inhibitor of factor Xa, which can be used in patients with a history of HIT. Standard prophylactic dosing for ► Fondaparinux is 2.5 mg SQ once daily, reduced to 1.5 mg in those with a creatinine clearance in the range of 30–50 mL/min. Fondaparinux should be avoided in those with a creatinine clearance <30 mL/min. If necessary, a dose reduction to 1.5 mg subcutaneously daily can be used.
- **Aspirin** is highly effective in reducing major **arterial** thrombotic events; there is little evidence that aspirin and/or other antiplatelet agents (e.g., ► clopidogrel) can prevent **venous** thromboembolic events in hospitalized medical patients. As such, aspirin should **not** be used, either alone or in combination, as prophylaxis against VTE.
- **Direct oral anticoagulants (DOACs).** ► Rivaroxaban has been approved for use in hospitalized medically ill patients. As such, under selected circumstances (e.g., low bleeding risk, ability to tolerate PO medications), DOACs may become VTE prophylaxis option.

2.4.2 Mechanical Methods of Thromboprophylaxis

Mechanical methods for the prevention of VTE are suggested over no prophylaxis in patients at high risk of bleeding or in whom anticoagulation is contraindicated. **When mechanical forms of prophylaxis are used, transition to a pharmacologic agent should occur as soon as the bleeding risk becomes acceptably low (e.g., often within 24–48 h) or has been reversed.**

Caution: Data to support this approach are derived mostly from surgical patients with few studies performed in ICU patients. Transition to a pharmacologic agent should occur as soon as the bleeding risk becomes acceptably low.

- **Intermittent pneumatic compression devices**
  (IPC or "flowtrons") devices prevent DVT by enhancing blood flow in the deep veins of the legs, thereby preventing venous stasis. Skin breakdown is a known complication, especially in frail or older patients. IPC devices are also contraindicated in patients with evidence of leg ischemia due to peripheral vascular disease. Optimal compliance to IPC use is essential (ideally >90% of time in bed), and the proper fit of the IPC device must be assured.
- **Graduated compression stockings** may be used in some units, but there is no evidence on the efficacy in ICU patients.

2.5 Positioning, Mobilization, and Rehabilitation

Acute critical illness, sedation/paralysis and ICU treatments including invasive devices often leave ICU patients bedbound for many days or even weeks. Immobility is a risk factor for ICU-acquired weakness, thromboembolism, respiratory dysfunction, and pressure ulcers. These complications often prolong mechanical ventilation

and are further associated with long-term physical, cognitive, and psychological disability. Typical ICU patient is increasingly old and frail, and the importance of the prevention of failed functional outcomes in contemporary ICUs is more important than ever. Accordingly, the process of regaining strength and function termed rehabilitation should begin at the earliest opportunity. Whenever the patients are sedated, unconscious, paralyzed or otherwise unable to actively move in the bed, their positioning and passive rehabilitation must be performed in a controlled way to protect skin integrity and prevent joint stiffness, or for therapeutic purposes. The use of prone position in ARDS or of semi-upright position to prevent ventilator-associated pneumonia (VAP—see below) are excellent examples of how appropriate positioning can change outcome. As soon as patients' condition allows, the active mobilization and rehabilitation begin, ideally through a protocolized goal-directed process. As with many other treatments in the ICU, rehabilitation involves the whole ICU team. Doctors and nurses need to reflect the patients' pathway to recovery in daily treatment plans (e.g., by minimizing the use of sedation and paralysis). Experts such as physiotherapists, occupational therapists, speech and language therapists, psychologists, and others are involved, too.

2.5.1 Positioning of the ICU Patient

ICU patients have an increased risk for developing pressure ulcers due to immobility in the context of severe illness, injuries, and sedation. Frequent changes (every 2h) in position between supine position and left or right lateral position are essential to prevent pressure ulcer formation. The care of skin integrity is generally the domain of nurses. Some nurses specialize in this as part of a tissue viability team that provides specialist advice and equipment tailored to the individual patient need.

> *Technical note: Most ICU beds are electrically powered and can be operated using a control panel allowing turning the bed in multiple directions, altering its height, and allowing positions like cardiac chair and Trendelenburg. Some ICUs use special air mattresses consisting of separated cylinders inflated with air under controlled pressure. Those air chambers are alternately inflated and deflated to consistently and evenly distribute pressure so that no part of the body remains in contact with the surface for a longer period.*

Apart from skin integrity, there is other issues regarding patient positioning that must be taken into consideration:

- Patients with unsecured spine and pelvic injuries or other trauma/neurotrauma patients are handled and moved according to specific instructions. Occasionally, patients will be too unstable for re-positioning.
- Intubated patients are to be placed in a semi-upright position (45° head elevation), if there are no contraindications for doing so, as part of the ventilator-associated pneumonia (VAP)—prevention bundle.
- Positioning can help to improve Ventilation-Perfusion (V/Q)-mismatch in injured lungs, for example, lateral position in unilateral lung injury or prone position in ARDS.

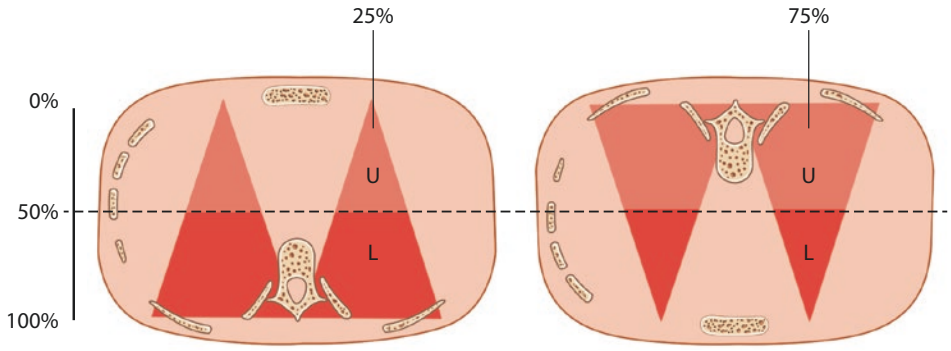


Fig. 2.4 Mechanism of prone position improving V/Q. The amount of tissue in the dorsal regions of the lung is greater than the one in the ventral part. Hypothesizing that a superimposed pressure may lead to collapse parts of the lungs below 50% of its height, it becomes clear that, if the dorsal 50% become nondependent (grey color) in prone position, the amount of tissue recruited is greater than the one de-recruited in the ventral part (now dependent, red color) and therefore gas-exchange improves (redraw).

Prone Position in ARDS became standard of care for moderate and severe ARDS because early and prolonged (minimum 12h) application significantly decreases mortality (see Ref. [1]). Prone position improves oxygenation due to improved V/Q--mismatch, improved respiratory mechanics, and reduced ventilator-associated lung injury as well as enhanced drainage of secretions (Fig. 2.4). It usually requires five persons (see video attached to PROSEVA trial how to prone here ► https://www.youtube.com/watch?v=E_6jT9R7WJs).

When the patient is placed in prone position, the arms go in swimmers' position (one arm up next to where the head is facing, other arm on the side, keep shoulder flexion <80° to avoid brachial plexopathy, avoid hyperextension, extensive rotation and lateral flexion of the cervical spine, alternate every 2 h). Make sure all lines are free, check pressure areas frequently and give special care to eyes, ears, mouth, nose, knees, and genitals.

2.5.2 ICU-Acquired Weakness

Critical illness can lead to the development of ICU-acquired weakness (ICUAW) within days. It can be viewed as a manifestation of multi-organ failure at the level of skeletal muscle (critical illness myopathy CIM), peripheral nerves (critical illness polyneuropathy, CIP), or both (critical illness neuromyopathy). The typical clinical signs are a generalized symmetric muscle weakness that affects the limbs (proximal > distal) and respiratory muscles, whilst sensation, facial, and ocular muscles are often spared. Additionally, these patients often fail to wean from the ventilator. On more detailed examination, there is no other cause apart from critical illness itself.

Risk factors for development of ICUAW include severity of illness, female sex, older age, hyperglycemia, parenteral nutrition, neuromuscular blocking agents in combination with corticosteroids, and immobility.

The natural course of ICUAW is very variable. Some patients regain muscle strength and recover quickly (within days), others may suffer complications and

Fig. 2.5 Medical Research Council (MRC) Score to evaluate muscle strength in critically ill patients

Movement tested on each side	Score for each movement
Arm abduction	0=no movement
Flexion at the elbow	1=flicker of movement
Wrist extension	2=movement with gravity eliminated
Hip flexion	3=movement against gravity
Extension at the knee	4=movement against resistance
Ankle dorsiflexion	5=normal power

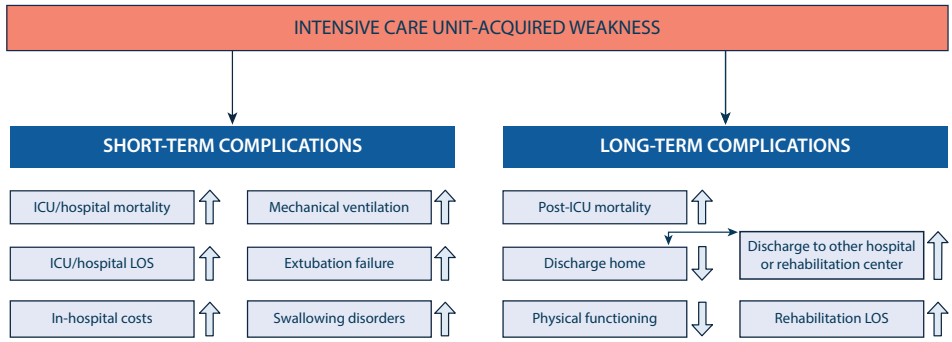


Fig. 2.6 Complications and consequences of ICUAW. Vanhorebeek et al., Intensive Care Med (2020)

long-term consequences such as impaired functional outcome, death, or fatiguability up to 5 years after critical illness survival.

The Medical Research Council (MRC) Sum-score serves to follow dynamics of ICUAW in time. Muscle strength in the cooperative ICU patient can be evaluated by the 5-point Oxford scale on 6 bilateral muscles (see Fig. 2.5). The summed final score (minimum 0, maximum 60) indicates ICUAW when below 48 (Fig. 2.6).

Prevention and treatment: There is no specific treatment for ICUAW but given its grave consequences all care must be taken to modify its risk factors, such as avoiding hyperglycemia and early parental nutrition, minimizing sedation/paralysis, and promoting early mobilization.

2.5.3 Protocolized Physiotherapy and Mobilization: The ABCDEF Bundle

Acutely ill patients still in the resuscitation phase of their disease need time until their condition stabilizes. However, as soon as stability is achieved, early and patient-oriented mobilization is important to promote timely recovery and potentially pre-

vent long-term sequelae from immobilization. As part of the ABCDEF ICU bundle, mobilization contributes to improved outcomes such as shorter length of ICU stay, shorter duration of mechanical ventilation, less delirium, less ICU re-admissions, and less post-ICU discharge disposition. This ABCDEF bundle is not to be confused with the one used in unstable patients. It includes:

A—**A**ssess, prevent, and manage pain
B—**B**oth spontaneous awakening and breathing trials
C—**C**hoice of Analgesia and Sedation
D—**D**elirium: assess, prevent, and manage
E—**E**arly Mobility and Exercise
F—**F**amily engagement/empowerment

Optimal timing of mobilization depends on the acuity of illness and the patients' condition. It is usually considered safe when cardiovascular, respiratory, and neurologic status are stable (vasoactive infusions or mechanical ventilation are not generally a barrier if the patient is otherwise stable) (Fig. 2.7).

Early mobilization protocols guide ICU clinicians through the process of rehabilitation (see protocol below). Typically, early rehabilitation starts with passive range of motion exercises and advances towards active exercises and functional tasks

System	Starting a Rehabilitation/Mobility Session[a]	Stopping a Rehabilitation/Mobility Session[a]
System	**Rehabilitation or mobility could be "started" when ALL of the following parameters are present:**	**Rehabilitation or mobility should be "stopped" when ANY of the following parameters are present:**
Cardiovascular	• Heart rate is between 60 and 130 beats/min, • Systolic blood pressure is between 90 and 180 mm Hg, or • Mean arterial pressure is between 60 and 100 mm Hg	• Heart rate decreases below 60 or increases above 130 beats/min, • Systolic blood pressure decreases below 90 or increases above 180 mm Hg, or • Mean arterial pressure decreases below 60 or increases above 100 mm Hg
Respiratory	• Respiratory rate is between 5 and 40 breaths/min • $Spo_2 \geq 88\%$ • $FIO_2 < 0.6$ and positive end-expiratory pressure < 10 • Airway (endotracheal tube or tracheostomy) is adequately secured	• Respiratory rate decreases below 5 or increases above 40 breaths per minute • Spo_2, decreases below 88% • Concerns regarding adequate securement of airway (endotracheal tube or tracheostomy)
Neurologic	• Able to open eyes to voice Further, the following clinical signs and symptoms should be "absent": • New or symptomatic arrhythmia • Chest pain with concern for myocardial ischemia • Unstable spinal injury or lesion • Unstable fracture • Active or uncontrolled gastrointestinal bleed	• Changes in consciousness, such as not following directions, lightheadedness, combative, or agitated Further, if the following clinical signs, symptoms or events develop and appear clinically relevant: • New/symptomatic arrhythmia • Chest pain with concern for myocardial ischemia • Ventilator asynchrony • Fall • Bleeding • Medical device removal or malfunction • Distress reported by patient or observed by clinician
Other	Mobility sessions may be performed with the following: • Femoral vascular access devices, with exception of femoral sheaths in which hip mobilization is generally avoided • During continuous renal replacement therapy • Infusion of vasoactive medications	

Fig. 2.7 Summary of safety criteria for starting and stopping physical rehabilitation or mobilization performed either in-bed or out-of-bed. Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption (PADIS) guideline (2018)

in conscious patients, for example, in-bed cycling, strength training, trunk balance, or sit-to-stand exercises. Great emphasis is given to protocolized mobilization of all eligible patients, whereby level and intensity is gradually increased based on previous tolerance. Example of goal-directed mobility protocol can be found in useful checklists and algorithms, page 266.

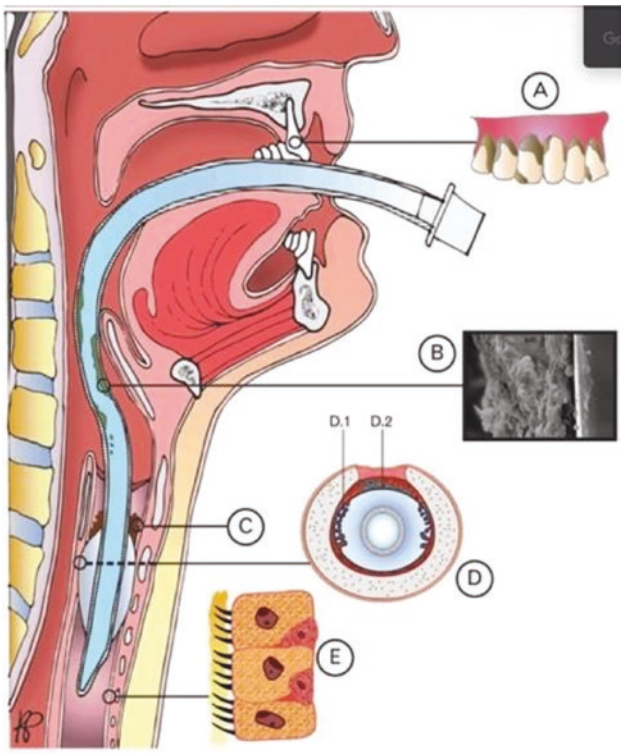
Note: In some units, physiotherapists will actively screen for patients meeting these criteria, in other doctors' prescription is necessary. Check the policy in your unit so early mobilization and physiotherapy is not neglected.

2.6 Ventilator-Associated Pneumonia (VAP) Prevention Bundle

Ventilator-associated pneumonia (VAP) is a nosocomial pneumonia that develops in ICU patients who have been mechanically ventilated for at least 48 h. Although intuitively obvious, there is no universal diagnostic criteria defining VAP—most definition requires a combination of clinical signs, microbiological isolates, and radiological findings. For healthcare quality assessment and audit purposes, scoring systems are used, such as Clinical Pulmonary Infection Score (CPIS, ▶ https://www.mdcalc.com/calc/3278/clinical-pulmonary-infection-score-cpis-ventilator-associated-pneumonia-vap). VAP is a major cause of morbidity and mortality in ICU patients. It increases the duration of mechanical ventilation, ICU stay and hospitalization, and healthcare costs.

Note: Notice whether there is a system in place to monitor the incidence of VAP on your unit and which criteria are used. Are processes preventing VAP (see below) being audited as well?

2.6.1 Pathophysiology and Preventability of VAP



VAP pathogenesis: (A) Oropharyngeal microflora can be directly passed down to the lung during intubation causing early VAP. Later, oropharynx becomes colonized by hospital MDR Gram negatives (B) endoluminal biofilm within the lumen of ETT as a source of bacterial colonization of the lower airway. (C) Secretions accumulate above the cuff, and (D1) leak into the lungs through the inflated cuff because of microscopic folds or (D2) mucosal damage because of tracheal wall ischemia. (E) Impaired tracheal mucociliary apparatus by a suboptimal humidification and heating of inhaled air. Adopted from Ref. [2]

The sequence of event leading to VAP is shown in Figure. It has been demonstrated that VAP is largely preventable and the incidence of VAP is one of the quality markers of intensive care. Incidence ranges between 2 and 16 cases per 1000 ventilator-days in most units in Europe, but it largely depends on the case mix and diagnostic criteria used.

2.6.2 Components of VAP Prevention Bundle

A care bundle is a set of interventions that, when used together, significantly improve ICU patient outcomes. VAP prevention bundle consists of a range of measures, which impact different aspects of VAP pathophysiology and, if used in combination, has been demonstrated to reduce the incidence of VAP.

> *Note: Care bundles may vary between regions/hospitals. It is fundamental to be aware of the local protocol.*

The following measures might be recommended:

1. General measures
   (a) Education and training of the staff: Both in the manipulation of the airway and in evidence-based strategies to prevent VAP. For *example: Inadequate ETT fixation can lead to cuff movement inside trachea and increase microaspiration.*
   (b) Implementation of standard precautions: Strict hand hygiene, personal protective equipment, general environmental cleaning.
   (c) Limiting the duration of mechanical ventilation: Daily sedation holds and weaning protocols. Reintubation should be avoided if possible.
   (d) Maintaining adequate staffing levels in the ICU can improve infection control practices.
   (e) Favour orotracheal over nasotracheal intubation.
2. Prevention of aspiration
   (a) Control and maintenance of cuff inflation pressure between 20 and 30 cmH_2O.
   (b) Aspiration of subglottic secretions—only use ET tubes with subglottic suction port.
   (c) Semi-recumbent position (elevation of the head of the bed to 30°–45°) unless contraindicated. In that case, consider rotation of the bed.
3. Prevention of contamination of equipment
   (a) Avoid scheduled changes of the ventilator circuit, only change the circuit when visibly contaminated.
   (b) Avoid reusing "single-use" items and use single patient nebulizers and resuscitation equipment whenever possible.
   (c) Heat-moisture exchanger are more effective than heated humidifiers at preventing VAP. The risk-benefit should be assessed for every patient.
   (d) Use of filters to protect mechanical ventilator circuits.
   (e) Condensate accumulating in the ventilator circuit should not be drained towards the patient.
4. Prevention of colonization of the aerodigestive tract
   (a) Regular oral hygiene as per local guidelines, but always including brushing teeth, gums, and tongue at least twice a day with a soft pediatric toothbrush.
   (b) Topical application of chlorhexidine gluconate (0.12%–0.2%) (every 6–8 h).
   (c) Stress ulcer prophylaxis with acid suppression predisposes patients to developing VAP by raising the gastric pH levels and allowing bacterial overgrowth.

It is only recommended in patients who are not on full enteral feeding and/or have other risk factor such as steroid treatment.

(d) Selective decontamination of the digestive tract is not routinely recommended but can be considered in settings with low prevalence of antibiotic resistance.

(e) Prophylactic administration of a short course of systemic antibiotic after emergent intubation for altered level of consciousness may decrease the rate of VAP but is not routinely recommended.

Take Home Messages

- Daily assessment of ICU patient should be done in a concise, structured way. It consists of carefully checking patients notes, gathering information from nurses and other allied healthcare professionals, performing a detailed head-to-toe physical examination, often extended by focused bedside ultrasound and checking the monitors, syringe drivers, and other equipment settings, bloods, and results of auxiliary tests.
- Treatment plans should be formulated, agreed, and shared within team members during the multidisciplinary ICU ward-round, and carefully documented in the notes. Goals of care should always be tailored to patients' values and wishes.
- Apart from the treatment of underlying disease and organ support, ICU care includes fluid management, nutrition, and bundles of care aimed at preventing complications of intensive care such as thromboembolic events, pressure ulcers (positioning), ICU-acquired weakness (rehabilitation), or ventilator-associated pneumonia.
- Fluids are drugs that should be prescribed as any other medication: clear indication, precise amount, and set date. Balanced crystalloids are the preferred fluids of choice in most critically ill patients.
- Insulin resistance, hyperglycemia, and feeding-resistant protein catabolism are hallmarks of critical illness. Sliding scale insulin is used to control blood glucose in critically ill patients.
- Most patients in ICU can be fed by enteral polymeric formula, targeting 25 kcals and 1.5 g of protein per kg and day.
- Critically ill patients are at high risk of venous thromboembolism, and pharmacologic prophylaxis (usually with LMWH) is a standard of care for all patients without active contraindications (i.e., high risk of bleeding or brain surgery).
- Special equipment and 2 hourly turns are needed to protect the skin of immobile critically ill patients unless special circumstances occur such as unstable spine or the need of prone position prone positioning for at least 12–16 h daily is standard of care when managing patients with moderate to severe ARDS (incl. with COVID-19)
- Once the resuscitation phase is completed, rehabilitation should begin based on a multidisciplinary bundle of interventions, which includes daily sedation holds and protocolized physiotherapy and mobilization.
- VAP is a major morbidity and mortality cause for critically ill patients. It is largely preventable by a care bundle, mostly consisting of daily sedation holds, bed head elevation, gastric ulcer prophylaxis, oral care, subglottic aspiration, and tracheal cuff pressure monitoring.

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Intra-hospital Transport

Anne Mecklenburg

Contents

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Intended Learning Outcomes

By the end of this chapter, the reader should be able to:

1. Discuss the risks and possible pitfalls of transporting a critically ill patient.

3

3.1 Introduction

Transportation of a critically ill patients requires the continuing delivery of organ support in an unfavorable environment. Often, junior ICU doctors take patients to CT scans or theaters and safe patient transfer is an important skill to learn [1, 2].

Risk factors for adverse events during transportation include:

- complications with equipment, e.g., dislocation of lines and tubes
- clinical deterioration of the patient, e.g., increased intracranial pressure, which may go unrecognized due to inadequate monitoring
- limited options in terms of therapy due to lack of appropriate equipment (e.g., it is not easy to deliver high-flow nasal oxygen during a transfer).
- limited staff available for emergency situations
- limited access to additional investigations, e.g., X-rays

Therefore, **meticulous planning is mandatory,** and this includes:

1. **Assessment of patients' condition and risk-benefit analysis regarding the transport**. Every transport needs a clear indication (e.g., Will the results of certain investigations change clinical management?). If in doubt, discuss with a senior member of the team. Adequately stabilize the patient before transport and discuss the measures that need to be taken in case the patient deteriorates during transport.
2. **Planning for resources (staff and equipment) for stabilization and resuscitation**

   Discuss who should be with the patient for the transport (Junior or senior doctors? Do they need to be airway trained? How many nurses? Special health professionals like perfusionists for ECMO? Transport personnel to push the bed/stretcher?) Use a checklist to go over the equipment and drugs needed on the transport (See Appendix "Useful Checklists and Algorithms," page 267). Make a final phone call to the accepting department or suite to make sure they are ready. Conduct a "team time out" just before leaving as a final check (see below).

   Note: If you do not feel comfortable to transfer a patient or have any other concern, speak up! Never ever cut corners.
3. **Handover and documentation**

   Full documentation of monitor readings and interventions is obligatory. For handover to other departments or colleagues use the ABCDE (airway, breathing, circulation, disabilities, environment) approach for primary survey and the AMPLE (allergies, medications, past history, last meal, events) approach for history, unless there are local differently structured communication protocols in use.

3.1.1 How to Do a "TEAM TIME OUT"?

One team member goes through a list and feedback is given by everyone to check off the items on that list, done just before leaving the unit. Follow the rules of "closed-loop-communication" and—if you are not using formalized checklist—do not omit:

- patients name and diagnosis including reason for transfer
- complete documentation (chart summary, lab work)
- destination department or suite
- back-up plan and personnel in case of complications
- checking all medical equipment and that you have enough supply of drugs for the transport
- duration of the transport and calculation of needed supply of medical gas
- check all battery-operated monitors, infusion pumps, ventilator, and other devices are adequately charged
- check appropriate alarm limits for monitoring

3.1.2 What MONITORING Do I Need During Transport?

Minimum standard for ICU patients includes:

- Minimum three-lead ECG with heart rhythm and ST-segment analysis.
- Blood pressure which is preferably invasive.
- Peripheral oxygen saturation monitor.
- End-tidal capnography is a minimum standard in some countries.

The choice of the monitoring depends on patients' stability and on operability of the monitoring and the ability to influence the measured value in the remote environment. For example, end-tidal capnography is highly recommended in ventilated patients and particularly for those with raised intracranial pressure. On the other hand, ICP or body temperature may be difficult to control in the CT scanner, and therefore their use *en route* should be considered individually and depends on local protocols. Patients with special devices, for example, ECMO, Impella, or balloon pump will need senior doctors and specialized nurses.

3.1.3 What EQUIPEMNT Do I Need to Bring on the Transport?

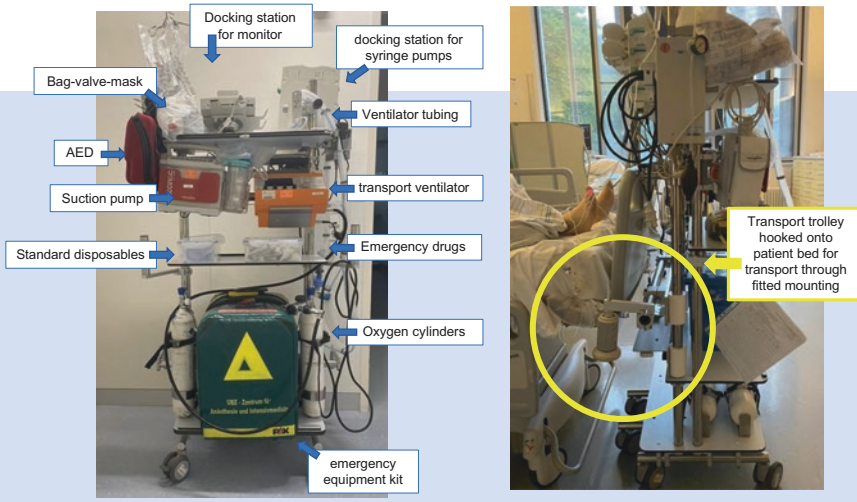
Most hospitals use dedicated transport trolleys that may be attached to the bed during transport (pictured) and include standard equipment:

- Monitor and monitoring equipment
- Defibrillator/AED
- Ventilator and oxygen cylinders (always make sure to know how much oxygen you have for the transport, see "How to calculate oxygen demand and supply?")
- Portable suction pump and catheters
- Syringe drivers and fully charged infusion pumps
- Emergency Kit (e.g., a frequently checked and sealed emergency bag with endotracheal intubation equipment, standard set of disposables such as syringes, needles and cannulae, and fluids) plus bag-valve-mask

- Drugs (sedatives and analgesia, resuscitation drugs, and scheduled medication like antibiotics if the patient is going to be out of the unit for a long time)

Practical note: In most cases, it is safe to interrupt maintenance of fluids, nutrition and low-dose insulin, potassium replacement, and other non-essential drugs. However, always take vasopressors and sedatives in syringe drivers with you. Draw extra syringes of sedatives and other medication as well as emergency drugs like ephedrine in case you need them. If the patient is on high F_iO_2 or PEEP, it is better to reconnect them to the transport ventilator while still in the ICU bed and see how the change effects their gas exchange.

► Example



Transport trolley, University Medical Center Hamburg-Eppendorf, Germany ◄

How Do I Calculate the Oxygen Supply and Demand During Transport?

Oxygen available (example):

- The barometer on the oxygen cylinder shows 200 bars (= 200 times the normal ambient pressure).
- The volume of the cylinder is 5 L.
- Therefore, the oxygen available will be 5 L × 200 bars = 1000 L.

Oxygen demand (example):

- The patient is ventilated with 15 L/min at FiO_2 of 50%.
- Therefore, 7.5 L/min of oxygen is needed.
- The time for the cylinder (5 L, 200 bar) to empty is 1000 L/7.5 L/min = 133 min *(Well, but always take an extra full cylinder, if you can, just in case!).*

Take Home Messages

- "CT monkey" is a misnomer as transferring critically ill patient is a responsible and important job that mandates adequately trained personnel.
- No transfer comes without risks and the benefits must clearly outweigh these.
- Don't go if you have concerns.
- Carefully prepare the patient, the team, and the equipment. Double check you have enough oxygen and enough drugs.
- "What if" is a relevant question—always have a plan B.
- Let the patient settle on the transport ventilator, make sure you are expected in the location you are taking the patient to, and do a quick time-out with your team just before you leave (a checklist is useful).

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Human Factors and Non-Technical Skills

Rahul Costa-Pinto and Carole Boulanger

Contents

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Intended Learning Outcomes (ILOs)

By the end of this chapter, you should be able to achieve ILO 1. You should also have the knowledge required to successfully achieve ILO 2 and 3.

1. Discuss the principles of communication in crisis and crisis resource management (leadership, membership, situational awareness) and relate them to your own experience and professional context.
2. Communicate in a professional but effective and assertive manner in a simulated emergency.
3. Demonstrate a succinct and structured handover in a simulated setting.

4.1 Introduction

Intensive care medicine involves the delivery of complex interventions by a multidisciplinary team. A team-based approach is essential to deliver optimal patient care in this environment but conversely can also lead to unintended patient harm in poorly functioning teams. An understanding of human factors (HF) and non-technical skills (NTS) is therefore of particular importance in delivering care to critically ill patients.

'Human factors' is an umbrella term for the environmental, organisational, and individual factors that allow us to work most effectively. Understanding and applying HF principles can help health professionals enhance patient safety, reduce medical error, and boost personal well-being within the team.

The HF 'Dirty Dozen', a term coined by Gordon Dupont working in the aviation industry, describes 12 elements that can be attributed to accidents and incidents (Fig. 4.1). These elements can help identify latent safety threats.

There are mitigating strategies for each of these human factors when working in the intensive care unit (ICU), but they require both individual and organisational-level change to implement successfully. Structured communication tools, multidisciplinary team handovers, and use of checklists and safety huddles can help to address problems with communication, knowledge, awareness, and resources. Speaking up for safety, promoting staff well-being and ensuring designated rest areas can help reduce complacency, stress, pressure, and fatigue.

Non-technical skills encompass cognitive and interpersonal skills that contribute to safe and efficient team performance. These include:

- leadership and followership
- team assembly and disassembly
- decision-making
- task management
- situational awareness
- communication within a team
- communication with patients and families

There is evidence to suggest that resuscitation teams with good non-technical skill performance also perform technical aspects of advanced life support (e.g. chest compressions with minimal interruptions, rhythm recognition) better.

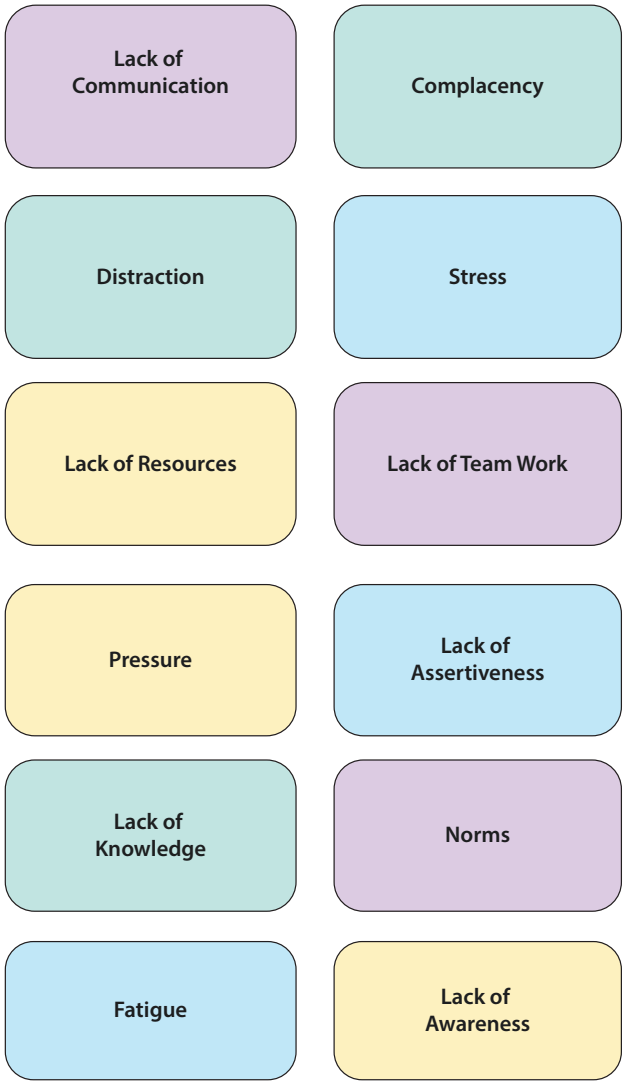

Fig. 4.1 Human factors 'Dirty Dozen', as described by Gordon Dupont

4.2 Team Performance

Intensive care is a team job and patient outcomes depend on the performance of the whole team rather than its individual members. In the ICU, there are four key teamwork processes which have been shown to predict patient outcomes:

- **Team communication.** ICU patients are particularly vulnerable to communication errors. Divergent goals between doctors, nurses, and allied health professionals (AHPs) regarding patient care can lead to team conflict, staff burnout, and decreased quality of patient care. Interdisciplinary communication is vital to develop shared goals for each patient. An example of this could be creating and communicating the daily plan for an ICU patient (see ▶ Chap. 4, page 51). Crisis communication is discussed below.

- **Team leadership.** Team leaders should facilitate the development of shared goals and oversee team decision-making (see below). In a crisis, it is necessary that the team leader is clearly declared (i.e. all team members know who the team leader is) and their responsibility is to maintain situational awareness, dynamically set and communicate goals and priorities whilst openly taking and encouraging input from team members. Specific tasks (e.g. airway management) may need so much focus that they consume an operator's entire attention span and makes them prone to fixation error. It is therefore advisable that demanding tasks are delegated to team members, whilst the team leader maintains general oversight.

Dangers of lack of leadership can be best seen when analysing death after airway emergencies. The Elaine Bromiley case is one such example (see supplemental reference). In this airway emergency, there was a pattern of continual unsuccessful attempts to intubate whilst neglecting profound and protracted hypoxia. In hindsight, it may seem unbelievable how experienced operators could neglect profound hypoxia for so long and allow a patient's death without attempt at a surgical airway. The major contributor to this was fixation error—the operators were so focused on the technical aspects of securing the airway that they completely lost situational awareness of a patient dying from hypoxia. Furthermore, other members of the team did not feel empowered to tell the operators this was a 'cannot intubate, cannot ventilate' scenario and that they should progress immediately to a surgical airway.

- **Team coordination.** Effective team coordination requires all team members to clearly communicate their status, progress, and needs to the rest of the team in a timely fashion. Situational awareness and sharing a mental model are important components for enhancing team coordination. A 'shared mental model' for goals, tasks, and the roles and responsibilities of all team members facilitates team decision-making and allows for rapid adaptation of the team to its task demands. Situational awareness ('seeing the bigger picture') is particularly challenging in the ICU as synthesis of a large amount of data is required and cognitive load is high. This can be exacerbated by frequent changes in team members (e.g. with locum or agency staff). A positive team culture is integral to seamlessly include new and transient members into the team. After a crisis scenario, it is advisable to have a short huddle away from the clinical environment to debrief the team, allow for emotional responses to be shared, and consider what could be improved for the next time. It is also an opportunity to assess if any team members need further support.
- **Team decision-making.** Encouraging collective leadership emphasises shared responsibility between all members of the multidisciplinary team. Team decision-making should be collaborative where possible. Junior team members should feel empowered to discuss decisions with the team leader and offer input. Flat hierarchy and a 'no-blame' culture encourage that attitude and are hallmarks of well-performing ICUs.

There are many tools that can be utilised to assess team performance. The Team Emergency Assessment Measure (TEAM) is one such tool that is commonly utilised in resuscitation training [2] (See Appendix 'Useful Checklists and Algorithms', page 268).

4.3 Crisis Communication

During a crisis scenario, nurses and doctors will often perform separate and distinct tasks in parallel. It is here where principles of effective communication are particularly important. Poor communication between doctors and nurses may account for up to 40% of preventable errors in the ICU.

For communication to be effective, it must be:

- Directed—it must be clear who the message is addressed to
- Complete—contain all relevant information
- Clear—delivered in an easily understandable manner
- Concise—kept as brief as possible
- Timely—offered at the right time for effective clinical action

Effective communication is a two-way process that requires delivering a message whilst also ensuring the message is correctly received and understood by the other person. The term 'closed-loop communication' is a standard terminology used to describe this process. In resuscitation scenarios, closed-loop communication has been shown to reduce the time to completion of key tasks, such as medication orders, placement of intravenous lines and obtaining blood samples. This communication style should involve a call and response (e.g. Call: 'Can you please administer Adrenaline 1 mg IV?'; Response: 'Adrenaline 1 mg given'.).

'Standardised communication' is the use of specific phrases that have universal meaning. Standardised phrases such as 'resume compressions', 'prepare for intubation', or 'tell me when you see the vocal cords' may also allow all members of a resuscitation team to share a common understanding of the situation.

4.4 Crisis Resource Management

Crisis resource management (CRM) is an educational curriculum derived from the aviation industry to improve safety, communication, and decision-making. The key tenets of CRM are shown in Fig. 4.2.

Simulation is a commonly used teaching modality for crisis resource management and teaching non-technical skills. Simulations are most effective when they reproduce the physical, conceptual, and psychological fidelity of resuscitation and other crisis scenarios (Table 4.1).

Fig. 4.2 The key tenets of crisis resource management. (*Adapted from Goldhaber-Fiebert et al (2013). Implementing emergency manuals: can cognitive aids help translate best practices for patient care during acute events?* [1])

Table 4.1 Application of crisis resource management principles for a peri-arrest patient in the intensive care unit (ICU)

CRM principle	*Examples in a peri-arrest scenario*
Anticipate and Plan	A patient has been in the ICU for 4 h with severe community acquired pneumonia, on high-flow oxygen therapy. The ICU nurse is concerned by the worsening trend in the patient's oxygen requirements. The ICU junior doctor is called to review the patient and communicate a management plan in case of further deterioration.
Call for Help Early	The ICU junior doctor recognises the high risk of deterioration with this patient and calls for senior medical assistance to review the patient immediately. The ICU nurse also notifies their in-charge nurse of the team's concerns.
Know the Environment	The patient's bedspace is cleared of unnecessary equipment and patient belongings to accommodate the additional space the resuscitation team will need to assess and manage the patient.
Designate Leadership	The ICU senior doctor reviews the patient and designates herself as team leader. She announces to the team that the patient appears critically unwell and will need to be intubated immediately.
Mobilise Resources	The ICU nurse summons additional team members to assist with airway setup and to manage the circulation. The 'difficult airway trolley' and 'crash cart' are also mobilised next to the patient's bedspace.
Establish Role Clarity	The ICU senior doctor assigns a role for each of the team members, clarifies their names, and ensures they are comfortable performing the role they have been assigned. A scribe is assigned to document the resuscitation.

Table 4.1 (continued)

CRM principle	*Examples in a peri-arrest scenario*
Allocate Attention Wisely	To reduce cognitive load, the ICU senior doctor delegates tasks. She asks the airway doctor and nurse to devise an airway plan and then report back to the team. She asks the circulation nurse to source the induction medications for intubation and report back once these are ready. She remains deliberately 'hands off' to maintain situational awareness at all times.
Use All Available Information	The ICU senior doctor asks direct questions to the ICU nurses and doctors who have been managing the patient to establish appropriate goals of care, treatments administered, investigations ordered, relevant past medical history, previous airway grade of intubation and to update the next-of-kin. The ICU senior doctor explicitly asks team members if they have any additional suggestions for this patient's management plan.
Distribute the Workload	The ICU senior doctor ensures tasks are allocated based on appropriate skill mix. She also ensures team members are not unequally assigned tasks and that workload is evenly distributed. Additional staff are called to assist as required.
Communicate Effectively	The ICU senior doctor ensures all team members use closed-loop communication when completing tasks. She also uses standardised phrases where possible when delivering instructions. She frequently summarises the situation to the team to ensure there is a shared mental model.
Use Cognitive Aids	An intubation checklist is utilised to ensure all necessary airway equipment is available. The Advanced Life Support algorithm is clearly visible on the 'crash cart'.

4.5 Handover

Handover is a transfer of critical information about a patient and responsibility of care from one team of clinicians to another. It is a frequent, complex process that poses significant patient risk if poorly completed. Critically ill patients present additional challenges to this process as their handover may require the transfer of large, complex chunks of information, delivered in a stressful environment with many distractions.

Standardising tools may improve transfer of information and quality of handover. One such tool is ISBAR (Identity, Situation, Background, Assessment, Recommendation) which may improve the handover process and increase confidence for junior doctors when giving and receiving handover [3]. An example of using this structured handover tool is provided in Table 4.2. The components of ISBAR are as follows:

- Identity—introduce self; name/age/hospital number/ward/team of patient
- Situation—symptom/problem; stability of patient
- Background—history of presentation/past medical history/brief list of ICU issues
- Assessment—impression of situation/vital signs/treatments administered
- Recommendation—ongoing plan/pending tasks to complete/review(s) required

Table 4.2 Application of handover principles for a peri-arrest patient in the intensive care unit (ICU)

Handover principle	*Examples in a peri-arrest scenario*
Identify	Hi Dr Jones, my name is David. I am the intensive care doctor on shift tonight.
Situation	I have just reviewed a 50-year-old patient who I think is very unstable.
Background	The patient has only been in the ICU for 4 h with severe community acquired pneumonia. He has a history of asthma, hypertension, and is a smoker.
Assessment	He has a rapidly escalating oxygen requirement and is failing high-flow oxygen therapy. He is now on 60% oxygen with oxygen saturation of 90%. He is tachypnoeic with a respiratory rate of 35, tachycardic with a heart rate of 120 but is maintaining his blood pressure without any additional support. He is diaphoretic and the nurse reports he is starting to become more agitated and non-compliant with care.
Recommendation	I am concerned about this patient and think he may require intubation urgently. I do not have formal airway training so would like you to review this patient and assist with this as soon as possible. Thank you.

4.6 Examples of Common Mistakes and Errors

- Having a plan without sharing it with the bedside nurse and other team members.
- Unaddressed messages—if you shout 'Get me a defibrillator, please', everyone may leave to fetch it, or no one will.
- Overreliance on memory and failure to double check, particularly when hungry, angry, tired, or late.
- Cutting corners instead of preparing plan B ('I will be just fine'; 'It won't happen to me')
- Fixation error and loss of situational awareness. Neglecting or suppressing new information that is not in keeping with initial diagnosis ('I am treating persistent bronchospasm, this cannot be a pneumothorax').
- Lost in translation—information may get lost or distorted during multiple handovers. Always check original notes.
- Loss of continuity of care due to multiple changeovers of staff. This particularly applies to communication with relatives. Document well.
- Asking who is to blame rather than what we can do to prevent this error from happening again.

Take Home Messages

- Non-technical skills encompass cognitive and interpersonal skills which contribute to safe and efficient team performance.
- For communication to be effective, it must be directed, complete, clear, concise, and timely. The receiver closes the loop.
- Team leaders should facilitate the development of shared goals and oversee team decision-making.
- Crisis resource management training may improve safety, communication, and decision-making. Simulation is an important teaching modality for CRM.
- Standardising tools, such as ISBAR, may improve quality of handover.

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Approach to Difficult Decisions and End-of-Life Care

Frauke Weidanz

Contents

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Intensive Care Fundamentals Intended Learning Outcomes (ILOs)

This chapter will help you achieve the following Intended Learning Outcomes (ILOs):

1. Explain the limitations of intensive care, and the principles of withholding and withdrawing treatment, including potential organ donation.
2. Describe a management and treatment plan for the patient at the end of life and adequately prescribe symptomatic therapy.

5.1 Introduction

5

The aim of Intensive Care is to provide organ support while the underlying acute illness improves over time with targeted treatment. Some conditions do not respond to treatment however, and sometimes the insult of the acute organ dysfunction is too severe, particularly if the patient is frail or has a high burden of chronic disease. Between 15 and 20% of patients do not survive their ITU admission, and in the majority of cases, their death follows a decision to withhold or withdraw therapy. These decisions pose complex ethical challenges, and while practice varies due to differences in legal frameworks, culture and religion, the principles of ethical decision-making are the same, irrespective of where you work.

We will discuss the principles underpinning decisions to withhold or withdraw life-sustaining therapy, the concept of capacity and some practical aspects of providing end of life care in the ICU, before reviewing the basic principles of organ donation.

5.2 Withholding and Withdrawing Therapy

Withholding treatment is usually defined as a decision not to start or increase a life-sustaining intervention, and withdrawing treatment as a decision to stop a life-sustaining intervention. Both are generally, but not in all belief systems, seen as ethically the same, and are different from actively shortening the dying process, which is unlawful in some most jurisdictions.

Reasons to withhold or withdraw therapies broadly fall into one of the following categories:

- Rapidly progressive single or multiple organ failure where additional therapies are not expected to prevent imminent death
- Survival to hospital discharge is not expected, either because the illness is progressive or unresponsive to treatment, or because underlying frailty or chronic disease burden limits the patient's ability to recover
- Survival is expected to be associated with a level of physical or cognitive impairment not consistent with the patient's wishes or best interest

5.3 Decision-Making When Patients Lack Capacity

The decision to withhold or withdraw life-sustaining therapy, like any decision about medical treatment, should respect the patient's right to autonomy and to be involved in decision-making. Many patients in Intensive Care have impaired capacity, either

because of the underlying illness or due to effects of treatment including sedation. Whenever a decision to withhold or withdraw therapy is made, capacity should be carefully assessed rather than assumed to be absent, and efforts made to maximise the ability of the patient to understand, retain, and weigh up the information provided and to reach a decision. When this is not possible, you should check whether any advanced directive or similar legal document is in place, or whether someone else holds legal authority to make decisions on their behalf. Legal frameworks for this differ between countries. If there is no legal representative, then make efforts to establish the patient's previously expressed wishes. This is particularly important for a decision to withdraw therapy in the third category listed above, based on whether or not expected quality of life would be acceptable to them. Involve family members or others close to the patient. The legal role of relatives in relation to making these decisions varies between countries and jurisdictions, and families may have different preferences for the role they take in making decisions on behalf of their relative.

The presumption should always be in favour of prolonging life. Carefully weigh up the expected benefits, harms and burdens of any therapy in question and consult widely with the entire multi-disciplinary team within the ICU and with any other clinicians involved in the patient's care.

Family Communication at the End of Life in the ICU

- Seek consensus with entire team and parent specialties before family meetings
- Aim for senior intensivist and nurse to be present
- Find out the family's understanding and value their perspective
- Take time to listen and acknowledge emotions
- Give information in clear language and small chunks and check understanding
- Leave pauses and time for questions

Communication at the end of life is a key skill in Intensive Care Medicine, but detailed discussion of strategies is outside the scope of this chapter. Take every opportunity you can to observe experienced clinicians.

5.4 End-of-Life Care in ITU

The process of withdrawing life-sustaining therapy and the practical aspects of subsequent end-of-life care vary between different hospitals and countries. The goal of pharmacological management should be the relief of distressing symptoms rather than sedation, but many patients will be obtunded due to the underlying organ failures and are unable to communicate. Assess and manage pain, nausea, dyspnoea, agitation, and anxiety and titrate medication to clinical effect. A table of commonly used drugs for symptom relief at the end of life in ICU can be found in (Table 5.1). Use your local protocols and seek advice if symptoms are not controlled.

Once symptom control has been optimised, all other treatments including vasopressors and ventilatory support are discontinued. Practice varies, and it is essential that a clear plan has been communicated so that all team members, the family, and the patient (if able to communicate) understand the process. Find out about any

Table 5.1 Commonly used drugs for symptom relief at the end of life in ICU

Drug	Indication	Typical starting dose (Titrate to effect and consider continuous infusions)
Morphine (or other opiate)	Pain or dyspnoea	Morphine: 1.25–2.5 mg i.v./s.c. hourly if required
Hyoscine butylbromide (or other anticholinergic)	Respiratory secretions	Hyoscine butyl bromide: 20 mg s.c. hourly if required (maximum usually 120 mg in 24 h)
Midazolam (or other benzodiazepine)	Dyspnoea, anxiety, or agitation	Midazolam: 1.25–2.5 mg s.c. hourly if required
Haloperidol (consider Levomepromazine if not effective)	Nausea, vomiting, or agitation	Haloperidol: 0.5–1.5 mg s.c. every 4 h if required or Levomepromazine: 2.5–5 mg s.c. every 12 h

specific cultural or religious needs that still need to be addressed. Ensure monitoring has been discontinued and alarms silenced. Organ support is often reduced in a stepwise fashion so that symptoms can be reassessed after each step, such as stopping vasopressors, then reducing oxygen and ventilatory support followed by extubation to room air. The plan for the process of withdrawal needs to be individualised and documented for each patient. Consider seeking support from your local palliative care services and offer bereavement support to the family according to your usual local practice.

5.5 Diagnosis of Death by Neurological Criteria

The concept of brain death or brainstem death, sometimes called diagnosis of death by neurological criteria, is widely accepted in Europe, but nomenclature and diagnostic criteria vary. The diagnosis relies on proof that consciousness, brainstem reflexes, and the ability to breathe are irreversibly lost. Brain death most commonly occurs when patients ventilated for traumatic brain injury, subarachnoid haemorrhage, meningitis or hypoxic brain injury develop coning as a result of extreme levels of intracranial pressure, or sometimes as a result of a more focal insult to the brainstem. The process of confirming death by neurological criteria varies between countries, but generally requires the underlying condition to be irreversible, and any contributing metabolic or pharmacological factors to have been excluded before confirming apnoea and the absence of brainstem reflexes (Fig. 5.1).

In most countries, death diagnosed by this method is legally equivalent to circulatory death. Particular care must be taken in communication with families after diagnosis of death by neurological criteria, as the concept can be difficult to understand and the patient will look much the same to them as before brain death

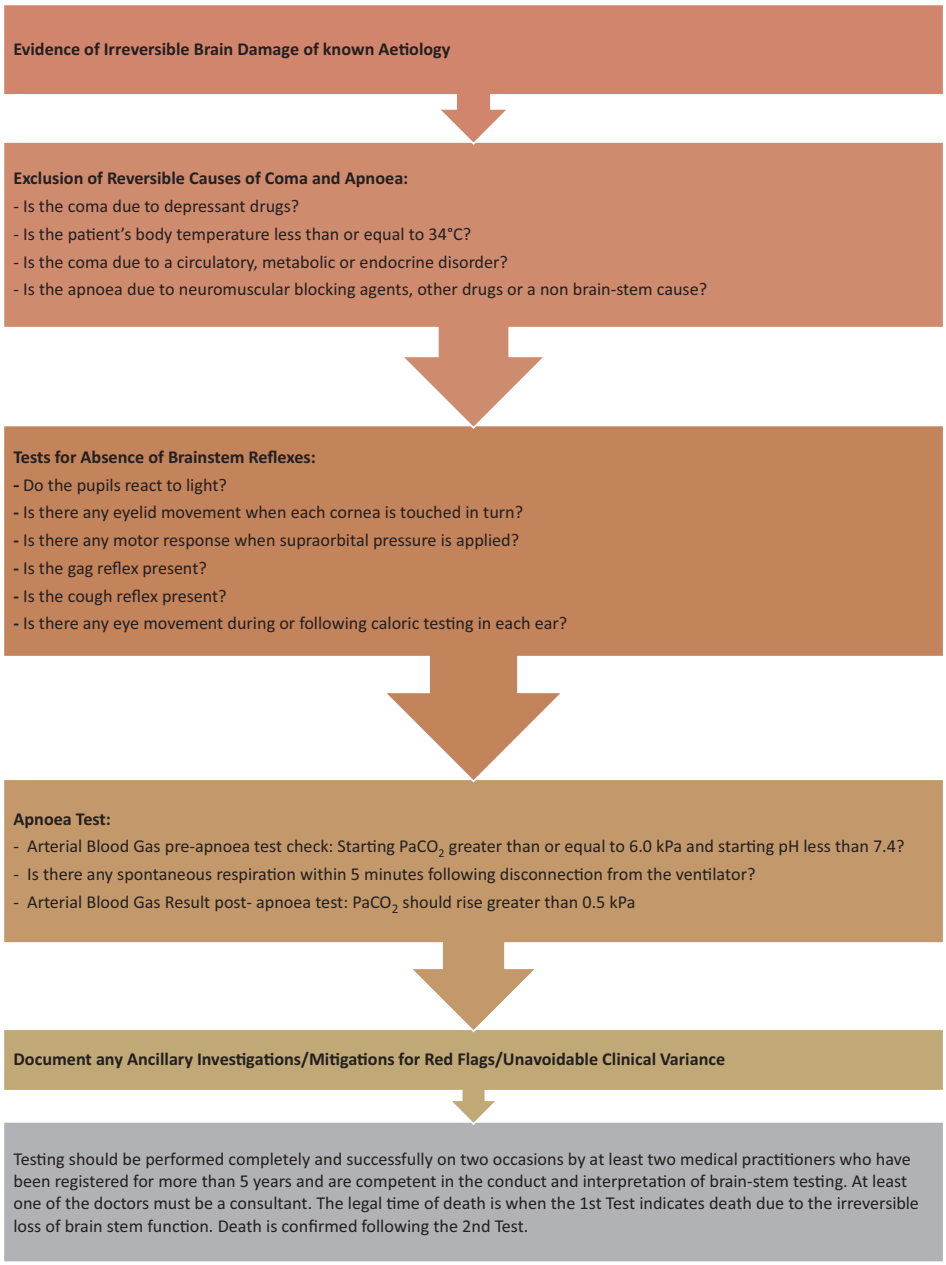

Fig. 5.1 Example of guidance for diagnosis of death by neurological criteria

occurred. If the patient had expressed a wish to donate their organs, this should be facilitated if possible. If donation is not an option, ventilatory and any other organ support is discontinued once the diagnosis of death has been communicated to the family.

5.6 Organ Donation

Due to its success in prolonging lives and improving the quality of life of many patients with chronic organ failures, the demand for organ transplantation is increasing. In addition to donation after death diagnosed by neurological criteria, donation after circulatory death is becoming more common in many countries, and outcomes are similar. Donation rates, clinical practice, and the legal frameworks governing donation vary considerably between countries.

Donation after death diagnosed by neurological criteria (or donation after brain death, DBD) is only possible when a ventilated patient has been declared dead after brainstem testing, where there is permanent loss of brainstem function due to a defined and irreversible brain injury. The organs remain perfused as circulation is still intact, but brain death typically results in marked physiological instability due the loss of central autonomic and endocrine regulation. You should have access to local protocols detailing cardiovascular targets, fluid, electrolyte and glucose management and replacement of pituitary hormones. Careful correction of the pathophysiological consequences of brainstem death improves the number and quality of donor organs.

Donation after circulatory death (DCD) describes retrieval of organs after confirmation of death by circulatory criteria and can in theory be considered in any patient where planned withdrawal of life-sustaining therapy is expected to result in death on the Intensive Care Unit. This includes but is not limited to patients with catastrophic brain injuries who do not meet criteria for brainstem death testing. Clearly, some conditions preclude successful transplantation, such as metastatic malignancy, uncontrolled infection or established multi-organ failure. Once a decision to withdraw organ support has been made by the treating team in consultation with the family, the transplant team can coordinate consent from the family, assess suitability of organs and prepare for organ retrieval. If cardiac arrest occurs within a certain timeframe without a prolonged period of hypoperfusion and hypoxaemia, organs can be retrieved after death has been confirmed. The typical processes for DBD and DCD are illustrated below (Fig. 5.2).

Offering organ donation is an important part of end-of-life care in ICU, but it is essential that this process remains separate from any decision to withdraw life-sustaining therapy in the case of DCD. The focus of the ITU team remains on delivering high quality end-of-life care and on supporting their patient's family. Relatives are not normally approached for consent until they understand and accept that withdrawal of organ support is in the patient's best interest or that brainstem death has been confirmed. Local practice around the process of consent varies in line with differences in legal frameworks, and your local specialist organ donation team will be able to offer support and advice. Following the expressed wishes of the dying patient is key.

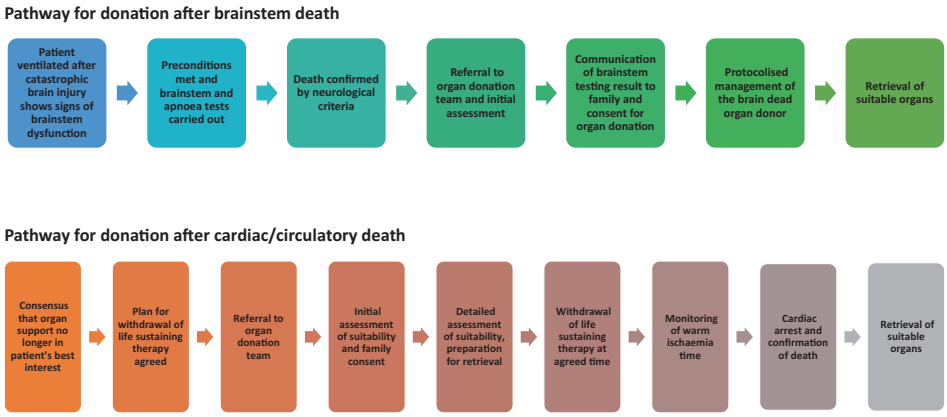

Fig. 5.2 Flow diagram of DBD and DCD processes

Take Home Messages

- There are limitations to what intensive care can achieve, and when the burden of prolonged invasive organ support outweighs the benefit or if recovery is no longer expected, then life-sustaining therapy is withdrawn and symptom control becomes the focus of care
- The decision to withhold or withdraw therapy is difficult and ethically challenging, particularly when patients lack capacity to be involved
- The benefit and burden of continuing or escalating therapy must be carefully considered. Any decision to withhold or withdraw therapy requires consensus within the multi-disciplinary ICU team and with other clinicians involved in the patient's care, and sensitive communication with relatives is essential
- End-of-life care in the ITU includes the pharmacological management of symptoms including pain, nausea, dyspnoea, distress, agitation, and anxiety, in addition to spiritual care and family support
- Organ donation can be considered after confirmation of death by neurological criteria or when planned withdrawal of therapy is expected to result in circulatory death. This process must be separated from end-of-life decision-making

Reference

1. Faculty of Intensive Care Medicine UK. https://www.ficm.ac.uk/index.php/diagnosing-death-using-neurological-criteria. Accessed Jan 2022

Organ Dysfunction and Suppsort

Contents

Respiratory Failure and Respiratory Support

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Contents

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Intended Learning Outcomes (ILOs)

By the end of this chapter, you should be able to achieve ILO 1. You should also have the knowledge required to achieve ILO numbers 2–5, successfully.

1. Describe the indications and modalities of oxygen therapy, non-invasive ventilation methods, and indications for intubation and invasive mechanical ventilation.
2. Apply basic physiological principles of mechanical ventilation—volumes, pressures, compliance, etc. in the management of the most common lung pathologies using basic modes of ventilation (in a simulated setting).
3. Demonstrate the ability to initially set a ventilator and adapt ventilatory settings for the most common types of ventilation disorders, including obstructive pulmonary disease and ARDS (in a simulated setting/app).
4. Select an adequate PEEP based on physiological values (in a simulated setting/app).
5. Identify the most common types of ventilator interference (in a simulated setting/app).

6.1 Introduction

Mechanical ventilator is essential for life support in the intensive care unit (ICU). Clinicians working in ICU have to become familiar with how to handle/use a ventilator and fulfill the tasks of initiating, maintaining, and weaning patients from mechanical ventilation. The primary purposes of instituting mechanical ventilation are (1) to decrease the work of breathing, (2) to support the gas exchange, and (3) to buy time for other interventions to reverse or treat the cause of respiratory failure. Apart from its role in the management of respiratory failure, mechanical ventilation is indicated to permit the pharmaceutic depression of the respiratory center during anesthesia or disease states of depressed consciousness. In this chapter, we assume medical student level knowledge of lung and gas exchange physiology.

6.2 Basic Physiology

Respiratory failure is when the respiratory system fails in one or both of its gas exchange functions: oxygenation and carbon dioxide elimination.

Respiratory failure types are:

- Type I or Hypoxemic respiratory failure
  - Definition: PaO_2 <60 mmHg [8 kPa] with normal or low $PaCO_2$ normal or high pH. There is impairment of oxygen transfer in the lung causes hypoxemia. It is the most common form of respiratory failure, where lung disease is severe enough to interfere with pulmonary O_2 exchange, but overall ventilation is maintained.
  - Causes:
    - Ventilation/Perfusion (V/Q) mismatch
    - Shunt

  - Hypoventilation (respiratory pump failure)
  - Impaired diffusion
  - Low inspired oxygen fraction
- Type II hypercapnic respiratory failure:
  - Definition: Inadequate ventilation leading to retention of CO_2, with hypercapnia ($PaCO_2$ >45 mmHg, [6 kPa]) and hypoxemia (pO_2 <60 mmHg, [8 kPa]). The value of pH depends on the concentration of HCO_3^-, which depends on the duration of hypercapnia. Type 2 respiratory failure results from absolute or relative hypoventilation.
  - Causes:
    - Increased CO2 production (fever, sepsis, burns, overfeeding)
    - Decreased CO_2 elimination by alveolar ventilation
      - Decreased CNS drive (CNS lesion, overdose, anesthesia)
      - Neuromuscular disease (Myasthenia Gravis, Amyotrophic Lateral Sclerosis, Guillian-Barre, myopathies, etc.)
      - Increased work of breathing (WOB) leading to respiratory muscle fatigue and inadequate ventilation
      - Asthma/COPD
      - Pulmonary fibrosis
      - Kyphoscoliosis
      - Increased physiologic dead space (hypovolemia, poor cardiac output, alveolar over distension)
- Type III (Peri-operative) respiratory failure.
  - Causes:
    - Atelectasis due to low functional residual capacity (FRC) in the setting of abnormal abdominal wall mechanics. Often results in type I or type II respiratory failure.
- Type IV (Shock) respiratory failure.
  - Causes:
    - Secondary to cardiovascular instability. Type IV describes patients who are intubated and ventilated in the process of resuscitation for shock, and the goal of ventilation is to stabilize gas exchange.

Note

Acute respiratory distress syndrome (ARDS) is one of the most common causes of hypoxemic acute respiratory failure in ICU. The diagnosis of ARDS is based on Berlin criteria:

Timing: Within 1 week of a known clinical insult or new/worsening respiratory symptoms.

Chest imaging: Bilateral opacities not fully explained by effusions. Lobar/lung collapse or nodules.

Origin of edema: Respiratory failure not fully explained by cardiac failure or fluid overload. Needs objective assessment (e.g., echocardiography) to exclude hydrostatic edema if no risk factor present.

Oxygenation:

Mild-PaO_2/FIO_2 ratio 200–300 mmHg [27–40 kPa] with a minimum of 5 cmH_2O PEEP (or CPAP)

Moderate-PaO_2/FIO_2 ratio 100–200 mmHg [13–27 kPa] with a minimum of 5 cmH_2O PEEP (or CPAP)

Severe PaO_2/FIO_2 ratio <100 mmHg [13 kPa] with a minimum of 5 cmH_2O PEEP (or CPAP)

6.3 Supplementary Oxygen Delivery Devices

The first and simplest method to increase the fraction of oxygen in inspired air (FiO_2) is to administer oxygen. Supplementary oxygen delivery devices are categorized into low-flow and high-flow systems depending on whether device flow can match the patient's peak inspiratory flow. Normally, peak inspiratory flow is 20–30 L/min and it increases with labored breathing.

- With low-flow systems, inspired oxygen (or therapeutic gas mixture) is diluted by ambient air at peak inspiration. For example, a patient with peak inspiratory flow 30 L/min on 100% oxygen 15 L/min will breathe 1:1 mixture of oxygen (FiO_2 1.0) and room air (FiO_2 0.21) at peak inspiration. In theory, this should be (1.0 + 0.21)/2 = 0.6, but inspiratory flow is not constant and different oxygen masks contain technical solutions aiming at reducing room air admixture during inspiration. In addition, the patient does not take in 30 L/min for the whole duration of the inspiratory cycle; this is only peak inspiratory flow. The result is a variable and not easily calculable FiO_2.
- High-flow systems deliver flow higher than peak inspiratory flow, and in theory there should be no admixture of room air to what the patient inspires (set FiO_2 = actual FiO_2).

The selection of oxygen devices and delivery systems depends on the degree of hypoxemia, the patient's underlying diagnosis, and patient preference.

Low-Flow Systems

- Nasal cannula (set to deliver flow 1–6 L/min, FiO_2 24–40%)
- Simple face mask (set to deliver 5–10 L/min, FiO_2 35–55%)
- Non-rebreathing mask (set to deliver 15/min, FiO_2 80–95%)

High-Flow Systems

- Rebreathing mask
- Venturi mask (precise FiO_2 delivery between 24 and 50%)
- High-flow nasal cannula (HFNC)

In a high-flow nasal cannula (HFNC), at a flow of up to 60 L/min, gas from an air/oxygen blender is heated and humidified with an active humidifier and subsequently

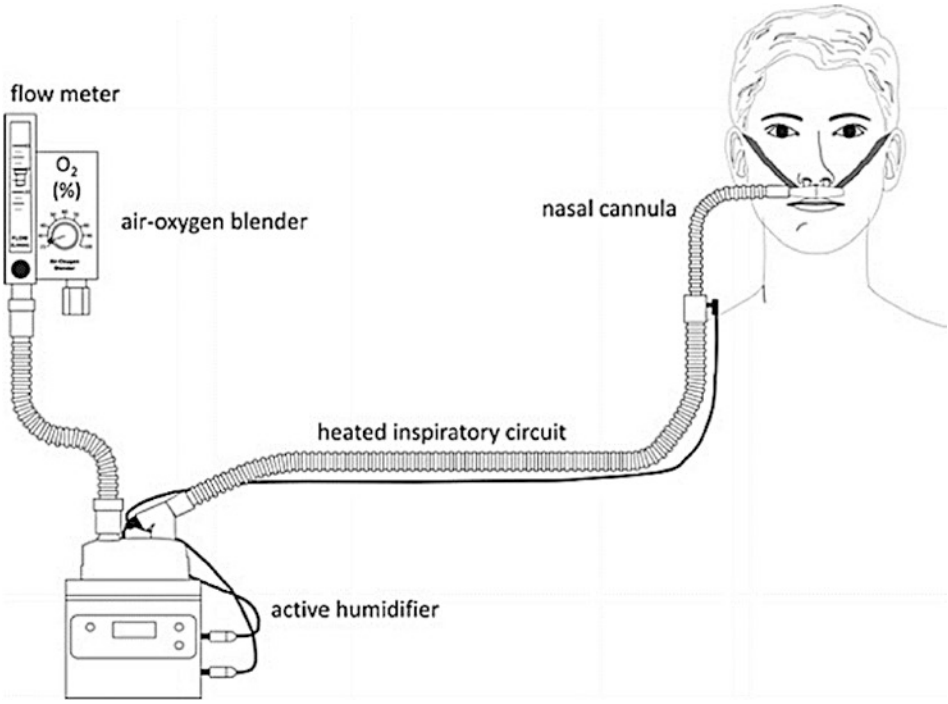

Fig. 6.1 Schematical presentation of a high-flow nasal cannula system

delivered through a heated circuit (Fig. 6.1). With HFNC, the delivered FiO_2 ranges from 24 to 100%. HFNC is the only oxygen delivery system in which actual FiO_2 is close to calculated (predicted) FiO_2. This system also has a PEEP effect (approximately 1 cmH_2O/10 L/min).

In practice: Typical indication of HFNO is type 1 respiratory failure in a patient who is not sick enough to require intubation. Although it reduces dead space, in type 2 respiratory failure, the first choice in hypercapnic failure would be non-invasive ventilation. It can help to avoid intubation in some patients, but the risk is that HFNO will cause an unnecessary delay in some patients in whom intubation is unavoidable. HFNC turned was very useful during the COVID-19 pandemic to treat patients with "happy hypoxia." It is tolerated well by most patients, but it can fail in mouth breathers. Contraindication to HFNC is injury of nose or base of skull.

6.4 Non-Invasive Ventilation (NIV)

NIV refers to the delivery of mechanical ventilation using techniques that do not require an artificial airway (endotracheal tube or tracheostomy). A typical arrangement and different interfaces for applying NIV are presented in Figs. 6.2 and 6.3. Typical patients for NIV are those with hypercapnic patients with COPD or cardiogenic pulmonary edema [1].

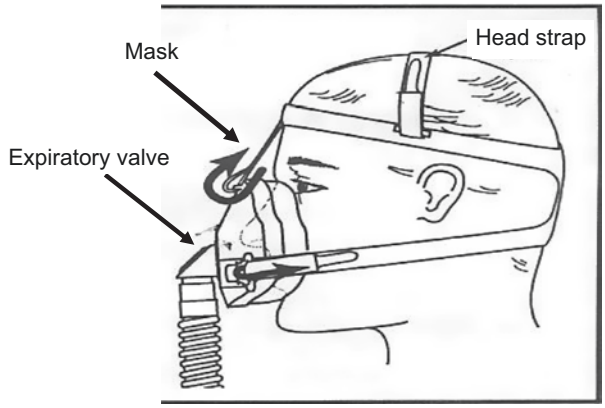

Fig. 6.2 Typical arrangement for applying NIMV. A typical arrangement for applying NIMV includes the musk secured firmly with a head strap and the expiratory valve, which is important to avoid CO_2 rebreathing

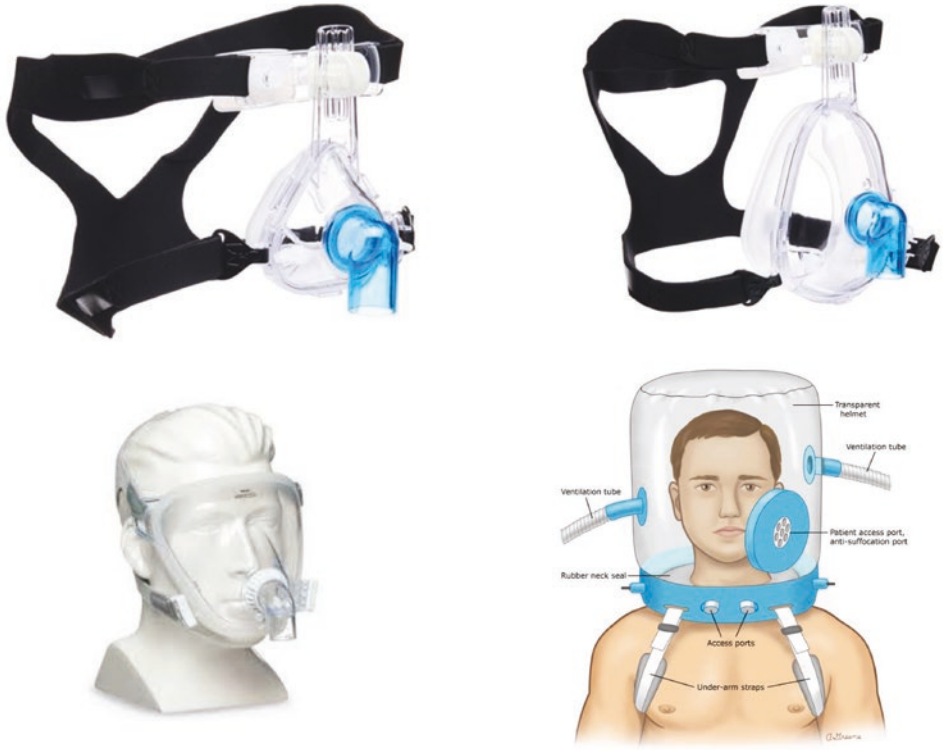

Fig. 6.3 Interfaces to deliver. Non-invasive mechanical ventilation. From Up left to bottom right: nasal mask, nose-mouth mask, total face mask and helmet

When to Start NIV

- Respiratory distress
- Respiratory failure (not corrected by oxygen therapy alone)
- PO_2/FiO_2 <300 mmHg [40 kPa]
- PCO_2 >45 [6 kPa]
- pH <7.35 (H^+ >42 nEq/L)
- Diseases in which NIV has proven to be effective are acute exacerbation of COPD and hypercapnic acidosis, pulmonary edema, and postoperative respiratory failure
- Absence of contraindications

When to Terminate NIV and Proceed to Intubation

- hemodynamic instability
- decrease level of consciousness
- worsening PH and $PaCO_2$
- worsening PaO_2
- tachypnea >30 b/min
- intense dyspnea
- signs of increased WOB
- inability to clear secretions
- agitation with or intolerance of NIV with progressive respiratory failure

Contraindications for the Use of NIV

- cardiac or respiratory arrest
- inability to keep a patent airway (coma or obtunded mental status) and/or to manage secretions
- anatomical abnormalities which prevent interface fitting (facial or upper airway trauma, surgery)
- intractable emesis or GI bleeding
- severe hemodynamic instability

In most hospitals, NIV can also be applied outside the ICU. It is typically used in emergency departments as a temporary measure or in respiratory wards. Yet, the success of NIV depends on the skills of the bedside nurse. Good care is time demanding and patients need constant attention and reassurance. The optimal location for patients receiving NIV depends on adequate monitoring capabilities, staff skills experience, awareness of potential complications, and, more importantly, the recognition of the patients' need for intubation and invasive mechanical ventilation.

NIV can be delivered using either NIV-dedicated devices or ICU ventilators. Typical patients on NIV are those with type 2 respiratory failure in COPD and cardiogenic pulmonary edema.

There are in essence, two commonly used settings:

- **CPAP** (continuous positive airway pressure) works by simply increasing the pressure in the circuit above atmospheric pressure. CPAP is the regime used at home by patients with variable airway obstruction (obstructive sleep apnea syndrome),

where positive pressure helps in keeping the airway open. In hospital, CPAP is mainly used in patients with hypoxemic respiratory failure due to cardiogenic pulmonary edema, where positive intrathoracic pressure reduces left ventricular afterload. Additional support can be added to CPAP: pressure support: when the ventilator registers patient's inspiratory effort, it may further increase the positivity of pressure in the circuit, further enhancing inspiration and reducing work of inspiration. Thus, CPAP becomes, in fact, pressure support ventilation (PSV, see below). Technically, CPAP is not a form of "ventilation" until this pressure support is added.

An example of typical initial settings for a hypoxic patient with cardiogenic pulmonary edema: CPAP: PEEP 6 cmH_2O*, pressure support PEEP+ 6* cmH_2O*,* FiO_2 *= 0.6, and titrate as per* SpO_2*. When tolerated, PEEP could be increased up to 10* cmH_2O.

- **BIPAP** (bilevel positive airway pressure) cyclically switches between two levels of pressure, which in an apneic patient would cause inspiration and expiration. On both pressure levels, the ventilator allows the patient to breathe spontaneously. In turn, not only does this regime increases intrathoracic pressure, but it also helps with the work of breathing, too. It is the preferred initial mode of ventilation in hypercapnic respiratory failure (e.g., in patients with COPD).

An e*xample of typical initial setting for a hypercapnic patient with COPD: PEEP 6* cmH_2O*, inspiratory pressure 20* cmH_2O*, RR 12/min, I:E 1:3,* FiO_2 *= 0.35 and titrate to* SpO_2 *= 88–92%.*

REMEMBER: Both HFNC or NIV are useful temporizing measures and they usually improve patient's physiological parameters. Yet, a significant proportion of patients will fail and require intubation and this should not be done too late, for example, in a patient *in extremis*. Early recognition of NIV failure requires a lot of experience. The clinical picture ("end-of-the-bed-ogram") is usually more helpful than blood gases in making decision to intubate.

6.5 Invasive Mechanical Ventilation

Invasive mechanical ventilation is delivered via an artificial airway (endotracheal tube or tracheostomy).

Indications of Intubation and Invasive Mechanical Ventilation

Inability to protect upper airway

- excessive secretions
- obtunded patient (GCS <8)

Failure of ventilation

- airway obstruction
- cardiac or respiratory arrest
- hypercapnia with impaired conscious level
- respiratory rate <10 breaths/min

Failure of oxygenation

- life-threatening hypoxemia
- PaO_2 <60 mmHg [8 kPa] or SaO_2 <90% despite FiO >0.6 and CPAP
- failure of NIV or CPAP
- deteriorating parameters despite optimal treatment
- exhaustion, e.g., RR > 40 breaths/min
- in patients with neuromuscular disease (vital capacity <15 mL/ kg (normal 65–75), <1 L or <30% predicted)

6.5.1 Basic Physiology of Respiratory System Related to Mechanical Ventilation

6.5.1.1 Respiratory System Compliance and Airway Resistance

Any flow of gas requires a pressure gradient. In spontaneous inspiration, inspiratory muscles increase the volume of thoracic cage, creating a subatmospheric ("negative") pressure in the pleural space. This causes air to move into the lungs. Exhalation in spontaneous and mechanical ventilation is passive, where the pressure gradient is created by the elastic recoil forces of the lung, which overcome airway resistance and drive exhalation. At end-expiration, lung volume rests in functional residual capacity (FRC), and alveolar pressure equals atmospheric (or the pressure in the circuit).

By mechanical ventilation in the following text, we mean positive pressure ventilation. This means that inspiration is driven by increased pressure in the ventilator circuit. In essence, the pressure gradient is used to (1) overcome the elasticity of the lungs and chest wall and (2) move air through the airways.

Let's look at these values further:

- Elastance (or rather its inversion value compliance, C = 1/elastance) is an important static parameter. Compliance determines the inhaled volume for each unit of pressure (unit is mL/mbar or cmH_2O). Reduced respiratory system compliance can be caused by reduced compliance of the lung (such as in ARDS) or chest wall (such as in morbid obesity or abdominal hypertension). Respiratory system compliance can be measured in patients without inspiratory effort by constructing a pressure-volume (PV) curve on the ventilator, or it is calculated on a breath-by-breath basis by ventilator software (but this is less precise as resistance also becomes a factor). Normal values are above 50 mL/cmH_2O, while in severe ARDS values are usually <40 mL/ cmH_2O.
- Resistance is defined as the pressure difference at a constant flow 1 L/s (or 60 L/min), and normal values are <10 cmH_2O.s/L. Resistance is elevated in airway diseases such as asthma or COPD.

Both static and dynamic parameters of the respiratory system need to be taken into consideration when setting the mechanical ventilator. General principles can be inferred when setting the ventilator in lungs with different pathologies:

- Reduced compliance (ARDS). Patients require lower tidal volumes (VT) to avoid excessive pressures damaging the lung (barotrauma). Increased elastic recoil of the lung requires higher PEEP to keep the lung open at end-expiration.
- Patients with increased resistance (e.g., due to COPD) may not exhale completely before the next inspiration begins. Therefore, pressures between alveoli and the ventilatory circuit may not equilibrate. This means that alveolar pressure remains positive at end-expiration (a condition called intrinsic PEEP or PEEPi). In turn, FRC increases (a phenomenon called dynamic pulmonary hyperinflation) until a new equilibrium is reached where PEEPi generates a high enough pressure gradient to complete exhalation. Therefore, for mechanically ventilated patients with airflow obstruction, it is crucial is to increase the time for exhalation This is achieved by using lower respiratory rates and tidal volume and extended expiratory:inspiratory time ratio.

6.5.1.2 Influence of Positive Pressure Ventilation on Hemodynamic Parameters

During mechanical ventilation particularly when high PEEP or large tidal volumes are employed, intrathoracic pressures are generally increased and swing during inspiration/inspiration cycle, which influences hemodynamic parameters in the following ways:

- Venous return (RV preload) and cardiac output is reduced due to increased intrathoracic pressure, at least temporarily as the heart can only pump what it gets. Practically, every intubation can lead to more profound hypotension than induction drugs alone would have caused. It is more pronounced in patients with high intrathoracic pressure (e.g., stiff lung or dynamic pulmonary hyperinflation) or in hypovolemic patients. Be prepared for this (arterial line first and have vasopressors ready).
- Pulmonary vascular resistance increases due to compression of the pulmonary capillaries thereby increasing right ventricle afterload and reducing stroke volume.
- Left ventricle afterload is reduced, which helps the LV, especially in patients with congestive heart failure. LV afterload is defined as the systolic blood pressure minus intrathoracic pressure. That is why the transition from positive pressure to spontaneous breathing in patients with congestive heart failure can be poorly tolerated (see weaning failure). There is also a reduction in intrathoracic pressure by quickly pushing out large volumes of fluid in the lungs.
- Reduced venous drainage of abdominal organs with the increase in intrathoracic pressure can worsen the function of splanchnic organs.
- There is also the influence of shock states on lung function. Most importantly, normal mixed venous blood saturation is around 70%. Low cardiac output causes mixed-venous blood to desaturate below 70%, and this exacerbates the influence of intrapulmonary shunt on arterial oxygenation (i.e., the same venous admixture causes lower arterial oxygen levels if the shunted venous blood has lower oxygen saturation).

6.5.2 Basic Features of Positive Pressure Ventilators

The function of positive pressure ventilators depends on **three different variables**: *the trigger variable,* which is the signal for the ventilator to initiate the mechanical breath, *the variable that controls pressure delivery* and the *cycling off* criterion, which is the signal for the termination of mechanical breath. It is useful to think in these terms when trying to understand ventilator modes. Manufacturers are using "innovative" modes and give them new names which can be very confusing for a novice. Ultimately, every ventilator can be viewed as a machine blowing gas into patients lungs following certain computer-driven instructions. Invariably, it measures FiO_2, flows, and pressures in both inspiratory and expiratory phases of the respiratory cycle [1].

6.5.2.1 Triggering Variables

- **Time**: Time as a triggering variable applies in controlled modes in which the operator sets the respiratory rate; a mechanical breath begins at constant intervals (every x sec, where respiratory rate = $60/x$)
- **Pressure**: (applies in assisted modes) The inspiration begins when the patient's effort decreases the pressure in the ventilator circuit by a predetermined level. A schematic presentation of ventilator triggering when the triggering variable is the pressure is presented in Fig. 6.5.
- **Flow**: (applies in assisted modes) A continuous flow (bias flow) is established in the circuit during the expiration and, the inspiration begins when the patient's effort decreases the flow by a predetermined value. A schematic presentation of ventilator triggering when the triggering variable is the flow is shown in Fig. 6.6.

Variables That Control Pressure Delivery

Depending on the variable that controls pressure delivery the modes are defined as volume or pressure targeted modes. Variables that control pressure delivery are

- **Volume** and **Flow** in volume-targeted modes (volume control [VC] and assist volume control [AVC]). In volume-targeted modes, volume and flow are the independent variables, and airway pressure the dependent variable, denoting that pressure provided by the ventilator depends on the elasticity and resistance of the respiratory system and the predefined flow or volume.
- **Pressure**: In pressure targeted modes (pressure control [PC] and pressure support [PS]). In pressure-targeted modes, airway pressure is the independent variable, and volume and flow the dependent variable, denoting that instant flow and volume is determined by the elasticity and resistance of the respiratory system and the predefined pressure

6.5.2.2 Cycling Off Variables

Time: (applies in controlled modes). The inspiration terminates at regular time intervals determined by the preset by the operator respiratory rate and the inspiration/expiration ratio (I:E)

Flow: (applies in assisted modes). The inspiration ends when the inspiratory flow decreases to a fixed value (25%) or operator-defined (featured in new generation ventilators) percentage of its peak value.

Pressure (applies in PS). It is used as a safety feature along with flow threshold for cycling off. The mechanical inspiration ends when airway pressure increases above a predefined threshold (1–3 cmH_2O).

6.5.3 Ventilation Modes

In all ventilator modes, **variables influencing oxygenation (i.e., FiO_2 and PEEP) are always set by the operator**. Setting parameters influencing CO_2 elimination, i.e., minute ventilation differs according to the ventilation mode [1].

6.5.3.1 Controlled Modes

In the controlled modes of mechanical ventilation, the patient is passive and it is the ventilator that triggers inspiration and delivers the work of breathing. In ICU, these modes are usually used in the initiation of MV

Volume Control Mode

In volume control mode (VC), the variable that controls pressure delivery is the preset volume. The dependent variable is the airway pressure (Paw). Figure 6.4 shows the Paw, flow, and volume waveforms in a patient ventilated on VC. Note that flow is roughly constant throughout inspiration. The operator has to set VT, the respiratory rate, and inspiratory to expiratory times (I:E) in VC mode, while pressures are monitored. Let's look a little closer at the pressure waveform of a volume-controlled breath Fig. 6.5.

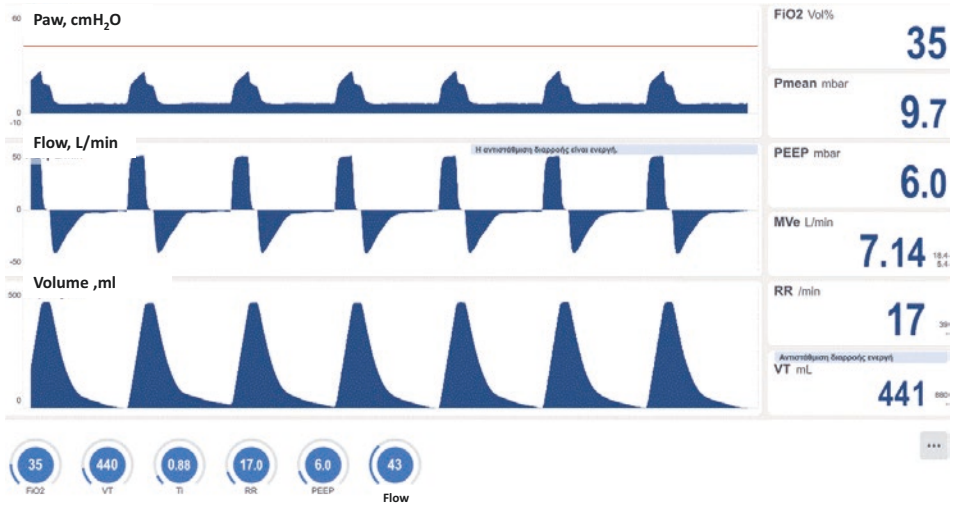

Fig. 6.4 From up to bottom airway pressure (Paw), flow and volume waveforms in a patient ventilated on volume control mode

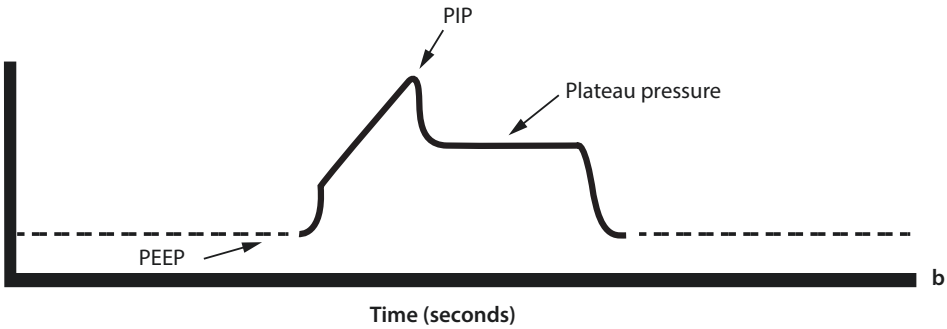

Fig. 6.5 Airway pressure waveform in volume control mode

Constant flow maintained during inspiration is achieved by increasing the pressure steadily until the end of inspiration, reaching PIP. When inspiratory flow stops, expiratory valve has not opened yet and pressure drops a bit to the plateau pressure (Pplat). The difference between PIP-Pplat reflects airway resistance as this was the part of the pressure gradient used to move the air through the airways. In contrast, the difference plateau pressure-PEEP (called driving pressure) reflects the pressure needed to distend the respiratory system beyond the airways. For a given setting, PIP increases in airflow obstruction diseases and Pplat increases in ARDS.

Remember: Pplat <30 mbars and driving pressure <14 mbar are important parameters for ventilation safety. On the other hand, PIP is not translated to the alveolar level pressure and its elevation, for example, in intubated asthma patients is much less concerning as long as Pplat is at a safe level.

Pressure Control Mode

In pressure control mode (PC), the variable set is the pressure, and flow and volume are the dependent variables. Figure 6.6 shows how Paw, flow, and volume waveforms look like in a patient ventilated on PC. Note that inspiratory flow decreases during inspiration because the pressure in the airways is the same, and the pressure gradient and hence flow are gradually reduced during inspiration. In PC mode, the operator has to set the inspiratory pressure, respiratory rate, and I:E ratio, while the VT achieved is monitored.

6.5.3.2 Assisted Modes of Ventilation

Unlike controlled modes, assisted modes of ventilation are designed to accommodate the patient's breathing efforts without causing patient-ventilator asynchrony and discomfort.

Pressure Support Ventilation (PSV)

PSV (some manufacturers label this mode as CPAP/ASB, as for Assisted Spontaneous Breathing) is the most commonly used mode of assisted ventilation in clinical practice. Once triggered, the ventilator provides a preset constant pressure support of the patient's effort during inspiration.

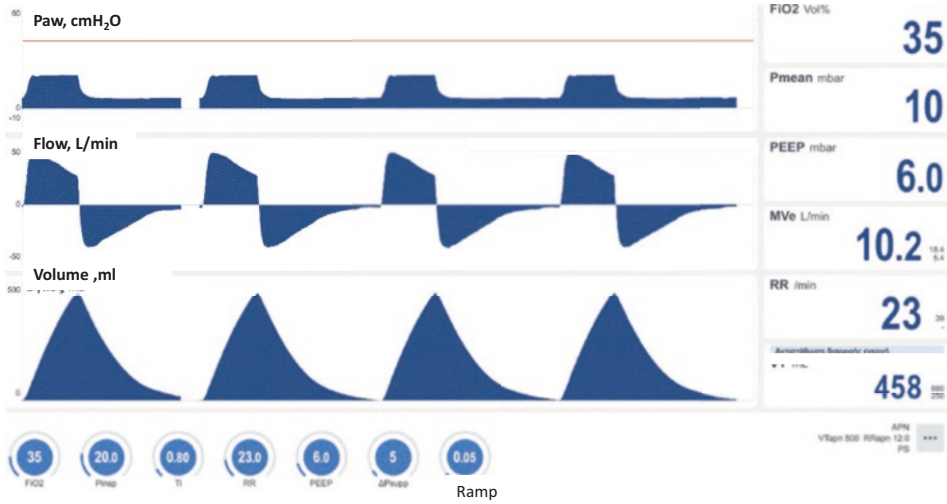

Fig. 6.6 From up to bottom airway pressure (Paw), flow and volume waveforms in a patient ventilated on pressure control mode

The ventilator maintains the appropriate flow needed to achieve the preset pressure during the inspiration phase. Cycling off occurs when inspiratory flow drops below 25% (usually) of peak inspiratory pressure. In PSV, the operator sets the level of pressure support (usually between 0 and 14 cmH_2O) and monitors the VT and RR achieved. PSV is the only mode that is entirely dependent on the patient to trigger a breath. Therefore, alarm limits are set to trigger based on apneic time (usually 15 s), after which the ventilator turns to a backup controlled mode of ventilation. Figure 6.7 shows the how Paw, flow, and volume waveforms look like in a patient ventilated on PSV.

BIPAP (Bilevel Positive Airway Pressure)

It can not only be used for NIV (Fig. 6.8c), but also in intubated patients. In patients without a breathing effort, this mode behaves as PCV. Unlike PCV, the ventilator can accommodate spontaneous breaths (which can also be pressure assisted). The setting of the ventilator and monitored values are identical to PCV. Reducing respiratory rate makes the patient more reliant on spontaneous breathing, which can be very useful during weaning (Fig. 6.8).

SIMV (Synchronized Intermittent Mandatory Ventilation)

In patients without a breathing effort, SIMV works as a VC mode and it is set as such. If it detects a patient's breathing effort during the breathing cycle (if set RR = 10, each cycle lasts 6 s), it will deliver the volume-controlled breath without waiting for the time-trigger to kick off. There is a lower chance of ventilator asynchrony compared to VC ventilation.

There are many other ventilation modes, but each unit usually uses only a couple of them depending on the ventilators in use and local preference. Try to understand how these work and use them. It is adherence to lung-protective ventilation princi-

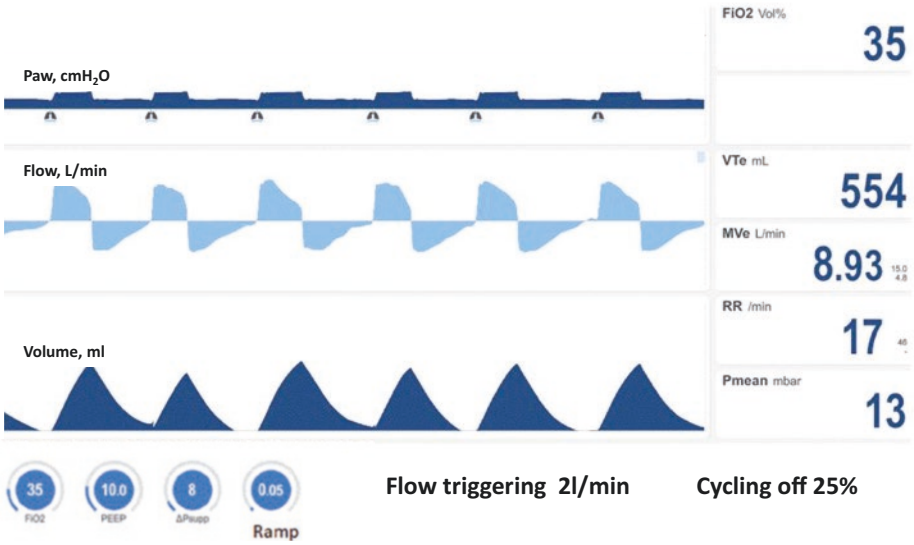

Fig. 6.7 From up to bottom airway pressure (Paw), flow and volume waveforms in a patient ventilated on pressure support mode

ples that changes the outcome, not the mode of ventilation. Therefore, if you are in Rome, do what the Romans do.

6.5.3.3 Initial Ventilator Settings

Choosing the Mode of Ventilation

Most patients will have spontaneous breathing efforts ablated by drugs given to facilitate ET tolerance. The initial choice of the mode ventilation should allow controlled breathing. Use whichever mode you are familiar with initially. The majority of intensivists probably would choose:

- Volume-controlled modes (e.g., VC) for patients with COPD/Asthma because it allows to separate PIP from Pplat (see above) and by tolerating a high PIP inspiratory flow can be high enough to allow for sufficiently long expiration. Volume control mode may also mandatory in patients with moderate and severe ARDS at the acute phase to ensure protective mechanical ventilation (low tidal volume and low distending pressures). Also, this could be the preferred mode for patients with raised intracranial pressure as minute ventilation and hence pCO_2 is better controlled.
- Pressure-controlled modes (e.g., PCV or BIPAP) for ARDS patients when you have to perform PEEP-optimizing maneuvers and both for ARDS and COPD patients following the acute phase of the disease at transition from controlled to assisted modes.

Indeed, further settings depends on the mode of ventilation chosen (see above). Indeed elimination of CO_2 depends on minute ventilation, while oxygenation depends on PEEP and FiO_2.

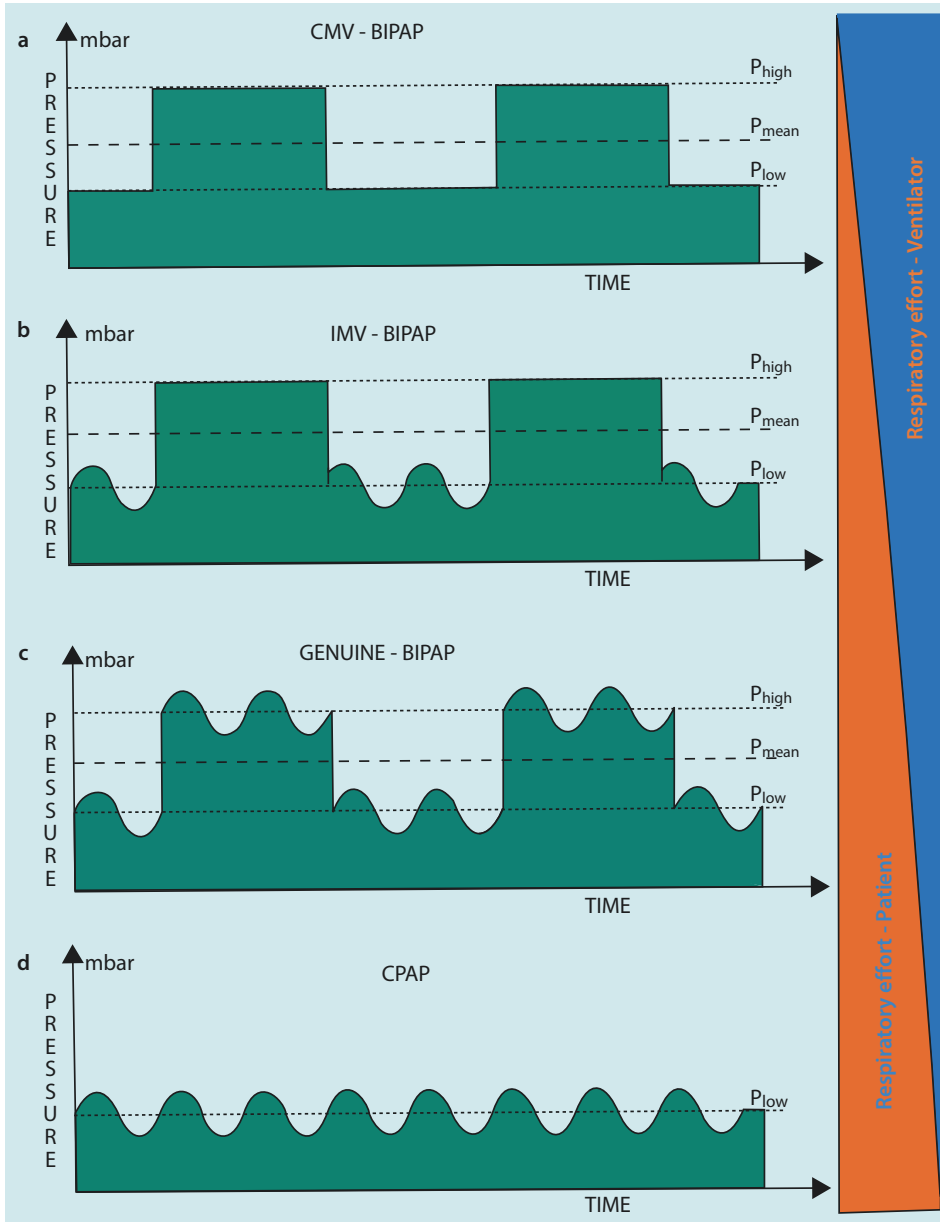

Fig. 6.8 Transition from controlled to assisted ventilation (**a**) in a patient on BIPAP (**b**). (**d**) and (**c**) represent Paw waveforms in patients ventilated on NIV on BIPAP (**c**) and continuous positive airway pressure (**d**) (CPAP) See text for details

Setting FiO_2

Initially, set FiO_2 to 1.0 and titrate down as per SpO_2 to achieve oxygen saturations of 93–96% or lower in patients with chronic hypoxia.

Setting PEEP

Applying PEEP aims to prevent alveoli collapse at end-expiration and promote reopening of closed alveoli (recruitment). On the other hand, high PEEP can overdistend some alveoli and impair perfusion in some regions. Therefore, in order to decrease shunt and improve V/Q mismatch, an optimum PEEP must be found. Clinical condition of the patient can help you to estimate initial setting of PEEP.

- *Healthy lung*. In all but patients with obstructive lung disease and severe dynamic hyperinflation on controlled modes, a PEEP of 5 to 8 cmH_2O should be applied to prevent atelectasis in the dependent lung regions.
- *Low compliance states.* In patients with ARDS, applying PEEP represents one of the cornerstones of protective mechanical ventilation. The application of PEEP mitigates the risk of ventilator-induced lung injury (VILI) by preventing the cyclical opening and closing of unstable alveoli. It also improves lung compliance and homogeneity by increasing the number of open alveoli. Initially, it is recommended to set a higher PEEP in ARDS, for example, in range 10–14 mbar or per ARDS net table:

FIO_2	0.3	0.4	0.4	0.5	0.5	0.6	0.7	0.7	0.7	0.8	0.9	0.9	0.9	1.0
PEEP	5	5	8	8	10	10	10	12	14	14	14	16	18	20–24

  Then, lung recruitability should be tested, for example, by titrating the PEEP for ideal lung compliance and oxygenation. Patients with ARDS respond varyingly to an increase in PEEP depending on whether they have high or low lung recruitability.
- *High airflow resistance*. In controlled modes, PEEP should be low to maximize the pressure gradient between the alveoli and circuit during expiration. However, this changes when the obstructed patient starts to breathe in assisted modes of ventilation. In patients with dynamic hyperinflation, the application of PEEP aims to improve ventilator performance at triggering (by counterbalancing PEEPi). External PEEP at about 80% of PEEPi can substantially decrease inspiratory elastic workload at triggering without further increasing dynamic hyperinflation.

Setting Tidal Volume

As a rule of thumb, 6 mL mL/kg **predicted** body weight (PBW) is appropriate for most patients. In patients with healthy lungs and in patients with obstructive lung disease, a slightly higher VT could be tolerated as long as Pplat is low. Low VT in patients with ARDS (Set VT of ≤6 mL/kg PBW) is one of the fundamental principles of protective mechanical ventilation.

- VT to target and end-inspiratory pressure (Pplat) <30 cmH_2O
- VT to target a driving pressure of the respiratory system (the difference between Pplat and PEEP; ΔP) <14 cmH_2O.

Note: Setting VT to achieve a ΔP <14 cm H_2O is independently associated with lower mortality in patients with ARDS.

Practical note: Changes in ventilator setting (e.g., effect of PEEP) may take a while to translate into a better SpO_2 as alveolocapillary reflex takes time to establish a new V/Q relation. Don't rush it. Think carefully about the ventilator changes you make and then give it a few minutes to see whether it works or not.

REMEMBER: After you have set the ventilator, come back and review both the patient and the ventilator screen. Is the patient OK? Are protective ventilation parameters being met? What is next plan with ventilation and physiological targets? Communicate with the bedside nurse and nurse in charge of the unit.

6.5.3.4 Ventilatory Strategies in Specific Conditions

Ventilatory Strategies in Patients with Acute Exacerbation of COPD and Asthma

The main pathophysiologic mechanisms leading to respiratory system inefficiency during an acute exacerbation of COPD and asthma are:

- dynamic hyperinflation
- respiratory muscle dysfunction at least due in part to increased FRC
- inefficient gas exchange
- cardiovascular abnormalities

Key features of ventilation of patients with airflow limitation is long expiration (low RR and I > E) and low PEEP. During transition to assisted modes of ventilation, PEEP needs to increase a bit to facilitate the triggering of pressure support for spontaneous breaths (see textboxs Targets in controlled modes and targets in assisted modes for details).

Targets in Controlled Modes

1. Acceptable PaO_2 (>60 mmHg [8 kPa]) and adequate O_2 delivery to tissues (consider Hb, cardiac output).
2. Correction of life-threatening respiratory acidemia (pH <7.2).
3. Relaxation of the respiratory muscles (deep sedation, consider short course neuromuscular sedation).
4. Reduction of dynamic hyperinflation.
   (a) **Set low minute ventilation** (↓RR, ↓ventilatory demands, accept hypercapnia and mild academia consider measures to reduce equipment dead space
   (b) **Increase expiratory time** (high inspiratory flow, low T_I/T_{TOT}, no end-inspiratory pause)
5. **Decrease resistance to expiratory airflow** (use bronchodilators, corticosteroids).
6. Switch to assisted modes as earlier as possible.

Practical advice for patients who are *in extremis* due to severe airflow limitation (e.g., occasionally seen in life-threatening asthma or severe reactive bronchospasm). These patients can be "stone" hard to ventilate despite full paralysis after intubation. When reconnected to a ventilator with a standard "COPD setting" (see textbox) there is no effective ventilation and the pressure limit alarm can go off immediately. Ensure deep sedation and paralysis, turn FiO_2 to 1.0. Disconnect the patient from the ventilator and leave to fully exhale for 30–60 s. In the meantime, set the ventilator to a VC mode, VT 4 mL/kg, RR = 10, PEEP = 0, I:E 1:5, set the pressure limit to 80 mbar. Reconnect the patient, don't worry about high pressures. Turn autoflow off and set flow manually to 60–80 L/min in order to make Pplat visible on the airway waveform. It will usually be well below 30 mbar despite a very high PIP. Then reduce the flow so that the full inspiratory time is used and PIP is decreased a bit. Titrate down FiO_2. Recheck frequently, as this setting will lead to hypercapnia. In most patients, the ventilator can soon be gradually reset to more standard settings as described in the textbox.

REMEMBER: Hypoxia is **not** a feature of COPD/asthma and these patients usually need FiO_2 in the range of 0.25–0.4. Look for other problems if such patients became hypoxic (pneumothorax, endobronchial intubation, etc.)

Targets in Assisted Modes

1. Acceptable PaO_2 (>60 mmHg [8 kPa]) and adequate O_2 delivery to tissues (consider Hb, cardiac output).
2. Promote patient-ventilator synchrony.
   (a) Maximize trigger sensitivity.
      i. Adjust the triggering threshold to the lowest level not associated with autotriggering.
      ii. Reduce dynamic hyperinflation (see previous text box).
      iii. Apply PEEP (80% of the PEEPi).
   (b) Decrease cycling off threshold to increase mechanical inspiratory time.
   (c) Avoid either insufficient or excessive levels of ventilation assist.
3. Consider the subjective feelings of comfort and breathlessness.

Ventilatory Strategies in Patients with ARDS

Mechanical ventilation in patients with ARDS should rely on established protective ventilation strategies to mitigate ventilator-induced lung injury (VILI). The hallmark of ventilation is using lower VT to keep Pplat<30 and driving pressure <14 mbar, most patients will need a high PEEP. Main ventilatory and non-ventilatory strategies are presented in the ◘ Table 6.1.

Table 6.1 Ventilatory and non-ventilatory strategies to avoid VILI in patients with ARDS. *PBW* Predictive body weight, *Pplat* End-inspiratory pressure, *PL* Transpulmonary pressure (the difference between Pplat and esophageal pressure), *ΔP* Respiratory system driving pressure (the difference between Pplat and PEEP), *Crs* Respiratory system compliance

Strategy	Target	Rationale-considerations
Ventilator strategies		
Tidal volume (VT)	≤6 mL/kg/PBW	Low VT improves outcomes in patients with ARDS.
	Pplat <30 cmH_2O	Pplat as a surrogate of stress
	PL at end-inspiration <18–20 cmH_2O	The stress in the lungs at a given lung volume. Consider in patients with suspected low chest wall compliance
	ΔP (driving pressure) <14 cmH_2O	Individualizes VT to lung size (Crs). The strongest predictor of mortality in recent studies
PEEP	Individualized based on the assessment of lung recruitability	Improves heterogeneity by recruiting closed alveoli and preventing cyclical collapse. Consider higher PEEP in patients with high lung recruitability
Non-ventilator strategies		
Prone position	16 h/sessions	Increases lung homogeneity and size of aerated lung improves V/Q mismatch and decreases shunt. Consider proning early in the course of mechanical ventilation in patients with moderate to severe ARDS
Neuromuscular blockade	<48 h by continuous infusion	Consider in patients with severe hypoxemia, significant patient-ventilator asynchrony that precludes lung-protective ventilation, and in patients with markedly high respiratory drive despite deep sedation

6.5.3.5 Weaning the Patient from Mechanical Ventilation

Most patients who are ventilated for a short period of time (hours or few days) for a non-pulmonary reason, will be able to breath normally after extubation. In these patients, a sedation hold is performed with a spontaneous breathing trial (see below) and the patient can be extubated. Other patients, particularly those with pulmonary pathology and/or ICU-acquired weakness will need a more gradual process of liberation from mechanical ventilation, called weaning. The principle of weaning is to retrain respiratory muscles by gradually loading more work of breathing on them, while protecting the lung from ventilator-induced injury, allowing the patients a good sleep and avoid exhaustion and anxiety.

Definitions

- Weaning is defined as the entire process of liberating the patient from mechanical support and the endotracheal tube.
- Spontaneous breathing trial (SBT): A trial of patients undertaking the entire WOB without assistance. In practice, the patient is put on PSV with PEEP = 6 + pressure support 6 cmH_2O for 30 min and observed. SBT in tracheostomized patient can also be performed using a T piece.

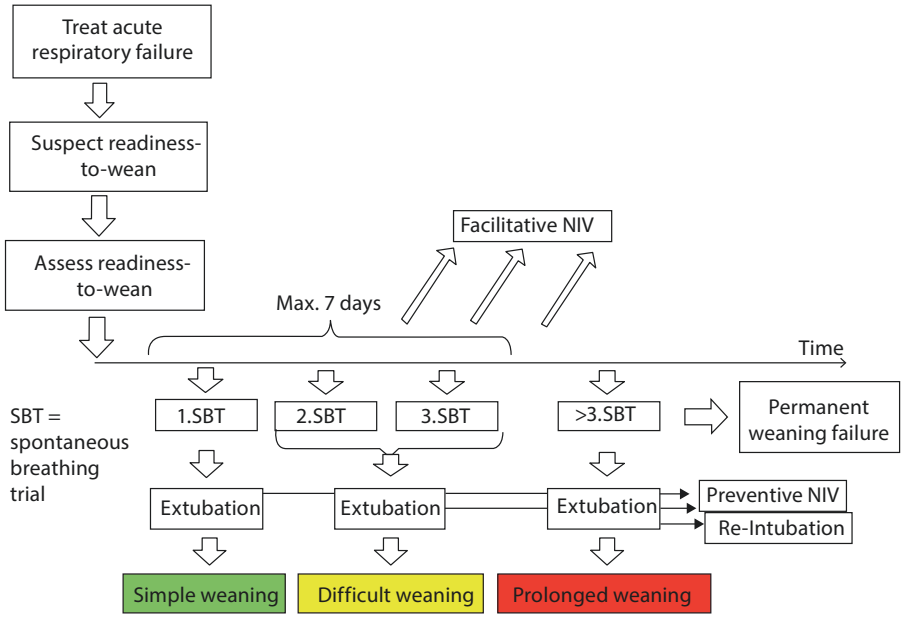

Fig. 6.9 The course of weaning and categorization of weaning. Based on the number of spontaneous breathing trials are required for extubation patients are categorized as having undergone simple, difficult, or prolonged weaning

- Weaning failure is defined as the failure to SBT or the need for reintubation or NIV support within 48 h (for some authors within 72 h) following extubation.
- Extubation failure is defined as the need for reintubation.

The course and categorization of weaning is illustrated in Fig. 6.9. As a general rule, at any given point in time, ventilator setting should be the least aggressive possible. The weaning process should be started as soon as the reason for intubated is resolved or improved and the patient's vital functions are stable. Then as the patient's condition improves, the support is gradually reduced, and the WOB is gradually given back to the patient. It could be done, for example, by gradually reducing pressure support or the rate of controlled breaths. Together with a sedation hold, all stable patients should have an SBT performed. When they pass an SBT (see textbox, they can be extubated).

Criteria of Successful SBT

- respiratory rate <35 breaths/min
- good tolerance to spontaneous breathing trials
- heart rate <140/min or heart rate variability of >20%
- $SatO_2$ >90% or PaO_2 >60 mmHg [8 kPa] on FiO_2 <0.4
- systolic blood pressure >80 and <180 mmHg or <20% change from baseline
- no signs of increased WOB or distress*

*Accessory muscle use, paradoxical or asynchronous rib abdominal cage movements, intercostal retraction, nasal flaring, profuse diaphoresis, agitation

Criteria of SBT Failure

1. Clinical criteria
   (a) diaphoresis
   (b) nasal flaring
   (c) increasing respiratory effort
   (d) tachycardia (increase in heart rate >40 bpm)
   (e) cardiac arrhythmias
   (f) hypotension
   (g) apnea
2. Gas exchange criteria
   (a) increase of $PetCO_2$ >10 mm Hg [1.3 kPa]
   (b) decrease of arterial pH <7.32
   (c) decline in arterial pH >0.07
   (d) PaO_2 <60 mmHg [8 kPa] with an FiO_2 >0.40 (PaO_2/FiO_2 ratio <150 [20 kPa])
   (e) fall in SpO_2 >5%

Weaning Failure

The main causes of weaning failure are incomplete resolution of critical illness, errors in assessing readiness to wean, and the presence of a new problem (see textbox). Some patients are very slow to wean despite addressing all the reversible causes. These patients usually need a tracheostomy and are very slow to wean; they may take weeks. In these patients, it is crucial that weaning is planned, predictable, includes overnight rest and is explained to the patient. It is also good that more support is given to the patient during exercise and mobilization. Exhaustion should be avoided as it can lead to anxiety. It is crucial to be attentive and reassure patients that help is always available whenever they develop shortness of breath or fatigue.

Practical advice: Find out whether nurse-led/physiotherapy-led weaning plans are in use for long-term patients in your unit? If yes, don't change them even if you think the patient can manage more. Continuity and predictability are very important.

Note: Patients older than 65 years and those with chronic cardiovascular or respiratory disease are at high risk of weaning failure.

The pathophysiology of weaning failure is multifactorial. The main pathophysiologic mechanisms associated with weaning failure are:

- **Hypoxemia**
- **Increased work of breathing**
  - increased ventilatory demand
  - increased resistive load
  - increased elastic load

- **Decreased neuromuscular capacity**
  - respiratory muscle weakness-fatigue
  - decreased ventilatory drive
- **Cardiac dysfunction**
  - myocardial ischemia
  - pulmonary edema
  - fluid overload
- **Psychological dysfunction**
  - delirium
  - anxiety
- **Metabolic, electrolyte, and endocrine abnormalities**

Take Home Messages

- High-flow nasal cannula is a good interim measure for patients with type 1 respiratory failure, while non-invasive mechanical ventilation is used mainly in cardiogenic pulmonary edema (CPAP) and exacerbation of COPD (BIPAP).
- Mechanical ventilation does not treat the lung pathology and care is needed to avoid ventilator-induced lung injury, but it offloads the WOB and supports gas exchange until underlying disease improves.
  - There are two types of pulmonary pathologies seen in ICU:
  - Low compliance states such as in ARDS where stiff lungs need a higher PEEP and lower VT. VT <6 mL/kg and Pplat <30 mbars are important safety parameters.
- High airflow resistance diseases such as COPD or asthma need a sufficiently long exhalation time to avoid dynamic pulmonary hyperinflation. PEEP is low in controlled modes and then increased on assisted modes of ventilation to facilitate triggering of pressure support.
- Positive pressure ventilation helps the failing left ventricle by reducing its afterload, but may overload the right ventricle, reduce venous return and cardiac output, particularly when using high pressures (PEEP, Pinsp).
- Allowing mild respiratory acidosis is less harmful for patients than damaging the lung by using aggressive ventilator settings.
- Weaning starts as soon as the underlying disease improves and the patient is otherwise stable.
- A sedation hold should be performed at least daily in all ICU patients who are ready for it.
- Nurse-led/physiotherapy-led weaning plans can be used for long-term patients who are difficult to wean.

Case Vignette

A 49-year-old man with confirmed COVID-19 pneumonia is admitted to ICU with acute hypoxemic respiratory failure. On admission in ICU:

Vital signs: BP 100/70 mmHg, Pulse 120/min, Respiration 38/min, Temperature 39.0 °C

Arterial blood gases: (on FiO_2 0.6), PH 7.35, PaO_2 45 mmHg [6 kPa], $PaCO_2$ 45 mmHg [6 kPa], HCO_3 24 mmol/L, PaO_2/FiO_2 75 mmHg [10 kPa], SaO_2 75%.

Chest X-ray reveals bilateral infiltrates. Transthoracic echocardiography shows: Ejection fraction 60%, normal left ventricular systolic and diastolic function.

Based on the clinical presentation, the imaging findings, and the arterial blood gases, what are the appropriate interventions to manage respiratory failure in this patient?

Reference

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Shock and Haemodynamic Monitoring

Mo Al-Haddad

Contents

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Intended Learning Outcomes (ILOs)

By the end of this chapter, you should be able to achieve ILO 1, 2, and 4. You should also have the knowledge required to successfully achieve ILO number 2.

1. Describe basic cardiovascular physiology and its monitoring in the context of the most common pathologies in ICU, including cardiac output and its measurement, left heart failure, and right heart failure.
2. Demonstrate assessment of fluid responsiveness in the simulated haemodynamically unstable patient/case.
3. Discuss the indications and use of vasopressor therapy.
4. Describe the different aetiologies of shock, recognise the role of POCUS to help assess the causes of haemodynamic instability.

7.1 Introduction

7

Haemodynamic instability and shock are some of the most common causes of referral to critical care services and are very common in critically ill patients in ICU. As a novice resident in ICU, you will commonly be asked to review patients with haemodynamic instability (i.e. hypotensive or with arrhythmias). In this chapter, I present fundamental concepts and give you a pragmatic approach to dealing with haemodynamically unstable patients until senior help arrives. This chapter is not meant to replace your local guidelines or international guidelines such as the Surviving Sepsis guidelines.

7.2 Basic Cardiovascular Physiology

One of the cardiovascular system's main functions is to deliver oxygen and nutrient-rich blood to tissues and remove waste products from these tissues and deliver them to organs—such as the kidneys and liver—for excretion.

The heart is the pump of the system. The perfusion of organs is achieved through a fine balance of flow and pressure. There is an inverse relationship between flow (Cardiac Output [CO]) and resistance (Systemic Vascular Resistance [SVR]) as demonstrated in Eq. (7.1). A high SVR leads to a higher mean arterial pressure (MAP) and reduces CO. An increase in CO also results in a higher MAP. A rise in MAP can therefore be caused by both those situations.

$$MAP = CO \times SVR \tag{7.1}$$

Equation (7.1). *Ohm's Law. MAP = Mean Arterial Pressure, CO = Cardiac Output and SVR = Systemic Vascular Resistance. This is analogous to: Voltage = Current * Resistance*

In turn, low blood pressure can either be caused by a low cardiac output, or by a loss of peripheral vascular resistance. Both the global flow (cardiac output) and peripheral vascular resistance can affect tissue perfusion, as demonstrated by the garden irrigation analogy in ◘ Fig. 7.1.

◘ Figure 7.1 is a garden irrigation analogy. The water and flow are analogous to the CO and the garden is analogous to tissues and organs. The upper diagram represents a situation where the water hose is completely open. In this case, the water flows freely and much more than the other situations. However, the pressure is not high

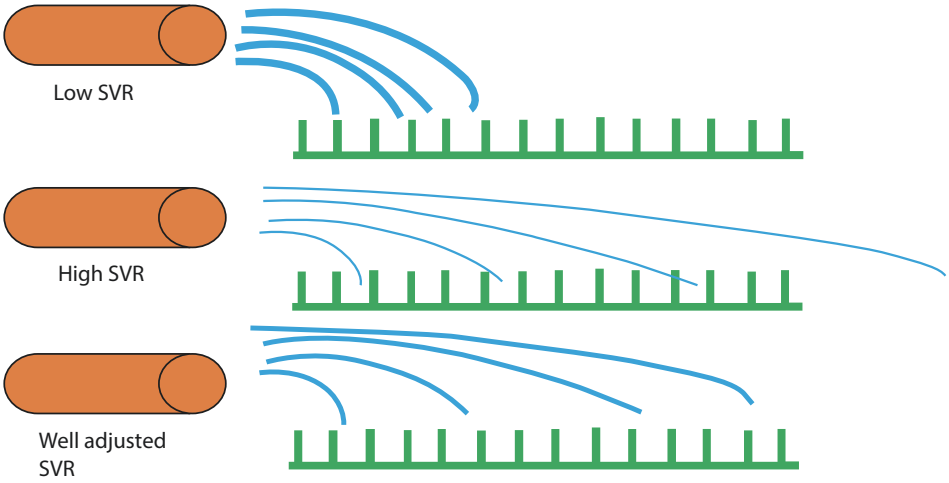
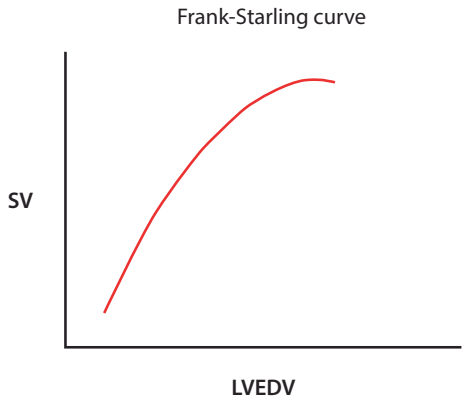


Fig. 7.1 Diagrammatic representation of a hose irrigating a garden with the tap completely open. The top, middle, and lower diagrams represent too little restriction (SVR), too much and just enough. *SVR* Systemic Vascular Resistance

Fig. 7.2 The Frank-Starling curve. On the upslope of this curve, increments in LVEDV leads to an increase in SV. *LVEDV* left ventricular end diastolic volume, *SV* stroke volume



enough to reach all areas of the garden. In the body, this is like distributive shock as we will see later. The middle diagram represents a situation where there is a restriction in the water hose outlet. This leads to high pressure which overshoots the area we want to irrigate and a significantly reduced flow. In the body, this is like situations where there is high SVR as in a hypertensive crisis or in the pathological response to cardiogenic shock, which puts further pressure on the heart and reduces CO. The lower panel represents a physiologically well adapted state. The interplay between MAP, SVR, and CO is crucial for understanding and dealing with shock states.

Cardiac output is determined by stroke volume (SV) and heart rate (HR): CO = HR * SV. Stroke volume is determined by:

- Preload. The heart can only pump what it gets. Frank-Starling's law dictates that increased end systolic volume increases stroke volume, Fig. 7.2. Blood returning to the heart through venous system distends the right ventricle and blood returning from the lungs distends the left ventricle. Most of the diastolic blood

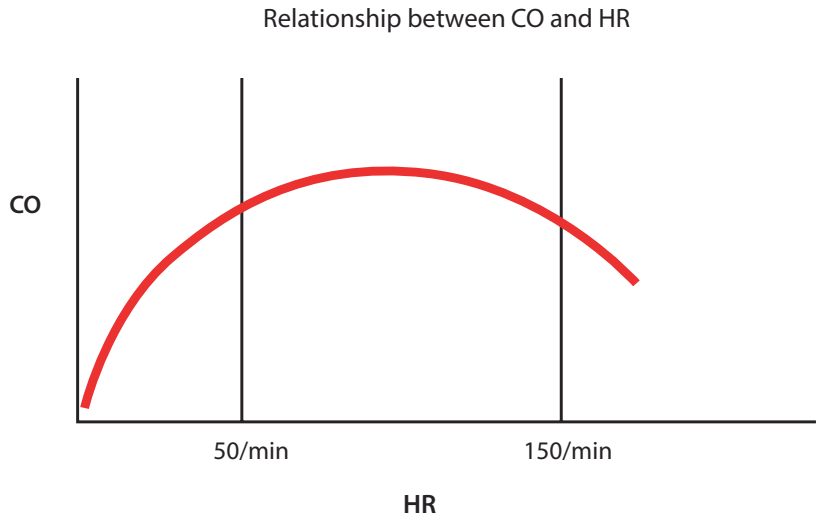


Fig. 7.3 The relationship between Cardiac Output (CO) and Heart Rate (HR)

flow is passive, whilst the last 20% of volume is generated by atrial systole ("atrial kick").
  - example of preload-related problem is hypovolaemic shock, e.g. in acute haemorrhage
  - example of clinical use: preload-responsiveness test such as passive leg-raise test
- Contractility: Is the ability of myocardium to contract and eject the blood during systole.
  - An example of contractility-related problem is cardiogenic shock, for example, after extensive myocardial infarction.
  - An example of clinical use: Echo parameters such as ejection fraction is used to assess contractility.
- Afterload: Is the resistance against which the blood is being ejected. For the left ventricle, it can be estimated as systolic blood pressure minus intrathoracic pressure. A failing ventricle is unable to cope with an increased afterload.
  - An example of afterload-related problem is a massive pulmonary embolism, when the RV dilates and fails.
  - An example of clinical use: Systolic blood pressure must be lowered to 100 mmHg when treating pulmonary oedema.

Therefore, the static value of CVP is a poor predictor of volume status and preload responsiveness and dynamic predictors such as a passive leg raise test are preferred.

The influence of heart rate on CO is inverse U-shaped, Fig. 7.3. Low HR is initially compensated by increased SV due to increased diastolic filling before each heartbeat, but reduction below 30/min reduces CO invariably. Tachycardia is a universal compensatory response to any reduction of SV or stress in general ("Sick, thus fast"), but too high HR (>150/min) may impair ventricular filling and reduce SV. Tachyarrhythmias >150/min can reduce CO and lead to further deterioration

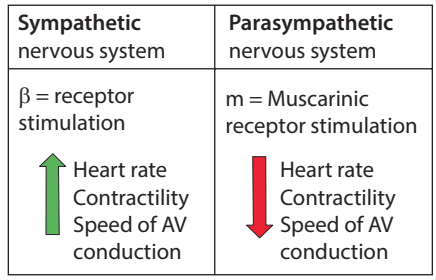


Fig. 7.4 Receptors and regulation of the heart

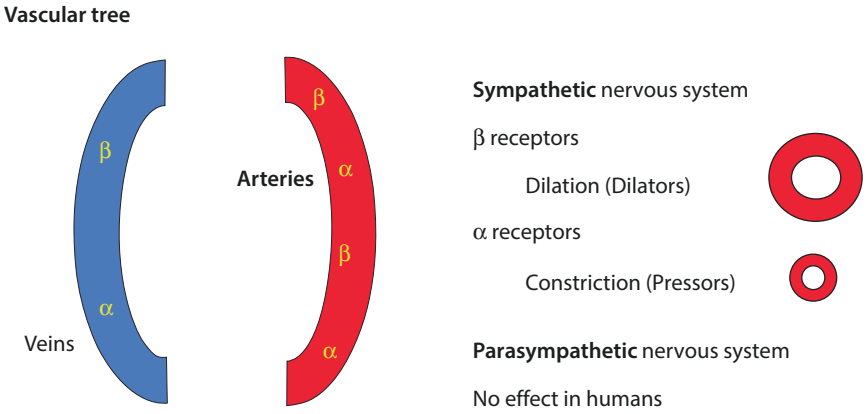


Fig. 7.5 Autonomic receptors and regulation of vascular beds

("Fast, thus sick"). The loss of the atrial kick in atrial fibrillation may further impair venous return and CO.

Figure 7.4 is a simple depiction of the main autonomic nervous system receptors responsible for regulating the heart functions

Figure 7.5 is a simple depiction of the main autonomic receptors regulating the diameter of vessels. It is important to note that this regulation is achieved solely by the sympathetic nervous system in Humans. Arteries are muscular vessels that are more elastic than veins. They are therefore more amenable to constriction and dilation by the sympathetic nervous system. A vasoconstrictor like noradrenaline, therefore, will constrict both arteries and veins but will constrict the former more than the latter. On the other hand, the pressure in the systemic arterial circulation is about six times that of the pulmonary arterial system.

A fundamental physiological principle worth mentioning is the Frank-Starling curve, Fig. 7.2. The premise of this principle is that an increase in preload or left ventricular end-diastolic volume (LVEDV) leads to an increase in stroke volume (SV). This occurs until the LVEDV reaches a certain volume after which further increases in volume will not lead to an increase in SV. Indeed, LVED volumes above this level lead to a decrease in SV or left ventricular failure due to fluid overload.

LVEDV is determined by the amount of blood delivered by the venous vascular system. This blood is also known as venous return. In a cardiovascular system at the left side of the Frank-Starling curve, an increase in venous return on the right side of the heart (e.g. by giving a fluid challenge, or straight leg raising) leads to an increase

in the output of the right ventricle. This leads to an increase in LVEDV causing an increase in SV. The venous return is always equal to the cardiac output if there is no change in circulating volume ("The heart can only pump what it gets").

Note on Venous Return

Right atrial pressure (clinically determined as central venous pressure) can be viewed from two sides:

- As a determinant of end-diastolic volume, which, as dictated by Frank-Starling principle increases stroke volume and in turn cardiac output.
- As a determinant of venous return. Because venous return is mostly a passive process, where blood flows from capillaries to the right atrium according to pressure gradient, it means that the higher CVP, the lower venous return and hence cardiac output.

7.3 Shock

Is the state of circulatory failure that leads to inadequate oxygen delivery to cells. This results in organ failure and cells switching to a predominantly anaerobic pathway of energy generation (respiration). Anaerobic respiration is less effective resulting in the generation of only two ATP molecules compared to a further 34 normally generated with aerobic respiration. Anaerobic respiration also results in the accumulation of lactate in both tissues and plasma, as lactate is a by-product of anaerobic glycolysis. If shock persists, it can lead to further multi-organ failure and ultimately death.

Lactate is therefore an important indicator of the severity of shock. The higher the level of lactate, the higher the risk of multiorgan failure and death. Lactate is also a useful molecule to monitor when managing patients with shock. A decrease in plasma lactate indicates response to management and an improvement in perfusion.

Figure 7.6 illustrates the four main types of shock. These are:

1. Hypovolaemic shock. As the name suggests, the cardiovascular system here is volume depleted. This can be due to haemorrhage or water loss, for example, severe diarrhoea. To maintain flow, the sympathetic nervous system is activated leading to peripheral vasoconstriction and tachycardia. Clinically, patients are anxious, diaphoretic, often pale, cold peripherally, and might have evidence of organ failure such as altered level of consciousness, reduced urine output, and sometimes chest pain.
2. Distributive shock. The main feature of this type of shock is vasodilation. There are many causes of this, for example, septic shock, anaphylaxis, and neurogenic shock. To maintain flow, the sympathetic nervous system is activated, and CO typically increases (This mechanism is lost if the level of spinal injury is high in neurogenic shock resulting in both hypotension and bradycardia.). As a result of the pathological vasodilatation, the circulation becomes relatively volume depleted; a term known as relative hypovolaemia. Clinically, patients with distributive shock are initially warm peripherally and can be flushed. Sometimes the

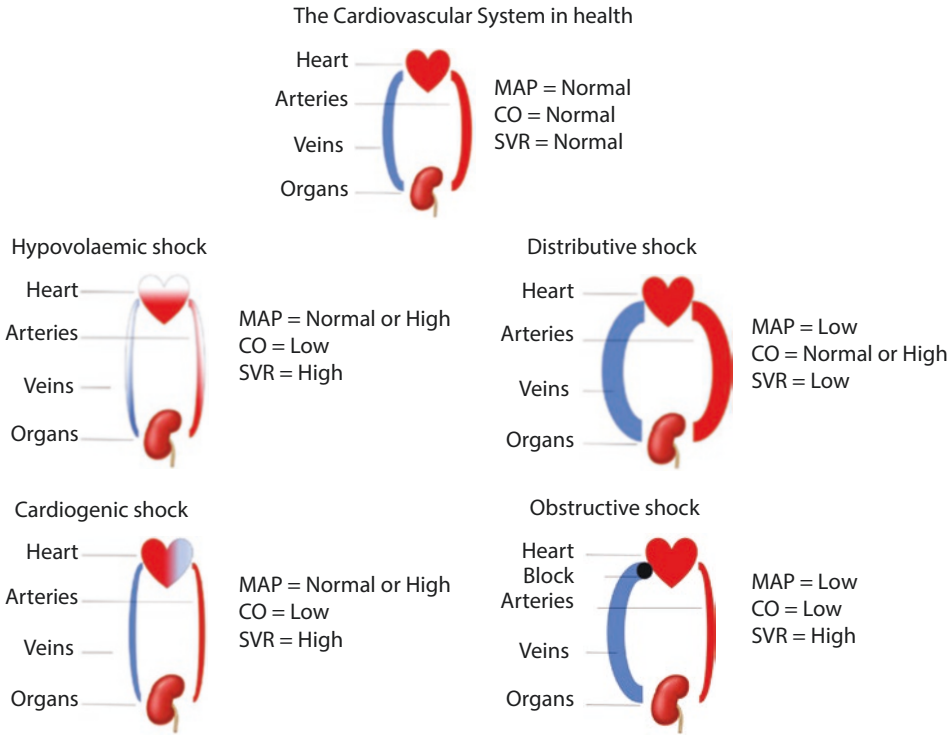


Fig. 7.6 The four main types of shock compared to the cardiovascular system in health

stroke volume (SV) is increased to such an extent that the chest or the whole patient can be seen moving (pulsating) with the heartbeat. Patients may also exhibit features of hypovolaemia.

3. Cardiogenic shock. Here there is pump failure. A sympathetic response is triggered to maintain perfusion, but this doesn't help as the failing heart is required to pump against a higher SVR. Patients with left ventricular heart failure are cold peripherally, pale, and eventually develop pulmonary oedema typified by shortness of breath, adopting a sitting posture if able, chest crackles and pink frothy sputum. Patients with right-sided heart failure are hypoxic and develop high pressures on the systemic venous side. This is manifested as peripheral oedema, a high central venous pressure, congested liver causing right upper abdominal quadrant pain, and gut oedema. An important cause of cardiogenic shock in critically ill patients that will not be discussed here is arrhythmia (see ► Chap. 13).
4. Obstructive shock. In this type of shock, there is blockage to the flow of blood. Examples are pulmonary embolism, and tension pneumothorax which leads to obstruction of the venous flow to the heart. In significant obstructive shock, the blood pressure drops as there is limited blood circulating. Features are those of very poor perfusion to the organs and peripheral tissues.

Septic shock is a common type of shock and is worth mentioning separately. It is defined as a condition in patient with sepsis where the MAP is < 65 mmHg despite adequate filling and serum lactate of >2 mmol/L (>18 mg/dL). Typically, septic shock

starts as a predominantly distributive shock with relative hypovolaemia. Due to disruption of the glycocalyx and the endothelium, the capillaries become "leaky". This leads to true hypovolaemia as fluid extravasates into the interstitial space. Moreover, sepsis-induced cardiac dysfunction can lead to a cardiogenic or relative cardiogenic shock as the heart fails to meet the demands of cells, tissues, and organs. In addition to this complex haemodynamic picture, mitochondrial dysfunction leads to a reduction in the cells' ability to utilise and extract oxygen. There is no predictable sequence with which these pathological haemodynamic states develop, making the management of septic shock particularly challenging.

In fact, shock is often present as a combination of the four "pure" types of shock illustrated in Fig. 7.6. That is where haemodynamic monitoring can be useful to gain further insights in the pathophysiological picture for each patient. It helps to determine the need for fluids (preload responsiveness), vasopressors (if peripheral vascular resistance is too low) or, quite rarely, inotropes (when contractility is the predominant problem).

The term haemodynamic instability is used either to indicate shock resistant to management with fluids and first line vasopressor, i.e. noradrenaline, or the state of going in and out of shock.

7.4 Haemodynamic Monitoring

Three clinical windows into the adequacy of perfusion:
- Capillary refill time reflects microcirculation (early peripheral shutdown).
- Urinary output reflects endocrine responses (fluid conservation).
- Consciousness reflects perfusion of the brain (affected late).

Clinical haemodynamic monitoring involves observing patients for symptoms and signs of shock. Initial signs are orthostatic hypotension, restlessness, or mild confusion. On physical examination, patient typically have tachycardia with or without hypotension, cold pale skin, anuria, and later mottled skin and coma. Heart rate monitoring (ECG), non-invasive blood pressure, and peripheral pulse oximetry are minimal requirements and often the only option available initially. It is vitally important to initiate the management of shock until further monitoring becomes available.

If the patient deteriorates or has ongoing shock or haemodynamic instability, invasive arterial monitoring is important. Central venous access is required if it becomes apparent that vasoconstrictors will be needed. Unless contraindicated, use the left internal jugular vein as the first option. The right internal jugular vein is best reserved for a renal replacement line which is commonly required in these patients. Central venous pressure is an unreliable parameter to monitor although high values are associated with conditions such as left ventricular failure and tension pneumothorax. Striving to insert invasive arterial and venous lines should not distract from ongoing clinical monitoring and resuscitation. In practice, these tasks are often performed simultaneously by different team members.

7.4.1 Lactate

Lactate is commonly used as a marker of overall organ perfusion. It is a by-product of anaerobic metabolism as mentioned above. It is an important target for resuscitation, especially in septic shock (see ▶ Chap. 11). Remember that there are other causes of a high lactate including concurrent administration of adrenaline or IV salbutamol, or liver failure, but during the initial assessment high lactate should be considered a sign of hypoperfusion unless proven otherwise.

7.4.2 Mixed and Central Venous Saturation, and PCO_2 Gap

The oxygen saturation of the blood in the pulmonary arteries (SvO_2) correlates with adequacy of overall organ perfusion. In a healthy circulation, the SvO_2 is around 75%. Since the decline in use of Pulmonary Artery Catheters (PACs), the SvO_2 is not readily available. Despite some evidence that there is a correlation between saturation of blood in the superior vena cava ($ScvO_2$) and SvO_2, neither of these values is routinely measured in critically ill patients. The reason is that an $ScvO_2$ below 65%–70% reflects inadequate oxygen delivery and the patient will likely benefit from measures aimed at the increasing it. However, normal or high $ScvO_2$ does not necessarily mean the opposite—this is because oxygenated blood may shunt at microcirculation level or there may be an oxygen extraction problem at cellular level, particularly in septic shock. At times when the $ScvO_2$ is normal, the difference between central venous and an arterial blood PCO_2 (PCO_2 gap) ≥0.8 kPa (6 mmHg) may better reflect potential benefit from measures to increase cardiac output and, hence, is incorporated in some algorithms for resuscitation of septic shock.

7.4.3 The Arterial Blood Pressure Waveform

To the trained eye, the shape of the arterial pressure waveform can say a lot about stroke volume, peripheral vascular resistance, and sometimes preload responsiveness. The physiology behind this is complex and learning pattern recognition needs time and exposure. Make sure that the arterial blood pressure monitoring system is working optimally and is correctly calibrated before drawing any conclusions.

Important facts worth remembering are:

- Systolic blood pressure determines LV afterload.
- Mean arterial pressure determines organ perfusion.
- Diastolic pressure determines coronary perfusion.
- Pulse pressure (systolic pressure-diastolic pressure) reflects.
  - Stroke volume (lower pulse pressure = lower stroke volume).
  - Peripheral vascular resistance and aortic stiffness which increases with age (higher pulse pressure = higher PVR or aortic stiffness).

    Clinically: a BP of 92/56 mmHg in an elderly lady is most likely due to very low stroke volume, a BP 110/38 in young patients with sharp spiky waves likely reflects maximum vasoconstriction.
- The cyclical (with breathing) fluctuation in arterial pressure, sometimes called "arterial swing", may reflect preload responsiveness (clinically interpreted as "under-filled" or hypovolaemic). However, this must be interpreted with caution as

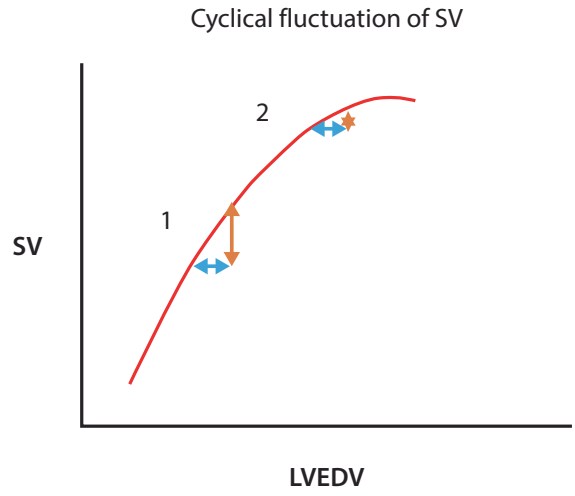


Fig. 7.7 The fluctuation of SV with the respiratory cycle is pronounced in situation 1 compared to situation 2. *SV* stroke volume; *LVEDV* left ventricular end diastolic volume

this phenomenon reflects complex heart–lung interactions. It occurs when the LVEDV is on the steep upslope of the Frank-Starling curve. Changes in intrathoracic pressures—because of breathing—lead to fluctuating volumes of blood delivered to the left ventricle at the end of diastole as shown in Fig. 7.7. The fluctuation in SV—Stroke Volume Variability (SVV)—can also be detected as a fluctuation in pulse pressure—Pulse Pressure Variability (PPV)—and in the invasive arterial blood pressure giving the classic "swing". An SVV or PPV of 15% may predict fluid responsiveness in patients with sinus rhythm and on fully controlled mechanical ventilation with minimal changes in intrathoracic pressures. However, arterial swing can also be caused by unusually high fluctuation in intrathoracic pressures, such as during ventilation of stiff lungs (ARDS) or a dilated and/or failing right ventricle, which limits filling of the ventricle in a constrained pericardial space ("interventricular interdependency").

Practical Tip

A large cyclical fluctuation or "arterial swing" does not always indicate fluid responsiveness and should not lead to you to automatically give a fluid challenge.

7.4.4 Point-of-Care Ultrasound

Basic critical care ultrasound is now a mandatory competence of an intensivist at the end of training. As a novice in ICU, you will not be expected to carry out ultrasound examination, unless you have been trained to do so, but it is important that you are aware of how it can help in the monitoring and management of patients with shock. Using point-of-care ultrasound (POCUS), we can diagnose left ventricular dilatation, left ventricular dysfunction, right ventricular dilatation and right ventric-

ular dysfunction, a hyperactive ventricle, severe hypovolaemia, and the presence of pericardial effusion. POCUS can therefore be carried out for patients with a complex haemodynamic picture to ascertain the type of shock. Specific protocols have been designed for this purpose (such as Rapid Ultrasound in Shock). It can also be used to monitor the response to ongoing management, for example, the effect of a fluid bolus or diuretic therapy.

There are now well-established training programmes and accreditation bodies in Europe and around the world. ESICM offers General Ultrasound in Intensive Care (GENIUS) training programme covering core competences and an advanced European Diploma in Echocardiography (EDEC).

7.4.5 Monitoring of Cardiac Output

Cardiac output is the volume of blood pumped out of the heart in one minute; normally about 70 mL/kg/min. It is not universally monitored in critically ill patients and is certainly never a priority in the management. Critical care practitioners tend to be on a spectrum from no to extreme enthusiasm for using them. Always follow local practice.

The thrust of the argument for using CO monitors is that they give a clearer picture and more data to incorporate when assessing the critically ill patient with shock. They allow the monitoring of parameters to guide fluid therapy. In other words, to use the Frank-Starling curve to administer intravenous (IV) fluids in boluses (200–250 mL over 5–15 min) until the SV no longer increases with fluid administration. Alternatively, proponents of CO monitors use parameters like stroke volume variation (SVV) or pulse pressure variation (PPV) that quantify the cyclical fluctuation or "swing" in the arterial pressure. These are sometimes referred to as dynamic indicators of preload responsiveness, ◘ Fig. 7.7.

The arguments against using CO monitors are that most CO monitors are not accurate. Even if they were accurate, we simply do not know what the best CO is for any given patient. None of the large studies that compared a protocol-driven haemodynamic resuscitation strategy compared to standard care demonstrated a survival benefit. As mentioned above, the use of SVV or PVV has not been demonstrated to consistently predict fluid responsiveness in critically ill patients. The reasons for this are twofold. The first is that a significant majority of mechanically ventilated patients in ICU are not paralysed. The second is that lung compliance in critically ill patients is often poor. This results in large fluctuations of intrathoracic pressure which amplify the variability in cyclical blood volume delivery to the left ventricle at the end of diastole. In some critically ill patients, it is simply not possible to eliminate the arterial "swing" no matter how much fluid is given. In addition, even if PPV or SVV were accurate predictors of fluid responsiveness that allow us to push the LVEDV to the peak of the Frank-Starling curve, there is no evidence that this is the best point to target on that curve. All this tells us is that further fluid administration will lead to fluid overload, which intuitively, seems precarious. There is also emerging evidence that a high total fluid balance during ICU stay is associated with worse outcomes. There are ongoing studies on restrictive fluid resuscitation strategies vs. liberal ones.

For these reasons, a global marker of tissue perfusion, namely dynamic lactate levels, is used to monitor improvements in perfusion and to guide therapy.

Note
Have you noticed that the CO is around 70 mL/kg/min normally, which is the same value as the Minute Ventilation (volume of air breathed in one min), and that the ventilation/perfusion ration is about 1?

PACs are considered the gold standard in terms of accuracy in measuring CO. Because of the invasive nature of these catheters, possible complications, and the uncertainty described above regarding targets of treatment, the use of PACs has declined this century. They remain in use in complex haemodynamic situations or in research to validate less invasive alternatives.

Cardiac output monitors can be broadly grouped from most invasive to least invasive into:

1. CO monitors that use pulse contour analysis. Examples are Pulse Contour Cardiac Output (PiCCO)™, LiDCO™, and Vigileo™. These apply a Fourier analysis of the invasive arterial waveform and use nomograms of aortic diameter to calculate SV and CO. Some require calibration using, for example, cold saline in PICCO™ or Lithium in LiDCO™ to mitigate the drift in signal over time which leads to calculation errors. Some require an arterial signal from a central artery, for example, PICCO™ while a peripheral arterial signal can be used for LiDCO™ and Vigileo™. These monitors calculate parameters such SVV and PPV which are used in some ICUs.
2. Oesophageal Doppler Monitors. For example, CardioQ-ODM™. This monitor receives a doppler signal from blood flowing in the descending aorta by using a soft probe inserted in the oesophagus. An equation calculates the distance the blood travels through the aorta in one heartbeat. This is then multiplied by the surface area of the aorta that is estimated from nomograms. The result is the SV. Fluid therapy can also be guided by targeting the flow time which is corrected for heart rate (FTc). A short flow time indicates a limited time for the blood to flow. This can be either due to hypovolaemia or a high SVR. Incidentally, this phenomenon can also be seen on a traditional invasive arterial waveform where a narrow arterial wave indicates similar conditions.
3. Bioimpedance CO monitors. The higher the fluid content of the thoracic cavity the lower the impedance to a small electrical current that is delivered using leads similar to ECG leads. The fluctuation of thoracic cavity fluid content between systole and diastole can be detected by these monitors to calculate SV. These are the least invasive monitors using only leads on the chest wall.

7.5 Management of Shock

The appropriate management of shock or haemodynamic instability relies on a correct assessment of the type of shock and what is causing it. The aim is to restore the cardiovascular system to the balance described in ◘ Fig. 7.1. Your role as a new resident in ICU is to assess the patient (see ▶ Chap. 2 on initial assessment of critically ill patient), start life-saving management and call for senior help. The time to call help depends on many factors including the urgency of the situation, your experi-

ence, and the time it will take senior help to arrive. It is always good practice to have a clear understanding between you and your immediate supervisor regarding triggers for calling them and establish effective ways to reach them, for example, using a mobile phone.

Most patients presenting with altered mental status, hypotension, and/or mottled skin should be considered to have a time-critical emergency as this situation may escalate to a peri-arrest situation quickly. Stick with ABCDE—protect airways, give oxygen, secure at least 1 IV line and basic monitoring. In most situation, initiating a fluid bolus, for example, by giving 250–500 mL of balanced crystalloid is appropriate. Then perform your clinical evaluation, search for information, and think of the resources available to help you and what is the best environment for ongoing care. Critical care is a team effort, and there are usually other members of the multidisciplinary team to help you. Using the history, clinical examination, lab, and chart data as well as your A-E assessment you will start to formulate a list of differential diagnoses as to what the type of shock is and what is causing it.

7.6 Haemorrhage

If the cause of shock is haemorrhage (hypovolaemic shock), you should take immediate action to stop the haemorrhage as soon as possible. This immediate action can be one of two broad strategies:

1. You or a member of your team can stop the bleeding, for example, apply pressure on a bleeding wound. In this case, do this immediately, while you continue managing the patient.
2. You need a member of another specialty to stop the bleeding, for example, surgeon or an endoscopist if the patient suffers an upper to lower gastrointestinal haemorrhage. In this case, make an urgent referral while you continue managing the patient.

The key principle is that management of the shock without stopping the bleeding is futile.

Depending on the extent of haemorrhage and your local setting, you might have to activate the major haemorrhage protocol in your hospital to gain quick access to blood and blood products (see ► Chap. 14). In brief, you will need four large peripheral lines and/or a vascath and give warmed blood products to maintain systolic blood pressure at around 80 mmHg until bleeding is stopped. Prevent hypothermia by warming the patient, give 1 g of tranexamic acid and watch and replace ionised Ca^{2+}. Avoid the use of vasopressors in the very early stage unless *in extremis* or perintubation.

7.7 Fluid Therapy

Unless the patient has cardiogenic shock or is fluid overloaded, the management of shock usually starts with the administration of an IV fluid bolus (250 mL in 5–15 min) of a balanced crystalloid. To achieve this, IV access is clearly required. You

can administer fluid quicker using a larger peripheral cannula compared to a long narrow central venous catheter. An improvement in MAP indicates fluid responsiveness. Further fluid boluses should be given to achieve an MAP of >65 mmHg.

Typically, at least 30 mL/kg of crystalloid is recommended for patients with septic shock within the first 3 h, some argue that smaller boluses of 4ml/kg should be given and repeated as long s the patient is fluid response; both strategies are acceptable. As a novice in ICU, and depending on your previous experience, you should not administer more than 1–2 L of fluid to a patient who is haemodynamically unstable without discussing with your supervisor. If you are having to administer this fluid quickly, for example, within an hour, you should discuss with your supervisor as soon as possible.

The debate regarding targets of fluid therapy was discussed above. Follow international guidelines, for example, Surviving Sepsis, and the practice in your local ICU. Monitor the response to management by monitoring the patient clinically, measuring lactate (e.g. every 30–60 min) and urine output. If the kidney suffers an AKI, urine output will cease to be a reliable or useful measure of successful fluid resuscitation. This can be a difficult judgement to make for a novice.

In case of rapid deterioration or profound hypotension, for example, septic shock or anaphylaxis, it might become apparent that vasopressors are required sooner rather than later to achieve the balance described in Fig. 7.1. This occurs either when there is no response to a fluid bolus or when the MAP or CO response to an IV fluid bolus is short lived and a further IV fluid bolus is required as soon as the previous one finishes.

As a novice, starting a patient on a vasopressor can be a difficult decision to make. Try to discuss it with your supervisor if circumstances permit. Do not delay this decision and persist with further fluid boluses knowing that vasopressors are required.

7.8 Vasopressors and Inotropes

Noradrenaline (norepinephrine) is by far the commonest vasopressor in use for patients with shock. It is a potent vasoconstrictor that works on the α receptors in the peripheral circulation, Fig. 7.5, to counteract the vasodilation that occurs with many types of shock. Pharmacology textbooks underplay the β adrenergic effects on the heart that noradrenaline exhibits clinically.

Vasodilation or vasoplegia (loss of vessel tone) is very common in critically ill patients. Almost all types of shock, especially if prolonged, can trigger a systemic immune response similar to sepsis. This leads to widespread endothelial and glycocalyx damage which results in vasoplegia. For example, a patient who suffers hypovolaemic shock due to massive haemorrhage can be managed by stopping the haemorrhage and restoring blood volume with blood, blood products, and fluid. However, the systemic immune response that might follow causes shock similar to septic shock. In addition, sedatives and analgesics cause vasoplegia and hypotension which is managed with noradrenaline.

Adrenaline (epinephrine) is given as a bolus in cases of cardiac arrest and extreme haemodynamic instability. Noradrenaline is not normally administered in this way. IV boluses of adrenaline can either be large, for example, 1 mg in the case of cardiac arrest or can be titrated in smaller doses, for example, 50–100 micrograms for extreme

haemodynamic instability. Titrating adrenaline in this manner requires experience and caution as the response might be extreme tachycardia and/or hypertension. For this reason, titrating adrenaline in this manner should only be carried out by an experienced practitioner or under the instructions of an experienced practitioner.

Adrenaline is the inotrope of choice to treat anaphylaxis but is also used in critically ill patients with other types of shock either to augment the pressor effect of noradrenaline or to add a positive inotropic effect. One of the side effects of adrenaline is that it increases lactate production which leads to hyperlactataemia. This needs to be considered when using plasma lactate to monitor the effectiveness of shock management.

Vasoplegia, especially in septic shock, that is unresponsive to noradrenaline can be treated using vasopressin which is a potent peripheral vasoconstrictor. You will rarely be expected to start vasopressin without discussing with your supervisor.

Hydrocortisone 50 mg four times a day is also widely used in sepsis-induced vasoplegia unresponsive to noradrenaline despite lack of evidence of its effect on outcome. Corticosteroids sensitise the α adrenergic receptors on the vessels making them more responsive to noradrenaline and adrenaline.

Dobutamine is a β adrenergic receptor agonist. It is used clinically for patients in cardiogenic shock to mitigate peripheral vasoconstriction and reduce afterload. In this situation, its positive inotropic effects are usually minimal. GTN (which is neither a vasopressor nor an inotrope) can also be used to achieve this vasodilatory effect.

As previously mentioned, some patients with septic shock can have a state of low CO or relatively low CO (normal CO but not enough to meet the cells' demands). In this situation, some practitioners use dobutamine as an inotropic agent not as a vasodilator. Here dobutamine should only be started once the patient is established on noradrenaline. Otherwise, the vasodilatory effect of dobutamine can lead to profound hypotension. This practice was more common in the early 2000s and is less common now.

All vasopressors and inotropes are administered via a central venous catheter. Using them peripherally can lead to intense venoconstriction and subsequent extravasation with resultant devastating tissue necrosis.

When vasopressors or inotropes are started, they can take a few minutes until they reach the tip of the central catheter lumen and into the circulation. If you want to reduce this time, increase the infusion rate slightly. Never give a bolus to purge the line.

Safety Tip!

- Never give a bolus of a vasopressor/inotrope infusion to purge the central line.
- Never run other drugs through the same line is vasopressors/inotropes, especially ones that might be given as a bolus.

Vasopressors and inotropes are diluted in a crystalloid. Check the standard concentration used in your ICU. It might differ from the concentration used in the operating theatre or in other ICUs you might have worked in. Watch out for this when admitting a patient transferred from the operating theatres or another facility.

Practical Points in the Management of Shock

- Call for senior help.
- Work with your team.
- Assess the patient using all sources of data available.
- Identify the type of shock.
- If the patient is bleeding, stop the bleed as a matter of priority.
- Establish IV access and give a fluid bolus unless the patient is in cardiogenic shock or is fluid overloaded.
- Use vasopressors or inotropes to achieve targets agreed with supervisor
- If you are using a CO monitor, be aware of its limitations.
- Monitor effectiveness of management by clinical assessment and measuring serum lactate and urine output.

There is no recommended dose for vasopressors and inotropes (other than in cardiac arrest). They are titrated to achieve certain haemodynamic targets; typically to achieve a certain MAP which is usually >65 mmHg. In some patients, for example, in septic shock, this target might not be achievable, and a lower MAP is targeted. This is done in discussion with the intensivist in charge of care or a senior clinician.

Take Home Messages

- CO, MAP, and SVR are physiologically regulated to achieve an optimum MAP and CO for cells, tissues, and organ perfusion.
- Disruption of this regulation leads to the four main types of shock.
- Shock is a life-threatening emergency—call for help and work with your team.
- Diagnose the type of shock using data from your clinical assessment, lab data, and monitors available to you.
- Follow international guidelines and local policy to manage shock and haemodynamic instability.
- Monitor the response to management by assessing organ perfusion and measuring serum lactate.

Further Readings

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4. Link to GENIUS and EDEC courses.

Disorders of Consciousness

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Contents

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Intensive Care Fundamentals Intended Learning Outcomes (ILOs)

This chapter will help you achieve the following Intended Learning Outcomes (ILOs):

1. Describe the pathophysiology of intracranial hypertension and its operative and non-operative management.
2. Describe a treatment plan for patients with various neurological injuries (TBI and stroke).
3. Plan neuroprotective strategies following cardiac arrest in a simulated patient or case.
4. Discuss the immediate actions needed when the patient is showing signs of coning.
5. Explain the meaning of neuroprotective measures in patients with brain injury.
6. Discuss the initial management of seizures and status epilepticus.
7. Describe the principles of post-resuscitation care and prognostic assessment post-CPR.

8.1 Introduction

Neurological Critical Care is a specialist area, but critically ill patients with neurological conditions frequently present to non-specialist centres and are often initially treated by general intensivists, sometimes before the underlying diagnosis is confirmed.

We will discuss the initial stabilisation of a patient with reduced conscious level and suggest a pragmatic approach to initial investigation of the underlying cause. After reviewing the causes, consequences, and management of raised intracranial pressure, we will discuss the importance of neuroprotective measures in preventing secondary brain injury.

We will then discuss the most important aspects treating specific conditions commonly encountered in a Neuro-Critical Care Unit. If you work in a specialist unit, you will have access to excellent local guidelines and to immediate specialist advice. However, working through this chapter will help you in your approach to these patients until more experienced help arrives. If you work in a general Critical Care Unit and are involved in stabilising patients prior to transfer to specialist centres, understanding the concepts of neuroprotective measures and management of raised intracranial pressure will be equally important [1].

8.2 Approach to the Comatose Patient: Initial Resuscitation and Investigations

Patients with reduced conscious level are frequently referred to Critical Care, and the underlying cause may not be immediately apparent. While many of the resuscitative and supportive measures will apply to most of these patients, some underlying pathologies require specific and often urgent targeted treatment, and it is important that you identify these early.

Disorders of consciousness may be caused by pathology of the brain and meninges, or by systemic problems affecting the brain, such as shock or hypotension, hypoxaemia, intoxication, or metabolic disturbances including hypoglycaemia or hypercapnia. Primary brain problems can be structural, such as trauma, stroke, or intracranial bleeds, or can be caused by infection of the central nervous system or by seizures or status epilepticus.

Your priority is to look for and treat the potential causes of coma and the life-threatening consequences of it, and to prevent secondary brain injury. Use an ABCDEF approach (see page 3) and consider the effects of coma on airway patency and airway protection. Measure blood glucose early in all patients with disordered consciousness.

Tip

Always check blood glucose in a patient with altered consciousness. Identifying hypoglycaemia as the cause of coma after a CT scan risks harm to the patient as well as an unnecessary scan!

Intubating early is usually the safest course of action, particularly of the underlying pathology and expected clinical course are unclear or before transferring the patient for CT scanning or to a different unit or hospital. This will prevent episodes of hypoxaemia, hyper- or hypocapnia and avoid aspiration of gastric contents. The downside is that following induction of anaesthesia to facilitate intubation you can no longer assess neurological status easily, and you should carefully examine the patient and document your clinical findings prior to intubation.

- **Focused Neurological Examination of a Patient with Altered Consciousness**
  - **Glasgow coma scale:** Commonly used to describe conscious level after traumatic brain injury but is useful in other causes of impaired consciousness too, particularly to track and document changes. Observe eye opening, speech, and movement of the right and left side in response to a verbal (spoken or shouted request) or painful stimulus (pressure on nailbed, trapezius muscle, or supra-orbital notch).

Behaviour	Response	Score
Eye opening	*spontaneously*	*4*
	to command or speech/sound	*3*
	to pain or pressure	*2*
	none	*1*
Verbal response	*orientated*	*5*
	confused answers	*4*
	inappropriate or incoherent words	*3*
	sounds/incomprehensible speech	*2*
	none	*1*
Motor response	*obeys commands (e.g. squeezes hand / sticks out tongue)*	*6*
	localises to pain	*5*
	normal flexion	*4*
	abnormal flexion	*3*
	extension	*2*
	none	*1*

- **Examine pupils** for size, symmetry, and reactivity to light.
- **Meningism** is resistance to neck flexion due to muscle spasm caused by meningeal irritation. If present, consider starting antibiotics for suspected bacterial meningitis urgently and before investigations are complete, particularly in febrile patients. Meningism can also occur in subarachnoid haemorrhage, where blood causes irritation and inflammation of the meninges and motor nerve roots.
- Assess the **respiratory pattern** in unconscious patients.
- **Focal or lateralising signs**: Look for asymmetry of movement and in unconscious patients, assess muscle tone and check for deviation of the eyes. Asymmetry or focal deficits suggest a structural cause, and imaging should be performed as soon as safely possible. If the CT brain is normal but lateralising signs are present, consider an urgent CT angiogram to look for stroke.

Take care to avoid periods of hypotension at any stage during intubation, stabilisation, and transfer, as this can cause secondary brain injury. Insert an arterial line early for continuous invasive blood pressure monitoring, give fluid boluses if required, and consider early central access and vasopressor support. Perform arterial blood gas analysis early, in addition to routine laboratory testing, to identify hypoglycaemia and other metabolic disturbances that may cause or contribute to coma, and to ensure adequate oxygenation and normocapnia. Appropriate specific initial ventilatory and blood pressure targets are considered as part of general neuroprotective measures below, but in general you should aim for a mean arterial blood pressure of at least 80 mmHg, ensure adequate fluid resuscitation, aim for normocapnia and a paO_2 of 9–10 kPa.

The history may give a clear indication of the likely underlying cause, but brain imaging is usually required. If there is any concern of a structural brain abnormality that might be amenable to surgical treatment, such as in our case vignette at the start of this chapter, then you should arrange a CT scan as soon as possible. Minimise any delays to imaging and surgical intervention. Sometimes, additional tests will be required if the cause of the coma remains uncertain. Consider a lumbar puncture and CSF analysis if CNS infection is a possibility and ask whether additional imaging such as CT angiography could help, especially if there is a suspicion of a vascular occlusion or injury. In the initial phase of stabilisation, you should prioritise tests that identify specific treatment targets. More specialist investigations such as MRI scanning or EEG can often be deferred until the patient has been stabilised and transferred to a Neuro-Critical Care unit.

8.3 Pathophysiology of Raised Intracranial Pressure (ICP)

Many types of acute brain injury lead to raised ICP, which in turn causes reduced blood flow to the brain and can cause brain shift (herniation) and compression of brain tissue. It is associated with poor neurological outcomes and increased mortality.

Intracranial pressure is determined by the combined volume of the components within the fixed container of the skull: brain tissue, blood, and cerebrospinal fluid (CSF). It is usually less than approximately 10–20 mmHg but can spike due to coughing or straining in health, without causing injury. Pathologically elevated ICP can be caused by intracranial bleeding or abscesses, brain swelling due to injured brain tissue, accumulation of CSF in obstructive hydrocephalus or reduced outflow of blood, such as in cerebral venous sinus thrombosis (Fig. 8.1).

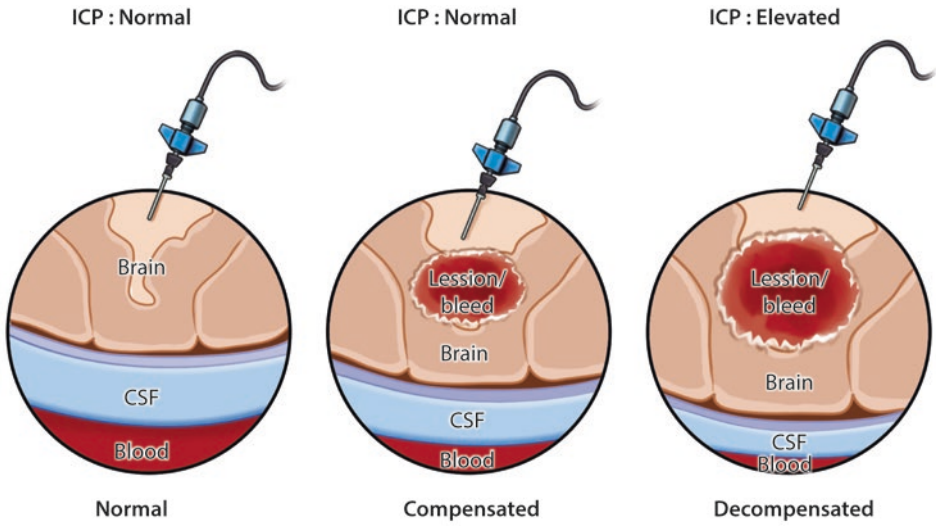

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Fig. 8.1 Brain compartments and ICP/Monroe—Kellie doctrine

Small increases in intracranial volume can be compensated for by displacement of CSF or displacement of blood from the venous sinuses. If the pathology progresses and the increase in volume exceeds compensatory capacity, ICP increases exponentially and can rapidly lead to inadequate brain perfusion and ischaemia, as well as causing herniation (Fig. 8.2).

Brain shift or herniation occurs when a large pressure gradient squeezes brain tissue across fixed, bony structures. This may be tentorial herniation, when part of the cerebrum, usually the uncus of the temporal lobe, is forced across the tentorium downwards, compressing the midbrain. Clinically, this can manifest as pupillary dilatation due to compression of the third cranial nerve. Tonsillar herniation—often referred to as 'coning'—is the movement of the cerebellar tonsils downwards through the foramen magnum. This causes compression of the medulla and results in brainstem dysfunction including the typical description of 'Cushing's reflex', a combination of hypertension, bradycardia, and abnormal respiratory pattern.

Both tentorial and tonsillar herniation are emergencies. Without rapid treatment and reduction of the critically elevated ICP, herniation can result in irreversible brain damage and death (Fig. 8.3).

Blood supply to the brain depends on the pressure gradient between the mean arterial pressure and ICP: cerebral perfusion pressure (MAP—ICP). Normally, cerebral blood flow is relatively constant even when cerebral perfusion pressure (CPP) changes. This is because autoregulation leads to vasoconstriction in response to an

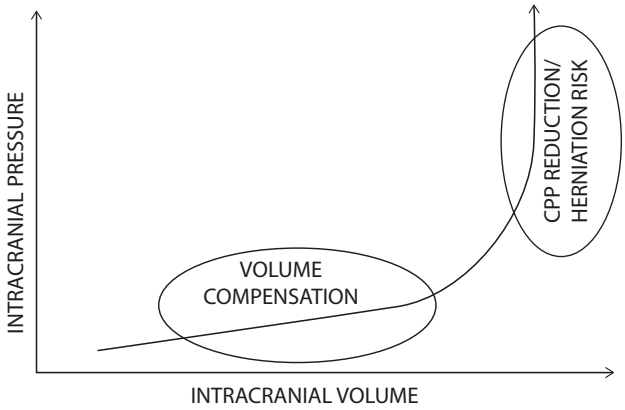

Fig. 8.2 Intracranial pressure/volume relationship

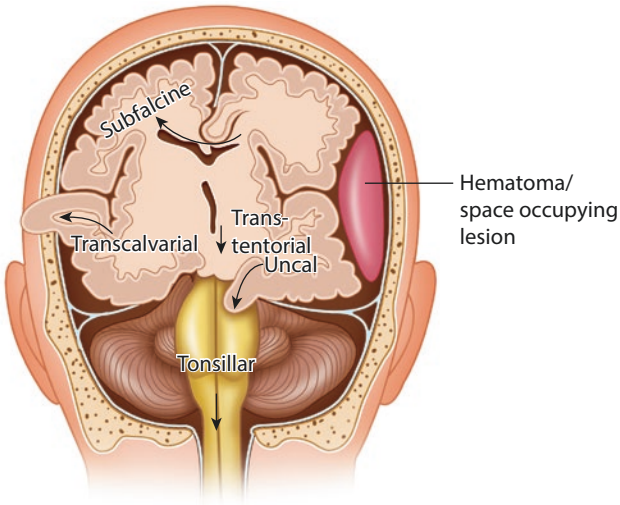

Fig. 8.3 Types of herniation

increased CPP in order to prevent hyperaemia, and vasodilatation occurs if the CPP is low so as to prevent ischaemia. Autoregulation is usually maintained at a range of CPP between approximately 60 and 160 mmHg. Below this level of CPP, brain perfusion will fall precipitously (Fig. 8.4).

Autoregulation is often impaired in acute brain injury, and when it is completely lost, ICP will follow CPP in a linear fashion as cerebral blood volume increases with higher arterial blood pressures. Several systemic factors also affect cerebral blood flow, most notably arterial CO_2 tension. Hypercapnia such as due to periods of hypoventilation or airway obstruction causes cerebral vasodilatation and increased cerebral blood flow, blood volume, and ICP. Conversely, hypocapnia causes cerebral vasoconstriction and reduces blood flow and ICP and blood flow.

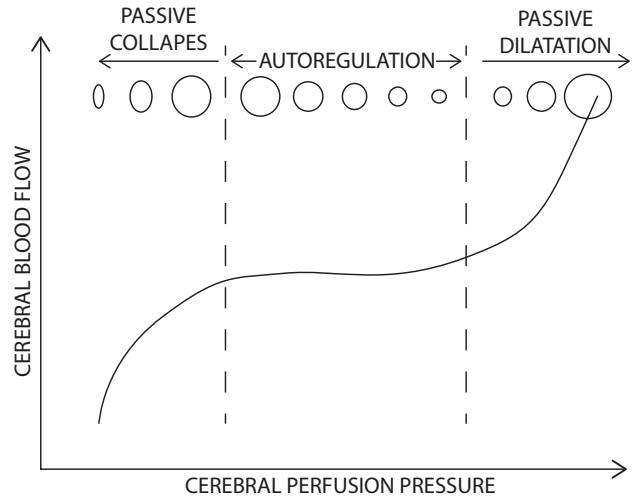

Fig. 8.4 Cerebral autoregulation

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8.4 Treatment of Raised ICP

Clinical signs of brain herniation such as pupillary dilatation in a comatose brain-injured patient require immediate treatment to lower the ICP and avoid irreversible brain damage.

'Medical' or non-operative management may be part of a strategy to control ICP until brain swelling resolves over time, or it can buy time to arrange urgent surgical treatment of raised ICP. This may be evacuation of a haematoma, decompressive craniectomy, or surgical CSF drainage if there is hydrocephalus (Fig. 8.5).

Initial non-operative treatments of critically elevated ICP are summarised below. Your aim is to reduce ICP and optimise brain perfusion while surgical options and a definitive management plan are considered. Seek expert help immediately.

Management of Critically Elevated ICP/'Coning'

- **Intubate** if not already done to protect airway and maintain oxygenation and normocapnia.
- **Elevate head** of bed to 30° to improve venous drainage and reduce ICP.
- **Deepen sedation and add/optimise neuromuscular blockade** as well as analgesia, to reduce cerebral metabolic demand and avoid coughing and straining.
- **Elevate MAP to at least 80 mmHg** to ensure adequate cerebral perfusion pressure—use isotonic fluid boluses and vasopressors, e.g. Noradrenaline.
- **A brief period of hyperventilation** will reduce cerebral blood flow through vasoconstriction and thus reduce ICP. This can be helpful if brainstem herniation is imminent but can cause prolonged reduction in cerebral blood flow.

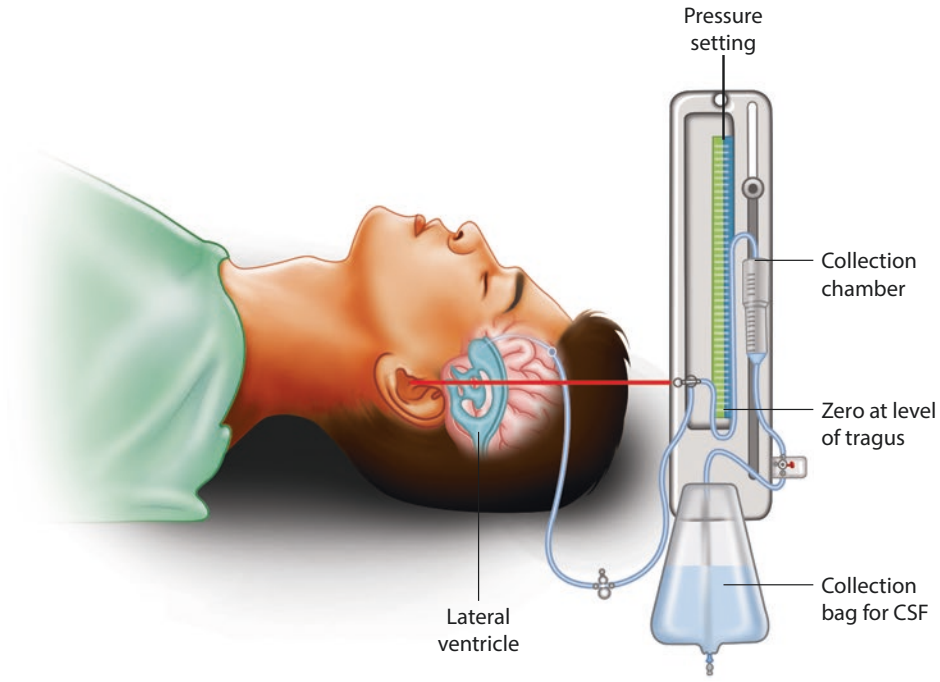


Fig. 8.5 External Ventricular Drain (EVD) for CSF drainage

- **Osmotherapy** reduces brain swelling by drawing water from the brain tissue into the vascular space along an osmotic gradient (depending on local protocols, give, e.g. 125 mL of 5% Sodium Chloride solution via central venous catheter, or 250 mL of 20% Mannitol intravenously).
- **Consider repeat CT imaging and neurosurgical opinion**: Always consider whether surgery or CSF drainage could help.

8.5 Secondary Brain Injury and Neuroprotective Measures

The injured brain frequently suffers secondary damage that happens over time to neurons unharmed by the initial insult. This is partly driven by an inflammatory response to the initial injury but is also caused by complications that reduce adequate brain oxygenation after the initial insult. Secondary brain injury is therefore at least partly preventable, and while the damage caused by the initial pathology—be this trauma, infarction, or a bleed—cannot be reversed, reducing secondary brain injury can improve functional outcomes.

The mechanisms of avoidable secondary brain injury are hypotension, hypoxaemia, anaemia, and elevated ICP, which reduce cerebral perfusion. All of these result in failure to deliver enough oxygen to the brain. Additionally, seizures and pyrexia can increase the metabolic and oxygen demand of brain tissue. Neuroprotective measures aim to prevent these mechanisms of secondary injury and apply to brain injuries of any aetiology although targets can be individualised if needed.

Oxygenation

Guidelines vary but it is sensible to aim for paO_2 > 10 kPa.

Anaemia

If brain oxygenation is impaired or ICP significantly elevated, aim for haemoglobin >90 g/L.

CO_2 Control

Avoid hypercapnia due to the associated rise in ICP. Generally, aim for low normocapnia to reduce ICP, but avoid hypocapnia in SAH to minimise risk of vasospasm.

Blood Pressure Control

Avoid hypotension and generally aim for MAP >80 mmHg. Ensure adequate fluid resuscitation, use vasopressors but diagnose potential causes of shock: consider bleeding particularly in context of trauma, consider sepsis and think of myocardial dysfunction in SAH. Avoid hypertension (aim systolic blood pressure <180 mmHg or <140 mmHg if significant risk of re-bleeding such as after SAH).

Sedation

If you think the ICP is elevated, aim for deep sedation to reduce metabolic demand of the brain. Don't forget analgesia and consider neuromuscular blockade if ICP is critically elevated.

Seizure Control

Treat any observed seizures with anticonvulsants in addition to sedation. Seizure prophylaxis is not routinely recommended.

Temperature Control

Treat hyperthermia with antipyretics and active cooling measures. Diagnose and treat infections, but remember fever is often due to the brain injury itself.

Glycaemic Control

Avoid hyper- and hypoglycaemia: use your local protocol.

General Supportive Measures

Pay attention to evidence-based general Critical Care. Prevent ventilator-associated pneumonia and pressure sores, use enteral nutrition, prevent stress ulceration and venous thrombo-embolism.

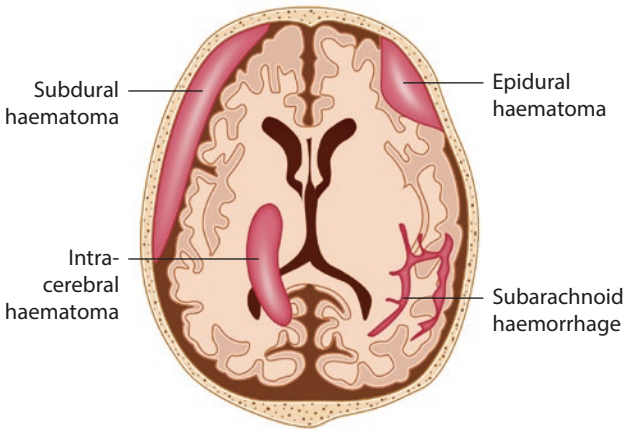
8.6 Specific Conditions in Neuro-Critical Care

8.6.1 Traumatic Brain Injury (TBI)

Head injuries are a common cause of death and disability, are often caused by road traffic accidents, and frequently present to non-specialist centres. TBI is commonly classified as mild, moderate, and severe based on the GCS (13–15, 8–13, and <8, respectively). Outcomes for patients with coma due to head trauma are better in specialist centres even if no surgical intervention is required, but you may be involved in managing these patients prior to transfer. Remember that other parts of the body can be affected by the trauma too, making the management of these patients complex and dependent on multiple specialties working together as a team.

Initial stabilisation will follow the ABCDE approach. Look for trauma to other organs causing life-threatening bleeding and maintain stability of the cervical spine. Reduced conscious level is a sign of elevated ICP, particularly if it persists after initial resuscitation. Seek help and intubate early if the patient is agitated or does not obey commands. Arrange a CT scan—this is essential in order to identify any intracranial bleeding requiring emergency surgery (◘ Fig. 8.6).

Surgery is usually indicated if there is a sizeable extra- or subdural haematoma causing significant mass effect, but consultation with your local specialist centre is advised for any patient with significant or prolonged reduction in conscious level regardless of CT appearance. Avoid preventable secondary brain injury by paying attention to neuroprotective measures.



◘ **Fig. 8.6** Types of post-traumatic intracranial haematoma

TBI: Initial Management Goals

- Airway—protected (remember C spine precautions); intubate if in doubt.
- Oxygenation—paO_2 at least 10 kPa.
- CO_2 control—$paCO_2$ 4.5–5 kPa (hypercapnia will increase ICP).
- Blood pressure—avoid hypotension, aim MAP >80 mmHg; insert arterial line.
- Use isotonic crystalloid solution for fluid resuscitation (look for bleeding from occult trauma to other organs).
- If there are signs of brainstem herniation, elevate head, deepen sedation, give osmotherapy, and seek expert help immediately.
- Arrange urgent CT scan and discuss with specialist centre.

Management in specialist centres following transfer will involve insertion of an ICP bolt in order to provide targeted medical management of the ICP using the measures outlined above: sedation, analgesia, neuromuscular blockade, head elevation, and maintaining CPP above 60 mmHg. Osmotherapy is used when ICP rises despite this. Increasing the CPP above 60 mmHg may reduce cerebral blood volume enough to decrease ICP while maintaining safe oxygenation, assuming cerebral autoregulation is intact. A safe target is to keep ICP <20 mmHg, but this may need to be tailored to individual circumstances. If the ICP rises, repeat imaging is considered to ensure opportunities for surgical intervention or CSF drainage are not missed, such as in the event of a re-bleed or development of obstructive hydrocephalus.

If these measures fail, then rescue therapies are considered. These including barbiturate coma or secondary decompressive craniectomy, where part of the skull is removed, allowing the swollen brain to expand. Both are not without controversy and decompressive craniectomy in particular is associated with a high proportion of patients surviving with significant disability. While decompression is effective at preventing death from brain herniation, it does not undo the extensive damage that has led to the catastrophic and refractory brain swelling in the first place (Fig. 8.7).

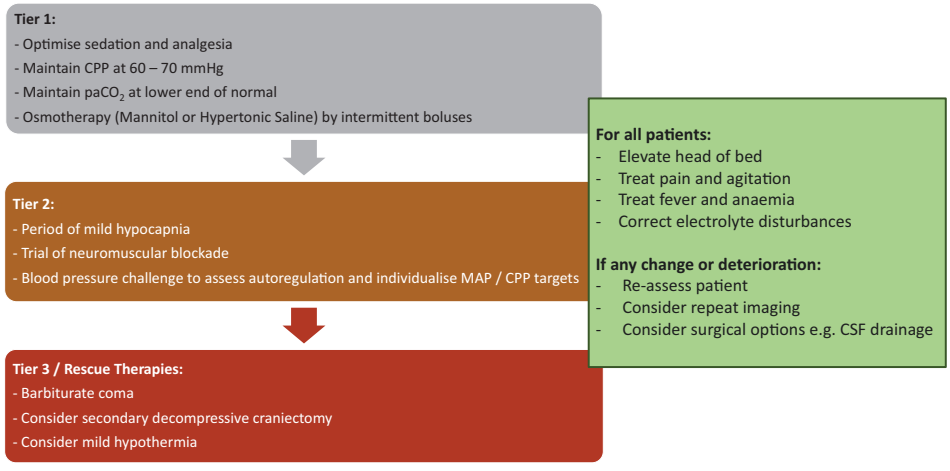


Fig. 8.7 Simplified tiers of ICP management in TBI

In the recovery phase, when the ICP is settling and no longer dependent on low $paCO_2$ and CPP, interventions can be gradually de-escalated, including stopping neuromuscular blockade and reducing sedation. Recovery can take a long time however and prognostication is often difficult in the early stages.

8.6.2 Subarachnoid Haemorrhage (SAH)

Subarachnoid haemorrhage is ► bleeding into the ► subarachnoid space, the area between the ► arachnoid membrane and the ► pia mater surrounding the ► brain. While this can be caused by trauma or occasionally happen spontaneously, the term SAH is often used for bleeding caused by cerebral aneurysms around the circle of Willis. The presenting symptoms can range from headache to coma.

SAH has a variable trajectory and patients often deteriorate in the days following the initial bleed, either because of a re-bleed, or because of sequelae of the initial bleed. The blood in the subarachnoid space causes inflammation and vasospasm, clinically apparent as 'delayed cerebral ischaemia' or DCI causing new focal neurological deficit or reduction in conscious level typically between 4 and 10 days after the bleed. If the bleed has extended into the ventricles, obstructive hydrocephalus can occur, but delayed non-obstructive hydrocephalus is also seen, caused by reduced absorption of CSF. Seizures are relatively common, and the physiological stress and catecholamine release after a large SAH can cause ECG changes, myocardial stunning, and neurogenic pulmonary oedema.

The early management follows the same approach as for all patients with altered conscious level. Arrange an early CT scan if SAH is suspected and remember that intubation prior to CT transfer is safer if the patient is agitated, has a poor motor response or if oxygenation or normocapnia cannot be maintained. Because of the requirement for blood pressure control, insert an arterial line. Speak to your specialist centre early if SAH is confirmed, as these patients are usually transferred early.

SAH: Initial Management Goals

- Airway—protected.
- Oxygenation—paO_2 at least 10 kPa.
- CO_2 control—$paCO_2$ 5–6 kPa (hypocapnia may increase risk of vasospasm).
- Blood pressure—avoid hypo- and hypertension, aim systolic 120–160 mmHg.
- Euvolaemia—use boluses of isotonic crystalloid solution.
- Commence Nimodipine 60 mg every 4 h enterally to reduce risk of vasospasm.
- Treat any persistent or recurrent seizures (prophylaxis not indicated).
- Defer pharmacological thromboprophylaxis until aneurysm is secured.
- Aim for early transfer to specialist centre to facilitate treatment of aneurysm.

The management of patients with SAH in specialist centres will involve securing of aneurysm, now usually performed by minimally invasive endovascular coiling unless craniotomy and clipping is required for technical reasons. Once the aneurysm is secured, the focus will be on prevention and management of complications. This includes blood pressure augmentation tailored to neurological response if there

are signs of DCI. Hydrocephalus is treated with external ventricular drains. Many patients with SAH require prolonged stays in Critical Care and the mortality overall is relatively high.

8.6.3 Stroke

Most stroke patients are managed on general wards or stroke units, but some benefit from Critical Care admission. Increasingly, invasive interventions are available for selected patients, often resulting in a period of more intensive monitoring in Critical Care.

The majority of strokes are ischaemic, caused by embolic or thrombotic occlusion of cerebral vessels. The focus of therapeutic interventions is to restore blood flow, and due to the short time window for preventing irreversible neurological deficit, early diagnosis, and imaging are key in any patient presenting with sudden onset neurological deficit consistent with a stroke. CT imaging is most widely used, and while a proportion of patients with ischaemic stroke will not have CT changes if scanned early, CT will help exclude important differential diagnoses such as intracerebral bleeds. CT angiography can add useful information about the nature of vascular occlusion and help determine whether it is amenable to invasive treatments.

Depending on the setup in your local area, you may have access to endovascular thrombectomy, where occlusive thrombus is retrieved with an intra-arterial catheter, usually inserted through the femoral artery under local anaesthesia. Only a small proportion of patients with ischaemic stroke benefit from thrombectomy, and only within a strict time window. Local protocols and pathways will determine which patients are eligible. Intravenous, systemic thrombolysis does not rely on specialist services and improves functional outcomes in selected patients if it is administered early enough, usually within 4.5–6 h of symptom onset.

Patients are sometimes admitted to Critical Care Units after thrombolysis, to monitor for complications such as intracerebral and gastrointestinal bleeding and for blood pressure control. Similarly, patients who have undergone thrombectomy are usually initially managed in a Critical Care environment.

Occasionally, patients develop severe brain swelling and raised ICP after ischaemic stroke involving the middle cerebral artery causing large hemispheric infarction. These patients develop features of progressive ICP rise in the days after their stroke: headache and vomiting followed by coma and signs of brainstem herniation. The mortality is high, but in selected patients, decompressive hemicraniectomy may be appropriate. It prevents herniation and death although it does not undo the neurological deficit caused by the large stroke. Younger patients at risk of this 'malignant middle cerebral artery syndrome' are sometimes monitored in a Critical Care in order to detect neurological deterioration early (Fig. 8.8).

Haemorrhagic stroke is caused by extravasation of blood into the brain tissue, frequently in the basal ganglia, and is associated with hypertension. It also presents with sudden onset neurological deficit but unlike ischaemic stroke, signs of increased ICP including headache, vomiting, and coma are common. The benefit from neurosurgical intervention such as clot evacuation is uncertain, but selected patients may be considered for this, and others may benefit from insertion of an external ventricular drain if the mass effect of the intraventricular haemorrhage or blood within the ventricles causes hydrocephalus.

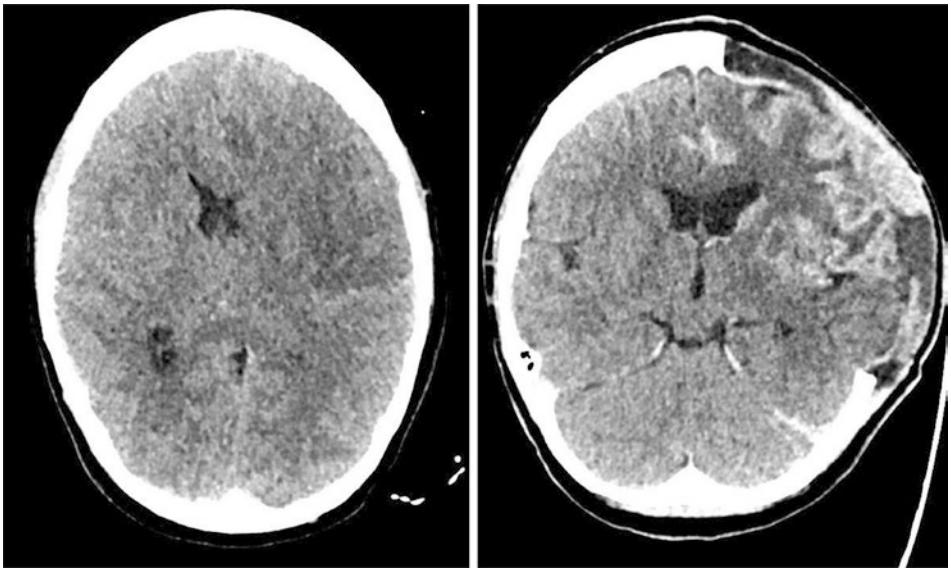


Fig. 8.8 Malignant Middle Cerebral Artery Syndrome (before and after hemicraniectomy)

Approach a patient presenting with a stroke using the ABCDE approach. Some patients will present comatose, particularly in the presence of large haemorrhagic strokes, and require intubation to protect their airway, and allow safe CT scanning. Many patients are hypertensive following a stroke, and you should treat this if the systolic pressure is above 180 mmHg to prevent re-bleeding or haemorrhagic transformation of ischaemic strokes. Sometimes, even tighter control is recommended for haemorrhagic stroke—seek specialist advice.

Some patients are frail or have devastating strokes, and careful consideration should be given to whether intensive, burdensome treatment in Intensive Care is likely to be of benefit and consistent with their wishes.

Immediate Management of a Patient with a Suspected Stroke

ABCDE assessment—protect airway if required

Intravenous access, routine bloods, and check glucose

Urgent CT scan (CT angiography often helpful!)

In acute ischaemic stroke:

- Check whether thrombectomy or thrombolysis are indicated.
- Commence antiplatelet therapy (Aspirin 300 mg—rectally if unsafe swallow).
- Keep systolic blood pressure below 180 mmHg.

In haemorrhagic stroke:

- Seek expert help/consult neurosurgical team.
- Watch for signs of raised ICP—if present, intubate and commence neuroprotective measures.
- Reverse coagulopathy if present.
- Keep systolic blood pressure below 140–180 mmHg—seek advice.

8.6.4 Seizures and Status Epilepticus (SE)

Seizures are transient episodes of altered behaviour or conscious level caused by abnormal neuronal activity. Generalised seizures usually result in loss of consciousness, and if a seizure persists for more than 5 min or if consciousness is not regained in between recurrent seizures, this is called status epilepticus. It is a medical emergency not only because it can cause airway obstruction, hypoxaemia, and aspiration, but because untreated prolonged seizure activity results in sympathetic activation and massively increased metabolic demand and ultimately severe acidosis, hypoglycaemia, and multi-organ failure, as well as raised ICP and neuronal damage. Common causes include medication withdrawal or intercurrent infection in those with underlying epilepsy, and TBI, stroke, meningitis, and encephalitis as well as toxic and metabolic disturbances in others.

When treating a patient in status epilepticus, use simple manoeuvres to maintain airway patency and give supplementary oxygen while attempts are made to stop the seizure activity. Ensure you look for and treat hypoglycaemia. Use a bolus of a benzodiazepine such as Lorazepam or Diazepam as first-line treatment, and repeat this after a few minutes if there is no effect. If the status persists, commence an intravenous infusion of either Phenytoin or Levetiracetam depending on local protocols.

Status epilepticus which persists despite two doses of an appropriate benzodiazepine and a first-line intravenous anticonvulsant is usually classed as ‘refractory’. The next step now is intubation. It is highly unlikely that additional non-sedating anticonvulsants alone will interrupt seizure activity at this stage. Seek help and use induction agents such as Propofol or Thiopentone, which are powerful anticonvulsants. Add an additional anticonvulsant agent such as Phenytoin, Levetiracetam, or Sodium Valproate, and consider using an infusion of Midazolam in addition to Propofol for ongoing sedation. If there is still evidence of seizure activity after 24 h of ventilation and intravenous sedation, or if the patient fails to wake during a sedation hold, EEG monitoring will become essential and care is best provided in a specialist centre. The term ‘super refractory status epilepticus’ is used to describe status that persists despite anticonvulsant therapy, intubation, and use of iv anaesthetic agents for at least 24 h.

The treatment of super-refractory SE in specialist centres involves use of high-dose sedative agents such as Midazolam, Ketamine, or Thiopentone to achieve ‘burst suppression’ on a beside EEG monitor, i.e. marked suppression of cerebral activity. This can interrupt seizure activity, but usually additional anticonvulsant agents and occasionally more than one period of ‘burst suppression’ are required.

Step-Wise Approach to Pharmacological Management of Status Epilepticus (Consult Local Protocols)

Stage 1—Early status epilepticus

- Diazepam emulsion 2 mg increments i.v. up to 10 mg over 5 min.
- Alternative: Lorazepam 4 mg i.v.
- Repeat above once if required.

Stage 2—Established status epilepticus

- Load with Phenytoin (e.g. 20 mg/kg iv) followed by maintenance dosing.
- Alternative: Levetiracetam (e.g. 60 mg/kg, max dose 4500 mg) followed by maintenance dosing.

Stage 3—Refractory status epilepticus

Induce general anaesthesia, intubate and ventilate. Consider using Propofol or Thiopentone as induction agents, followed by continuous infusions:

- Propofol infusion of up to 4 mg/kg/h.
- If using additional Midazolam: Loading dose followed by infusion 0.05–0.4 mg/kg/h.
- Consider adding Phenytoin and/or Levetiracetam (if not already used) and Sodium Valproate.

Stage 4—Super-refractory status epilepticus

Requires specialist treatment and continuous EEG monitoring. Involves periods of very deep sedation with, for example, Midazolam, Ketamine, or Thiopentone titrated to 'burst suppression' pattern on EEG.

Following the initial stabilisation, start thinking about underlying cause of the status epilepticus. Arrange a CT scan of the brain in the first instance and consider a lumbar puncture for CSF analysis if no structural abnormality has been found. Routine laboratory tests and microbiology samples should be sent to look for infection. If no obvious cause is identified or if the patient fails to respond to treatment, seek specialist advice. Further tests can be carried out in specialist centres, including MRI scanning and more detailed CSF analysis and immunology, to look for rare causes, such as auto-immune encephalitis.

The prognosis of status epilepticus depends on the cause, and patients with structural brain abnormalities often do worse. The longer the status persists the poorer the outcome, reflecting a more aggressive underlying process. In addition, intensive specialist management of SE is burdensome and brings with it the complications of prolonged deep sedation and organ support, and older patients with comorbidities are at much higher risk of harm.

8.6.5 Central Nervous System Infection

Patients with infective meningitis or encephalitis can be referred to ITU due to reduced conscious level, features of sepsis or with complications such as seizures. CNS infection is often diagnosed late, and treatment delay can lead to increased mortality and complications, so a high index of suspicion is essential. Always ask yourself whether you could be missing CNS infection when assessing a patient with altered neurology or with infection of uncertain source.

Meningitis is inflammation of the meninges, the protective layers surrounding the brain and spinal cord. It is often caused by either bacterial or viral pathogens although viral meningitis tends to be milder and self-limiting. Typical clinical features

include headache, neck stiffness, fever, and altered mental state, but presentation can be variable and rapid deterioration is common in bacterial meningitis. Encephalitis is inflammation of the brain tissue, most commonly caused by viral infection. The presentation tends to be subacute with confusion and headache, sometimes fever and later focal neurological deficit and seizures (◘ Fig. 8.9).

Confirm the diagnosis with CSF analysis, but arrange a CT scan before performing a lumbar puncture if the patient has focal neurological signs, seizures, or a reduced conscious level. This is in case a brain abscess or significant brain swelling is present, which could result in herniation after lumbar puncture. Measure the opening pressure if it is safe to proceed to LP, and send the CSF for microscopy and cell count, bacterial culture, viral PCRs, and biochemistry. Unless lumbar puncture can be performed immediately, start empirical treatment (see ◘ Table 8.1 for common organisms, examples of empirical antimicrobial choice and adjunctive steroid

	Opening Pressure	Cell Count	Protein	Glucose
Bacterial	↑	↑ (Polymorphs)	↑	↓
Viral	↑ or normal	↑ (Lymphocytes)	↑ or normal	Normal
Fungal or Tuberculous	↑	↑ (Lymphocytes)	↑	↓

◘ **Fig. 8.9** CSF findings in meningitis and encephalitis

◘ **Table 8.1** Empirical treatment for suspected CNS infection (use local guidelines, and remember to clarify travel history)

	Meningitis	Encephalitis
Common organisms (consider opportunistic infection in immunocompromised patients)	*Neisseria meningitidis* *Streptococcus pneumoniae* *Haemophilus influenzae* *Staphylococcus aureus* (common post neurosurgery) *Listeria monocytogenes* (commoner in elderly and young children)	Herpes simplex virus Varicella zoster virus Enteroviruses
Example of empirical antimicrobial regimen	Cephalosporin, e.g. Ceftriaxone 2 g iv 12 hourly Add Amoxicillin 2 g iv 4 hourly in elderly/if Listeria is suspected Add Vancomycin if Penicillin-resistant pneumococcus occurs locally or if relevant travel	Aciclovir 10 mg/kg iv 8 hourly
Adjunctive steroid therapy	Commence Dexamethasone 0.15 mg/kg 6 hourly if pneumococcal infection is suspected, to reduce risk of neurological complications	

therapy). Once the diagnosis is confirmed and an organism identified, you can de-escalate the antimicrobial treatment.

In addition to antimicrobial treatment, remember neuroprotective measures. Look out for complications of CNS infection: Hydrocephalus and cerebral venous sinus thrombosis can occur in bacterial meningitis, and seizures and status epilepticus are particularly common in encephalitis. If the diagnosis remains uncertain after initial investigations or if the patient fails to respond to treatment, seek specialist advice and consider transfer to a specialist centre.

8.6.6 Post-Cardiac Arrest Brain Injury

Patients who are comatose after a cardiac arrest are usually managed in general Critical Care Units rather than specialist neuroscience centres. Many will have sustained hypoxic–ischaemic brain injury during the time of cardiac arrest, which is the leading cause of death in this patient group. In addition to prevention of a further cardiac arrest, the management focuses on prevention of secondary brain injury by using neuroprotective measures.

These patients are intubated early and if the cause is a myocardial infarction, will often undergo coronary intervention prior to admission to Critical Care. Investigation and management of the underlying cause should be addressed in parallel to the management of the hypoxic-ischaemic brain injury.

Use your local protocol for the management of post-cardiac arrest patients. This will include sedation and analgesia to reduce cerebral metabolic demand, ventilation to achieve neuroprotective targets, and blood pressure control to maintain cerebral perfusion pressure. Remember glycaemic control, nutrition, and prophylaxis of thromboembolism. Pyrexia frequently occurs even if there is no evidence of infection, and it can worsen neurological outcomes. The evidence for how aggressively temperature should be controlled is controversial, but temperatures above 37.8° should definitely be avoided: Follow your local protocol. To achieve 'targeted temperature management', both external cooling in the form of cooling blankets and pads, or internal cooling devices such as special central venous catheters perfused with cold water can be used. Use deep sedation, analgesia, and neuromuscular blockade to avoid shivering, and Magnesium replacement to supra-normal targets may help. Most protocols recommend a period of at least 24 h at the selected target temperature, followed by slow rewarming if applicable.

Prognostication in comatose patients after out-of-hospital cardiac arrest is unreliable in the first 72 h after the arrest and should only be performed after a period of neuroprotective measures and targeted temperature management. Ensure sedation has worn off completely before your assessment.

Poor prognostic clinical signs if observed a minimum of 72 h after cardiac arrest:

- absent pupillary response to light
- absent corneal reflex
- absent motor response to painful stimulus, or extensor response only
- presence of myoclonic status epilepticus (prolonged, generalised, and repetitive or continuous myoclonic jerks)

Additional investigations may be performed to supplement the clinical assessment. These include EEG, SSEPs (somatosensory evoked potentials) and CT or MRI imaging. Not all units use of these ancillary investigations routinely in all patients. A thorough assessment by an experienced clinician is essential, and if in doubt, allow more time for observation, repeat the clinical assessments, and arrange ancillary investigations. If the conclusion is that neurological recovery is not expected, then life-sustaining therapy is withdrawn and end of life care provided.

8.7 Prognostication

Many patients with brain injuries require prolonged stays in ITU, some do not survive and others are left with significant long-term disability. Prognostication in many of these patients is complex and outside the scope of this ster although some markers predictive of poor outcomes in comatose patients following cardiac arrest are described.

In many patients, a prolonged period of time is required to allow for any residual neurological deficit after treatment to become clearer, and to assess the rehabilitation potential. Sometimes continued invasive organ support may no longer be beneficial. The team caring for the patient will try to ascertain the patient's previously expressed wishes and seek consensus with everyone involved in their care including family members.

Take Home Messages

- Use an ABCDE approach and intubate if airway at risk, reduced motor response or agitation.
- Use neuroprotective measures to prevent secondary brain injury: Good oxygenation, normocapnia, fluid resuscitation, and keep MAP above 80 mmHg.
- Take a pragmatic diagnostic approach and rapidly identify treatable causes of coma: Blood tests for metabolic causes, imaging to look for surgical targets, consider LP if CNS infection is a possibility.
- Manage signs of 'coning' immediately to prevent brainstem damage and death: Seek expert help, intubate, and optimise sedation, elevate the head, hyperventilate briefly, and give osmotherapy. Arrange urgent CT and consider whether surgery could help.
- Consult experienced clinicians, specialists, and local guidelines for definitive management plans and to individualise treatment targets.

Reference

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Interpreting Blood Gas Analysis

František Duška

Contents

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Intended Learning Outcomes

1. Interpret arterial blood gases

9.1 Why a Blood Gas is Important in ICU?

Stable volume, ion composition, osmolarity, and pH of the extracellular fluid ("Milieu internal" by C. Bernard) is mandatory for maintaining ATP production in cells and hence is considered the fourth vital function. Human body evolved a range of physiological mechanisms of keeping internal environment steady and critical illness sometimes put these mechanisms to their limits, requiring a careful intervention from a clinician. Or rather, derangements of internal environment can be first sign of patient's deterioration that require attention and action. In this chapter and related workshop, you should learn to recognise "what is going on" the blood gas strip, frequently laid on a table at the patient's bedside [1].

In an ICU patient, milieu internal is frequently monitored by means of:

- Arterial[1] blood gas analysis is performed usually at least twice a day on a bedside analyser ("point-of-care testing"). The result is available within a minute and contains pO_2, pCO_2, acid-base parameters, usually also ions (Na^+, Cl^-, K^+, Ca^{2+}), lactate, blood glucose, and often other metabolites.
- Other ions and biochemical parameters are usually checked once daily.
- Clinical parameters reflecting volume status such as urinary output, vital functions are indeed monitored continuously

Blood gas strip design, displayed variables, and their labelling may vary from unit to unit. Don't get confused—most blood gas strips contain a lot of derived variables, which are of very little or no value for most clinicians (e.g. FHHb).

1 In some ICUs, blood gas is sampled rather from central venous catheters to measure central venous saturation. In conjunction with pulse oxymetry, there is a sound physiological basis for this approach. Yet, arterial or paired samples are still most common.

SYRINGE SAMPLE

ACID/BASE 37°C		Units	Reference Range
pH	7.240↓		(7.350 - 7.450)
pCO2	5.53	kPa	(4.67 - 6.00)
pO2	15.55↑	kPa	(10.00 - 13.33)
HCO3-act	17.4	mmol/L	
HCO3-std	16.9	mmol/L	
ctCO2	18.7	mmol/L	
BE(B)	-9.5	mmol/L	
BE(ecf)	-10.0	mmol/L	

OXYGEN STATUS 37°C			
ctHb	131	g/L	(120 - 180)
Hct	39	%	
ctO2(a)	18.1	mL/dL	(15.0 - 23.0)
BO2	18.0	mL/dL	(16.0 - 24.0)
pO2	15.55↑	kPa	(10.00 - 13.33)
sO2	98.3	%	(92.0 - 98.5)
FO2Hb	97.4↑	%	(94.0 - 97.0)
FCOHb	0.3	%	(0.0 - 1.5)
FMetHb	0.6	%	(0.0 - 1.5)
FHHb	1.7	%	(0.0 - 5.0)

ELECTROLYTES			
Na+	145.9	mmol/L	(135.0 - 148.0)
K+	5.37↑	mmol/L	(3.50 - 5.30)
Ca++	0.67↓	mmol/L	(1.13 - 1.32)
Ca++(7.4)	0.63	mmol/L	
Cl-	107↑	mmol/L	(98 - 106)
AnGap	26.9	mmol/L	

METABOLITES			
Glucose	5.5↑	mmol/L	(3.7 - 5.2)
Lactate	10.25↑	mmol/L	(0.50 - 2.00)

↑ or ↓ = exceeds reference range

THINK: Blood gas is done frequently in ICU and many minor adjustments ("fine-tuning") of routine treatments are blood gas-driven. Can you think of some?

- ventilatory support adjustments incl. setting of mechanical ventilator (e.g. changing minute ventilation according to pCO_2)
- insulin infusion rate according to glucose level
- potassium chloride infusions

- resuscitation fluid choice and rate
- dialysis machine setting and bags (according to acid base, K, Ca)
- hypertonic saline treatment in neuro-patients, etc.

Hence, blood gas is a tool to achieve physiological targets. Most importantly, blood gas analysis for an intensivist is a window into patients' physiology and often "What is going on?" is much more important question than "How do I get the values back to normal range?"

pH, pO_2, and pCO_2 are actually measured by the respective electrodes in the sample. Remaining acid-base values are calculated, and hence labelled by some machines with "c". See text below for more details.

The concentration of total haemoglobin (ctHb) in blood, haematocrit (Hct), measured saturation of the blood with oxygen (sO_2), blood O_2 binding capacity (ctO_2a), and content (BO_2), fractions of haemoglobin derivatives such as oxyhaemoglobin (FO_2Hb), deoxyhaemoglobin (FHHb), as well as the dysfunctional haemoglobin species carboxy-(FCOHb) and methaemoglobin (FMetHb).

Ions and metabolites are directly measured, derived values are anion gap (AnGap) = $Na^+ + K^+ - Cl^- - HCO_{3\,act}^-$ and Ca++ is ionised calcium corrected to pH 7.4

Tip

At induction day, look very carefully at blood gas print-out in your ICU, look up what all values mean and decide, which are relevant for you.

9.2 Technical Notes to Blood Gas Measurements

- All analyses in the machine are done in a sample preheated to 37 °C. These are reported as "uncorrected" or indexed "37 °C" or without a specific labelling. Some machines also display "corrected" values, which are numerically adjusted to actual body temperature of the patient, which nurses enter into the blood gas machine. The difference is very small unless extremes of body temperature, but if you have choice, always **look at uncorrected values**.
- Ions are measured by direct ion selective electrodes and in a well-maintained machine very trustworthy. Even more precise than a value from central laboratory (!) because it does not use sample dilution and avoids error derived from nonstandard water content of plasma ("pseudohyponatraemia"). Notable exception is

K^+ measurement—sample haemolysis cannot be detected by blood gas machine—always think about the possibility of sample haemolysis when K^+ is unexpectedly high on a blood gas strip.

- Haemoglobin measurement is only reliable if sample is well shaken immediately before the measurement. RBC sedimentation in a syringe occurs quickly and can lead to errors. Haemoglobin derivatives are good in detecting carbon monoxide poisoning (FCOHb > 10%) and FMetHb needs to be monitored in patients treated with i.v. vasodilator nitroprusside, others are of no value for clinicians and only contribute to cognitive overload[2].

Tip

Never start treatment for hyperkalaemia that came as a surprise on a single POCT measurement.

What More Do You Need to Know About These Values?

- pH (normal range 7.35–7.45, with pH <7.35 termed "acidaemia" and >7.45 "alkalaemia") reflects final result or the sum of respiratory (reflected by pCO_2) and metabolic (reflected by SBE or $HCO_{3\ st}^-$, see below). Disease processes (or acid-base disorders) shifting pH down or up, are termed acidoses or alkaloses, respectively.
  - Treatment of an ICU patient rarely aims to normalise pH. Notable exceptions when pH can be a plausible target are (1) setting the ventilator for a COPD patient with significant bicarbonate retention or (2) extremes acidaemia or alkalaemia with clinical symptoms (e.g. noradrenaline-resistant vasodilation in extreme acidaemia or apneic pauses in patient with alkalaemia).
  - Although pH outside normal range will inform us, which acid/base disorder dominates, a normal pH does not exclude the presence of acid-base disorders as these can offset each other.
- Oxygenation parameters: pO_2 (normal range 10.0–13.3 kPa, usually acceptable >8 kPa) is used to titrate oxygen therapy (or FiO_2 and PEEP in mechanically ventilated patients) or for physiological calculations. Note, that as >98% of blood O_2 content is O_2 bound to haemoglobin, saturation of haemoglobin with oxygen (SO_2), measured either with pulse oximetry or by blood gas analyser is much more important for oxygen delivery[3]. Relation between pO_2 and SO_2 is defined by well-known haemoglobin saturation curve.
  - Central venous oxygen saturation (normally 70%) is an integral measure of the adequacy of oxygen content of the arterial blood (influenced by Hb concentration, saturation, and pO_2) and cardiac output.

2 If you ever wondered why sO_2 and FO_2Hb on a blood gas strip give different readings, it is because sO_2 refers to oxygen binding to functional Hb species, whilst FO_2Hb is a fraction of all Hb species, i.e. including Met-Hb and CO-Hb. It is unclear to the author of this text why FHHb and FO_2Hb are displayed at the first place.

3 Yet, most doctors and nurses prefer to look at pO_2 rather than sats when assessing oxygenation. The reason is probably historical, when pulsion oximetry was not available and Hb saturation in old blood gas machines was calculated and—unlike pO_2—notoriously unreliable.

- Oxygenation target for most critically ill patient would be 93–97%, for patients with chronic hypoxia such as these with COPD 88–92% and rarely lower in exceptional circumstances.

- pCO_2 (normal range 4.7–6.0 kPa) is reflective of the balance between pCO_2 production and elimination. In spontaneously breathing patients, minute ventilation (and hence CO_2 elimination) is regulated by central receptors in the brain (in fact, sensing is via CO_2-driven pH changes). In patients in controlled ventilation, minute ventilation. Because CO_2 is in equilibrium with carbonic acid, it makes human blood more acidaemic and alterations of pCO_2 cause respiratory disorders of acid-base balance.
  - Too high pCO_2 (termed hypercapnia or hypercarbia) is in principle caused by alveolar hypoventilation: In conjunction with hypoxia, it is a hallmark of type 2 respiratory failure (see there). In ICU patient, it can also reflect reduced respiratory drive due to sedatives or opioids or too low minute ventilation set on a controlled mode ventilation.
  - Clinical signs if severe: hypertension, tachycardia, reduced consciousness.
  - In COPD and other patients with chronic hypercapnia, bicarbonate retention compensates, and hence pH better reflects respiratory status—aim for pH 7.2–7.3. The same applies in patients with most severe forms of respiratory failure when a certain degree of hypercapnia is tolerated to avoid too aggressive ventilator setting and lung damage (this strategy is called "permissive hypercapnia").
  - Too low pCO_2 is a sign of hyperventilation. Most likely causes are pain, agitation, pregnancy (compensated—normal pH) or—in ICU setting hypoxia, shock, or metabolic acidosis or too high MV set on ventilator.
    - Clinical signs: per se most often silent, muscle spasms, or hyperirritability (Chvostek sign) may occur.
    - In profound metabolic acidosis, hyperventilation occurs as a compensation (clinically described as Kussmaul's breathing) and hence pCO_2 decreases. But how low it should be? It has been empirically determined, that pCO_2 can be predicted as $\mathbf{pCO_2 = HCO_3^-{}_{act}/5 + 1\ kPa\ (\pm 0.3)\ kPa}$. This so-called Winter's formula is one of the few worth remembering. In spontaneously breathing acidotic patients, it will enable you to detect superimposed respiratory disorders. For example, in a patient with profound diabetic ketoacidosis due to pneumonia, pCO_2 can still be below "normal range" and yet too high for the condition, suggesting life-threatening respiratory failure. It can also serve as a rough guide to adjust ventilator setting in acidotic patients.
    - In neuro-patients with (or at risk of) intracranial hypertension, mechanical ventilator is usually set to maintain pCO_2 at the lower end of normal range (e.g. 4.5–5.0 kPa), but hyperventilation should be avoided.

- Bicarbonates and base excesses. Traditional (Danish, Copenhagenian) approach primarily assesses acid-base status according to bicarbonate buffer system described by Henderson-Hasselbalch equation $pH = 6.1 + \log (HCO_3^-{}_{act}/0.03pCO_2)$. This equation is used to calculate actual bicarbonate ($HCO_3^-{}_{act}$, or just bicarbonate without an index). Also, if pH is viewed as being determined by ratio $HCO_3^-{}_{act}/pCO_2$ in this equation (the rest are constants), it is easy to understand mechanisms of compensation, i.e. shift in either pCO_2 or $HCO_3^-{}_{act}$ causing pH deviation

to one direction, can be offset by the shift in the other parameter to the same direction, bringing pH back into or closer to normal range.

- Actual bicarbonate is used for electroneutrality calculations and to assess respiratory compensation. Of note, actual bicarbonate is influenced by pCO_2 (because of shifts in the reaction $H_2O + CO_2 \leftrightarrow H_2CO_3 \leftrightarrow HCO_3^-{}_{act} + H^+$) making it poor marker of metabolic acid/base disorders.
- Standard bicarbonate ($HCO_3^-{}_{std}$ or $stHCO_3^-$) is bicarbonate concentration that would have been present had pCO_2 return to 5.33 kPa. Deviation of $HCO_3^-{}_{std}$ from 24.4 mmol/L used by some to assess metabolic component of acid-base disorder.
- Base excess of the blood (BE_B, normal range 0 ± 2 mmol/L) was developed to outperform and replace $HCO_3^-{}_{std}$ in the assessment of metabolic acid-base disorders. Base excess is the amount of strong acid that needs to be added in vitro to 1 litre of fully oxygenated whole blood to return the sample to standard conditions (pH of 7.40, pCO_2 of 5.33 kPa, and temperature of 37 °C). As the final improvement, the blood has been replaced by virtual standard extracellular fluid, forming the concept of standard base excess (SBE or BE_{ecf}). Out of all possible indicators of metabolic disorders, SBE is probably the most useful for a clinician at the bedside.

9.3 How to Assess Acid-Base Status?

In real life, intensivists rarely give the blood gas a long thought and rather use a quick pattern recognition. For example, on the blood gas shown at the beginning of this chapter, lactate 10.2 mM will likely be instantly spotted. The acid-base disorder (SBE −10 mM and low pH) well matches with lactate elevation. Normal pCO_2 means no compensation and minute ventilation should be increased. All looks fine and likely no further analysis will be attempted.

Tip

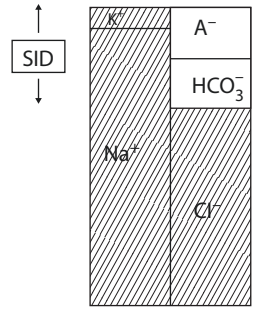
Develop your own systematic way how you will be looking at the blood gas strip. Having a mental checklist will reduce the chance you overlook something important.

Sometimes the situation in less clear and a systematic way of deciphering acid-base disorder is needed. This is because various acid-base disorders can offset each other and may not be visible (see example below). There are many approaches to more thorough assessment of acid-base status, and most are based on two important principles:

- pH is determined by ratio $HCO_3^-{}_{act}/pCO_2$. This explains directions into which pH is driven, for example, by increase of pCO_2 in respiratory acidosis and also compensations, for example, why bicarbonate retention by the kidney would restore pH back towards normal in respiratory acidosis.
- Electroneutrality—this simple rule dictates that in all body compartments the sum of cations must equal the sum of anions. Electroneutrality is the hallmark of Stewart approach, but some extensions of classical approach (such as the use of anion gap) are based on electroneutrality, too.

9.3.1 Simplified Electroneutrality-Based Method[4]

The image of ion gamblegram in your mind is a very useful tool in the assessment of complex acid-base situation:



In this graph, hatched area represent strong ions, i.e. ions that are always ionised. The difference between strong cations and ions (SID, strong ion difference) is an important variable determining acid-base status. A^- represents negative charges on non-bicarbonate weak acids, mostly albumin and phosphate.

When looking at the gamblegram, you may notice that the marker of metabolic acid-base disorders—bicarbonate—is determined as $HCO_3^- = SID - [A^-]$. In turn, any increase of SID or reduction of $[A^-]$ will cause proportional increase in HCO_3^- (metabolic alkalosis). Analogously, metabolic acidoses could be caused either by a reduction in SID or increase in $[A^-]$. More importantly, the quantity of the change can also be assessed, for example, a reduction of SID by 10 mEq will cause a reduction of SBE by 10 mEq. This concept is particularly useful for quantitatively dissecting combined acid-base disorder. In order to be able to proceed by mental arithmetic, we can simplify SID to $[Na^+]$–$[Cl^-]$ with middle reference value 35 mEq and $[A^-]$ to 0.3 Alb [in g/L], i.e. 40 g/L of albumin would hold 12 mEq of negative charges. These simplifications induce some error, but it is acceptable for clinical purposes.

Then, the analysis of acid-base status may occur in the following steps:

1. Assess $[Na^+]$–$[Cl^-]$ deviation from 35 mEq and predict influence on BE.

- <35 mEq = low SID acidosis ("hyperchloridemic"[5]), SBE would be negative.
- >35 mEq = high SID alkalosis, SBE would be positive.

For example, the patient in the vignette $[Na^+]$–$[Cl^-]$ = 146–107 = 39, which would lead to SBE = +4 mEq/L.

2. Assess weak acids and their influence on SBE. Note that $[A^-]$ should be 12 mEq can be calculated as 0.3 Alb [g/:]

- <12 mEq/L = metabolic alkalosis: hypoalbuminaemic
- (>12 mEq/L = metabolic acidosis: hyperalbuminaemic, would be rare)

4 This is based on the work of Boyle, Lawrence, Story, Mallat, Agrafiotis, Morgan, and others. I owe them the credit.

5 Hyperchloridaemic is a misnomer as what really matters is the difference between $[Na^+]$ and $[Cl^-]$. Of note, this difference can be increased by removing free water in the system (such as in polyuria in diabetes insipidus)—concentration of both $[Na^+]$ and $[Cl^-]$ increases proportionally and so does the difference between them, causing phenomenon termed concentration alkalosis.

SYRINGE SAMPLE

ACID/BASE 37°C		Units	Reference Range
pH	7.240↓		(7.350 - 7.450)
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ELECTROLYTES			
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Ca++(7.4)	0.63	mmol/L	
Cl-	107↑	mmol/L	(98 - 106)
AnGap	26.9	mmol/L	

METABOLITES			
Glucose	5.5↑	mmol/L	(3.7 - 5.2)
Lactate	10.25↑	mmol/L	(0.50 - 2.00)

↑ or ↓ = exceeds reference range

For example, if the patient in the vignette has 30 g/L of albumin, we would estimate [A^-] = 9 mM, which would lead to SBE = +3 mEq/L. The logic of it can be inferred from the gamblegram. Less [A^-] leaves within given SID more space for HCO_3^- and hence cause alkalosis.

3. Detect unmeasured anion by comparing predicted SBE (in steps 1 and 2) to the one on blood gas strip. The difference between the two determine the quantity of non-chloride circulating strong anions such as:

- lactate (can immediately be checked on the blood gas)
- unmeasured anions such as ketones (starvation, diabetic ketoacidosis), sulphates (renal failure), or organic acids derived from toxic alcohols or other species

For example, in the patient in the vignette, we predicted SBE from changes in SID and $[A^-]$ *to be +4 and +3 mEq/L, respectively, giving together predicted SBE +7 mEq/L. On the blood gas, we see SBE = −10 mEq/L, i.e. 17 mEq/L lower and therefore 17 mEq/L of strong anions are in search. We see that only 10 mEq/L is explained by lactate, and therefore there must be 7 mEq/L of another strong acid, unknown at present.*

4. Assess respiratory disorder by comparing pCO_2 with predicted value. If metabolic component is near-normal (SBE near 0), compare with normal range. For pCO_2 in metabolic acidosis, we have already learned Winter's formula. $pCO_2 = HCO_3^-{}_{act}/5 + 1$ kPa (±0.3) kPa

   For example, the patient in the vignette has $HCO_3^-{}_{act}$ *= 17 mEq and therefore,* pCO_2 *should be 17/5 + 1 = 4.4 ± 0.3 kPa. In reality, it is 5.5 kPa, suggesting insufficient respiratory compensation or superimposed respiratory acidosis.*

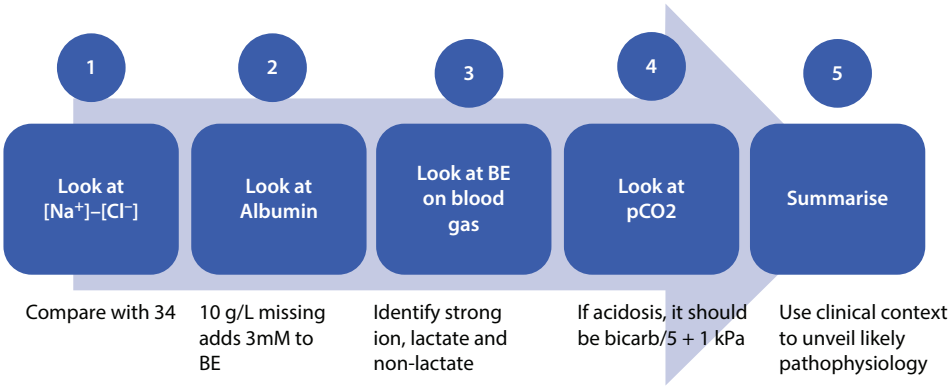
5. Making sense out of it—distinguishing causes from consequences, summarising the finding and putting them into clinical context. Start with summarising acid-base disorders found so far and link them to patient's pathophysiology. This might be obvious, but in some cases it is from ICU trainee perspective the most difficult part as it sometimes requires a lot of experience.

   For example, in the vignette is the first blood gas which was obtained in emergency room from a 67-year-old lady with a history of type 2 diabetes on metformin and chronic liver disease attributed to alcohol consumption in the past who was brought in with 3-day history of worsening back pain and vomiting. Now she is febrile 38.9 °C, confused and hypotensive. Oxygen at 15 L/min was applied, blood cultures were taken and she was given i.v. piptazobactam.

   After performing steps 1–4 of our acid-base analysis above, we have identified following disorders:

   - *High SID metabolic alkalosis (SBE +3)*
   - *Hypoalbuminaemic alkalosis (SBE +4)*
   - *Lactic acidosis (SBE -10)*
   - *Unknown anion acidosis (SBE -7)*
   - *Respiratory acidosis (*pCO_2 *1 kPa higher)*

     Given the clinical context, first two alkaloses are attributable to chronic liver disease (poor nutrition explains hypoalbuminaemia and secondary hyperaldosteronism and mild high SID alkalosis are often seen in patients with cirrhosis). Elevated lactate is worrisome, as it could be a sign of sepsis, which was suspected and acted upon. Unknown ion requires attention—plausible options are non-diabetic ketosis (starvation, alcoholism), renal failure, or toxic alcohols. Renal failure was confirmed as creatinine was 385 µmol/L and her urinary output was low. Alcohol level was 0. Hypoventilation is probably a result of altered consciousness. In light of this, this lady was treated by i.v. fluids, glucose, thiamine, and antibiotics. She later grew Staphylococcus aureus from blood cultures and was found to have spondylodiscitis as the source of sepsis.



Indeed, there are other approaches allowing a comprehensive acid-base analysis, which will give very similar results, such as corrected AG approach, delta/delta, or others. Feel free to use them if you are used to.

You will practice acid-base analysis on real cases during very interactive workshop.

Influence of iv. fluids on acid-base status: It is no surprise that strong ions in infused fluids influence acid-base status of the patients by changing SID of extracellular fluid and to a lesser extent by diluting weak acids (albumin). As a rule of thumb, following rules may apply

- Fluids with SID <24 mEq (such as normal saline or Ringers with SID =0) are acidifying. They may be used in the treatment of high SID alkaloses.
- Fluids with SID 24–40 mEq[6] (e.g. IsoLyte or Hartmanns) are considered balanced, i.e. not significantly altering acid base. This is achieved by replacing chloride by metabolisable organic anion such as lactate, acetate, or gluconate.
- Fluids with SID >40 mEq are alkalising. Some of these fluids (such as Plasma-Lyte SID = 50) could be used as maintenance fluids to compensate for normal saline used as a dilutant for most ICU drugs. Others (e.g. 8.4% Na-bicarbonate SID = 1600 mEq/L) only to treat metabolic acidosis.

6 In fact, the exact SID of the fluid that is balanced depends also on (1) plasma SID of the patients and (2) the degree of the plasma dilution effect. For fluids that would stay in intravasal compartment and cause weak acid dilution, SID 24 mEq is closest to no acid-base effect. On the other hand, if no plasma dilution is expected, such as in haemodialysis or maintenance fluids, SID 40 mEq/L is closest to electroneutrality.

Take-Home Messages

- Blood gas is one of the most frequently performed point-of-care tests performed in intensive care and can help achieving physiological targets of treatment and get insight into patient underlying pathophysiology.
- pO_2 and sHb inform about oxygenation, which is acted upon by altering FiO_2 (and PEEP in ventilated patients) to achieve oxygenation targets. pCO_2 is a measure of the adequacy of minute ventilation. For both, treatment targets are individualised.
- Winters formula $pCO_2 = HCO_{3\ act}^{-}/5 + 1$ kPa (±0.3) kPa helps to determine desired pCO_2 in patients with metabolic acidosis.
- $[Na^+]$–$[Cl^-]$ deviation from 35 mEq, rather than chloride level itself is a useful measure of SID-related disorders such as hyperchloridaemic acidosis or hypochloridaemic alkalosis. This also explains why solutions with $[Na^+]$–$[Cl^-] = 0$, such as normal saline makes patients more acidotic.
- Low albumin = alkalosis (SBE +3 mEq/L for every 10 g/L below normal albumin levels).
- Deciphering acid-base disorders is important for understanding the pathophysiology of patents condition and detecting underlying disease and complications that need to be acted upon.
- Unless in extremis or specific circumstances, pH itself seldom requires a "correction".

Reference

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Acute Kidney Injury

Karin Belch and Mo Al-Haddad

Contents

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Intended Learning Outcomes

After studying this chapter, you should be able to achieve ILO 2 and have the knowledge required to achieve ILO 1.

1. Recognise patients requiring urgent renal replacement therapy (in a simulated setting/case-based discussion)
2. **Describe common renal replacement therapy modes and compare haemodialysis, haemofiltration and haemodiafiltration**

10.1 Introduction

Acute kidney injury (AKI), previously termed acute renal failure, refers to the sudden decline in kidney function after an insult to the kidneys. It leads to retention and accumulation of waste products, dysregulation of extracellular fluid volume and electrolyte disturbances. AKI is commonly seen in the intensive care unit (ICU), affecting up to 60% of patients. It may be the primary reason for ICU admission or, more frequently, develop as a complication of shock, toxins or as part of multi-organ failure (MOF). Higher mortality is strongly linked to AKI in ICU, not only as a result of the underlying illness, but also from the direct complications of AKI and our methods of managing AKI.

In this chapter, we will discuss the basic physiology of the renal system, highlight the causes of AKI, explore the diagnostic and treatment modalities, and cover some aspects of care that an ICU resident might be asked to contribute to.

10.2 Basic Renal Physiology

Knowledge of the anatomy of the kidney is important for understanding renal pathophysiology. The two kidneys lie retroperitoneally against the posterior abdominal wall musculature. They receive about 20–25% of cardiac output (CO), which becomes the renal blood flow. The role of the kidney is to filter this blood and excrete the waste products as urine.

The functional unit which carries out this filtration process is the nephron. These are microscopic filtering systems, for which a healthy adult can have around 1 million of per kidney. The nephron traverses both parts of the renal parenchyma: the cortex and the medulla. The sections of the nephron located in the cortex are the glomerulus, Bowman's capsule and convoluted tubules. The medulla is where the loops of Henle and the collecting ducts are located.

Filtration of blood plasma begins at the glomerulus followed by reabsorption and secretion of electrolytes along the tubules as illustrated in Fig. 10.1. The collecting duct receives urine from many nephrons. The urine flows into the renal pelvis and then into the ureteric system.

The kidneys have many important functions that are summarised in Table 10.1.

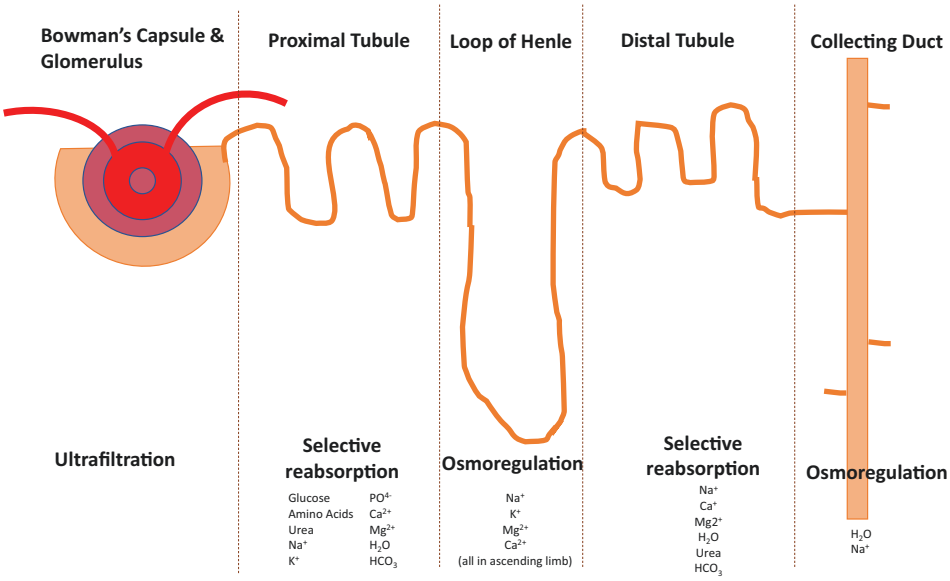

Fig. 10.1 Structure of a nephron detailing the route of filtration and location of reabsorption

Table 10.1 Functions of the kidney

Functions of the kidney
– Maintenance of fluid balance – Electrolyte regulation: potassium, sodium, magnesium and phosphate – Acid-base balance – Excretion of waste products: urea, creatinine, uric acid and ammonia – Excretion and metabolism of drugs/toxins – Blood pressure control through the renin-angiotensin-aldosterone system – Vitamin D activation – Production of erythropoietin

10.3 Assessment of Renal Function

Renal function can be assessed by calculating the glomerular filtration rate (GFR). This is the rate at which the protein-free plasma is filtered from the glomeruli into the Bowman's capsule per unit of time. Normal GFR is 90–120 mL/min. This can be assessed either directly or indirectly.

Direct measurements, such as the clearance of injected substances, are invasive and indirect measurements are preferred. GFR can be indirectly measured through serum measurement of endogenous filtration markers such as creatinine. In critically ill patients, however, creatinine levels may be deceivingly high or low through abnormal fluid distribution and catabolic illness or due to the patient being immobilised and malnourished.

Table 10.2 Investigations to assess renal function

Bloods	Urate	**Urine**
Urea and Electrolyte panel	Glomerulonephritis screen	Urine output
Glucose	Arterial Blood Gasses	Urinalysis
Full Blood Count	Blood film	Urine sodium and osmolality
Coagulation panel		**Imaging**
Blood culture		Ultrasound: kidneys, renal tract, aorta
Creatine kinase		
Ca, PO_4, Liver Function Tests, albumin		

Urine production can also be used as a method of measuring renal function; however, the relationship between urine output and GFR is complex.

10.3.1 Investigations

Clinically, many patients exhibit no specific symptoms when they have an AKI. However, as the damage progresses, symptoms and signs such as oliguria, fluid overload, arrhythmias and complications of uraemia may be seen.

Investigations that assist in the management of AKIs include blood tests, close monitoring of urine output and imaging of the kidneys. These investigations are listed in Table 10.2.

10.4 Acute Kidney Injury: Definition

AKI is an abrupt decline in kidney function. It is usually reversible after the cause is treated but can sometimes lead to chronic kidney disease.

The Kidney Disease: Improving Global Outcomes (KDIGO) criteria are widely used to stage the AKI. These criteria are displayed in Table 10.3.

10.4.1 Aetiology

The aetiology of AKI can be divided into pre-renal, intra-renal and post-renal causes. Pre-renal causes account for about 20% of AKIs and stem from a reduction in renal perfusion and oxygen supply. This is usually secondary to hypovolaemia or hypotension, for which careful fluid resuscitation is key to recovery.

Intra-renal causes account for 70% of AKIs and occurs as a result of structural damage to the kidneys. They can be subdivided based on the location that is damaged within the kidney. The tubules within the kidney can be injured leading to acute tubular necrosis. When the tubular cells die, they cause blockage and back pressure within the tubular system, resulting in AKI. The glomerulus can become inflamed from antigen-antibody complexes, leading to glomerulonephritis. Damage to these cells inhibits their function, allowing large molecules like blood and protein to pass

Table 10.3 The Kidney Disease: Improving Global Outcomes (KDIGO) criteria

	Creatinine	Urine output
Stage 1	Increase in creatinine to **1.5–1.9** times baseline OR Increase in creatinine by ≥26.5 μmol/L	Reduction in urine output to **<0.5** mL/kg/h for **6–12 h**
Stage 2	Increase in creatinine to **2.0–2.9** times baseline	Reduction in urine output to **<0.5** mL/kg/h for **≥12 h**
Stage 3	Increase in creatinine to **≥3.0** times baseline OR Increase in creatinine to ≥353.6 μmol/L OR The initiation of kidney replacement therapy OR In patients <18 years, decrease in eGFR to <35 mL/min/1.73 m^2	Reduction in urine output to **<0.3** mL/kg/h for **≥24 h** or Anuria for >12 h

Table 10.4 Aetiologies of acute kidney injury based on the location of disruption to renal function

Pre-renal (20%)	Intra-renal (70%)	Post-renal (10%)
Hypovolaemia: • Haemorrhage Hypotension: • Cardiogenic shock • Hypotension Afferent arteriole constriction: • ACE inhibitors • Renal artery stenosis • Hepato-renal syndrome	Acute tubular necrosis • Ischaemia • Drugs: gentamicin, radiocontrast dye, NSAIDs, ACE inhibitors, ethylene glycol, uric acid • Rhabdomyolysis Glomerulonephritis Acute interstitial nephritis: • Drugs: NSAIDs, penicillin, diuretics • Other: tuberculosis, sarcoidosis or systemic lupus erythematous	Renal calculi Ureteric: • Stones • Stricture • Prostatic hypertrophy • Tumours • Clots Extrinsic pressure: • Gynaecological cancer • Colorectal cancer

across the membrane. The interstitium within the kidney can become inflamed most commonly due to drug reactions. This is known as interstitial nephritis. Finally, the vascular system within the kidneys is subject to damage from vasculitis, renovascular disease or emboli.

Post-renal causes account for an estimated 10% of AKIs and occur from obstruction of renal flow. This leads to back pressure within the kidney and loss of concentrating ability. This is often seen on radiographic imaging as hydronephrosis.

It is important to note that there may be more than one aetiology contributing to a patient's AKI. A list of these is summarised in Table 10.4.

Sepsis is one of the most common causes of AKI in the ICU. However, the pathophysiology of this is complicated and multifactorial in nature with a combination of

endothelial dysfunction, intrarenal haemodynamic changes, intraglomerular thrombosis, inflammatory cell infiltration to the renal parenchyma and tubular necrosis. AKI as a result of sepsis is therefore thought to be due to a combination of both pre-renal and intra-renal aetiologies.

10.4.2 Risk Assessment for AKI

Particular patient groups are at increased risk of developing AKI in the critical care setting. These include patients with chronic kidney disease, diabetes, advanced age, black race and chronic diseases (heart, lung, liver). It is important that renal function is closely monitored in these patients during their acute illness.

10.4.3 Complications and Management of AKI

Complications of AKI can include metabolic acidosis, hyperkalaemia (see chapter on acid-base disturbances and chapter on electrolyte imbalances), fluid overload, hypocalcaemia and hypophosphataemia, anaemia and uraemia. Symptoms of uraemia can be encephalopathy, pericarditis and bleeding. It is imperative that these life-threatening complications are recognised promptly and corrected in the first instance when considering the management of a patient with AKI.

The management of AKI, therefore, involves ensuring the stabilisation of the patient whilst trying to improve or maintain renal function; looking for reversible causes of AKI; and commencing renal replacement therapy (RRT) at the appropriate time.

10.5 Renal Replacement Therapy

Renal replacement therapy is frequently used for the management of critically ill patients with AKI. It is used to remove excess fluid, correct electrolyte abnormalities and normalise acid-base status. Renal replacement therapy, however, cannot carry out the other functions of the kidney that have been discussed earlier in this chapter. Indications for urgent RRT are:

- Diuretic-resistant fluid overload
- Hyperkalaemia refractory to medical management
- Metabolic acidosis refractory to medical management
- Complications of uraemia
- Medication toxicity, for toxins removeable by RRT, e.g. salicylates, lithium and toxic alcohols

Practical Tips!

- You are mostly expected to start RRT in the following emergency situations:
  - Diuretic-resistant (anuria/oliguria) fluid overload
  - Rapidly rising K^+ (when the trajectory is for the K^+ to rise above 6 mmol/L) despite medical management (see chapter on electrolyte imbalances)
  - Rising H^+ levels despite medical management
- You only require clinical assessment (and chest X-ray in fluid overload) or a simple ABG (with electrolyte analysis) to make the decision to instigate RRT. Formal lab sample tests can be sent, but you do not need to wait for the results to start RRT, e.g. in the case of rising K^+ levels.
- It can take up to half an hour and sometimes longer to prepare a RRT machine. Prepare early and communicate your clinical decision process with members of the multidisciplinary team, especially bedside nurse and nurse in charge.
- If in doubt (and especially if you are not experienced), discuss with your supervising clinician.

Renal replacement therapy works by facilitating diffusion and/or convection, which are referred to as haemodialysis (HD) or haemofiltration (HF), respectively. The difference between these two modalities will be discussed later in this chapter.

As an overview, the RRT system consists of an extracorporeal circuit of blood that connects to the patient using a wide-bore double-lumen central venous catheter. These lines can be inserted in—through order of preference—the right internal jugular, femoral, left jugular or subclavian vein. Blood is removed from the patient through the afferent line and enters a cylindrical synthetic system that has multiple pores and fibres where dialysis and/or filtration takes place. The filtered blood is then returned to the patient through the efferent line.

10.5.1 Which RRT Mode?

The choice of RRT in AKI depends largely on local availability and practice. As a new resident, you will not be expected to make that choice. Historically, patients who were haemodynamically unstable received HF rather than HD, but that is not the case anymore. RRT can be ran continuously, intermittently or as a hybrid of the two, and it can be in the form of HF, HD or haemodiafiltration (HDF). These modalities are summarised in Fig. 10.2:

Intermittent HD is less commonly used in ICU as there is an increased risk of haemodynamic instability which may not be tolerated by patients, e.g., with acute brain injuries. These two RRT modalities are compared in Table 10.5.

Hybrid methods have been developed to combine the benefits of both intermittent and continuous RRT: working for long enough to ensure haemodynamic stability but short enough to avoid the necessities of anticoagulation and allow mobilisation periods for the patient.

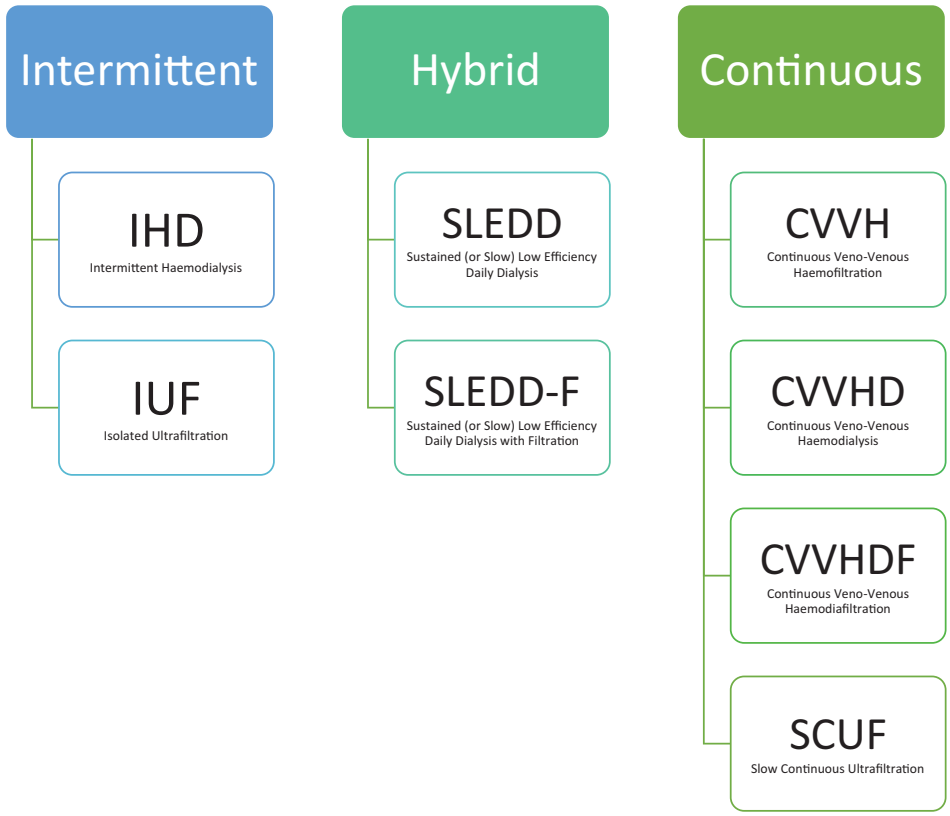

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Fig. 10.2 Types of renal replacement therapies

Table 10.5 Continuous RRT vs. intermittent RRT

	Advantages	Disadvantages
Continuous	Haemodynamic stability Predictable and stable volume control Predictable and stable control of biochemistry Stable intracranial pressure	Patient must be relatively immobile during treatment Requires anticoagulation → increased risk of bleeding Expensive Filter line at risk of clotting
Intermittent	Shorter duration Flexible timings Rapid electrolyte correction Rapid correction of fluid overload Minimal use of anticoagulation Rapid removal of dialysable drugs	Risk of cerebral oedema due to rapid removal of fluid Hypotension (especially when fluid is removed)

10.5.2 Haemofiltration vs. Haemodialysis

The key principle in haemodialysis is detoxifying the blood by **diffusion** of solutes across a semi-permeable membrane. The diffusion gradient is determined by the choice of solute in the dialysis fluid and a counter-current flow (Fig. 10.3).

In contrast, HF uses **convection** to detoxify the blood (Fig. 10.4). Convection refers to bulk flow of solutes and fluids crossing the semi-permeable membrane in a

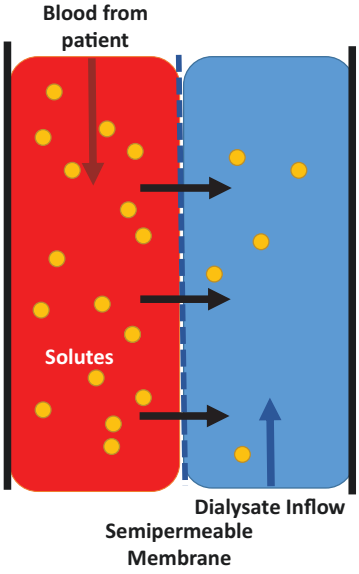

Fig. 10.3 Haemodialysis using a diffusion gradient to detoxify the blood

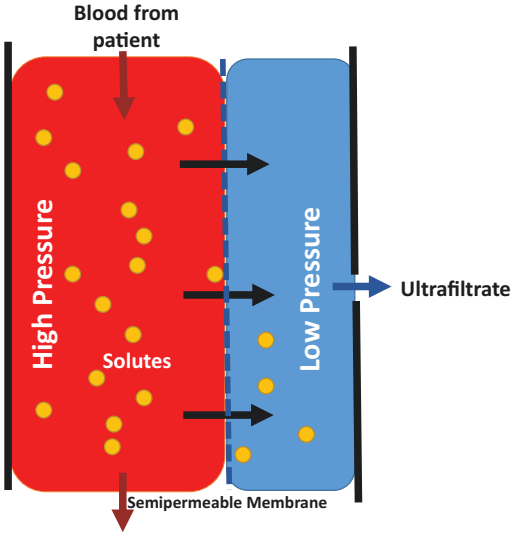

Fig. 10.4 Haemofiltration using a transmembrane pressure gradient to detoxify the blood

manner that is dependent on a transmembrane pressure gradient. This is independent of solute concentration but can be influenced by the semi-permeable membrane characteristics. Large volumes of fluid are required to create a pressure gradient high enough to detoxify the blood. This means that large amounts of fluid and essential electrolytes will be removed, which necessitates returning a balanced crystalloid replacement to the patient.

Haemodiafiltration (HDF) is a combination of HD and HF. This is achieved through using the haemodialysis diffusion gradient and increasing the transmembrane pressure to cause an increase in the filtration volume. As before, this removal of large fluid volume requires replacement to maintain the patient's blood volume.

10.5.3 RRT Prescription

When it comes to prescribing RRT, there are many factors to consider. Firstly, the decision regarding the choice of RRT is made depending on the patient needs and local availability as previously discussed. The second important prescribing consideration is anticoagulation. As the blood is being removed from the circulation into a plastic circuit, we must prevent blood clotting. Traditionally, heparin was the anticoagulant of choice, but recently the prescription of citrate has been favoured. Unlike heparin, the blood is anticoagulated using citrate within the filter machine rather than in the patient. This minimises side effects and allows the use of anticoagulation in situations where it would have been otherwise contraindicated. Like the choice of RRT, the choice of anticoagulation is determined by local practice.

We must also prescribe the appropriate exchange fluid. Again, this is patient dependent but is usually buffered bicarbonate fluid with varying concentrations of potassium. Dose and exchange rate is patient dependent, but the standard starting prescription is 25–35 mL/kg/h. Excess fluid removal can range from 0 to 250 mL/h. This process is known as ultrafiltration and is used for patients with fluid overload where we often aim to achieve a net negative balance. Remember—the higher exchange rate and the more fluid removed, the higher the risk of cardiovascular instability.

Whether to start RRT early or late in patients developing MOF is still a matter of debate. Follow your local ICU's practice.

10.5.4 Stopping RRT

There are no fixed guidelines on when a patient should discontinue RRT. The decision is usually based on the return of renal function. This could be through the production of urine, sufficient renal function to maintain safe electrolyte concentrations or if the patient has passed the catabolic phase of their illness. In practice, stopping RRT is individualised to each patient and is a decision made by a senior clinician.

Among the survivors of AKI, a proportion of patients fail to be weaned from RRT and will become dialysis dependent. A further subset of patients will not quite require RRT but never regain their baseline renal function.

Take Home Messages

- Stabilise the patient, ensuring appropriate volume status and perfusion pressure.
- Identify and manage acute life-threatening complications such as:
  - Hyperkalaemia
  - Pulmonary oedema due to fluid overload
  - Metabolic acidosis
- Find reversible causes of AKI and treat them.
- Start RRT if medical management of the life-threatening complications is failing or unlikely to succeed.

Case Study

You are called to review a 42-year-old lady in the Surgical High Dependency Unit following a road traffic accident in which she was entrapped. She suffered a proximal tibia and fibular fracture and underwent a fasciotomy yesterday in theatre secondary to compartment syndrome. The patient has not passed urine in over 10 h. On examination, she is maintaining her own airway, she has a respiratory rate of 32 and SpO_2 88%, chest has bilateral basal crackles, heart rate 110 bpm, and blood pressure 100/65. GCS was 13–E3, M6, V4, with temperature at 37.5 °C. How would you proceed? What are the management priorities?

Further Reading

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Sepsis and Septic Shock

Anne Le Roy

Contents

F. Duška et al. (eds.), *Intensive Care Fundamentals*, Lessons from the ICU,
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Intended Learning Outcomes (ILOs)

By the end of this chapter, the reader should be able to:

1. Discuss the warning signs of life-threatening infection
2. Discuss the 1-h bundle of treatment of patients with sepsis
3. Describe the most common ICU-acquired infections and propose an adequate initial antibiotic treatment
4. Describe the basics of antibiotic stewardship

11.1 Introduction

Management of sepsis and septic shock is the bread and butter of every intensivist's practice. Mortality from sepsis is around 20% and from septic shock around 40%. Sepsis causes up to 11 million deaths per year worldwide and is one of the leading causes of admission to ICU. Timely recognition of sepsis and its management in terms of haemodynamic support and early and appropriate antibiotic treatment can make the difference between life and death. The enormous burden that sepsis puts on society led to the launch of the Surviving Sepsis Campaign (SCC) in 2002, a worldwide initiative aiming to promote sepsis awareness, produce evidence-based guidelines and implement performance improvement programmes. Recommendations in this chapter are consistent with the 2021 SCC guidelines.

11.2 The Definition of Sepsis and Septic Shock

Sepsis has been defined by international consensus as a life-threatening organ dysfunction caused by a dysregulated response to infection (Sepsis 3 definition, 2016). Organ dysfunction is at the core of the definition and is defined as an increase in SOFA score by two points. Septic shock is a severe form of sepsis defined as the need for vasopressors to maintain a MAP >65 mmHg with a lactate level ≥2 mmol/L. Compared to previous definitions, the current one recognises the complex nature of the immune response in sepsis—it is no longer considered a hyperinflammatory state, but a state in which pathologic proinflammatory and anti-inflammatory processes are intertwined and are both of equal importance. Remember: Sepsis is an organ dysfunction due to acute infection.

11.3 Pathophysiology

Any infection will and should provoke an immune response from the host. The inflammatory reaction that is intended to eliminate the pathogen needs to be in balance with an anti-inflammatory reaction, which prevents inflammation from overshooting and allows it to end when it is no longer needed.

In sepsis, the immune response induced by the presence of microorganisms (bacteria, fungi or viruses) is dysregulated and generalised. By entering the body, the microorganisms activate several immune pathways simultaneously by activating the production of cytokines in host endothelial and white blood cells—just as in a phys-

iological response to infection, some of these pathways are proinflammatory and other anti-inflammatory. These pathways will be briefly explained in the following text and summarised in ◘ Fig. 11.1.

The prevailing responses and their extent are determined by both host factors (genetics, age, chronic conditions, medications, etc.) and pathogen factors (load and virulence factors). This explains the varied possible presentations of sepsis in different patients. It is tempting to speculate that different virulent factors (e.g. lipopolysaccharides of G-bacteria or exotoxin A of *Pseudomonas aeruginosa*) will cause distinct immune responses and hence distinguishable clinical pictures. Unfortunately, the pathogen-host interplay is so complex that this is rarely seen—perhaps with the exception of meningococcal sepsis or staphylococcal toxic shock syndrome, which can both have typical clinical presentations.

11.3.1 Proinflammatory Pathways

The proinflammatory pathways explain organ damage, multiorgan dysfunction and failure. The following four components explain the main mechanisms of multiorgan dysfunction syndrome (MODS) and the possible therapeutic interventions available.

11.3.1.1 Activation of the Endothelium

The endothelium is activated in sepsis in a generalised manner, which leads to:

- The expression of adhesive molecules, adhesion of white blood cells and activation of neutrophils
- The expression of tissue factor leading to procoagulation effects
- The expression of NO, leading to vasodilation
- The increased permeability of capillaries

From a macrocirculatory point of view, this leads to hypotension and a loss of intravascular volume. This hypovolaemic state is both absolute (loss of fluids into the interstitium) and relative (vasodilation). Treatment of hypotension therefore consists of the replacement of circulating volume with balanced crystalloids, and vasoconstriction with vasopressors, especially noradrenaline which is a potent alpha-1 agonist. See ► Chap. 8 (page 107).

At a microcirculation level, microthrombi can further impair the delivery of oxygen into tissues and organs. Sepsis can also cause disseminated intravascular coagulopathy (DIC), leading to prolonged coagulation times and thrombocytopaenia, and/or thromboembolic complications.

11.3.1.2 Cytopathic Hypoxia

Not only is oxygen delivery limited during sepsis, but the utilisation of oxygen in tissues is often impaired as well. This happens at a mitochondrial level and explains the possible elevation of lactate in patients with sepsis who are (still) normotensive due to compensatory mechanisms such as increased endogenous catecholamine production. Lactate is an excellent marker of oxygen utilisation in cells during sepsis, and its sequential measurement is useful to monitor the response to therapy.

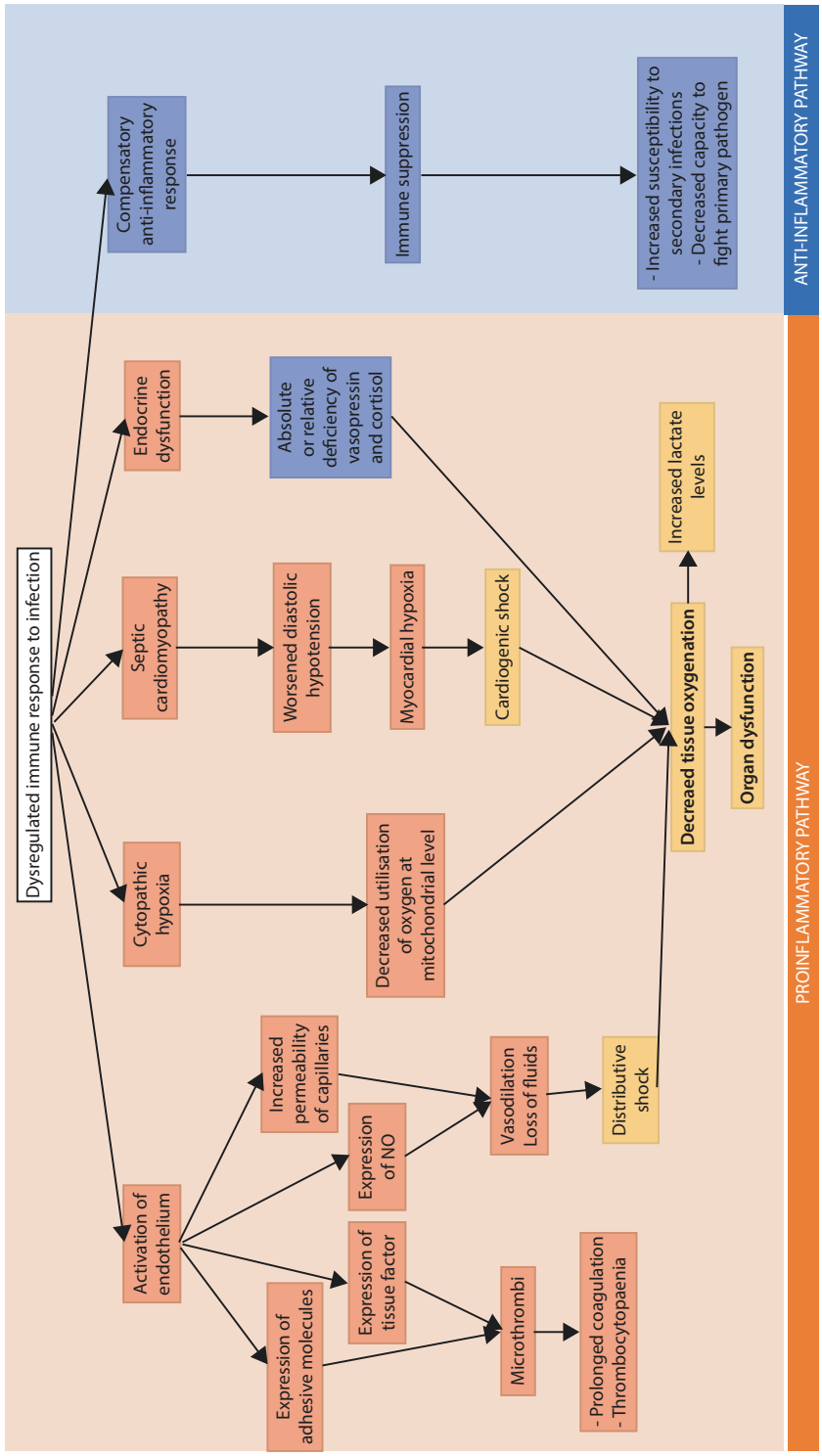


Fig. 11.1 The pathophysiological pathways of sepsis and septic shock

11.3.1.3 Septic Cardiomyopathy

Some cytokines have direct cardiodepressive effects. This further reduces diastolic blood pressure, which leads to myocardial hypoxia, pushing the patient with sepsis into a spiral of worsening hypotension. Cardiogenic shock is often present on top of distributive septic shock, which warrants the use of inotropes and can be diagnosed by echocardiography. See ► Chap. 7 (page 100).

11.3.1.4 Endocrine Dysfunction

There can be relative or absolute deficiency of hormones involved in the stress response—especially vasopressin and cortisol which might lead to worsening of septic shock. For this reason, vasopressin in substitution dose is the preferred second-line agent for refractory septic shock. Hydrocortisone in substitution dose can also be given in refractory septic shock.

11.3.2 Anti-inflammatory Pathways

In order to compensate for the systemic activation of proinflammatory pathways, anti-inflammatory pathways, sometimes called compensatory anti-inflammatory response syndrome, are activated as well. This can lead to significant immunosuppression causing a decreased capacity to fight against the primary pathogen and an increased susceptibility to secondary nosocomial infections. The capacity of the organism to adequately react to secondary infections is diminished in patients with sepsis, and this second hit can be fatal.

11.4 Diagnostics

11.4.1 Clinical Symptoms

Once you understand the basic pathophysiology of sepsis, the symptoms and signs are easy to extrapolate.

11.4.1.1 Symptoms Related to the Source of Infection

Sometimes, the source of infection is easy to recognise at presentation: for example, cough and chest pain in a patient with pneumonia or specific skin findings of erysipelas. However, this is not always the case, and a lack of a clear infection locus does not rule out sepsis.

11.4.1.2 Symptoms of Systemic Inflammation

The classic hyperinflammatory symptoms of the systemic inflammatory response syndrome (fever, tachycardia, tachypnoea) are easy to recognise and should lead to a prompt diagnosis. They are often accompanied with signs of vasodilation (warm and red skin), hypotension and signs of organ dysfunction. However, this typical "textbook" presentation will not always be present and is more commonly found in immunocompetent younger patients. Typically, geriatric patients' immune response is

milder and they can present with hypothermia and leukopenia. Some drugs such as beta-blockers can also mask the clinical picture.

11.4.1.3 Symptoms of Organ Dysfunction

Practically, all organs can be affected in sepsis and septic shock. The dysfunction of two or more organs is called multiorgan dysfunction syndrome (MODS). The severity of MODS can be assessed using the SOFA score (Sequential Organ Failure Assessment) and is directly linked to survival.

- **Kidneys**: acute kidney injury, oliguria, anuria. See ▶ Chap. 10, page….
- **Lungs**: respiratory failure with ARDS. See ▶ Chap. 6, page….
- **Central nervous system**: altered mental status, confusion. See ▶ Chap. 8, page….
- **Cardiovascular system**: cardiomyopathy, hypotension, altered microcirculation, mottled skin, elevated lactate. See ▶ Chap. 7, page….
- **Gastrointestinal tract**: enterocyte apoptosis, feed intolerance in ICU patients, translocation of bacteria and toxins
- **Bone marrow**: emergency haematopoiesis, thrombocytopenia
- **Liver**: liver dysfunction, hypoalbuminaemia, impaired detoxification

11.4.2 Laboratory Signs of Sepsis

11.4.2.1 Specific Biomarkers

At this time, there is no specific biomarker with reasonable specificity and sensitivity that could be used as a stand-alone method for the diagnosis of sepsis. Traditional biomarkers of sepsis (WBC, CRP, procalcitonin) lack specificity and can be elevated in a range of critical states. They are relatively sensitive but have a diagnostic window period (especially CRP which peaks 3 days after the primary insult), which can result in low values in hyperacute infections.

11.4.2.2 Lactate

As explained above, sepsis is a state characterised by both organ hypoperfusion and reduced utilisation of intracellular oxygen. Lactate is a marker of anaerobic metabolism and is a key marker of possible organ damage in sepsis. Its investigation is mandated by the current guidelines at presentation and sequentially during the treatment. Lactate levels are useful to the clinician for three reasons: it can be used to monitor response to haemodynamic stabilisation, it is a prognostic marker for mortality and a lactate ≥2 mmol/L is a diagnostic criterion for septic shock. Lactate can be elevated in a range of other states such as seizures, localised hypoperfusion such as mesenteric ischaemia and others.

11.5 Initial Management

The current Surviving Sepsis Campaign recommendation for the initial therapy is summarised in a 1-h bundle of care (◘ Fig. 11.2). This bundle focuses on three pillars of therapy: stabilisation of haemodynamic parameters, early antibiotic therapy

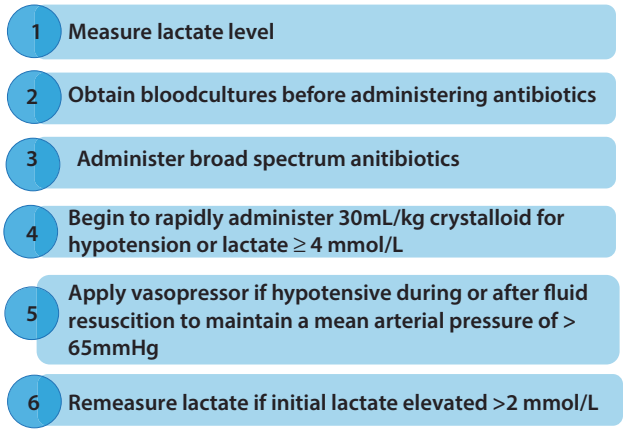


Fig. 11.2 The first hour bundle of care. Give 3 (oxygen, IV fluids, antibiotics) and take 3 (lactate, culture, urine)

and source control. All patients requiring ICU should be admitted within 6 h and should not be kept for an extended period in the emergency department.

11.5.1 Stabilisation of Haemodynamic Parameters

The goal is to reverse the circulatory disorders caused by sepsis: hypovolaemia, vasodilation, and myocardial and endocrine dysfunction. The target MAP is usually set at 65 mmHg for most patients (with the notable exception of previously uncontrolled hypertensive patients), and an arterial line should be inserted early.

- **Correction of hypovolaemia with balanced crystalloids**. The initial recommended dose of IV fluids is 30 mL/kg within 3 h, but current practice is to focus on a more individualised approach. This generally means more aggressive fluid replacement for patients with combined hypovolemia such as diarrhoea and sepsis, and more restrictive fluid replacement for patients with ARDS or pre-existing cardiac compromise.
- **Correction of peripheral vascular resistance with vasopressors**. The vasopressor of choice in septic shock is noradrenaline, titrated to effect. Noradrenaline is a potent alpha-1 agonist, markedly increasing peripheral vascular resistance. In practice, noradrenaline infusion is started concomitantly with fluid resuscitation in all hypotensive patients as soon as a CVC has been inserted. See ▶ Chap. 7 ….
- **Endocrine substitution.** Vasopressin 0.03C IU/min is added in patients with refractory hypotension on high doses (>0.5 μg/kg min) of noradrenaline. At the same time, hydrocortisone 100–200 mg/day is added as a treatment or prophylaxis for critical illness-related adrenal dysfunction.
- Inotropes such as dobutamine or adrenaline are very rarely considered for patients in refractory septic shock but are sometimes used for such patients with low cardiac output.

Giving too much or too little fluid can cause harm. The patient with septic shock should be very regularly reassessed for the signs of fluid responsiveness, lactate level trends and organ function (see ▶ Chap. 7 …):

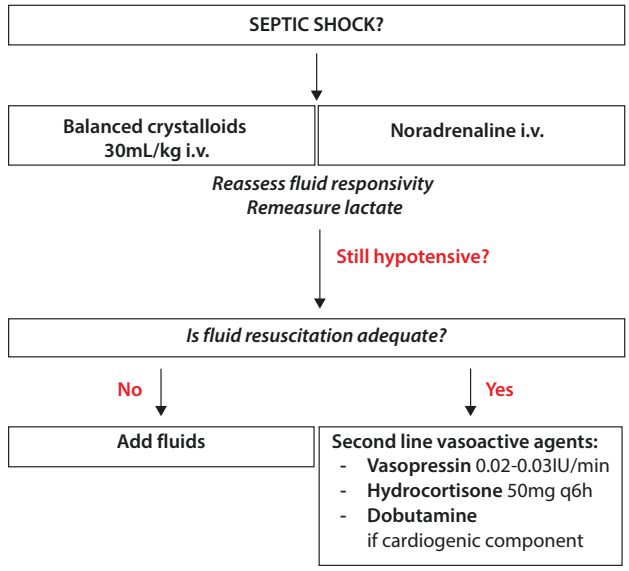
Note: A one-off CVP measurement is no longer considered a valid indicator of volume resuscitation. Nonetheless, sudden increase in CVP in the context of fluid resuscitation of septic shock can mean impeding right ventricular failure. Call for senior help.

Practical Tips!

- If the patient is not preload responsive (e.g. does not respond to a passive leg raise manoeuvre), it means that further fluids are not even temporarily able to increase cardiac output and will likely cause more harm than good. Stop fluids and reassess later.
- In patients who seem to be improving (lactate, vasopressor dose, organ function), reduce fluids and reassess later. Tests of fluid responsiveness are pointless as improving patients will not benefit from further fluids even if preload responsive.
- Boluses rather than continuous infusion and frequent reassessment are the key to giving the right dose of fluid in patients with sepsis.

11.5.2 Early Antibiotic Therapy

Early and adequate antibiotic therapy directly impacts mortality and is a core component of effective treatment of patients with sepsis. If sepsis is likely, empirical antibiotic therapy should be initiated as soon as possible and no later than 1 h after recognition of possible presence of sepsis. If the diagnosis of sepsis is uncertain but possible and the patient shows signs of shock, antibiotics should be given in the same time frame. If the patient is haemodynamically stable and sepsis is considered among other diagnoses, a rapid assessment of other causes can be performed before starting antibiotics. However, if concern over infection persists, start antibiotics within 3 h of recognition (Fig. 11.3).



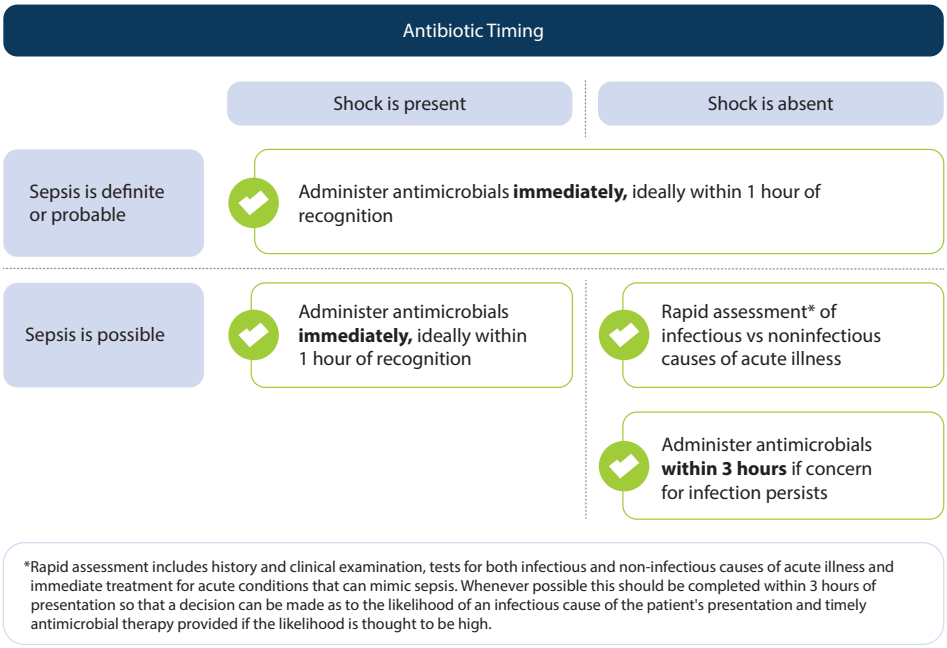


Fig. 11.3 Antibiotic timing [1]

The principles of antibiotic therapy are as follows:

- Antibiotic therapy should be started within 1 h from the diagnosis of sepsis.
- Take cultures before administering antibiotics, but do not delay antibiotic treatment. At least two sets of blood cultures should be taken from a vessel (not from a non-sterile line) 20–30 min from each other. Timing with the highest levels of bacteriaemia (chills and rising fever) increases the chances of identifying the infectious agent but is not critical.
- Familiarise yourself with local guidelines for empirical treatment of infection. In some countries, a clinical microbiologist is also available 24/7 for advice.
- Use broad-spectrum bactericidal antibiotics (or a combination of antibiotics) that achieve high concentration in the blood to cover all possible pathogens:
  - Beta-lactam + (one-off dose) aminoglycoside is a typical synergic combination.
  - Some antibiotics such as clindamycin are able to inhibit bacterial protein synthesis and should be used if a toxin-synthetising G+ is suspected (e.g. toxic shock syndrome).
  - Antibiotics with large volume of distribution and low blood concentration (quinolones, tigecycline, chloramphenicol) are generally less useful in sepsis.
- Give full (loading) dose regardless of organ function. Then consult clinical pharmacist for dosing and drug-level monitoring. Consider prolonged infusions of beta-lactams.
- Re-evaluate after 2 days (or earlier if results become available) with microbiology results, and consider de-escalation. If source control is adequate, the preference is to use shorter (5 days) over longer durations of therapy.

Figure 11.4 includes an example of empirical regimens for the most common sources of sepsis in the ICU.

Infection	Antibiotics	Example and dosage	Length of therapy
Community acquired pneumonia	Cephalosporins III generation + macrolide or respiratory chinolone	Ceftriaxone 2g q24h + Clarithromycin 500mg q12h	5 days *Prolong to 7-14 days if complicated pneumonia, bacteremic pneumococcal pneumonia, non-fermenting Gram-negative rods (pseudomonas aeruginosa, Acinetobacter, stenotrophomonas) or staphylococcus aureus*
Hospital acquired pneumonia	Pip/tazo *where ESBL pathogens are not widely present* or Carbapenems and consider adding vancomycine (30 mg/kg loading dose) if MRSA suspected	Pip/tazo 4.5g q6h or Meropenem 2g loading dose, then 1g q6h	5 days *Prolong to 7-14 days if complicated pneumonia, non-fermenting Gram-negative rods (pseudomonas aeruginosa, Acinetobacter, Stenotrophomonas) or staphylococcus aureus*
Peritonitis and intraabdominal absceses	Pip/tazo + one dose aminoglycoside + fluconazole if perforation of upper gastrointestinal tract	Pip/tazo 4.5g q6h + single dose Gentamicin 7mg/kg IBW[1] *+ Fluconazole 800mg loading dose, then 400mg q24h*	7 days *Consider prolonging if source control is not adequate*
Urinary tract infection	Aminopenicillin + aminoglycoside for 3 days	Ampicillin + sulbactam 3g q6h + Gentamicin 7mg/kg IBW[1] *(5mg/kg IBW in elderly or known renal impairment)*	5-7 days *Consider prolonging if source control is not adequate*

Fig. 11.4 An example of antibiotic treatments for the most common infections in the ICU in immunocompetent patients. *Note: The local microbiological situation should always be taken into consideration when choosing antibiotics. Consult local guidelines* [2]

11.5.3 Source Control

The third pillar of management of patients with sepsis is the identification and control of the source of infection as soon as possible (within the first 12 h). A focused history and examination will often give sufficient information to formulate a working diagnosis, but often imaging is needed to make the diagnosis or exclude others. For example, sepsis with typical signs of pyelonephritis might be due to a wedged ureteric stone, and hydronephrosis needs to be ruled out by ultrasound. On the same note, any treatment failure should again raise a question about the possibility of an uncontrolled source of infection (e.g. interloop abscess in a post-op patient).

Practical Tips!

- Sudden-onset chills with rigour, shivering and hypertension followed by hypotension should trigger a high suspicion of catheter-related bloodstream infections. Take cultures and change old catheters, starting with the CVC.
- A CT abdomen should be considered in all surgical patients with rising inflammatory biomarkers or sepsis in the post-operative period: things to search for are anastomosis leaks, hidden abscesses or deep wound infections.

11.6 Follow-Up Management

After initial resuscitation, empirical antibiotics and source control procedure, patients should start showing signs of improvement, mostly reflected by a decrease in lactate levels and/or vasopressor requirement. Inflammatory markers and other organ function may take more time to improve. The following needs to be considered:

- De-escalation of fluid therapy: While fluid resuscitation is necessary in the initial phases of sepsis treatment, it is later detrimental. Fluid overload leads to increased duration of ICU stay, mechanical ventilation and increased intra-abdominal pressure and is associated with an increased need for therapeutic interventions such as diuretic use and thoracocentesis. After meeting haemodynamic targets, the rate of fluid administration should be reduced or stopped.
- Review of antibiotic therapy: The antibiotics chosen initially are usually broad spectrum in order to treat all possible pathogens. After 2–3 days, the first culture and susceptibility results are usually back allowing for antibiotic de-escalation. De-escalation means narrowing the spectrum of antibiotics to avoid selection of resistant pathogens. Ideally, antibiotic treatment should be targeted to the pathogen that caused the sepsis, but this might not always be possible as often no pathogen is identified. In this case, clinical judgement should guide de-escalation (e.g. discontinuing macrolide treatment when legionella antigen is negative). De-escalation should ideally be performed in collaboration with a microbiologist or infectious diseases specialist. In patients with adequate source control and rapid resolution of sepsis, short antibiotic courses of less than 7 days are usually recommended. However, some notable exceptions exist where longer treatments are warranted:

- **Impossible source control:** undrainable focus of infection, endocarditis, osteomyelitis, large abscesses
- **Pathogen factors:** biofilm-forming microorganisms: *Staphylococcus aureus*, *Candida* spp., non-fermenting Gram-negative rods (*Pseudomonas aeruginosa, Acinetobacter, Stenotrophomonas*), viral infections (Herpes spp., CMV), highly resistant pathogens with limited sensitivity
- **Patient factors**: neutropenia, immunosuppression (haematologic malignancies, bone marrow transplant, AIDS, etc.)

If infection has been thoroughly excluded and another cause for critical illness has been found that satisfactorily explains the condition of the patient, antibiotics can be stopped at any time (there is no need to wait for 5 or 7 days).

11.6.1 Antibiotic Stewardship

Antibiotics save life, but inappropriate use of antibiotics can cause harm to the individual patients and to the bacterial ecology of the unit. At individual level, exposure to antibiotics will adversely affect gut microbiota and expose patients to the risk of *Clostridium difficile* infection and other types of antibiotic-associated diarrhoea. Increased colonisation with multi-drug-resistant flora may lead to difficulty in treating nosocomial infections, in addition to antibiotic-induced organ toxicities of antibiotics which are associated with increased morbidity and mortality. It is, therefore, of utmost importance to reduce unnecessary use of antibiotics. This policy is named "antibiotic stewardship". In ICU, the most important principles are the following:

1. Strict adherence to protocols for antibiotic prophylaxis—in particular, not to extend recommended duration of administration in surgery.
2. Policy of early antibiotic review and de-escalation (see above).
3. Avoidance of antibiotic use when there is evidence of no benefit such as in base-of-skull fractures, early uncomplicated pancreatitis, aspiration pneumonitis and viral infections. Also, neither the finding of raised inflammatory markers nor finding bacteria in a normally sterile site means the automatic requirement of antibiotic therapy. Findings from microbiological cultures should be interpreted critically, and infection should be differentiated from colonisation and contamination.

Colonisation: growing microbial agents that are physiologically not present in the sampled organ but are not causing a disease in the patient. Examples of this could be any bacteria in the lower respiratory tract, *Neisseria meningitidis* in the upper respiratory tract, etc.

Contamination: finding of microbes that have been sampled by error—e.g. blood cultures sampled from a non-sterile line.

Take-Home Messages

- Sepsis is a life-threatening organ dysfunction caused by a dysregulated response to infection.
- Early recognition and treatment are key to patient survival, and a high clinical suspicion should be maintained.
- The early management of sepsis and septic shock focuses on three pillars: stabilisation of haemodynamics, antibiotics and source control. The Surviving Sepsis Campaign guidelines provide a first-hour bundle to guide therapy.
- The three causes for multiorgan disorder syndrome that can be targeted by therapy are endothelial dysfunction leading to extravasation of fluids and vasodilation, myocardial dysfunction and endocrine dysfunction.
- The approach for initial antibiotic treatment in sepsis is "hit hard, hit early and hit appropriately". After stabilisation, de-escalation of therapy is equally necessary.

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Common Challenges and Troubleshooting in ICU

Contents

Hypoxia and Ventilator Asynchronies

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Contents

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Intended Learning Outcomes (ILOs)

By the end of this chapter, you should be able to achieve ILO 1, 2, and 3. You should also have the knowledge required to complete ILO number 4 successfully:

1. Describe the five pathophysiological mechanisms of hypoxia and the representative disease entities associated with them.
2. Define hypoxia, recognize its most common causes in the critically ill patient, and discuss ways to manage it.
3. Describe the most common types of ventilatory asynchronies in mechanically ventilated patients, and discuss interventions to handle them.
4. Recognize the different types of ventilatory asynchronies whilst assessing the waveforms in the ventilator screen.

12.1 Hypoxia

12.1.1 Basic Respiratory Pathophysiology: Five Mechanisms of Hypoxia

Hypoxaemia refers to the low oxygen content in the blood, whereas hypoxia means low oxygen supply in bodily tissues. Because these two are interconnected, we use these terms interchangeably in this book and clinical practice. Hypoxaemia is defined as PaO_2 <60 mmHg or 8kPa (normal range 75–100 mmHg, 10–13.3 kPa). Its mechanisms can be viewed as derangements of physiological processes of gas exchange. Because dealing with hypoxia is the hallmark of intensive care, we will discuss them in a bit more detail.

Oxygen serves as an acceptor of electrons in the mitochondrial matrix where the electron transfer chain drives ATP synthesis. To get there from atmospheric air, O_2 always follows a diffusion gradient. Let us follow the oxygen diffusion cascade in more details now (see Fig. 12.1) as these processes underly mechanisms of hypoxia:

1. Atmospheric air (760 mmHg = 100 kPa at sea level, 21% O_2 has $pO_2 = 760 \times 0.21 = \mathbf{159\ mmHg} = 21$ kPa).

> Note: A high altitude reduces barometric pressure and hence pO_2 in the gas entering airways, so does breathing an anaesthetic mixture with too low an FiO_2. This is the first cause for hypoxia.

2. First reduction of pO_2 occurs when air is humidified in the airways, when P_{H2O} (the water vapour pressure) of 47 mmHg [6.2 kPa] needs to be subtracted, and leaves pO_2 $p_IO_2 = 0.21 \times (760–47) = \mathbf{149\ mmHg}$ or 20 kPa.
3. In the alveolar air, P_AO_2 is determined by the equilibrium between alveolar ventilation (adds O_2) and pulmonary blood flow (removes O_2).

   The alveolar gas equation describes this equilibrium as $P_AO_2 = p_IO_2 - pCO_2/R$, where R is the gas exchange ratio, usually 0.8. It means that normally $P_AO_2 = 149 - 40/0.8$, i.e. **99 mmHg** 13.2 kPa.

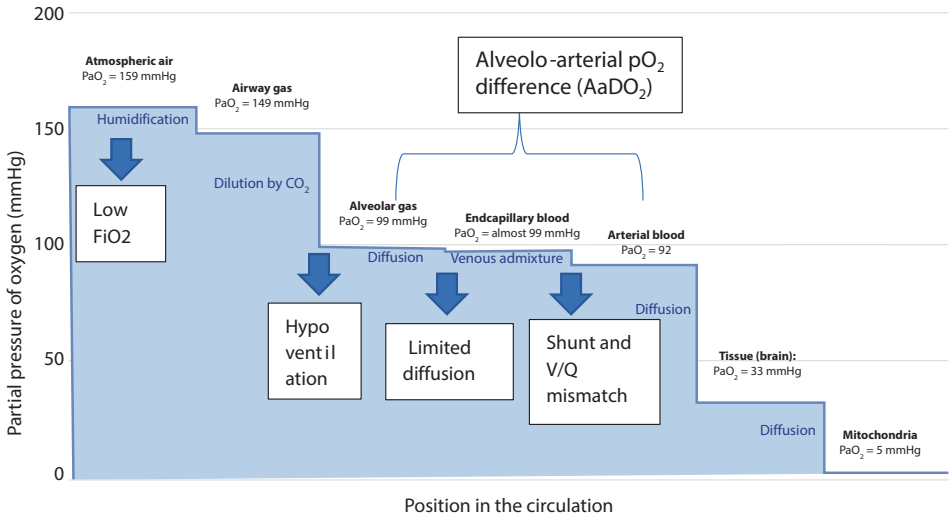


Fig. 12.1 Oxygen cascade in normal physiology: See text for details

(a) Alveolar hypoventilation causes pCO_2 to rise. As all the exhaled CO_2 comes from alveolar air, it can be easily inferred that pCO_2 is inversely proportional to MV_{alv}. For example, halving the MV_{alv} from 5 to 2.5 L/min would double pCO_2 from 40 to 80 mmHg (5.3–10.6 kPa).

(b) The same degree of hypoventilation would in turn reduce P_AO_2 to 149 – 80/0.8 = 149 – 100 = 49 mmHg (6.5 kPa). If we wanted to restore P_AO_2 back to the normal 99 mmHg in this hypoventilated patient, we would need a p_IO_2 of 199 kPa. This is achieved by FiO_2 0.28, as $p_IO_2 = 0.28 \times (760 - 47) = 199$ mmHg.

The Same as Multiplied?

Notice: Alveolar hypoventilation is the second cause of hypoxia, which arises from a disturbed balance between oxygen removal from lungs and its addition from the atmosphere, leading to low partial pressure of oxygen in the alveolar air. This hypoxia can be easily treated by a minimal increase in FiO_2. Of note, alveolo-arterial difference calculated as $AaDO_2 = [FiO_2 * (Pb\text{-}PH_2O) - PaCO_2/R] - PaO_2$ is normal, i.e. 2.5 + 0.21 × age [mmHg] or 0.3 + 0.03 × age [kPa] in room air.

4. Diffusion of oxygen through the alveolo-capillary barrier is the next step of the oxygen cascade. It normally takes 0.25 s for pO_2 to equilibrate between the alveoli and capillary blood, whilst red blood cell travel time through pulmonary capillary is 0.75 s at rest and 0.3 s during heavy exercise.

Notice: Thickening of the alveolo-capillary barrier in interstitial lung diseases such as in pulmonary fibrosis limits diffusion of oxygen, and this is the third cause of hypoxia. Typically, it worsens with exercise (because of the reduction in RBC transit time), responds well to an increase in FiO_2 (as this increases diffusion gradient), and does not affect CO_2 elimination (as CO_2 is known to be 20x more diffusible compared to O_2).

5. Partial pressure of oxygen in the arterial blood (**92 mmHg** = 12.2 kPa) is normally slightly lower than pO_2 at the end of the capillary adjacent to the aerated alveolus. This is because of the admixture of deoxygenated blood from bronchial veins and thebesian veins of the heart. In healthy people, this shunt represents about 2% of the cardiac output.

   Notice: Increased admixture of venous blood through shunts is the fourth possible cause of hypoxia. There are two types of shunts:
   (a) *Intracardiac:* blood passes through an anatomic channel in the heart and does not pass through the lungs
   (b) *Intrapulmonary shunt:* blood flows through pulmonary capillaries without participating in gas exchange (see causes in the box)

A shunt is the only cause of refractory hypoxia, i.e. hypoxia that persists despite ventilating with FiO_2 = 1.0. Analogously, a failure to respond to increase FiO_2 by increase in arterial saturation always means that there is a significant shunt. It is possible to calculate the % of the shunt by letting the patient breathe FiO_2 = 1.0 and using the Berggren equation, which uses oxygen content (not partial pressure) in arterial and mixed venous blood. You can find more on this in Refs. [1, 2].

Causes of Shunt

Intrapulmonary

- Cardiogenic pulmonary oedema
- ARDS
- Pneumonia
- Lung haemorrhage
- Atelectasis

Intracardiac

- Ventricular septal defects
- Congenital heart disease
- Open foramen ovale

Note

When thinking about hypoxia, also think about the haemodynamics: The degree to which a given intrapulmonary shunt contributes to arterial hypoxaemia depends also on the saturation of mixed venous blood. Indeed, the more desaturated venous admixture, the lower saturation in the arterial blood. When dealing with hypoxaemia, not only gas exchange but also the haemodynamics should always be considered. For example: further increase in PEEP in a patient with ARDS and a 30% shunt may improve gas exchange a little bit, but it may reduce cardiac output, which in turn leads to lowering of oxygen saturations in mixed venous blood, and the overall effect of this might be worsening arterial saturation (in addition to the compromise of oxygen delivery due to lowering cardiac output).

6. During spontaneous ventilation in the upright position, ventilation and perfusion are well matched. However, the distribution of ventilation and perfusion is not uniform throughout the lungs, with the bases receiving substantially more of both than the apices. The difference between apices and bases is more marked for perfusion, and hence, *V*/*Q* is the highest at apices and the lowest at lung bases. The distribution of perfusion throughout the lung is partly due to the effects of gravity and partly anatomical with improved flow to the bases. Most of the effects of prone positioning are from improving the perfusion of the aerated part of the lung.

Practical Point!
The alveolo-capillary reflex is pulmonary vasoconstriction in poorly ventilated areas, which redirects the blood flow to better ventilated regions. It takes some time, so if you change the patient's position or ventilator setting, the effect is not usually immediate. Wait until the pulmonary circulation adapts to the new setting.

Notice: *V*/*Q* mismatch is the fifth and the most important cause of hypoxia. Unlike shunt, it responds to an increase in FiO_2. Its effects are understood by looking at its extreme forms (Fig. 12.2).

Left on the figure is the nonventilated alveolus (*V*/*Q* = 0). Indeed, the blood leaving the adjacent capillary is identical to mixed venous blood as no gas exchange occurs (pO_2 = pCO_2 = 45 mmHg = 6 kPa). This is the intrapulmonary shunt mentioned before, and an increase in FiO_2 will have minimal effect on oxygenation. Importantly, as long as there is some ventilation, increasing FiO_2 would improve hypoxia. The other extreme is an alveolus that receives no perfusion. Here, the partial pressures of gases are that of inspired air (pCO_2 = 0, pO_2 = 149 mmHg) as no gas is added or removed from it. This is called alveolar dead space. Alveolar dead space added to anatomical dead space in large airways forms the physiological dead space. To achieve the same CO_2 elimination, patients with increased dead space have to increase minute ventilation. Spontaneous breathing is not sustainable above a certain

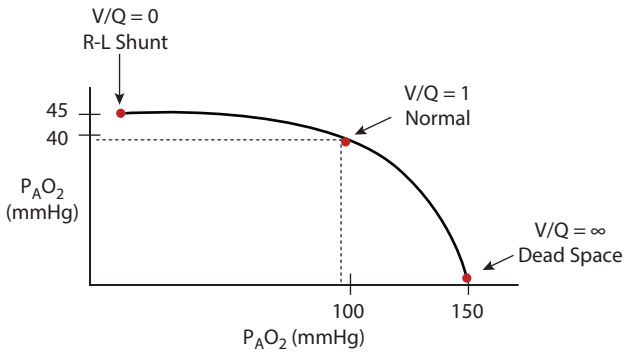


Fig. 12.2 *V*/*Q* mismatch. See text for detailed explanation

threshold, as the increased breathing work generates more CO_2 than the lungs can eliminate. In addition, hyperventilation not only increases the work of breathing but also leads to damage to lung parenchyma (called self-inflicted lung injury (SILI)).

Causes of *V/Q* Mismatch:
- Atelectasis
- Pulmonary embolism
- Patient position
- Bronchospasm
- Obstruction of the airways (acute exacerbation of COPD and asthma)
- Pneumonia
- ARDS
- Pneumothorax

In practice, in severely hypoxaemic patients in ICU, V/Q mismatch combines with a degree of intrapulmonary shunt, and we see the effect of both:
- Shunt, i.e. admixture of venous blood leading to oxygen-refractory hypoxia
- Increased dead space, which means that increased MV is required to eliminate CO_2

Summary: five pathophysiologic mechanisms of hypoxia:
1. Low FiO_2
2. Alveolar hypoventilation
3. Diffusion limitation
4. Shunt
5. Ventilation/perfusion (V/Q) mismatch

12.1.2 A Practical Approach to a Ventilated Patient with Worsening Hypoxia

The approach to a patient with hypoxaemia vastly differs depending on severity and circumstances. Mild hypoxaemia with saturations in the range of 85–90% could be very worrying in a young patient with asthma exacerbation but could represent a treatment goal for a patient with COPD. The most worrying consequence of severe hypoxaemia is the damage to the central nervous system.

Hypoxia Consequences
- Mild hypoxaemia causes few changes.
- Severe hypoxaemia (PaO_2 approximately 40 mmHg or 5.3 kPa) in those not adapted to it causes:

- CNS effects: headache, somnolence, and clouding of consciousness. Profound acute hypoxaemia can cause convulsion and permanent brain damage.
- CVS effects: tachycardia, arrhythmia and hypertension, bradycardia, hypotension, and pulmonary hypertension.
- Renal: sodium retention and proteinuria.

The most common scenario in ICU in which you can be called to assist is a sudden worsening of oxygenation in a patient receiving mechanical ventilation.

12.1.3 Causes

Hypoxia in a mechanically ventilated patient may be caused by:

1. Equipment failure
2. Endotracheal tube-related problems
3. Patient-related problems

The key question is whether the problem is in the equipment or the patient. An experienced nurse would have checked the ventilator, the circuit, and the tube, and before calling you, the patient is already on 100% oxygen. Nonetheless, it is worth double-checking. Ask what preceded the deterioration as this may provide a clue (e.g. change of position of the patient), and check both the equipment and the patient.

1. Equipment failure and ventilator malfunction

Practical points to assess failure in oxygen source:

- Increase FiO_2 to 100% and check FiO_2 in ventilator monitor:
  - If it does not reach 100%, check the oxygen source probe for disconnection.
  - If oxygen source probe is in place, change to another wall source and call medical physics for support.

2. Endotracheal tube (ETT)-related problems

Endotracheal tube (ETT)-related problems include:

(a) ETT malposition
(b) ETT cuff damage
(c) ETT obstruction by mucus plug or foreign body (rarely)

(a) ETT malposition

i. ETT has been displaced superiorly, and the tip of the tube is above the vocal cords and outside the trachea.
ii. ETT has been displaced inferiorly (endobronchial intubation), and the tube's tip is in one of the mainstem bronchi. Confirmation: In clinical examination,

there are decreased lung sounds and/or decreased expansion in the one lung. Chest radiography would confirm the position of ETT in this situation.

(b) ETT cuff damage

Confirmation: On clinical examination, this can usually be heard as a loud, low-pitched breath sound escaping through the mouth. The air leak is also evident by a difference between the set and expired tidal volume on the ventilator.

(c) ETT obstruction by mucus plug or foreign body (rarely)

Confirmation: In the ventilator, monitor increased Paw and low tidal volume. Unable to pass a suction catheter through the ETT.

Practical points for endotracheal tube-related problems:

(a) ETT malposition
- If a superiorly malpositioned tube is suspected, consider removing it and reintubating the patient with a new endotracheal tube. Alternatively, the endotracheal tube can be advanced into the proper position under direct vision (flexible bronchoscope or laryngoscope).
- If endobronchial intubation is suspected, consider pulling the ETT out by 2 cm, preferably under direct vision.

(b) ETT cuff damage
- Reintubate the patient with a new ETT. Consider exchanging the ETT over a bougie.

(c) ETT obstruction
- Make sure that the tube is not blocked or kinked outside or between the teeth.
- Attempt to pass a suction catheter down the ETT to assess for obstruction from mucus plugging. If available, the integrity of the endotracheal tube and upper airway can also be assessed with flexible bronchoscopy.
- If mucus plugs are not removed by suctioning or bronchoscopy, the tube should be removed and the patient reintubated with a new ETT.
- Obstruction of the ETT may also occur when a patient bites the tube. Consider increasing sedation or adding intravenous neuromuscular blocking agent.

3. Patient-related problems

Once technical problems have been ruled out, we can turn our attention to the patient. *V*/*Q* mismatch and shunt are the main pathophysiologic mechanisms of hypoxaemic respiratory failure in critically ill patients. These are distinguished from each other by their response to oxygen. *V*/*Q* mismatch without shunt responds well to an increase in FiO_2. Alveolar dead space may cause problems with CO_2 elimination. The less the patient responds to an increase in FiO_2, the more significant the shunt. The main causes of changes of *V*/*Q* ratio or worsening of shunt are the following:

(a) Mucus plugs blocking segmental or lobar bronchi (complete block = shunt): the solution for this is bronchoscopic suctioning, but less invasive options could be tried first.

(b) Lung derecruitment and collapse (typical after change of patient position, collapsed, nonaerated lung also creates collapse). For this, gentle recruitment and increase of PEEP may help.
(c) Worsening of underlying disease (see table) or a sudden onset of a new such disease (e.g. pneumothorax, aspiration pneumonitis, pulmonary embolism). Here, the treatment is specific according to the cause.

Perform physical (and sonographic) examination of the chest, suction the patient's airway, and try gentle recruitment of the lung (by hand or by a ventilator). Try response to increase in PEEP. Rule out quick killers, such as pneumothorax. Review the last CXR and consider obtaining a new one. Consider decreasing the shunt by patient positioning, e.g. lateral with healthy lung down in a patient with lobar pneumonia or prone or semi-prone positioning in a patient with ARDS. Remember to call for help.

Practical Tip!

Manual bagging by high-flow bag with a PEEP valve connected to 15 L/min O_2 can be very useful in a desaturated intubated patient, e.g.

- If unsure if the ventilator is working
- To perform manual recruitment
- To feel how stiff the lung is

A capnograph from the airway trolley should be attached, if not already present.

Remember: The first priority is to improve profound hypoxia as soon as possible to avoid neurological damage. The second priority is to protect the lung. It is much more important to find out what is going on than to make numbers look nice by an aggressive ventilator setting. It is important to come back to your patient again, and check whether the current setting is in keeping with lung-protective ventilation ($p_{plat} < 30$ mbar, $V_T < 6$ mL/kg, driving pressure <14 mbar) but also what are the haemodynamic effects of your intervention (change in $S_{cv}O_2$, urinary output).

The table below summarizes the diagnostic and therapeutic approach of the most common causes of hypoxia in the ICU.

Cause	Diagnosis	Specific treatment
Acute exacerbation of COPD and asthma	Previous history of COPD or asthma Clinical signs (wheezing)	• Inhalation therapy (b2 adrenergic agonists, corticosteroids) • Systemic corticosteroids Consider antibiotic therapy
Pneumonia	Clinical symptoms (fever cough, purulent secretions) Chest X-ray Lung ultrasound Blood tests Microbiologic examination of lower respiratory tract specimen	• Empiric antibiotic therapy • Supportive therapy
Cardiogenic pulmonary oedema	Previous medical history of cardiac disease, clinical symptoms, and signs ECG Transthoracic echocardiography Chest X-ray: accentuated hilum, bat wings Lung ultrasound Blood tests Hallmark = quickly improved oxygenation and CXR on positive-pressure ventilation	• Diuretics • Inotropes • iv nitrates • CPAP • Treat acute coronary syndrome if indicated • Treat arrhythmia if present
ARDS	Berlin criteria Chest X-ray: bilateral infiltrates Lung ultrasound Presence of a causative factor (pulmonary or extrapulmonary)	• PEEP • Recruitment manoeuvres • Prone position • Treat causative factor • Conservative fluid management
Pneumothorax	Chest X-ray Lung ultrasound Clinical examination Possible haemodynamic instability	• Placement of an intercostal drain
Pulmonary embolism	Presence of risk factors CT pulmonary angiography Transthoracic echocardiography—RV stain Possible haemodynamic instability	• Anticoagulation therapy • Consider thrombolysis in case of massive pulmonary embolism

12.2 Patient-Ventilator Asynchronies

Another common task of a doctor in ICU is to troubleshoot a frequently alarming ventilator or patients who are "fighting" the ventilator. A very tempting solution to this problem is to deepen the sedation of the patient, suppress spontaneous breathing

efforts, and use a controlled mode of ventilation. Although this approach would be effective in most cases in the short term, it would deprive patients of exercising their respiratory muscles and clearance of airways by coughing and expose them to the adverse effect of excessive sedation. In addition, by regularly looking on the screen of the ventilator and respiratory pattern of the patient, an intensivist should be able to recognize the most common asynchronies, even though they may not trigger any alarms. Unrecognized asynchronies can adversely affect gas exchange and haemodynamics, lead to patient exhaustion and anxiety, and worsen outcomes. During unrecognized asynchronies, swings in intrathoracic pressures may invalidate haemodynamic tests such as measuring pulse pressure variation. Recognizing the type of asynchrony is a prerequisite for solving the problem by improving ventilator setting, but it requires advanced knowledge and experience (see Refs. [3–5] for a more advanced review of the topic). For the novice in ICU, ineffective efforts, autotriggering, and air hunger are probably the most relevant asynchronies to focus on.

During assisted mechanical ventilation, the main target is the synchronization of mechanical (ventilator) and neural breath (patient) both in terms of timing (matching mechanical and neural inspiratory times) and ventilator assist (avoiding either excessive or insufficient assistance). Patient-ventilator asynchrony is common, especially with conventional modes of assisted mechanical ventilation (pressure support (PS) and assist volume control (AVC)). Patient-ventilator asynchrony may present in all three phases of the mechanical breath: the triggering phase, the pressure delivery, and the cycling-off phase. The most common types are presented below.

Types of ventilator asynchronies:

1. Asynchronies during the triggering phase:
   (a) Ineffective efforts
   (b) Triggering delay
   (c) Autotriggering
2. Asynchronies during the pressure or flow delivery phase:
   (a) Excessive ventilatory assist
   (b) Insufficient ventilatory assist
3. Asynchronies during the cycling-off phase:
   (a) Delayed opening of the expiratory valve
   (b) Premature opening of the expiratory valve
   (c) Double-triggering

12.2.1 Asynchronies During the Triggering Phase

In order to support inspiration in assisted modes, e.g. by delivering pressure support, the ventilator must detect the patient's inspiratory effort. Most contemporary ventilators use the flow trigger to detect patients' inspiratory activity. There is a constant flow through the circuit, and when the patient starts to inspire, the ventilator detects the difference between flows in the inspiratory and expiratory branches of the circuit. The magnitude of this difference is called trigger sensitivity, and it is usually set by

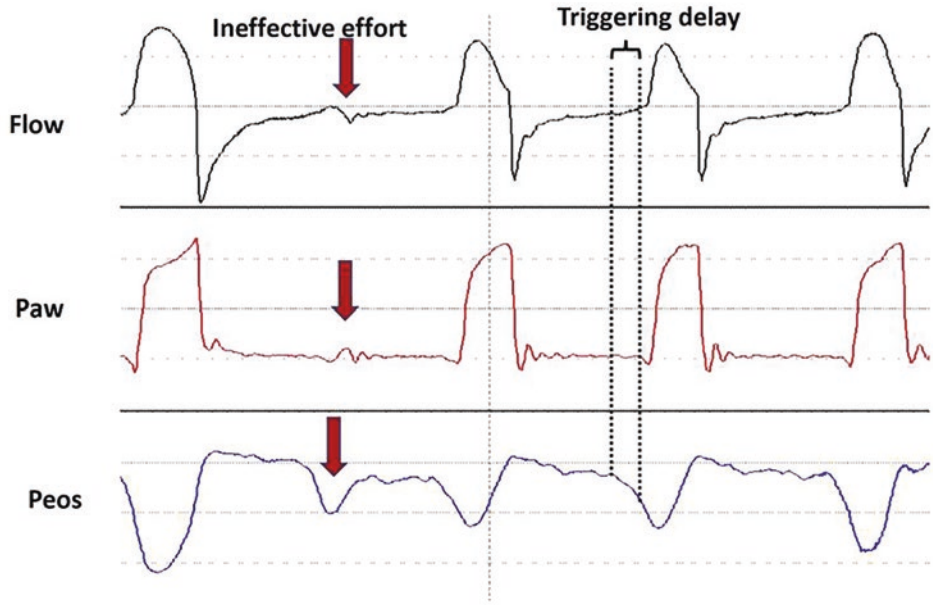
default to 2–5 L/min, but the operator can change it. This sensitivity can be manipulated in advanced settings. Indeed, a conventional ventilator can only detect a patient's inspiratory effort that has already begun; therefore, patient effort is needed to do so.

12.2.1.1 Ineffective Efforts and Triggering Delay

The definition of *ineffective efforts* is inspiratory efforts not followed by ventilator triggering (red arrows in ◘ Fig. 12.3). Clinically, you may notice the patient's "wasted" inspiratory efforts.

Causes: dynamic hyperinflation in COPD, too high a triggering threshold, too high a ventilator assist, low respiratory drive (sedation, alkalaemia), low inspiratory muscle output, delayed opening of the exhalation valve in the previous breath.

Suggested interventions: (i) interventions to increase respiratory drive (**decrease** assist level, decrease sedation, correct alkalaemia); (ii) interventions to decrease dynamic hyperinflation (decrease airway resistance, lower assist level, increase flow threshold for cycling off, application of external PEEP (positive end-expiratory pressure) to balance for PEEPi (intrinsic PEEP).



◘ **Fig. 12.3** *This is a COPD patient on pressure support ventilation. Looks uncomfortable on the ventilator*. Flow, airway pressure (Paw), and oesophageal (Poes) pressure waveforms. Poes (surrogate for pleural pressures) is not routinely measured, but in this picture, it is displayed in order to demonstrate the patient's inspiratory effort. Observe that the second decrease in oesophageal pressure (Poes), which represents the patient's inspiratory effort, is not followed by a mechanical breath. This is an ineffective effort during the expiration and is manifested by a slight decrease in airway pressure (Paw) associated with a simultaneous decrease in expiratory flow (red arrows). Also, observe that in every mechanical breath, there is a time lag between the start of neural inspiration (first dotted line) and the start of mechanical inspiration (second dotted line). This time lag is the triggering delay and is due to dynamic hyperinflation indicated herein by the presence of end-expiratory flow

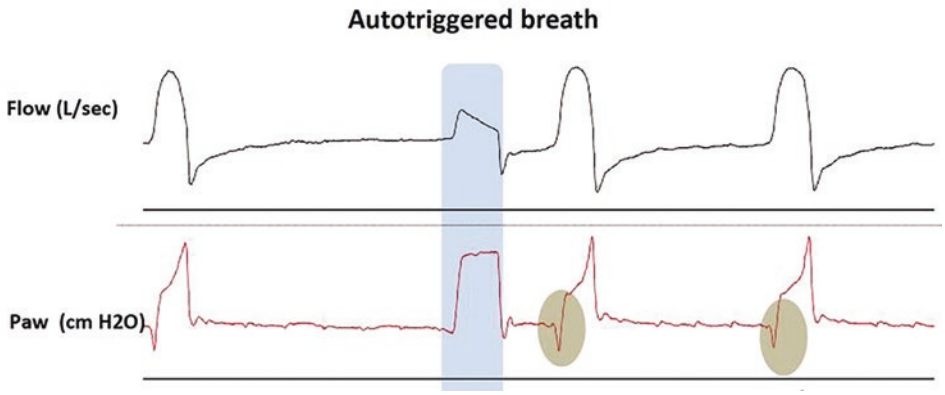


Fig. 12.4 *Autotriggering*. Flow and airway pressure (Paw) waveforms in a patient ventilated on pressure support. There is no inspiratory effort before the second mechanical breath. Observe that, in comparison to patient-triggered breaths, there is no decrease before the start of mechanical inflation (grey shaded areas) and there is no distortion in the Paw- (no decrease in Paw) and flow-time curve in the autotriggered breath. Moreover, the shape of the inspiratory flow and Paw waveforms is different compared to that of patient-triggered breaths

Note: Wasted efforts especially when present at clusters result in fatigue and tachycardia and are associated with adverse patient outcome.

12.2.1.2 Autotriggering

Definition: ventilator triggering in the absence of patient effort (blue shaded area in Fig. 12.4)

Causes: Low triggering settings, circuit leaks, presence of water in the circuit, cardiogenic oscillations, hiccups. *Ventilator waveform characteristics*: absence of the initial pressure dip below PEEP, triggering occurring synchronously with cardiogenic oscillations. *Suggested interventions*: increase triggering threshold, elimination of circuit leaks, enhance the respiratory drive by reducing sedation, correct alkalosis by reducing the level of assist, aspirate secretions, change triggering variable from flow to pressure.

12.2.2 Asynchronies During the Pressure or Flow Delivery Phase

Patient ventilator asynchrony during the pressure delivery phase occurs when the assistance provided by the ventilator is either excessive or inadequate in respect to the patients' ventilatory demands. Most common asynchronies are from flow starvation (in volume-controlled modes) or insufficient pressure support, e.g. during weaning.

12.2.2.1 Inspiratory Airflow Asynchrony: Flow Starvation

Ventilator waveform characteristics: Downward V-shaped distortion of the inspiratory part of the Paw waveform or any concavity in pressure tracing; see Fig. 12.5.

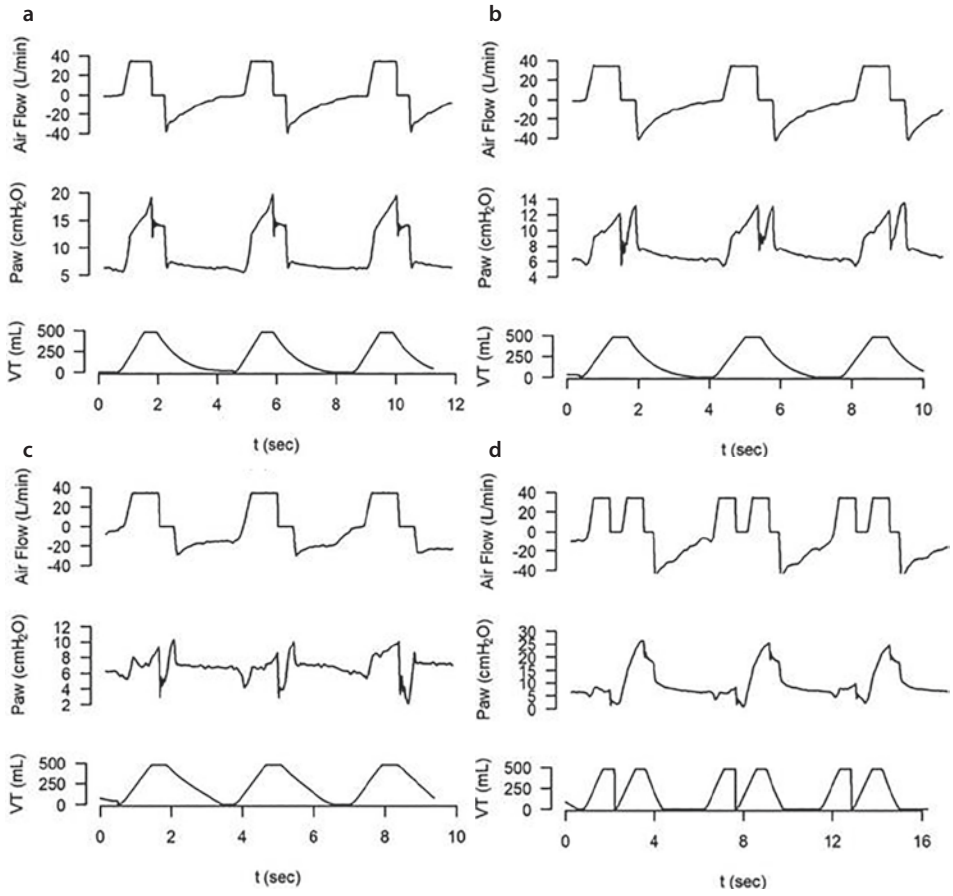


Fig. 12.5 Inspiratory airflow asynchrony. Sequence of airflow and airway pressure waveforms corresponding to a same patient in the same day ventilated in assist volume control mode. Set airflow is insufficient for the patient's needs and originated different degrees of airflow dyssynchrony or starvation. **a** Mild airflow dyssynchrony. **b**, **c** The progression of airflow dyssynchrony through a more severe stage. **d** The appearance of double cycling secondary to a huge and large inspiratory effort (adopted from Ref. [3])

Causes: This asynchrony occurs in patients with strong inspiratory efforts and insufficient flow settings on the ventilator. Think of pain, delirium, substance withdrawal, or metabolic acidosis.

Suggested intervention: Find and treat the cause of the patient's strong inspiratory efforts, deepen sedation, increase flow and/or minute ventilation.

12.2.3 Insufficient Ventilator Assist

Ventilator waveform characteristics: rounded or constant inspiratory flow waveform Fig. 12.6. *Causes*: Same as above, but in patients on pressure support modes.

Suggested interventions: decrease ventilation demands (sedation), increase ventilator assistance.

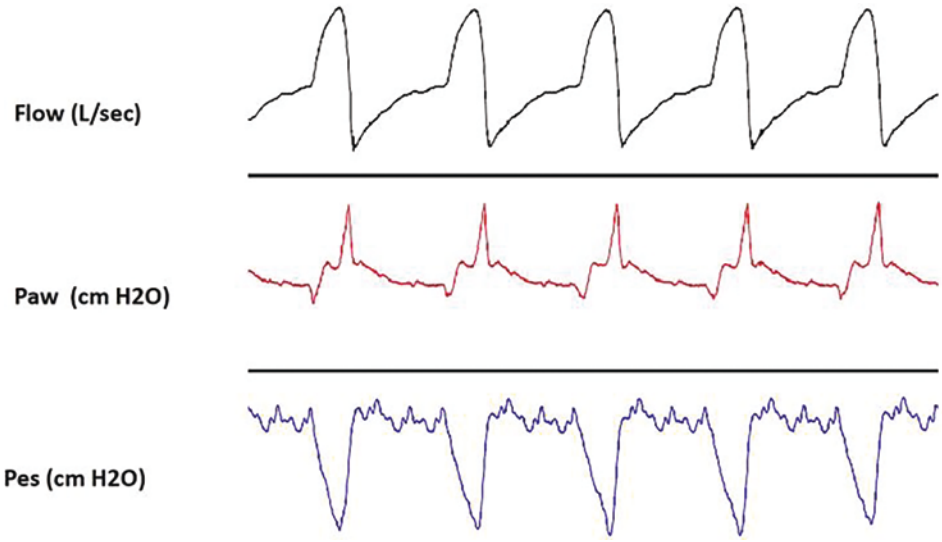


Fig. 12.6 *Insufficient ventilator assist.* Flow, airway pressure (Paw), oesophageal pressure (Peos) waveforms in a patient ventilated on pressure support. Observe the vigorous inspiratory efforts (Pes decreases) that result in the rounded inspiratory flow and a considerable decrease of Paw from the expected square-shaped form

12.2.4 Asynchronies During the Cycling-Off Phase

The third group of asynchronies arises at the cycling-off phase, when the ventilator terminates the mechanical inspiration and opens the expiratory valve. Expiratory trigger is used in pressure support mode to detect the end of patients' inspiratory effort. This is accomplished by calculating the % of peak inspiratory flow (PIF), terminating pressure support, and opening the expiratory valve at a certain % of PIF. In most ventilators, this is set by default at 25% PIF, but the operator can change this, e.g. in a range of 5% (very late cycling off) to 90% (very early termination).

As a general rule:

- ARDS patients ("stiff, fast-to-exhale lung") tend to synchronize better with late cycling off (e.g. 5% PIF), and they tend to suffer from premature cycling-off asynchronies, in particular with low pressure support.
- COPD patients ("slow-to-exhale lung") tend to synchronize better with early cycling off (e.g. 40–70% PIF), and they tend to suffer from delayed cycling-off asynchronies, in particular with high pressure support.

There are distinct recognizable waveforms for both these asynchronies; the easier one to recognize is premature cycling off in an ARDS patient. Typical reversed-tail wing-shaped expiratory flow curve is detected by a concavity (blue arrows in Fig. 12.7). Suggested intervention is reducing % of PIF with or without increasing pressure support.

For more detailed knowledge about asynchronies, see Refs. [3–5].

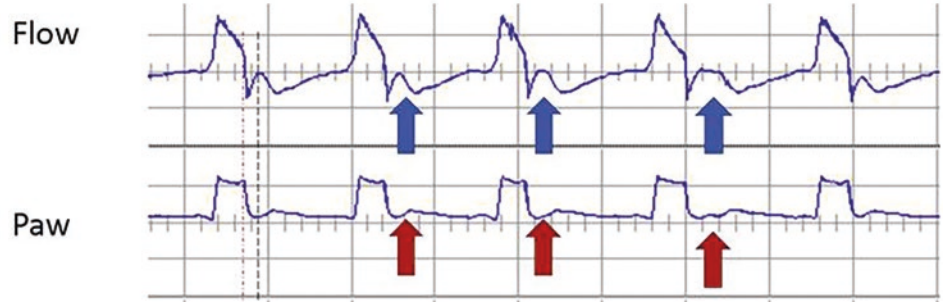


Fig. 12.7 Premature opening of the expiratory valve. Flow and airway (Paw) pressure waveforms in a patient ventilated on pressure support. Observe the flow (blue arrows) and Paw (red arrows) distortion early in expiration caused by continuing contraction of inspiratory muscles

Take-Home Messages

- There are five pathophysiological mechanisms of hypoxia. In critically ill patients, *V*/*Q* mismatch and shunt are the most common.
- Hypoxia poorly responding to increases in FiO_2 is due to a shunt.
- When facing a hypoxic ICU patient, first ensure that the ventilator is working, the patient is on FiO_2 1.0, and the tube is in the right place. If unsure, manually ventilate the patient with high-flow bag with a capnometer.
- The standard workout is a physical exam and the lung ultrasound. Some patients may need CXR and bronchoscopy.
- Mucus plugging and atelectasis are the most common causes of refractory hypoxaemia in patients with copious secretions and after positioning. Hand ventilation may help, but the patient may require bronchospopy and suction.
- Patient-ventilator asynchronies, which may worsen patients' outcomes, are common and may be present in all three phases of the mechanical breath: the triggering, the pressure delivery, and the cycling-off phase.
- Patient-ventilator asynchronies are recognized by looking at both the patient and ventilator screen—learn to do so by frequently looking at the ventilator screen and thinking about what you see.

Case Vignette

A 50-year-old man with a past medical history of hypertension and diabetes presents to the emergency department with fever, dyspnoea, and productive cough lasting for a week. On clinical examination, the airway is patent, respiratory rate is 32 breaths/min, there are diminished breath sounds in the right lower lung field on chest auscultation, SpO_2 is 85% on room air, heart rate is 120/min, blood pressure is 100/70 mmHg, GCS is 15/15, blood glucose value is normal, and temperature is 38.5 °C. Arterial blood gas samples demonstrate PaO_2 = 50 mmHg, PCO_2 = 32 mmHg, PH = 7.47, and FiO_2 = 21%. What are the management priorities?

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Arrhythmias

Katie Duncan and Mo Al-Haddad

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Intended Learning Outcomes

After studying this chapter, you should have the knowledge required to:

1. Recognise life-threatening brady- and tachyarrhythmias and provide treatment options in a simulated setting.

13.1 Introduction

Critically ill patients commonly have cardiac arrhythmias. These arrhythmias are often detected quickly as most patients are connected to continuous cardiac monitoring. Arrhythmias are more often a complication that occurs during the ICU stay rather than being the reason for admission to ICU. Recognition, treatment and prevention of arrythmias can be life-saving. In this chapter, we will explore the most common types of arrhythmias you will encounter in critically ill patients, as well as the key stages in the recognition and management of patients with each arrhythmia. It is likely that you will be called to a patient with sudden-onset atrial fibrillation during one of the first night shifts in ICU..

13.2 Causes of Arrhythmia in ICU Patients

Damage to the heart tissue, for example due to myocardial infarction, may lead to an interruption of the electrical conduction in the myocardium and result in arrhythmia. However, non-cardiac causes of arrhythmias are much more common in critically ill patients.

Non-cardiac causes of arrhythmia include:

- Hypovolaemia
- Electrolyte disturbances, in particular hypokalaemia, hyperkalaemia and hypomagnesaemia
- Hypercapnia and hypoxia
- Drugs, such as inotropes or those which prolong the QT interval
- Sepsis and infections, e.g. pneumonia
- Acute pain
- Acidosis
- Hypothermia

13.3 Arrythmia Classification

We will describe arrhythmias in two groups—tachyarrhythmias and bradyarrhythmias. To administer prompt and appropriate treatment, it is important to be familiar with the different types of arrhythmias in each group. Further information on the pathophysiology of each arrhythmia, including ECG examples, can be found elsewhere, such as the European Resuscitation Council guidelines. Please note that crucial for the management decisions is not only the type of arrhythmia, but also whether

it causes adverse haemodynamic features (see below) and whether there is a risk of further deterioration.

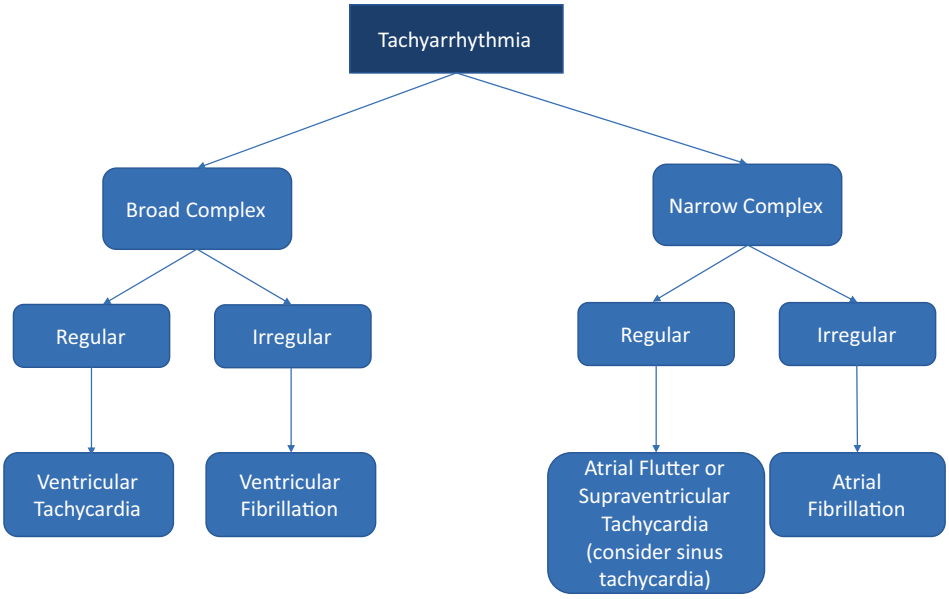
13.3.1 Tachyarrhythmias

Although classification of tachyarrhythmias could be extremely complex, for the "Friday night" initial management in intensive care practice, it is usually sufficient to classify them according to two features, which can be read from a standard cardiac monitor using the width of the QRS complexes and the regularity of the rhythm (see ◘ Fig. 13.1). It is always better to capture the arrhythmia using a 12-lead ECG.

Broad complex tachyarrhythmias are those in which the QRS complex is greater than 120 ms in duration, and they usually require immediate action. Narrow complex tachyarrhythmias are usually less of an immediate threat to life but can lead to cardiac ischaemia if left untreated. Coronary perfusion occurs during diastole, and therefore an increased heart rate reduces blood flow to the myocardium by shortening the duration of diastole.

13.3.2 Bradyarrhythmias

Take note of:
1. The presence of P-waves
2. The relation of P-waves to QRS complexes (AV conduction)
3. The shape and width of QRS complex



◘ **Fig. 13.1** A simplified flow chart for classifying tachyarrhythmias

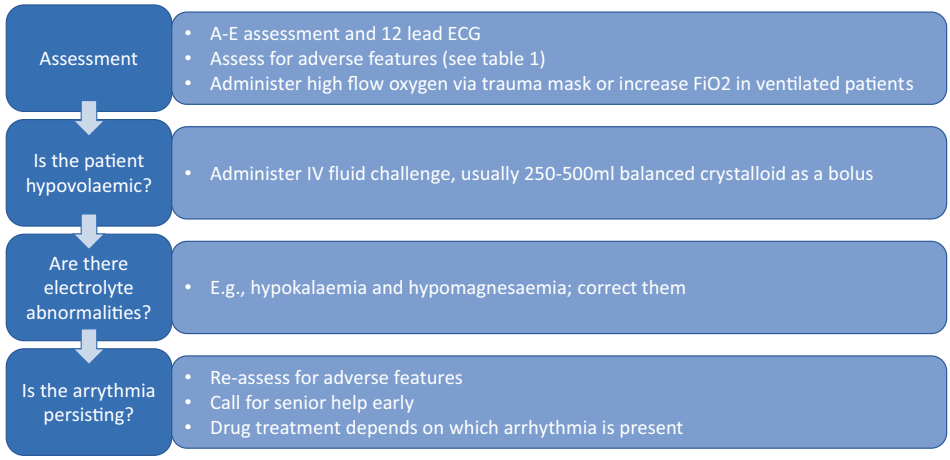
Sinus bradycardia usually has a reversible extracardiac causes (hypoxia, hypothermia, drugs), whilst AV blocks are more commonly caused by structural disease of the heart and tend to deteriorate further. Most worrisome are broad complex bradyarrhythmias, which usually precede cardiac arrest, unless the cause is found and treated (e.g. severe hyperkalaemia).

13.4 Initial Approach

The following steps refer to patients with an arrythmia and who have a palpable pulse, i.e. are not in cardiac arrest. If a patient has an arrhythmia and no pulse, CPR should commence immediately, and cardiac arrest resuscitation guidelines should be followed.

The general principles for assessing a patient with a new arrhythmia are outlined in ◘ Fig. 13.2. All patients should be assessed using an A–E approach; see ▶ Chap. 2. The purpose of the assessment is the following:

- Ensure that the patient is physiologically safe, and identify whether or not the patient has any **adverse features** such as heart failure, cardiac ischaemia, syncope or shock, as outlined in ◘ Table. 13.1. The presence of any of these features will influence the choice and the urgency of treatment.
- Identify the type of arrhythmia as described above. This will determine the risk of deterioration including the progression to cardiac arrest. A 12-lead ECG is not only important to better identify the arrhythmia, but it also helps to rule out acute myocardial ischaemia.
- Identify and manage potential **underlying causes** of the arrhythmia. Factors such as hypovolaemia, hypoxaemia, hypokalaemia and hypomagnesaemia can and should be corrected quickly. These interventions alone may be enough to correct the arrythmia. After these corrections are made, consider specific drug treatments depending on the arrhythmia.



◘ **Fig. 13.2** Steps to take when assessing a patient with a new arrhythmia

Table 13.1 Adverse features which may be present in patients with arrhythmias

Adverse Feature	Signs and Symptoms
Heart Failure	Peripheral and/or pulmonary oedema, chest X ray changes, shortness of breath, reduced oxygen saturation.
Cardiac Ischaemia	Patient may report chest pain, chest tightness, shortness of breath, and nausea. ECG may exhibit ST segment changes.
Syncope	The patient may report feelings of dizziness or light-headedness, or, in severe cases, they may lose consciousness.
Shock	Low mean arterial blood pressure/cardiac output, reduced urine output, altered conscious level, cool peripheries, prolonged capillary refill time, weak and thready pulses.

The condition of a patient with arrhythmias may rapidly change. It is, therefore, important to continually reassess the patient. After initial assessment, consider informing your supervisor and discuss further management.

The most common antiarrhythmics used in ICU are Outlined in Appendix A (page 249).

13.5 Management of Tachyarrhythmias

Please see the Algorithm for Tachyarrhythmias in Appendix B (page 263).

13.5.1 Management of Unstable Patients with a Tachyarrhythmia

As a general rule, tachyarrhythmias that cause adverse features (see Table 13.1) require synchronised DC cardioversion. However, in critically ill patients, the myocardium can be very irritable. As a result, there is sometimes a brief conversion to sinus rhythm after synchronised DC cardioversion, only to be followed by a return of the tachyarrhythmia shortly after. Clearly, repeated synchronised DC shock is not possible. In this situation, it is important to administer amiodarone 300 mg over 10–20 min and wait for a few minutes before delivering another pulse of synchronised DC shock (see Fig. 13.3).

After stabilisation of the patient's condition, reassess and try to answer the key question of what was the cause of arrhythmia. Repeat the ECG, consider biomarkers, measure ions and acid-base status, perform an echocardiography (whether regional wall motion abnormalities or right ventricular strain suggesting pulmonary embolism) and last, but not least, think sepsis. Without finding and addressing the cause, any improvement will be temporary.

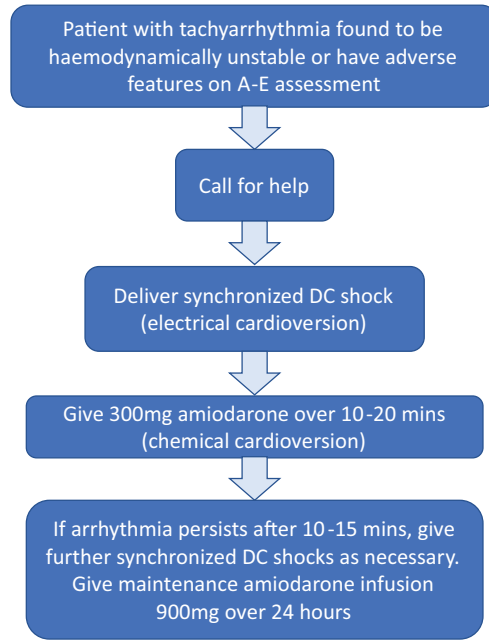


Fig. 13.3 Algorithm for treating patients who have tachyarrhythmia with haemodynamic instability

13.5.2 Management of Stable Tachyarrhythmia

13.5.2.1 Atrial Fibrillation

All irregular tachyarrhythmias with narrow QRS complexes are considered AF in the following text.

The most common **causes** of AF in the community ("big five") are hypertension, ischaemic heart disease, hyperthyroidism, pericarditis and mitral stenosis. Although all of these can cause AF in critically ill patients, the most common causes in the ICU setting are hypokalaemia, hypomagnesaemia, drugs (such as betamimetics, levosimendan or other inotropes) and infections. Often, new-onset AF is the first manifestation of sepsis.

The haemodynamic **effects** of AF on the circulation are many. The ventricles have impaired filling due to irregular duration of diastole and loss of atrial contraction ("atrial kick"). If the heart rate is very fast, this is even more pronounced. Coronary perfusion decreases, which worsens diastolic compliance of the left ventricle. In the long term, blood stagnating in the ventricles dilates the atria, which makes a successful restoration of sinus rhythm unlikely. After 48 h, blood clots may form in the left atrial appendage putting the patient at risk of stroke. This risk is greatest shortly after restoration of sinus rhythm. Whilst in new-onset AF with normal atria the aim is to restore sinus rhythm ("rhythm control"), in patients with dilated atria and chronic AF, the goal is usually to slow down the heart rate ("rate control").

The management of atrial fibrillation and atrial flutter is dependent on how long the arrythmia has been present. The following steps should be taken for all patients

in atrial flutter or atrial fibrillation who are haemodynamically stable. Firstly, obvious reversible causes should be addressed. Check the blood gas and give potassium if serum potassium is less than 4 mmol/l; try administering 10 mL of 20% magnesium sulphate over 20-30 min, as Mg slows conduction through the AV node and sometimes leads to cardioversion. Then, the approach differs depending on arrhythmia duration.

1. **Less than 48 h**—You have the following options:
   (a) Amiodarone 5 mg/kg over 20 min as a loading dose, followed by a 24-h maintenance infusion of 15 mg/kg, is the drug of choice for patients with impaired left ventricular function or those at greatest risk of haemodynamic deterioration. It will control heart rate and also restore sinus rhythm.
   (b) Beta-blockers or propafenone (where available) can be given only to stable patients with normal systolic function.
2. **Greater than 48 h, or onset unknown**—The goal of the treatment should be rate control. Restoration of sinus rhythm is unlikely and, in patients without adequate anticoagulation, risks stroke and other embolic complications. Rate control can be achieved using a beta-blocker or digoxin. Digoxin is the preferred option in most critically ill patients.

Note
IV magnesium is used to treat tachyarrhythmias due to its calcium channel blocking properties. The serum level of magnesium at the time is not relevant (unless the patient is known to have hypermagnesaemia or is already on a magnesium infusion).

13.5.2.2 Supraventricular Tachycardia

These are recognised as regular tachyarrhythmias with narrow QRS complexes. First, check the 12-lead ECG carefully to rule out the following:

- Atrial flutter—which is managed similarly to AF (see above).
- The presence of regularly shaped P-waves preceding QRS complexes suggests that we are likely dealing with an extreme sinus tachycardia—which is not an arrythmia causing deterioration ("fast, thus sick"), but rather a non-specific sign of a serious condition ("sick, thus fast"). Priority should be given to finding and treating the cause of the sinus tachycardia, e.g. hypovolaemia, hyperpyrexia and pain.

For supraventricular tachycardia (SVT), treatment should take a stepwise approach:

1. **Vagal manoeuvres** are usually the first choice of management, as they can often terminate the arrythmia without the use of drugs by stimulating the vagal nerve to increase parasympathetic stimulation to the heart. The most commonly applied vagal manoeuvre is carotid sinus massage.
2. **Adenosine** 6–12–18 mg given through a large peripheral or a central vein followed by a large saline flush, as the half-life is only 10 s. Whilst receiving adenosine, the patient should undergo continuous cardiac monitoring with a defibrillator readily available. If alert, the patient must also be warned that adenosine may make them

feel very unwell. Also, alert inexperienced members of the team as adenosine causes several seconds of asystole.
3. Beta-blocker or verapamil should be tried if adenosine fails to restore sinus rhythm.

13.5.2.3 Broad Complex Tachyarrhythmias

These are usually life-threatening arrhythmias presenting with cardiac arrest or severe haemodynamic instability. In the rare circumstance of a stable patient with broad complex tachyarrhythmia, get the crash trolley and call for help anyway and remember:

- Regular (ventricular tachycardia): give amiodarone
- Irregular (torsades de pointes or AF with aberrant conduction): give magnesium and treat as AF

13.6 Management of Patients with Bradyarrhythmia

Bradycardia is well tolerated by a normal heart as the prolonged diastolic time leads to an increased end-diastolic volume of both ventricles, which—in turn—increases stroke volume, as dictated by Frank-Starling law. Increased stroke volume compensates for reduced heart rate, and cardiac output remains normal. Impaired compliance of the ventricle (due to ischaemia or hypertrophy) or impaired contractility may dramatically change this. Key considerations for the management of bradyarrhythmias are the following:

1. Is there haemodynamic instability, i.e. adverse features listed above?
2. What is the risk that the arrhythmia deteriorates further or progresses into a cardiac arrest?

Please see the Algorithm for Bradyarrhythmias in Appendix B (page 264).

13.6.1 Stable Bradyarrhythmia

Bradyarrhythmias are commonly asymptomatic. If the patient is haemodynamically stable and has sinus bradycardia, they often do not require any specific treatment. Manage reversible causes such as:

- Drugs, in particular beta-blockers, digoxin and calcium channel blockers
- Raised intracranial pressure (Cushing reflex = bradycardia + hypertension)
- Hypo/hyperkalaemia
- Hypothermia

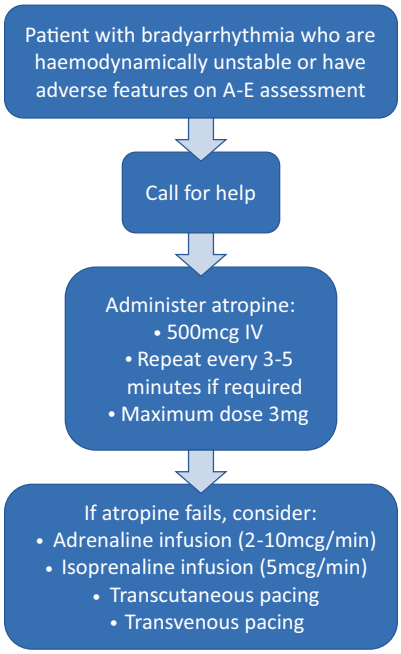


Fig. 13.4 Algorithm for treating bradyarrhythmias with haemodynamic instability

13.6.2 Unstable Bradyarrhythmia

Certain factors will influence whether a bradyarrhythmia is at high risk of progressing to asystole and subsequent cardiac arrest. These include:

- Ventricular pauses lasting longer than 3 s
- Second-degree heart block (Mobitz II subtype)
- Third-degree heart block
- Previous episodes of asystole

Although patients may be initially stable, patients with bradyarrhythmias are at high risk of deterioration and should have continuous cardiac monitoring. They should be reviewed by a cardiologist as early as possible.

If the patient is haemodynamically unstable due to the bradyarrhythmia, they should be treated urgently to prevent asystole. As in Fig. 13.4, patients should receive atropine as a first-line treatment. If this does not improve their condition after a total of 3 mg, an adrenaline (epinephrine) or isoprenaline infusion can be used. If you have not called your supervisor already, call them at this stage to discuss further management. Transcutaneous pacing using the pacing function of a defibrillator should be considered until a cardiologist arrives to consider temporary cardiac pacing. Please note that transcutaneous pacing is painful, and you should provide adequate analgesia to the patient if this is used.

Take Home Message

- Assess early for any adverse features or haemodynamic instability using the A–E approach (► Chap. 2).
- Adverse features are heart failure, myocardial ischaemia, syncope or shock.
- Identify and manage triggers of the arrhythmia, e.g., hypoxia, hyovolaemia, hypokalaemia or sepsis.
- If the patient is unstable with tachyarrhythmia, early DC cardioversion is the priority.
- If the patient is unstable with bradyarrhythmia, atropine, a chronotropic agent, or transcutaneous pacing are mainstays of management.
- In stable patients, identifying the arrhythmia is important to guide medical management.
- Continuously reassess patients with arrhythmias as they may become unstable at any time.

Further Reading

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An Approach to the Critically Ill Bleeding Patient

Nathan D. Nielsen

Contents

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Intended Learning Outcomes (ILOs)

By the end of this chapter, you should be able to achieve ILOs #2 and #3. You should also have the knowledge required to successfully achieve ILO #1.

1. Apply the principles of safe blood transfusion to a simulated patient with life-threatening haemorrhage/trauma.
2. Diagnose and propose a treatment plan for the common coagulopathies in a simulated patient or case.
3. Discuss the management of haemorrhage in a patient who is receiving an anticoagulant/antiplatelet agent.

14.1 Introduction

Much of the guidelines and medical literature on the acutely bleeding critically ill patient come from the trauma population. And while this population does encompass the majority of the haemorrhagic shock cases seen in the ICU, the management principles developed for trauma patients may not be directly or uniformly applicable to non-trauma patients. As such, there is a distinct set of skills and knowledge that a clinician needs to have in order to optimally manage this complex patient population. Among these are the ability to identify the severity of haemorrhage and the urgency of needed intervention(s); understand the tools available to identify the source of bleeding; appreciate the importance of proper vascular access and the options available to obtain it; recognize the factors that contribute to impaired haemostasis and how to correct them; and, should the situation require it, use anticoagulant and antiplatelet reversal agents. There are also key principles guiding resuscitation and transfusion that even new residents in the ICU should be aware of. This chapter should provide you a basic understanding of all of the above but should not replace local or institutional haemorrhage management or transfusion protocols. References for international guidelines on the management of major bleeding are given at the end of the chapter.

14.2 Classification of Haemorrhage

A useful framework to approaching the management of haemorrhage begins with classification of the severity of bleeding. One such classification scheme is that developed by the American College of Surgeons:

- Class I haemorrhage involves a blood volume loss of up to 15%. The heart rate is minimally elevated or normal, and there is no change in blood pressure, pulse pressure or respiratory rate. Ambulatory patients may have orthostatic hypotension.
- Class II haemorrhage (moderate haemorrhage) occurs when there is a 15–30% blood volume loss. Clinical manifestations include tachycardia (HR 100–120), tachypnoea (RR 20–24) and a decreased pulse pressure, although systolic blood pressure (SBP) changes minimally, if at all, and so does cardiac output. Sympathetic system is activated, with clinical signs of centralized circulation. The skin may be cool and clammy, and capillary refill may be delayed.

- Class III haemorrhage (severe haemorrhage) involves 30–40% blood volume loss, resulting in a significant drop in cardiac output, blood pressure and changes in mental status. Any hypotension (SBP <90 mmHg) or drop in blood pressure greater than 20–30% is cause for concern. Heart rate (≥120 and thready) and respiratory rate are markedly elevated, while urine output is diminished. Capillary refill is delayed.
- Class IV haemorrhage (also severe haemorrhage) involves more than 40% blood volume loss leading to significant depression in blood pressure and mental status. Most patients in Class IV shock are hypotensive (SBP <90 mmHg). Pulse pressure is narrowed (≤25 mmHg), and tachycardia is marked (>120 beats per minute). Urine output is minimal or absent. The skin is cold and pale, and capillary refill is delayed. Any further minor blood loss can cause collapse of circulation (usually PEA arrest). Even if such patients are successfully resuscitated, they often suffer from organ damage and failure at later stage.

Mnemonic:
0–15, 15–30, 30–40 and >40% volume loss in the respective four ACS grades of haemorrhage gave this scale a nickname: The Tennis Classification!

14.3 Identification of the Source of Haemorrhage

In order to best stabilize an acutely bleeding patient, it is essential to identify the source of bleeding. Source identification in turn leads to potential haemorrhage control options, be it endoscopic, endovascular, interventional radiology or surgical interventions. Prompt consultation with relevant specialists is essential to avoid wasted time and prevent further decompensation or blood loss. In the case of readily identifiable external haemorrhage, direct pressure remains the mainstay of haemorrhage control, including possible tourniquet use.

Ultrasound is an integral part of the initial evaluation of the trauma patient (and can be appropriately applied to the diagnosis of non-trauma bleeding patients, particularly if no bleeding site is readily apparent). Ultrasound can reliably identify free intra-abdominal fluid in the hands of proficient ultrasonographers. During the initial resuscitation, the extended Focused Assessment with Sonography for Trauma (eFAST) exam is performed to assess first for pericardial blood and then for intraperitoneal bleeding and pneumothorax.

Mnemonic:
"Blood on the floor plus four more" is a saying in the trauma arena, meaning that along with the chest and abdomen, pelvic and femoral fractures are the primary potential sources of significant blood loss.

In the non-trauma context, the most common sources are upper and lower GI bleeds, leaking aortic aneurysms and soft-tissue haemorrhage in coagulopathic patients.

Gauge	Approximate Flow Rate to Gravity (mL/min)	Time to Infuse IL (min)
14G	250	4
16G	150	7
Cordis	130	8
18G	100	10
15G Humeral IO	80	13
16G Distal Port Triple Lumen	70	15
15G Tibial IO	70	15
20G	60	17
22G	35	29
18G Prox Port Triple Lumen	30	34

Fig. 14.1 Flow rates through different types and sizes of IV and IO access [1]

14.4 Establishing Vascular Access

Vascular access should be established as soon as possible, with (ideally) two or more short, large-bore (16-gauge or lower) peripheral intravenous (PIV) lines in the antecubital fossa. Intraosseous (IO) devices can be placed rapidly and should be considered as an alternative in situations where IV access is delayed or insufficient. (N.B.: Contrary to some beliefs, blood products *can* be reliably administered through IO devices.)

Placement of a large-bore (8 French, dialysis catheter or Swan sheath) central venous catheter can be considered when adequate PIV access cannot be obtained and also allows for the safe administration of vasopressor support.

Note: Using small-bore PIVs or long catheters (e.g.: PICC lines or multi-lumen CVC catheters) is not ideal for the resuscitation of a haemorrhaging patient, as blood product or IV fluid administration will be relatively slow through such catheters. (See Fig. 14.1 for a comparison of flow rates through various catheters commonly used in the ICU.)

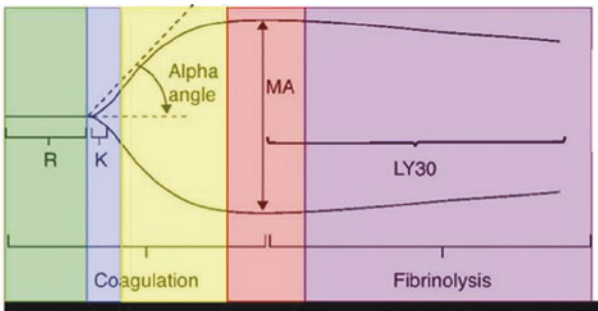
14.5 Key Resuscitation and Transfusion Principles

The management of haemorrhage will vary depending upon the source of blood loss, vital signs, degree of haemorrhage and available resources (e.g. haemorrhage control options, blood products, anticoagulant reversal agents).

Important principles guiding the management of haemorrhage beyond those detailed above include the following [2–4]:

- Minimize the use of IV fluids in the resuscitation of haemorrhagic shock—IV fluids should only be used to resuscitate hypotensive patients (MAP <65 mmHg), and administration should cease as soon as blood products become available. If IV fluids must be administered, balanced crystalloid solutions are preferred.
- Blood products should be administered as soon as they are available.

- The optimal RBC:plasma:platelet ratio is not well established, though multiple professional societies recommend a 1:1:1 ratio in the acutely haemorrhaging *trauma* patient. For non-trauma patients, this ratio is far less clear and may result in a higher incidence of complications and lower survival rates.
- Tranexamic acid (TXA) is an inhibitor of fibrinolysis. Hyperfibrinolysis can contribute to coagulopathy, particularly in the setting of trauma. A 1g IV TXA bolus should be given followed by a 1g infusion over 8 hours in bleeding trauma patients whenever hyperfibrinolysis is suspected or detected by viscoelastic testing (e.g. thromboelastography or thromboelastometry) (see below). TXA can also be considered in non-trauma patients in the setting of confirmed or strongly suspected hyperfibrinolysis.
- Whole blood would, in theory, be the ideal product to replace blood loss. It is being investigated for the resuscitation of trauma patients, but data are not yet available, and most importantly, whole blood is not routinely available in blood banks.
- The use of viscoelastic testing (thromboelastography (TEG)/thromboelastometry (ROTEM)) or comparable rapid point-of-care assessment of coagulation should be the guide for trauma resuscitation whenever possible and can also be considered as a guide for non-trauma resuscitation. (See ◘ Fig. 14.2 for an illustration of viscoelastic test results and recommended transfusion responses.)



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rebelem.com

Thromboelastogram (TEG)

Components	Definition	Normal Values	Problem with...	Treatment
R Time	Time to start forming clot	5 – 10 minutes	Coagulation Factors	FFP
K Time	Time until clot reaches a fixed strength	1 – 3 minutes	Fibrinogen	Cryoprecipitate
Alpha angle	Speed of fibrin accumulation	53 – 72 degrees	Fibrinogen	Cryoprecipitate
Maximum Amplitude (MA)	Highest vertical amplitude of the TEG	50 – 70 mm	Platelets	Platelets and/or DDAVP
Lysis at 30 Minutes (LY30)	Percentage of amplitude reduction 30 minutes after maximum amplitude	0 – 8%	Excess Fibrinolysis	Tranexemic Acid and/or Aminocaproic Acid

◘ **Fig. 14.2** Thromboelastogram (TEG) tracing with associated treatment options. (n.b.: DDAVP = desmopressin) [5]

- While typed and cross-matched blood products are preferable, the preparation and vetting of fully cross-matched products may take 20 min or more. If warranted by the situation, emergency-release blood products (uncross-matched Group O RBCs and Group AB plasma (sometimes "low-titre" Group A)) should be requested and administered—these can usually be obtained rapidly, though procedures for approving the use of such products may vary.

14.6 Resuscitation Targets in the Bleeding Patient

Resuscitative efforts should proceed in parallel with source control and not cause delays. Before definitive source control is obtained, ongoing blood loss can be minimized by targeting a lower-than-normal blood pressure, e.g.: SBP of **80–90 mmHg**. This blood pressure should be sufficient to perfuse vital organs but not interfere with haemostasis. (N.B.: An important exception is in patients with traumatic brain injury where the SBP goal should be ~100 mmHg.) Practically, blood pressure control can usually be achieved by titrating the infusion rate of blood products. Hypovolaemic bleeding patients usually respond very nicely to adjustments in the rate of volume replacement. Physicians skilled in managing haemorrhage resuscitation always think ahead and work to have enough blood products available in time. (N.B.: It is also extremely important to regularly communicate with the blood bank, especially in a massive haemorrhage situation [2].)

Norepinephrine (noradrenaline) and other vasopressors have a very limited role in the resuscitation of haemorrhagic shock and, as can be inferred from physiology, are minimally effective in the absence of blood volume replacement (i.e.: transfusion).

Important Note:
Haemoglobin levels are NOT useful targets in actively bleeding patients.

Only after the bleeding has been controlled and shock resolved can transfusion needs be determined by haemoglobin levels.

14.7 Correction of Factors that Contribute to Delayed Haemostasis

Multiple complications that develop during both the bleeding process and resuscitative efforts can contribute to delayed haemostasis. The following factors should be monitored and, if possible, corrected in order to optimize the likelihood of achieving haemostasis (see ◘ Fig. 14.3):

- Hypocalcaemia: Hypocalcaemia contributes to impaired clotting factor function (as calcium is Factor IV in the classic clotting cascade). The citrate used as an anticoagulant in the majority of blood products worldwide can chelate ionized

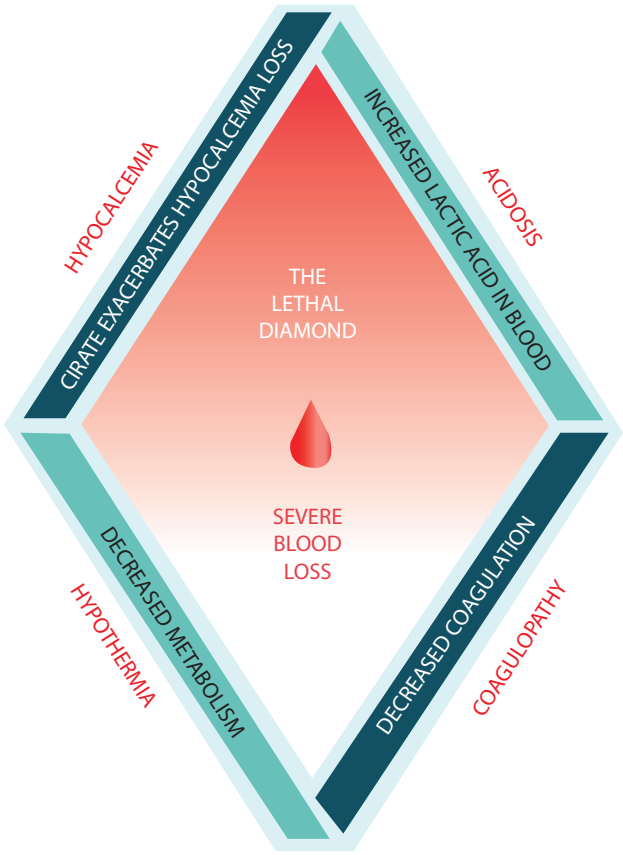

Fig. 14.3 The lethal diamond: hypocalcaemia, acidosis, hypothermia, coagulopathy. (Adapted from: Ditzel RM Jr, Anderson JL, Eisenhart WJ, et al. A review of transfusion- and trauma-induced hypocalcemia: Is it time to change the lethal triad to the lethal diamond? J Trauma Acute Care Surg. 2020;88(3):434-439. doi:10.1097/TA.0000000000002570)

calcium, making it unavailable to aid in the activation of other clotting factors. If possible, ionized calcium levels should be closely monitored during resuscitation with large quantities of blood products and replaced aggressively. If ionized calcium levels cannot be measured in a timely fashion, empiric replacement of calcium with 1g of IV calcium (gluconate or chloride) can be considered following every 3–4 blood products transfused.

- Acidosis: Severe acidosis (pH <7.2) impairs both clotting factor function and platelet activity. Though options to address severe acidosis may be limited, you should minimise interventions that can potentially worsen acidosis.
- Hypothermia: Hypothermia can impair clotting factor function, particularly as core temperatures approach <32 °C. External warming (e.g.: air warming devices, blankets) should be applied whenever possible to the bleeding patient. Further, if large quantities of blood products are to be administered, a blood warming device

should be used if accessible—as RBCs and thawed plasma are typically transported at 6–10 °C, transfusion of these products in even moderate quantities can result in a substantial drop in core temperature.

14.8 Reversal of Anticoagulant and Antiplatelet Agents

Many patients, particularly older adults with comorbidities, may be taking anticoagulants. While a comprehensive review of anticoagulant reversal is out of the scope of this chapter, the following anticoagulant:reversal agent pairings are worth noting [6]:

- Warfarin: Vitamin K PO or IV (the effect will only appear after 24 hours); plasma transfusion; pro-thrombin complex concentrates (PCCs) can be used in the setting of CNS haemorrhage or life-threatening haemorrhage from other sources.
- Direct thrombin inhibitors (e.g.: dabigatran): idarucizumab; haemodialysis may also help reduce the amount of circulating anticoagulant.
- Factor Xa inhibitors (e.g.: rivaroxaban, apixaban, edoxaban): PCCs; factor eight inhibitor bypassing activity (FEIBA); andexanet alfa.
- Heparin: protamine sulphate.
- Low-molecular-weight heparin (LMWH): protamine sulphate (n.b.: will only partially reverse the anticoagulant effect); andexanet alfa.

Many of these reversal agents (PCCs, FEIBA, andexanet alfa) are associated with significant rates of venous thromboembolism (VTE) following their use—appropriate surveillance for this complication should be implemented if these agents are used.

The options for reversing the effects of antiplatelet agents (e.g.: aspirin, clopidogrel) are far more limited. As a general rule, platelet transfusions should be avoided unless significant thrombocytopenia ($<50 \times 10^9$/L) is also present, as transfusions in this context are ineffective and may even worsen clinical outcomes, including mortality. However, if antiplatelet drug reversal is deemed necessary to obtain haemostasis, the following options can be considered:

- Desmopressin (ddAVP)
- Cryoprecipitate transfusion *(n.b.: very limited data to support this recommendation)*

Finally, as a novice in the ICU, you are not expected to manage haemorrhage on your own. Call for help from your supervisors early as the situation can deteriorate rapidly. A clinical pharmacist or haematologist can be useful for getting advice on anticoagulants and their antagonists. You might also need to activate the major haemorrhage protocol in your hospital depending on the trigger threshold in your institution. This activates contact with a transfusion medicine physician, lab, blood bank and porters in the hospital, in addition to key clinical staff.

Take-Home Messages

- Call for help early!
- The classification of haemorrhage severity proposed by the American College of Surgeons links the volume of blood loss with pathophysiology and clinical signs.
- Identification of the source of bleeding is essential, as source identification guides potential haemorrhage control options.
- Vascular access should be established as soon as possible, with a minimum of two short large-bore (16-gauge or lower) IV lines in the antecubital fossa. Other options include dialysis catheters or short large-bore central venous catheters.
- Blood products should be transfused as soon as possible, and IV fluids should be minimized; a RBC:plasma:platelet ratio of 1:1:1 is used for life-threatening traumatic haemorrhage in many institutions.
- In a rapidly bleeding patient, transfusion-based resuscitation targeting an SBP of 80–90 mmHg is generally appropriate, and haemoglobin levels are irrelevant.
- Hypocalcaemia, hypothermia and acidosis can impair haemostasis and should be monitored and corrected whenever possible.
- In the event of haemorrhage in the setting of anticoagulant use, the use of a reversal agent matched to the anticoagulant should be strongly considered.

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Analgesia and Sedation

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Contents

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Intended Learning Outcomes

After reading this chapter you should be able to achieve ILO #2 and have the knowledge necessary to achieve ILO #1

1. Safely prescribe sedation and analgesia in a simulated ICU setting or case, including adequate use of sedation holds.
2. **Discuss suitable options for perioperative pain management**.

15.1 Introduction

The relief of suffering is a fundamental principle in practice of all health professionals. In patients admitted to intensive care units, the degree of pain seems to be disproportionately higher, as many of them are at the limit of their injury or illness. Additionally, the discomfort associated with the components of ICU care routines, such as aspiration of secretions, positioning, changes in wake/sleep pattern or changing dressings/bandages, is significant and often undervalued [1, 2].

In addition to that, many ICU patients are also given sedatives to relieve anxiety and induce amnesia. In the early days, high doses of hypnotics used to be administered, sometimes together with neuromuscular blocking agents, to provide "rest for recovery". Over the last two decades, this paradigm has changed. Overuse of sedation is be associated with adverse outcomes like delirium, disturbed sleep, prolonged ICU and hospital stay, and death—mostly as a consequence of reduced mobility and prolonged unconsciousness.

In modern intensive care, much emphasis is therefore put on pain control, whilst the use of sedatives and hypnotics is minimised by strict adherence to goal-targeted sedation, with deep sedation being only reserved for specific subgroups of patients (e.g. in patients with increased intracranial pressure and status epilepticus seizure or to facilitate mechanical ventilation in severe ARDS). Also, protocolised sedation and/or daily sedation holds (i.e. interrupting the infusion of sedatives) have become the standard of care for stable ICU patients to prevent drug accumulation and allow for spontaneous breathing and awakening trials.

15.2 Pain in the ICU

15

Pain is an unpleasant multidimensional experience involving a sensory component and an emotional component associated with actual or potential tissue damage. Severe pain negatively affects the critically ill patient on several levels beyond the mere unpleasant experience.

Consequences of pain and the consecutive stress response to it are the following:

- *Physiological*: increased myocardial oxygen consumption, impaired healing and immune function, excess muscle loss, hyperglycaemia, increased stress hormone release, vasoconstriction, limited cough reflex, increasing the risk of atelectasis and other pulmonary complications
- *Psychosocial*: development of chronic pain, anxiety and post-traumatic stress disorder, impaired quality of life

Typical sources of pain for critically ill patients are the following:

- *At rest*: site of surgery/injury, back or limb pain, abdomen (constipation, spasms), endotracheal tube, indwelling tubes/devices.
- *Procedural pain*: chest drain removal, wound drain removal, arterial line insertion and suctioning have been found to be most painful in critically ill patients.

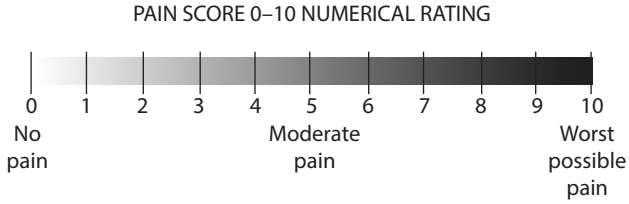
15.3 Assessment of Pain in Critically Ill Patients

A consistent approach to pain assessment and management is paramount as the inability of some of our ICU patients does not negate their experience of pain or the need for appropriate pain management. Systematic and repeated assessment is associated with improved pain management, improved patient satisfaction, reduced sedative use and reduction in the duration of mechanical ventilation and ICU stay.

Note: Normal blood pressure and heart rate in an unresponsive ICU patient do not rule out pain. Vital signs alone should not be used as assessment of pain.

15.3.1 Patients, Who Can Self-Report (Conscious)

The numerical rating scale NRS (1–10) with or without visual support has very good validity and reliability for assessing pain.



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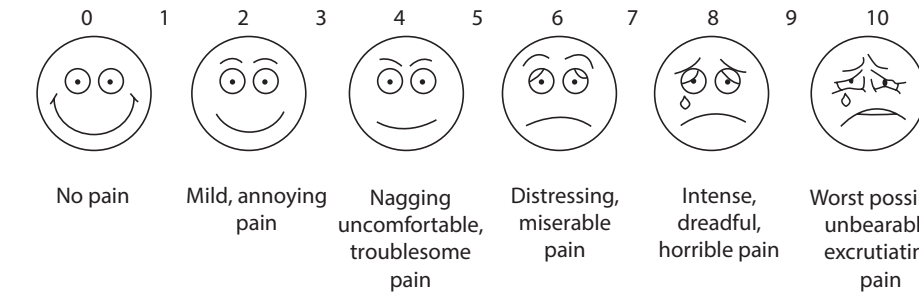
The visual analogue scale VAS (1–10) is the modification of NRS with visual support.



Derived from ► https://operativeneurosurgery.com/doku.php?id=visual_analog_scale

15.3.2 Patients, Who Cannot Self-Report Due to Sedation or Disorders of Brain or Mind

The assessment of pain is an essential part of routine medical assessment of an ICU patient, and it is regularly performed and recorded by nurses. The tools used for detecting pain in patients who cannot self-report are based on the observation of facial expression, body position, muscle tone and compliance with the ventilator. The most used tools are the *Behavioural Pain Scale* (BPS) and the *Critical Care Pain Observation Tool* (CPOT). It is important to acknowledge that they can identify pain but do not determine the severity of pain.

BPS: score of >5 indicates 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 limbs	No movement	1
	Partially bent	2
	Fully bent with finger flexion	3
	Permanently retracted	4
Compliance with ventilation	Tolerating movement	1
	Coughing but tolerating ventilation for most of the time	2
	Fighting ventilator	3
	Unable to control ventilation	4

Payen et al., Crit Care Med (2001)

CPOT: score of >2 indicates pain

Indicator	Description	Score	
Facial expression	No muscular tension observed	Relaxed, neutral	0
	Presence of frowning, brow lowering, orbit tightening, and levator contraction	Tense	1
	All of the above facial movements plus eyelid tightly closed	Grimacing	2
Body movements	Does not move at all (does not necessarily mean absence of pain)	Absence of movements	0
	Slow, cautious movements, touching or rubbing the pain site, seeking attention through movements	Protection	1
	Pulling tube, attempting to sit up, moving limbs/ thrashing, not following commands, striking at staff, trying to climb out of bed	Restlessness	2
Muscle tension Evaluation by passive flexion and extension of upper extremities	No resistance to passive movements	Relaxed	0
	Resistance to passive movements	Tense, rigid	1
	Strong resistance to passive movements, inability to complete them	Very tense or rigid	2
Compliance with the ventilator (intubated patients)	Alarms not activated, easy ventilation	Tolerating ventilator or movement	0
	Alarms stop spontaneously	Coughing but tolerating	1
OR	Asynchrony: blocking ventilation, alarms frequently activated	Fighting ventilator	2
Vocalization (extubated patients)	Talking in normal tone or no sound	Talking in normal tone or no sound	0
	Sighing, moaning	Sighing, moaning	1
	Crying out, sobbing	Crying out, sobbing	2
Total, range			0-8

Gélinas et al., Am J Crit Care (2006)

15.4 Assessment of Sedation in ICU Patients

The most common scale used to assess and target the level of sedation is the *Richmond Agitation and Sedation Scale* (RASS). For most ICU patients, the goal is to achieve excellent pain control first and then a RASS of 0 to −1.

RASS (Richmond Agitation Sedation Scale)		
4	Combative	Overtly combative, violent, immediate danger to staff
3	Very agitated	Pulls or removes tubes or catheters; aggressive
2	Agitated	Frequent non-purposeful mvmt, fights ventilator
1	Restless	Anxious but movements not aggressive or vigorous
0	Alert and calm	
−1	Drowsy	Sustained awakening to voice (≥10sec)
−2	Light sedation	Briefly awakens with eye contact to voice (<10 sec)
−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
−5	Cannot be aroused	No response to voice or physical stimulation

Derived from ► https://www.grepmed.com/images/9144/agitation-nursing-richmond-diagnosis-rass

15.5 Analgesia-Based Sedation/Analgosedation

15.5.1 Principles

To make sure that oversedation is avoided whilst adequate pain relief is provided, modern analgesia-based sedation follows some important rules:

- Prioritise analgesia before anxiolysis/hypnosis/sedation. This in turn means that significantly less hypnotic is required to have an awake and comfortable patient. This is very important: ensure adequate analgesia BEFORE titrating sedatives (so-called **A1—analgesia first—strategy**).
- Use the Analgesic Ladder proposed by the World Health Organization (WHO), since it proposes a structured and gradual approach to pain.
- Anticipate pain (e.g. administration of a bolus of opioid before mobilisations), as pain prevention is more effective than treatment of previously established pain.
- Goal-directed sedation and analgesia avoid unnecessary treatment. Take the time to carry out drug titration until the patient is well.
- Use of a multimodal pharmacological approach (use of different classes and modes of analgesic drugs) reduces side effects and increases quality of analgesia. Use co-adjuvants (i.e. magnesium, lignocaine, ketamine, α_2-agonists and gabapentin, according to local protocols).
- Understanding the interplay between drugs, organ dysfunction and adverse effects, especially in critically ill patients, helps to individualise analgesic regimen (if unsure, discuss with your clinical pharmacist or supervisor).
- If the patient is well on analgesia with a specific therapeutic regimen from another department, this should not be modified.
- Use local guidelines and protocols for pain management and sedation (Fig. 15.1).

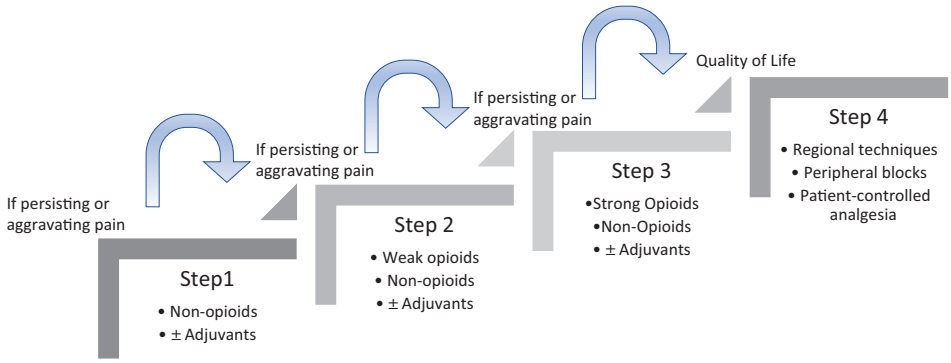


Fig. 15.1 Revised WHO fourth-step pain ladder. The additional step 4 is an "interventional" step and includes invasive and minimally invasive techniques. Such a four-step ladder reflects the advances in non-opioid modalities for better pain relief. Integrative medicine therapies can be adopted in each step for reducing the use of analgesics. If the non-opioids and weak opioids fail, invasive interventions (step 4) can be recommended before upgrading to strong opioids

15.5.2 Pharmacokinetic and Pharmacodynamic Considerations

The uptake, metabolism, effect, elimination and excretion/clearance of analgesics and sedatives (plus other medications) are often deranged during critical illness. In turn, there is a high inter-individual variability in drug-effect relation and in pharmacokinetics of analgesics and sedatives.

Examples include but are not limited to:

- Unpredictable absorption of oral drugs due to ileus or reflux, which limits the use of drugs that are only available in oral form in some patients (e.g. quetiapine, trazodone). Whenever possible, intravenous administration is preferred as it allows faster onset of action and titration.
- Context-sensitive half-life means that the duration of residual analgesic or sedative effect after stopping the infusion depends on the duration of its previous administration. This phenomenon is explained by the initial distribution of the drug into slow compartments (e.g. fat) and subsequent slow release during redistribution after discontinuation of the infusion. Drugs with a long context-sensitive half-life are less favourable choices when prolonged treatment is necessary. This is the reason why daily sedation holds are important—they prevent the accumulation of sedatives and failure to wake up.
- Old age and renal and hepatic dysfunctions are associated with impaired drug metabolism, elimination/excretion and risk of over-treatment.
- Drug tolerance may develop quickly (typically to opioids), and some ICU patients may require very large doses. Actively consider and account for withdrawal, and never stop opioids abruptly in patients on high opioid doses or long-term treatment.

The dosage and basic pharmacological consideration for individual drugs are in the ICU Drug Chart (Appendix B).

15.5.3 Practical Approach to Pain Control in the ICU Patient

15.5.3.1 Modalities of Pain Management

- Start with non-pharmacological means, such as checking for comfortable position, not too tight dressing and applying cooling where reasonable. The use of a psychological approach—a calm, empathetic and explanatory attitude towards diagnostic and therapeutic actions—reduces anxiety and enhances the analgesic effect of drugs. Music therapy is also recommended. The use of physical treatments as massages, cold or heated packs and fracture immobilisation in case of trauma reduce pain and vascular and nervous complications.
- Systemic analgesia can generally be facilitated through different routes of administration (intravenous, enteral, transdermal, subcutaneous, intramuscular, nasal) that may be considered in certain settings. However, in critically ill patients, intravenous administration is preferred due to the altered pharmacokinetic and pharmacodynamic profile in these patients, and it also allows faster onset of action and titration.

- Patient-controlled analgesia (PCA) through PCA pumps is useful in conscious post-surgery or malignancy patients. The use of PCA increases patient comfort and feeling of self-control and reduces the risk of opioid overdose. Importantly, the patient must be pain free when PCA is being started.
- Regional or neuraxial analgesia (e.g. epidural or regional catheters) or use of local anaesthetics should always be considered especially in surgical patients or trauma (e.g. fractured ribs). In most centres and countries, insertion of neuraxial catheters (e.g. epidural catheter) is performed by anaesthetists. Those interventions follow strict guidelines regarding coagulation status and use of anticoagulants.

15.5.3.2 Analgesic Drugs

In the following part, we provide some general thoughts on analgesic drugs and their characteristics for practical consideration. Detailed information on commonly used analgesics is given in the ICU Drug Chart Appendix B.

- Modern analgesia follows a multimodal approach, meaning combining different classes of analgesics (non-opioids and opioids) and adjunctive drugs that may not have analgesic properties per se but reduce opioid use.
- **Paracetamol** (e.g. 1 g i.v. every 6 h) is often the first-choice non-opioid analgesic in ICU patients. Administer slowly as rapid infusion causes transient hypotension. Caution is required in liver failure.
- **Intravenous opioids** are the cornerstone of pain management in critically ill patients. Use a step-up approach for acute pain control (e.g. dilute 10 mg of morphine to 10 mL and give 1–2 mg every 3–5 min until pain is controlled). Only then start opioid infusion or PCA. Typical adverse effects of opioids may be aggravated in the critically ill patient and include respiratory depression, hypotension, bradycardia, histamine release, ileus, constipation, nausea, vomiting, delirium, hallucinations and hyperalgesia. There is a whole range of opioids in use in ICU (see table in Appendix A) in the ICU Drug Chart Appendix. However, morphine, sufentanil and remifentanil are most frequently used in ICU.
  - Morphine is the oldest and cheapest and has least pharmacokinetic interaction with other drugs. Accumulation of active metabolites makes its use in renal dysfunction problematic.
  - Sufentanil is a synthetic opioid 500 times as potent as morphine. It is widely used in anaesthesia. In ICU patients, it has an advantage over morphine as it accumulates less in patients with renal dysfunction and has a more rapid onset of action.
  - Remifentanil has an extremely rapid onset of action and a short half-life due to its specific mode of elimination. That is why it offers an advantage in rapidly waking up patients. However, one needs to keep in mind to provide other pain relief when stopping remifentanil as its analgesic effect wears off so quickly.

  Frequently reassess pain and use goal-directed stepwise down-titration of opioid infusion or switch to bolus treatment where possible. Prolonged opioid use is associated with tolerance and withdrawal. Nonetheless, this is unavoidable in some ICU patients. Note: Fentanyl can be used as a bolus, but it is not recommended for prolonged infusions due to its extremely long context-sensitive half-life.
- **Analgesic adjunctives** include agents like gabapentinoids, tricyclic antidepressants, alpha-2-agonists and ketamine. They may reduce pain intensity and opioid consumption in post-operative patients in a multimodal concept.

15.5.4 Refractory Pain and Special Circumstances

It is not uncommon to encounter a patient in ICU with pain that is difficult to control. Start with reviewing the drug history of such a patient first. If the patient is on long-term opioid use (medical or illicit), continue the equivalent dose whilst in ICU and add opioid to control acute pain on top of this chronic dose. Similarly, do not discontinue chronic tricyclic antidepressants or gabapentinoids unless you have a good reason to do so.

Here are other tips for refractory pain:

- Ketamine in subanaesthetic dose (bolus 0.3–0.5 mg i.v. and/or continuous infusion usually started at 0.1–0.2 mg/kg per hour) can be very effective and reduce opioid doses in perioperative setting (e.g. spinal surgery, burns) and facilitate procedures in ICU (e.g. dressing change).
- In patients with pain that is seemingly unusual to circumstances, always ask yourself what else is going on. Always consider surgical complications such as bowel content leak, haemoperitoneum, deep wound infections or limb compartment syndromes.
- Reconsider neuraxial and regional analgesia techniques and ask anaesthetists for advice. Some hospitals provide consultation services for specialists in the management of chronic and acute pain; consider presenting your case to them.

15.5.5 Practical Approach to Sedation in ICU Patients

The word "sedation" comes from the Latin "sedare", or "to caress", and consists of the relief of anxiety/agitation whilst inducing a state of tranquillity. The purpose of sedation depends primarily on the acute process and the necessary interventions that the patient goes through. Currently, light levels of sedation are recommended (unless special circumstances), as these are associated with a reduction in the length of stay in the ICU. Sedation is a dynamic process determined by the patient's condition at any given time. Thus, the desired level of sedation must be defined at the beginning of therapy and reassessed daily as the clinical situation changes.

15.5.5.1 Principles of Sedation in ICU

- Sedation of agitated patients should be started only after providing adequate analgesia and treating reversible physiological causes ("A1 Strategy").
- A sedation goal should be established and regularly redefined for each patient using a validated sedation assessment scale.
- The dose titration of the sedative to a defined goal is recommended, with systematic tapering of the dose or daily interruption with re-titration to minimise prolonged sedative effects.
- Using propofol is preferable to midazolam, as this strategy has been shown to improve patients' outcomes.
- The use of sedation guidelines, an algorithm or a protocol is recommended.

15.5.5.2 Commonly Used Sedatives

Here, you find some specifics and practical considerations on frequently used sedatives in the ICU setting. For detailed information see Appendix A (page 248).

- **Propofol** is the most used hypnotic agent. Common side effects are (profound) hypotension and green-coloured urine. Prolonged administration and/or high doses may induce rare but fatal propofol infusion syndrome (PRIS): arrhythmias, lactic acidosis, heart failure and rhabdomyolysis.

Practical Tips on Propofol Titration

1. Indicate the desired sedation level, according to the RASS.
2. Start propofol infusion:
   (a) Maintain initial infusion at 1 mg/kg/h.
   (b) Titrate until the desired RASS level is reached (up to 3 mg/Kg/h).
   (c) Optimise sedation level: If the patient is oversedated, stop the infusion until the target RASS is reached and then restart with 50% of the dose.
   (d) Daily interruption of sedation (in the morning, after hygiene).

Notes: If infusions last longer than 7 days, consider progressive weaning and pay attention to complications (propofol infusion syndrome—PRIS, hyperlipaemia).

- **Alpha-2-mimetics** (clonidine, dexmedetomidine) reduce the release of endogenous catecholamines and have mild sedative and anxiolytic effects without causing respiratory depression. They are used to treat agitation and withdrawal syndromes and, in some units, replace propofol as the main sedatives for light sedation.

Practical Tips on Dexmedetomidine Titration

1. Indicate the desired sedation level, according to the RASS.
2. Start infusion:
   (a) Give a loading dose of 1 μg/kg over 10 min.
   (b) Followed by continuous infusion of 0.2 μg/kg/h.
   (c) Titrate until the desired RASS level is reached (up to 0.7 μg/kg/h).
   (d) Optimise sedation level: if the patient is oversedated, decrease the infusion by 50% of the dose.
   (e) Daily interruption of sedation (in the morning, after hygiene).

Notes: DEX has very good safety profile considering that there have been no adverse effects, except for oversedation in the cases of an accidental overdose of 2.5–60 times of intended dosages. Side effects include hypotension (transient hypertension may develop following high dose of DEX through activation of peripheral vascular α2B receptor), bradycardia and decreased cardiac output. It is frequently used in weaning and extubation periods.

- **Midazolam** is a benzodiazepine. Its use has declined dramatically through recent years as it is associated with delirium. It may accumulate in renal failure and lead to oversedation. It is mostly reserved for the treatment of status epilepticus, withdrawal syndromes and overdose of stimulant drugs or in patients in whom the desired level of sedation cannot be achieved by propofol infusion alone.

15.5.5.3 Therapeutic Use of Deeper Sedation

Deep sedation (i.e. RASS −4 to −5) with or without the use of neuromuscular blocking agents is still occasionally needed for specific purposes in the ICU setting. Most commonly, this strategy is implemented in patients:

- With increased intracranial pressure (here, even i.v. barbiturates such as thiopentone may rarely be indicated—senior decision only)
- With refractory status epilepticus (EEG monitoring is usually required)
- Who are very difficult to ventilate as in life-threatening asthma or severe ARDS
- Who have suffered post-cardiac arrest to facilitate targeted temperature management

In these subgroups, daily sedation holds are not routinely performed. However, the ongoing need of deep sedation must be evaluated daily. Before sedation is lifted, always make sure that the effect of neuromuscular blocking agents has worn off had they been used.

Take-Home Messages

- The overarching goal of analgesia and sedation is to make ICU stay bearable for the patient and to avoid negative physiological and psychosocial consequences.
- The treatment target and current degree of analgesia, sedation and anxiety should be documented at least once per shift with the use of validated scales.
- Pain must be dealt with first. Only then hypnotics and sedatives are added if required to achieve the desired level of sedation.
- Multimodal pain therapy means integration of non-pharmacological means with pharmacological options like non-opioid and opioid analgesics as well as analgesic adjuncts and, where appropriate, also neuraxial and regional analgesia techniques.
- Intravenous opioids are the cornerstone of pain treatment in ICU.
- Stand at the bedside of a patient in pain and top up the analgesic until pain control is achieved. It may take several minutes before i.v. opioids kick in. Only then start i.v. opioid infusion or PCA.
- For all ICU patients, a target RASS of 0/−1 is recommended and deeper sedation must only be reserved for patients with specific indications.
- Daily spontaneous awakening trials and spontaneous breathing trials are recommended in patients with a RASS ≤−2, if there are no contraindications.

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Agitation and Delirium

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Contents

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Intended Learning Outcomes

After reading this chapter you should be able to achieve ILO #1 and #2.

1. Discuss the physical and psychosocial needs of hospitalised patients with regard to the prevention of delirium.
2. Describe the signs of hypo- and hyperactive delirium and treatment options.

16.1 Introduction

Delirium is an acute and fluctuating disturbance of consciousness and cognition, with inattention or disorganised thinking. It affects up to 80% of mechanically ventilated adult ICU patients and is associated with increased mortality, prolonged ICU and hospital LOS, and development of post-ICU cognitive impairment. Nearly half of the patients admitted to a hospital with an acute condition will undergo some form of *delirium* during their admission [1–4]. There are three subtypes of delirium, described in ◘ Table 16.1.

Besides minimising the use of sedation and avoiding benzodiazepines, there are other modifiable risk factors in reducing ICU *delirium* incidence, like preventing sleep disruption, maintaining euglycaemia, controlling pain, and judicious use of steroids and neuromuscular blockers. Pre-existing dementia appears to be the strongest predictor for the occurrence of delirium. ◘ Fig. 16.1 states the main risk factors for developing *delirium*.

◘ **Table 16.1** Subtypes of delirium

Hyperactive *delirium*	**Hypoactive *delirium***	**Mixed *Delirirum***
• Abnormal psychomotor activity (agitation) • Emotional disturbances (fear, anxiety, anger, euphoria) • Hallucinations and delusions	• Calm or lethargic • Depression, apathy • Confusion and sedation	• The fluctuation between the other two subtypes

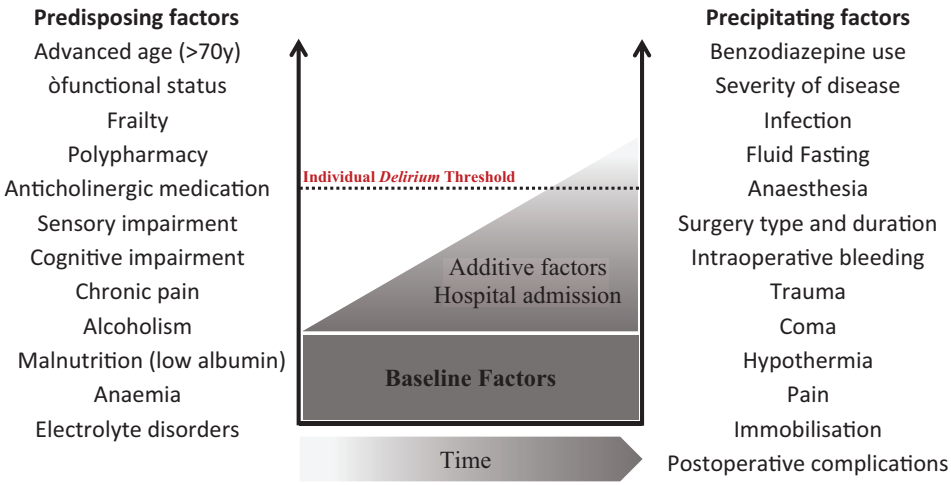

Fig. 16.1 Diagram of predisposing and precipitating factors of delirium. As the number of baseline factors increases, the more it approaches the individual delirium threshold, therefore needing fewer additional precipitating factors to cross that threshold and develop delirium

16.2 Risk Factors

Delirium is a multifactorial disorder. Factors that increase the risk for delirium can be classified into those that increase baseline vulnerability (predisposing factors) and those that precipitate the disturbance (precipitating factors). Bear in mind that risk factors for developing delirium are additive. Fig. 16.1 states the main risk factors for developing delirium.

16.3 Delirium Prevention

ICU interprofessional daily practices are the most important factors to decrease delirium incidence and its consequences. Delirium prevention strategies can be categorised as non-pharmacologic, pharmacologic, and combined pharmacologic/non-pharmacologic approaches. The features of each are described in Table 16.2 below.

Table 16.2 Delirium prevention strategies

Non-pharmacologic (recommended)	Pharmacologic
• Noise reduction • Sleep promotion at night (avoid routine procedures at night, reduce lights) • Time and space orientation (glasses and hearing aids) • Physical activity and early mobilisation • Mental stimulation with occupational therapy • Regular visits of family and friends • Avoid dehydration • Avoid physical restraints	• Minimise use of sedation • Avoid benzodiazepines • Avoid anticholinergic drugs • Use of α_2-agonists (not evidence based)

There is no official recommendation for using a pharmacologic *delirium* prevention protocol in adult ICU patients, as no compelling data demonstrates that this reduces delirium incidence or duration. The use of propofol for the sole purpose of improving sleep is not recommended, because it changes the normal sleep stages with the suppression of rapid eye movement (REM).

Do Not Forget!

At least once per shift:

- Screen for POD, anxiety, and pain.
- Check for cognition stimulation, and support day-night rhythm with non-pharmacological treatment.
- Check for oral nutrition and enough oral fluid intake.
- Check for early mobilisation.
- Check for catheters and foreign material → take it out if no more indication.

16.4 Assessment of *Delirium*

Assessment of ICU patients for delirium should be done on a daily routine basis, using checklist tools. The Confusion Assessment Method for the ICU (CAM-ICU) Table 16.3 and the Intensive Care Delirium Screening Checklist (ICDSC) are the most reliable delirium diagnosis and monitoring tools in adult ICU patients. It is likely that a translated version is used in your ICU.

Table 16.3 Confusion Assessment Method for the ICU (CAM-ICU). Adapted from [5]

Confusion Assessment Method for the ICU (CAM-ICU) flow chart		
1. **Acute change or fluctuating course of mental status**:		**Delirium present**
• Is there an acute change from the mental status baseline? **OR** • Has the patient's mental status fluctuated during the past 24 h?	If yes, go to 2	
2. **Inattention**:		
• "Squeeze my hand when I say the letter 'A'". Read the following sequence of letters: SAVEAHAART or CASA-BLANCA or ABADBADAAY ERRORS: No squeeze with "A" and squeeze on letter other than "A".	>2 errors, go to 3	
3. **Altered level of consciousness**:		
Current RASS level	RASS not zero → RASS zero, go to 4	
4. **Disorganised thinking**:		
1. *Will a stone float on water?* 2. *Are there fish in the sea?* 3. *Does one pound weigh more than two?* 4. *Can you use a hammer to pound a nail?* Command: "Hold up these many fingers" (hold up two fingers) "Now do the same thing with the other hand" (do not demonstrate) OR "Add one more finger" (if the patient is unable to move both arms)	>1 error →	

16.5 Bundle ABCDEF (the "ICU Liberation" Bundle)

The ABCDEF bundle represents one method of approaching the organisational changes that create a culture shift in our treatment of ICU patients. The ABCDEF bundle includes Assess, prevent, and manage pain; Both spontaneous awakening trials (SATs) and spontaneous breathing trials (SBTs); Choice of analgesia and sedation; Delirium: assess, prevent, and manage; Early mobility and exercise; and Family engagement and empowerment. This evidence-based strategy uses goal-directed sedation protocols associated with applying spontaneous ventilation tests (spontaneous breathing trials or SBTs) and early mobilisation. The implementation of this bundle demonstrated a decrease in mechanical ventilation time and incidence of delirium. The potential benefits of these recommended strategies outweigh the minimal risks of costs and coordination. Ultimately, the ABCDEF bundle is one path to well-rounded patient care and optimal resource utilisation resulting in more interactive ICU patients with better pain control. They can safely participate with their families and healthcare providers in higher order physical and cognitive activities at the earliest point in their critical illness.

16.6 Algorithm for the Coordinated Approach to Pain, Sedation, and Delirium in the ICU

See Fig. 16.2.

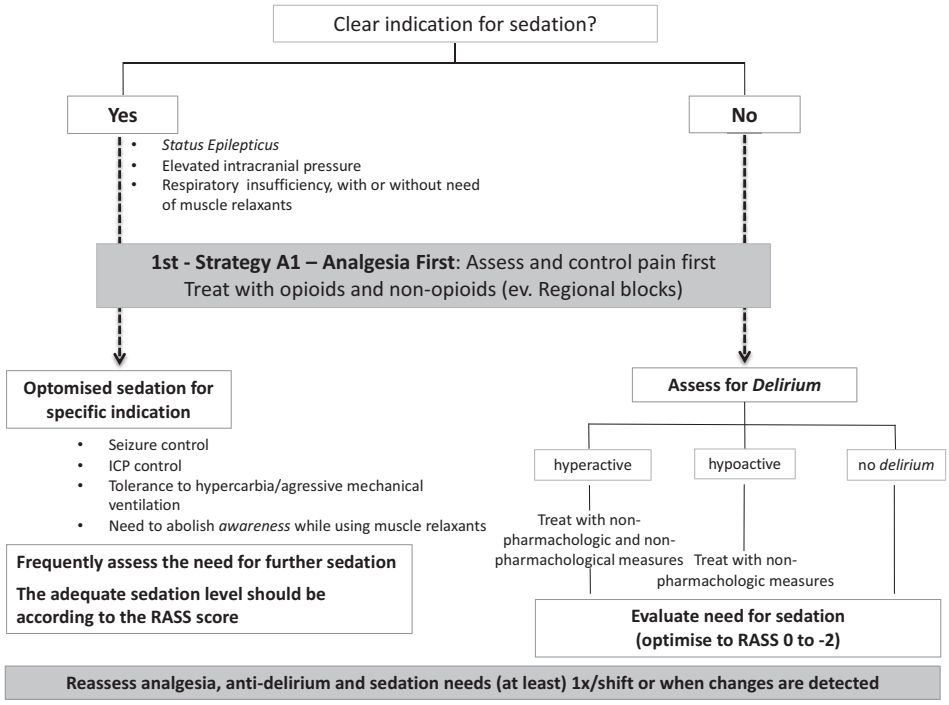

Fig. 16.2 Algorithm for the coordinated approach to pain, sedation, and delirium in the ICU. Adapted from [2]

16.7 Practical Approach to Acutely Agitated Patient in ICU

Agitation is a non-specific symptom which includes a combination of confusion with compulsory physical activity, with or without verbal or physical aggressivity. Acute agitation or verbal aggression could be a frequent reason why an intensivist is called to a patient in and outside ICU, such as in hospital ward or emergency department.

Of note, agitation may be caused by or result in a life-threatening condition. In turn, the traditional "restrain and medicate" strategy may lead to catastrophic outcomes. A systematic approach is advised instead.

1. De-escalate: Prior further steps are taken, always try to establish verbal and eye contact with acutely agitated patients, and try to calm them down. Show sincere interest in helping them. Mind your own safety.
2. Evaluate: Acute agitation may be a sign of acute deterioration of the medical condition of the patient. Start with ABCDE examination (incl. blood glucose) to ensure that vital functions are stable, and a more thorough evaluation is performed once the patient is calmer. Simultaneously gather information about present illness, medication, and a history of alcohol or drug abuse and psychiatric illnesses.
3. Pharmacotherapy is usually needed to buy time for further evaluation of the cause. It is always needed whenever physical restraint of the patient is required to prevent injuries and complications associated with resisting restraint.
   - Haloperidol 2.5–5 mg i.v. is usually the first choice unless alcohol or benzodiazepine withdrawal is suspected, and it can be repeated in 30 min. Most common side effects are QT prolongation, extrapyramidal symptoms, and QTc prolongation.
   - Benzodiazepines (e.g. midazolam 2–5 mg boluses, repeat as needed): first choice in alcohol or benzodiazepine withdrawal and backup for all other non-manageable agitation.
   - Ketamine (1–2 mg i.v.) is rarely used in ICU, but i.m. administration (5 mg/kg) can be useful for severely excited patients without i.v. access.
4. Physical restraints may be needed as a last-resort temporary therapy to prevent injuries to the patient and staff. Restraints themselves carry its own risk of injury to patients, are experienced as coercion or aggression, and can lead to psychological trauma.
   - Five trained persons are needed to apply restraints.
   - Patient comfort and dignity must be maintained at all times.
   - Local guidelines should be followed.
   - It is not acceptable to physically restrain patients for longer periods of time, e.g. to facilitate care.
   - In most extreme cases, it may be safer to sedate and intubate until the underlying cause of agitation is found and addressed.
5. When the patient is calmer, reassess ABCDE with emphasis on the fact that airway control and breathing have not been altered by eventual pharmacotherapy. Make sure that vital functions are monitored continuously and try to find and address the cause (see above for delirium). Think sepsis.

Take-Home Messages

- Delirium is a common complication of ICU stay, which is associated with morbidity and mortality.
- Delirium can be prevented by minimising sedation and sensory deprivation and maximising early mobility and cognitive stimulation.
- No pharmacological prevention is effective, with the exception of benzodiazepines in patients addicted to them or to alcohol.
- A proportion of ICU patients suffer from delirium, which is triggered by a treatable cause such as new-onset sepsis, pain, thirst from hypernatraemia, or withdrawal syndromes.
- "Restrain and medicate" is not enough: prevent, evaluate, and treat the cause of delirium and agitation.

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Common Electrolyte Disturbances

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Contents

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Intended Learning Outcomes

After studying this chapter, you should be able to achieve ILO 1 and have the theoretical knowledge to achieve ILO 2:

1. **Describe a treatment plan for patients with life-threatening electrolyte and metabolic disturbances**.
2. Propose the appropriate management for patients with the most common metabolic disorders, especially hyperkalaemia and hypernatraemia.

17.1 Diagnostic and Therapeutic Approach to Dysnatraemias

17.1.1 Key Physiological Principles

Sodium is the central electrolyte for both osmoregulation and volume regulation.

The main elements of osmoregulation and volume regulation are summarised in Table 17.1.

Osmoregulation is the control of plasma osmolality (P-osm) between 275 and 290 mOsm/kg. It is sensed by osmoreceptors located in the hypothalamus. The effect of hyperosmolality is the retention of water by antidiuretic hormone (ADH) and water intake via thirst. Urinary osmolarity (U-osm) increases in response to ADH stimulation: U-osm >300 mOsm/L means ADH is being secreted and is effective. On the other hand, U-osm <100 mOsm/L is seen if ADH is maximally suppressed.

Table 17.1 Sensors and effectors of osmoregulation and volume regulation. Note: Equation for glucose and urea in mg/dL would be $Posm = 2 \times [Na+] + [glucose]/18 + [urea]/6$. Urea in mg/dL = blood urea nitrogen in mg/dL * 2.14. *P-osm* plasma osmolality, *ADH* antidiuretic hormone, *ANP* atrial natriuretic peptide [1–3]

	Osmoregulation	Volume regulation
Regulation of	Proportion	Absolute amount
	of Na^+ to water	of Na^+ and water
What is being sensed?	$Posm = 2 \times [Na^+] + [glucose] + [urea]$ for all values in mmol/L	Effective circulating volume
Sensor	Hypothalamic osmoreceptors	Different pressure sensors in carotid, artery, renal afferent arterioles
Effector	ADH	Sympathetic nervous system
	Thirst	Renin-angiotensin-aldosterone
		ANP
		ADH (non-osmotic secretion)
Effect	Excretion or intake of water	Haemodynamics
		Excretion or retention of sodium

An important exception in ADH axis regulation is non-osmotic secretion—a phenomenon of ADH secretion disproportional to osmolarity during hypovolaemia or stress—when the body tries to maintain circulating volume at the expense of decreased osmolarity.

Volume regulation effects the circulating volume and thus the absolute amount of sodium (and water). The effective circulating volume is part of the extracellular fluid present in the vascular compartment. In practice, this volume is sensed indirectly by measuring the pressure that perfuses the arterial baroreceptors. Since different systems are regulated separately, various baroreceptor systems are present throughout the body, e.g. in the carotid sinus and the glomerular afferent arterioles. Multiple effectors are involved in volume regulation, mainly influencing haemodynamics directly (e.g. norepinephrine and angiotensin II) and urinary sodium (UNa) retention or excretion. The most important hormones involved are aldosterone, which increases reabsorption of sodium and chloride in the distal nephron, and the counterregulatory atrial natriuretic peptide (ANP), which causes Na^+ excretion.

Note: Plasma osmolarity is largely determined by the concentration of Na^+ in the plasma, but the effectors of osmolarity regulation are intake and excretion of free water (not of Na^+). Sodium intake and excretion, in turn, influence volume status and are regulated by the hormones aldosterone and ANP, which reflect volume status, or more specifically kidney perfusion and preload, respectively. U-osm reflects the status of ADH axis (U-osm >300 mOsm/L = ADH active), and UNa^+ reflects the renin-angiotensin-aldosterone axis (UNa^+ <40 mmol/L = aldosterone active, the body sensing hypovolaemia).

17.1.2 Hyponatraemia

17.1.2.1 Practical Diagnostic Workup

Measuring P-osm, U-osm and UNa^+ is the basic workup for patients with an osmolarity disorder. It will provide the insight into the actual status of the main regulatory axes: ADH and renin-angiotensin-aldosterone systems.

Step 1: Start with the Story

First start with the clinical picture, as this will often clarify the diagnosis up front. Important in the medical history are heart failure, chronic liver disease, chronic kidney disease, and food and fluid intake during the last few days, including drinking habits, current reasons to suspect volume depletion and concomitant medications such as diuretics. Many hyponatraemic states are encountered in typical patient profiles and patterns: the elderly individual with diarrhoea who has ingested only hypotonic fluids, an alcoholic with advanced cirrhosis or a patient with chronic heart failure on diuretics. You will learn more and more typical patterns of hyponatraemia over time. If you cannot recognise the "pattern of hyponatraemia", you are left with a systematic physiology-based approach described below.

Note: Carefully look into patients' symptoms and signs as symptoms of hyponatraemia such as new seizures, headache or stupor, which are important for management decisions (see below).

Step 2: Check Plasma Osmolality P-osm

Plasma osmolarity should be checked whenever the cause of hyponatraemia is not obvious. It will help to rule out two conditions:

- *Pseudohyponatraemia* is a laboratory artifact occurring due to plasma sample dilution in a lab in situations where there is less water in plasma than expected, e.g. due to extreme hyperlipidaemia or hyperproteinaemia. On the contrary, blood gas machine measures [Na^+] in an undiluted sample and will give you a true reading.
- *Dilutional* hyponatraemias will be revealed by measuring P-osm, which in this case will be high. When other solutes cause an increased P-osm, water will move from the intracellular to the extracellular compartment, diluting plasma sodium. The most common example is hyperglycaemia (empirically 1 mmol/L of glucose will reduce [Na^+] by 0.25 mM); other textbook examples are the administration of mannitol. Hyperosmolality caused by molecules rapidly crossing cell membranes such as ethanol or urea does not cause sodium shifts. The treatment of dilutional hyponatraemias focuses on correcting the responsible osmotically active solute, e.g. glucose control.

Tip

A well-maintained blood gas machine gives more reliable readings of [Na^+] than a central lab.

Step 3: Determine ADH Activity by Measuring U-osm

U-osm is the most efficient way to assess whether ADH is both secreted and functional.

- When U-osm is low (<100 mOsm/kg), ADH is maximally suppressed and the hyponatraemia must have been caused by excessive water ingestion (or administration). In healthy subjects, even large volumes of water can easily be excreted, but when the intake exceeds 10–15 L, or is ingested very rapidly, important levels of hyponatraemia can ensue. The phenomenon of "tea-and-toast hyponatraemia" or the hyponatraemia associated with beer potomania is a variant of this type of hyponatraemia. Here, mostly malnourished individuals lack the intake of dietary solutes (sodium, potassium, ammonium, chloride, urea) to produce a sufficient volume of diluted urine. These patients can develop hyponatraemia after the ingestion of no more than a few litres of free water (beer or otherwise).
- A value of U-osm that is higher than P-osm indicates the clear presence of ADH, and the reason for this should be investigated in step 4.

- Between U-osm values below 100 mOsm/kg and values that are higher than P-osm, there is a grey zone where excessive fluid intake can outweigh ADH secretion that is not fully suppressed. In this area, combined reasons for hyponatraemia are often present.

The alternative to measuring U-osm is to measure urine specific gravity and estimate U/osm as per the conversion table, see Appendix B (page 269).

Step 4: Assess Volume Status by Measuring UNa

When impaired water excretion has been excluded by the steps above, the next step is to consider UNa.

- When urine sodium concentration is low (e.g. below 30 mmol/L), the presence of aldosterone and thus a depletion of the effective circulating volume can be suspected. This could be due to
  - *True* volume depletion
  - *Perceived* (by baroreceptors) volume depletion as seen in heart failure and liver cirrhosis

  Notice: The pattern of hyponatraemia, high U-osm and low UNa suggests the situation where the body is trying to increase the circulating volume depletion by non-osmotic ADH secretion. It could be called "syndrome of ***appropriate*** *ADH secretion". Although aldosterone causes sodium and chloride reabsorption from the urine, U-osm is increased (not decreased) in hypovolaemic states. This is because of (1) concomitant reabsorption of water caused by increased ADH and (2) increased potassium and ammonium excretion, which replace sodium and chloride in the urine.*
- When UNa is high (e.g. more than 30 mmol/L or equalling dietary sodium intake), this suggests that either
  - The body senses adequate (or excessive) circulating volume, suppressing aldosterone secretion and/or triggering ANP release. The presence of hyponatraemia in this context means that ADH is being secreted without appropriate reason (such as hyperosmolarity of low volume), defining SIADH. SIADH has a wide array of causes; many of them are medication induced or due to the presence of neurological of pulmonary disease. In ICU patients, relative adrenal insufficiency, prolonged shock, inadequately controlled pain or hypothermia can all contribute to SIADH.

Note: These patients usually have normal volume status and urinary output. The reason why patients with SIADH are not clinically fluid overloaded is that, although osmoregulation is deranged, volume regulation is still intact.

- The excretion of Na^+ in the urine is inappropriately high due to
  - Diuretics
  - Cerebral salt wasting (CSW): a condition not uncommon in patients with subarachnoid haemorrhage or other neurological injuries including high C-spine lesions. Typically, UNa^+ is very high, $\geq P\text{-}Na^+$. A similar picture can also be seen in neuro-ICU patients in whom the treatment with hypertonic saline has been abruptly stopped, whilst the induced counterregulatory natriuresis continues for some time.

Note: These patients tend to be volume depleted and may be polyureic.

Step 5: Summarise

By measuring serum and urine Na^+ and serum and urine osmolarity, you should be able to determine what is the actual status on the two regulatory axes (ADH and aldosterone/ANP) and how the kidney is responding to it. Together with fluid balance, urinary output, assessment of intravascular volume status (see page 98), and checking of patients' drug chart and indeed the story, you should be able to determine the acuity of the process and the underlying cause and distinguish it from physiological regulatory responses. This will help you to decide on the management.

17.1.2.2 Therapeutic Principles: Should Be Guided by Symptoms, Not Sodium Levels

Two main principles are important to consider in the treatment of hyponatraemia:

- First, it is the presence of symptoms associated with hyponatraemia, rather than the sodium level itself, that determines the urgency and necessity of the treatment. Symptoms of hyponatraemia are mostly neurological by nature and are caused by osmotic water shifts and brain swelling.
  - Moderately severe symptoms are nausea, headache or confusion.
  - Severe symptoms are vomiting, cardiorespiratory distress and a Glasgow Coma Scale ≤8.

  Symptomatic hyponatraemia is mostly seen when sodium levels have dropped rapidly and are usually completely absent in chronic hyponatraemias. Depending on the seriousness of the symptoms (of which you must be confident that they are caused by hyponatraemia), hypertonic saline can be used to rapidly increase sodium levels, as summarised in Table 17.2. In this case, you could administer

Table 17.2 Therapeutic principles of hyponatraemia according to the associated symptoms

	Severe symptoms (vomiting, cardiorespiratory distress, deep somnolence, seizures, coma)	Moderately severe symptoms (nausea, confusion, headache)	No severe or moderately severe symptoms
Acute (<48 h)	150cc NaCl 3% over 20′	150cc NaCl 3% over 20′ if decrease with >10 mmol/L	Stop non-essential fluids and medications associated with hyponatraemia
	Check after 20′ whilst repeating 150cc NaCl 3% over 20′	Cause-specific treatment. Check after 1, 6 and 12 h	Diagnostic assessment
	Repeat maximum twice until 5 mmol/l increase		
Chronic (>48 h)	Limit first-day increase to 10 mmol/L or sodium levels of 130 mmol/L		Cause-specific treatment

repeated (under close monitoring of sodium levels) 150 mL infusions of 3% hypertonic saline until the serum sodium concentration has increased by 5 mmol/L, or until the symptoms improve, whichever comes first.

Tip

In the units where 3% NaCl is not available, an equivalent of 150 mL of 3% NaCl (4.5 g NaCl in 150 mL) can be prepared by mixing 110 mL of normal saline (1 g NaCl) and 40 mL of 10% NaCl (3.6 g). Alternatively, if you have central venous access, use slow boluses of 50 mL 10% NaCl (4.5 g NaCl).

- Second, the speed of correction is of paramount importance and should not exceed 10–12 mmol per day, even when treating severely symptomatic hyponatraemias. In acute symptomatic hyponatraemias, e.g. after water poisoning or drug-related SIADH, very often renal compensatory mechanisms are already in action and the patient will be self-correcting very fast. Therefore, sodium levels will increase much more rapidly than anticipated with the risk of the development of osmotic demyelination syndrome. An important feature of this self-correction is a brisk early urine output after the initiation of the correction. In neuro-ICU patients, who are more prone to complications of hyponatraemia such as the rise of intracranial pressure or vasospasms, the threshold for substitution might be lower. In addition, if excessive natriuresis is the underlying mechanism (such as in CSW), the administration of fludrocortisone 0.1 mg twice daily might be considered.

Tip

If the patient with symptomatic severe hyponatraemia starts to produce large amounts of diluted urine and serum sodium increases too rapidly putting the patient at risk of osmotic demyelination syndrome, i.v. 5% glucose may be used to slow down the increase of sodium. Rarely 2–4 µg of desmopressin intravenously or 10 µg intranasally is required to stop the overcorrection.

17.1.3 Hypernatraemia

Compared to the wide array of causes of hyponatraemia, hypernatraemia is rather straightforward and—besides some rare instances where it is caused by sodium administration—is **mostly caused by a deficit of free water**. Since thirst is the most distinctive symptom of hypernatraemia, it is rarely encountered in patients who are able to drink *ad libitum*, and it is almost without exception seen in patients that have no access to water, such as the elderly or indeed ICU patients.

The first step in the differential diagnosis of hypernatraemia is checking the drug chart to rule out the administration of hypertonic solution, such as hypertonic saline or 8.4% bicarbonate.

After ruling out hypertonic solutions as the cause, the main question in hypernatraemia is where the patient is losing water from. This could be due to losses via the gastrointestinal tract (e.g. diarrhoea), through skin and soft tissue (e.g. fever, wounds or burns) or through urine. In the former two causes, urine output will be reduced to a small amount of concentrated urine, and further investigation of urine biochemistry is not necessary.

Tip

It is a common misunderstanding that the administration of isotonic solutions commonly leads to hypernatraemia. Urine concentration will usually be able to retain sufficient free water. On the same note, it is a common mistake to try find and reduce all sources of sodium in a critically ill patient with hypernatraemia or even try to increase sodium excretion by, e.g., a thiazide diuretic. This misses the point as hypernatraemia is a state of free water deficit rather than sodium excess.

When urine output is unexpectedly high in view of hypernatraemia, we first need to know whether ADH, that should be acting maximally in the presence of a hyperosmolar state, is being secreted and is effective. To investigate this, the U-osm needs to be assessed.

- *U-osm is very low* = ADH is not secreted = central diabetes insipidus: This is frequently encountered in the setting of neurological injuries. Typically, the patient develops hypernatraemia relatively quickly after having produced large amounts of diluted urine. Usually, the diagnosis is straightforward, and the treatment is to administer 2–4 μg of desmopressin intravenously or 10 μg intranasally and carefully replace solute-free water if needed (S-Na^+ around 150 mmol/L might be set as a target in the context of raised intracranial pressure).
- *U-osm is close to S-osm* = ADH is not working and/or the kidneys are unable to concentrate urine = nephrogenic diabetes insipidus. The reasons include the following:
  - Polyureic phase of AKI: In patients recovering from AKI, glomerular filtration is usually restored first, whilst it takes more time for the tubules to regain their concentrating ability. Fluids being lost need to be replaced.
  - Prolonged administration of furosemide: Concentration of urine in the collecting ducts is dependent on the presence of hyperosmolar environment in the kidney medulla. This is maintained by sodium, potassium and chloride reabsorption in the ascending limb of the loop of Henle—a process which is inhibited by loop diuretics. Their prolonged administration may cause the washout of hyperosmolarity of the kidney medulla, loss of concentration ability of the kidney and, in turn, hypernatraemia.
- *U-osm is very high* = osmotic diuresis: Free water is dragged along and lost when the body must excrete large amount of osmotically active substances such as mannitol, glucose (if blood glucose is >10 mmol/L for prolonged periods of time) or, most commonly, urea. Hypercatabolism in acute illness, along with high-protein alimentation, leads to the formation of large amounts of urea, which

requires large amounts of free water for its excretion. Indeed, U-osm can be very high under these circumstances.*Notice: In the post-acute phase of critical illness, ICU patients often end up oedematous, with fluid mostly in the extracellular compartment. It is the right approach to restrict further fluid intake and aim for a negative fluid balance. Nonetheless, enough solute-free fluid intake, e.g. in the form of nasogastric water, should always be given not only to cover insensible losses, but also to enable urea excretion. The development of hypernatraemia accompanied with a rise in plasma urea (disproportionally to creatinine) in patients with prolonged hypercatabolism or pyrexia, such as those with pancreatitis, is usually a sign that the patient needs more solute-free water, which should be given despite the patient's oedematous state. See the textbox for the tip on how to assess patients' needs of solute-free water.*

When treating patients with hypernatraemia, a few things are important to consider. First, the cornerstone of the treatment is the administration of free water. Compared to this, avoiding the administration of sodium, e.g. by dissolving medication in glucose or dextrose 5% instead of in isotonic fluid, is of much less importance.

Free water can be administered as glucose or dextrose 5%, but when used in large amounts over a short time, these solutions could lead themselves to osmotic diuresis. Therefore, the use of tap water or bottled water via a nasogastric tube is preferred in those with functional gastrointestinal tract. Outside the context of neurocritical care or paediatrics, the rate by which hypernatraemia is corrected is not as important as previously thought as faster correction rate appears safe.

Tip

Whenever the ICU patient is stable enough and tolerating enteral nutrition, it is an established practice in some units to replace isotonic i.v. maintenance fluids with repeated boluses of enteral water.

17.2 Disorders of Potassium Cation Concentration

Potassium cation (K^+) is mainly an intracellular ion. Its plasma concentration represents only a minute fraction of total body potassium, and it is prone to transmembrane shifts.

17.2.1 Hypokalaemia

Hypokalaemia is common in ICU patients, and most of the patients in ICU require potassium replacement at some stage. Untreated hypokalaemia puts patients at risk of atrial fibrillation and other arrhythmias (particularly in patient on digoxin) and may worsen muscle weakness and catabolism.

Causes in ICU Patients:

- Sympathetic surge of acute illness causes K^+ to rapidly enter the cells, so does adrenaline or betamimetics. This hypokalaemia is usually short-lived.
- Aldosterone axis activation as a part of the stress response increases urinary K^+ loses, and this is exacerbated by the lack of intake (unless K^+ is a part of maintenance fluids).
- Catabolism leads to K^+ release from cells and wasting to urine, which slowly leads to K^+ depletion. Glucose intake and insulin release then shift the extracellular K^+ into the cell, often leading to profound hypokalaemia as a part of the refeeding syndrome.
- Metabolic acidosis increases K^+ excretion in urine and can lead to K^+ depletion. However, low pH increases K^+ concentration due to transmembrane shifts. Therefore, K^+ depletion may only be seen after acidosis correction (as typically seen in diabetic ketoacidosis).
- Hypothermia (both accidental and induced) increases urinary K^+ excretion.
- Furosemide treatment.

Management of hypokalaemia means K^+ replacement after excluding lab error (if low K^+ is unexplained or unexpected). Check and replace other intracellular ions where appropriate, such as Mg^{2+} and phosphates. K^+ replacement can be done by:

- Continuous 8.45% = 1 mmol/mL KCl solution via central line, usual rate 5–15 mmol/h via central line.
- Normal saline with 40 mmol/L KCl in pre-prepared 1 L bags, max rate 500 mL/h, can be administered into peripheral vein.
- KCl tablets (1 g), usually 2 tablets 8 hourly p.o. or into BG tube, in those with intact GI tract.

Notice: Hypokalaemia in ICU patients often comes hand in hand with metabolic alkalosis, hypomagnesaemia and hypophosphataemia.

17.2.2 Hyperkalaemia

Hyperkalaemia is a medical emergency, which—if severe enough—can cause cardiac arrest. Healthy kidneys are able to excrete vast amounts of potassium and therefore hyperkalaemia is caused by:

- Renal failure which causes not only K^+ retention in the body, but also acidosis that further worsens hyperkalaemia by transmembrane shifts (see below).
- Drug related: ACE inhibitors and spironolactone if overdosed or in patients with AKI or dehydration
- Rapid intravenous administration, such as in the case of medical error or rarely suicide or homicide
- Rapid release from intracellular compartment due to membrane destruction such as in rhabdomyolysis or crush syndrome
- Transmembrane shifts as a result of acidosis

Note: For every 0.1 pH drop below 7.4, extracellular [K^+] increases by 0.6 mmol/L. This increase will be corrected once underlying acidosis has been treated. Acidosis from a circulating anion increases [K^+] less than hyperchloraemic acidosis.

Management of hyperkalaemia in the emergency room setting is summarised in ERC guidelines (see Algorithm in Appendix A) https://www.cprguidelines.eu/assets/guidelines/European-Resuscitation-Council-Guidelines-2021-Ca.pdf. The treatment is based on [K^+] level and the presence of ECG changes such as peaked T waves and/or broad QRS complexes. The cornerstones of treatment include the following:

- Administration of Ca^{2+} (10 mL 10% $CaCl_2$ or 30 mL 10% Ca-gluconate by a slow i.v. bolus): This will not decrease K^+ levels, but it will protect the myocardium against the effects of hyperkalaemia.
- Nebulised salbutamol will shift K^+ into the cells and reduce K^+ levels by up to 1 mmol/L. Its effect is very short-lived, but will buy time for other measures to kick in.
- Glucose 25 g with 10 IU of insulin i.v. (i.e. a bolus of, e.g., 50 mL 50% glucose or 500 mL 5%).
- Then, final treatment such as renal replacement therapy (see ▶ Chap. 10, page 144) should be commenced. At the same time, the underlying condition should be found and addressed.

In ICU, the treatment of hyperkalaemia is similar to treatment elsewhere, and it is very rarely revealed suddenly or as a surprise. If it does, always check for possible measurement error. Typical examples are sample haemolysis or inadvertent admixture of K^+-containing fluid with the blood sample.

Notice: Never start treatment for hyperkalaemia that surprised you without first verifying that it is genuine. Consider other K^+-containing solutions before giving K^+, e.g. penicillin G 5 MIU contains 8 mmol K^+, and packed red blood cells much more.

For the management of hyperkalaemia in ICU patients, the context and cause are very important and often lead to deviation from classical guideline-driven approach. For example, the treatment required for hyperkalaemia in the early stages of diabetic ketoacidosis could be renal replacement therapy if the patient also has an AKI. In addition, most symptomatic will have rapidly evolving hyperkalaemias caused by transmembrane shifts, in contrast to slowly evolving hyperkalaemias such as in chronic kidney diseases.

17.3 Magnesium

Hypomagnesaemia is common in ICU patients, in particular in those with sepsis or malnutrition or those on loop diuretics or long-term renal replacement therapy with Mg-free dialysis solutions. Magnesium sulphate 20% is commonly used for Mg^{2+} substitution but also to treat arrhythmias, bronchospasms or pre-eclampsia.

Magnesium [Mg^{2+}] is mainly (99%) an intracellular cation. Half of the total body stores it in bones. Circulating Mg^{2+} is a sum of free Mg^{2+} (66%) and protein- and organic acid-bound Mg^{2+} (33%). Only free Mg^{2+} is biologically active, but total Mg^{2+} is measured and reported by laboratories (normal range 0.65–1.05 mmol/L

Table 17.3 Link between physiology, sign and symptoms of magnesium deficit and its therapeutic use. Note: *AF* Atrial fibrillation, *NMDA* N-methyl-D-aspartate, *PTH* Parathormone, *SAH* Subarachnoid haemorrhage, *TBI* Traumatic brain injury

Function of Mg^{2+}	Related hypomagnesemia signs/symptoms	Rationale for therapeutic use of Mg^{2+}
Cofactor of membrane Na^+/K^+ ATPase in cardiac tissue	ECG changes similar to $\downarrow K^+$ Atrial fibrillation (and other supraventricular arrhythmias) Torsades de pointes (and other ventricular arrhythmias)	Mg^{2+} is the first-line drug in the treatment of torsades de pointes Many intensivists give magnesium to treat patients with new-onset AF
Cofactor of renal K^+ reabsorption	Losses of K^+ and hypokalaemia refractory to substitution	Check/replace Mg^{2+} whenever you treat hypokalaemia
Promotes pre-synaptic inhibition and directly inhibits NMDA receptors	Neuromuscular irritability: both central (seizures) and peripheral (Chvostek sign)	High-dose Mg^{2+} for (pre) eclampsia Strict normomagnesaemia in TBI and to reduce the risk of vasospasm in SAH
Relaxes smooth muscle	–	Mg^{2+} for bronchospasms in asthma
Indispensable for PTH secretion	Ionised hypocalcaemia	Mg^{2+} for unexplained hypocalcaemia

[1.6–2.5 mg/L]). There is no specific hormonal regulation; filtered free magnesium is reabsorbed, mostly in the loop of Henle.

Magnesium has a range of functions in the body, most of them linked to the role of Mg^{2+} in binding to the ATP molecule. These functions are linked to signs and symptoms of hypo- and hypermagnesemia. They also explain the therapeutic use of Mg^{2+} (Table 17.3):

Plasma total Mg^{2+} is a poor reflection of Mg^{2+} stores in the body. Nonetheless, in ICU patients, Mg^{2+} is usually checked daily and maintained within normal range by substitution. Intravenous 20% $MgSO_4$ contains 2 g (8 mmol, i.e. 0.8 mmol in 1 mL) in each 10 mL vial. For torsades de pointes or urgent treatment, a slow bolus of 2 g should be given and repeated once. For other conditions, a continuous treatment at a rate of 2 g/h is recommended. Check plasma Mg^{2+} after 5 h.

Hypermagnesaemia occurs as part of a complex homeostasis derangement in renal failure or rarely from iatrogenic causes. Symptoms are hypoventilation, muscle weakness and coma. Renal replacement would usually be required for the treatment of the underlying renal failure. If not, generous hydration and loop diuretics can be used.

17.4 Phosphate

Phosphate is 99% an intracellular anion. Extracellular levels poorly reflect body stores. The laboratory measures the sum of $H_2PO_4^-$, HPO_4^{2-} and PO_4^{3-} with a normal range being 0.9–1.4 mmol/L [2.8–4.5 mg/dL]. Phosphate metabolism is regulated

by parathormone and vitamin D (together with Ca^{2+}) and also by specific regulatory peptides called phosphatonins.

Phosphate depletion in the body (with or without hypophosphataemia) can be caused by malnutrition including the prolonged catabolism of critical illness or by increased renal losses due to long-term diuretic use or osmotic diuresis (e.g. in untreated type 1 diabetes). Hypophosphataemia, however, most commonly occurs because of transcellular phosphate shifts such as in refeeding syndrome or during the treatment of diabetic ketoacidosis with insulin. A recent international study found the incidence of hypophosphataemia to be 15% in the general ICU population. The clinical picture of hypophosphataemia is primarily muscle weakness including type 2 respiratory failure and cardiomyopathy. Potassium dihydrogen phosphate (KH_2PO_4) 13.6% contains 1 mmol of K^+ and 1 mmol of phosphates in each millilitre. This solution is usually given continually (e.g. 10 mmol over 6 h); renal failure not treated by dialysis is a relative contraindication. In some countries, sodium phosphate salts are available, too.

Hyperphosphataemia, on the other hand, occurs in renal failure (phosphate levels are higher in chronic as compared to acute renal failure). It also occurs acutely in states when intracellular content is suddenly released such as in rhabdomyolysis or tumour lysis syndrome. The main consequence of hyperphosphatemia is a decrease in ionised Ca^{2+} (see below), which is refractory to substitution due to the fact that calcium phosphate is poorly water soluble and, in turn, any administered calcium will cause metastatic calcification. The treatment is to remove excessive phosphate by either dialysis or generous hydration if renal functions are preserved.

17.5 Calcium

Ca^{2+} is an extracellular cation (intracellular concentrations are several orders of magnitude lower than in the extracellular space), which is half bound to plasma proteins. The other half is free or ionised (Ca^{2+}). Alkalaemia reduces the proportion of ionised Ca^{2+}.

The ionised Ca^{2+} (normal range 1.1–1.4 mM/l) is the fraction that is responsible for the biological activity and is frequently and directly measured by the blood gas machine in ICU patients. The level of total Ca^{2+} is normally 2.25–2.75 mM and is determined by the lab. Indeed, patients with chronic hypoproteinaemia would have a reduced total Ca^{2+} as it is the ionised Ca^{2+} which is subject to regulations. This is not a reason for substitution as ionised Ca^{2+} and Ca^{2+} biological activity remains normal.

> *Note: Ionised Ca^{2+} reported from the laboratory may be calculated from total Ca^{2+} and albumin and could be less reliable than ionised Ca^{2+} measured by a blood gas analyser.*

The regulation of ionised Ca^{2+} is by a simple feedback loop. A reduction in ionised Ca^{2+} leads to a release of PTH, which increases plasma Ca^{2+} by the following mechanisms:

1. Release from bones
2. Increase Ca^{2+} reabsorption in the kidney (together with an increase in phosphate excretion)

3. Increase activation of vitamin D, which increases Ca^{2+} absorption from the intestines

Calcitonin, which increases Ca^{2+} incorporation into bone, plays a less important role.

Ionised hypocalcaemia is frequent in the critically ill, and it is often multifactorial. Factors playing a role include:

- Reduced intake prior to ICU admission: malnutrition, vitamin D deficiency
- Ca^{2+} precipitation in hyperphosphataemia
- Ca^{2+} chelation in citrate toxicity (use of citrate as an anticoagulant in sepsis or in transfusions >4 RBC/hour) or as calcium oxalate in ethylene glycol poisoning
- Ca^{2+} sequestration (binding to saponificated retroperitoneal fat in pancreatitis)
- Impaired renal reabsorption due to impaired PTH secretion and/or action such as in sepsis

Most cases of ionised hypocalcaemia in ICU patients are asymptomatic. Symptoms of hypocalcaemia are increased neuromuscular irritability (such as Chvostek or Trousseau signs, carpopedal spasms) or cardiac arrhythmias, prolonged QT and reduced contractility. Impaired coagulation occurs only in most extreme forms.

Treatment of ionised hypocalcaemia can be summarised as follows:

- Specifically look for and address treatable causes such as hyperphosphataemia or hypomagnesaemia or citrate toxicity in patients on citrate anticoagulation.
- Substitution is indicated only if ionised Ca^{2+} is <0.8 mM/L or the patient has symptoms of hypocalcaemia such as prolonged QT, severe haemodynamic instability or forearm muscle spasms on inflation of blood pressure cuff.
- There is no evidence of benefit and possible harm of Ca^{2+} substitution in asymptomatic ICU patients with mild (≥0.8 mM/L) ionised hypocalcaemia.
- Specific indications for Ca^{2+} treatment are hyperkalaemia with ECG changes or overdose with Ca^{2+} channel blockers.

Calcium gluconate 10% contains 0.22 mmol of Ca^{2+} in 1 mL, whilst calcium chloride 10% contains 0.46 mmol of Ca^{2+} in 1 mL. The treatment usually begins with 20 mL of 10% calcium gluconate or 10 mL of 10% calcium chloride administered at a very slow (over 10 min) bolus, followed by a re-check of ionised Ca^{2+}. The effect is usually short-lived and may necessitate repeating the dose or a continuous infusion (e.g. 10 mmol of Ca^{2+}/day).

Hypercalcaemia is rare in ICU patients and occurs in bone-destructing malignancies such as multiple myeloma or parathyroid tumours, or as a consequence of dehydration as a result of thiazide diuretics. The first measure is generous i.v. hydration followed by administration of furosemide. Further investigation and treatment (pamidronate, salmon calcitonin or bisphosphonate] are usually led by the endocrinologists.

Take-Home Messages

- Serum concentration of Na^+ is the major determinant of plasma osmolarity. Nonetheless, it is controlled by free water movements, which are regulated by antidiuretic hormone, released in response to hyperosmolarity or hypovolaemia.
- Total body Na^+ content is regulated by haemodynamic parameters: it is increased by aldosterone and reduced by atrial natriuretic peptide.
- A systematic approach to hyponatraemia can unveil underlying physiology. It is based on verification by plasma osmolarity, determination of ADH activity by measuring urinary osmolarity and aldosterone axis by measuring urinary [Na^+].
- Hypernatraemia is the lack of free water rather than total sodium excess. Consider urea-driven osmotic diuresis and make sure that your patients are given enough solute-free water.
- Treatment of hyponatraemia is guided by symptoms. Most patients with hyponatraemia do not require treatment other than the management of the underlying cause. Hypertonic saline is reserved for rare cases of acute hyponatraemia with neurological symptoms.
- Hyponatraemia must be corrected slowly due to the risk of osmotic demyelination. However, hypernatraemia can be corrected quickly in adults who do not have neurological symptoms.
- Most ICU patients require K^+ supplementation during their ICU stay. The most common complication of hypokalaemia is atrial fibrillation, especially in patients with sepsis or who are on digoxin.
- Mg^{2+} substitution is always required in hypomagnesaemia and is used therapeutically for (pre)eclampsia, torsades, bronchospasms and AF in critically ill patients.
- Calcium administration is not recommended for mild asymptomatic hypocalcaemia in ICU patients. It is required only if ionised Ca^{2+} is <0.8 mM/L or in specific situations, such as hyperkalaemia with ECG changes, Ca^{2+} channel blocker overdose or profound shock.

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Failure to Wean from Mechanical Ventilation

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Contents

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Intended Learning Outcomes

By the end of the chapter, you should be able to:

1. Describe the principles of weaning from mechanical ventilation, readiness testing and risk factors for weaning failure.

18.1 Introduction

Many critically ill patients are in need for respiratory support during their stay in the ICU. As much as mechanical ventilation is a lifesaving intervention, it comes with risks and bears possible complications, like ventilator-induced lung injury (VILI) or diaphragmatic dysfunction (VIDD) and ventilator-associated pneumonia (VAP). Therefore, weaning and liberation from mechanical ventilation are an important aspect of ICU care and need to be a top priority for every ICU team member from the moment mechanical ventilation is instigated.

Successful liberation from ventilation is defined as the entire process of liberating the patient from mechanical support and removing the endotracheal tube (Fig. 18.1). The practice of liberation may vary widely but usually follows a three-step approach that involves testing for readiness, weaning and extubation. Indeed, in many patients in ICU, particularly those ventilated for a short time (e.g. patients after elective surgery), the process of liberation from mechanical ventilation towards extubation is short and straightforward; in others, it requires planning and time.

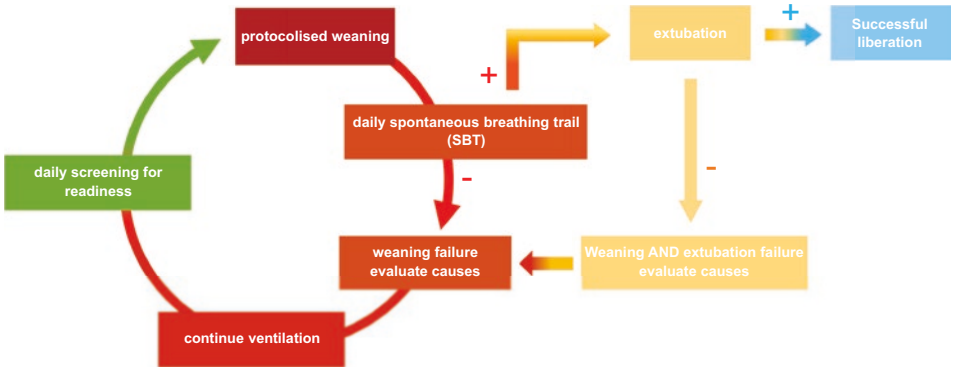


Fig. 18.1 Process of liberation from mechanical ventilation. The three steps include daily screening for readiness (green), weaning (red) and extubation (yellow). Daily spontaneous breathing trials are part of the weaning process. If successful (+), continue with extubation; if unsuccessful (−), evaluate the causes for weaning failure and continue ventilation. The patient is successfully liberated from ventilation when showing a sufficient gas exchange 48 h after extubation (+). In case the patient is in need for respiratory support within 48 h of extubation (−) and has therefore failed extubation, evaluate the causes.

18.2 Screening for Readiness

Several clinical and sometimes physiological criteria may be used to determine whether a patient is ready to start the process of weaning from mechanical ventilation.

A patient should meet all the following **clinical criteria** to be considered for weaning:

- Adequately treated cause for mechanical ventilation/improved respiratory failure
- Respiratory stability (adequate oxygenation, e.g. PaO_2/FiO_2 >200 mmHg (with PEEP ≤5 cmH_2O; arterial pH >7.25))
- Ability to take spontaneous breaths
- Haemodynamic stability (e.g. low vasopressor infusion)

An appropriate mental state (target goal of RASS −2 to +1) is preferrable. An altered mental state is not an exclusion criterion for weaning as long as the patient can protect their airway. It is important to acknowledge that up to 30% of patients who do not meet the clinical criteria can still be successfully weaned from mechanical ventilation.

Apart from clinical observations, there are physiological tests that can help predict whether a patient may successfully wean from ventilation. Those so-called weaning predictors should be used in addition to the clinical criteria above and not instead of. The most often used test is the ***rapid shallow breathing index*** (RSBI), which is the ratio of respiratory rate per minute to tidal volume (f/Vt) usually measured at zero support and zero PEEP in a pressure support mode for 1 min. A RSBI ≥105 breaths/minute/L indicates that a patient is not ready for weaning and may fail. However, a RSBI <105 breaths/minute/L does not automatically mean the patient will successfully wean. Other predictors use measurement of respiratory drive (e.g. airway occlusion pressure $P_{0.1}$ which is the pressure (cmH_2O) measured 100 ms after starting inspiration performed against a closed respiratory system) or are multi-component indices like the CROP index (**C**ompliance, **R**ate, **O**xygenation, **P**ressure). They have limited predictive value and should not be used solely.

If a patient is deemed ready for weaning, a protocolised weaning approach is favourable, especially in settings with limited resources. In patients who do not seem ready, continue to treat the underlying cause for respiratory failure and frequently re-evaluate readiness. Ultimately, if they do not improve, a tracheostomy and long-term ventilation may be required.

18.3 Weaning

In clinical practice, the capacity of ventilated patients to breath on their own is frequently underestimated. Data show that a protocolised liberation strategy with daily assessments of readiness and protocolised weaning reduces the duration of mechanical ventilation and ICU length of stay significantly. Weaning protocols can be personnel driven or automated.

18.3.1 Techniques

Frequently used approaches to assess readiness for weaning include daily spontaneous breathing trials (SBTs) or a progressive reduction of pressure support during pressure support ventilation (PSV). Recently, computer-driven automated PSV weaning protocols were introduced but show no superiority over personnel-driven protocols. Keep in mind that patients intubated for less than 24 h (e.g. post-surgery) may not need a weaning trial at all and are extubated if appropriate.

18.3.1.1 Spontaneous Breathing Trial (SBT)

- Simulates patients' ability to undertake the entire workload of breathing without assistance
- Usually between 30 min and 2 h on a T-piece or pressure support ventilation ≤8 cm H_2O or CPAP

18.3.2 Weaning Failure

Weaning failure is defined as the failure to maintain appropriate spontaneous breathing during a weaning trial and having to revert to partial or full ventilatory support. Certain clinical and physiological criteria indicate weaning failure regardless of the approach chosen. If you notice the following signs, stop the weaning trial and put the patient back on adequate ventilation support.

18.3.2.1 Signs of Weaning Failure

Clinical Criteria

- Sweating
- Nasal flaring
- Increasing respiratory effort (respiratory rate >35/min)
- Tachycardia (increase in heart rate >140 bpm)
- Cardiac arrhythmias
- Hypotension or hypertension (>20% change from baseline)
- Use of accessory muscles
- Agitation

Practical Tip

Apnoeic pauses that trigger alarms and backup modes of ventilation can have different causes requiring different approaches:

- Residual effect of sedation—re-evaluate and eventually reduce or stop opioids, switch back to mandatory ventilation mode and wait.
- Respiratory alkalosis: reduce mandatory minute ventilation, re-check blood gases soon after and try again.
- Metabolic alkalosis: find and treat the cause.

Repetitive apnoeic pauses with Cheyne-Stokes breathing occur in patients with a damage to the brainstem or heart failure and usually predict the need for longer respiratory support.

Gas Exchange Criteria

- Increase in $P_{et}CO_2$ by >10 mmHg (1.5 kPa)
- Decrease of arterial pH <7.32 or a decline in arterial pH >0.07
- PaO_2 <60 mmHg (8 kPa) with an FiO_2 >0.40 (PaO_2/FiO_2 ratio <150 mmHg [20 kPa])
- Decrease in SpO_2 by >5%

Patients who fail their first SBT and require up to three SBT attempts or 7 days to be liberated from ventilation are considered difficult to wean (25–40% of patients). Patients who require more than 3 SBTs or more than 7 days until liberation are considered to have prolonged weaning (6–14% of patients). However, most of the mechanically ventilated patients in ICU are in the simple-to-wean category (50–75% of patients).

18.3.3 Evaluate Causes of Weaning Failure

The main causes of weaning failure are usually the incomplete resolution of critical illness, errors in assessing readiness to wean or presence of a new problem (e.g. delirium or medication side effects). Older patients (>65 years of age), patients with chronic cardiovascular or respiratory disease and patients with a positive fluid balance <24 h before extubation have an increased risk for failure.

The pathophysiology of weaning failure is complex and multifactorial but is best described as an imbalance between possible work of breathing and demand. The most common pathophysiologic mechanisms associated with weaning failure are:

1. **Increased work of breathing**
   (a) Increased ventilatory demand (e.g. hypoxemia, fever, agitation)
   (b) Increased resistive load (e.g. bronchoconstriction, tracheal stenosis)
   (c) Increased elastic load (e.g. pleura effusion, rib fractures, infiltrates, fibrosis)
2. **Decreased neuromuscular capacity**
   (a) Respiratory muscle weakness/fatigue (e.g. VIDD, ICU-acquired weakness)
   (b) Decreased ventilatory drive (e.g. sedation, neurologic disorders or neurotrauma)
3. **Cardiac dysfunction** (specifically left ventricular dysfunction)
   (a) Myocardial ischaemia
   (b) Pulmonary oedema
   (c) Fluid overload
4. **Psychological dysfunction**
   (a) Delirium
   (b) Anxiety
5. **Metabolic, electrolyte and endocrine abnormalities**

Goal-directed sedation and analgesia as well as early mobilisation in addition to protocolised weaning approaches may reduce the risk for weaning failure and support timely liberation from mechanical ventilation.

18.4 Extubation

Extubation is the final step of liberation from mechanical ventilation. Before removing the endotracheal tube, it is important to assess the patient for airway patency and their ability to protect their airway, and for the amount of respiratory secretions. Ideally, you want a conscious haemodynamically and respiratory stable patient to be able to effectively cough, gag and swallow. However, especially in neurological or neurosurgical patients, this might not be achievable.

All patients must be closely monitored during and after extubation and need appropriate oxygen therapy. If there is any doubt that the patient can sustain liberation from ventilation, consult senior clinicians and discuss reintubation or non-invasive ventilatory support. Patients in need for reintubation within 48–72 h after extubation are considered to experience extubation failure.

Take-Home Messages

- Liberation from mechanical ventilation includes three steps: testing for readiness, weaning and extubation.
- Use protocolised weaning strategies and assess readiness and weaning daily, e.g. using SBT.
- Be aware of clinical and physiological signs of weaning failure.
- In established weaning failure/extubation failure, identify the causes of failure and treat effectively before resuming a new trial of weaning or extubation.
- Goal-directed sedation, early mobilisation and neutral/negative fluid balance support timely liberation from ventilation.

References

1. ESICM Academy ACE Course: Mechanical ventilation, Weaning (Part 5) at https://www.academy/esicm.org
2. Perren A, Brochard L. Managing the apparent and hidden difficulties of weaning from mechanical ventilation. Intensive Care Med. 2013;39(11):1885–95. https://doi.org/10.1007/s00134-013-3014-9. Epub 2013 Jul 18.
3. Goligher EC, Ferguson ND, Brochard LJ. Clinical challenges in mechanical ventilation. Lancet. 2016;387(10030):1856–66. https://doi.org/10.1016/S0140-6736(16)30176-3. Epub 2016 Apr 28.
4. Jung B, Vaschetto R, Ten Jaber S. tips to optimize weaning and extubation success in the critically ill. Intensive Care Med. 2020;46:2461–3. https://doi.org/10.1007/s00134-020-06300-2.

Supplementary Information

F. Duška et al. (eds.), *Intensive Care Fundamentals*, Lessons from the ICU,
https://doi.org/10.1007/978-3-031-21991-7

Appendix A: Common ICU Drugs

Only includes most common drugs in ICU that are worth getting familiar with early during your ICU training. Check the local prescription guidelines and policies or ask clinical pharmacist.

ABW = adjusted body weight = 0.4 × (actual weight − IBW) + IBW, where IDW is ideal body weight. Use ► https://www.mdcalc.com/calc/68/ideal-body-weight-adjusted-body-weight. Patients actual weight can be used instead unless in patients in extremes of BMI.

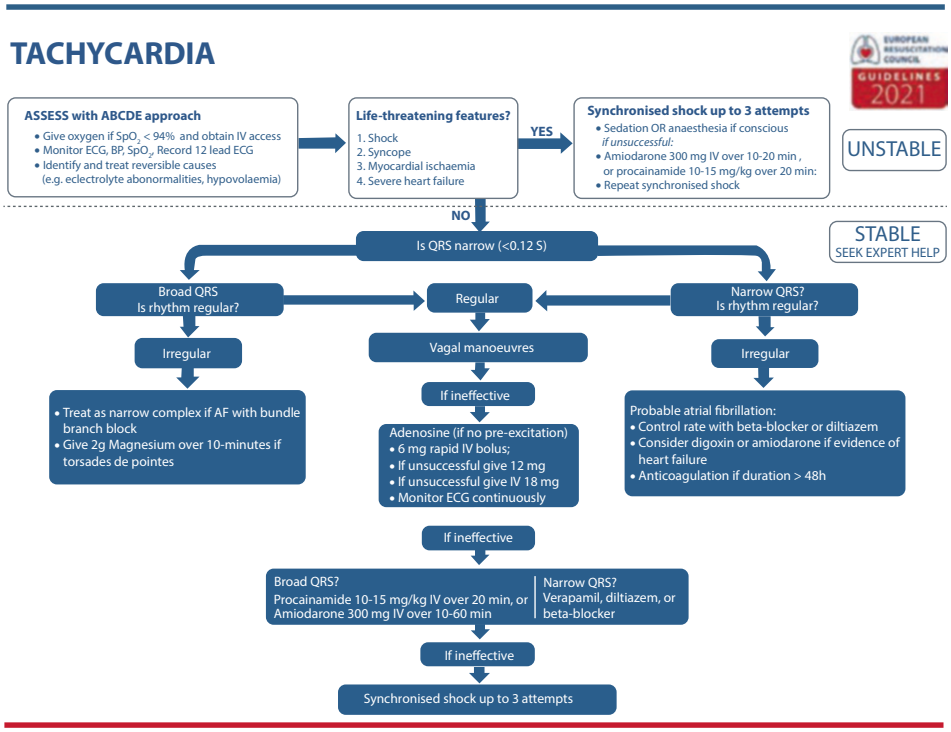
Induction/intubation drugs. Sedatives.

Drug	Dose and administration	Mechanism of action	Uses	Common adverse effects
Propofol	Induction: 50–200 mg i.v., old and very sick need less Deepening sedation in ICU 30–50 mg i.v., repeat as needed Sedation: up to 4 mg/kg h i.v.	Sedative, half-life in minutes	Induction to anaesthesia Sedation in ICU Seizure control	Hypotension Pain if given peripherally Do not get confused by 1% and 2% concentrations. Rare and serious Propofol Infusion Syndrome.
Midazolam	Induction 5–20 mg Sedation 2–10 mg/h	Sedative, GABA receptor agonist, half-life 20 min, context-sensitive much longer	Induction to anaesthesia (less commonly) Sedation in ICU Seizure control	Can be deliriogenic, tend to accumulate, avoid in AKI or do sedation holds daily
Ketamine	Induction 100 mg i.v., analgesia: 0.1–0.3 mg/kg/h, ev. 10–30 mg/h or 10–20 mg p.o.	Incisive neuroleptic, analgesic, NMDA receptor antagonist	Induction in shock/hypotension Analgesia (burns and spines) Critical asthma	Hallucinations, psychosis
Rocuronium	Rapid sequence induction: 1.0–1.5 mg/kg	Non-depolarising paralytics, inhibits	Paralysis to facilitate intubation or other procedures	Hypotension Anaphylaxis
Ephedrine	10 mg i.v. boluses (can go peripherally)	Alpha agonist, half-life very short in minutes	Hypotension and no central access	Tachyarrhythmias

Example: For intubation of an ICU patient, draw 20 mL 1% propofol, 5 mg of midazolam, and 50 mg rocuronium and 2 mL (100 µg) of sufentanyl. Make sure you are ready to deal with hypotension (get ready noradrenalin infusion if CVC is in place or ephedrine 50 mg diluted in 5 mL if no central access)

Vasopressors				
Drug	**Dose and administration**	**Mechanism of action**	**Uses**	**Common adverse effects**
Noradrenaline	Continuous infusion into a dedicated lumen of a central line (no boluses, no peripheral administration) For dose/dilution, respect local protocol. No maximum dose, but for doses >0.5 µg/kg min, vasopressin is usually added	Alpha1 agonist (beta agonist, too, but does not cause tachycardia unless very high doses)	Hypotension refractory to fluids. Excellent for vasoplegia, does not work in hypovolaemia	Arrhythmias, splanchnic ischaemia. If dose ≥0.5 µg/kg min, consider adding vasopressin
Vasopressin	Continuous infusion to CVC. Respect local protocol, if none, dilute 20 IU in 50 mL and start at 6 mL/h	V1 receptor agonist	Second line vasopressor in severe vasoplegia (septic shock)	Splanchnic and limb ischaemia

Antimics



Tachycardia algorithm. ABCDE airway, breathing, circulation, disability, exposure BP blood pressure; DC direct current; ECG electrocardiogram; IV intravenous; SpO_2 arterial oxygen saturation; VT ventricular tachycardia.

Analgesics				
Drug	**Dose and administration**	**Mechanism of action**	**Uses**	**Common adverse effects**
Morphine	Bolus i.v.: 2–10 mg Infusion i.v.: 1–5 mg/h PCA regime: 1 mg bolus, 5 min lock-out time	Opioid receptors, onset 5–10 min, half-life 3–4 h	First choice opioid in most ICUs, few drug–drug interactions, cheap	Significant hepatic metabolism: M6G more potent than morphine and accumulates in renal impairment, M3G can cause neuroexcitatory effects Morphine can cause histamine release Caution in hepatic and renal impairment
Sufentanil	Bolus i.v.: 5–10 µg (1–2 mL) Infusion i.v.: 5–25 µg/h (1–5 mL/h)	Opioid receptors, onset 3 min, half-life 3 h (context sensitive)	Used in OR and ICUs, preferred in patients with AKI	Many drug interactions, e.g. effect increased by fluconazole or clarithromycin
Paracetamol	0.5–1 g × 4 daily (i.v., p.o.) max: 4 g/day	Central (serotoninergic) and peripheral analgesic action. Minimal anti-inflammatory effect	Analgesic and antipyretic, Synergic effect with opioids	Extensive hepatic metabolism produces hepatotoxic reactive metabolite, which requires conjugation with glutathione. Dose reduction in low weight, liver or renal impairment, and glutathione deficiency. *N*-acetylcysteine is used in paracetamol overdose

Drugs used in ICU delirium, seizures, and withdrawal syndromes Always assess reversible causes of delirium!				
Drug	**Dose and administration**	**Mechanism of action**	**Uses**	**Common adverse effects**
Diazepam	5–20 mg i.v. or p.o. can be repeated 6 hourly, or tapered down	Long-acting benzodiazepine (GABA agonist)	Alcohol and/or benzodiazepine withdrawal syndrome Seizures	Avoid benzodiazepines in the management of delirium of other causes. Think also thiamine when treating alcohol withdrawal
Haloperidol	2.5–5 mg i.v. bolus, then 6-hourly	Atypical neuroleptic	Agitated delirium	Prolongs QT and may decrease seizure threshold

Drugs used in ICU delirium, seizures, and withdrawal syndromes				
Always assess reversible causes of delirium!				
Drug	**Dose and administration**	**Mechanism of action**	**Uses**	**Common adverse effects**
Clonidine	Bolus i.v.:2–5 µg/kg Infusion i.v.: 0.3–2 µg/kg/h p.o.: 50–150 µg Never stop infusion abruptly	Alpha-2-agonists analgo-sedative, anxiolytic and anti-hypertensive effects	Opioid withdrawal, anxiety, agitation	Hypotension, bradycardia, first degree heart block, nausea, vomiting, with abrupt discontinuation: hypertension, nervousness, withdrawal
Dexmedetomidine	Bolus i.v. 1 µg/kg Infusion i.v.: 0.2–1 µg/kg/h	Highly selective alpha-2 agonist	Used as primary sedative in some ICUs	Cardiovascular side effects as above, decreased clearance with obesity. Expensive, no solid evidence of superiority yet over traditional sedation
Levetiracetam	500–1500 mg twice a day i.v. or p.o. (loading for status epilepticus 60 mg/kg, max. 4.5 g i.v. over 10 min), after 12 h continue 1000–3000 mg/day	Inhibits the release of excitatory mediators	Usually second choice drugs (after benzodiazepines) for epileptic seizures	None
Phenytoin	Give slow (over 30 min) bolus for status epilepticus 20 mg/kg (max. 2 g) i.v., after 6–8 h continue 3–5 mg/kg/day (every 8 h)	Sodium channel blockade	Usually third-choice drug for refractory seizures	Narrow therapeutic range: send blood levels before third maintenance dose (target 10–20 mg/L) A lot of drug interactions. Cardiac toxicity (arrhythmias) Neurotoxicity (nystagmus, ataxia, delirium)
Valproate	Give slow (over 30 min) bolus for status epilepticus 20–40 mg/kg i.v (max 3000 mg)., after 12 h continue 3–5 mg/kg 12 hourly	Sodium channel blockade	Usually third-choice drug for refractory seizures, hypoxic myoclonus (weak evidence of efficacy)	Narrow therapeutic range: send blood levels before third maintenance dose (target 80–100 mg/L) Hyperammonaemia Never co-administer with meropenem

Most Common Antimicrobials				
Drug	**Dose and administration**	**Mechanism of action**	**Uses**	**Common adverse effects**
Ampicillin/ Sulbactam (beta-lactamase inhibitor)	1.5–3 g every 6 h	Inhibition of the synthesis of the peptidoglycan layer of bacterial cell walls. Bactericidal, time-dependent killing	sCAP, UTIs	none
Piperacillin/ tazobactam (beta-lactamase inhibitor)	4.5 g every 4–6 h		HAP (covers also anaerobes and pseudomonas)	none
Flucloxacillin	2 g every 4–6 h		MSSA infections	none
Meropenem	1 g every 6 h or 2 g every 8 h		VAP and other nosocomial infections incl. ESBL1 and Amp C bacteria	seizures
Vancomycin	30 mg/kg i.v. (max. 3 g) bolus over 60 min, followed by 15 mg/kg every 12 h (C.dif. colitis: 125 mg. p.o. every 4 h for 10 days)	Inhibits cell wall synthesis by inhibition of the transpeptidase	MRSA infections, C.dif infection (p.o. treatment)	Red man syndrome if infused too fast, nephrotoxicity, monitor levels, aim for 15–20 mg/L before next dose)
Amikacin	20–25 mg/kg ABW loading first day, followed by 1 g i.v. once daily	Inhibits bacterial protein synthesis, concentration-dependent killing	Monotherapy for UTIs, co-treatment with beta-lactam for G-sepsis	Nephrotoxicity after 3–5 days, monitor blood levels before and after second dose
Trimethoprim/ sulfamethoxazole	960 mg every 12 h i.v. or p.o. every 12 h (PCP prophylaxis: 480 mg once daily)	Folate synthesis inhibition	UTIs, stenotrophomonas PCP	Hyperkalaemia, agranulocytosis
Fluconazole	400 mg i.v. or p.o. daily	Inhibits yeast cell wall synthesis (by inhibiting ergosterol synthesis)	Candida albicans prophylaxis (e.g. upper GI perforation) or treatment	None
Acyclovir	5–10 mg/kg IV every 8 h for 21 days	Inhibits viral DNA polymerase	Severe HSV infections (e.g. encephalitis)	None

Drugs influencing gastrointestinal system				
Drug	**Dose and administration**	**Mechanism of action**	**Uses**	**Common adverse effects**
Famotidine	20 mg i.v. twice a day	H2 blocker	GI prophylaxis	–
Omeprazole	20–40 mg. i.v. twice a day for GU prophylaxis, 240 mg/day continuous infusion for GI bleed	Proton pump inhibitor	Prophylaxis and treatment of GI ulcers and bleeding	Increases risk of C. dif. infections
Metoclopramide	10 mg i.v. every 6–8 h for a maximum of 5 days	Stimulates gut motility by affecting different receptors in the GI tract, antiemetic by central D2 receptor inhibition	Gastric nutrition intolerance (high residues)	Usually none, rarely tardive dyskinesia or neuroleptic malignant syndrome

Top Ten Line Incompatibilities

Drug	Incompatible drug/solution	Compatibility information
Ceftriaxone	Calcium containing solutions	Precipitation
Potassium or sodium phosphate	Calcium, magnesium containing solutions	Precipitation
Amiodarone	Sodium chloride 0.9%	Loss of amiodarone (5% in 6 h)
Noradrenaline	Sodium chloride 0.9%	Loss of oradrenaline (10–20% in 24 h)
Amphotericin B	Sodium chloride 0.9%	Loss of amphotericin V (50% in 2 h)
Phenytoin	5% dextrose Noradrenaline Dobutamine Midazolam Morphine Heparin Sufentanyl Fentanyl Propofol	Visible crystals within 10–20 min Precipitation
Aminoglycosides	B lactams	Loss of amikacin (30% in 2 h)
Thiopental	Noradrenaline Dobutamine Midazolam Morphine Sufentanil	Precipitation

Drug	Incompatible drug/solution	Compatibility information
Furosemide	Noradrenalin Midazolam Insulin Morphine Fluconazole Vasopressin	Precipitation

Top Ten Drug–Drug Interactions

Drug affected	Interacting drugs	Effect of interaction
Valproic acid	Carbapenems	Carbapenems dramatically reduce valproate serum levels, loss of efficacy
Sufentanil, Fentanyl	Fluconazole, voriconazole, and other azoles, clarithromycin	Opioids levels can be enhanced by interacting drugs, risk of adverse reactions
Amiodarone	Clarithromycin, citalopram, trazodone, haloperidol, quetiapine, olanzapine, ciprofloxacin, moxifloxacin, fluconazole, voriconazole, and other azoles	QTc prolongation, risk of torsades de pointes
Theophylline	Ciprofloxacin	Theophylline levels are markedly increased, risk of adverse reaction and toxicity
Linezolide	Citalopram, sertraline, fluoxetine, paroxetine, trazodone, mirtazapine, duloxetine, venlafaxine, tramadol	Risk of serotonin syndrome
Clopidogrel	Omeprazole	Reduction in clopidogrel efficacy, risk of thrombosis
Ticagrelor	Fluconazole, voriconazole, and other azoles, clarithromycin	Ticagrelor cumulation, risk of bleeding
Ticagrelor	Rifampicin, phenytoin	Reduction in ticagrelor efficacy, risk of thrombosis
Benzodiazepines	Fluconazole, voriconazole, and other azoles, clarithromycin	Plasma levels of benzodiazepines are very markedly increased, risk of adverse reactions, and prolongation of their effect
Benzodiazepines	Rifampicin, dexamethasone, phenytoin	Plasma levels of benzodiazepines are very markedly decreased, loss of efficacy
Digoxin	Clarithromycin, verapamil, propafenone, amiodarone	Interacting drugs cause increase in digoxin levels, risk of toxicity

Note: Epidural Analgesia

Epidural analgesia is highly effective in controlling acute postoperative pain from abdominal surgery, post-trauma or acute pancreatitis pain and is associated with minimal side effects and high patient satisfaction. However, it can lead to potentially fatal complications like any other technique, so effective management requires a coordinated multidisciplinary approach. The primary complications of continuous epidural analgesia include hypotension, motor blockade, urinary retention, pruritus, pressure ulcers, respiratory depression, post-dural puncture headache, epidural haematoma or abscess, neurological damage, and inadequate analgesia. Epidural catheters are placed using an aseptic technique and, when manipulated, asepsis must always be respected (treat as a central venous line). Epidural catheters tend to remain in place for up to 48–72 h for postoperative analgesia, but in selected cases, they can be tunnelled so that they can remain in place for up to 15 days. In patients with risk factors for nosocomial infection (such as diabetics, patients taking steroids, or immunosuppression), the tip of the catheter should be sent for bacteriology once removed. The epidural route of administration must be marked with a different colour (yellow for identification of nerve blocks) and must not have any stopcock for additional drug administration. An antibacterial filter should always be used at the junction between the protractor and the epidural catheter. All drugs administered through the epidural catheter must be clearly discriminated. Never administer local anaesthetic drugs—often administered through an epidural catheter—by another route, as this increases the risk of death from cardiotoxicity and neurotoxicity. In case of cardio-respiratory arrest, prolonged resuscitation manoeuvres (>1 h) should be carried out and concomitant use of lipid solution is recommended.

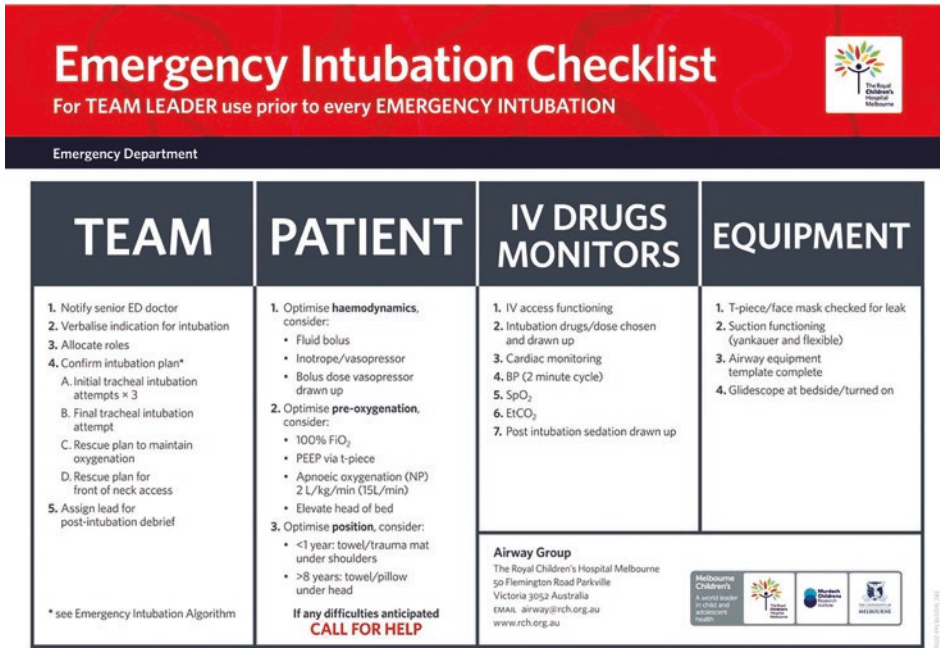
Usual concentration of bupivacaine is 0.125%, which allows maximum infusion rate 15 mL/h. Local anaesthetic can be used alone ("plain epidural") or opioids are added to it. Systemic (i.v.) and epidural opioids should not be administered concomitantly.

Appendix B: Useful Checklists and Algorithms

Note: Most of these figures will need to be redrawn to get unique graphical design. In case of copyright issues, these need to be solved.

Airway Management

ICU Intubation Checklist



Emergency Intubation Checklist

For TEAM LEADER use prior to every EMERGENCY INTUBATION

Emergency Department

TEAM

1. Notify senior ED doctor
2. Verbalise indication for intubation
3. Allocate roles
4. Confirm intubation plan*
   - A. Initial tracheal intubation attempts × 3
   - B. Final tracheal intubation attempt
   - C. Rescue plan to maintain oxygenation
   - D. Rescue plan for front of neck access
5. Assign lead for post-intubation debrief

* see Emergency Intubation Algorithm

PATIENT

1. Optimise **haemodynamics**, consider:
   - Fluid bolus
   - Inotrope/vasopressor
   - Bolus dose vasopressor drawn up
2. Optimise **pre-oxygenation**, consider:
   - 100% FiO_2
   - PEEP via t-piece
   - Apnoeic oxygenation (NP) 2 L/kg/min (15L/min)
   - Elevate head of bed
3. Optimise **position**, consider:
   - <1 year: towel/trauma mat under shoulders
   - >8 years: towel/pillow under head

If any difficulties anticipated
CALL FOR HELP

IV DRUGS MONITORS

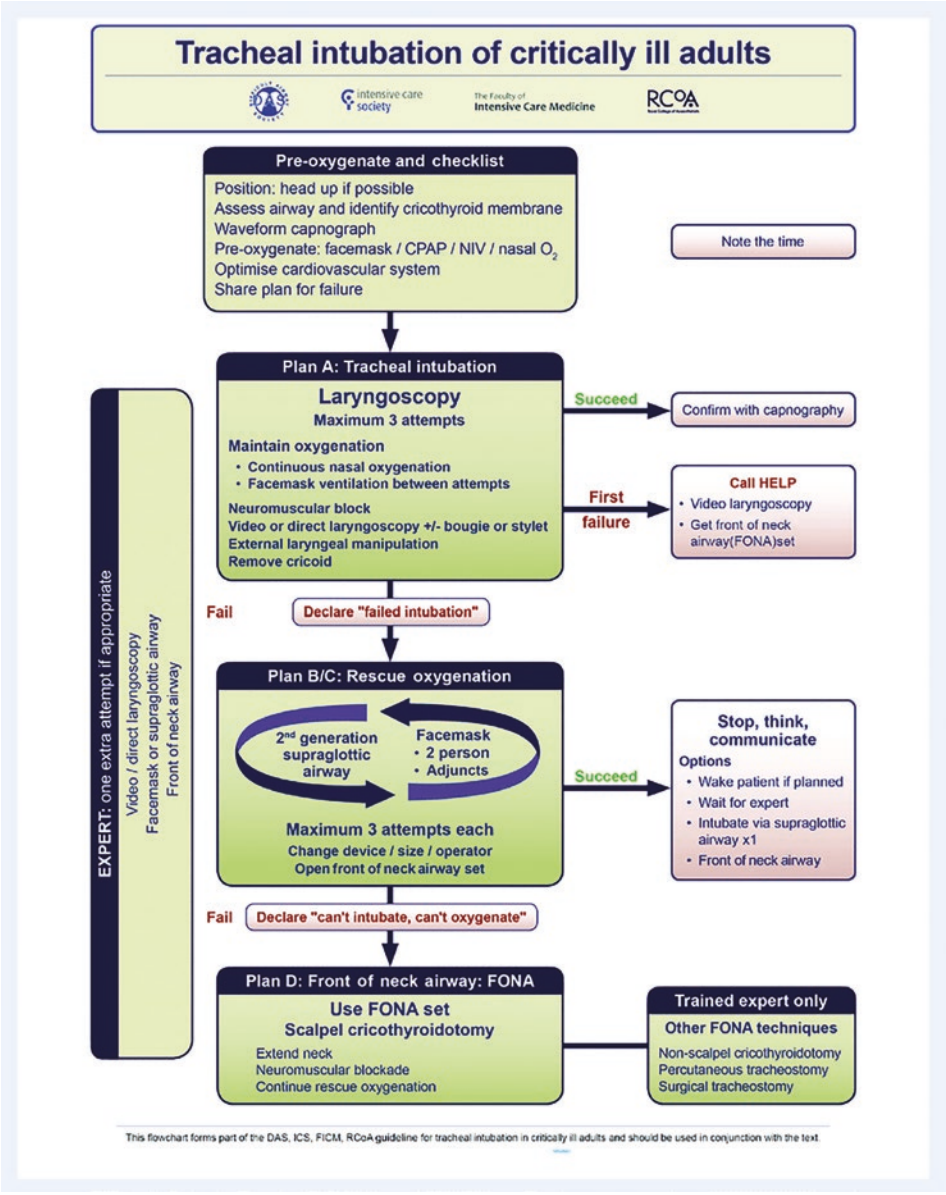
1. IV access functioning
2. Intubation drugs/dose chosen and drawn up
3. Cardiac monitoring
4. BP (2 minute cycle)
5. SpO_2
6. $EtCO_2$
7. Post intubation sedation drawn up

EQUIPMENT

1. T-piece/face mask checked for leak
2. Suction functioning (yankauer and flexible)
3. Airway equipment template complete
4. Glidescope at bedside/turned on

Airway Group
The Royal Children's Hospital Melbourne
50 Flemington Road Parkville
Victoria 3052 Australia
EMAIL airway@rch.org.au
www.rch.org.au

Difficult Airways Society Algorithm

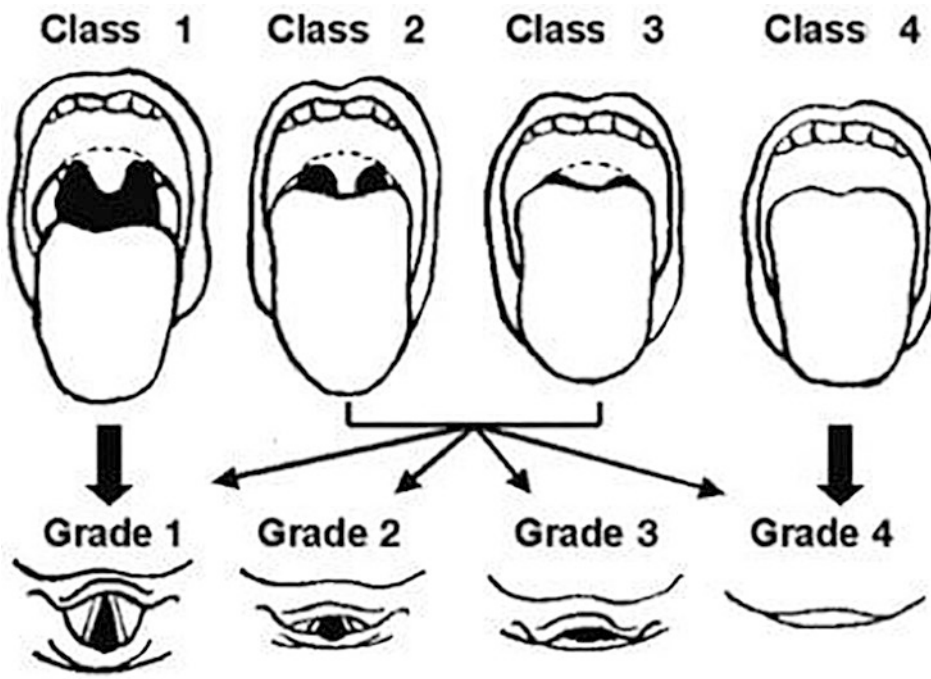


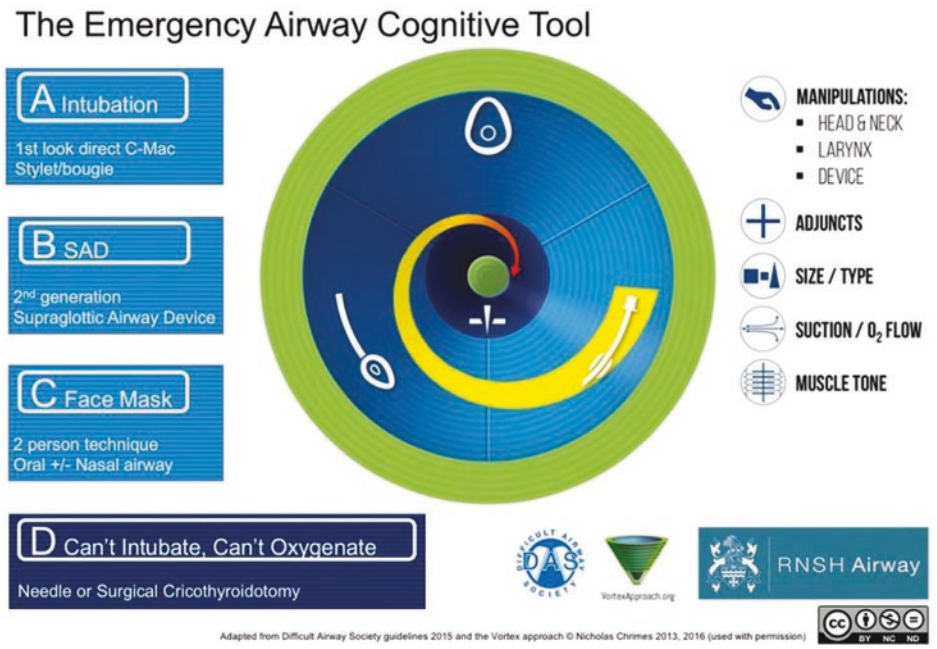
Predicting Difficult Intubation in Critically Ill: The MACOCHA Score

The MACOCHA Score is the only tool has been validated for predicting the difficulty of endotracheal intubation in critically ill adults. It is a graduated score ranging from 0 (anticipated easy) to 12 (anticipated very difficult) based upon seven clinical features.

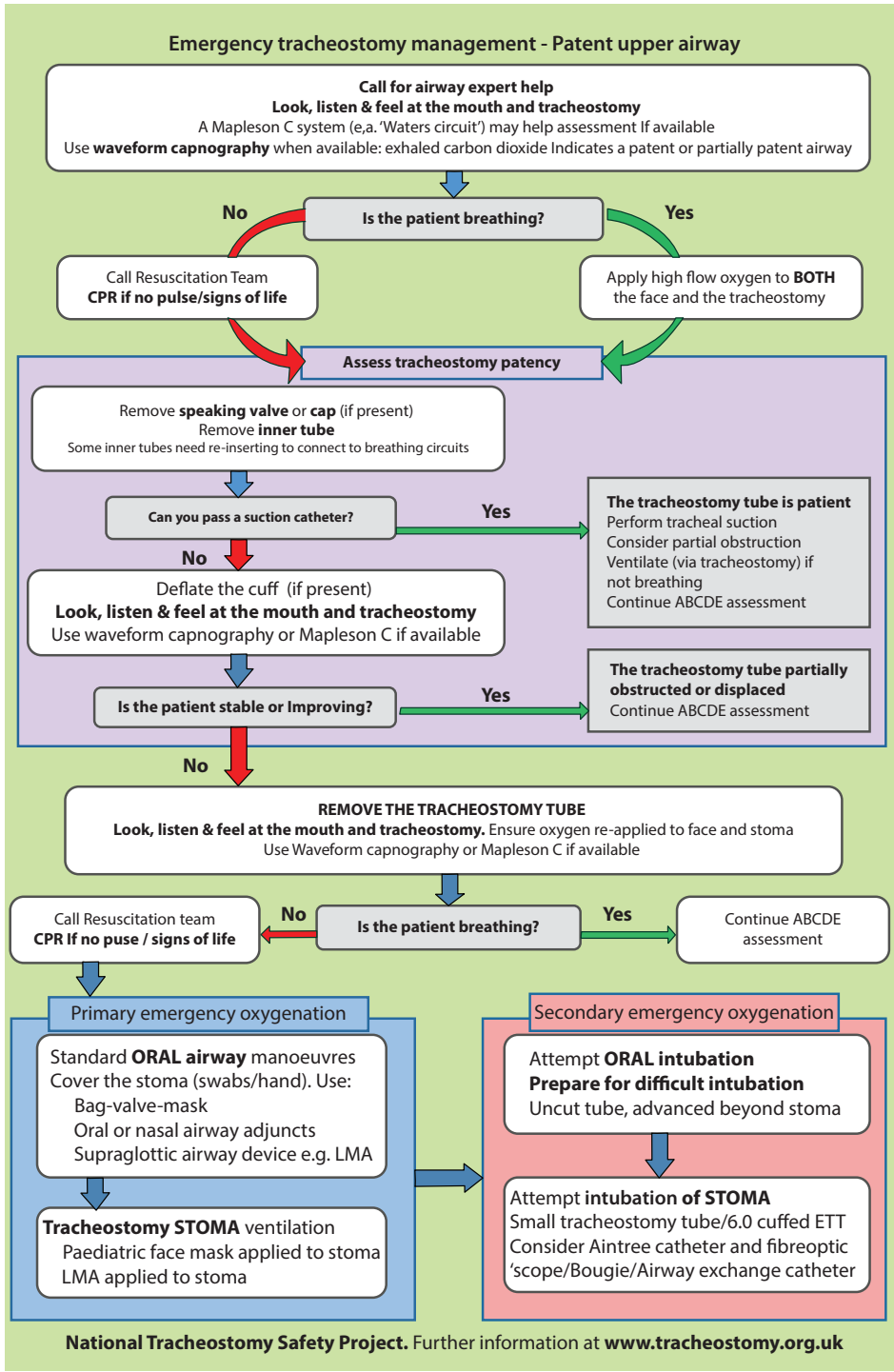
Factors points	
Factors related to patient	
Mallampati score III or IV	5
Obstructive sleep apnoea syndrome	2
Limited mouth opening <3 cm	1
Reduced mobility of cervical spine	1
Factors related to pathology	
Coma	1
Severe hypoxaemia (<80%)	1
Factor related to operator	
Non-anaesthesiologist	1

Mallampati Classes



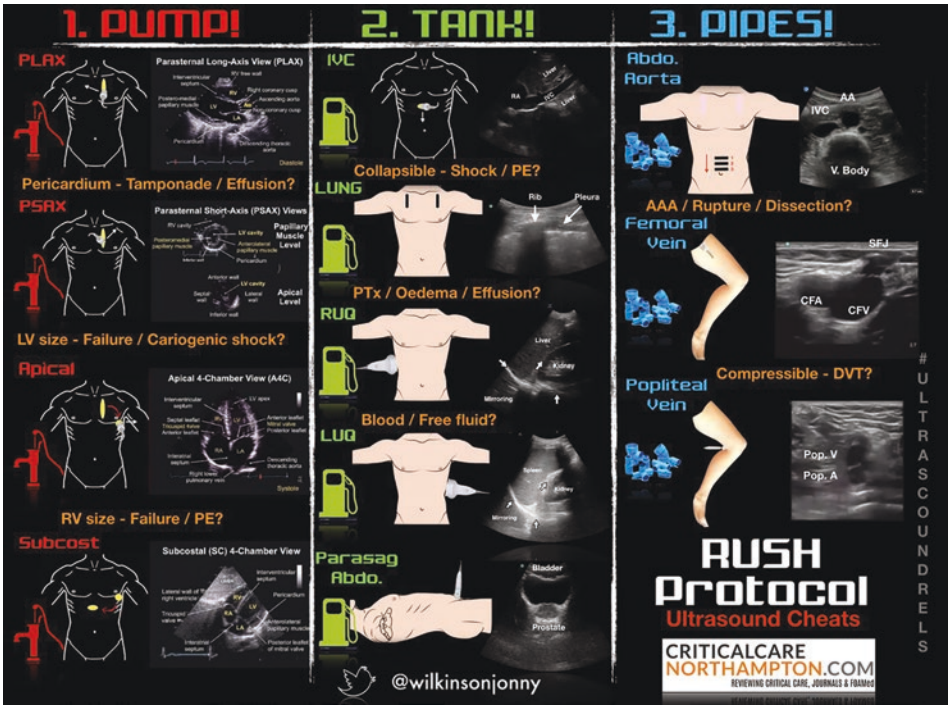


Comment: The principle of "vortex approach" is a cycle of attempts in securing airways with intubation, supraglottic devices, and oxygenating the patient with a facemask. In each cycle, intubating conditions (see on the right) are manipulated. Oxygenation is always a priority and once the patient spirals down the vortex to hypoxia, bougie-assisted cricoidotomy is performed.



Focused Ultrasound Protocols

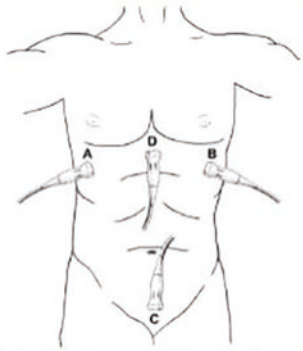
RUSH Protocol: Rapid Ultrasound in Shock



Focused Assessment Using Sonography in Trauma (FAST)

Views in FAST & Extended-FAST

Four views of original FAST[1]



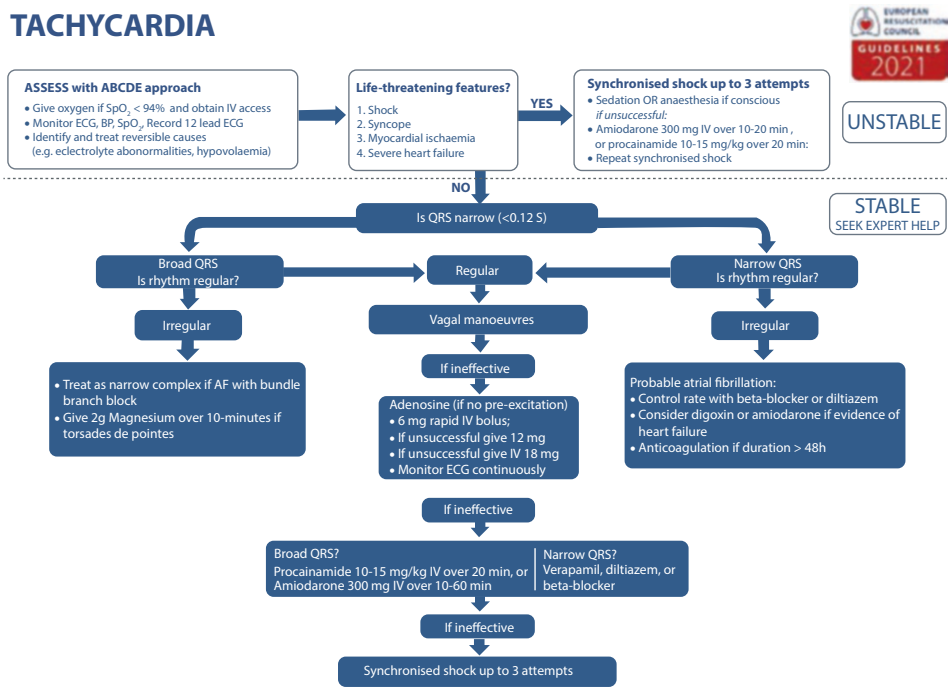
A: Right upper quadrant view
B: Left upper quadrant view
C: Pelvic view (axial & transverse)
D: Subxiphoid heart view

Additional views in E-FAST[2]

A: Right anterior longitudinal chest view
B: Left anterior longitudinal chest view
C: Longitudinal view of IVC

[1] Tso P et al. J Trauma 1992; 33: 39–43.
[2] Kirkpatrick AW et al. J Trauma 2004;57(2):288–295.

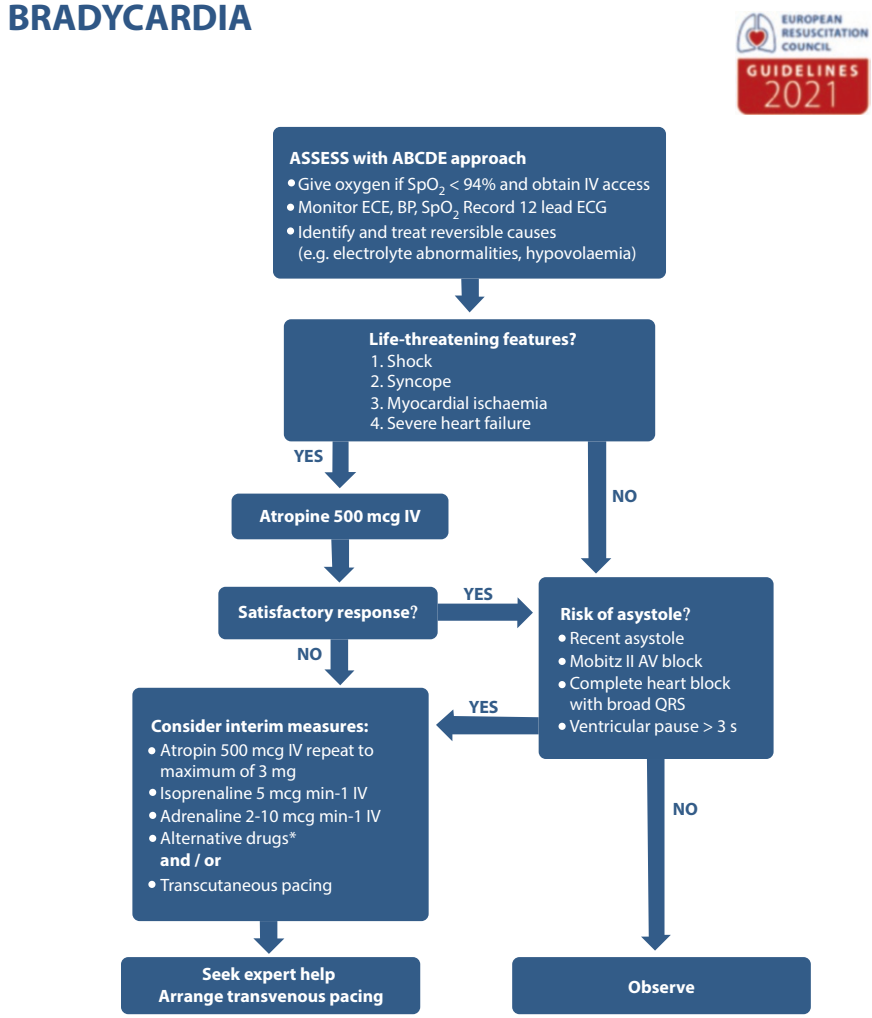
Arrhythmias
Tachyarrhythmias Algorithm



Tachycardia algorithm. ABCDE airway, breathing, circulation, disability, exposure BP blood pressure; DC direct current; ECG electrocardiogram; IV intravenous; SpO_2 arterial oxygen saturation; VT ventricular tachycardia.

Cite ERC 2021 Guidelines

Bradyarrhythmia Algorithm



* Alternatives include:
- *Aminophylline*
- *Dopamine*
- *Glucagon (if bradycardia is caused by beta-blocker or calcium channel blocker)*
- *Glycopyrrolare (may be used instead of atropine)*

Bradycardla algorithm. ABCDE aiiway, breathing, circulation, disability, exposure BP blood pressure; ECG electrocardiogram; IV intravenous; SpO_2 arterial oxygen saturation.

Routine Daily Assessment Checklist

ABCDEFG: Daily Checklist

A

Airway:
- Tube position
- Cuff pressure

B

Breathing:
- Ventilator setting – **focus on safety**
- Mode (synchronised, non-synchronised?)

1. RR
2. Pressures
3. PEEP
4. FiO2

- Blood gases: pH, PaO2, PaCO2
- Secretions
- Lung sounds

C

Cirulation:
- Capillary refill time
- Arterial blood pressure
- Heart rate
- Central Venous Pressure CVP
- ScvO2 (venous blood gas)
- Lactate
- Urinary output, fluid balance/24h

D

Disability:
- GCS
- RASS status
- CAM-ICU / delirium
- Pupil size and reactiveness to light

E

Exposure:

Check access sites
Check skin colour and pathologies
Drains, tubes, lines
Body temperature
Lab results – pathological values

F

Feeding:
- Blood glucose
- Enteral feeding tolerance
- Bowel movements

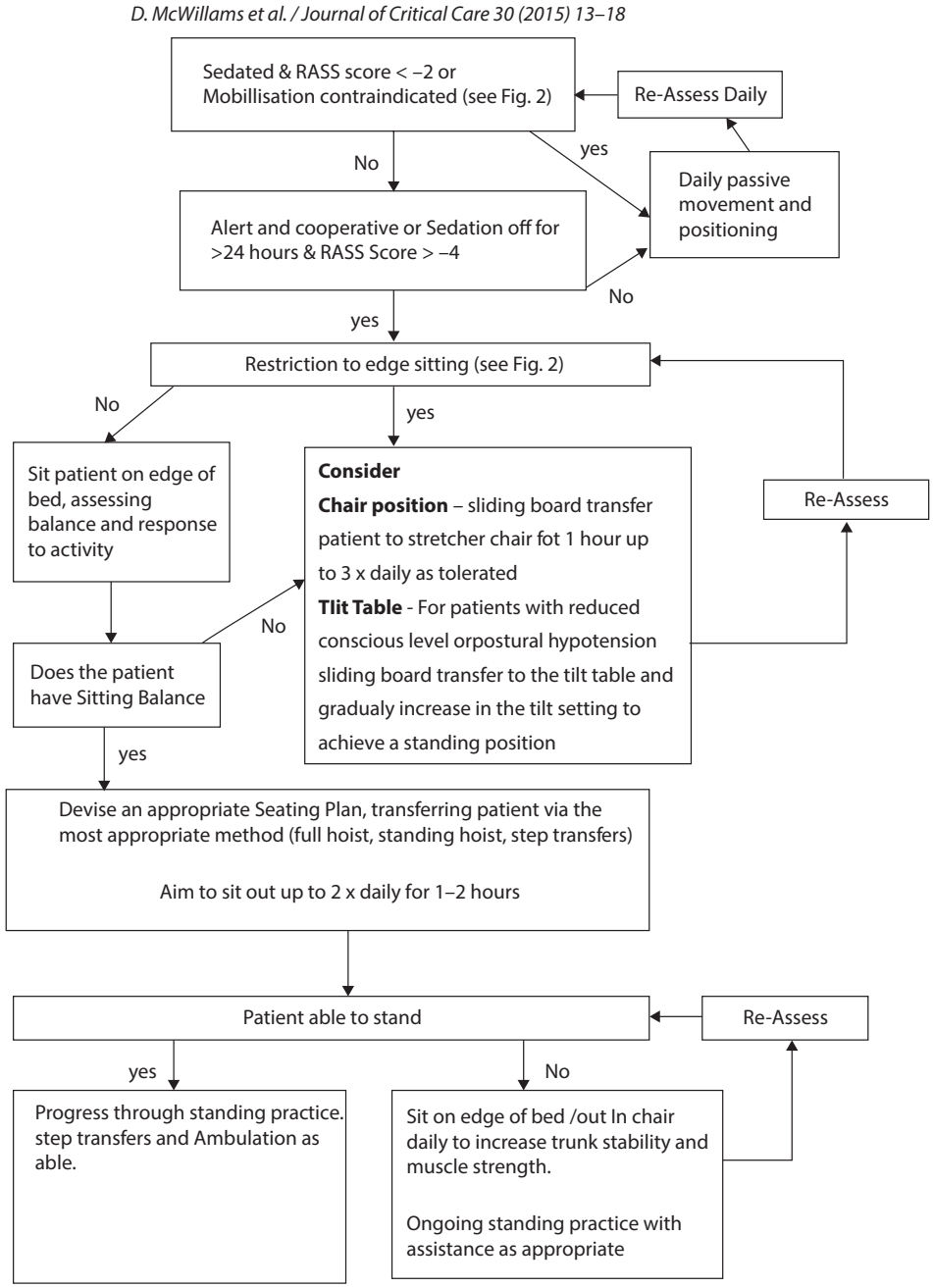
G

General other aspects:
- Gastric ulcer prophylaxis
- VAP prophylaxis
- Positioning, mobilisation and physical therapy

Daily Reassess care plan

1. Resuscitation status
2. Sedation
3. GI prophylaxis
4. DVT prophylaxis
5. Fluids and electrolytes
6. Nutrition
7. Intravenous and other accesses
8. Duration of antibiotics and steroid use
9. Delirium prevention

Example of Goal-Directed Mobility Protocol



Transfer of ICU Patient—Drug and Equipment Checklist

Patient label	Date (dd/mm/yyyy)	
	Time of start transport (hh/mm)	
	Time of arrival in ICU (hh/mm)	
	Procedure	
	☐ CT-Scan ☐ MRI ☐ Angiography	
	☐ Other	
	Purpose of transport	
	☐ Diagnostic ☐ Intervention	
	☐ Diagnostic and Intervention	

Pre-transport

Equipment/materials	YES	NO	NA
Transport bag present			
Transport trolley fully charged			
Defibrillator present			
Manual resuscitation bag present			
Sufficient oxygen level			
Checklength of i.v. tubes			
In case of MRI; extend length i.v. tubes			
Shut off necessary i.v. tubes			

Medication	YES	NO	NA
Sufficient intravenous medication			
Additional intravenous sedatives			
Additional intravenous inotropics			
Additional medication			
Additional infusion pump			
Additional intravenous fluids			
Stop enteral nutrition			
Stop enteral insulin			

In case of CT-Scan with contrast	YES	NO	NA
Intravenous cannula 18GA present			
Oral contrast administered			
If "YES":			
Renal protection according to protocol			

Monitor	YES	NO	NA
$EtCO_2$ monitoring present			
Check and set visual and audible alarm			

Transport ventilator	YES	NO	NA
Turn on the oxygen			
Put HME filter between ventilator and ET/TT			
Check and set visual and audible alarms			

ET/TT depth (cm)	

Administrative	YES	NO	NA
Resister baseline vital signs overleaf			
Switch patient in PDMS to "Transport"			
Radiology department informed			
Fill In MRI Safety Questionnaire			

Example of ICU transfer checklist.

Ref.: Brunsveld-Reinders AH, Arbous MS, Kuiper SG, de Jonge E. A comprehensive method to develop a checklist to increase safety of intra-hospital transport of critically ill patients. Crit Care. 2015 May 7;19(1):214. doi: 10.1186/s13054-015-0938-1. PMID: 25947327; PMCID: PMC4438434.

Team Emergency Assessment Measure (TEAM™)

Introduction

This form has been designed as a teamwork observational scale to assess the performance of emergency medical teams (e.g. resuscitation and trauma teams). The form should be completed by expert clinicians to enable accurate performance rating and feedback of leadership, teamwork, situation awareness and task management. Rating prompts are included where applicable. Please rate the first 11 items using the following scale and the last item using the 10 point scale.

Never/Hardly ever	Seldom	About as often as not	Often	Always/Nearly always
0	1	2	3	4

Team Identification

Date _____ Time _____ Place _____

Team Leader _____ Team _____

Leadership: *It is assumed that the leader is either designated, has emerged, or is the most senior – if no leader emerges allocate a '0' to questions 1 & 2.*	0	1	2	3	4
1. The team leader let the team know what was expected of them through Tdirection and command	☐	☐	☐	☐	☐
2. The team leader maintained a global perspective *Prompts: Monitoring clinical procedures and the environment? Remaining 'hands off' as applicable? Appropriate delegation?*	☐	☐	☐	☐	☐

Team Work: *Ratings should include the team as a whole i.e. the leader and the team as a collective (to a greater or lesser extent).*	0	1	2	3	4
3. The team communicated effectively *Prompts: Verbal, non-verbal and written forms of communication?*	☐	☐	☐	☐	☐
	☐	☐	☐	☐	☐
5 The team acted with composure and control *Prompts: Applicable emotions? Conflict management issues?*	☐	☐	☐	☐	☐
6. The team morale was positive *Prompts: Appropriate support, confidence, spirit, optimism, determination?*	☐	☐	☐	☐	☐
7. The team adapted to changing situations *Prompts: Adaptation within the roles of their profession? Situation changes: Patient deterioration? Team changes?*	☐	☐	☐	☐	☐
8. The team monitored and reassessed the situation	☐	☐	☐	☐	☐
9. The team anticipated potential actions *Prompts: Preparation of defibrillator, drugs, airway equipment?*	☐	☐	☐	☐	☐

Task Management	0	1	2	3	4
10. The team prioritised tasks	☐	☐	☐	☐	☐
11. The team followed approved standards/guidelines *Prompt: Some deviation may be appropriate?*	☐	☐	☐	☐	☐

Overall	1	2	3	4	5	6	7	8	9	10
12. On a scale of 1–10 give your global rating of the team's performance	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

Comments: _____

_____

_____

Ref.: Cooper S, Cant R, Porter J, et al. Rating medical emergency teamwork performance: Development of the Team Emergency Assessment Measure (TEAM). *Resuscitation* 2010, 81(4), 446–452. doi:10.1016/j.resuscitation.2009.11.027

Conversion of Urine-Specific Gravity to Urine Osmolarity

Specific gravity	Refractometry Osmolality
1.010	300
1.012	341
1.014	381
1.016	422
1.018	462
1.020	503
1.022	544
1.024	584
1.026	625
1.028	665
1.030	706

Relationship between urine-specific gravity and plasma osmolality.

Appendix C: ICU Trainee Survival Guide

Gabriel Garcia Rosenbaum

Pre-rounding:

- Make sure you know at what time your team start to round.
- It is possible that in your first days, you may need to start pre-rounding earlier, so, try to keep a balance between duty hours and good patient care.
- Find the overnight nurse before their morning shift change, they can give you more detailed information about overnight events on your patients.
- Start your daily progress note. Time management is the key. Go systematically through vitals, labs, review medications, imaging, or diagnostics, consults/referral inputs, and other ancillary recommendations from physiotherapy, occupational therapy, speech therapy, or the dietitian.
- The patient: Your goal is to get as much information as you can. Try to know your patient better than anyone else. Try to follow your "Ds" (Dying, Discharging, Diagnostics). See first whoever is sick and likely dying. Make sure your senior is aware of these patients. Then, try to see the rest ones, especially those that you think can head out of the ICU to the floor. Lastly, you can always discuss your patient with your senior for additional workup.

Rounding:

- This is the time for you to shine like a rock star!
- You will be presenting to your attending/consultant, fellow, and the rest of the team. Usually, there is a pharmacist, social worker, dietitian, and medical students. It can be nerve-wracking, but you will be alright! I trust you!
- You can present your patient from a printed note on paper, mobile computers from the ICU, or your tablet or laptop.
- Presentation:
  - Quick ID statement, especially if your attending knows the patient. Please, include the reason why the patient is needing ICU care.
  - 24 h events, usually what the overnight nurse or team told you, plus any pertinent information you saw on the chart.
  - Assessment and plan system by system. Always go neuro, cardiovascular, respiratory, gastrointestinal, renal/genitourinary, haematology and infectious disease, endocrine, musculoskeletal and ICU issues, like DVT prophylaxis, diet, lines, stress ulcer prophylaxis, and code status.
  - Mention things only once, even if it is in your note multiple times. Please try to keep your diagnostics up to date. You might not want to mention the same chest X-ray 3 days on a row.
- Teamwork. There is usually more than one junior and there might also be medical students. Your teammate can put orders in while you are presenting, and it is very nice if someone else can update the daily task for the team at the same time, so when you are done presenting, your orders are in. Also, if possible and you have time, you could sign your notes while rounding, which means, the work is almost done after rounds.

After Rounds:

- Run the list. This is very helpful, usually done by the senior resident, advance provider, or fellow. Here, you can catch up with the rest of the team on what is going on with the rest of the patients. Also, it is time to double-check all orders.
- Make sure you get your diagnostic test in, consults are called, and discharges from the unit are happening.
- Procedures. If you are willing to do a procedure, reach out to your senior who can supervise you.
- Family updates. These are extremely important, yet, sometimes forgotten. Please, try to call or speak to the family every day, especially if they are not allowed to visit their loved ones.
- Notes. Yes, they come at last. Sign them after you are done.

Before Going Home:

- Have your own checklist. But, it is helpful to review that your note is in and sent to your consultant, the daily task list is updated, consults/referrals are called, recommendations are appropriately followed or considered, and laboratory tests are prepared for the next day.

References/Further Reading/Additional Resources

- At your programme or home institution, look for prior experiences and note templates from your co-residents, look for the senior working with you and ask many questions you like, including who you are likely to see on the following day.

Take-Home Message

ICU could be overwhelming at first glance, multiple things will be happening at the same time, infusion rates or ventilator settings might not be the same from last seen, or some decisions may not make any sense to you. But if you keep up the hard work, you are going to really enjoy your ICU rotation and learn a ton!

I wish you success!