

ICU Clinical Review

Haytham Abbas
Editor



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Department of Internal Medicine, Critical Care
Medicine and Cardiovascular Critical Care

Dr. Soliman Fakeeh Hospital

Jeddah, Saudi Arabia



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Preface

Since completing my clinical exam for the Fellowship in Critical Care Medicine, I was inspired to write a book that contains all the approaches, diagrams, and topics I prepared, so I could share them with others. I truly enjoyed every second I spent writing, and my happiness grew even more with the exceptional support and collaboration of my incredible team at Dr. Soliman Fakeeh Hospital, Jeddah. I am truly grateful, thank you all for everything.

A sincere thank you also goes to everyone who supported us by sharing their knowledge or resources, which helped make this book successful and engaging. I warmly welcome your feedback and suggestions, which will inspire me further and be invaluable in shaping future editions of this resource.

Jeddah, Saudi Arabia

Haytham Abbas

Acknowledgments I would like to extend my gratitude to Dr. Soliman Fakeeh Hospital for their generous sponsorship and support in the publication of my book, *ICU Clinical Review*. Their contribution has been instrumental in bringing this work to fruition and in promoting knowledge in the field of critical care.

Introduction

ICU Clinical Review is a focused and comprehensive guide designed to enhance clinical insight and build familiarity with common scenarios encountered in ICU exams and real-life practice. The primary goal of this book is to serve as a practical, concise resource that highlights the most critical points needed by ICU practitioners, both in their clinical exams and during daily ICU duties.

Grounded in evidence-based medicine, this book includes the most essential ICU clinical trials and key references. It comprises 13 chapters covering various ICU subspecialties, each focused on the core skills ICU physicians are expected to master.

These essential skills include electrocardiogram (ECG) interpretation, arterial blood gas (ABG) analysis, hemodynamic assessment, both noninvasive and invasive mechanical ventilation, and continuous renal replacement therapy (CRRT) orders. They also cover the operation and interpretation of various ICU machines, such as cardiac devices, monitors for intra-abdominal and intracranial pressure, etc. Additional key skills include communication, statistical analysis, and more. All major clinical scenarios and conditions are covered in a clear, concise, and practical manner, designed to provide definitions, clinical presentations, scoring systems, common investigations, and management plans. Each topic is supported by current evidence and landmark clinical trials relevant to the ICU setting.

The book also features over 200 diagrams, images, and tables to make the information more engaging, accessible, and easier to retain.

To ensure accuracy and comprehensive coverage, each chapter has been peer-reviewed by experts from relevant departments, assigned based on their subspecialties.

Finally, practice is key. The knowledge presented in this book must be applied in clinical settings to reinforce understanding and improve proficiency.

Jeddah, Saudi Arabia

Haytham Abbas

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About the Editor

Haytham Abbas is a consultant in Critical Care Medicine at Dr. Soliman Fakeeh Hospital in Jeddah, Saudi Arabia, where he has been practicing since 2019. He obtained the Saudi Board in Internal Medicine in 2016 and the Saudi Critical Care Fellowship in 2019. In 2023, he was awarded the European Diploma in Critical Care Medicine and, in 2025, the Cardiac ICU Fellowship at Western University in London, Ontario, Canada.

From 2021 to 2024, he served as the program director for the Critical Care Medicine Residency Program. He has contributed to multiple clinical trials in Saudi Arabia and co-authored a chapter on “Proximal Myopathy” in *Skills of Rheumatology* by Dr. Hani Almoallim, published by Elsevier.

Dr. Abbas is also passionate about medical education and has been organizing and leading a focused course on ICU skills for the past several years. This course, aimed at mastering ICU techniques, spans three months and is offered annually. His interest in creating diagrams and figures to enhance learning has also driven his work in writing this book.

Chapter 1

Cardiovascular System



Haytham Abbas  and Ayman Eissa

Introduction

Cardiovascular system is one of the most important chapters that must be mastered by critical care practitioners. It contains multiple skills and diseases with which intensivists need to be familiar. Examples of these skills include hemodynamic assessment, the use of various cardiac devices for rhythm control or mechanical support, interpretation of electrocardiograms (ECG), the approach to shock, particularly cardiogenic shock, and the management of key clinical conditions.

Hemodynamic Assessment

The goal of initial resuscitation in any patient with shock is to restore mean arterial pressure (MAP) to sustain organ perfusion pressure and minimize tissue hypoperfusion which ends by organs damage.

Such hypoperfusion usually happens due to difference between oxygen delivery and oxygen demands. Figure 1.1 shows the oxygen delivery (DO_2) and oxygen consumption (VO_2) equations.

Patients with shock need a focused hemodynamic assessment method. Generally, hemodynamic assessment consists of three points to be addressed: volume responsiveness, cardiac status, and hypoperfusion markers.

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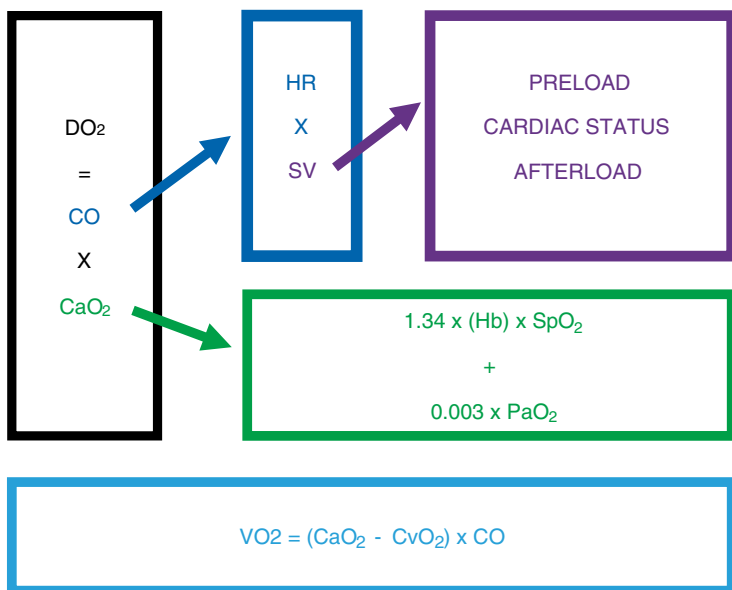


Fig. 1.1 Oxygen delivery and oxygen consumption equations. DO_2 = oxygen delivery, CO = cardiac output, CaO_2 = arterial oxygen content, HR = heart rate, SV = stroke volume, Hb = haemoglobin, SpO_2 = oxygen saturation, PaO_2 = arterial oxygen pressure, VO_2 = oxygen consumption, CvO_2 = venous oxygen content. (Adapted from Kumar [1]. Used with permission)

Volume Responsiveness

Any shocked patient must be assessed for volume responsiveness, and based on that, restoration of the hemodynamics can be predicted with volume expansion or to be ineffective and sometimes harmful if it was provided for unresponsive patient. Multiple assessment tools can be used for volume responsiveness assessment, which are generally classified either static or dynamic.

Static Parameters

They are predictors, which seek a single value to assess volume responsiveness; those values do not reflect the heart/lung interaction as in the dynamic maneuvers. Examples for static parameters are central venous pressure (CVP), pulmonary artery occlusion pressure (PAOP), global end diastolic volume (GEDV), and central venous oxygen saturation ($ScvO_2$).

One of the common protocols that used static maneuvers in the management of shocked patients is early goal-directed therapy (EGDT) (Fig. 1.2).

Despite *RIVERS trial* [2] showing mortality benefits from using EGDT, the subsequent studies *ARISE* [3], *ProMISE* [4], and *ProCESS* [5] did not show any clinical significance in comparison to usual care. Based on those trials, EGDT currently is not recommended as a standard protocol for management of shocked patients.

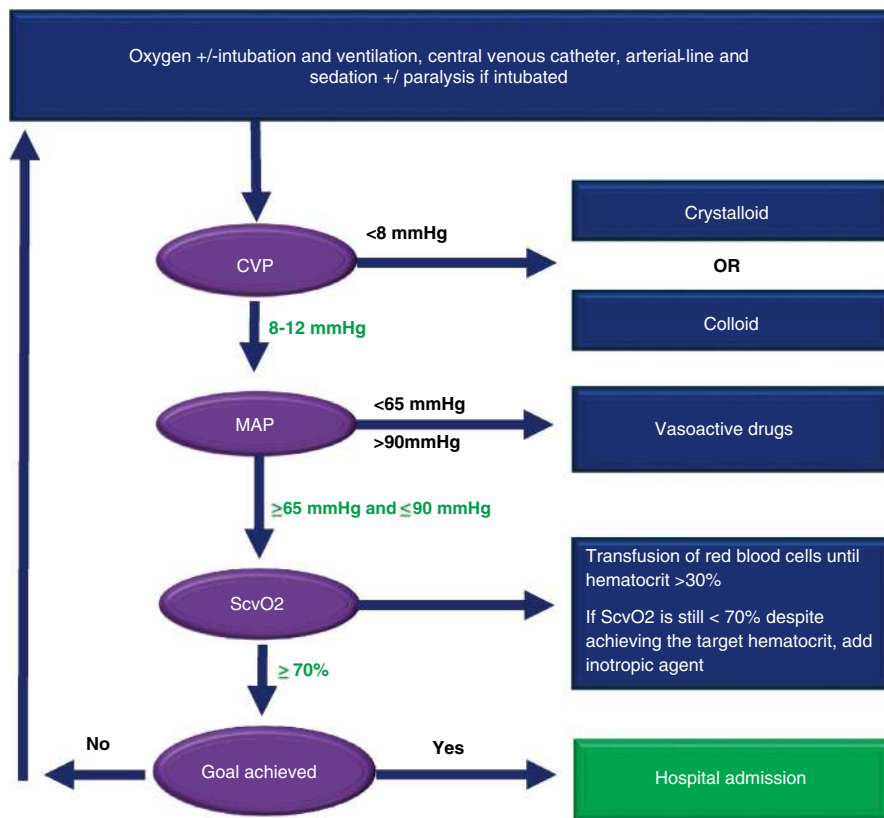


Fig. 1.2 Early goal directed therapy strategy. CVP = central venous pressure, MAP = mean arterial pressure, ScvO₂ = central venous oxygen saturation. (Adapted from Rivers et al. [2]. Used with permission)

Dynamic Maneuvers

Variable values that depend on heart/lung interaction for the hemodynamic assessment.

They are more sensitive than static maneuvers in prediction of volume responsiveness [6].

Common examples of these maneuvers are:

- Pulse pressure variation (PPV) and stroke volume variation (SVV)
- Mini-fluid challenge test
- Expiratory occlusion test
- Passive leg raise
- Pleth variability index (plethysmography)
- Point of care ultrasound (POCUS), e.g., lung ultrasound and inferior vena cava (IVC) assessment

Pulse Pressure Variation (PPV) and Stroke Volume Variation (SVV)

Changes in stroke volume (SV) or pulse pressure (PP) are markers of volume responsiveness; both are considered positive when they exceed 13% (Fig. 1.3) [7].

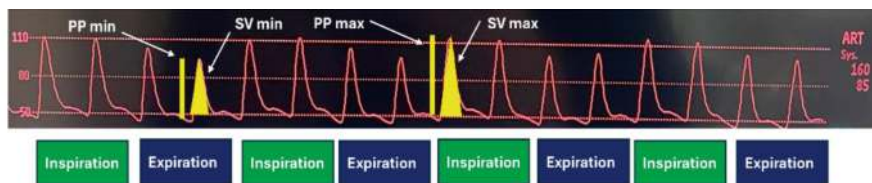
$$PPV = \left[(PP \text{ maximum} - PP \text{ minimum}) / PP \text{ mean} \right] \times 100$$

$$SVV = \left[(SV \text{ maximum} - SV \text{ minimum}) / SV \text{ mean} \right] \times 100$$

To consider the values are accurate, multiple conditions must be achieved: the patient should be sedated to the point of no spontaneous breathing, he should receive at least a tidal volume (TV) of 8 mL/kg/ideal body weight (IBW) [8], he must have a sinus rhythm with no arrhythmias, his lung compliance should be >30 mL/cmH₂O, and his heart rate to respiratory rate ratio must exceed 4.

The arterial (A) line connection and positioning must be accurate; the steps for setting are:

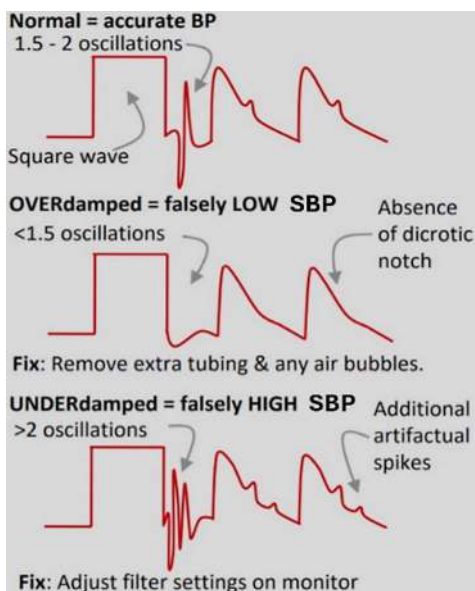
- Attachment of saline bag with pressure calf and the pressure must be set on 250–300 mmHg.
- Attach the saline bag to a transducer, and from the other side of the transducer, the A line must be connected.
- Leveling of the transducer to the phlebostatic point, which is the level of 4th intercostal space midaxillary line reflecting the right atrium.
- Zeroing: the line then will be connected to the monitor, the valve will be opened to atmospheric pressure, zeroing of the A line on the monitor, and once it is zero, the valve will be closed again to get A line waveform on the monitor.
- For confirmation of setting, the transducer must be flushed, the waveform will be box shaped and followed by one or two smaller oscillations. Abnormal connection makes the waveform overdamped or underdamped (Fig. 1.4).



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Fig. 1.3 Change in PP and SV is seen in the arterial line during mechanical positive pressure ventilation and considered a marker for volume responsiveness

Fig. 1.4 Normal and abnormal arterial line connection. SBP = systolic blood pressure. (Adapted from One Pager ICU, courtesy of Dr. Nick Mark's, used with permission)



Overdamped waveform: It has underestimated systolic pressure and overestimated diastolic pressure.

It is caused by loose connections, air bubbles in the line, blood clots, kinked line, or arterial spasm.

Underdamped waveform: It has overestimated systolic pressure and underestimated diastolic pressure.

It is caused by stiff tube and cardiac arrhythmias.

Neither overdamped nor underdamped waveforms alter the mean arterial pressure.

Mini-Fluid Challenge

A bolus of a small fluid volume (100 mL administered over 1 min, using crystalloids or colloids) is given, and hemodynamic parameters are compared before and after the bolus. An increase in stroke volume of >10% generally indicates volume responsiveness.

End Expiratory Occlusion Test

It consists of a respiratory pause of 15 s at end of the expiration phase during mechanical ventilation. An increase in venous return and cardiac output is observed, and 5% increase in cardiac output or stroke volume is a marker for volume responsiveness.

Passive Leg Raise (PLR)

Generally, the patient is kept in semi-sitting position before putting him supine with elevated lower limbs for 1–3 min, and improving of hemodynamics considers him as a responder (Table 1.1) [9].

Pleth Variability Index (Plethysmography) [10]

Variation in the plethysmography waveform of the pulse oximeter has been proposed as a predictor of fluid responsiveness (Fig. 1.5).

Point of Care Ultrasound (POCUS)

IVC Diameter

Patients who are spontaneously breathing and show an IVC diameter of ≤ 2.1 cm which collapses $>50\%$ during inspiration can be considered fluid responders (Fig. 1.6).

Table 1.1 Passive leg raise test

Measurement	Modality	Values to predict volume responsiveness
Stroke volume	Pulse contour analysis LVOT VTi using TTE or TEE	$>10\text{--}15\%$
Pulse pressure	Arterial waveform	$>10\text{--}15\%$
Cardiac output, cardiac index	Pulse contour analysis LVOT VTi using TTE or TEE PAC	$>10\text{--}15\%$
Quantitative end tidal CO_2		$>5\%$

LVOT VTi left ventricular outflow tract velocity time integral, *TTE* transthoracic echocardiography, *TEE* transesophageal echocardiography, *PAC* pulmonary artery catheter

Fig. 1.5 Plethysmography

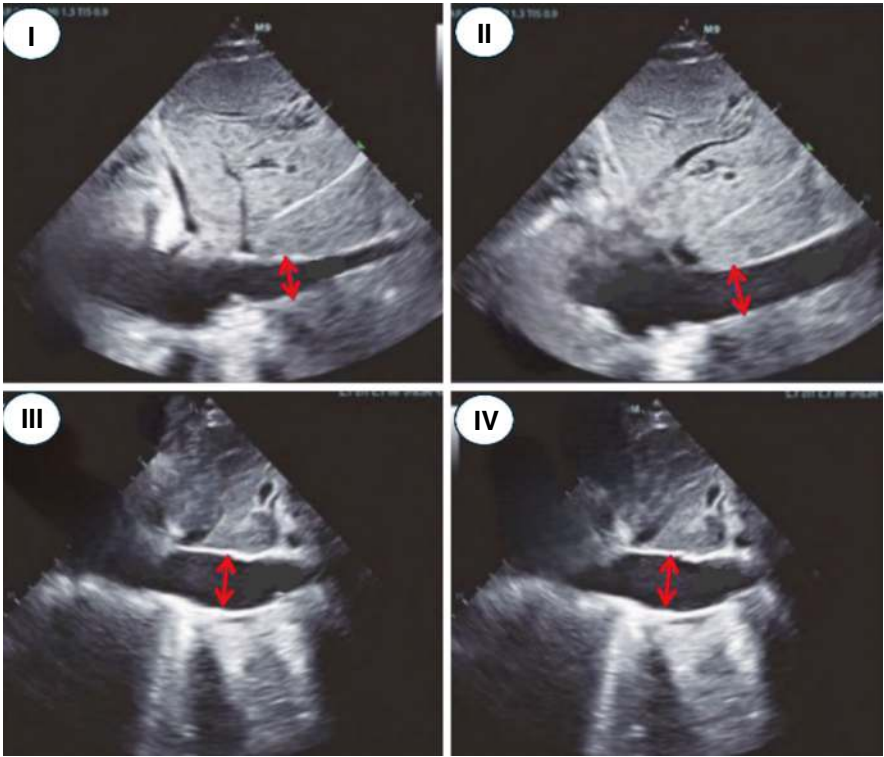
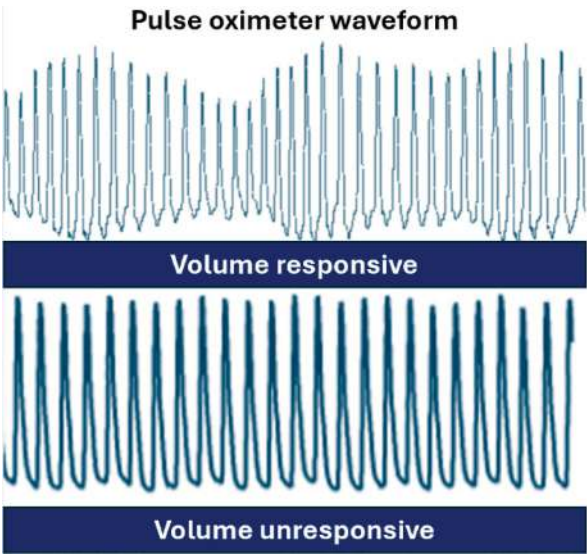


Fig. 1.6 I and II showed a collapsing IVC during the respiratory cycle, and III and IV showed poor IVC collapse

Collapsibility Index of IVC

It is used in spontaneously breathing patients by measuring the maximum and minimum diameter of the IVC, and the patient will be considered a responder when the collapsibility index is significantly high (>50%).

$$\text{Collapsibility Index} = \left[\left(\frac{\text{maximum diameter} - \text{minimum diameter}}{\text{maximum diameter}} \right) \right] \times 100$$

Distensibility Index of IVC

It is used in mechanically ventilated patients, and they are considered responders when the value exceeds 18%.

$$\text{Distensibility Index} = \left[\left(\frac{\text{maximum diameter} - \text{minimum diameter}}{\text{minimum diameter}} \right) \right] \times 100$$

Collapsibility and distensibility may be limited in some conditions like high right cardiac pressure, chest hyperinflation, increased intrabdominal pressure, or low lung compliance.

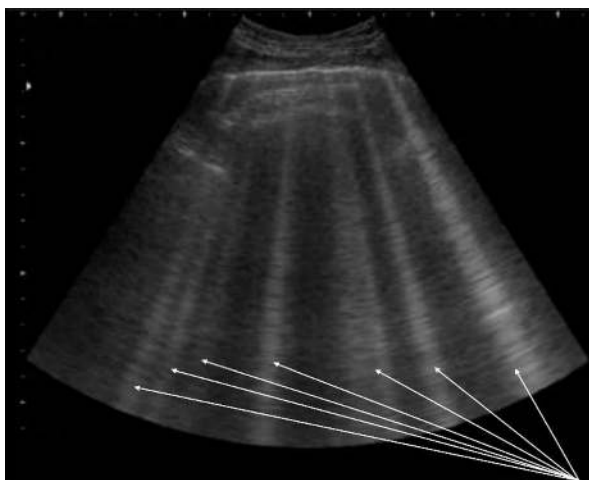
As the distensibility is applied for mechanically ventilated patients, they must be deeply sedated with no spontaneous breathing, taking a TV of at least 8 mL/kg/IBW, and having a normal respiratory rate.

Lung Ultrasound

The view of exaggerated B lines is a marker of pulmonary edema, and fluid unresponsiveness must be considered (Fig. 1.7).

Figure 1.8 summarizes the approach of volume responsiveness assessment.

Fig. 1.7 The arrows are targeting B lines in the chest



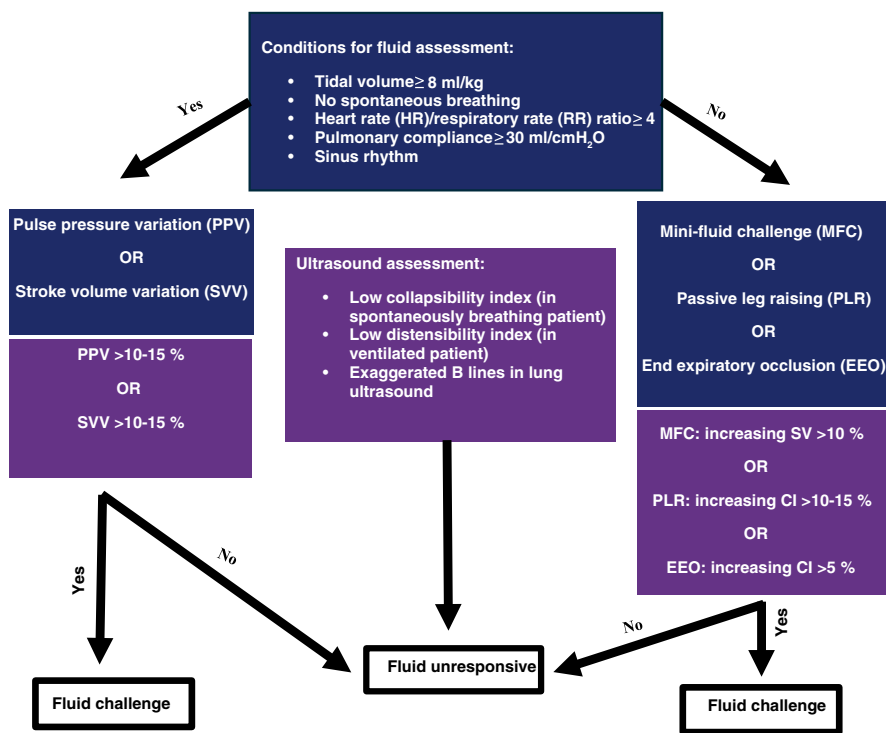


Fig. 1.8 Summary for volume responsiveness assessment tools. SV = stroke volume, CI = cardiac index

Cardiac Output (CO) Assessment

Multiple tools are used to measure CO, including echocardiography (Fig. 1.9), arterial line monitoring, central venous catheterization, and equations that estimate CO, such as the Fick equation.

Several machines are used to measure the CO by different mechanisms, and the most common modalities are:

- Lithium dilution-based devices (LIDCO)
- Thermodilution (e.g., PiCCO and pulmonary artery catheter)
- Pressure waveform analysis (Vigileo) (Fig. 1.10)

Pulse Index Continuous Cardiac Output (PiCCO)

PiCCO is a cardiac output monitor that combines pulse contour analysis and trans-pulmonary thermodilution technique.

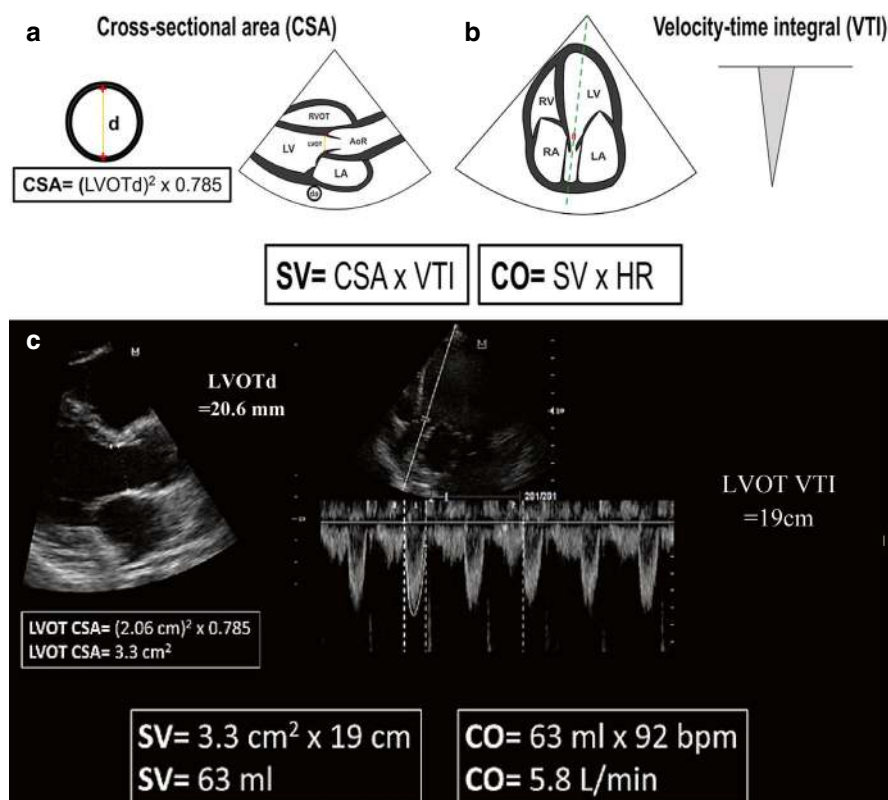


Fig. 1.9 Assessing the cardiac output by using the echocardiography. LVOT = left ventricular outflow tract, LVOTd = left ventricular outflow tract diameter, LV = left ventricle, LA = left atrium, RVOT = right ventricular outflow tract, AOR = aortic root, RA = right atrium, RV = right ventricle, SV = stroke volume, CO = cardiac output, HR = heart rate. (a) Is showing the parasternal long axis view to assess the LVOTd and CSA which = $(LVOTd)^2 \times 0.785$. (b) Is showing the apical 5 chamber view to assess LVOT VTI. (c) Is showing an example for a patient who has LVOT VTI of 19 cm and LVOT diameter of 2.06 cm so he will have a CSA of $(2.06)^2 \times 0.785 = 3.3 \text{ cm}^2$, $SV = VTI \times CSA = 63 \text{ mL}$, $CO = HR \times SV = 5.8 \text{ L/min}$. (Adapted from the original source: Blanco [11])

The thermodilution technique calculates volumetric measurements of preload and cardiac output after injection of cold saline.

Pulse contour continually estimates the stroke volume and CO from the arterial waveform.

The common uses of PiCCO are estimation of the types of shock, volume responsiveness, preload, cardiac status, pulmonary edema, and its causes.

The thermodilution parameters with their normal ranges include:

- CO: 4–8 L/min
- Cardiac index (CI): 3–5 L/min/m²

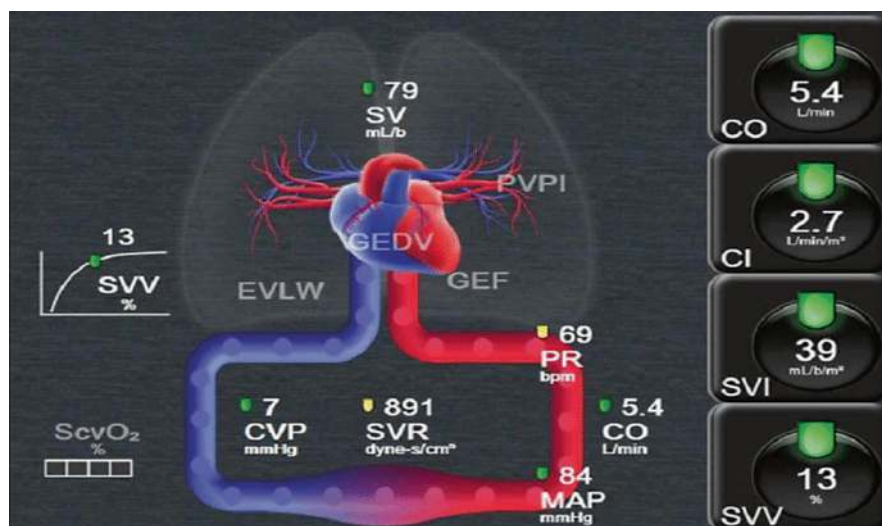


Fig. 1.10 Pressure waveform analysis (Vigileo) [12]

For preload assessment:

- Global end diastolic index (GEDI): 680–800 mL/m²
- Intra-thoracic blood volume index (ITBVI): 850–1000 mL/m²

For pulmonary edema assessment:

- Extravascular lung water index (ELWI): 3–7 mL/kg
- Pulmonary vascular permeability index (PVPI): 1.0–3.0

For cardiac contractility assessment:

- Cardiac function index (CFI): 4.5–6.5%
- Global ejection fraction (GEF): 25–35%

Pulse contour parameters include:

- Pulse contour cardiac output (PCCO)
- Arterial blood pressure (ABP)
- Heart rate (HR)
- Stroke volume (SV)

For volume responsiveness assessment:

- SVV and PPV

For afterload assessment:

- Systemic vascular resistance index (SVRI): 1700–2400 dyn*s*cm⁻⁵*m²

Pulmonary Artery Catheter (Swan-Ganz)

Despite controversy regarding its use, remains one of the best tools for CO assessment.

It provides information about intracardiac pressures, CO, mixed venous oxygen saturation (SvO₂), and the causes of shock status (Table 1.2).

It is still the gold standard tool for assessment of pulmonary hypertension etiology and response to vasodilators.

It measures CVP, right ventricular pressure (RVP), pulmonary arterial pressure (PAP), and PAOP.

CO is measured by thermodilution after injection of 10 mL of room temperature saline.

Intracardiac pressures and waveforms are displayed on the monitor; Figs. 1.11 and 1.12 illustrate normal and abnormal waveforms.

Complications That Might Happen from Pulmonary Artery Catheter

Complications associated with central venous access:

- Bleeding/hematoma
- Vascular injuries
- Pneumothorax
- Tamponade

Complications associated with advancement of the catheter:

- Arrhythmias
- Tamponade
- Valvular trauma
- Misplacement
- Knotting of catheter

Table 1.2 Hemodynamic parameters in shock

Type of shock	CVP	PCWP	CO	SVR	Comments
Hypovolemic	Low	Low	Low	Normal/high	
Cardiogenic	High	High	Low	Normal/high	
Distributive	Low	Low	Normal/high	Low	Examples are sepsis and anaphylaxis
RHF	High	Normal	Low	Normal/high	Examples are pulmonary embolism and right ventricular infarction
Tamponade	High	High	Low	Normal/high	It will show equalization of the diastolic pressure in all cardiac chambers

CVP central venous pressure, *PCWP* pulmonary capillary wedge pressure, *CO* cardiac output, *SVR* systemic vascular resistance, *RHF* right side heart failure

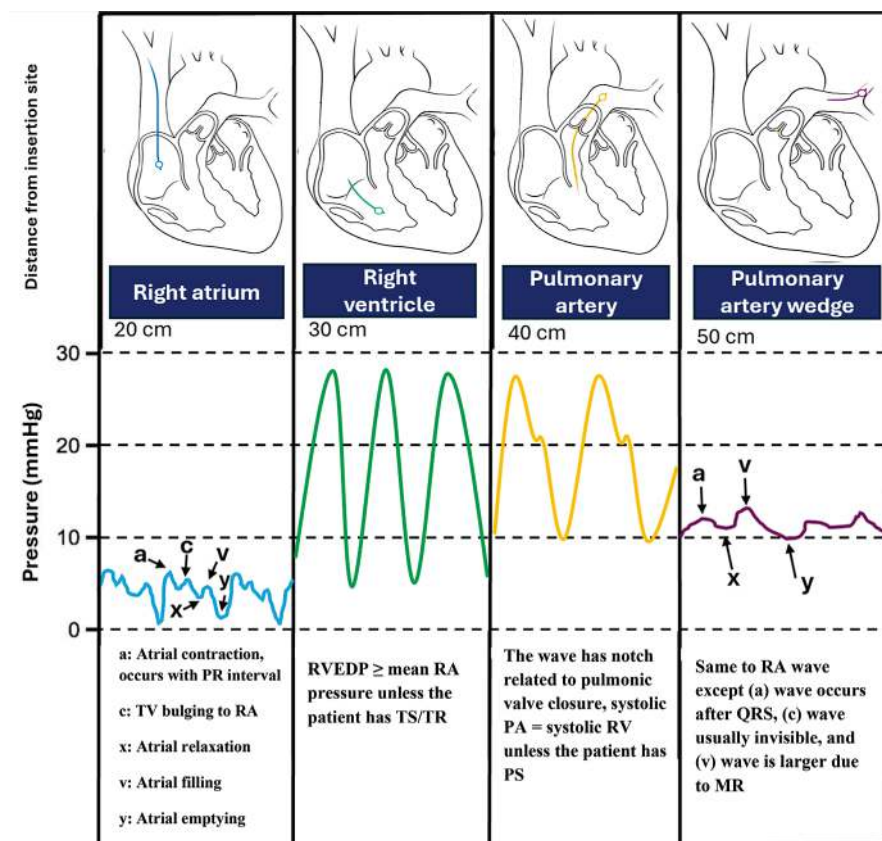


Fig. 1.11 Normal waves of pulmonary artery catheter. RA = right atrium, RV = right ventricle, PA = pulmonary artery, LA = left atrium, LV = left ventricle, TV = tricuspid valve, RVEDP = right ventricular end diastolic pressure, TS = tricuspid stenosis, TR = tricuspid regurgitation, PS = pulmonary stenosis, MR = mitral regurgitation. (Adapted from the original source: Bootsma et al. [13])

Complications associated with the catheter's continued presence.

- Venous thromboembolism
- Pulmonary arterial rupture

Contraindication for Pulmonary Artery Catheter Insertion Includes

- Coagulopathy
- Local infection at the site of insertion
- Prosthetic right heart valve
- Left bundle branch block (may end by complete heart block)
- Right-sided endocarditis
- Right ventricular thrombus

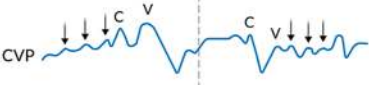
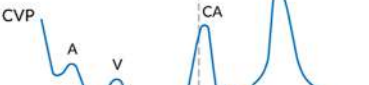
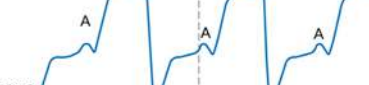
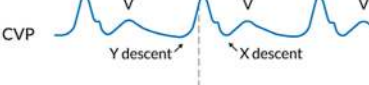
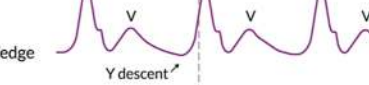
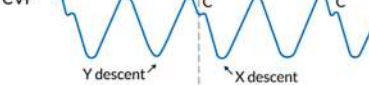
A. Atrial fibrillation/flutter Characteristics: • Absence of A-wave • C and V-waves most prominent peaks • Beat to beat changing morphologies • Small amplitude pressure waves (fibrillation/flutter waves)	
B. AV dissociation <i>Ventricular tachycardia, AVNRT, Complete heart block</i> Characteristics: • Cannon A-wave during ventricular systole	
C. Tricuspid insufficiency Characteristics: • Early holosystolic large V-wave • Merge with the C-wave • Disappearance of X-descent	
D. Mitral valve insufficiency Characteristics: • Early holosystolic large V-wave • V-wave merge with the C-wave • Disappearance of X-descent	
E. Tricuspid valve stenosis Characteristics: • Large A-wave • Slow Y-descent	
F. Mitral valve stenosis Characteristics: • Large A-wave • Slow Y-descent	
G. Pericardial constriction, RV infarction or restrictive cardiomyopathy. Characteristics: • Tall A-wave • Tall V-wave • Steep X-descent • Steep Y-descent	
H. Tamponade Characteristics: • Tall A-wave • Tall V-wave • Absent or diminished Y-descent	

Fig. 1.12 Abnormal waves of pulmonary artery catheter. CVP = central venous pressure, AV = atrioventricular, AVNRT = Atrioventricular nodal reentrant tachycardia, CA = cannon A, RV = right ventricle. (Adapted from the original source: Bootsma et al. [13])

Multiple trials have studied the effect of pulmonary artery catheter-directed therapy on ICU patients. The *PAC-man trial* [14] examined its effect on patients in shock and found no mortality benefit, along with an increased risk of mechanical complications. The *ESCAPE trial* [15] evaluated its use in patients with decompensated heart failure and similarly showed no mortality benefit, while also increasing the risk of mechanical complications.

Fick Equation

$$\begin{aligned} CO &= VO_2 / (CaO_2 - CvO_2) \\ VO_2 &= BSA * 125 \\ CaO_2 = CvO_2 &= 1.34 * Hb * 10 * (SaO_2 - ScvO_2) \end{aligned}$$

VO_2 = oxygen consumption, BSA = body surface area, CaO_2 = arterial oxygen content, CvO_2 = venous oxygen content, Hb = hemoglobin, SaO_2 = arterial oxygen saturation, $ScvO_2$ = central venous oxygen saturation.

Example

A patient who has BSA 1.68 m^2 , Hb 15 g/dL , SaO_2 90% , $ScvO_2$ 70% , calculation of the CO by using Fick equation will be as following:

$$\begin{aligned} CO &= VO_2 / 1.34 * HB * 10 * (SaO_2 - ScvO_2) \rightarrow CO \\ &= 1.68 * 125 / 1.34 * 10 * 15 * (90 - 70) = 5.2 \text{ L / min} \end{aligned}$$

Tissue Hypoperfusion

Perfusion status can be assessed using multiple clinical and laboratory indicators, such as level of consciousness, urine output, capillary refill, extremity examination, serum lactate, and renal and liver function. Abnormalities in these findings suggest hypoperfusion.

Serum Lactate

Lactate clearance is used as a reliable marker of tissue reperfusion. Lactate is produced by hypoxic tissues as a result of anaerobic metabolism. However, lactate levels may also be elevated in well-perfused patients due to other underlying etiologies. In general, hyperlactatemia is classified into Type A and Type B as follows:

- Type A: Associated with tissue hypoperfusion, such as in shock, severe hypoxemia, organ ischemia (e.g., mesenteric or limb ischemia), and severe anemia.
- Type B: Associated with other clinical conditions, including alcoholism, liver or renal disease, malignancy, thiamine deficiency, and drug-related adverse effects (e.g., beta₂-agonists, propofol, metformin, linezolid, salicylates, paracetamol, and isoniazid).

Several studies compared lactate to other perfusion parameters, e.g., capillary refill and ScvO₂.

Jones trial [16] studied resuscitation of shocked patients aiming to normalize lactate vs normalization of ScvO₂ and did not recognize any difference in the clinical outcomes.

ANDRO-MEDA SHOCK [17] studied the difference between normalization of the capillary refill vs normalization of lactate in shocked patient, and it also did not show any difference.

Carbon Dioxide (CO₂) Gap

CO₂ is about 20 times more soluble than oxygen, so it more reliably diffuses out of ischemic tissues into the circulation making it a sensitive marker of hypoperfusion.

$$\text{PCO}_2 \text{ gap} = \text{PcvCO}_2 - \text{PaCO}_2$$

PcvCO₂ = central venous CO₂ pressure, PaCO₂ = arterial CO₂ pressure

PCO₂ gap >6 mmHg suggests a hypoperfusion state that may be amenable to fluid resuscitation +/- vasoactive agents and inotropic support.

Microcirculatory Blood Flow

Sublingual mucosa is the preferred means to evaluate the microcirculation in critically ill patients.

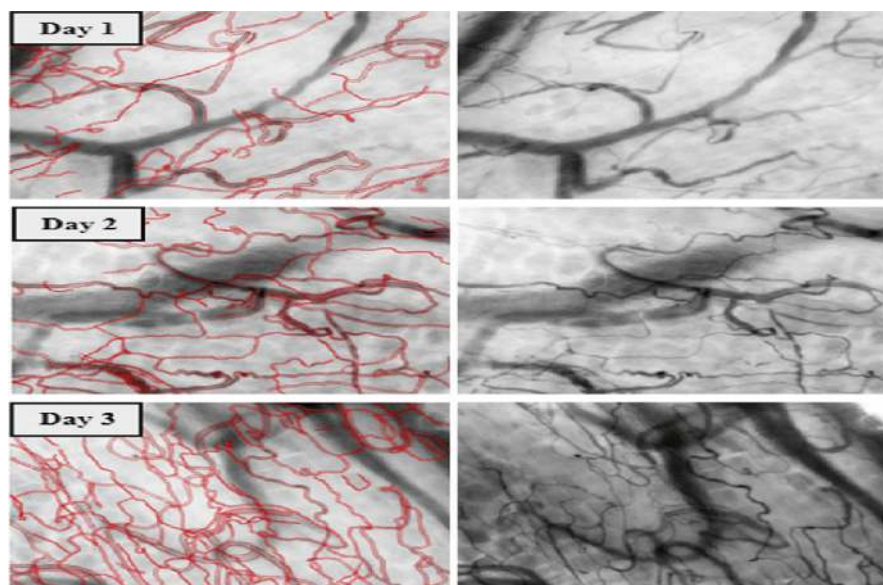


Fig. 1.13 Images of sublingual microcirculation—a visual representation of the increase of the total vascular density (TVD). Images of sublingual microcirculation video clips obtained from one patient on day 1 (T0), day 2 (T1), and day 3 (T2) after ICU discharge. The red lines indicate the TVD within the entire image. (Sourced from: Uz et al. [18])

Imaging of the sublingual microvasculature is typically obtained using a near-infrared spectroscopy (NIRS) (Fig. 1.13).

Review Questions

1. A 77-year-old man with a history of atrial fibrillation is intubated for respiratory distress secondary to community-acquired pneumonia (CAP). He received a 1-L bolus of intravenous fluids, and his lactate decreased from 6 to 2 mmol/L. His central venous pressure (CVP) is 9 mmHg. He is mechanically ventilated with a tidal volume of 6 mL/kg of ideal body weight, but he is asynchronous with the ventilator and exhibits multiple spontaneous breaths.

Which of the following statements is most accurate regarding intravascular volume assessment in this patient?

- A. Stroke volume variation can accurately predict his fluid responsiveness.
- B. A positive passive leg raise will predict his fluid responsiveness.
- C. CVP can accurately predict his fluid responsiveness.
- D. A low pulmonary artery occlusion pressure will best predict his fluid responsiveness.



CI = cardiac index
 SVV = stroke volume variation
 SVRI = systemic vascular resistance index
 ScvO₂ = central venous oxygen saturation
 Normal values:
 CI 2.5–5 L/min/m²
 SVRI 1700–2400 dyn*s*cm⁻⁵*m²

2. Based on the values in the figure, what is the most likely diagnosis:
 - A. Septic shock
 - B. Hypovolemic shock
 - C. Cardiogenic shock
 - D. Anaphylactic shock
3. Which of the following hemodynamic parameters are suggesting cardiac tamponade?
 - A. RA 17, PA 34/22, PAOP 25 mmHg
 - B. RA 17, PA 34/10, PAOP 12 mmHg
 - C. RA 20, PA 50/22, PAOP 12 mmHg
 - D. RA 22, PA 34/22, PAOP 21 mmHg

RA = right atrium, PA = pulmonary artery, PAOP = pulmonary artery occlusion pressure

Answers

1. B.

Dynamic maneuvers are more accurate than static measures in assessing volume responsiveness (C and D are incorrect). Stroke volume variation cannot be used when the patient has arrhythmia and spontaneous breathing or is receiving an inadequate tidal volume (<8 mL/kg/IBW), making option A incorrect. Passive leg raise is the best choice for assessment in this case.

2. C.

The patient has low CO with normal SVRI (A and D are incorrect), and SVV is low which is going with volume unresponsiveness (B is incorrect), with these parameters and also low ScvO₂; the most likely diagnosis is cardiogenic shock.

3. D.

The picture of intracardiac pressures for patients having pericardial tamponade will show high CVP, RVP, PAP, and PAOP with equalization of the diastolic pressure in all cardiac chambers (D is the most reliable numbers).

Cardiac Devices for Rhythm Control

Pacemaker (PM)

Indications of PM Insertion

Atrio-ventricular block (AVB): Mobitz type II AVB, 3rd degree AVB, alternating right and left bundle branch block (RBBB and LBBB), symptomatic 1st degree and 2nd degree Mobitz type 1 (rare but can be considered in severe cases).

Sinus node dysfunction: symptomatic bradycardia, sick sinus syndrome (SSS) with pauses.

Types of Pacemaker System (Pacemaker Codes)

1st letter for chamber which is paced: A (atrial), V (ventricular), D (dual)

2nd letter for sensing chamber: A (atrial), V (ventricular), D (dual), O (none)

3rd letter for response to sensed beat: I (inhibition), T (trigger), inhibition and trigger (D), or none (O)

4th letter for rate regulation: heart rate regulation (R) or none (O)

VVI: It is a ventricular pacemaker, which is sensing and inhibited when there is normal native beat, it is used in cases of AVB with atrial fibrillation (AF) (Fig. 1.14).

AAI: It is an atrial pacemaker, which is sensing and inhibited when there is normal native impulse, it is used in sinus node abnormalities e.g. SSS with pauses (Fig. 1.15).

DDD: Both atrial and ventricular pacing and both are sensing. When there is normal native atrial impulse, the atrial pace will be inhibited and when it is slower than the lower limit, the atrium will be paced. The ventricle will be triggered by the native impulse if it is normal and will be paced if the native impulse is slower than

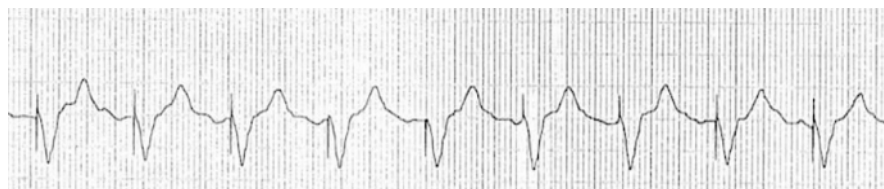


Fig. 1.14 VVI pacemaker



Fig. 1.15 AAI pacemaker

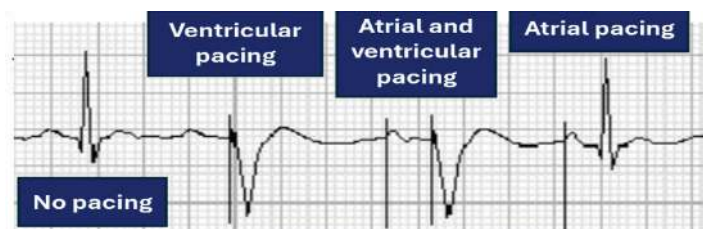


Fig. 1.16 DDD pacemaker

the lower limit. This type is used in patients who have AVB with or without sinus node abnormalities (Fig. 1.16).

DDDR: It is DDD pacemaker with heart rate regulation according to physical activity.

DDI: Both atrial and ventricular, both are sensing, and when there is normal native impulse, both will be inhibited.

AOO, VOO, and DOO: A magnet is attached to the PM during some procedures, e.g., electrical cautery, so the PM will work asynchronously (Figs. 1.17 and 1.18).

Fig. 1.17 Chest X-ray showing magnet over the site of a pacemaker

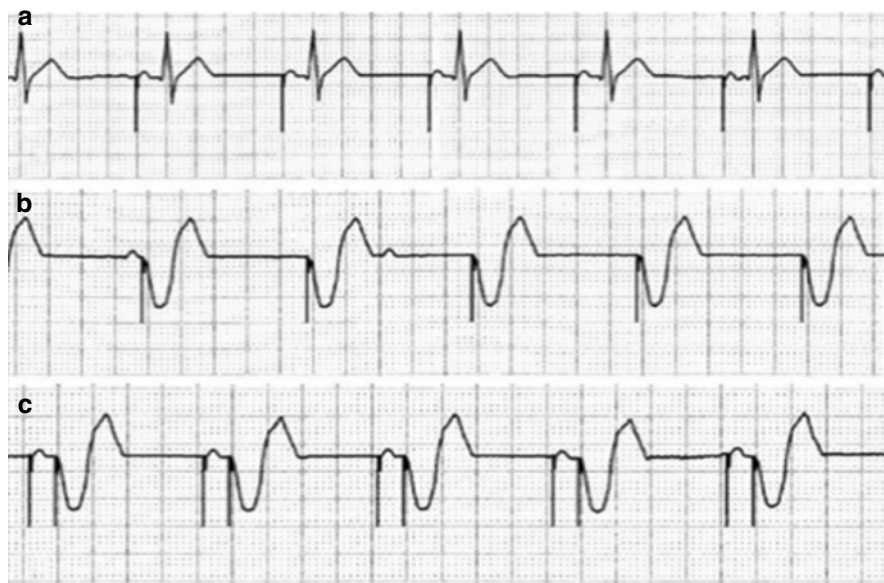
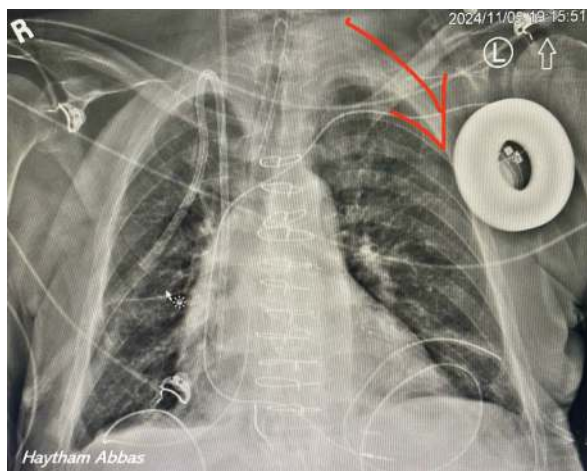


Fig. 1.18 (a) Is AOO, (b) is VOO, (c) is DOO pacemakers after magnet be attached

Implantable Cardioverter Defibrillator (ICD)

ICD insertion is indicated in some cardiac conditions to provide primary or secondary prevention of sudden cardiac death.

Secondary Prevention

ICD is indicated if the patient has a non-reversible cardiac disease, and one of the following conditions:

- History of resuscitation due to ventricular fibrillation (VF)/ventricular tachycardia (VT)
- Sustained VT
- History of syncope with suspicion to be due to VF/VT

Primary Prevention

The indications are:

- Ischemic cardiomyopathy (ICM), after 40 days of myocardial infarction (MI) when the patient meets any of the following criteria: (1) an ejection fraction (EF) <30%, (2) NYHA* class II or III with EF <35%, and (3) EF <40% with inducible VF/sustained VT.
- Non-ischemic cardiomyopathy (NICM), after 90 days of proper medical therapy when the patient has an EF <35% and NYHA class II or III.
- Patients with cardiac condition associated with high risk for life-threatening VF/VT, such as congenital Long QT syndrome, hypertrophic cardiomyopathy (HCM), arrhythmogenic right ventricular cardiomyopathy, cardiac sarcoidosis, and Brugada syndrome.

Examples of high-risk criteria in HCM include history of syncope, sudden cardiac death for first degree family member <50 years age, exercise induce VT and left ventricular hypertrophy >30 mm. *NYHA = New York Heart Association.

Cardiac Resynchronization Therapy (CRT)

It is indicated for patients with heart failure who have the following criteria:

- EF <35%
- NYHA class II to IV
- Left bundle branch block

Use of CRTD (CRT+ ICD) in patients with these criteria showed improvement of mortality in comparison to ICD alone (*RAFT trial*) [19].

Advanced Cardiac Life Support (ACLS)

Assessment of unstable patients by healthcare providers aims to quickly identify and categorize these patients using specific approaches. The ABC approach (appearance, breathing, and color) is employed for this purpose, classifying patients as collapsed, distressed, hypo-perfused, or stable [20].

The cardiac arrest, bradycardia, and tachycardia algorithms are key components of the ACLS protocols and must be mastered by all ICU team members. These algorithms are illustrated in Figs. 1.19, 1.20, and 1.21.

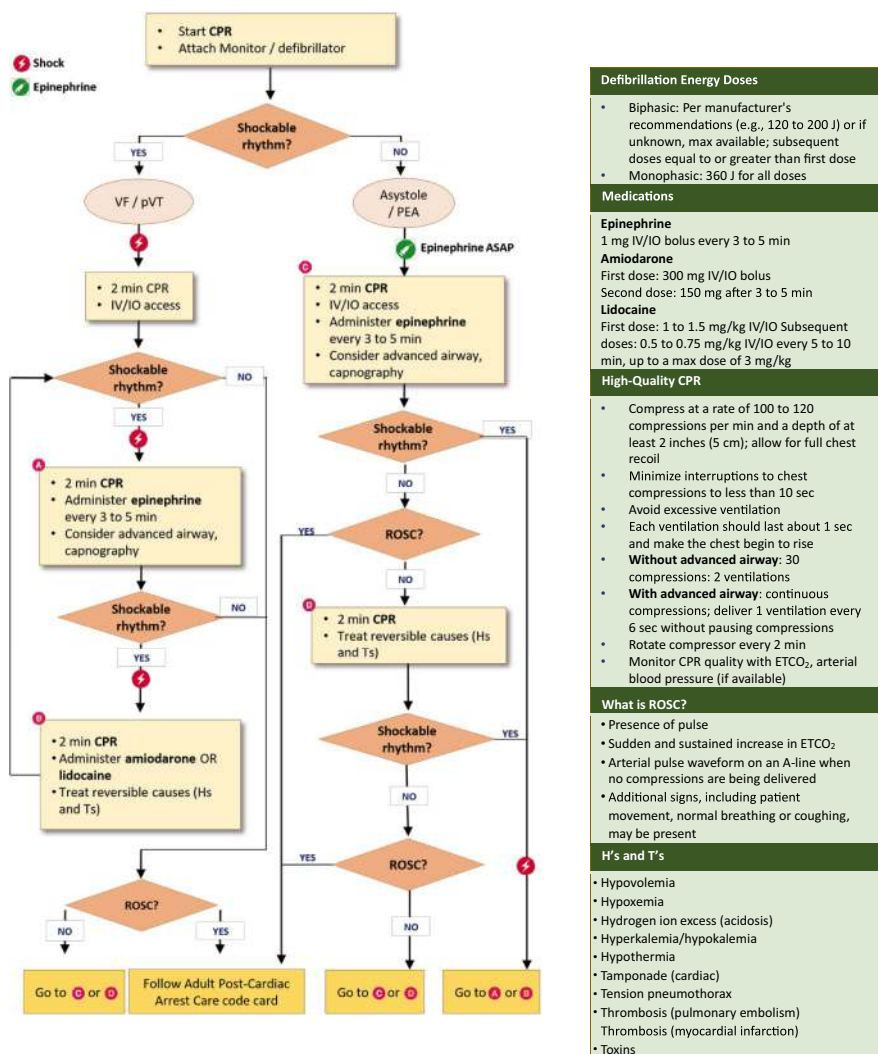


Fig. 1.19 Adult cardiac arrest algorithm. CPR = cardiopulmonary resuscitation, PEA = pulseless electrical activity, VF = ventricular fibrillation, pVT = pulseless ventricular tachycardia, IV = intravenous, IO = intraosseous, ETCO₂ = end-tidal carbon dioxide, ROSC = return of spontaneous circulation. (Sourced from Saudi Heart Association [20]. Used with permission)

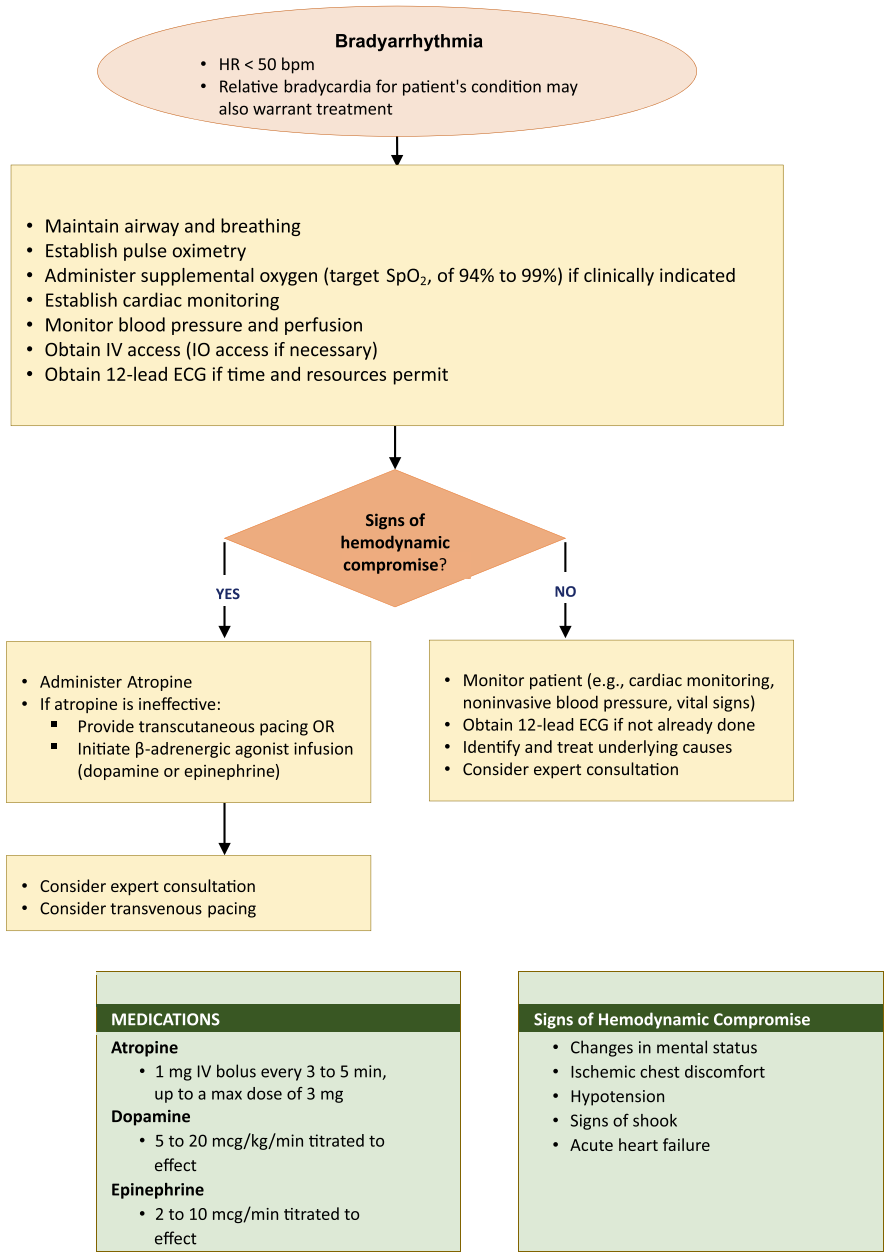


Fig. 1.20 Adult bradycardia algorithm. HR = heart rate, SpO₂ = oxygen saturation, IV = intravenous, IO = intraosseous, ECG = electrocardiogram. (Sourced from Saudi Heart Association [20]. Used with permission)

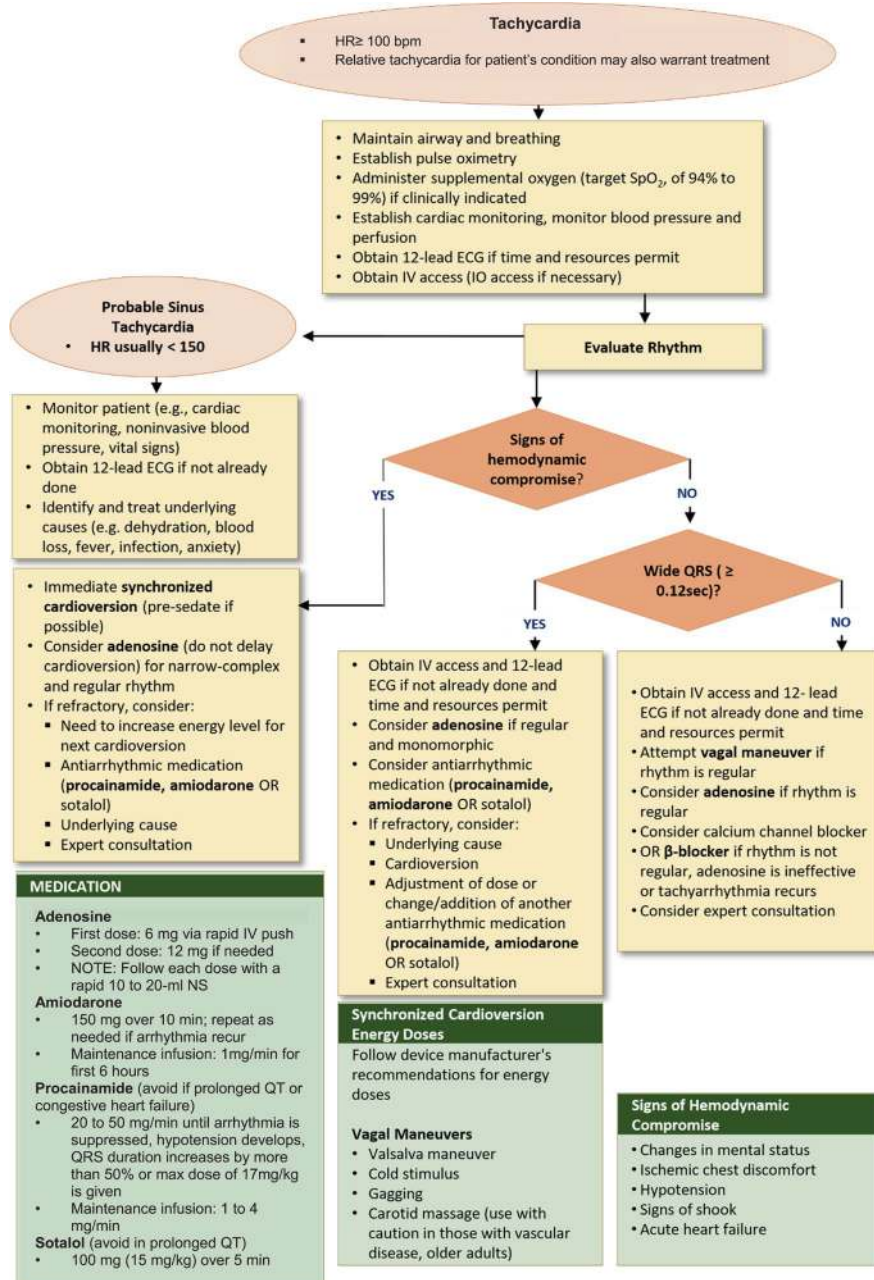


Fig. 1.21 Adult tachycardia algorithm. HR = heart rate, SpO₂ = oxygen saturation, IV = intravenous, IO = intraosseous, ECG = electrocardiogram, NS = normal saline. (Sourced from Saudi Heart Association [20]. Used with permission)

Post-Return of Spontaneous Circulation (ROSC) Management

Patient post-ROSC should be managed using the ABCD approach, with continuous evaluation for the reversible causes, the Hs and Ts.

Airway: If the patient cannot maintain his airway like in case of hypoventilation or coma, he should be intubated and ventilated.

Breathing: The patient should be assessed for signs of respiratory distress. Vital signs, including respiratory rate and oxygen saturation, should be monitored. The chest should also be examined for any abnormalities that may explain the cause of cardiac arrest or may have arisen as complications following effective cardiopulmonary resuscitation (CPR).

Circulation: An electrocardiogram (ECG) should be performed to look for signs of acute coronary syndrome. Blood samples should be obtained for blood gas analysis and basic chemistry. The patient's volume status should also be assessed and treated accordingly.

Disability: If the patient has a decreased level of consciousness, targeted temperature management (TTM) should be activated for the first 24–48 h. The section “[Post ROSC Neurological Assessment and Brain Death](#)” is explained in the Chap. 3.

Evidence of TTM post-ROSC

Multiple trials have been conducted to study the effect of hypothermia on patients post-ROSC, with some showing favorable outcomes, including mortality benefits.

HACA trial [21]: This trial studied the effect of hypothermia (target temperature of 32–34 °C) on patients who experienced out-of-hospital cardiac arrest due to VF or pVT. It demonstrated improvements in both mortality and neurological outcomes.

HYPERION [22]: It studied the effect of hypothermia post-ROSC in patients who developed cardiac arrest due to unshockable rhythm, temperature was targeted at 33 °C, and the study showed improvement in neurological outcomes.

TTM [23]: It did not show any differences in outcomes between targeting a temperature of 33 or 36 °C post-cardiac arrest.

TTM2 [24]: It showed no difference in long-term mortality between normal temperature (<37.8 °C) vs hypothermia (33 °C).

In clinical practice, for patients with severe neurological complications post-ROSC, such as deep coma, massive cerebral edema, or severe encephalopathy on electroencephalogram (EEG), a lower target temperature (33–36 °C) is preferred. For patients with milder neurological impairment, maintaining normothermia is generally suggested.

Cardiogenic Shock

Definition of Cardiogenic Shock [25]

Cardiogenic shock is a clinical condition characterized by organ hypoperfusion due to cardiac dysfunction.

Patients with cardiogenic shock have the following characteristics:

- Hypotension with a systolic blood pressure (SBP) <90 mmHg for ≥ 30 min, or the need for support to maintain SBP ≥ 90 mmHg. However, cardiogenic shock may present with normal blood pressure in some cases.
- Clinical and biochemical markers of hypoperfusion (e.g., cold extremities, encephalopathy, acute kidney injury, acute hepatic injury, elevated lactate).
- Cardiac dysfunction confirmed by echocardiography.
- Hemodynamic monitoring demonstrating a cardiac index (CI) <2.2 L/min/m² and evidence of increased cardiac filling pressures, with a pulmonary capillary wedge pressure (PCWP) ≥ 15 mmHg.

Causes of cardiogenic shock: (Table 1.3)

Investigations to Diagnose and/or to Follow Patient with Cardiogenic Shock

- *Brain natriuretic peptide (BNP/pro-BNP)*: It has a good sensitivity in diagnosis of congestive heart failure (CHF) [26].
- *Cardiac enzymes*: High sensitivity troponin and creatine kinase-myocardial band (CK-MB) will be elevated in cardiogenic shock and acute coronary syndrome (ACS) as a cause for cardiogenic shock.
- *Electrocardiogram (ECG)*: Multiple abnormalities can be discovered according to etiology of cardiomyopathy or as complications, e.g., ST and T wave changes, right or left bundle branch block, ventricular hypertrophy, arrhythmias, etc.
- *Chest x-ray*: Looking for pulmonary edema, pleural effusion, cardiomegaly, etc.
- *Complete blood count (CBC), chemistry and blood gas*: To rule out anemia, end organ damage and acidemia with high lactate.

Table 1.3 Causes of cardiogenic shock

Acute coronary syndromes (ACS)	
Arrhythmias	
Valvular pathology	Acute valvular regurgitation, e.g., rupture of chordae tendineae, endocarditis Decompensation of severe aortic stenosis
Viral myocarditis	Coxsackie virus, adenovirus
High output cardiac failure	Thyroid storm, severe anemia
Decompensation of chronic heart failure	Hypertensive heart disease Peripartum cardiomyopathy Restrictive cardiomyopathy due to infiltration (sarcoidosis, amyloidosis, and haemochromatosis), connective tissue disorders or radiation Congenital, e.g., hypertrophic cardiomyopathy

- *Echocardiography*: The gold standard investigation to assess heart failure and its etiology.
- *Other investigations*: These depend on the clinical situation and etiology of the disease, e.g., coronary angiography, magnetic resonance imaging (MRI) for the heart, electrophysiological studies.

Management of Patients with Cardiogenic Shock

As in any critical case, cardiogenic shock is approached by ABC and management of each step accordingly.

Treatment of the etiology is essential, e.g., percutaneous coronary intervention (PCI) in ACS.

If the patient has respiratory distress and signs of pulmonary edema, initiate management. This management can be remembered using the mnemonic LMON and it includes:

- **L**: Lasix (intravenous frusemide), given at double the usual dose.
- **M**: Morphine improves the symptoms and decreases pre/afterload.
- **O**: Oxygen and/or noninvasive ventilation (NIV) improve the oxygenation and decrease the afterload.
- **N**: Nitroglycerin decreases pre-/afterload.

As initial resuscitation, the patient must be kept on two large peripheral cannulas for extraction and administration of drugs. He should also be attached to a cardiac monitor.

Investigations include CBC, renal and liver function tests, blood gas analysis, pro-BNP, cardiac enzymes, chest X-ray, and ECG.

If the patient is in shock with MAP <60–65 mmHg, inotropic support must be started. The choices of inotropic support are summarized in Table 1.4.

If the patient is still in shock despite the maximum medical therapy, mechanical support should be considered. The choices are:

- Intra-aortic balloon pump (IABP)
- Veno-arterial extracorporeal membrane oxygenation (VA-ECMO)
- Left ventricular assistant device (LVAD)
- Microaxial flow pump (Impella)

Intra-Aortic Balloon Pump (IABP)

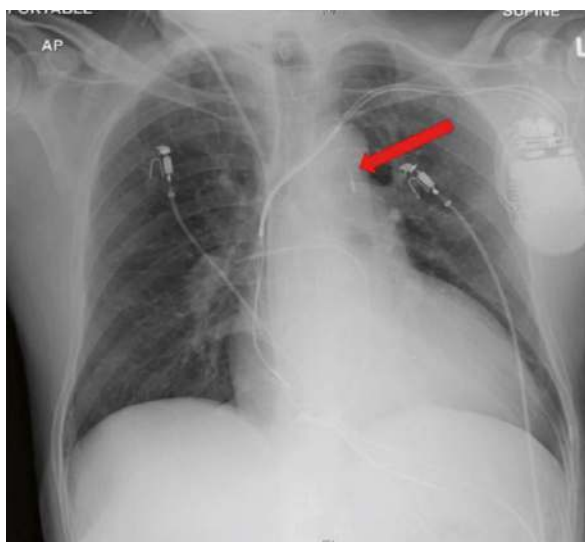
IABP is one of the most commonly used mechanical support modalities in the management of cardiogenic shock. It is inserted via the femoral artery, with the balloon positioned in the descending aorta, just distal to the origin of the left subclavian artery; this position is confirmed by chest X-ray (Fig. 1.22). The balloon is inflated with low-density helium during diastole, producing diastolic augmentation to enhance coronary perfusion. It is then deflated during systole, as the aortic valve opens, to reduce myocardial afterload. The timing of balloon inflation and deflation

Table 1.4 Choices of inotropic agents in cardiogenic shock

Drug	Mechanism of action	Comment
Norepinephrine	α , β agonist	The 1st choice in cardiogenic shock
Dobutamine	β_1 , weak β_2 agonist	Good choice, side effect is tachycardia
Dopamine	Low dose 2–5 mic/kg/min acts on dopamine receptor in kidneys, moderate dose 5–10 mic/kg/min on β receptor, high dose 10–20 mic/kg/min on α receptor	Currently, it has weak recommendations in cardiogenic shock [27] Side effects: tachycardia and arrhythmias
Epinephrine	α , β_1 , β_2 agonist	Good choice, side effect is tachycardia
Milrinone	Phosphodiesterase inhibitor	Positive inotropic, minimally chronotropic (does not cause tachycardia), vasodilator (decreasing the afterload)
Digoxin	It works on potassium-sodium ATPase channels which increases the intracellular calcium leading to increase the myocardial contractility without tachycardia	Good choice in heart failure with atrial fibrillation Side effects: Arrhythmias, CNS, gastrointestinal and visual side effects (green and yellow vision)
Levosimendan	Calcium sensitizer, acting on troponin C receptors	Improves myocardial contractility without increasing the oxygen demand, vasodilator which improves the afterload; it has weak evidence in cardiogenic shock [28]

α alpha, β beta, *ATPase* adenosine triphosphatase, *CNS* central nervous system

Fig. 1.22 IABP with proper positioning in chest x-ray at the level of the carina and at least 2 cm below the aortic knob



is synchronized with either the ECG or the arterial line waveform. Inflation occurs in the middle of the T wave or at the dicrotic notch, while deflation occurs at the peak of the R wave or just before the systolic upstroke on the arterial waveform. Expected hemodynamic effects include a 20% decrease in systolic blood pressure, a 30% increase in diastolic pressure, improvement in MAP, and an increase in cardiac output (CO) by approximately 0.5–1 L/min. Normal IABP waveforms are illustrated in Fig. 1.23, and abnormal waveforms are summarized in Figs. 1.24 and 1.25.

Indications of IABP

- Cardiogenic shock refractory to medical therapy.
- Refractory myocardial ischemia in patients who are planned for coronary reperfusion.
- High risk PCI, e.g., in patients with severe cardiomyopathy.
- Other possible indications include mechanical complications of acute myocardial infarction, e.g. ventricular septal defect and mitral regurgitation.

IABP-SHOCK II trial [29] was conducted in patients who have cardiogenic shock related to ACS to study the effect of IABP and it did not show mortality benefits.

Contraindications of IABP Insertion

- Significant aortic regurgitation
- Aortic dissection/aneurysm
- Severe peripheral vascular disease

Complications of IABP

- *Vascular*: bleeding, hematoma, dissection, perforation, etc.
- *Balloon related*: ischemia (mesenteric, renal or lower limbs if positioned low, left upper limb, cerebral if positioned high), hemolysis

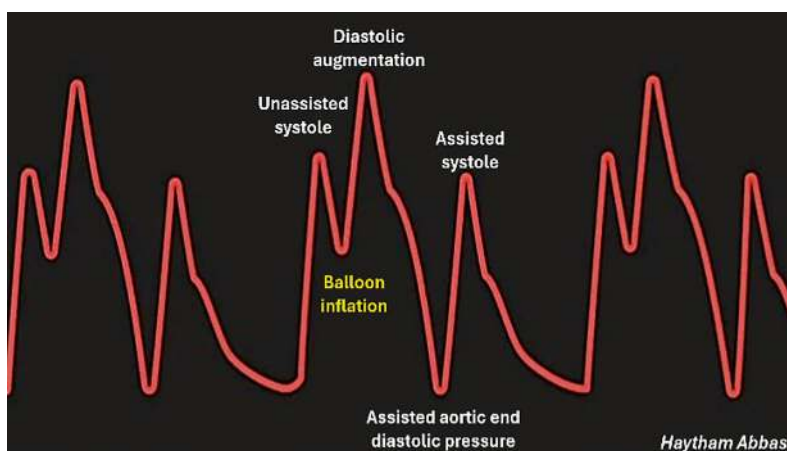


Fig. 1.23 Normal waveform of IABP

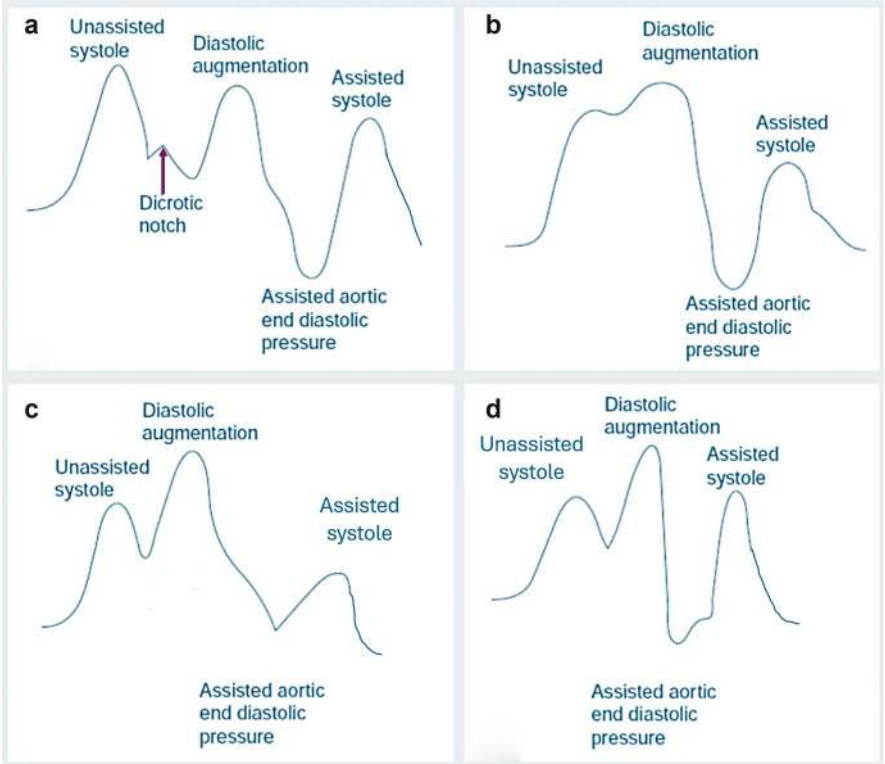


Fig. 1.24 IABP waveform abnormalities, (a) late inflation, (b) early inflation, (c) late deflation, and (d) early deflation

Fig. 1.25 IABP wave showing early inflation



Veno-Arterial Extracorporeal Membrane Oxygenation (VA-ECMO)

It Is Indicated in the Following Situations [30]

- Cardiogenic shock related to reversible causes, e.g., ACS, acute myocarditis, peripartum-cardiomyopathy, drug intoxication, etc.
- Bridging therapy until definitive intervention be conducted, e.g., cardiac transplantation or LVAD
- In massive pulmonary embolism, as bridge to definitive therapy, e.g., mechanical thrombectomy
- Persistent anaphylactic shock
- Weaning after cardiac surgery
- Arrhythmic storm

Contraindications

- End stage organ failure which is not amenable for recovery or transplantation e.g. end stage renal disease (ESRD), liver cirrhosis, chronic lung disease, end stage malignancy, etc.
- If cardiac recovery is unlikely and no indication for cardiac transplantation or LVAD.
- CNS catastrophe, e.g., massive stroke or traumatic brain injury (TBI).
- Aortic dissection.
- Severe aortic regurgitation.
- Severe peripheral vascular disease.

Complications

- Lower limb ischemia (in peripheral VA-ECMO particularly if large cannula is used).
- Differential hypoxemia, also known as Harlequin syndrome or north-south syndrome, is a complication of peripheral VA-ECMO that occurs when the patient experiences an improvement in cardiac function alongside worsening respiratory function. As a result, the patient will exhibit hypoxia in the upper part of the body, while the lower part remains normally oxygenated.
- Left ventricular (LV) load: classic management should be initiated, e.g., diuresis and inotropes. In severe cases, unloading by using invasive intervention is recommended, e.g., LV venting, IABP, or Impella (VA-ECMO + Impella = ECMELLA) [31].
- Bleeding.
- Sepsis.

Left Ventricular Assistant Device (LVAD)

LVAD (Fig. 1.26) is a surgically implanted mechanical device designed to support the function of the left ventricle. It decreases myocardial workload, allowing the ventricle to rest while maintaining forward blood flow and adequate organ perfusion.

Indications of LVAD

- Bridging to recovery in acute heart failure.
- Bridge to transplantation in chronic heart failure.
- It may also be used as a long-term treatment modality.

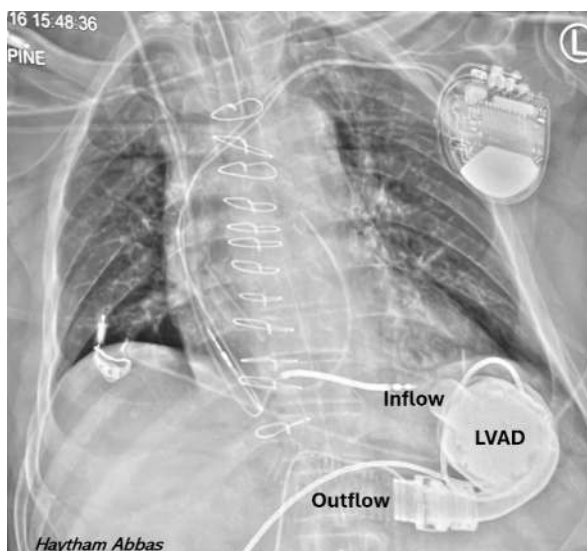
Complications of LVAD Include

- Bleeding
- Cardiac tamponade
- Right ventricular failure
- Infection
- Intra-cardiac thrombosis

Microaxial Flow Pump (Impella)

It is an intravascular microaxial blood pump that provides temporary mechanical circulatory support to reduce workload of the heart while improving systemic circulation. It provides continuous anterograde blood flow from the LV into the ascending aorta.

Fig. 1.26 Chest x-ray showing LVAD



Indications [32]

- Cardiogenic shock, particularly in ACS, as it showed survival benefit (*DanGer Shock trial* [33])
- Bridging to recovery or definitive intervention, e.g., cardiac transplantation or LVAD
- LV unloading in patient who is on VA-ECMO (ECMELLA)
- High risk PCI

Contraindications

- LV thrombus
- Mechanical aortic valve
- Severe aortic regurgitation/stenosis
- Aortic dissection
- Ventricular septal defect (VSD)

Complications

- Hemolysis (the most common)
- Bleeding
- Stroke
- Peripheral ischemia
- Malposition

Right Side Heart Failure (RHF)

Right side heart failure (RHF) is more challenging to manage than left-sided heart failure. This is related to the smaller size of the right ventricle (normally about one-third the size of the left ventricle), which makes treatment more difficult.

The etiology can be related to abnormality of preload, afterload, or contractility of the right ventricle (Table 1.5).

Clinically, patients with RHF may exhibit signs of right-sided congestion, including raised jugular venous pressure (JVP), hepatomegaly, and/or peripheral edema.

Investigations to Diagnose and/or Follow Patient with RHF

- *Brain natriuretic peptide (BNP/Pro-BNP)*: can be elevated in congestive heart failure (CHF).

Table 1.5 Causes of right-side heart failure

Etiology	Examples
Increased afterload	Pulmonary embolism (PE), pulmonary hypertension, positive mechanical ventilation
Decrease contractility	Right ventricular (RV) infarction, cardiomyopathy
Decreased preload	Severe hypovolemic shock, pericardial tamponade
Increased preload	Cardiomyopathy, left to right intracardiac shunt

- *Cardiac enzymes*: increase in right ventricular infarction, myocardial infarction, high-risk PE, and cardiomyopathy.
- *Complete blood count (CBC), chemistry and blood gas*: to rule out anemia, end organ damage and acidemia with high lactate.
- *Chest X-ray*: cardiomegaly may be present. PE may show prominent pulmonary artery, triangular wedge-shaped opacity (Hampton hump), or oligemia in the effected side (Westermark's sign).
- *Electrocardiogram (ECG)*: may show right axis deviation, right bundle branch block (RBBB), right ventricular hypertrophy (RVH), S1Q3T3 in PE (Fig. 1.28).
- *Echocardiography*: may show RV hypokinesia and/or dilatation, pulmonary hypertension, D-shaped septum, paradoxical movement of the septum, low tricuspid annular plane systolic excursion (TAPSE) <16 mm and provides data about the etiologies; left side cardiac function, pericardium, cardiac valves, intra-cardiac shunt, etc.
- *CT pulmonary angiography, VQ scan*: For suspected PE.
- *Pulmonary artery catheter*: for assessment of pulmonary hypertension and cardiac output.

Management of Patients with RHF

As in any critical case, RHF must be approached by ABC and management of each step accordingly.

If the patient is severely hypoxic, distressed, and needs urgent intubation, several challenges must be considered:

- Hypoxia should be treated appropriately as it can worsen the afterload with pulmonary vasoconstriction.
- High positive ventilation pressure can also worsen the afterload; try to maintain the oxygenation without increasing the mean airway pressure.
- Oversedation can decrease the preload which worsens the hemodynamics; try not to over-sedate and/or use agents, which do not affect hemodynamics.

Maintaining the Preload

Keep the patient euvolemic. If the patient is hypotensive, e.g., in high risk PE, or RV infarction, give a gentle dose of fluid. Overload should also be treated with gentle diuresis.

Decreasing the Afterload

- Avoid hypoxia.
- Avoid acidemia and hypercapnia.
- Avoid high positive airway pressure.
- For persistent high pressure, give a trial of vasodilators, e.g., inhaled nitric oxide, nitroglycerin, sildenafil, prostacyclin, etc.

Improving Contractility and Output

- For RHF with signs of poor contractility, inotropic support should be considered; norepinephrine, epinephrine, dobutamine, milrinone, digoxin, etc.

- Patients should be in sinus rhythm, and any tachy/bradyarrhythmia must be treated.
- For persistent shock related to RHF, mechanical support can be used, e.g., right ventricular assistant device (RVAD) and veno-arterial extracorporeal membrane oxygenation (VA-ECMO).

Treating the cause is the mainstay for recovery.

Pulmonary Embolism (PE)

Etiology of PE

Table 1.6 explains the risk factors for PE.

Classification of PE

PE is currently classified based on the risk of early mortality into high, intermediate-high, intermediate-low and low risk (Fig. 1.27) [34].

It was previously divided into massive and submassive based on specific criteria. Massive PE is diagnosed when the patient has one of the following:

- Hypotension or need to start inotropic support
- Pulselessness

Submassive PE is diagnosed when the patient is hemodynamically stable but has evidence of myocardial necrosis or right ventricular (RV) dysfunction as diagnosed by cardiac enzymes, brain natriuretic peptide (BNP), or cardiac imaging.

Investigations for Diagnosis and Follow Up of Patient with PE

- *Electrocardiogram (ECG)*: it may show sinus tachycardia, right bundle branch block (RBBB), right axis deviation, and/or S1Q3T3 (Fig. 1.28).
- *Troponin*: it is a marker for myocardial necrosis in high risk/massive and intermediate risk/submassive PE.
- *Pro-BNP*: marker for RV dysfunction.
- *D dimer*: it has a negative predictive value, can be used in low-risk probability.

Table 1.7 shows Wells criteria to estimate the probability of PE.

Table 1.6 Risk factors of PE

Venous stasis	Immobility, long travel, varicose veins
Endothelial injury	Surgery, indwelling catheters, burns, trauma
Hypercoagulable status	Pregnancy and puerperium Malignancy Medical conditions (IBD, nephrotic syndrome [loss of ATIII], HIT) Thrombophilia (factor V Leiden, activated protein C resistance, antiphospholipid syndrome, antithrombin, and protein C and S deficiencies) Drugs (oral contraceptive, chemotherapy, hormone replacement therapy)

IBD inflammatory bowel disease, *ATIII* antithrombin III, *HIT* heparin induced thrombocytopenia

Early Mortality Risk		Parameter for Risk			
		Haemodynamic instability	Clinical parameters of PE severity and/ or comorbidity: PESI class III –V or sPESI ≥ 1	RV dysfunction on TTE or CTPA	Elevated cardiac troponin levels
High					
Intermediate	Intermediate-high				
	Intermediate-low			One of them or none	
Low					
Parameter		PESI	Simplified PESI	PESI	
Age	Age in years		1 point if age >80	Class	Score
Male sex	10 points	_____		I	≤ 65
Cancer	30 points		1point	II	66-85
Heart failure	10 points		1point	III	86-105
Chronic respiratory disease	10 points		1point	IV	106-125
Pulse ≥ 110 bpm	20 points		1point	V	>125
Systolic blood pressure <100 mmHg	30 points		1point	Simplified PESI	
Respiratory rate ≥ 30 bpm	20 points	_____		Score	Risk
Temperature <36 °C	20 points	_____		0	Low
Altered mental status	60 points	_____		≥ 1	High
Oxygen saturation $<90\%$	20 points		1point	_____	_____

Fig. 1.27 Classification of PE based on mortality risk. CTPA = computed tomography pulmonary angiography, PE = pulmonary embolism, PESI = pulmonary embolism severity index, RV = right ventricular, sPESI = simplified pulmonary embolism severity index, TTE = transthoracic echocardiogram. (Adapted from the original source: Konstantinides et al. [34]. Used with permission)

- *Complete blood count (CBC) and coagulation profile:* to rule out coagulopathy before administration of thrombolytic therapy.
- *Renal/liver function and blood gas:* to rule out end organ damage related to shock status or RV failure.
- *Chest X-ray:* it may show prominent pulmonary artery, triangular wedge (Hampton hump), oligemia in the effected side (Westermarck's Sign).
- *Echocardiography* (Fig. 1.29), possible findings include:
 - RV dilatation
 - RV hypokinesia
 - McConnell's sign: hypokinesia of the RV with sparing of apex

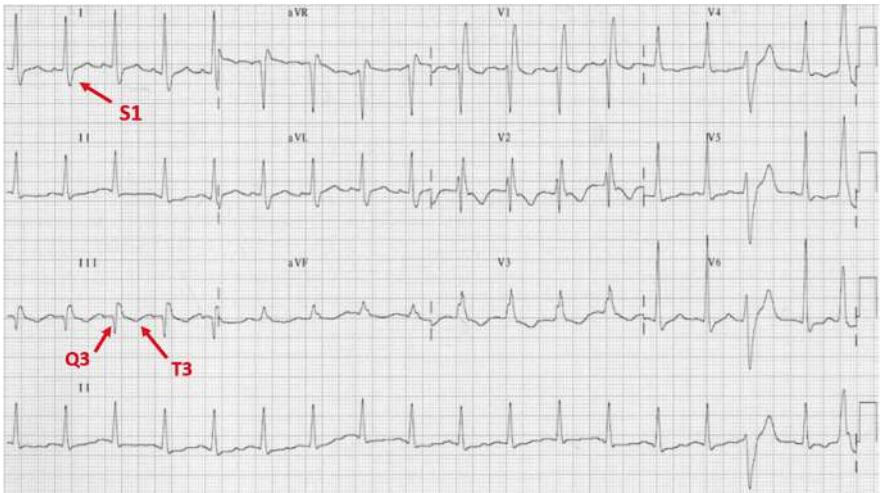


Fig. 1.28 ECG showing sinus tachycardia and S1Q3T3 in patient who has PE

Table 1.7 Wells criteria to estimate the probability of PE

Criteria	Points ^a
Clinical signs of DVT	3
Other differential diagnosis than PE is unlikely	3
Previous PE or DVT	1.5
Heart rate >100 bpm	1.5
Recent surgery or immobilization	1.5
Hemoptysis	1
Malignancy	1

Adapted from Wells et al. [35].
PE pulmonary embolism, DVT deep vein thrombosis
^aScore of 0–1 low, 2–6 intermediate, ≥7 high risk

- Pulmonary hypertension
- D shaped septum
- Paradoxical movement of the septum
- Low tricuspid annular plane systolic excursion (TAPSE) <16 mm
- *Computed tomography pulmonary angiography (CTPA):* the gold standard for diagnosis of PE (Fig. 1.30).

Management of High Risk/Massive and Intermediate Risk/Submassive PE
As in any critical case, PE should be approached with ABC and management of each step accordingly.
If right-side heart failure (RHF) is present, it must be managed as outlined in the section “[Right Side Heart Failure \(RHF\)](#)”.

Fig. 1.29 Echocardiogram is showing an enlarged right ventricle (RV) with D shaped septum. LV = left ventricle

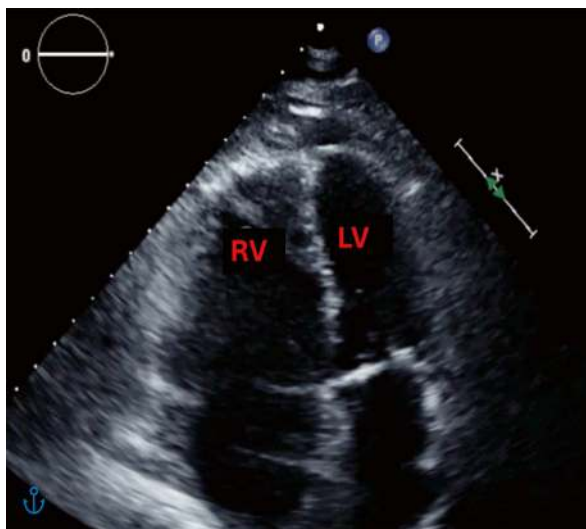
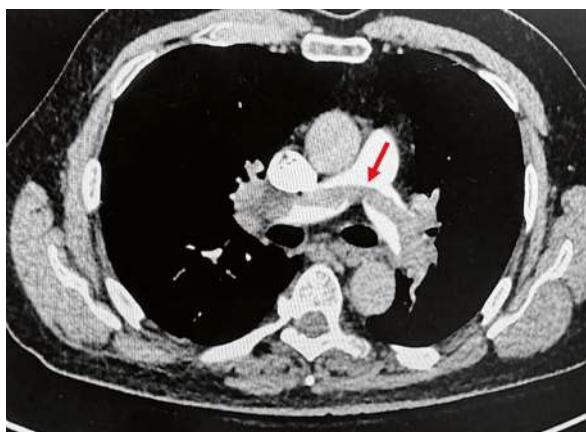


Fig. 1.30 The CT shows bilateral saddle shape pulmonary embolism of right and left main trunks. (Courtesy of Dr. Ahmad Bafaraj)



The patient should be treated in a critical care area, attached to a cardiac monitor, and maintained with two large-bore peripheral cannulas for investigations and treatment.

Anticoagulation, either with a heparin infusion or a therapeutic dose of enoxaparin, must be initiated.

For high-risk/massive PE, thrombolysis using a tissue plasminogen activator (TPA) should be administered unless an absolute contraindication exists (Table 1.8). Alteplase and tenecteplase are commonly used agents. If thrombolysis is contraindicated or ineffective, mechanical thrombectomy should be considered. Veno-arterial extracorporeal membrane oxygenation (VA-ECMO) may be used as a bridging therapy to maintain hemodynamic stability until reperfusion is achieved.

Table 1.8 Contraindications of thrombolysis in PE

<i>Absolute contraindications</i>
Prior intracranial hemorrhage
Ischemic stroke within 3 months
Known intracranial neoplasm or malformation
Recent head trauma
Recent brain/spinal surgery
Suspected aortic dissection
Active bleeding or bleeding diathesis
<i>Relative contraindications</i>
Severe uncontrolled hypertension (>180/110 mmHg)
History of ischemic stroke >3 months
Cardiopulmonary resuscitation
Major surgery/invasive procedure
Recent (non-CNS) bleeding
Pregnancy
Pericarditis or pericardial effusion
Diabetic retinopathy
Current use of anticoagulant
Age >75 years

Adapted from Kearon et al. [36]
CNS central nervous system

Evidence of Using Thrombolysis in Intermediate Risk/Submassive PE

Despite limited evidence, some experts use thrombolysis to treat submassive PE based on the results of clinical trials. The *MAPPET 3 trial* [37] showed that adding thrombolytic therapy to heparin reduces the need for escalation to thrombolysis in cases that deteriorate. The *PEITHO trial* [38] demonstrated a reduced rate of hemodynamic instability when thrombolytics are used in submassive PE; however, it also reported an increased risk of major bleeding.

Aortic Dissection

Classification of Aortic Dissection

The Stanford and DeBakey systems are the most used to classify aortic dissection (Fig. 1.31) [41].

The Stanford Classification

- Type A: involves the ascending aorta.
- Type B: involves only the descending aorta.

The DeBakey Classification

- Type I: originates in the ascending aorta and propagates at least to the aortic arch and beyond that.
- Type II: involves the ascending aorta only.
- Type III: originates in the descending aorta.

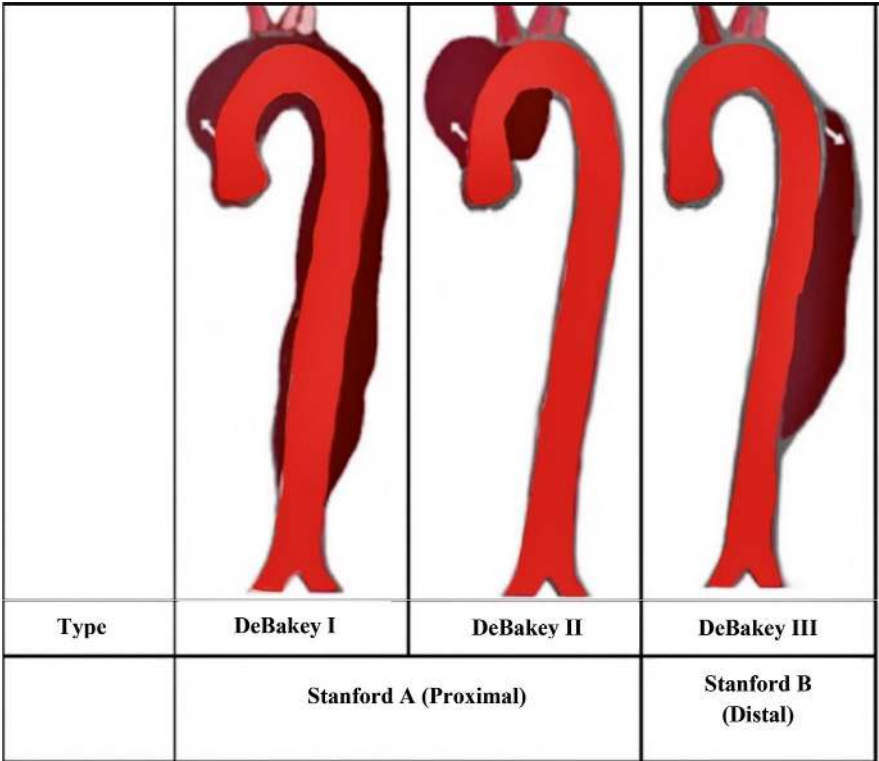


Fig. 1.31 Classification of aortic dissection. (Adapted from DeBakey et al. [39] and Daily et al. [40])

Risk factors for Aortic Dissection Include

- Hypertension
- Advanced age
- Smoking
- Trauma
- Congenital disorders, e.g., Marfan syndrome, Ehlers-Danlos syndrome, aortic coarctation, Turner’s syndrome, congenital aortic stenosis, bicuspid aortic valve
- Vascular inflammation, e.g., giant cell arteritis, Takayasu arteritis, Behcet’s disease, syphilis
- Iatrogenic factors, e.g., catheter/instrument intervention, valvular/aortic surgery

Symptoms and Signs of Aortic Dissection

- Pain:
 - Type A dissection classically presents with sudden onset, severe chest pain, radiated to the back.
 - Type B dissection classically presents only with back pain.

- Different or absent pulses in the extremities
- Blood pressure differences between limbs, with the arm opposite the dissection typically exhibiting higher blood pressure
- Aortic regurgitation (AR), early diastolic decrescendo murmur, best heard along the right sternal border
- Syncope, resulting from impairment of cerebral blood flow or stroke

Complications of the Aortic Dissection

- *Cardiovascular:*
 - Cardiac tamponade
 - Acute aortic regurgitation
 - Myocardial ischemia
 - Shock related to cardiac tamponade, acute AR, dissection of the coronary arteries, blood loss, etc.
 - Limb ischemia
- *Neurological:*
 - Ischemic stroke
 - Acute paraplegia related to spinal cord ischemia
- *Pulmonary:* plural effusions
- *Renal:* acute kidney injury
- *Gastrointestinal:* acute mesenteric ischemia
- *Hematological:* anemia and coagulopathy

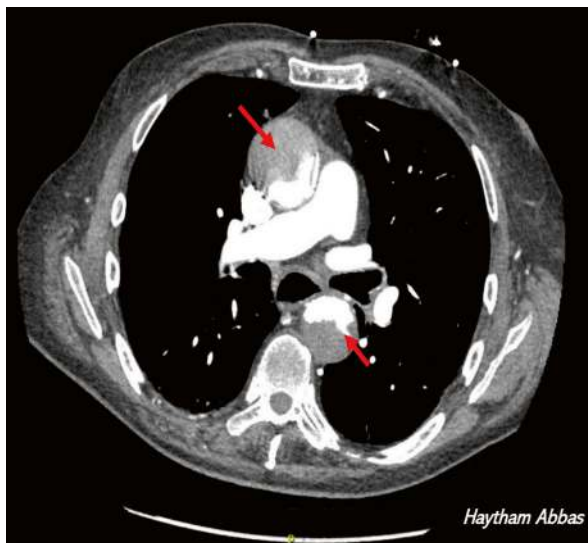
Investigations of Patients Suspected or Diagnosed with Aortic Dissection

- *Electrocardiogram (ECG)/cardiac enzymes:* patients may be complicated by myocardial ischemia.
- *Renal/liver function, blood gas:* to rule out end organ damage related to hypoperfusion.
- *Complete blood count (CBC) and coagulation profile:* to rule out anemia and coagulopathy.
- *Chest x-ray:* possible findings include:
 - Pleural effusion (in the same side)
 - Widened mediastinum
 - Tracheal shift to the opposite side
 - Cardiomegaly (in the case of pericardial effusion)
 - Calcium sign which is defined as separation of calcified intima at the aortic knuckle (Fig. 1.32)
- *Trans-thoracic echocardiography (TTE):* rarely shows the intimal dissection, but may reveal cardiac complication, e.g., aortic regurgitation, tamponade, hypokinesia, etc.

Fig. 1.32 Chest X-ray showing calcium sign in aortic dissection



Fig. 1.33 CT scan showing dissection of the ascending and descending aorta



- *Trans-esophageal echocardiography (TEE)*: more sensitive for detecting intimal dissection.
- *Computed tomography angiography (CTA)*: The diagnostic modality of choice to detect aortic dissection and assess its extent (Fig. 1.33)

Management of Aortic Dissection

As in any critical case, aortic dissection must be approached by ABC and management of each step accordingly.

The patient must be treated in critical care area, attached to a cardiac monitor, and maintained with two large peripheral cannulas for investigations and management.

Management of Hypertension

The main aim is to keep systolic blood pressure (SBP) between 100 and 120 mmHg and the heart rate (HR) ≤ 60 bpm. The first choice is an intravenous beta blocker (BB), e.g., labetalol or esmolol. If SBP is still not within target, adding a vasodilator is indicated, e.g., nicardipine, sodium nitroprusside, etc.

Management of Hypotension

A bolus of crystalloid $\pm$ inotropic support should be administered, aiming to maintain SBP between 100–120 mmHg. Urgent crossmatching and activation of the massive transfusion protocol should be considered if hemorrhagic shock is suspected. Echocardiography is also recommended to assess the etiology of shock, e.g., cardiac tamponade, cardiogenic, or hypovolemic shock. Treatment of the underlying cause should be implemented accordingly.

Definitive Management

Stanford type A and complicated type B require surgical intervention.

Uncomplicated type B requires only medical therapy to control blood pressure (BB $\pm$ vasodilators).

Hypertensive Emergency

It is defined as high blood pressure exceeding 180/120 mmHg with evidence of end organ damage. The target blood pressure and pharmacological choices depend on the type of end-organ damage; Tables 1.9 and 1.10 illustrate these points [45, 46].

Infective Endocarditis

Infective endocarditis (IE) is an infection of a native or prosthetic heart valve, leading to vegetation formation and subsequent tissue destruction. It is classically a multi-system disorder due to its hematogenous spread.

Risk Factors for IE Include

- Congenital heart disease
- History of endocarditis
- Valvular heart disease, e.g., rheumatic fever
- Prosthetic heart valves

Table 1.9 Clinical manifestations and management of hypertensive emergencies

End organ damage	Clinical symptoms/signs	Investigations	Target blood pressure (BP)	Treatment	Comments
<i>Cardiovascular complications</i>					
Acute pulmonary edema	Dyspnea and crackles	Chest x-ray Echocardiography	↓ SBP <25% within 1 h, <160/100 mm hg within 2–6 h, then achieve normal BP within 1–2 days	Nitroglycerin Nicardipine Nitroprusside	Add loop diuretic Avoid BB
Myocardial infarction	Chest pain, diaphoresis, etc.	ECG and cardiac enzymes	↓ SBP <25% within 1 h, <160/100 mmHg within 2–6 h, then achieve normal BP within 1–2 days	Nitroglycerin Labetalol Esmolol	
Aortic dissection	Chest pain radiated to the back	CT aortography	SBP 100–120 mmHg	Labetalol or esmolol first, nicardipine or nitroprusside if needed	Target HR ≤60 bpm
<i>CNS complications</i>					
Hemorrhagic stroke	Focal deficit according to the site	CT brain	Target SBP >130 to <140 mmHg	Labetalol Esmolol Nicardipine	
Ischemic stroke	Focal deficit according to the site	CT/MRI/CT angiography of brain	<220/120 mmHg if no interventions <185/110 mmHg before IV thrombolysis and should be maintained below 180/105 mmHg for at least the first 24 h ≤180/105 mmHg during and for 24 h after mechanical thrombectomy	Labetalol Esmolol Nicardipine	

(continued)

Table 1.9 (continued)

End organ damage	Clinical symptoms/signs	Investigations	Target blood pressure (BP)	Treatment	Comments
Hypertensive encephalopathy	Confusion, headache, visual disturbance	CT head to exclude ischemic stroke or hemorrhage	↓ SBP <25% within 1 h, <160/100 mmHg within 2–6 h, then achieve normal BP within 1–2 days	Labetalol Esmolol Nicardipine	
<i>Other conditions</i>					
Sympathomimetic use	Palpitation, agitation, diaphoresis, mydriasis	History and toxicology screen	Requires rapid lowering of BP	Nicardipine Phentolamine	Start by benzodiazepine Avoid BB as an initial agent
Preeclampsia/eclampsia	SBP >160 mmHg, DBP >110 mmHg, lower limb edema, symptoms and signs related to end organ damage	Proteinuria, workup for end organ damage	Requires rapid lowering of BP Keep SBP 130–150 mmHg and DBP 80–100 mmHg	Labetalol Hydralazine Nicardipine	Delivery of the fetus is essential Avoid ACEi, ARB, renin inhibitors, and nitroprusside
Acute kidney injury	Usually, asymptomatic	Renal function test	↓ SBP <25% within 1 h, <160/100 mmHg within 2–6 h, then achieve normal BP within 1–2 days	Fenoldopam Nicardipine BB	ACEi in scleroderma renal crisis
Pheochromocytoma	Palpitation, agitation, diaphoresis, tremor	Urine and serum metanephrines	Requires rapid lowering of BP	Phentolamine Nicardipine	Avoid initiation of BB before the alpha blocker
Perioperative hypertension	NA	NA	Control the BP immediately	Esmolol Nicardipine Labetalol	It happens after anesthesia induction and airway management

Adapted from: Writing Committee Members et al. [42], Marik and Varon [43], and Varon [44]
 ACEi angiotensin-converting enzyme inhibitors, ARB angiotensin receptor blockers, BB beta blockers, BP blood pressure, CT computed tomography, DBP diastolic blood pressure, ECG electrocardiogram, HR heart rate, IV intravenous, MRI magnetic resonance imaging, SBP systolic blood pressure

Table 1.10 Common agents used to treat hypertensive emergency

Class	Drug(s)	Usual dose range	Comments
CCB— dihydropyridines	Nicardipine	Initial 5 mg/h, increasing every 5 min by 2.5 mg/h to maximum 15 mg/h	Contraindicated in advanced aortic stenosis; no dose adjustment needed for persons aged ≥ 65 y. No negative inotropic or chronotropic effects.
	Clevidipine	Initial 1–2 mg/h, doubling every 90 s until BP approaches target, then increasing by less than double every 5–10 min; maximum dose 21 mg/h; maximum duration 72 h	Contraindicated in patients with soybean, soy product, egg, and egg product allergy and in patients with defective lipid metabolism (e.g., pathological hyperlipidemia, lipoid nephrosis [minimal change disease] or acute pancreatitis). No negative inotropic or chronotropic effects. Decreased risk of reflex tachycardia.
Vasodilators— nitric-oxide dependent	Sodium nitroprusside	Initial 0.3–0.5 mcg/kg/min; increase in increments of 0.5 mcg/kg/min every 5 min to achieve BP target; maximum dose 10 mcg/kg/min; duration of treatment as short as possible	Due to potency, intra-arterial BP monitoring is recommended to prevent “overshoot.” Lower dose required for older adults. Tachyphylaxis is common with extended use. No negative inotropic or chronotropic effects. Due to increased mortality risk, should be avoided in acute cerebrovascular disease unless other agents are not available. Use cautiously in pregnancy or older adults. Cyanide toxicity (increased risk in liver dysfunction and chronic kidney disease) and thiocyanate toxicity (increased risk in kidney dysfunction, $sCr > 3$) may occur for infusion rates ≥ 3 mcg/kg/min and/or duration ≥ 3 d. Cyanide toxicity and thiocyanate toxicity may present similarly with metabolic acidosis, altered mental status, and cardiac arrhythmia. For either toxicity state, nitroprusside should be discontinued and sodium thiosulfate or cyanocobalamin should be administered.
	Nitroglycerin	Initial 5 mcg/min; increase in increments of 5 mcg/min every 3–5 min to a maximum rate of 200 mcg/min	Use only in patients with acute coronary syndrome and/or acute pulmonary edema. Do not use in volume depleted patients. Tachyphylaxis is common with extended use.

(continued)

Table 1.10 (continued)

Class	Drug(s)	Usual dose range	Comments
Vasodilators— direct	Hydralazine	Initial 10 mg via slow IV infusion (maximum initial dose 20 mg); repeat every 4–6 h as needed. Adjust rate up to total cumulative dose of 200 mg/24 h	BP begins to decrease within 10–30 min, and the fall lasts 2–4 h. Hydralazine is an undesirable first-line agent for acute treatment in most patients due to unpredictability of response and prolonged duration of action.
Adrenergic blockers—beta-1 receptor selective antagonist	Esmolol	Loading dose 500–1000 mcg/kg/min over 1 min followed by a 50-mcg/kg/min infusion. For additional dosing, the bolus dose is repeated, and the infusion increased in 50-mcg/kg/min increments as needed to a maximum of 300 mcg/kg/min	Contraindicated in patients with concurrent beta blocker therapy, bradycardia, or decompensated HF. Monitor for bradycardia. Higher doses may block beta-2 receptors and impact lung function in reactive airway and obstructive pulmonary disease.
Adrenergic blockers— combined alpha-1 and nonselective beta receptor antagonist	Labetalol	Initial 0.3- to 1.0-mg/kg dose (maximum 20 mg) slow IV injection every 2 min or 0.4–1.0-mg/kg/h IV infusion up to 3 mg/kg/h. Adjust rate up to total cumulative dose of 300 mg/24 h	Contraindicated in reactive airway or obstructive pulmonary disease. Especially useful in hyperadrenergic syndromes. May worsen HF and should not be given in patients with second- or third-degree heart block or bradycardia.
Adrenergic blockers— nonselective alpha receptor antagonist	Phentolamine	IV bolus dose 5 mg. Additional bolus doses every 10 min as needed to lower BP to target. Adjust rate up to total cumulative dose of 50 mg/24 h	Used in hypertensive emergencies induced by catecholamine excess (pheochromocytoma, interactions between monoamine oxidase inhibitors and other drugs or food, cocaine toxicity, amphetamine overdose, or clonidine withdrawal).

Dopamine-1-receptor selective agonist	Fenoldopam	Initial 0.1–0.3 mcg/kg/min; may be increased in increments of 0.05–0.1 mcg/kg/min every 15 min until target BP is reached. Maximum infusion rate 1.6 mcg/kg/min	Contraindicated in patients at risk of increased intraocular pressure (glaucoma) or intracranial pressure and those with sulfite allergy.
ACE inhibitor	Enalaprilat	Initial 1.25 mg over a 5-min period. Doses can be increased up to 5 mg every 6 h as needed to achieve BP target. Adjust rate up to total cumulative dose of 50 mg/24 h	Contraindicated in pregnancy and should not be used in acute MI or bilateral renal artery stenosis. Mainly useful in hypertensive emergencies associated with high plasma renin activity. Poorly defined dose adjustments for kidney failure and may worsen kidney injury in those with CKD. Relatively slow onset of action (15 min) and unpredictability of BP response.

Reproduced with permission from: Writing Committee Members et al. [42]

CCB calcium channel blocker, *BP* blood pressure, *sCr* serum creatinine, *HF* heart failure, *ACE* angiotensin converting enzyme, *MI* myocardial infarction, *CKD* chronic kidney disease, *IV* intravenous

- History of intravenous drug use
- Indwelling devices, e.g., intravenous catheters and implanted cardiac devices
- Poor dentition/dental infection

Clinical Presentation of IE

- *General symptoms:*
Including anorexia, weight loss, night sweats, fever, etc.
- *Valvular involvement:*
 - New murmur
 - Symptoms and signs of congestive heart failure due to valvular incompetence
- *Systemic embolization:*
 - Janeway lesions (macular, painless plaques on the palms and soles)
 - Splinter hemorrhages (tiny linear lesions in the nail bed)
 - Septic emboli: these may lodge in any organ, leading to symptoms and signs specific to the affected organ as following:
 1. Cerebral emboli: focal neurological deficit and stroke
 2. Coronary emboli: myocardial infarction and arrhythmias
 3. Pulmonary emboli: dyspnea, chest pain and signs of right-side heart failure
 4. Splenic emboli: left upper quadrant pain, left-sided pleural effusion
 5. Renal emboli: hematuria and flank pain
- *Immune complex formation*
 - Glomerulonephritis, secondary to deposition of circulating immune complexes in kidneys
 - Inflammatory synovitis
 - Osler nodes: immune complex deposition on hands and feet (painful and red raised lesions)
 - Roth's spots: retinal immune complex mediated vasculitis (retinal hemorrhage)

Causative Organisms of IE

Generally, *Staphylococcus aureus* is the most common organism to cause IE.

- Native valve endocarditis is caused by the following organisms:
 - *Staphylococcus aureus:*
 - Methicillin-sensitive *Staphylococcus aureus* (MSSA) is more frequent in community-acquired IE.
 - Methicillin-resistant *Staphylococcus aureus* (MRSA) is predominantly related to nosocomial infection.
 - *Streptococcus viridans:*
 - *Streptococcus bovis* is frequently associated with colon cancer.
 - *Enterococcus faecalis*
 - Gram-negative bacilli:

- HACEK organisms: *Haemophilus*, *Actinobacillus actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella corrodens*, and *Kingella kingae*
- Prosthetic valve endocarditis is caused by the following organisms:
 - *Staphylococcus aureus* (the most common)
 - Coagulase-negative *Staphylococci*
 - Non-tuberculous mycobacteria
 - Fungi (mainly *Candida*)
 - Gram-negative organisms

Investigations and Diagnosis of IE

IE is diagnosed by using Duke’s criteria; see Tables 1.11 and 1.12 [47].

Table 1.11 Duke criteria for diagnosis of IE including the major and minor criteria

Major criteria
Microbiological
Positive blood cultures: Microorganisms that commonly cause IE isolated from 2 or more separate blood culture sets (<i>Staphylococcus aureus</i> ; <i>Staphylococcus lugdunensis</i> ; <i>Enterococcus faecalis</i> ; all streptococcal species [except for <i>S. pneumoniae</i> and <i>S. pyogenes</i>], <i>Granulicatella</i> and <i>Abiotrophia</i> spp., <i>Gemella</i> spp., HACEK group) (In the setting of intracardiac prosthetic material, the following additional bacteria should be included as “typical” pathogens: coagulase negative staphylococci, <i>Corynebacterium striatum</i> and <i>C. Jeikeium</i> , <i>Serratia marcescens</i> , <i>Pseudomonas aeruginosa</i> , <i>Cutibacterium acnes</i> , nontuberculous mycobacteria [especially <i>M. chimaera</i>], and <i>Candida</i> spp.).
Or
Microorganisms that rarely cause IE isolated from 3 or more separate blood culture sets.
Positive laboratory tests: Positive polymerase chain reaction (PCR) for <i>Coxiella burnetii</i> , <i>Bartonella species</i> , or <i>Tropheryma whippiei</i> from blood.
Or
Serology detection for <i>Coxiella burnetii</i> , <i>Bartonella henselae</i> or <i>Bartonella quintana</i> .
Imaging
Echocardiography and cardiac computed tomography (CT) imaging: Vegetation, valvular/leaflet perforation, valvular/leaflet aneurysm, abscess, pseudoaneurysm, or intracardiac fistula.
Or
Significant new valvular regurgitation on echocardiography as compared to previous imaging.
Or
New partial dehiscence of prosthetic valve as compared to previous imaging.
Positron emission computed tomography with 18F-fluorodeoxyglucose ([18F] FDG PET/CT imaging): Abnormal metabolic activity involving a native or prosthetic valve, ascending aortic graft, intracardiac device leads or other prosthetic material.
Surgical
Evidence of IE documented by direct inspection during heart surgery neither major imaging criteria nor subsequent histologic or microbiologic confirmation.

(continued)

Table 1.11 (continued)

<i>Minor criteria</i>
<i>Predisposing factors:</i> Previous history of IE, prosthetic valve, previous valve repair, congenital heart disease, endovascular cardiac implantable electronic device, hypertrophic obstructive cardiomyopathy, or injection drug use.
<i>Fever:</i> Documented temperature greater than 38 °C.
<i>Vascular manifestations:</i> Clinical or radiological evidence of arterial emboli, septic pulmonary infarcts, cerebral or splenic abscess, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages, Janeway lesions, purulent purpura.
<i>Immunologic manifestation:</i> Positive rheumatoid factor, Osler nodes, Roth spots, or immune complex-mediated glomerulonephritis.
<i>Microbiological not achieving the major criterion:</i> Positive blood cultures for a microorganism consistent with IE but not meeting the requirements for major criterion. Positive culture, PCR for an organism consistent with IE from a sterile body site other than cardiac tissue, cardiac prosthesis, or embolus; or a single finding of a skin bacterium by PCR on a valve or wire without additional clinical or microbiological supporting evidence.
<i>Imaging:</i> Abnormal metabolic activity as detected by [18F] FDG PET/CT within 3 months of implantation of prosthetic valve, ascending aortic graft (with concomitant evidence of valve involvement), intracardiac device leads, or other prosthetic material.
<i>Physical examination:</i> New valvular regurgitation identified on auscultation if echocardiography is not available. Worsening or changing of pre-existing murmur not sufficient.

Fowler et al. [47]. Used with permission

Management of IE

In critical cases such as cardiogenic or septic shock, management of IE is approached with ABC and management of each step accordingly.

The main line of management is antibiotics targeting the causative organism. Empirical antibiotics in IE should include vancomycin, as *Staphylococcus aureus* is the most common organism, and MRSA infection should be covered. The initial dose of vancomycin is 15–20 mg/kg administered intravenously. Subsequent doses depend on creatinine clearance and are adjusted to maintain area under the curve (AUC)/minimum inhibitory concentration (MIC) >400, or trough level of 15–20 mcg/mL [48].

If the infection involves a native valve, gentamicin or ceftriaxone should be added to vancomycin.

If the infection involves a prosthetic valve, the empirical primary regimen should include rifampin in addition to vancomycin and gentamicin.

Other antibiotic choices target the causative organism (these are explained in the section “[Use of Antibiotics](#)”, Chap. 8).

Table 1.12 Duke criteria for diagnosis of IE including the definite, possible and the rejected diagnosis**I. Definite endocarditis****A. Pathologic criteria**

Microorganisms identified (by culture, staining, immunologic techniques, polymerase chain reaction) in the context of clinical signs of active endocarditis in a vegetation; from cardiac tissue; from an explanted prosthetic valve or sewing ring; from an ascending aortic graft (with concomitant evidence of valve involvement); from an endovascular intracardiac implantable electronic device (CIED); or from an arterial embolus

Or

Active endocarditis (may be acute or subacute/chronic) identified in or on a vegetation; from cardiac tissue; from an explanted prosthetic valve or sewing ring; from an ascending aortic graft (with concomitant evidence of valve involvement); from a CIED; or from an arterial embolus

B. Clinical criteria

2 major criteria

Or

1 major criterion and 3 minor criteria

Or

5 minor criteria

II. Possible endocarditis

1 major criterion and 1 minor criterion

Or

3 minor criteria

III. Rejected endocarditis

Firm alternate diagnosis explaining signs/symptoms

Or

Lack of recurrence despite antibiotic therapy for less than 4 days.

Or

No pathologic or macroscopic evidence of IE at surgery or autopsy, with antibiotic therapy for less than 4 days

Or

Does not meet criteria for possible IE, as above

Fowler et al. [47]. Used with permission

Indications for surgery in IE: see Table 1.13 [50].

Antibiotic Prophylaxis for IE

It should be given to patients undergoing invasive dental procedures involving manipulation and have any of the following:

- A prosthetic cardiac valve
- A previous history of IE
- A cardiac transplant with valvopathy
- Congenital heart disease (CHD) with any of the following criteria:
 - Any type of cyanotic CHD
 - Any CHD repaired with a prosthetic material placed surgically or percutaneously within 6 months of the procedure
 - Repaired CHD with residual defects

Table 1.13 Indications of cardiac surgery in IE

<i>Congestive heart failure</i>
Infective endocarditis (IE) with: Severe acute aortic/mitral regurgitation or valve obstruction causing refractory pulmonary edema/shock (emergency) Severe acute aortic/mitral regurgitation or valve obstruction and persisting heart failure (urgent) Severe regurgitation and no heart failure (elective)
<i>Uncontrolled infection</i>
Paravalvular extension with formation of abscess, fistula or false aneurysm (urgent) Persisting fever and positive blood culture for ≥ 5 –7 days after administration of appropriate antimicrobial therapy (urgent) Infection caused by fungi or multi-resistant micro-organisms (urgent/elective)
<i>Systemic embolism</i>
Aortic or mitral IE with large vegetations (>10 mm) resulting in one or more embolic episodes despite appropriate antibiotic therapy (urgent) Isolated very large vegetations >15 mm (urgent)
<i>Prosthetic valve</i>
Prosthetic valve dehiscence or obstruction Infection caused by <i>Staphylococcus aureus</i> or non-HACEK gram-negative bacteria

Adapted from: Delgado et al. [49], Prendergast and Tornos [50], and Pettersson and Hussain [51]

Shock

Shock is defined as hypoperfusion that causes tissue hypoxia and results in multiorgan dysfunction.

Blood pressure(*BP*) = cardiac output(*CO*) $\times$ peripheral vascular resistance(*PVR*)
 $CO = \text{stroke volume} (SV) \times \text{heart rate} (HR)$

SV is affected by preload, cardiac contractility, and afterload.
By analyzing these equations, all causes of shock can be identified.

Causes of Shock

- *Hypovolemic shock*: Severe volume depletion causes decreased preload, which is reflected in a reduced SV and CO. The main causes include:
 1. Hemorrhage (trauma, gastrointestinal bleed, and retroperitoneal bleed)
 2. Dehydration (vomiting, diarrhea, and gastrointestinal fistula)
 3. Third spacing (burns, pancreatitis, and sepsis)
- *Cardiogenic*: Cardiac dysfunction (systolic or diastolic) leads to decreased SV and CO. Causes include myocarditis, cardiomyopathy, valvular heart disease, Arrhythmias, myocardial infarction (MI), etc.

- *Distributive*: Systemic vasodilation results in decreased PVR. The most common causes are:
 1. Septic shock
 2. Anaphylaxis
 3. Liver failure
 4. Neurogenic shock
 5. Adrenal insufficiency
- *Obstructive*: This type of shock is caused by either:
 1. Obstruction of circulation, leading to impaired preload, as seen in cardiac tamponade, constrictive pericarditis, or tension pneumothorax or
 2. A sudden increase in afterload, as seen in pulmonary embolism (PE)

Clinical Manifestations of Shock

Hypotension

Tachycardia

Tachypnea

Delayed capillary refill

Cool extremities

Altered mental status

Decreased urine output

General Management of Shock

As in any critical case, shock must be approached with ABC and management of each step accordingly.

Each type of shock has a specific management approach (explained in detail in its respective chapter).

Key components include:

- Fluid resuscitation and assessment for fluid responsiveness
- Blood transfusion if needed
- Vasopressors to increase PVR
- Inotropes to increase CO (see Table 1.14)
- Hemodynamic monitoring; central venous catheter, arterial line, pulmonary artery catheter, echocardiogram, CO monitoring, etc.
- Monitoring for reperfusion markers, e.g., lactate clearance, clinical assessment using Glasgow coma scale (GCS), urine output, capillary refill time, etc.

Table 1.14 The common vasopressors and inotropes

Pharmacological agent	α	$\beta 1$	$\beta 2$	Dopamine	Other	CO	SVR	BP	HR
Norepinephrine	✓✓	✓✓	×	×	×	↑↑	↑↑	↑↑	↑↑
Epinephrine	✓✓	✓✓	✓	×	×	↑↑	↑↑	↑↑	↑↑
Phenylephrine	✓✓	×	×	×	×	↓	↑↑	↑↑	–
Vasopressin	×	×	×	×	V1, V2	–	↑↑	↑↑	–
Dobutamine	×	✓✓	✓	×	×	↑↑	↓	↓	↑↑
Milrinone	×	×	×	×	PDEi	↑↑	↓	↓	–
Dopamine 2–5 mic/kg/min	×	✓	×	✓✓	×	↑	–	–	↑
Dopamine 5–10 mic/kg/min	✓	✓✓	✓	✓✓	×	↑↑	↑	↑	↑↑
Dopamine 10–20 mic/kg/min	✓✓	✓✓	✓	✓✓	×	↑↑	↑↑	↑↑	↑↑

α alpha, β beta, CO cardiac output, SVR systemic vascular resistance, BP blood pressure, HR heart rate, V1,2 vasopressin receptors 1 and 2, PDEi phosphodiesterase inhibitor

Cardiac Tamponade

Definition and Clinical Presentation of Cardiac Tamponade

Accumulation of fluid in the pericardial space may lead to diastolic dysfunction and progress to obstructive shock. Clinically, the patient may present with the classic triad of hypotension, distended neck veins, and muffled heart sounds. Pulsus paradoxus may also be observed, defined as a decrease in systolic blood pressure of more than 10 mmHg during inspiration.

Causes of Cardiac Tamponade

- Infectious causes: commonly viral pericarditis, other causes are bacterial, tuberculous, or fungal.
- Malignancy.
- Vasculitis.
- Traumatic.
- Post-myocardial infarction.
- Complicated aortic dissection.
- Metabolic, e.g., uremia, hypothyroid, and ovarian hyperstimulation syndrome.

Investigations of Cardiac Tamponade

- *Cardiac enzymes*: can be elevated.
- *Metabolic profile*: renal function, thyroid, etc., to rule out metabolic causes of pericardial effusion.
- *Complete blood count (CBC) and coagulation profile*: looking for changes related to infectious causes and hemorrhagic effusion.
- *Electrocardiogram (ECG)*: expected findings are low voltage and diffuse ST elevation.
- *Chest x-ray*: cardiomegaly may be seen.
- *Echocardiography*: The diagnostic modality of choice for tamponade is echocardiography, which typically shows pericardial effusion with systolic/early diastolic collapse of the right atrium (the most sensitive sign [52]) and diastolic collapse of the right ventricle. Septal shift with respiratory variation can also be seen; the interventricular and interatrial septa move leftward during inspiration, and these septa shift rightward during expiration. The respiratory variation of mitral and tricuspid flow velocities is also seen in cardiac tamponade with >30% variation across the mitral valve and >60% across the tricuspid valve.
- *Pulmonary artery catheter*: It shows an increase in central venous pressure (CVP), right ventricular pressure (RVP), pulmonary artery pressure (PAP), and pulmonary capillary wedge pressure (PCWP), with equalization of diastolic pressures in all cardiac chambers. The right atrial waveform typically demonstrates a prominent x descent and an absent y descent (Fig. 1.12).

Management of Cardiac Tamponade

As in any critical case, cardiac tamponade must be approached with ABC and management of each step accordingly. If the patient needs intubation, oversedation must be avoided as it may compromise hemodynamics.

For hypotension, it is recommended to support the preload with volume and bolus of crystalloid will be required.

Also, systolic function should be preserved by giving inotropic support, e.g., norepinephrine, epinephrine, and/or dobutamine.

The main line of management is pericardiocentesis.

In traumatic or post-cardiac surgery cases, surgical intervention is recommended.

Investigation and treating the cause is mandatory after stabilization of the patient.

Anaphylactic Shock

Definition of anaphylaxis: see Table 1.15.

The pathophysiology of anaphylaxis is described as an immediate hypersensitivity reaction (Type I), characterized by immunoglobulin E (IgE) stimulation leading to histamine release, which causes the signs and symptoms of allergy.

Anaphylactic shock is a clinical syndrome that is diagnosed clinically.

No specific investigations are indicated in the acute setting. After stabilization, some workup such as total IgE and allergy skin tests can be performed.

Management of Anaphylactic Shock [54]

As in any critical case, anaphylaxis must be approached with ABC and management of each step accordingly.

Table 1.15 Definition and criteria for diagnosis of anaphylaxis

Anaphylaxis is likely when any one of the three criteria is fulfilled:
1. No known allergen exposure: Acute onset of disease (minutes or hours) with involvement of skin/mucosa And either: A. Respiratory involvement B. Cardiovascular involvement
2. Likely or known allergen exposure: Sudden onset of two or more of the following: A. Skin/mucosal involvement B. Respiratory involvement C. Cardiovascular involvement D. Severe gastrointestinal involvement
3. Known allergen exposure: Sudden onset of either: A. Respiratory involvement after exposure to a non-inhaled allergen B. Cardiovascular involvement
<i>Organ involvement presentation</i> Skin/mucosa: urticaria, flushing, erythema, facial swelling, lips-tongue-orpharyngeal swelling, difficult swallowing Respiratory: dyspnea, wheezing, strider, hypoxemia, cough, voice change Cardiovascular: hypotension, collapse, syncope Gastrointestinal: severe abdominal pain, repetitive vomiting, diarrhea

Adapted from Dribin et al. [53]. Used with permission

Anticipate a difficult airway (e.g., suspected laryngeal edema or inflamed mucosa) and seek assistance from an expert early.

Identify and immediately stop the causative agent, such as an ongoing intravenous medication.

Attach the patient to a cardiac monitor.

Establish two large-bore peripheral intravenous (IV) cannulas.

In cases of hypotension, initiate a bolus of crystalloids.

Epinephrine 1:1000 at a dose of 0.5 mg should be administered subcutaneously or intramuscularly every 5–10 min as needed.

Steroids must also be administered to prevent delayed-phase anaphylaxis.

Administer bronchodilators in cases of bronchospasm.

Antihistamines (e.g., diphenhydramine) should be given if there is skin or soft tissue involvement.

For persistent shock, IV infusion of the epinephrine +/- mechanical circulatory support such as veno-arterial extracorporeal membrane oxygenation (VA-ECMO) should be considered.

Acute Coronary Syndrome (ACS)

Causes of ACS

- *Unstable angina*: It is related to subtotal occlusion of the coronary artery. Clinically, the patient will experience typical acute chest pain with the electrocardiogram (ECG) showing ST depression +/- T wave inversion and normal cardiac enzymes (e.g., high-sensitive troponin and creatine kinase-myocardial band [CK-MB]).
- *Non-ST elevation myocardial infarction (NSTEMI)*: It is also related to subtotal occlusion of the coronary artery. Clinically, patients will experience typical chest pain with the ECG showing ST depression +/- T wave inversion. However, cardiac enzymes will be elevated.
- *ST elevation myocardial infarction (STEMI)*: It is related to total occlusion of the coronary artery. Clinically, patients will experience typical chest pain, ST elevation in ECG or new left bundle branch block (LBBB), and elevated cardiac enzymes.

Clinical Presentation of Patients with ACS

Usually, patients are presented with acute chest discomfort. Women, older adults, and patients with diabetes may have “atypical” presentations. Other symptoms include shortness of breath, cardiac symptoms related to complications, e.g., palpitation, syncope, etc.

Clinical examination may reveal signs of heart failure with or without overload, arrhythmia, valvular heart disease, or signs of hypoperfusion related to complicated cardiogenic shock.

Investigations for ACS

- *ECG and cardiac enzymes*: used to confirm ACS and to identify which type. 12-lead ECG should be obtained within 10 min of arrival. If the initial ECG is nondiagnostic but clinical suspicion remains high, it should be repeated frequently. Table 1.16 shows the sites of ischemia in relation to cardiac leads. All the important ECGs are illustrated in the section “[Electrocardiogram \(ECG\)](#)”.
- *Blood gas with lactate*: possible findings are respiratory failure, metabolic acidosis, high lactate related to severe heart failure.
- *Chemistry/renal function*: to rule out cardiorenal syndrome and to address the renal function base before giving the contrast in coronary angiography.
- *Brain Natriuretic peptide (BNP/Pro-BNP)*: increases in heart failure.
- *Liver function test*: may be elevated in shocked patient or with right side heart failure.
- *Chest x-ray*: may show cardiogenic pulmonary edema, cardiomegaly, pleural effusion, etc.
- *Echocardiography*: Possible findings include cardiomyopathy, hypokinesia, and mechanical complications such as ruptured chordae tendineae or a ventricular septal defect (VSD).
- *Coronary angiography*: it is the gold standard modality for diagnosis and management of ACS.
- *Stress test and computed tomography (CT) coronary angiography*: for low probability cases.

Management of ACS [55]

As in any critical case, ACS must be approached with ABC and treatment of each step accordingly.

Attach cardiac and oxygen (O₂) saturation monitors and provide supplemental oxygen as needed to maintain O₂ saturation >90% [56]. Establish intravenous access and send for basic workup. Obtain an ECG and chest X-ray as well.

Life-Threatening Complications Should Be Treated Immediately

- *Cardiogenic shock*: pharmacological and mechanical support. See the management in the section “[Cardiogenic Shock](#)”.
- *Arrhythmias*: as per advanced cardiac life support (ACLS) guidelines.

Table 1.16 Sites of ischemia in relation to the cardiac leads

Leads	Site of ischemia
V1, V2	Septal
V3, V4	Anterior
V5, V6	Apical
I, AVL	Lateral
II, III, AVF	Inferior
RV4	Right ventricular infarction
Tall R wave in V1–V3 with ST depression	Posterior wall infarction

- Right ventricular infarction (RVI) with shock: gentle hydration, right side heart failure management and avoidance of vasodilators (e.g., Nitrate). See the management in the section “[Right Side Heart Failure \(RHF\)](#)”.
- Mechanical complications, e.g., ruptured chordae tendineae or VSD: cardiac surgery +/- mechanical support such as intra-aortic balloon pump (IABP).

Direct Therapies

- Anti-platelets:
 - Aspirin 325 mg (non-enteric coated) to be chewed and swallowed or given as rectal suppository if the patient cannot swallow. The subsequent doses are 81 mg daily.
 - P2Y₁₂ inhibitors: ticagrelor or prasugrel are the preferred agents particularly for percutaneous coronary intervention (PCI) patients and patients with NSTEMI. The dose of ticagrelor is 180 mg oral loading dose with subsequent doses of 90 mg twice daily. The dose of prasugrel is 60 mg loading dose followed by 10 mg daily. Clopidogrel is used for patients who will receive thrombolytic therapy with a dose of 300 mg loading dose and 75 mg daily for the subsequent doses.
 - Glycoprotein IIb/IIIa inhibitors (GPI): such as abciximab, eptifibatide, and tirofiban, can be given peri-PCI.
- Anticoagulation: unfractionated heparin (UFH) is the preferred choice especially for patients going to PCI, and therapeutic dose of enoxaparin is an alternative.
- Anti-ischemic and analgesics:
 - Nitroglycerin: given sublingually or intravenously if the patient has persistent chest discomfort, hypertension, or signs of heart failure.
 - Morphine: relieves pain and decreases pre-/afterload.
- Cardioprotective agents:
 - Beta Blocker (BB) if no contraindications, i.e., metoprolol given orally every 6 h with a target heart rate of 50–60 bpm.
 - Lipid management: high intensity statins e.g. atorvastatin 80 mg or rosuvastatin 40 mg are recommended. Non-statins, e.g., ezetimibe are recommended for more lipid control when statins are maximally tolerated.
 - Angiotensin-converting enzyme inhibitors (ACEi) or angiotensin II receptor blockers (ARBs): start once hemodynamics and renal function are stable.
- Reperfusion therapy in STEMI:
 - Primary PCI: it is the preferred modality [57], especially for patients with cardiogenic shock, heart failure, late presentation, or contraindications to fibrinolysis (see Table 1.17). Activate cardiac catheterization with an aim of (door-to-balloon) within 90 min.
 - Fibrinolysis: it can be used when PCI is unavailable within 120 min of first medical contact, symptoms occurred in <12 h, and no contraindications for its use. Activate thrombolysis with an aim of (door-to-needle) within 30 min.

Table 1.17 Contraindications of thrombolytic therapy in STEMI

<i>Absolute contraindications</i>
Previous intracranial hemorrhage
Ischemic stroke within 3 months
Recent significant closed-head trauma
Recent intracranial or intraspinal surgery
Intracranial neoplasm
Cerebral vascular lesion (e.g., arteriovenous malformation)
Aortic dissection
Active bleeding (except menses)
Severe uncontrolled hypertension (SBP >180 mmHg or DBP >110 mmHg)
<i>Relative contraindications</i>
History of prior ischemic stroke >3 months
Other intracranial pathologies (not mentioned in the absolute contraindications)
Chronic, poorly controlled hypertension
Oral anticoagulant therapy
Traumatic or prolonged CPR
Recent major non-CNS surgery
Recent internal bleeding (within 4 weeks)
Noncompressible vascular punctures
Pregnancy
Active peptic ulcer
Infective endocarditis

Adapted from: Ibanez et al. [58] and Rao et al. [55]
SBP systolic blood pressure, DBP diastolic blood pressure, CNS central nervous system, CPR cardiopulmonary resuscitation

Table 1.18 TIMI score used in unstable angina and NSTEMI, Total points 0–7, a score of 0 or 1 point are at lower risk of adverse outcome

<i>From history</i>
Age ≥65 years
≥3 CAD risk factors: Family history, hypertension, hyperlipidemia, diabetes mellitus, smoking.
Known CAD (stenosis ≥50%)
ASA used in the last 7 days
<i>At presentation</i>
Recent severe angina (≤24 h)
Elevated cardiac enzymes
ST deviation ≥0.5 mm

Adapted from Antman et al. [59]
CAD coronary artery disease, ASA acetylsalicylic acid (aspirin)

- Unstable angina or non-STEMI: early invasive vs conservative approach depends on hemodynamic stability, ongoing chest pain, or high TIMI (thrombolysis in myocardial infarction) or Grace scores. (Table 1.18 shows the TIMI score).

Post-Cardiac Surgery Care

Introduction: There are multiple cardiac surgery procedures; the most common surgery is coronary artery bypass graft (CABG) for various indications such as left main coronary artery stenosis or triple-vessel disease. Other surgeries include valvular replacement/repair, aortic surgeries, and others.

To perform the surgery, the patient is usually put on “the pump” or cardiopulmonary bypass (CPB). This involves cannulation of the right atrium and aorta. The heart is usually cooled. The patient is also usually systemically cooled to $<32^{\circ}\text{C}$ to minimize peripheral oxygen consumption. During this time, the patient must be systemically anticoagulated with heparin to prevent clotting in the bypass circuit. Long pump times are associated with increased postoperative complications such as bleeding, myocardial stunning, and multi-system organ failure. CPB may also be associated with systemic inflammatory response syndrome (SIRS).

It is sometimes difficult to liberate the patient from CPB or “get him off the pump,” that is, to restart the heart contracting normally. Pressors or inotropes are often used to facilitate “coming off the pump.” A variety of dysrhythmias may also occur during this period, including bradycardias requiring pacing. Most often, these dysrhythmias are transient and resolve spontaneously. By the end of surgery, the patient should have a normal activated clotting time (ACT), as he should receive protamine sulphate to counteract the effect of heparin [60].

Immediate Post-Op Care *History:* The following information should be collected from the surgeon, anesthesiologist, and the chart:

- Patient background (age, sex)
- Comorbidities: diabetes, hypertension, hyperlipidemia, smoking, family history, lung diseases, renal failure, hepatic failure, etc.
- Pre-operative medications
- Allergies
- Type of operation (CABG, valve, aorta, and whether it is elective or urgent)
- Indications for surgery
- Pre-operative results: catheterization laboratory (vessels involved), echocardiography, etc.
- Success of the operation (complete or incomplete, any complications)
- CPB time and aortic cross-clamp time
- Ease of separation from CPB (dysrhythmias, need for inotropes, pacing, etc.)
- Current inotropes, vasopressors, or anti-hypertensives
- Need for cardiac pacing
- Use of mechanical support, e.g., intra-aortic balloon pump (IABP), venoarterial extracorporeal membrane oxygenation (VA-ECMO), etc.
- Significant bleeding
- Attached lines: chest tubes, pacing wires, arterial line, central venous catheter (CVC), endotracheal tube (ETT), etc.

- *Physical exam and assessment:*
 - Follow the ABC approach. Ensure the ETT is correctly positioned and that bilateral air entry is equal. Keep in mind that tube displacement or pneumothorax may occur.
 - Confirm adequate oxygen saturation and review arterial blood gas (ABG) results as soon as they become available.
 - Verify ventilator settings.
 - Assess initial hemodynamic parameters (heart rate, blood pressure, cardiac output, and index, etc.) and determine the type and dosage of any vasoactive agent.
 - Check the patient's heart rhythm. If a pacemaker is in use, confirm its settings and functionality.
 - Inspect chest and mediastinal drains to ensure patency and assess for signs of excessive bleeding.
 - Auscultate heart sounds, with particular attention to murmurs, especially in patients who have undergone valve surgery.
 - Palpate all peripheral pulses.
 - Perform an abdominal examination.
 - Assess pupillary reflexes. A more detailed neurological examination should be conducted once the patient has recovered from general anesthesia.
- *Investigations:*
 - *Electrocardiogram (ECG):*
 - Changes from pre-operation: new right bundle branch block (RBBB) is not uncommon, usually temporary and of little clinical significance, shifts of the axis are also common and usually benign.
 - Rhythm: bradycardias, blocks, or atrial fibrillation, all are common.
 - ST-T changes: diffuse non-specific changes may reflect pericardial inflammation, ST elevation in two or more contiguous leads in a territory that was grafted, may indicate an acute graft failure.
 - *Chest X-Ray:*
 - Check the position of all tubes and drains; the nasogastric tube (NGT), ETT, pleural and mediastinal tubes, etc.
 - Check for pneumothorax.
 - Check for lobar collapse, atelectasis, effusions, pulmonary edema, etc.
 - *Laboratory Results:*
 - Complete blood count (CBC) and coagulation profile.
 - Blood gas: check for respiratory failure, high lactate, central venous oxygen saturation (ScvO₂), etc.

- Renal function and chemistry.
- Glucose: must be controlled, use an insulin drip or sliding scale to keep the blood glucose between 140 and 180 mg/dL.

Post-Cardiac Surgery Complications

Hypothermia

CPB is usually accompanied by hypothermia to $<32^{\circ}\text{C}$. Patients are usually rewarmed to at least 34°C prior to transfer to the intensive care unit (ICU). Further rewarming can be achieved postoperatively using a perioperative forced-air warming device.

Effects of hypothermia:

- Induces ventricular arrhythmias and lowers ventricular fibrillation (VF) threshold.
- Increases systemic vascular resistance (SVR); increases afterload and myocardial workload.
- Patient shivering causes increased peripheral oxygen consumption.
- Coagulopathy: it impairs platelet function and the coagulation cascade. Rewarming is an important part of the treatment of a bleeding patient.

Bleeding

It can be divided into:

- *Medical bleeding*: secondary to defects in the coagulation cascade, platelets count, platelets function, or fibrinogen. Treatment of medical bleeding include:
 - Correct hypothermia.
 - Control blood pressure if elevated.
 - Protamine 50–100 mg if ACT is elevated.
 - Desmopressin (DDAVP) 20 mcg intravenously, it might improve platelet function although has no strong evidence.
 - Platelet transfusion: aiming to keep platelets count for at least $50 \times 10^3/\mu\text{L}$.
 - Fresh frozen plasma (FFP) for coagulopathy.
 - Cryoprecipitate/fibrinogen: for hypofibrinogenemia.
 - Antifibrinolytic agents like tranexamic acid.

- Packed red blood cells (PRBC); to maintain a hemoglobin level target at ≥ 8 g/dL.
- Thromboelastogram (TEG) can help to identify the actual cause for coagulopathy and treat it accordingly.
- *Surgical bleeding*: secondary to operative trauma including leaks at sites of vascular anastomosis or cannulation sites or bleeding from small mediastinal arteries or veins. Surgical bleeding requires re-exploration to achieve hemostasis. Consider a surgical source of bleeding in the following situations:
 - Persistent bleeding in absence of coagulopathy
 - Sudden onset of fresh, rapid bleeding
 - Bleeding which is >500 mL in the first postoperative hour, >400 mL/h $\times$ 2 h, >300 mL/h $\times$ 3 h or >200 mL/h $\times$ 4 h [61]

Shock

Causes of shock in post-cardiac surgery cases are:

- Hypovolemic/bleeding.
- Cardiogenic; due to arrhythmia, myocardial infarction (MI), acute graft failure, myocardial stunning, etc.
- Obstructive shock; due to pericardial tamponade, pneumothorax, or pulmonary embolism.
- Distributive shock: due to vasoplegia; it is a common complication and may occur in 5–25% of the cardiac surgery cases, it is treated with hydration, vasopressors, i.e., norepinephrine +/- vasopressin, and in refractory cases, other agents can be used like methylene blue, hydroxocobalamin, corticosteroids, and angiotensin II [62].

Patients should undergo frequent clinical assessments and continuous hemodynamic monitoring to enable timely and appropriate therapeutic interventions.

Advanced Cardiac Life Support (ACLS) Approach in Arrested Patients Post-Cardiac Surgery

Summarized in Fig. 1.34 [63].

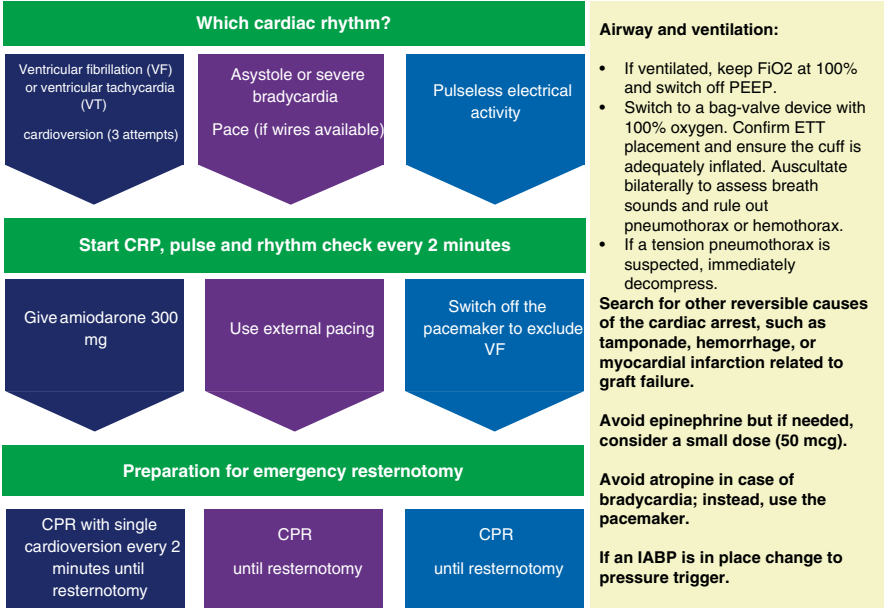


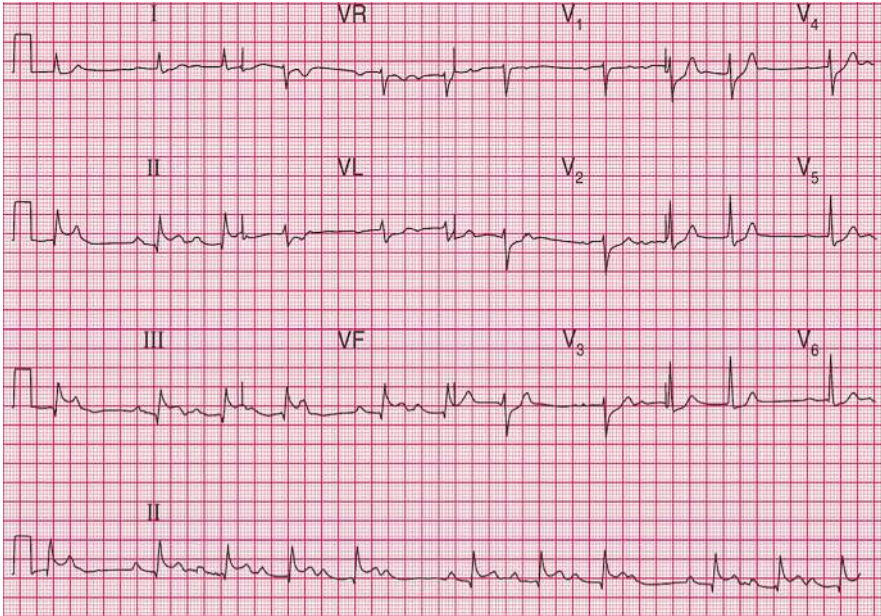
Fig. 1.34 Management of postoperative cardiac arrest after cardiac surgery. CPR = cardiopulmonary resuscitation, FiO₂ = fraction of inspired oxygen, PEEP = positive end expiratory pressure, ETT = endotracheal tube, IABP = intra-aortic balloon pump. (Adapted from the original source: Brand et al. [63]. Used with permission)

Electrocardiogram (ECG)

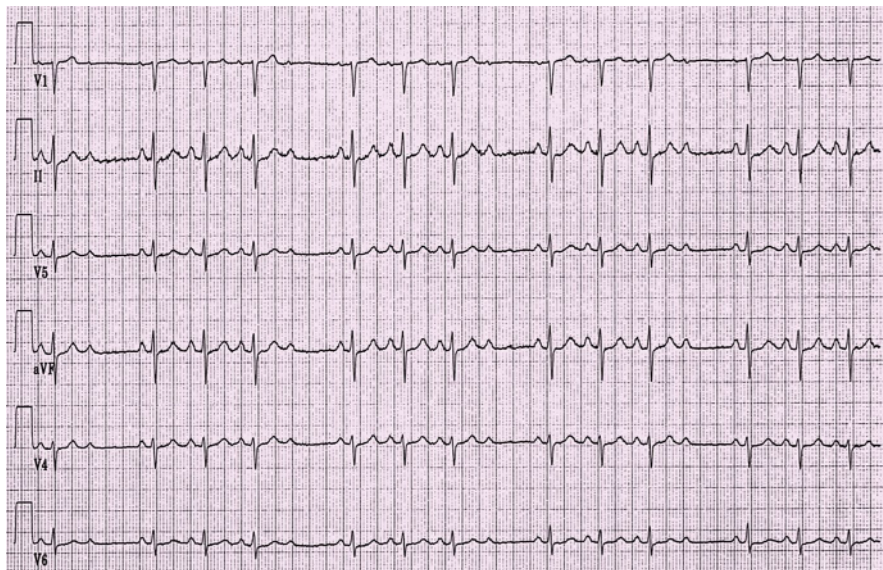
This topic involves multiple ECGs related to different cardiac conditions, providing focused information about their etiology, pathogenesis, and/or management.



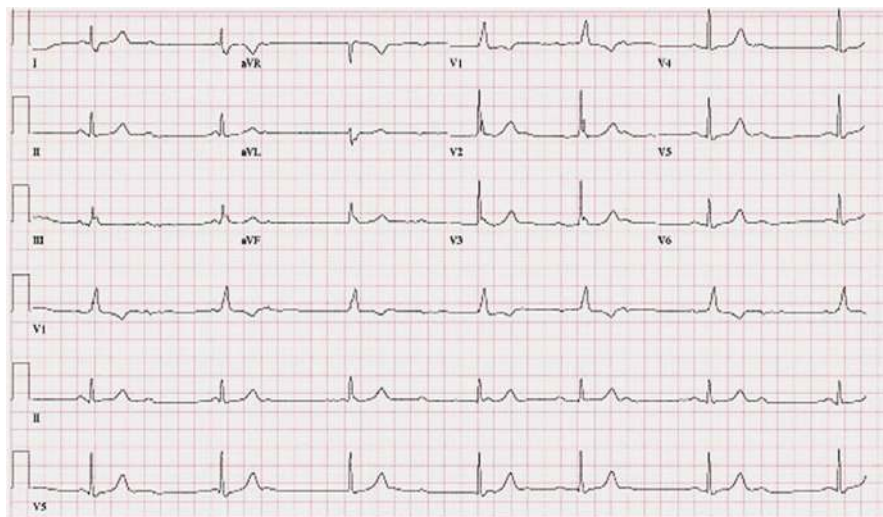
Fixed prolonged PR interval in first degree heart block.



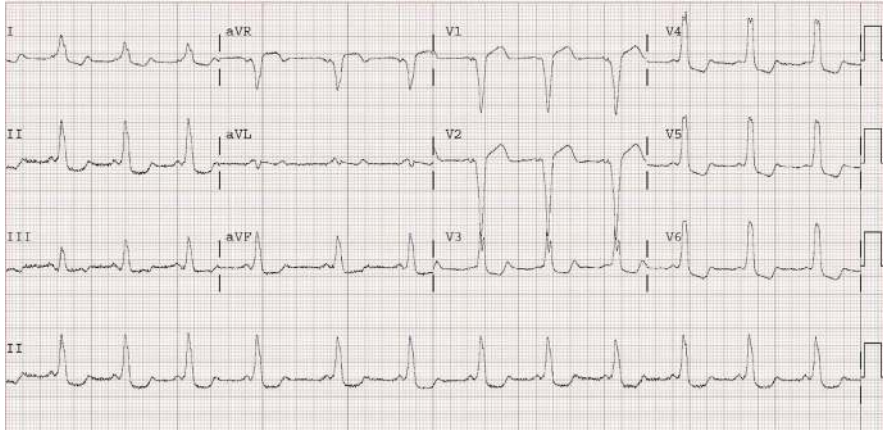
1. Progressive increase in PR interval until missing one complex in second degree Mobitz type I heart block.
2. Inferior wall ST elevation myocardial infarction (STEMI).



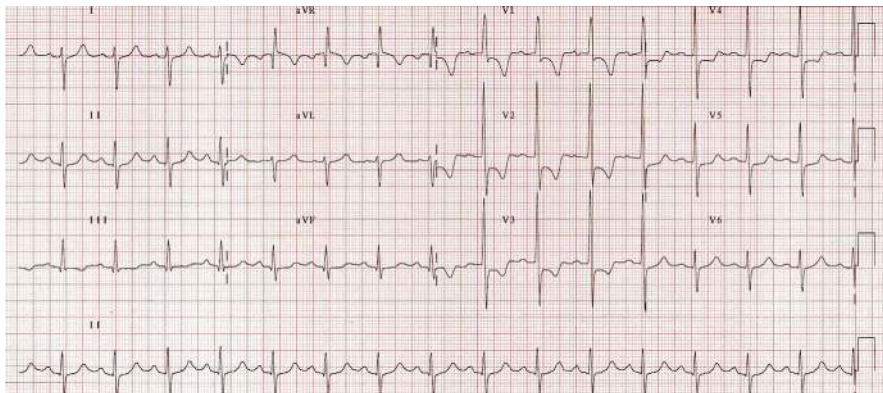
Second degree, Mobitz type II heart block with 2:1 ratio.



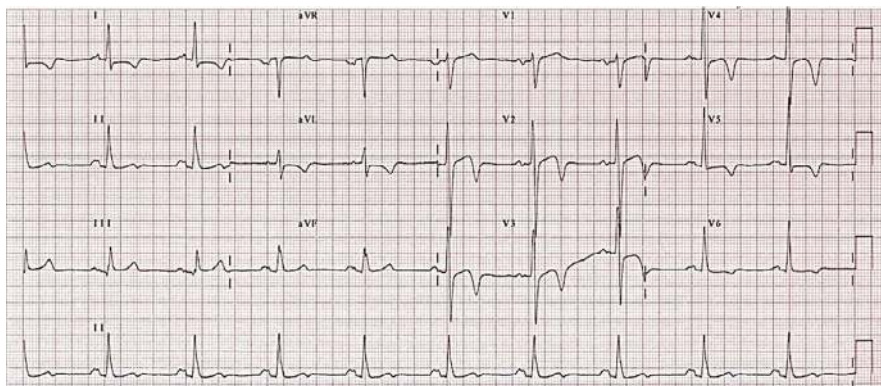
Complete loss of the relationship between P waves and QRS complexes is characteristic of third-degree (complete) heart block.



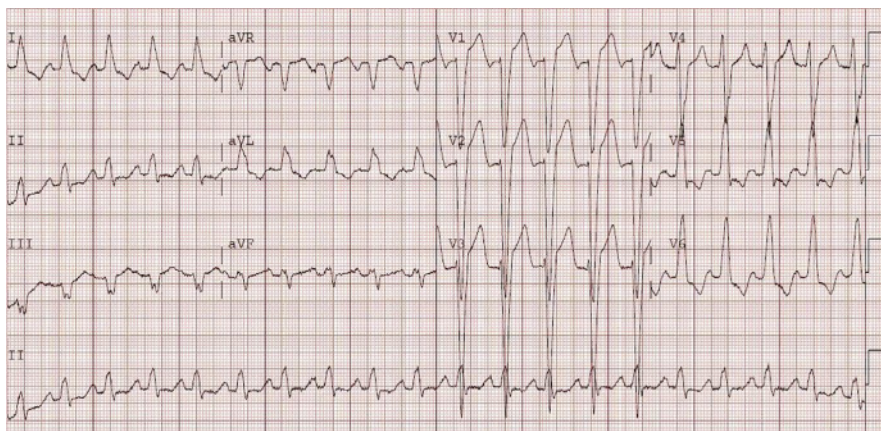
Short PR interval, wide QRS and delta wave in Wolff-Parkinson-white (WPW) syndrome. Treatment of such cases includes radiofrequency ablation of the accessory pathway. If the condition is associated with arrhythmia, use procainamide or ibutilide and avoid calcium channel blockers (CCB), beta blockers (BB), amiodarone, digoxin and adenosine.



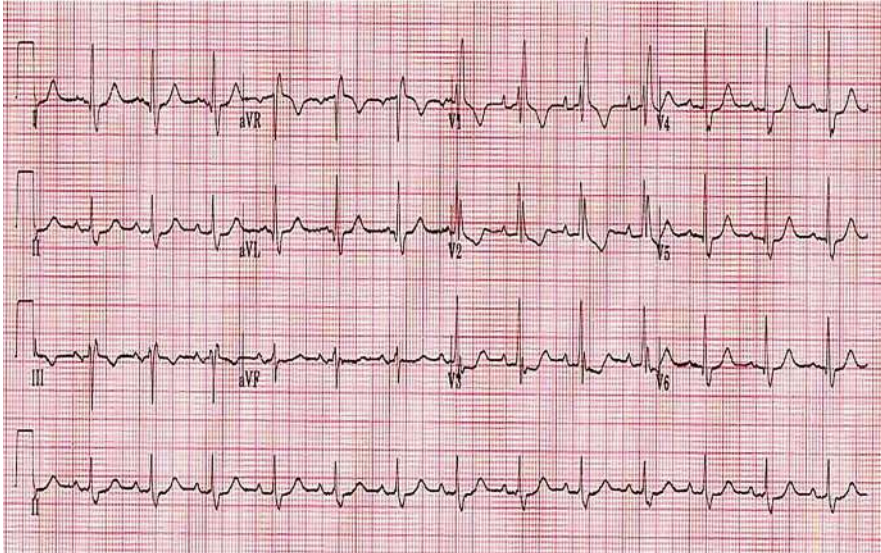
Right ventricular hypertrophy (RVH) with strain pattern (ST changes in V1, V2).



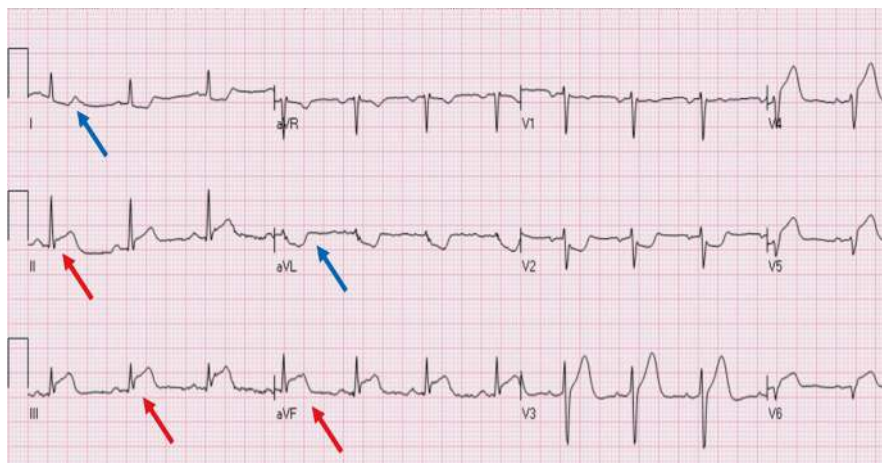
Left ventricular hypertrophy (LVH) with high precordial voltages, deep T-wave inversions in the precordial and high-lateral leads and left atrial enlargement (P mitrale) are seen in patients with hypertrophic cardiomyopathy (HCM). On clinical examination, such a patient will have an ejection systolic murmur at the left lower sternal border, which increases with standing and the Valsalva maneuver. An S₄, paradoxical splitting of S₂, and a mitral regurgitation (MR) murmur may also be present. Echocardiography typically shows LVH, usually involving the septum; systolic anterior motion (SAM) of the mitral valve which might end by left ventricular outflow tract (LVOT) obstruction; and MR. Treatment includes beta-blockers (BB), hydration, and $\pm$ alpha-agonists such as phenylephrine. For persistent symptomatic cases, surgical myomectomy or alcohol septal ablation may be considered. An implantable cardioverter-defibrillator (ICD) is also recommended for high-risk patients. Contraindicated medications include inotropic agents (e.g., nor-epinephrine, digoxin, epinephrine), vasodilators (e.g., nitrates), and diuretics.



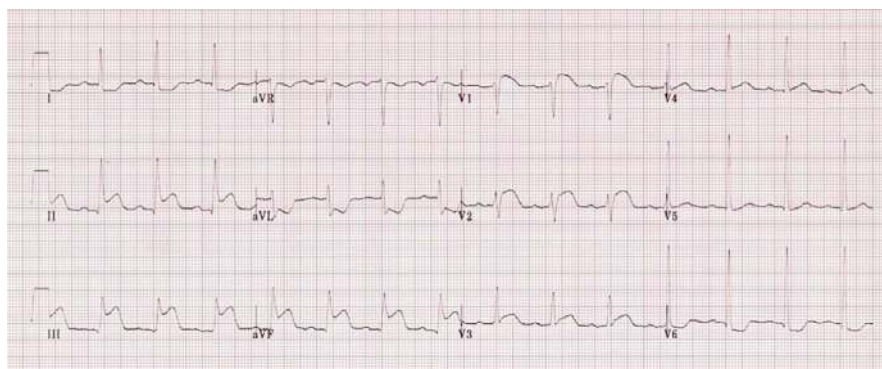
Left Bundle Branch Block (LBBB) with positive Sgarbossa as there is discordant ST elevation >5 mm in the antero-septal leads (positive Sgarbossa criteria are: concordant ST elevation >1 mm in leads with a positive QRS complex, concordant ST depression >1 mm in V1–V3, or discordant ST elevation >5 mm in leads with negative QRS).



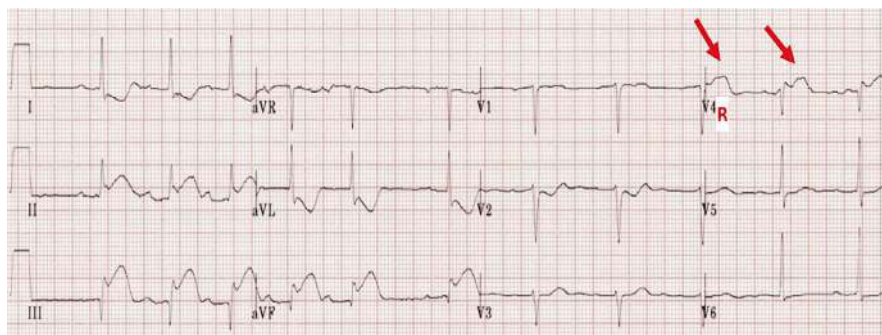
Right bundle branch block (RBBB).



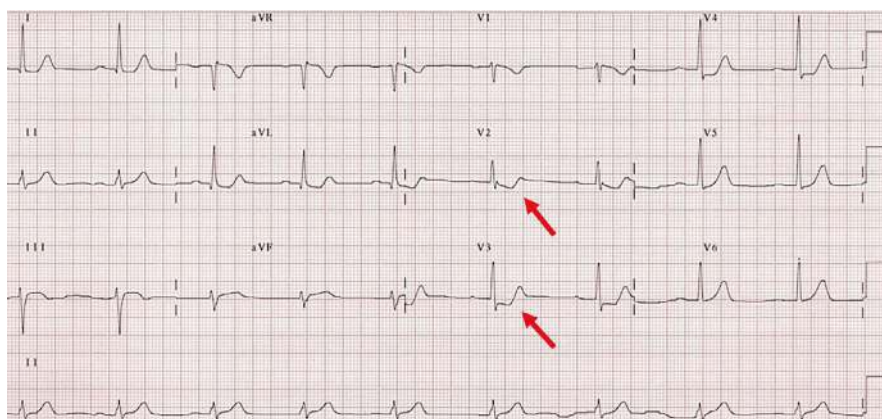
ST elevation in II, III, AVF, related to inferior wall STEMI with reciprocal changes in lateral leads (AVL, I). Classically, there is reciprocal changes between lateral and inferior leads.



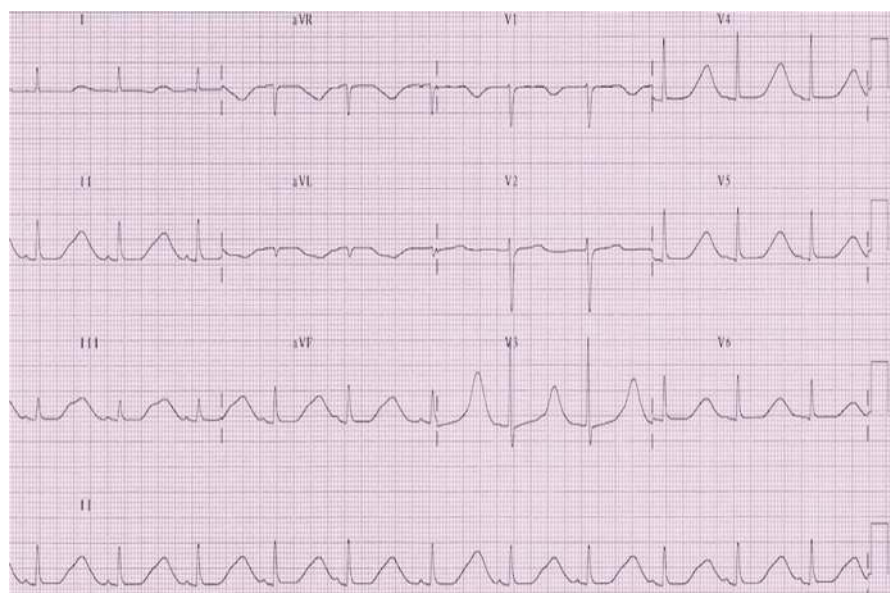
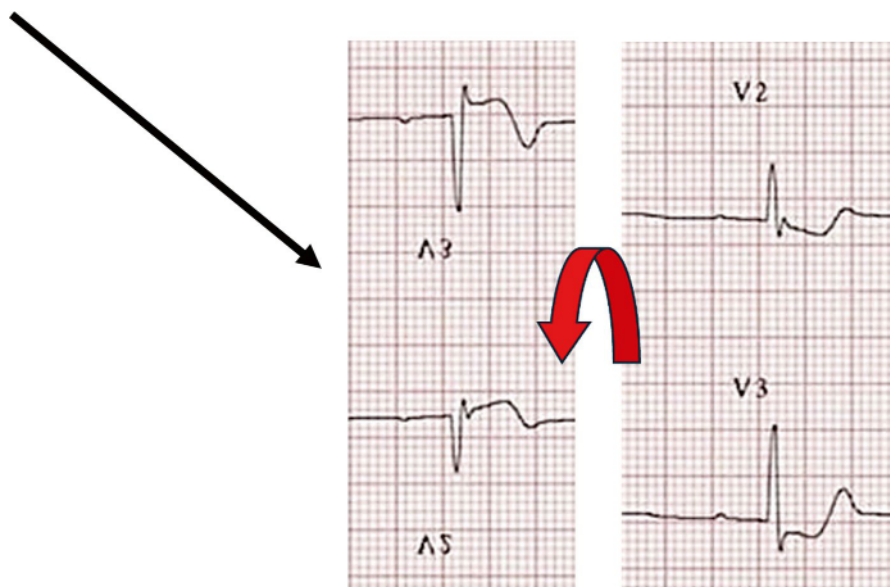
Inferior wall STEMI with elevated ST III > II and elevated ST in V1 and V2, suggesting right ventricular infarction (RVI); patient should do right-sided ECG as shown in next ECG.



Right sided ECG for patient with inferior wall STEMI showing RV4 ST elevation related to right ventricular infarction (RVI).



Tall R wave in V2 and V3 with ST depression in posterior wall STEMI.



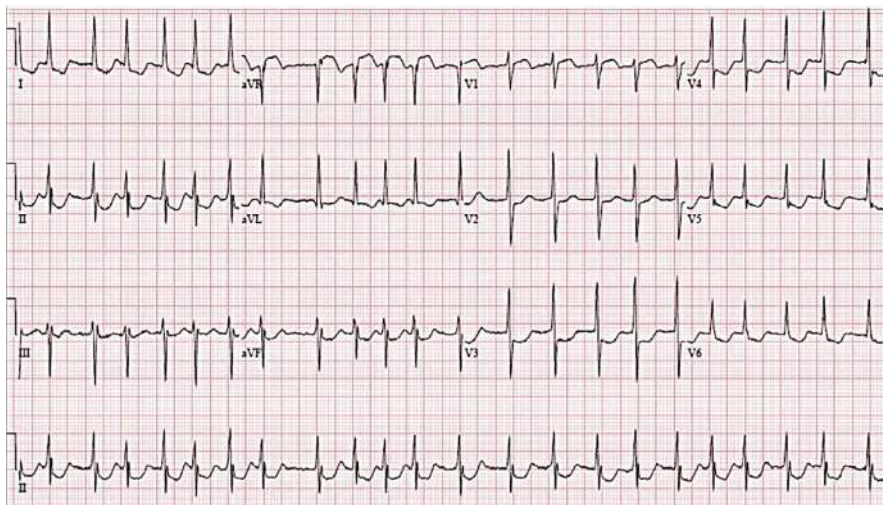
Long QT interval: causes are congenital, metabolic (hypokalemia, hypocalcemia, hypomagnesemia, hypothermia), intracranial hemorrhage, medications (macrolides, quinolones, fluconazole, antiarrhythmic drugs, antipsychotic, selective serotonin reuptake inhibitors [SSRI], tricyclic antidepressant).



Torsades de Pointes: A polymorphic ventricular tachycardia associated with a prolonged QT interval. Management depends on the hemodynamic stability of the patient, as outlined in the Advanced Cardiac Life Support (ACLS) protocol. Definitive treatment includes intravenous magnesium sulfate (MgSO_4) and addressing the underlying cause.



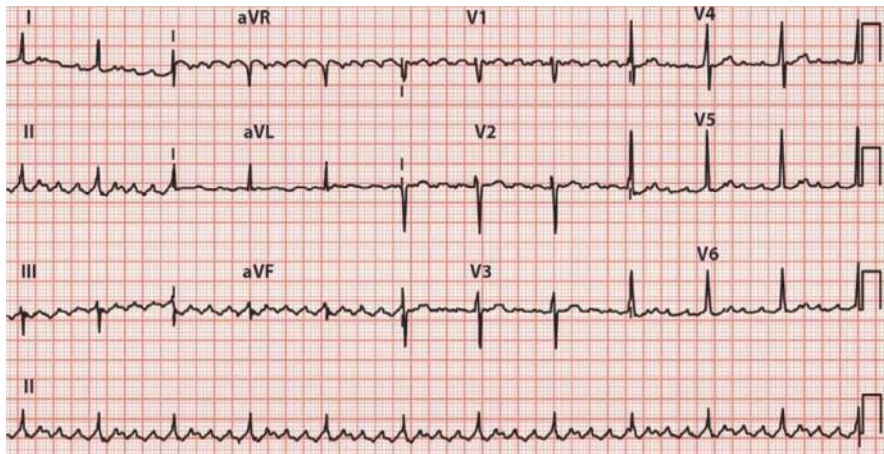
Multifocal atrial tachycardia (MAT): the most common cause is respiratory failure, e.g., chronic obstructive pulmonary disease (COPD), and treatment of the respiratory disease often leads to resolution of the arrhythmia.



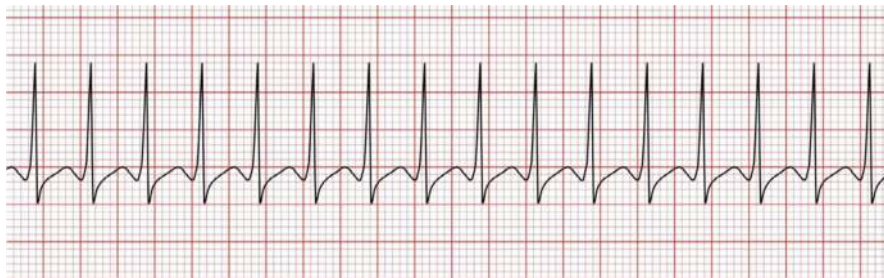
Atrial fibrillation (AF): management include [64]:

- Cardioversion:
 - If the patient is hemodynamically unstable, proceed with emergency electrical cardioversion.
 - If the patient is stable and cardioversion is not needed immediately, the patients should be anticoagulated for 3 weeks prior to cardioversion.
 - If the patient is stable but cardioversion cannot be delayed, management depends on the onset of symptoms:
 - <48 h: cardioversion can be performed immediately.
 - >48 h or unknown duration: perform trans-esophageal echocardiography (TEE) guided cardioversion.
- Rate control:
 - If ejection fraction (EF) $\leq 40\%$ use beta blockers (BB) or digoxin, and if EF $>40\%$ other agents like verapamil and diltiazem can also be used.
 - Target heart rate to be <110 b.p.m. as it was found to be non-inferior to <80 b.p.m. (*RACE II trial*) [65].

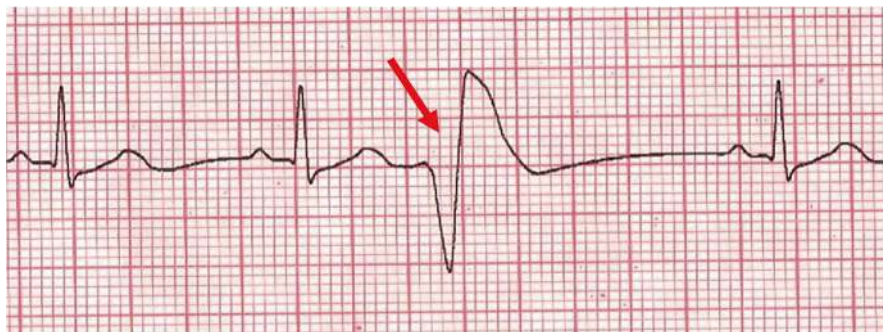
- Rhythm control: evidence has not shown significant benefit of rhythm control over rate control [66], but it can be considered in persistently symptomatic cases.
- Anticoagulation: for patients with CHA2DS2-VASc score ≥ 2 (congestive heart failure, hypertension, age [$>65 = 1$ point, $>75 = 2$ points], diabetes, previous stroke/transient ischemic attack [2 points], vascular disease, e.g., peripheral arterial disease or previous myocardial ischemia and sex of female). Choices include direct oral anticoagulants (DOAC), e.g., apixaban and dabigatran, other choice is warfarin.
- Catheter ablation for refractory cases.



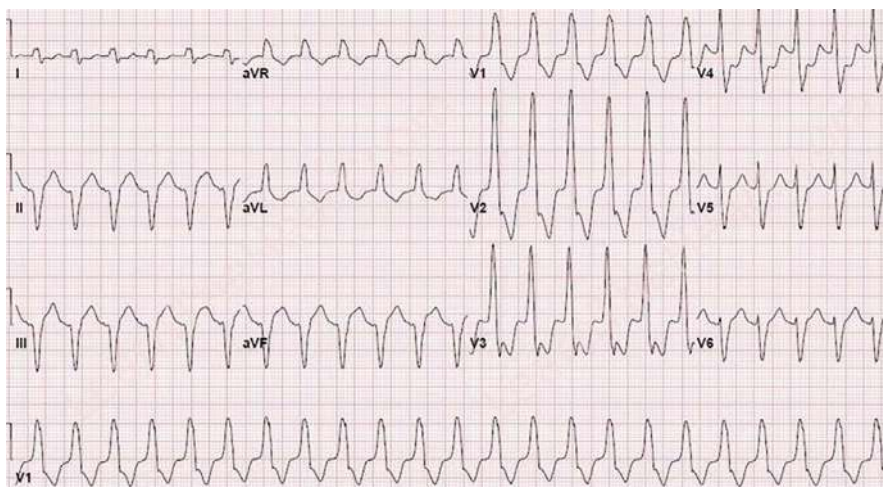
Atrial flutter: management is same as in AF including the anticoagulation for the high-risk group.



Supraventricular tachycardia (SVT)



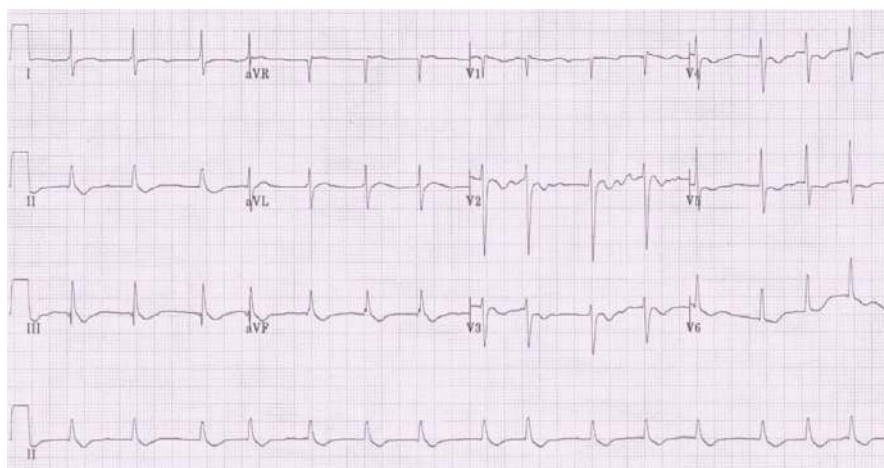
Premature ventricular contraction (PVC)



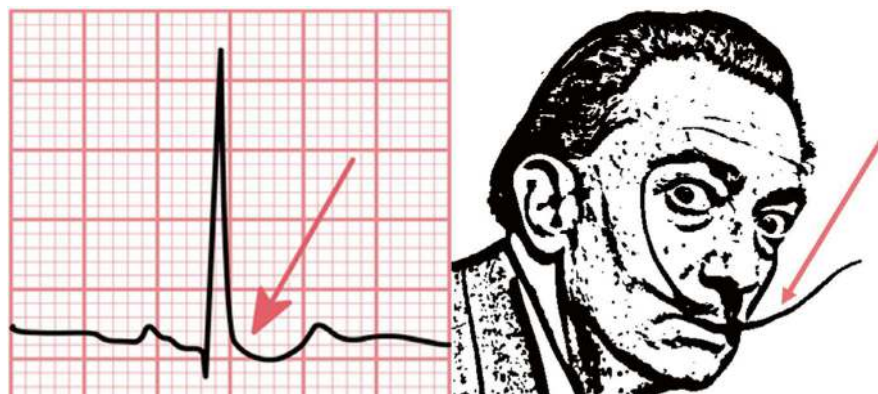
Ventricular tachycardia

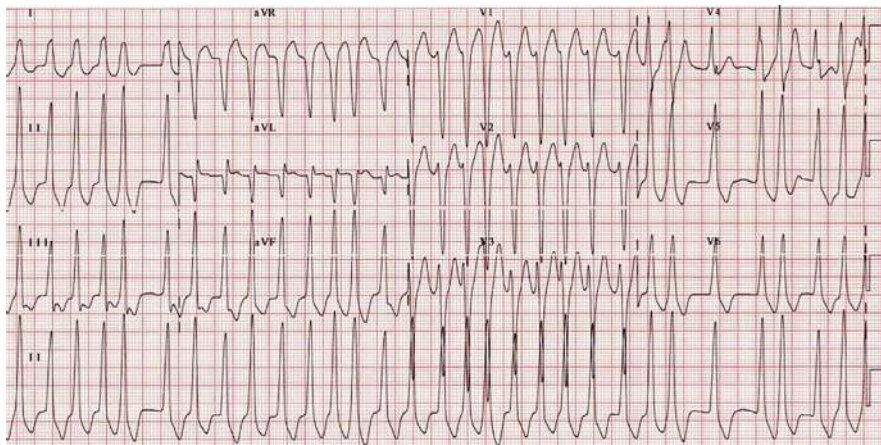


Ventricular fibrillation

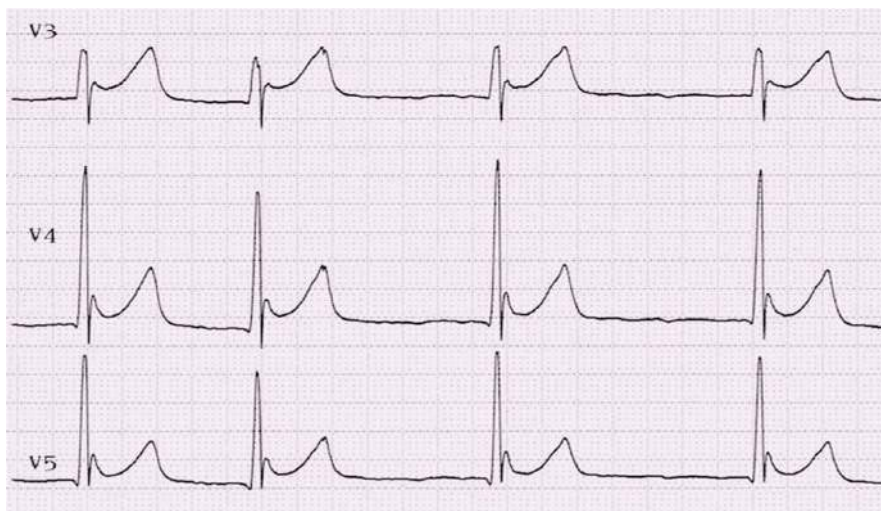


Sagging of ST wave, “*Salvador Dali’s moustache*” related to digoxin effect.

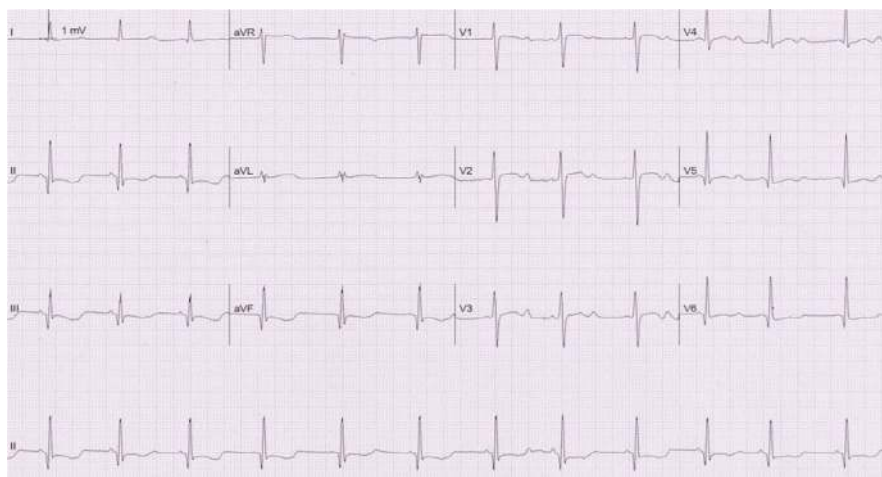


Salvador Dali's moustache

Atrial fibrillation (AF) + Wolff-Parkinson-white (WPW): management includes procainamide. While beta-blockers (BB), calcium channel blockers (CCB), digoxin, amiodarone, and adenosine should be avoided.



Osborn wave (J wave) in hypothermia cases.



U wave, flat T wave, ST depression in case of hypokalemia.

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Chapter 2

Pulmonology



Haytham Abbas  and Ans Ahmed

Introduction

Pulmonology is another one of the most important chapters for critical care practitioners to master. It focuses on key ventilation skills, including both invasive and noninvasive modalities. Practitioners must also be familiar with ventilation complications, weaning strategies, and other essential aspects of respiratory support. This chapter covers major respiratory conditions commonly seen in the ICU, such as acute respiratory distress syndrome (ARDS), status asthmaticus, hemoptysis, and others. As with every chapter in this book, the information is concise and focused on practical application.

Noninvasive Ventilation (NIV)

Positive Airway Pressure (PAP)

Positive airway pressure ventilation involves the delivery of oxygen into the lungs via positive pressure without the need for endotracheal intubation. There are different types of PAP therapy, including continuous positive airway pressure (CPAP), bilevel positive airway pressure (BiPAP), auto-titrating positive airway pressure (APAP), and adaptive servo-ventilation (ASV). Table 2.1 shows the comparison between the different modalities.

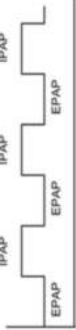
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Table 2.1 Types of non-invasive positive pressure ventilation

Type of PAP	Parameters and aims	Waveform
CPAP	Fixed expiratory pressure to maintain the airways open and therefore improves oxygenation	
BiPAP	Fixed inspiratory pressure (I-PAP) to control minute ventilation, and expiratory pressure (E-PAP) to control oxygenation	
APAP	Continuously adjusting expiratory pressure according to patient's needs to maintain the airways open and improving oxygenation	
ASV	Continuously adjusting I-PAP and E-PAP according to patient's needs for ventilation and oxygenation, with backup rate if needed	

Uses of PAP

- TYPE II respiratory failure (RF), e.g., chronic obstructive pulmonary disease (COPD), obesity hypoventilation syndrome (OHS) [BiPAP].
- Weaning of ventilator in patients with type II RF, applied post extubation [BiPAP].
- Cardiogenic pulmonary edema.
- Hypoxemic respiratory failure in immunocompromised patients.
- Obstructive sleep apnea (OSA) [CPAP].
- Central sleep apnea [ASV].

Contraindications of PAP

- Hemodynamic instability (cardiac arrest, ischemia, arrhythmia).
- Severely impaired consciousness (inability to protect the airway).
- Excessive upper airway secretions.
- Upper airway trauma or deformities.

High Flow Nasal Cannula (HFNC)

High-flow nasal cannula is a noninvasive respiratory support modality that can deliver up to 100% oxygen at flow rates of up to 60 L/min. The high flow helps wash out nasopharyngeal dead space and provides heated and humidified air, making it more comfortable and better tolerated by patients.

Uses of HFNC

- *Hypoxemic noncardiogenic respiratory failure*: it has shown improvement of mortality in acute noncardiogenic respiratory failure, the *FLORALI trial* [1] compared HFNC, with non-re-breather mask (NRM) and noninvasive positive pressure ventilation (NIPPV) and found that HFNC was associated with lower mortality, despite no significant difference in intubation rates among the groups.
- *Post-extubation hypoxia*: it has shown to decrease the re-intubation rate after unsuccessful extubation in hypoxic respiratory failure, the *HERNANDEZ trial* [2] compared it with conventional oxygen therapy in patients experiencing post-extubation hypoxia, HFNC decreased the need of re-intubation.
- *Pre-intubation oxygenation*: HFNC is also used to optimize oxygenation before intubation, helping to extend safe apnea time and reduce the risk of desaturation during airway management.

HFNC success prediction: it can be predicted by using ROX index (Fig. 2.1).

Disadvantages of HFNC

- Not as effective in type II respiratory failure compared to NIPPV.
- The machine does not display waveforms or values like in PAP, e.g., RR and tidal volume (TV).
- The jet flow can induce epistaxis or nasal mucosal injury.

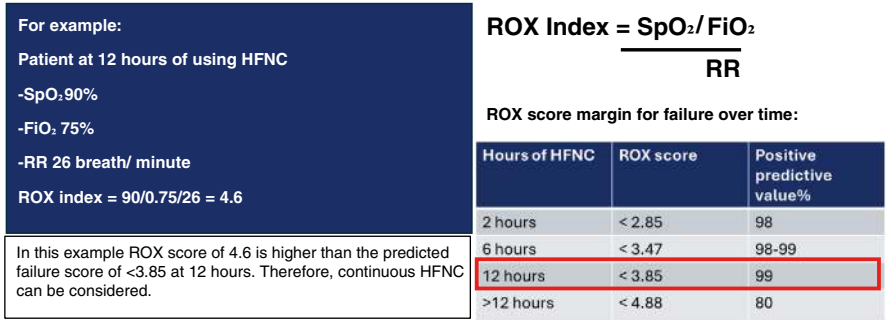


Fig. 2.1 ROX index for prediction of succession of HFNC. SpO₂ = oxygen saturation, FiO₂ = fraction of inspired oxygen, RR = respiratory rate. (Adapted from Roca et al. [3])

Contraindications of HFNC

- Hemodynamic instability, e.g., cardiac arrest, arrhythmia, shock.
- Nasal cavity deformity.
- Severely impaired consciousness (inability to protect the airway).

Mechanical Ventilation

Modes of Mechanical Ventilation

The respiratory cycle, which is provided by the machine, has three levels for each cycle:

- Trigger: the respiratory cycle can be initiated by the patient or the machine (time).
- Target: a fixed maximum value that the variable can reach during inspiration; this variable can be volume and flow, or pressure.
- Cycle: the final variable when inspiration ends and expiration starts; it can be related to time, flow, or volume.

Based on these dynamics, the ventilator modes can be classified as:

- Spontaneous: e.g., continuous positive airway pressure (C-PAP).
- Supported: e.g., pressure support ventilation (PSV) or volume support ventilation (VSV).
- Assisted: e.g., assisted control ventilation (ACV) or synchronized intermittent mandatory ventilation (SIMV).
- Mandatory: volume control ventilation (VCV), pressure control ventilation (PCV), or pressure regulated volume control (PRVC).
- Special modes: e.g., airway pressure release ventilation (APRV).

Figures 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, and 2.10 are examples for each mood.

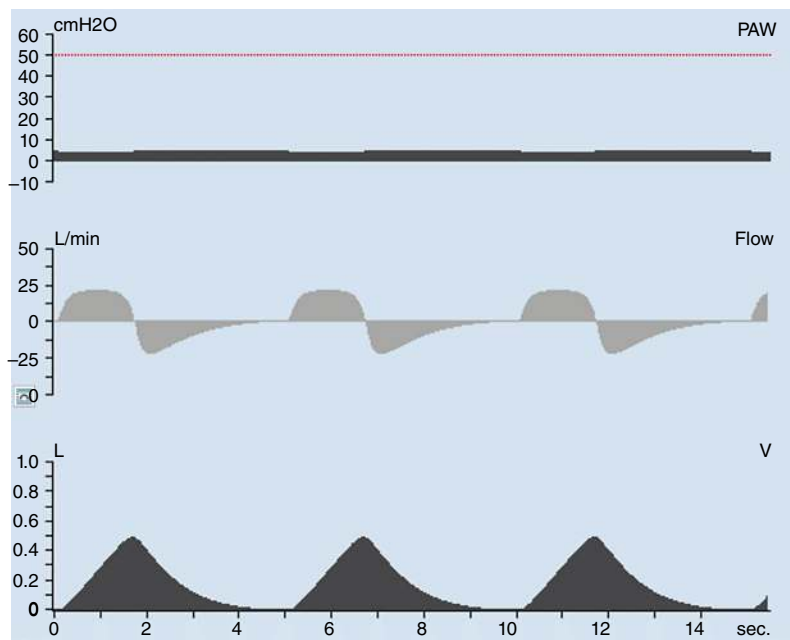


Fig. 2.2 C-PAP, the respiratory cycle is triggered and cycled by the patient (sinusoidal flow waves are a marker of spontaneous breathing with the patient’s trigger), and no target is adjusted. (Courtesy of Dr. Mazen Kherallah)

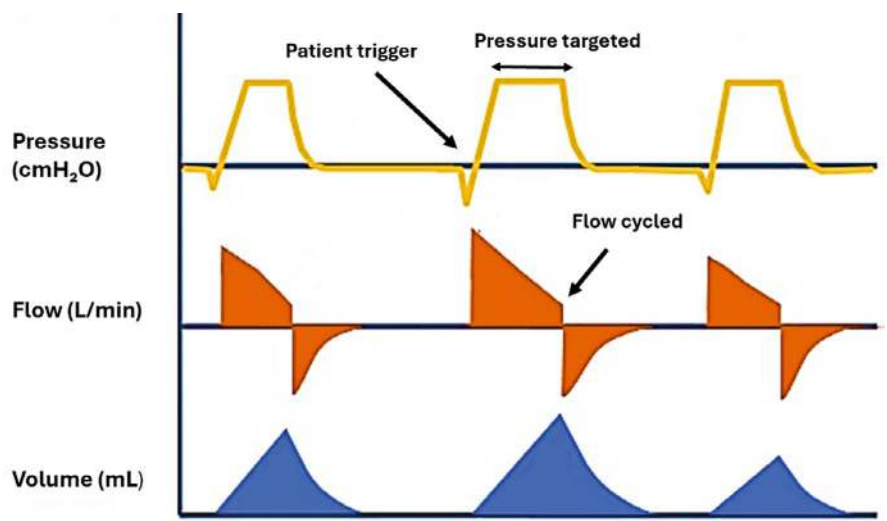


Fig. 2.3 PSV, the patient is triggering the respiratory cycle as negative pressure is seen in the pressure waves. It is pressure targeted (box-shaped pressure waves, and flow cycled as inspiration ends when the flow decreases to 25%)

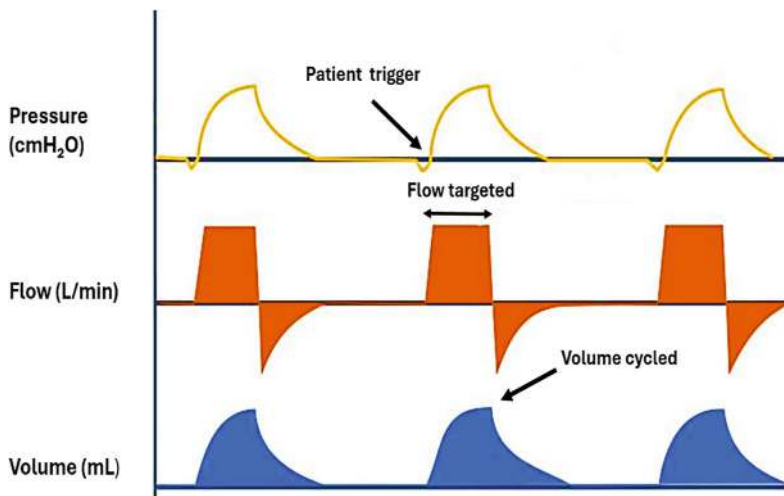


Fig. 2.4 ACV—volume targeted, the respiratory cycle is triggered by patient (negative pressure in the pressure wave), flow targeted (box-shaped flow waves), and volume cycled

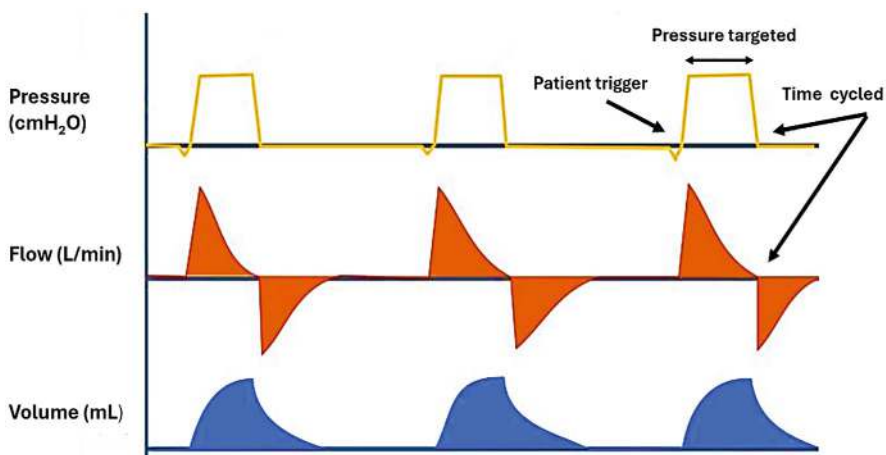


Fig. 2.5 ACV—pressure targeted, the respiratory cycle is triggered by patient (negative pressure in the pressure wave), pressure targeted (box-shaped pressure waves), and time cycled

Airway Pressure Release Ventilation (APRV) (Fig. 2.10):

- This mode provides alveolar recruitment; patients with acute respiratory distress syndrome (ARDS) may benefit from its use.
- It offers an inverse inspiratory/expiratory (I:E) ratio, i.e., T_{high} = inspiration, T_{low} = expiration.
- This mode allows spontaneous breathing, so the patient should not be paralyzed.
- It has four main parameters: T_{high} , T_{low} , P_{high} , P_{low} .

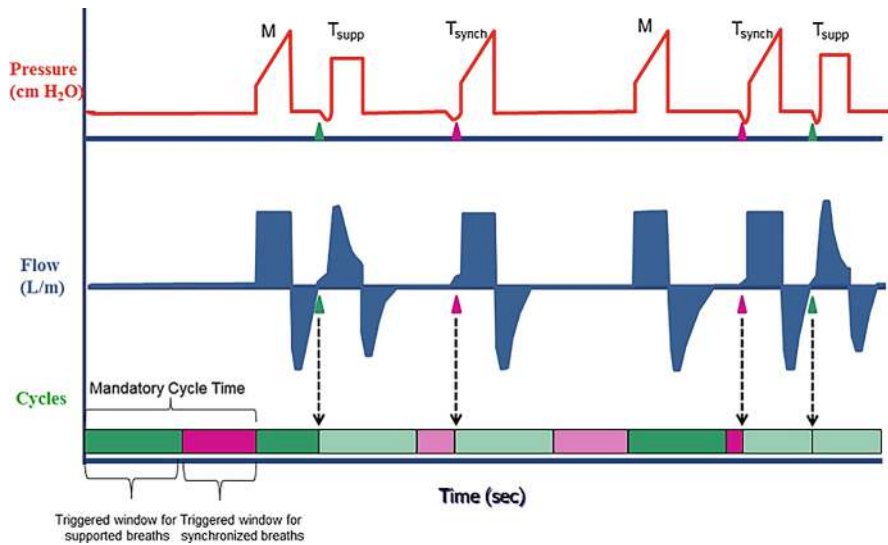


Fig. 2.6 SIMV/volume targeted: *M* (mandatory respiratory cycle with time triggered and flow targeted), *T_{supp}* (patient triggered and supported), *T_{synch}* (patient triggered and synchronized). (Sourced from Prasad and Patil [4])

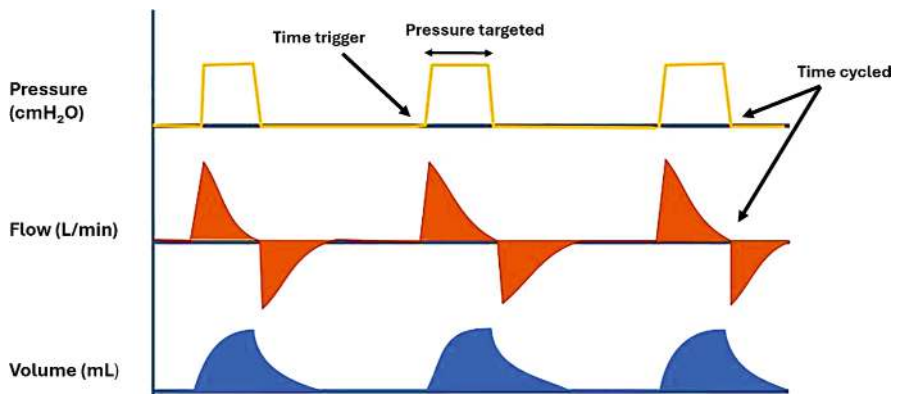


Fig. 2.7 Mandatory PCV, the respiratory cycle is time triggered (no negative pressure in the pressure wave), pressure targeted (box-shaped pressure waves), and time cycled

- *T* high: is set at 4–6 s; the higher the *T* high, the lower the respiratory rate (RR).
- *T* low: is set at 0.4–0.8 s.
- *P* high: should be between 20 and 30 cmH₂O, it increases the mean airway pressure (MAP).
- *P* low: is set at 0–5 cmH₂O.
- In hypoxia: increase fraction of inspired oxygen (FiO₂), *P*_{high} and *T*_{high}.
- In respiratory acidosis: increase *P*_{high} and *T*_{low} and decrease *T*_{high}.

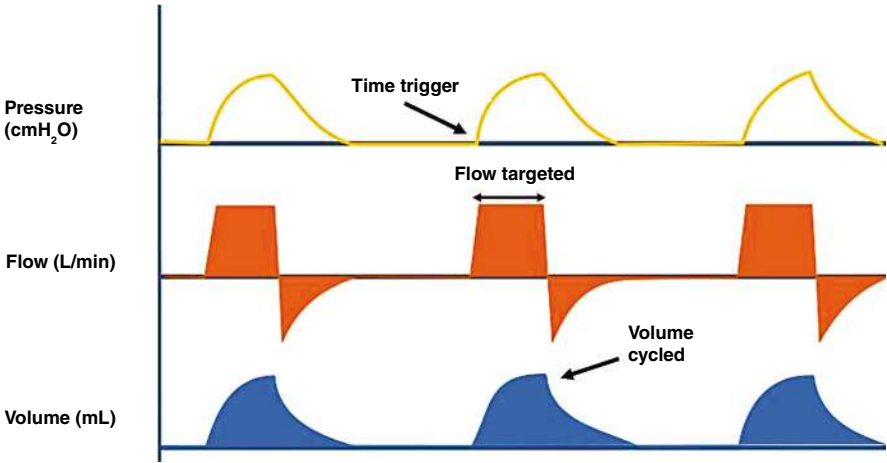


Fig. 2.8 Mandatory VCV, the respiratory cycle is time triggered (no negative pressure in the pressure wave), flow targeted (box-shaped flow waves), and volume cycled

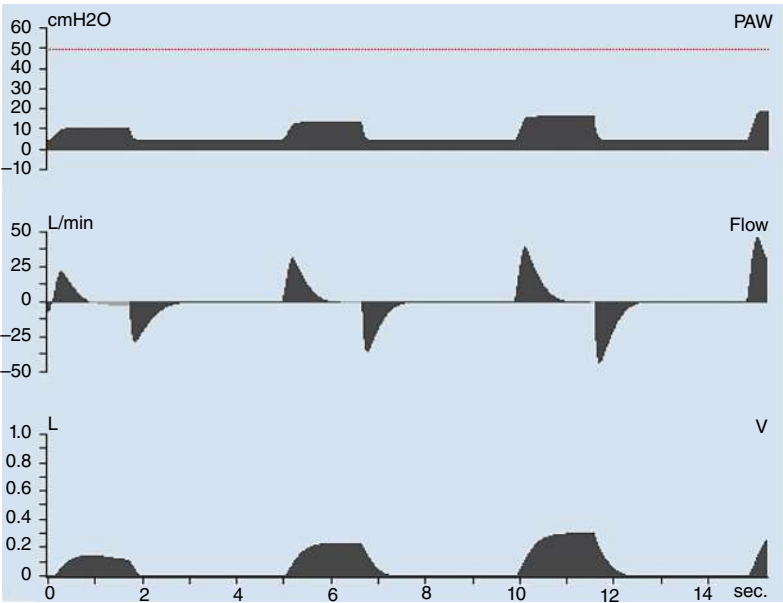


Fig. 2.9 Mandatory PRVC ventilation mode, it is time triggered and cycled. The target here is regulated pressure aiming to achieve specific tidal volume. (Courtesy of Dr. Mazen Kherallah)

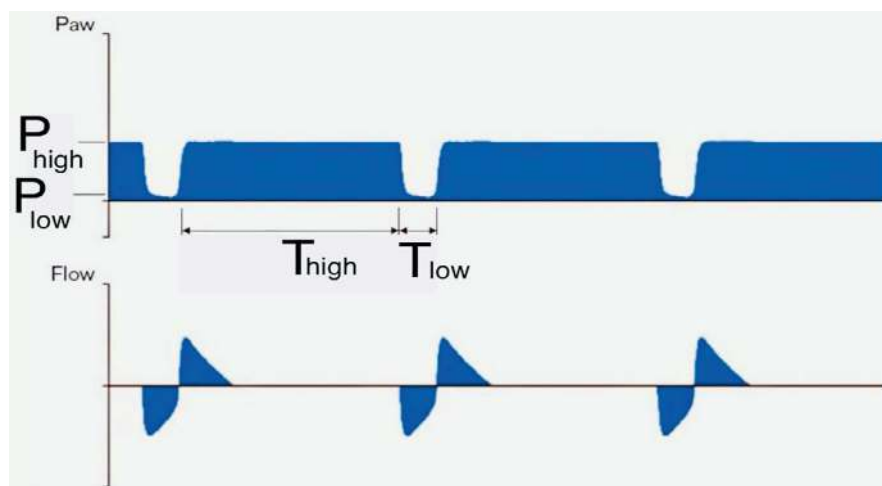


Fig. 2.10 APRV mode

Oxygenation

To improve oxygenation by using the ventilator, two changes can be considered:

- Increase FiO_2
- Increase mean airway pressure (MAP):

$$\text{MAP} = \left(T_{\text{ins}} / T_{\text{cyc}} \right) \times (\text{PIP} - \text{PEEP}) + \text{PEEP}$$

T_{ins} = inspiratory time, T_{cyc} = time of respiratory cycle, PIP = peak inspiratory pressure, PEEP = positive end expiratory pressure

Any of the following parameters when increased, can raise the MAP and therefore improve oxygenation:

- Positive end expiratory pressure
- peak inspiratory pressure
- Tidal volume (TV)
- Respiratory rate
- I:E ratio

Carbon Dioxide (CO₂) Removal

CO₂ removal can be achieved by increasing the minute volume (MV).

MV = TV × RR. Therefore, increasing TV and/or RR will help to clear CO₂. Another approach is to decrease the I:E ratio (e.g., 1:3 or 1:4).

Normally, patients need a minute volume of 100 mL/kg/IBW. (IBW = ideal body weight).

Compliance and Resistance

The principles of compliance and resistance depend on the equation of motion of the respiratory system, which defines the total pressure required to overcome elastic recoil and airway resistance during breathing.

$$\Delta P = \text{flow} \times \text{resistance} + \text{TV} / \text{compliance}$$

$$\text{Resistance} = (\text{PIP} - \text{Pplat}) / \text{flow}$$

$$\text{Compliance static} = \text{TV} / (\text{Pplat} - \text{PEEP})$$

$$\text{Compliance dynamic} = \text{TV} / (\text{PIP} - \text{PEEP})$$

ΔP = pressure gradient = P muscle + P ventilator

TV = tidal volume

PIP = peak inspiratory pressure

Pplat = plateau pressure

PEEP = positive end expiratory pressure

Lung compliance decreases when lung parenchyma is compromised; for example, in ARDS, consolidation, and auto-PEEP. It also decreases when extrapulmonary conditions interfere with lung expansion, such as pneumothorax, pleural effusion, or abdominal compartment syndrome. On the ventilator, this is reflected by increased PIP and Pplat. The normal compliance value in ventilated patients is 50–100 mL/cmH₂O.

Airway resistance increases with airway obstruction, such as in cases of mucus plugs, asthma exacerbations, or a kinked endotracheal tube (ETT). The ventilator will show an increase in PIP without an increase in Pplat. The normal resistance value is 1–8 cmH₂O/L/s (see Fig. 2.11).

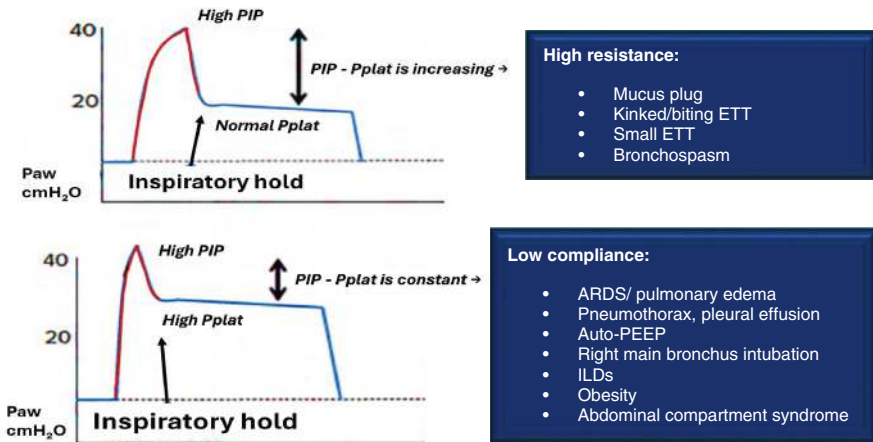


Fig. 2.11 The pressure wave shows the differences in airway pressure changes when resistance increases and compliance decreases. PIP = peak inspiratory pressure, Pplat = plateau pressure, ETT = endotracheal tube, ARDS = acute respiratory distress syndrome, PEEP = positive end expiratory pressure, ILDs = interstitial lung diseases

Changes in lung compliance and resistance as seen on the ventilator are illustrated in Figs. 2.12, 2.13, 2.14, and 2.15.

Pressure Volume (PV) Tool/Flow Volume (FV) Loop

Normal waveforms of the PV tool and the FV loop are illustrated in Figs. 2.16 and 2.17.

The PV tool can provide data on:

- Changes in pulmonary compliance and resistance
- Determination of the optimal PEEP setting
- Detection of air leaks (see Figs. 2.18, 2.19, and 2.20)

The FV loop can provide data on:

- Airway obstruction
- Auto-peep
- Air leak (Fig. 2.21)

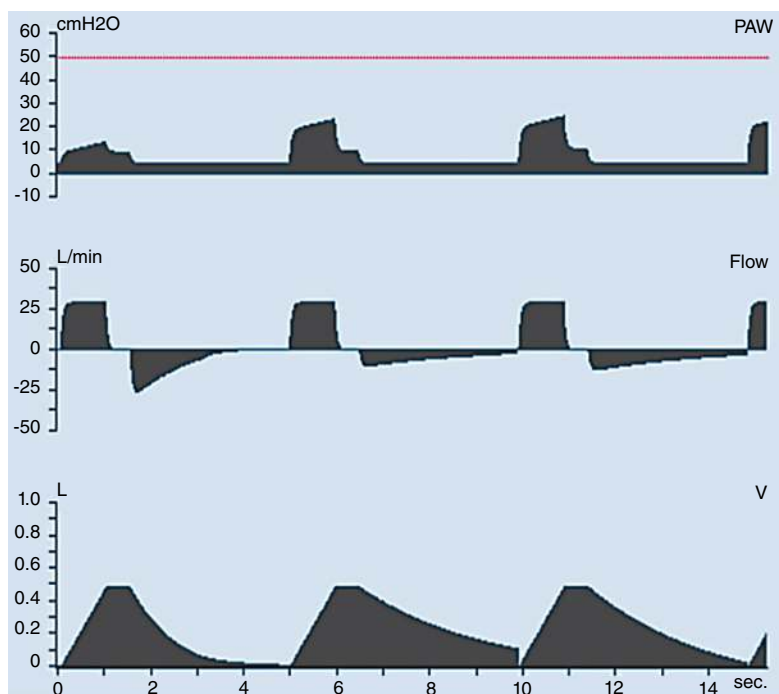


Fig. 2.12 The volume control ventilator mode, with an increase in PIP without an increase in Pplat, and prolonged expiration seen in the flow wave. This pattern typically occurs when airway resistance is increasing. (Courtesy of Dr. Mazen Kherallah)

Auto-PEEP

Auto-PEEP is a common ventilator complication, especially in patients with obstructive lung disease, when ventilator settings are adjusted with parameters that exceed the lungs' ability to fully exhale the TV in each respiratory cycle.

Patients with auto-PEEP may present with hypotension, hypoxia, and/or type II respiratory failure. On the ventilator, there will be signs of a sudden decrease in lung compliance, reflected by a significant increase in both PIP and Pplat. The expiratory flow waveform will show incomplete exhalation, indicating air trapping during the expiratory phase (Fig. 2.22).

Management of Auto-PEEP

If the patient is hemodynamically unstable, he or she should be disconnected from the ventilator immediately.

If the patient is stable, or after reconnection to the ventilator, the following ventilator settings should be adjusted:

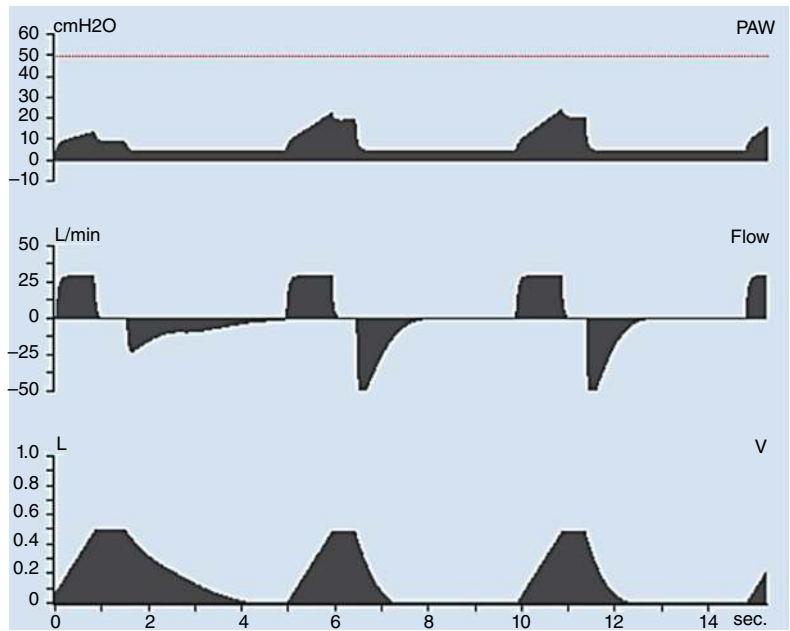


Fig. 2.13 The volume control ventilator mode, with increases in both PIP and Pplat, and a shortened expiratory phase in the flow wave. This pattern is seen when lung compliance is decreasing. (Courtesy of Dr. Mazen Kherallah)

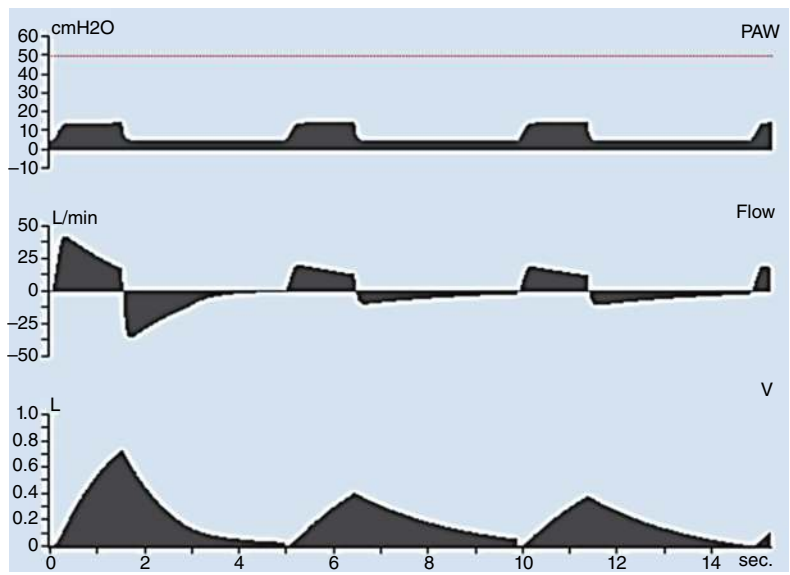


Fig. 2.14 Pressure-controlled ventilation with decreased inspiratory flow, prolonged expiratory flow, and reduced tidal volume. This pattern is seen when airway resistance is increasing. (Courtesy of Dr. Mazen Kherallah)

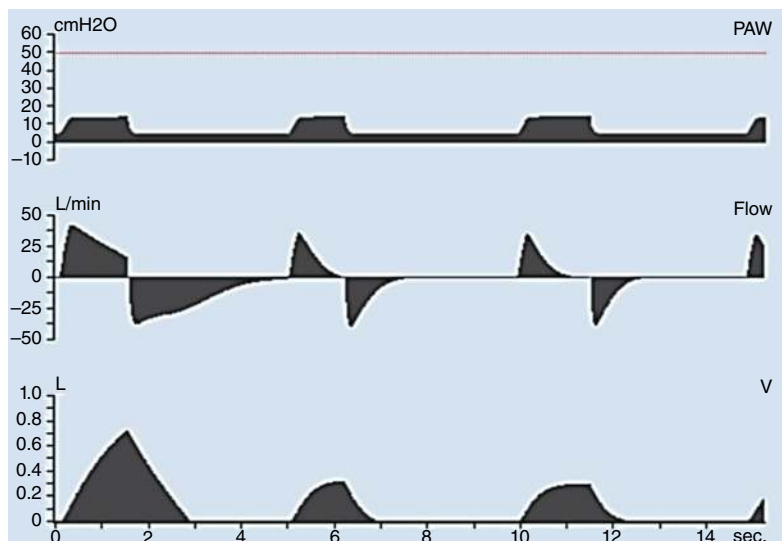
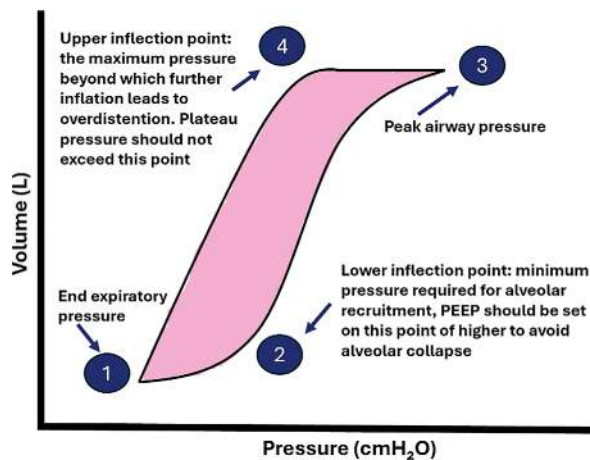


Fig. 2.15 Pressure-controlled ventilation with decreased inspiratory flow, shortened expiratory flow, and reduced tidal volume. This pattern is seen when lung compliance is decreasing. (Courtesy of Dr. Mazen Kherallah)

Fig. 2.16 Pressure volume tool. PEEP = positive end expiratory pressure



- Decrease the RR
- Increase the expiration time (by using lower I:E ratio)
- Increase the inspiratory flow rate
- Decrease the TV

In addition to auto-PEEP, other causes of a sudden increase in PIP, also referred to as high peak airway pressure (HPAP), should be excluded. These include the following:

Fig. 2.17 Flow volume loop

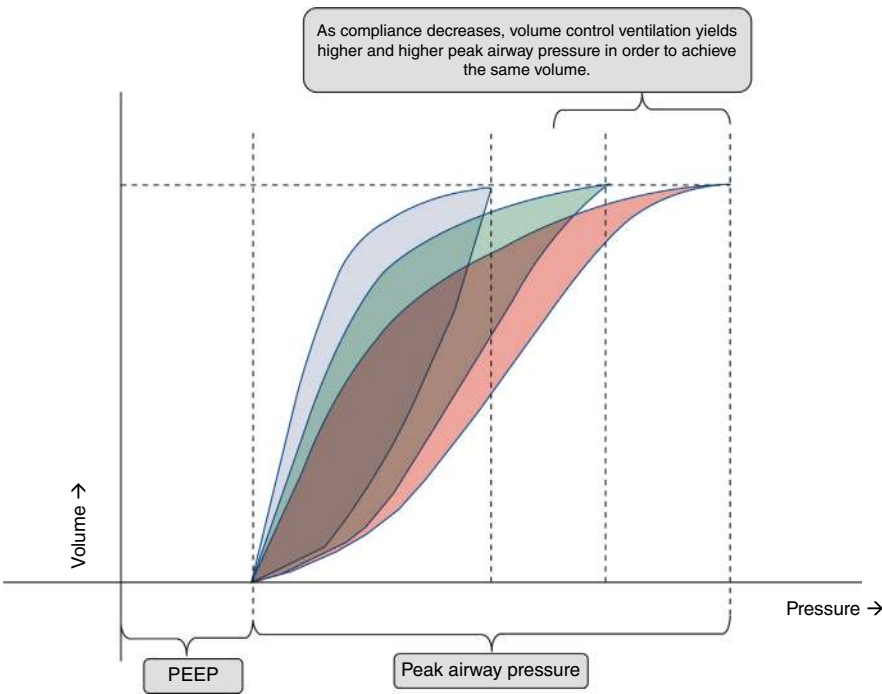
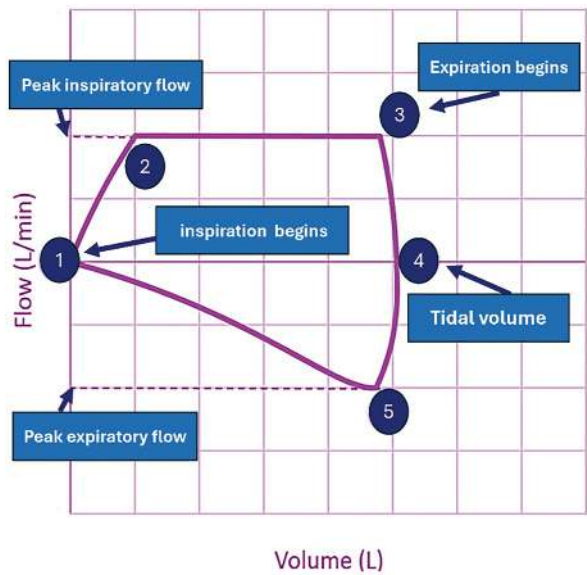


Fig. 2.18 Pressure volume loop in VCV shows increasing PIP and Pplat due to decreased lung compliance; appears as a leftward shift of the curve. (Courtesy of Dr. Alex Yartsev, used with permission)

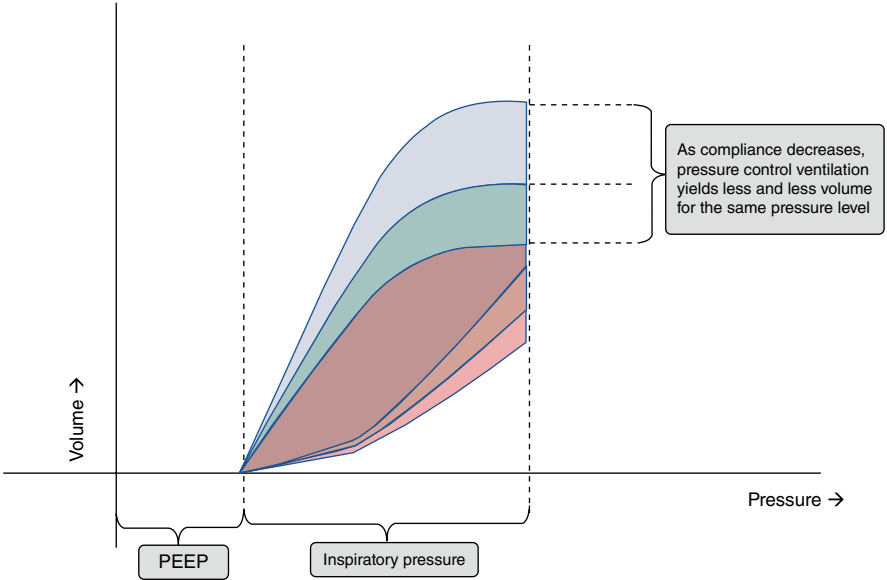


Fig. 2.19 Pressure volume tool in PCV shows decreasing volume due to worsening of pulmonary compliance or increased airway resistance. (Courtesy of Dr. Alex Yartsev, used with permission)

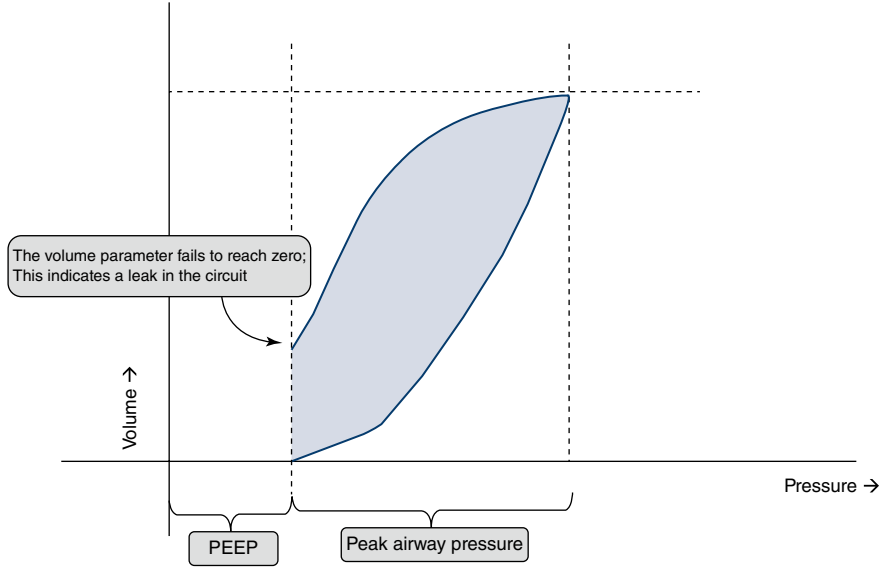


Fig. 2.20 Pressure volume tool showing air leak. (Courtesy of Dr. Alex Yartsev, used with permission)

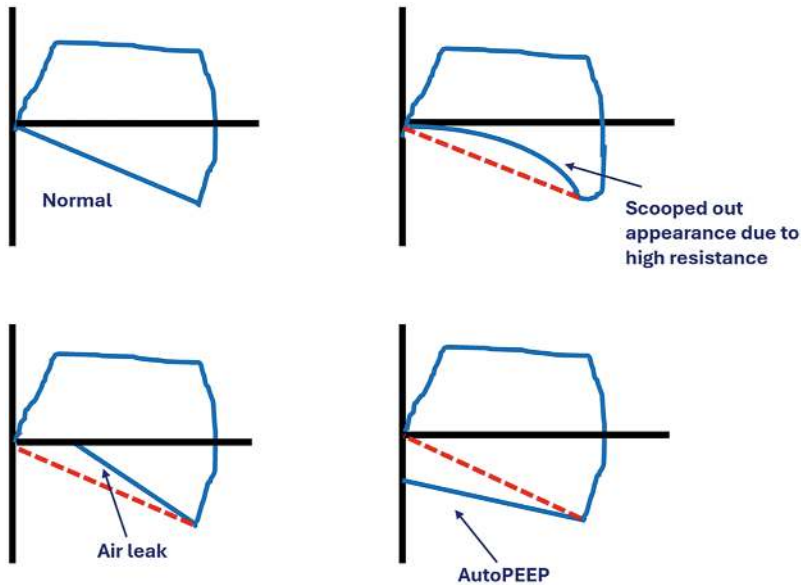


Fig. 2.21 Flow volume loop for different medical conditions

Fig. 2.22 Auto-PEEP. Flow waveform shows incomplete exhalation during the expiratory phase, with flow not returning to baseline before the next breath



- Tension pneumothorax (causing low lung compliance)
- Kinked or dislodged endotracheal tube (causing high airway resistance)
- Large mucus plug (causing high airway resistance)

If the diagnosis is not clear, manage each potential cause step by step:

- Disconnect the patient from the ventilator to allow exhalation of trapped air (auto-PEEP).
- If there is no improvement, check the patency of the ETT and perform suctioning to address a possible kinked ETT or mucus plug.
- If still no improvement, examine the chest for signs of pneumothorax (e.g., asymmetrical chest movement, decreased breath sounds), and treat accordingly.

Also, since auto-PEEP can cause sudden hypoxia, other potential causes should be considered. The approach to sudden hypoxia can be remembered using the mnemonic DOPE:

- D—displacement of the ETT: the endotracheal tube may be dislodged (e.g., out of the airway or advanced into a main bronchus). Look, listen, and feel, assess the patient and ventilator, and adjust the ETT position as needed.
- O—obstruction: perform suctioning to clear the airway of any secretions or mucus plugs.
- P—pulmonary embolism, auto-PEEP or pneumothorax: assess clinically and treat accordingly.
- E—equipment: assess the connections, oxygen supply, and the ventilator for any malfunctioning.

Proper PEEP Setting

PEEP setting can be adjusted by multiple modalities:

1. Measuring the Pplat and set the PEEP with value to keep driving pressure (DP) <15 cmH₂O.

$$DP = P_{plat} - PEEP$$

2. Use the FiO₂–PEEP table as outlined in the ARDSnet protocol (Fig. 2.23).
3. Pressure volume tool: PEEP is set at or just above the lower inflection point (Fig. 2.16).
4. Esophageal pressure monitoring: This method estimates pleural pressure, allowing for more precise adjustment of PEEP. The goal is to maintain:
 - Transpulmonary pressure (TPP) between 0 and 10 cmH₂O at the end of expiration.
 - TPP < 25 cmH₂O at the end of inspiration [6].

TPP = alveolar pressure – pleural pressure.

5. Stress index (SI): PEEP is adjusted to keep SI around 1 (Fig. 2.24).

Ventilator Asynchrony

Asynchrony is a common ventilator troubleshooting that can result from various causes, such as improper ventilator settings, over or under-sedation, critical illness–associated weakness, and other patient-related or equipment-related factors. Identifying and addressing abnormal patterns on the ventilator can help determine

Lower PEEP/ higher FIO ₂														
FIO ₂	0.3	0.4	0.4	0.5	0.5	0.6	0.7	0.7	0.7	0.8	0.9	0.9	0.9	1.0
PEEP	5	5	8	8	10	10	10	12	14	14	14	16	18	18-24
Higher PEEP/ lower FIO ₂														
FIO ₂	0.3	0.3	0.3	0.3	0.3	0.4	0.4	0.5	0.5	0.5-0.8	0.8	0.9	1.0	1.0
PEEP	5	8	10	12	14	14	16	16	18	20	22	22	22	24

Fig. 2.23 FiO₂-PEEP table, in hypoxic patients, increase both parameters step by step. (Sourced from: ARDS Network [5])

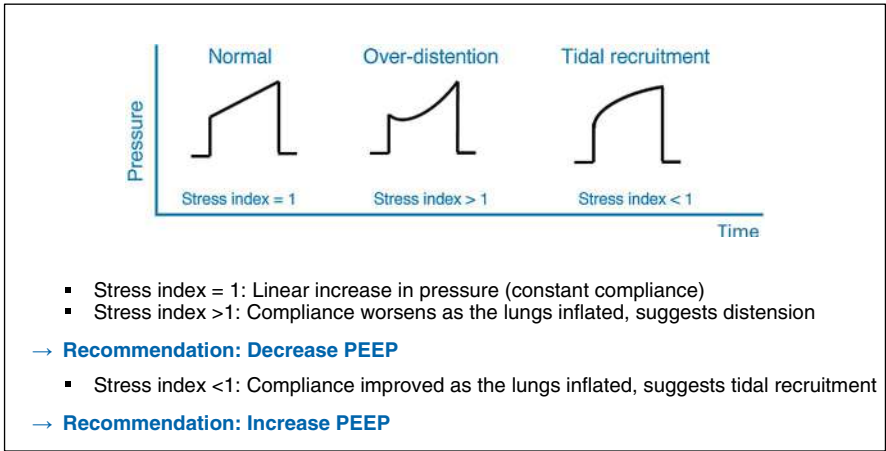


Fig. 2.24 Stress index indicates whether alveoli are normal, overdistended, or tidally recruited; helps guide PEEP adjustment

the underlying cause and guide appropriate management. The most common types of ventilator asynchrony include the following:

- *Ineffective triggering* (Fig. 2.25): causes include the following:
 - Over sedation
 - ICU acquired weakness
 - Electrolyte disturbances
 - Auto-PEEP
 - Low sensitivity trigger (flow trigger is high)

Management: assess and treat the cause and decrease the flow trigger.

- *Double triggering* (Fig. 2.26): it is caused by:
 - Low set of inspiratory time
 - Under sedation

Fig. 2.25 Ineffective triggering: the patient attempts to initiate a respiratory cycle, but the effort does not trigger the ventilator

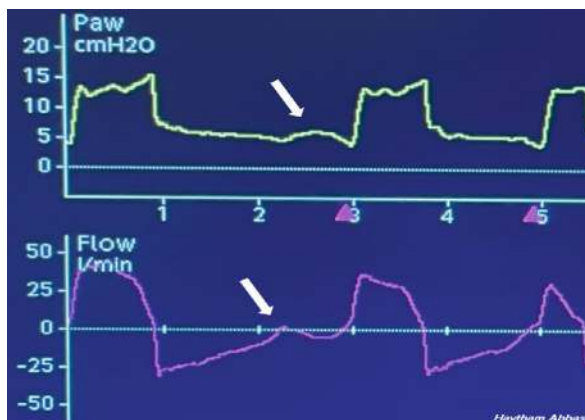
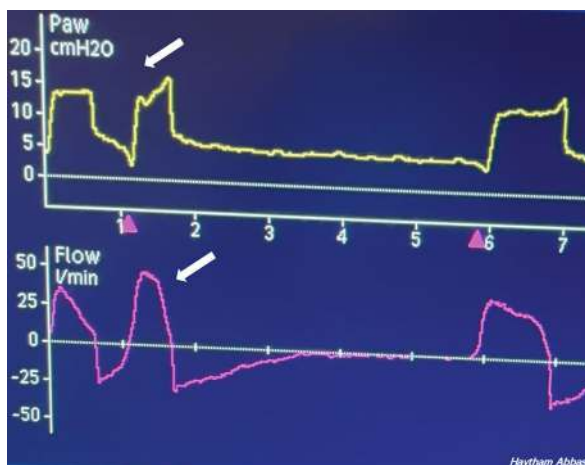


Fig. 2.26 Double triggering



Management: adjust the sedation regiments and increase inspiration time.

- *Auto-triggering* (Fig. 2.27): causes include the following:

- Air leak
- High trigger sensitivity

Management:

- Assess for and correct any air leaks
- Increase the flow trigger threshold to reduce false triggering

- *Flow asynchrony* (Fig. 2.28):

This occurs when the inspiratory flow setting is too low and does not meet the patient's demand. It appears as a concave (scooped) shape on the inspiratory limb of the pressure waveform. Adjusting the inspiratory flow can correct this asynchrony.

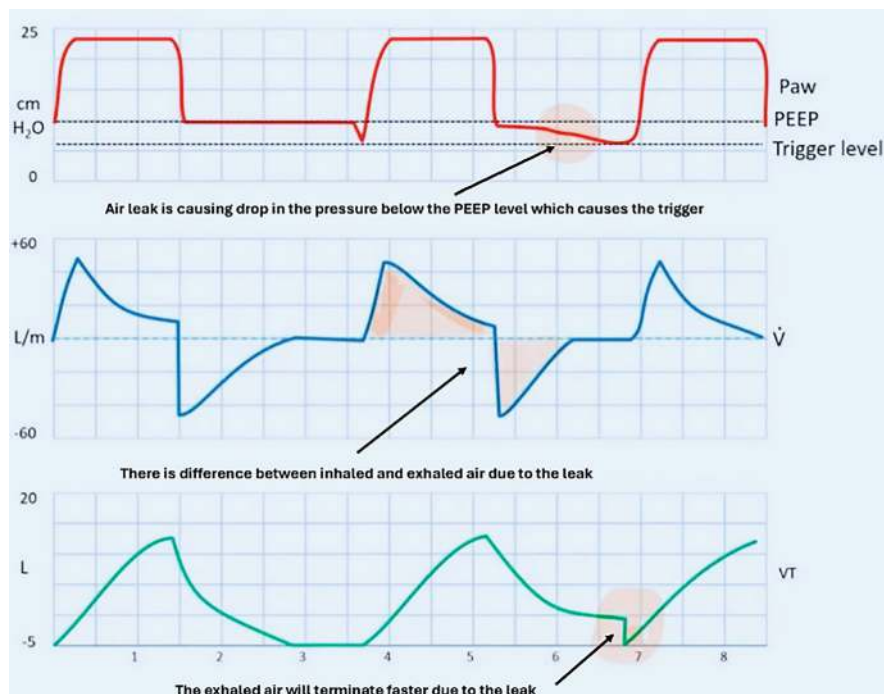


Fig. 2.27 Auto-triggering. (Courtesy of Dr. Mazen Kherallah)

- *Late cycling* (Fig. 2.29):

This occurs when the set inspiratory time is too long, causing the patient to attempt to terminate the breath before the ventilator does. This effort appears as a dip in the pressure waveform at the end of the inspiratory phase.

Management: decrease the inspiratory time to better match the patient's effort.

Complications of Ventilator

Ventilator-Associated Pneumonia (VAP)

VAP is a common complication in patients ventilated for >48 h. Along with new infiltrates on chest radiograph, diagnosis involves clinical and lab findings, classified as:

- Ventilator-associated condition (VAC)
- Infection-related ventilator-associated complication (IVAC)
- Possible/probable ventilator-associated pneumonia (VAP)

Figure 2.30 explains the criteria for each phase [7].

Fig. 2.28 Concavity of the inspiratory pressure wave indicates patient effort due to low set inspiratory flow; a typical sign of flow asynchrony

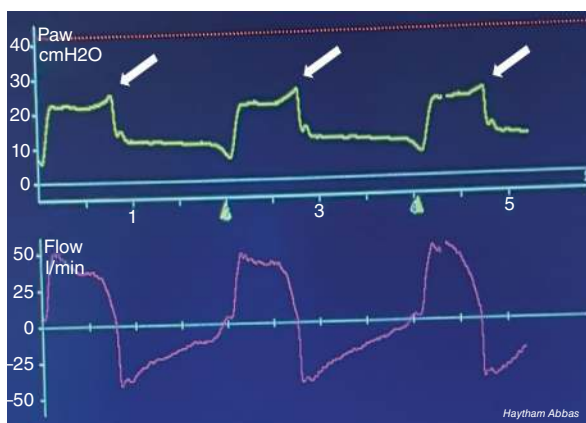
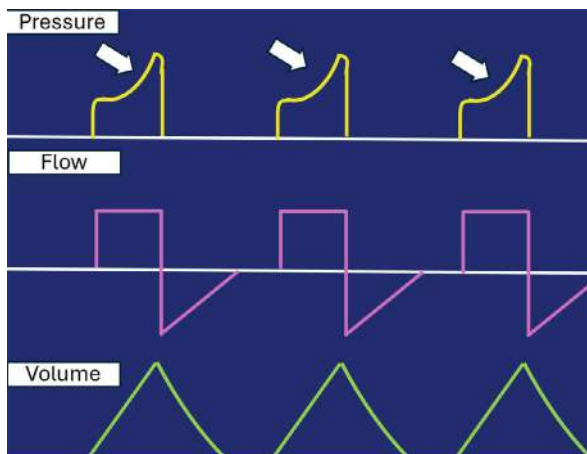


Fig. 2.29 Late cycling asynchrony

Mechanical Complications of Ventilator

They are classified as:

- Barotrauma
- Volutrauma
- Atelectotrauma
- Biotrauma
- Oxygen toxicity

Table 2.2 explains the difference between those complications and the proper management [8, 9].

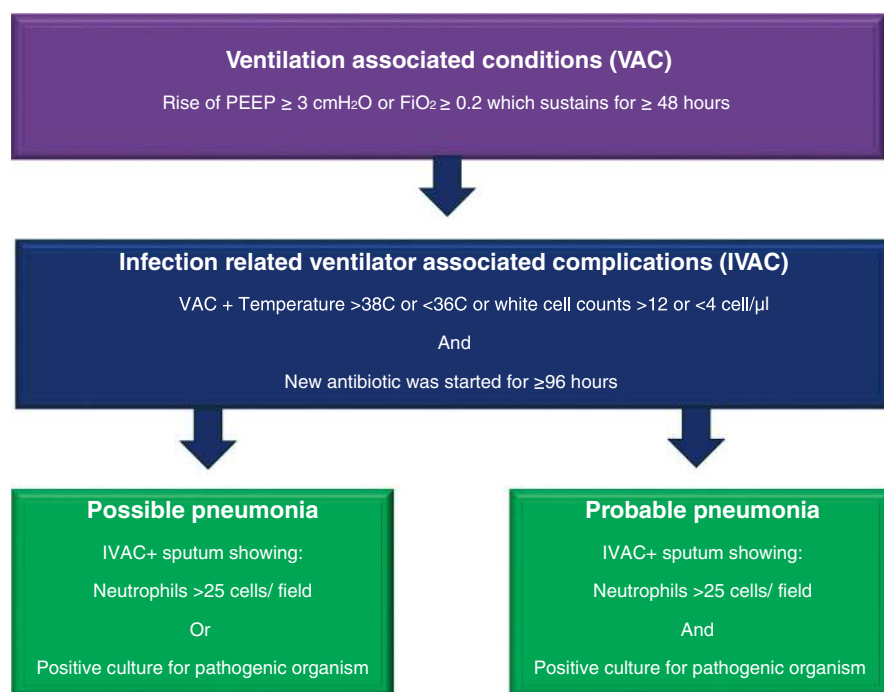


Fig. 2.30 VAC, IVAC, possible- or probable-VAP. FiO₂ = fraction of inspired oxygen; PEEP = positive end-expiratory pressure. (Adapted from the original source: Pearson et al. [7]. Used with permission)

Capnography

Types of capnography

Qualitative (colorimetric) (Fig. 2.31)

Quantitative (infrared technique) (Fig. 2.32)

Capnography waveform: normal waveform is illustrated in Fig. 2.33.

Alveolar-arterial CO₂ gradient (PaCO₂ – ETCO₂) is normally 0–5 mmHg. The gradient increases with increased dead space ventilation. PaCO₂ = partial pressure of arterial carbon dioxide, ETCO₂ = end-tidal carbon dioxide.

Causes of increased and decreased ETCO₂: summarized in Table 2.3.

Uses of capnography

1. Verification of endotracheal tube (ETT) placement:

- Colorimetric method: indicator turns yellow if the ETT is correctly placed in the trachea and remains purple if placed in the esophagus.
- Infrared capnography: a capnography waveform appears when the ETT is properly placed in the airway. No waveform is seen if the tube is in the esophagus or dislodged.

Table 2.2 Mechanical complications of ventilator

Injury	Mechanism	Management
Volutrauma	Overdistention of the alveoli causing basement membrane stretching and stress on intracellular junctions	Avoid overdistention and apply lung protective strategy: Tidal volume (TV) 6 mL/kg/IBW Plateau pressure (Pplat): ≤30 mmHg
Barotrauma	Increasing transpulmonary pressure causing disruption of the basement membrane	Avoid high transpulmonary pressure and apply lung protective strategy: Tidal volume (TV) 6 mL/kg/IBW Plateau pressure (Pplat): ≤30 mmHg
Atelectotrauma	Collapse and expansion of the alveoli leading to shearing injury	Optimization of positive end expiratory pressure (PEEP) Consider recruitment
Biotrauma	Tissue damage leading to cytokines and chemokines release resulting in systematic inflammatory response syndrome	Lung protective strategy Higher PEEP Prone positioning Neuromuscular blocking agents
Oxygen toxicity	High oxygen supply will increase the oxygen free radicals which induce lung injury	Avoid over-oxygenation and target oxygen supply depending on blood gas, PaO_2/FiO_2 ratio and oxygen saturation

IBW ideal body weight, *PaO₂* partial pressure of arterial oxygen, *FiO₂* fraction of inspired oxygen

Fig. 2.31 Colorimetric capnography gives a range in which end-tidal carbon dioxide (ETCO₂) is expressed by color change. It is used mainly to confirm endotracheal tube (ETT) position



Fig. 2.32 Quantitative capnography provides both a numerical value and waveform display of ETCO₂ on the monitor. It is commonly used in mechanically ventilated patients



Fig. 2.33 Capnography waveform

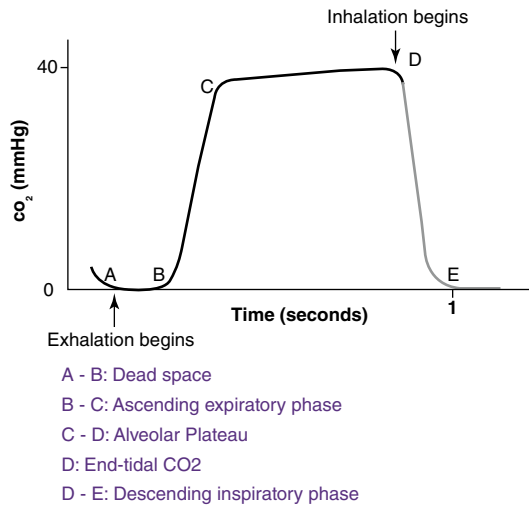


Table 2.3 Physiological and clinical factors that can lead to elevated or reduced end-tidal CO₂

Causes of increased ET _{CO} ₂	Causes of decreased ET _{CO} ₂
<i>Metabolic:</i> shivering, hyperthermia, hyperthyroid, bicarbonate infusion	<i>Metabolic:</i> muscle relaxant, hypothermia, hypothyroid
<i>Hypoventilation</i>	<i>Hyperventilation</i>
<i>Increased cardiac output</i> , e.g., during resuscitation	<i>Decreased cardiac output</i> (cardiac arrest, pulmonary embolism, heart failure or hypovolemia)

2. Confirmation of ETT position during transportation.
3. Use in cardiopulmonary resuscitation (CPR) [10]:
 - During CPR, if $\text{ETCO}_2 < 10$ mmHg, CPR quality must be improved.
 - Abrupt increase of ETCO_2 is a marker for return of spontaneous circulation (ROSC).
 - Failure to achieve $\text{ETCO}_2 > 10$ mmHg in 20 min, ROSC will be unlikely.

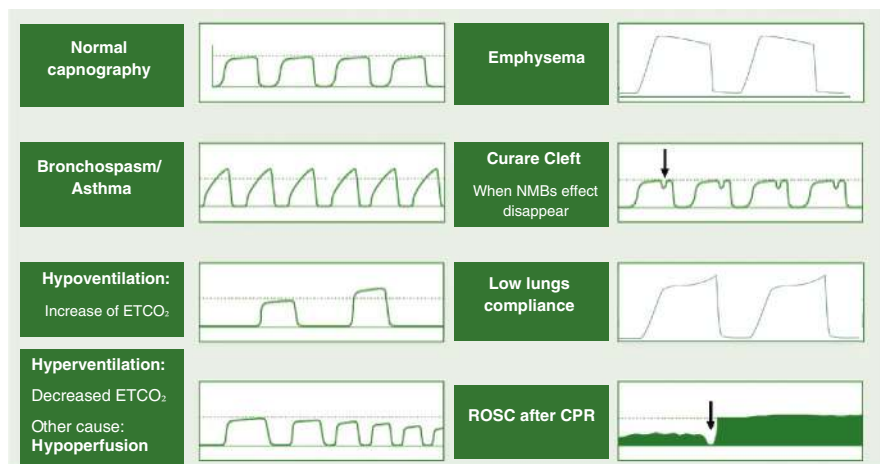


Fig. 2.34 Common shapes of ETCO_2 waveforms. NMBs = neuromuscular blockers, CPR = cardiopulmonary resuscitation, ROSC = return of spontaneous circulation, ETCO_2 = end-tidal carbon dioxide

4. Use in trauma patient:

- The aim is to keep the patient normocapnic, hypo-/hypercapnia can worsen the outcomes.

Common shapes of ETCO_2 waveforms: Different clinical conditions produce characteristic capnography waveform patterns; Fig. 2.34 illustrates some of the most important waveform shapes and their clinical significance.

Percutaneous Tracheostomy

Indications of Tracheostomy

- Difficult weaning of ventilator, usually due to neurological complications, e.g., stroke, ICU acquired weakness, and neuropathy.
- Inability to maintain airway, e.g., bulbar symptoms.
- Airway obstruction, e.g., edema, oropharyngeal/tracheal trauma, extrinsic compression from hematoma or mass.

Advantages of Tracheostomy

- Facilitate weaning of ventilator.
- Facilitate weaning of sedation.
- Allow oral use, e.g., hygiene, feeding, speech.
- Allow rehabilitation, e.g., mobility, physiotherapy.
- Decreases the ICU stay.
- Decreases the risk of nosocomial infections.
- Decreases the complication related to endotracheal tube (ETT), e.g., laryngeal edema.

Proper Timing for Tracheostomy

The timing of tracheostomy is controversial and depends on the underlying disease and its progression. However, it is usually performed within 10–14 days. Some trials have compared early versus late tracheostomy. The *Trac-Man trial* [11] studied early tracheostomy (within 4 days) versus late tracheostomy (after 10 days) and found no significant difference in mortality between the two groups. Additionally, some patients in the early group ultimately did not require the procedure.

Contraindications for Percutaneous Tracheostomy

Absolute contraindications:

- Patient or family refusal.
- Lack of indication for the procedure.

Relative contraindications:

- Coagulopathy.
- Hemodynamic instability.
- High oxygen requirements.
- Anatomy related:
 - Morbid obesity.
 - Cervical instability.
 - Thyroid or neck mass.

Local infection.

Complications of Tracheostomy

Immediate:

- Hypoxia and ventilation failure.
- Bleeding.
- Mechanical complications:
 - Pneumothorax and surgical emphysema.
 - Esophageal cannulation.
 - Injury to thyroid gland or recurrent laryngeal nerve.
 - Cartilage fracture or laceration.
 - Early: within days-weeks:
- Local infection and ventilator associated pneumonia (VAP).
- Obstruction.
- Malposition.
- Erosion related, e.g., tracheoinnominate fistula and tracheoesophageal fistula.

Late: weeks to months:

- Same as early complication.
- Tracheomalacia.
- Tracheal stenosis.

Approach to Sudden Hypoxia in Patients on Tracheostomy

As in any critical case, sudden hypoxia in patients on tracheostomy is approached with ABC and management of each step accordingly.

As a difficult airway is anticipated, early involvement of otolaryngology and anesthesia experts is essential. The approach is summarized in Fig. 2.35 [12].

Approach of Sudden Bleeding from Tracheostomy Tube

Sudden bleeding from tracheostomy tube is also an emergency especially if caused by tracheoinnominate fistula. It must be approached with ABC.

Difficult airway must be anticipated, and involvement of anesthesia and otolaryngology experts is essential.

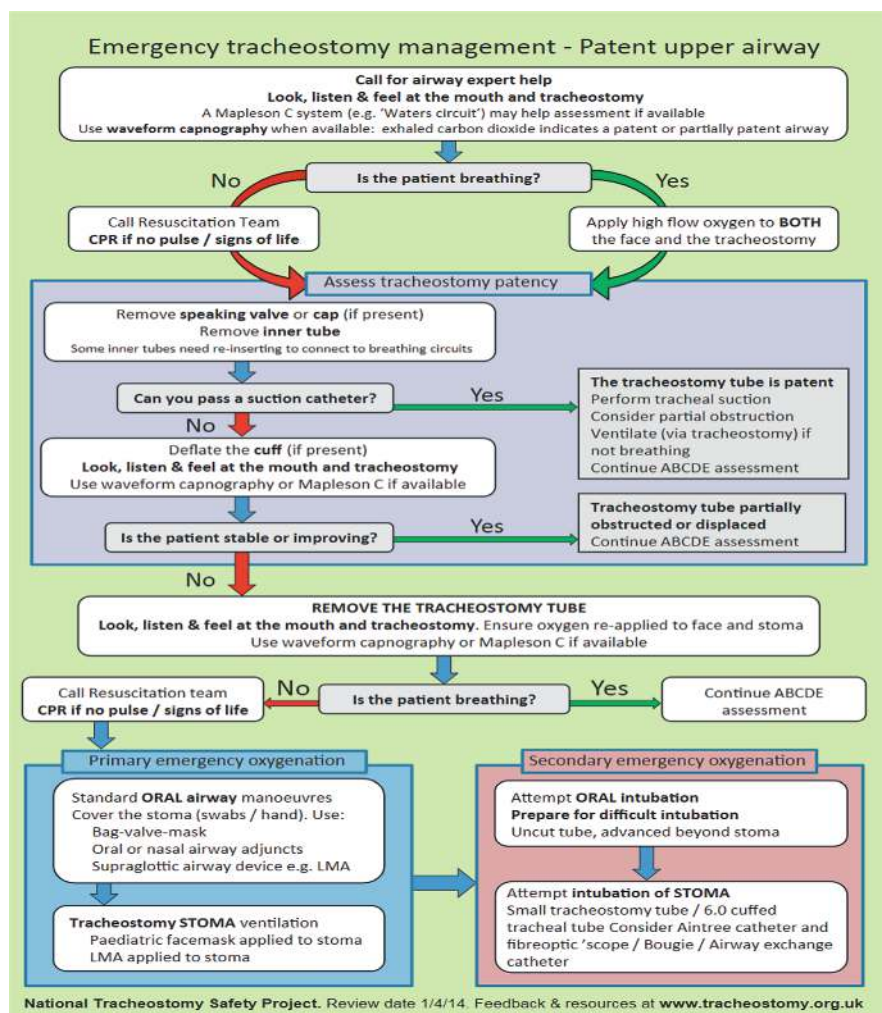


Fig. 2.35 Emergency tracheostomy management. CPR = cardiopulmonary resuscitation, LMA = laryngeal mask airway. (Reproduced with permission from McGrath et al. [12])

Assess if the patient is in cardiac arrest and start cardiopulmonary resuscitation (CPR) accordingly.

Send crossmatch, complete blood count (CBC), and coagulation profile; prepare blood products.

Overinflate the tracheostomy tube cuff to tamponade the bleeding site.

If bleeding persists, urgently remove the tracheostomy, apply digital compression to the artery, and insert an endotracheal tube (ETT) deeply to bypass the bleeding site.

Once bleeding is controlled and the airway is secured, proceed with surgical intervention.

Weaning of Ventilation

Weaning is the process of reducing ventilatory support, allowing the patient to gradually assume more spontaneous or independent ventilation.

This can be achieved either through an immediate trial of unassisted breathing, known as a spontaneous breathing trial (SBT), or by gradually decreasing the level of ventilatory support.

Regardless of the method, extubation is considered once the patient demonstrates adequate spontaneous breathing and both airway patency and airway protection are confirmed.

Tools and Criteria Used for Weaning

- *Initial criteria for weaning of ventilator:* summarized in Table 2.4 [13].
- *Maximal inspiratory pressure (MIP)/negative inspiratory force (NIF):*
An MIP or NIF of -30 cmH₂O or lower (i.e., more negative) is associated with a higher likelihood of successful weaning, whereas values of -20 cmH₂O or higher (i.e., less negative) may be associated with weaning failure.
- *Rapid shallow breath index (RSBI):*
RSBI is calculated as respiratory rate (RR) divided by tidal volume (TV).
A value of <105 is considered a reliable predictor of weaning success.
Evidence suggests that RSBI is one of the most accurate parameters for assessing weaning readiness. In the *RSBI trial* [14], multiple weaning predictors were evaluated, and an RSBI cutoff of 100 was found to be the most sensitive and specific indicator of successful weaning.
- *Airway occlusion pressure P0.1:*
P0.1 is the airway pressure generated during the first 0.1 s of an inspiratory effort against an occluded airway. In healthy individuals, it is typically <2 cmH₂O. Values >4 – 6 cmH₂O may indicate increased respiratory drive and are associated with a higher risk of weaning failure.

Table 2.4 Initial criteria for weaning of ventilator

<i>Underlying cause of respiratory failure has resolved or significantly improved</i>
<i>Good oxygenation: $PaO_2/FiO_2 \geq 150$–200 or $SpO_2 \geq 88$–90% on $FiO_2 \leq 40$–50%, and $PEEP \leq 5$–8 cmH₂O</i>
<i>No acidosis: pH >7.25–7.3</i>
<i>Good cough and minimal secretion</i>
<i>Able to initiate an inspiratory effort</i>
<i>Hemodynamic stable: no or low-dose vasopressors</i>
<i>Hemoglobin ≥ 7–8 g/dL</i>
<i>Afebrile: temperature ≤ 38 °C</i>
<i>Good mental status: awake and alert</i>

Adapted with modifications from MacIntyre et al. [13]

PaO_2 partial pressure of arterial oxygen, FiO_2 fraction of inspired oxygen, SpO_2 oxygen saturation, $PEEP$ positive end expiratory pressure

Steps of Weaning

Spontaneous awaking trial (SAT) and spontaneous breathing trial (SBT):

The steps of SAT and SBT are illustrated in Fig. 2.36. The *ABC trial* demonstrated that combining SAT with SBT was superior to SBT alone in reducing mortality and the duration of mechanical ventilation [15].

Pressure support ventilation (PSV):

PSV is considered the most effective mode for weaning. It is recommended to continue PSV for 30–120 min to determine if the weaning trial is successful. The *BROCHARD trial* compared PSV with other weaning methods, including the T-piece and synchronized intermittent mandatory ventilation (SIMV), and found significantly better outcomes in the PSV group [16].

Cuff leak test [17]:

A cuff leak test is recommended for high-risk patients who may develop laryngeal edema, such as those with traumatic intubation, prolonged intubation (>6 days), use of a large endotracheal tube, female patients, or those requiring reintubation after unplanned extubation.

If the cuff leak test is positive, extubation can proceed. If the test is negative, administering systemic steroids at least 4 h before extubation is recommended, as this has been shown to reduce the risk of post-extubation stridor and the need for reintubation.

Causes of Unsuccessful Weaning

Patients who require more than 7 days to complete the weaning process are at higher risk for poor outcomes and are more likely to experience extubation failure compared to those who undergo simple weaning. Most underlying causes can be identified through routine clinical evaluation, including physical examination, laboratory tests, arterial blood gas analysis, electrocardiography, chest radiography, and a review of sedative use and ventilator settings.

Table 2.5 summarizes the systems involved and the causes of weaning failure.

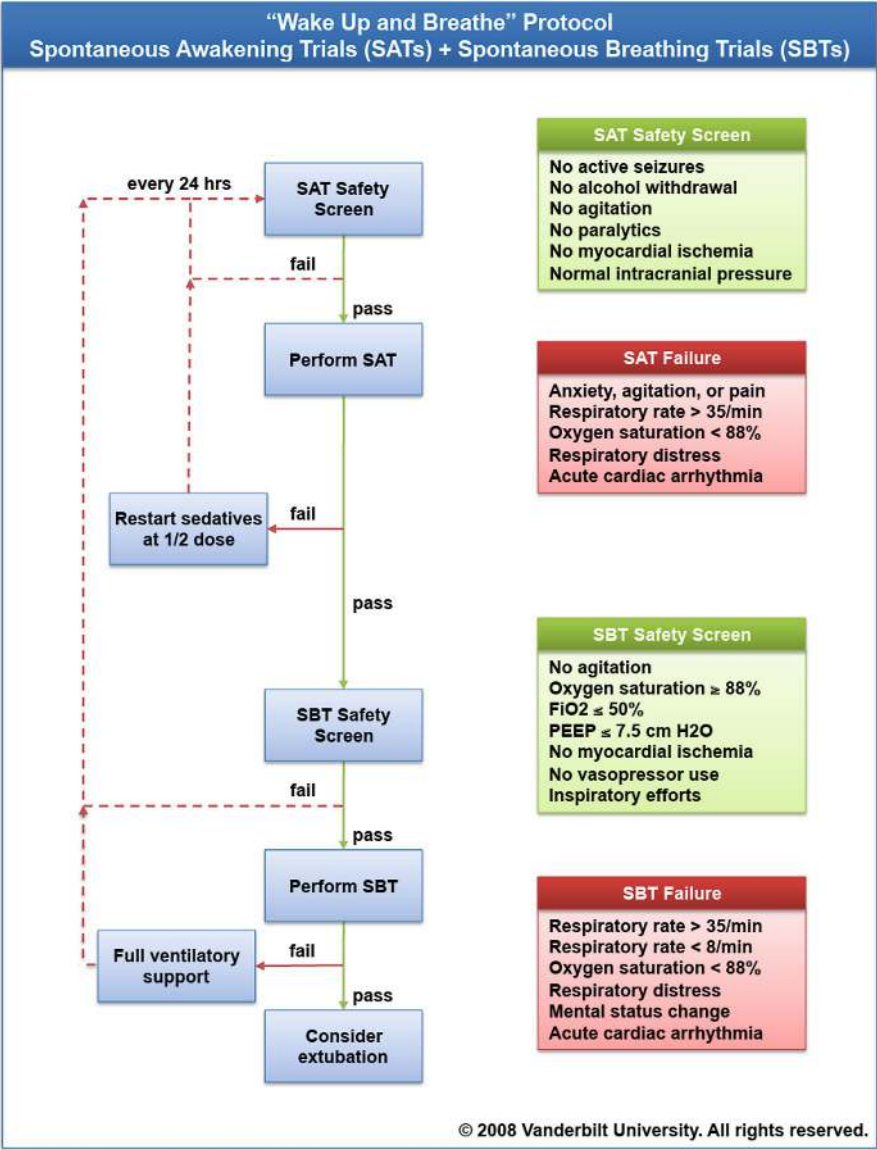


Fig. 2.36 Spontaneous awakening trial (SAT) and spontaneous breathing trial (SBT). FiO₂ = fraction of inspired oxygen, PEEP = positive end expiratory pressure. (Used with permission, for more details visit ICUdelirium.org)

Table 2.5 Causes of weaning failure

Pathophysiology	Examples	Exam/workup
<i>Respiratory causes</i>		
High resistance	COPD, asthma, small ETT, mucus plug	<i>Clinical exam:</i> chest, cardiac, neurology, and abdominal exams;
Low compliance	Auto-PEEP, ARDS, pneumonia, pneumothorax, pleural effusion, abdominal compartment syndrome	ETT (including suction), equipment, and ventilator parameters (e.g., auto-PEEP, compliance, resistance)
Dead space	Atelectasis, pulmonary embolism, severe dehydration, heart failure	<i>Investigations:</i> chest X-ray, blood gas, POCUS. If etiology is unclear, other investigations might be considered such as CT pulmonary angiography, and CT head
Hypoventilation	OHS, central sleep apnea, CNS diseases, sedation, ICU acquired weakness	
<i>Cardiovascular causes</i>		
Myocardial ischemia, low cardiac output, increased cardiac filling pressure, and/or volume overload	Myocardial infarction (SAT may induce myocardial ischemia in high risk patients), heart failure +/- cardiogenic shock or overload	Cardiac and pulmonary exam ECG, cardiac markers, echocardiography, POCUS. If etiology is unclear, other investigations might be considered such as PAC and TEE
<i>Neuropsychiatry causes</i>		
Localized weakness	Stroke, mononeuropathy	Medications review, neurology exam, and ICU-CAM assessment
Generalized weakness	ICU acquired weakness, polyneuropathy, oversedation, electrolytes disturbances (e.g., k, PO ₄ , Mg), anemia	CT head, CBC, chemistry, and electrolytes. If the etiology is not clear, consider other workup like NCS/EMG
Delirium	Hyper/hypoactive or mixed	
<i>Nutritional causes</i>		
Improper diet	Malnourishment or overfeeding	Assess caloric requirements, indirect calorimetry, nitrogen balance, etc.

COPD chronic obstructive pulmonary disease, *ETT* endotracheal tube, *PEEP* positive end expiratory pressure, *ARDS* acute respiratory distress syndrome, *OHS* obesity hypoventilation syndrome, *CNS* central nervous system, *POCUS* point of care ultrasound, *CT* computed tomography, *SAT* spontaneous awaking trial, *ECG* electrocardiogram, *PAC* pulmonary artery catheter, *TEE* transesophageal echocardiogram, *CBC* complete blood count, *k* potassium, *PO₄* phosphate, *Mg* magnesium, *CAM* confusion assessment method, *NCS* nerve conduction study, *EMG* electromyography

Airway Management

Airway Assessment

1. History

Ask for medical and surgical history that help to rule out difficult airway such as:

- Previous difficult airway:
Have you ever had any difficulty with intubation or airway management during previous surgeries or procedures?
- Head and neck surgeries or radiation:
Have you had any surgeries or radiation therapy to your head, neck, or throat?
- Facial or airway trauma:
Have you experienced any trauma, burns, swelling, tumors, or masses involving your face, neck, or airway?
- Obstructive sleep apnea (OSA):
 - Have you been diagnosed with sleep apnea?
 - Do you snore loudly, feel tired during the day, or have been told you stop breathing during sleep?
- Temporomandibular joint (TMJ) dysfunction:
Do you have any jaw problems, such as pain, limited mouth opening, or clicking?
- Cervical spine disease:
Do you have any neck issues such as arthritis, previous neck trauma, stiffness, or conditions like rheumatoid arthritis or ankylosing spondylitis?

2. Clinical examination

Use mnemonic LEMON (Look, Evaluate, Mallampati, Obstruction, Neck mobility)

- *Look externally:*
Assess for facial abnormalities, limited mouth opening, obesity, dental issues (e.g., loose or missing teeth, dentures), and any facial or neck masses or pathology.
- *Evaluate:*
Use 3-3-2 rule; 3 fingers for mouth opening, 3 fingers for mento-hyoid, 2 fingers for hyoid-thyroid (Fig. 2.37)
- *Mallampati:*
The Mallampati classification (Fig. 2.38) is used to assess airway visibility and ranges from Class I to Class IV as following [19]:
 - Class I: Soft palate, uvula, fauces, pillars visible.
 - Class II: Soft palate, major part of uvula, fauces visible.
 - Class III: Soft palate, base of uvula visible.
 - Class IV: Only hard palate visible.

Fig. 2.37 3-3-2 rule for airway assessment

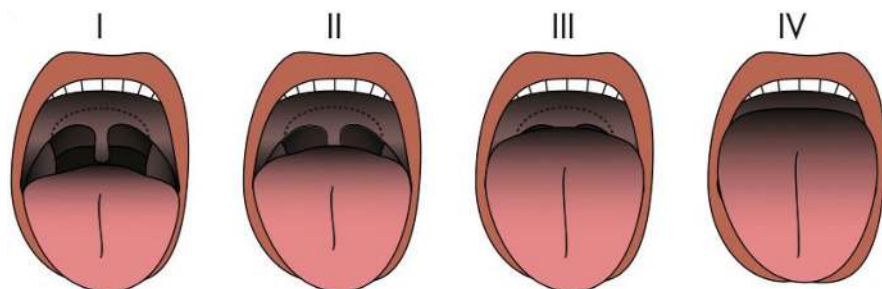
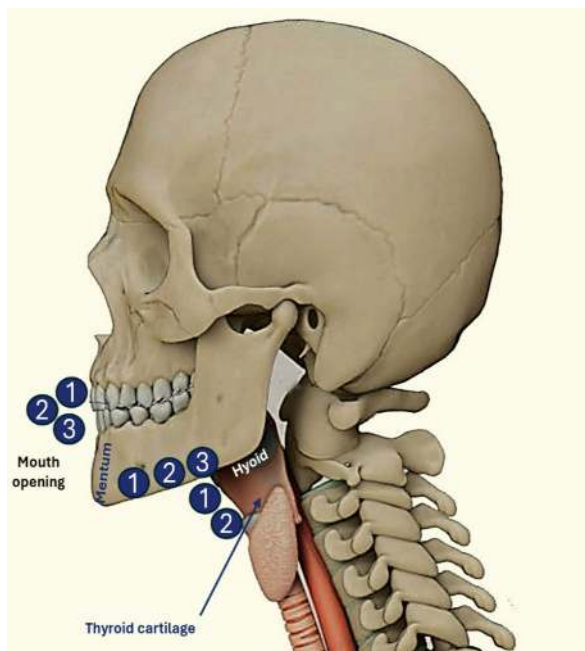


Fig. 2.38 Mallampati classification. (Sourced from Nørskov et al. [18])

- *Obstruction:*
Assess for any mass or pathology can interfere with intubation.
- *Neck mobility:*
Assess the range of motion of the neck to identify any restrictions or limitations.

Airway Devices and Tools

If intubation is planned, ensure the following are prepared in advance, especially if a difficult airway is anticipated:

1. *Oral and nasal airways:*

- Indication: used to maintain airway patency in patients with impaired consciousness, where soft tissue collapse (e.g., tongue or epiglottis) may obstruct airflow.
- Oral airway sizing: approximated by measuring from corner of mouth to angle of the mandible.
- Nasal airway sizing: determined by measuring from nares to tragus of ear.
- Avoid or use extreme care with insertion of nasal airway in patient on anti-coagulation or with basal skull fracture.

2. *Mask ventilation:*

- Allows ventilation and oxygen delivery up to 100%.
- Left hand to fix the mask, right hand for positive pressure.
- Holding the mask by C-E maneuver (Fig. 2.39).
- Look (chest rise), listen (air escape from the mask and air entry to the chest), feel (air escape from the mask).
- If difficult single mask ventilation, following steps are recommended:
 - Call for help to assist with two-persons mask ventilation.
 - Insert oral or nasal airway.
 - Perform head tilt chin lift and/or jaw thrust (Fig. 2.40).



Fig. 2.39 C-E maneuver for single person using mask ventilation

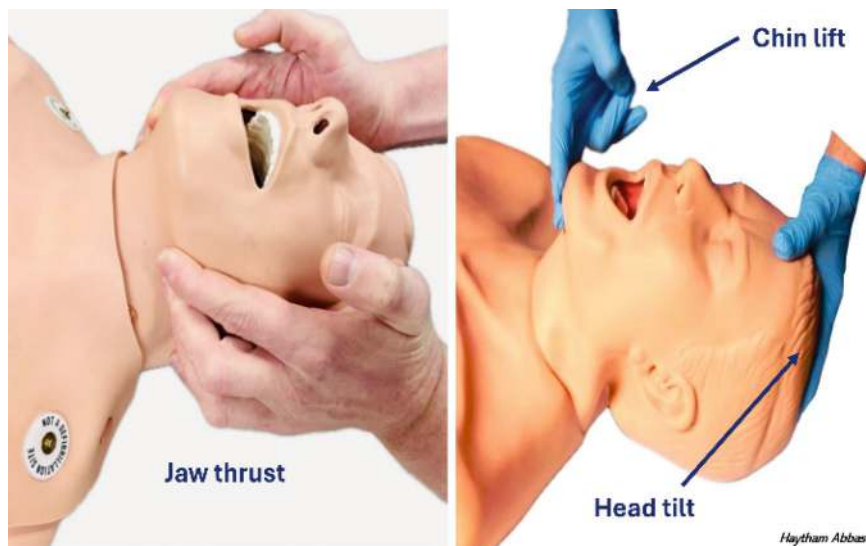


Fig. 2.40 Head tilt, chin lift, and jaw thrust

3. *Laryngeal mask airway (LMA)* (Fig. 2.41):

Indications:

- Rescue device in difficult airway
- Conduit for stylet, fiberoptic bronchoscopy, or small diameter endotracheal tube (ETT)

Contraindications:

- Pharyngeal pathology
- Obstruction
- High aspiration risk
- Long surgeries

Disadvantages:

- Does not protect the airway
- Can be dislodged

4. *Endo-tracheal tube (ETT)*:

- Diameter in females 7–7.5 mm, males 7.5–8 mm
- Length at the level of lips in females 20–21 cm, males 21–22 cm
- Patency of the balloon has to be checked before using the tube

Fig. 2.41 Laryngeal mask airway



5. *Laryngoscope:*

It has multiple types such as:

- Macintosh blade (curved)
- Miller blade (straight)
- Video laryngoscopes: e.g., glidescope, C-MAC (Fig. 2.42)

The *Cormack–Lehane* system classifies views obtained by direct laryngoscope based on the structures seen (Fig. 2.43)

6. *Fiberoptic bronchoscope*

Uses:

- Difficult airway
- C-spine pathology
- Upper airway obstruction

7. *Cricothyroidotomy kit*

8. *Malleable stylet*

9. *Airway bougie*

10. *Tools to confirm successful intubation:* e.g., stethoscope and capnography

Pharmacological agents used for intubation: (see Table 2.6).

Approach to difficult airway: (see Fig. 2.44).



Fig. 2.42 Types of laryngoscopes

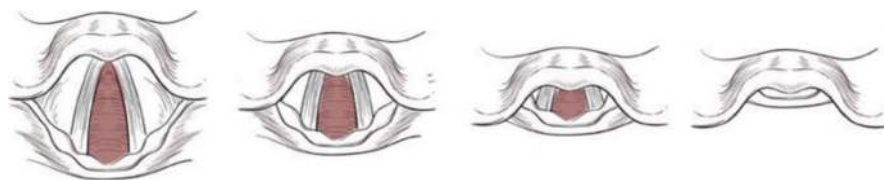


Fig. 2.43 Cormack–Lehane system classification. (Sourced from Zeger et al. [20])

Complications of Intubation

- Laryngospasm: may occur during or after intubation. Management includes the following:
 1. Applying gentle positive pressure ventilation
 2. Performing the laryngospasm maneuver (firm pressure behind the mandibular ramus, near the earlobe)
 3. Administering succinylcholine (0.25–1 mg/kg) for muscle relaxation
- Negative pressure pulmonary edema: typically seen post-extubation. Management involves the following:
 1. Securing the airway
 2. Providing supplemental oxygen
 3. Considering positive pressure ventilation or reintubation

Table 2.6 Pharmacological agents used for intubation

	Mode of action	Comments
<i>Sedative agents</i>		
Midazolam	Gamma-aminobutyric acid(GABA)- α agonist	Sedative and good choice in status epilepticus (SE). Side effects: hypotension and delirium.
Propofol	GABA- α agonist	Sedative, and good choice for increased intracranial pressure (ICP) and SE. Side effects: hypotension, propofol infusion syndrome, and green urine.
Etomidate	Positive modulation of GABA activity	It is a good choice in trauma and hemodynamic unstable cases. Side effects: myoclonus and adrenal insufficiency.
Ketamine	N-methyl-D-aspartate (NMDA) receptor blocker	Good choice in status asthmaticus, does not cause hypotension and has an analgesic effect. Side effects: demand ischemia with hypertension and tachycardia, hypersalivation and may increase ICP and intra-ocular pressure (IOP).
Fentanyl	Opioid	Analgesic. Side effects: abdominal pain, constipation, vomiting, and respiratory depression.
<i>Neuromuscular blockers</i>		
Succinylcholine	Depolarizing neuromuscular blocker (NMB)	Side effects: increased ICP and IOP and may cause malignant hyperthermia (MH). Contraindicated in immobility, muscle dystrophy and in trauma or burn >24–72 h (risk of severe hyperkalemia), and previous history of MH.
Vecuronium	Non-depolarizing NMB	Hepatobiliary excretion, overdose is reversed by sugammadex.
Rocuronium	Non-depolarizing NMB	Hepatobiliary excretion, overdose is reversed by sugammadex.
Cisatracurium	Non-depolarizing NMB	Degenerated by Hofmann degradation.

- Recurrent laryngeal nerve injury: it may result in hoarseness or vocal cord dysfunction
- Post-intubation stridor: it indicates upper airway edema
- Subglottic stenosis (acquired): often due to prolonged intubation or trauma
- Iatrogenic trauma (e.g., broken teeth, upper airway hemorrhage)
- Mechanical ventilation-related complications, outlined in the section [“Complications of Ventilator”](#)

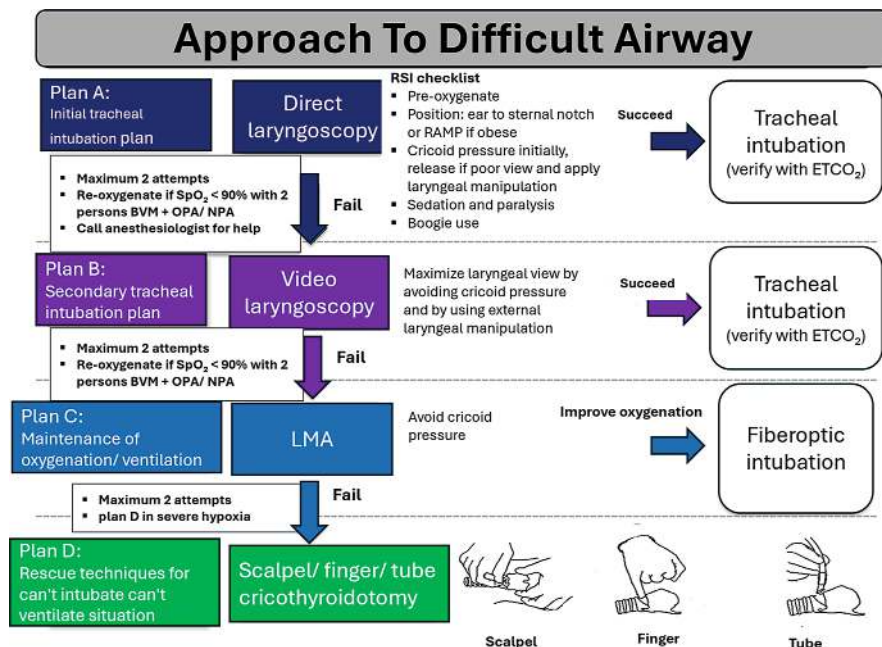


Fig. 2.44 Approach to difficult airway. RSI = rapid sequence intubation BVM = bag valve mask, OPA = oropharyngeal airway, NPA = nasopharyngeal airway, LMA = laryngeal mask airway, SpO₂ = oxygen saturation, ETCO₂ = end-tidal carbon dioxide, RAMP = rapid airway management positioner. (Adapted from a previously used diagram by www.das.uk.com, used with permission)

Life-Threatening Asthma

Clinical Findings of Life-Threatening and Near Fatal Asthma

- Drowsiness/altered consciousness
- Talks in words
- Exhaustion
- Hypotension
- Arrhythmia
- Pulsus paradoxus (defined by decreasing of systolic pressure for >10 mmHg during inspiration)
- Cyanosis
- Silent chest
- Poor respiratory effort and using accessory muscles
- Peek expiratory flow rate (PEFR) <33%
- Hypoxemia with oxygen saturation (SpO₂) <90%
- Near fatal asthma: if the blood gas showed high partial pressure of carbon dioxide (PaCO₂) level

Management of Life-Threatening Asthma [21]

As in any critical case, life-threatening asthma must be approached with ABC and management of each step accordingly.

If the patient requires intubation, difficult airway must be anticipated, call for help and prepare the equipment of difficult airway.

Keep the patient on oxygen to maintain oxygenation with target oxygen saturation $\geq 93\text{--}95\%$.

Insert two peripheral intravenous cannulas, extract basic labs, obtain a blood gas to follow PaCO_2 , and order chest X-ray. Start the first line management which includes the following:

- Salbutamol 5 mg nebulizer: it is short-acting beta (β)₂ agonist (SABA) acting as a bronchodilator, and it should be given as a continuous nebulization for the first hour.
- Ipratropium bromide 500 mic nebulizer: it is short-acting anti-muscarinic (SAMA) also acting as a bronchodilator, continuous nebulization for the first hour can be initiated.
- Systemic steroid: methylprednisolone 40–60 mg twice or three times daily, it reduces the relapse, hospitalization, and the need of β_2 agonist [22].
- Intravenous magnesium sulfate (MgSO_4): can be used as it avoids smooth muscle contraction and inhibits acetylcholine release.

If the patient is not responding to the first-line management or deteriorated up to need for intubation, rescue therapies must be initiated after the intubation, and they include the following:

- Ketamine infusion: it is a sedative agent with inhibitory action on N-methyl-D-aspartate (NMDA) receptors, and it has a bronchodilator effect and one of the good choices for patients who are intubated due to asthma exacerbation.
- Neuromuscular blockers (NMBs), e.g., rocuronium: they avoid smooth muscle contraction and provide bronchodilation. Atracurium may induce histamine release and better be avoided.
- Inhalational anesthesia, e.g., sevoflurane, also has a bronchodilator effect.
- Heliox: it is a gas combining helium with higher percentage and oxygen with lower percentage (e.g., 70:30 or 80:20). The helium is very light gas and decreases the turbulent flow, such therapy with low fraction of oxygen cannot be used in severely hypoxic patients and only provided to patients who are maintaining oxygenation.
- Back-to-back nebulization continuously, the serum potassium must be monitored frequently due to risk of hypokalemia.
- Veno-venous extracorporeal membrane oxygenation (VV-ECMO): if all measures failed to manage the asthma exacerbation (the patient has persistent hypercapnia, high airway pressures, silent chest, etc.), VV-ECMO can be used as a rescue modality.

Ventilator Settings in Patients with Life-Threatening Asthma

Asthmatic patients on mechanical ventilation are at high risk of air trapping and auto-PEEP.

If auto-PEEP occurs with hemodynamic instability, manifested by high peak inspiratory pressure (PIP), hypotension, hypoxia, etc., immediate ventilator disconnection is the appropriate next step to allow exhalation of trapped air.

Ventilator settings to minimize risk of auto-PEEP:

- Lower respiratory rate
- Lower inspiratory-to-expiratory (I:E) ratio (i.e., prolonged expiratory time)
- Lower tidal volume
- Increased inspiratory flow rate

Chronic Obstructive Pulmonary Disease (COPD)

COPD is chronic respiratory symptoms due to progressive airflow limitation caused by airway and parenchymal inflammation and obstruction. It has two common syndromes which are emphysema and chronic bronchitis.

Emphysema is characterized by parenchymal destruction and formation of emphysematous bullae, clinically the patients may have the appearance of pink buffer (thin, non-cyanotic).

Chronic bronchitis is defined as a chronic productive cough for more than 3 months per year in more than 2 years; clinically the patients may have the appearance of blue bloater (obese, cyanotic, and edematous).

The most common etiology is smoking; other causes include recurrent airway infection, occupational exposure, and alpha 1 antitrypsin deficiency.

Frequently, there is an overlap between the syndromes which are causing airway obstruction, e.g., emphysema, chronic bronchitis, asthma, and bronchiectasis.

Diagnosis of COPD

COPD is an obstructive lung disease. In addition to history, clinical examination, and risk factors, a pulmonary function test (PFT) is required for diagnosis. During exacerbation, clinical findings may include wheezing, use of accessory muscles, pulsus paradoxus (>10 mmHg drop in systolic pressure during inspiration), cyanosis, and signs of respiratory distress. The PFT findings include the following:

- Forced expiratory volume in 1 s (FEV1)/forced vital capacity (FVC) of <0.7 .
- Poor response to bronchodilators to increase the FEV1 $> 12\%$ or 200 mL.
- Decreased diffusing capacity of the lungs for carbon monoxide (DLCO) of $<75\%$ in emphysema.

Other investigations:

- Chest X-ray: it may show hyperinflation, flat diaphragm, or emphysematous bullae.
- Blood gas: it may show acute or chronic type II respiratory failure according to the patient's presentation.

Table 2.7 GOLD classification for COPD staging

In COPD patients (FEV1/FVC < 0.7):		
GOLD 1	Mild	FEV1 ≥ 80% predicted
GOLD 2	Moderate	50% ≤ FEV1 < 80% predicted
GOLD 3	Severe	30% ≤ FEV1 < 50% predicted
GOLD 4	Very severe	FEV1 < 30% predicted

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Staging of COPD Patients

GOLD Classification (Global Initiative for Chronic Obstructive Lung Disease) categorizes COPD based on FEV₁ from PFT into four severity stages (Table 2.7).

For symptom assessment, tools include the following:

- COPD assessment test (CAT)
- Modified medical research council (mMRC) dyspnea scale

The GOLD ABE classification integrates:

- FEV₁ severity
- Symptom scores (CAT, mMRC)
- Exacerbation history

It provides a comprehensive scale with treatment recommendations (Figs. 2.45 and 2.46) [23].

Management of COPD Exacerbation [23]

As in any critical case, COPD exacerbation is approached with ABC and management of each step accordingly.

BiPAP is indicated for hypoxia and type II respiratory failure. Its use has been shown to improve survival and reduce the need for intubation, as demonstrated in the Brochard et al. (1995) trial [24].

The target oxygen saturation is 88–92%; hyperoxia can worsen the hypercapnia for multiple reasons:

- Increase in dead space; hyperoxia will worsen ventilation/perfusion (V/Q) matching due to loss of hypoxic pulmonary vasoconstriction leading to perfusion of non-functioning airways.
- Haldane effect: Increased oxygen binding to hemoglobin promotes the release of carbon dioxide from the blood into the lungs.

If the patient is ventilated, consider risk of auto-PEEP and adjust the ventilator accordingly.

Keep the patient on two peripheral cannulas, extract basic labs, blood gas, and order chest X-ray.

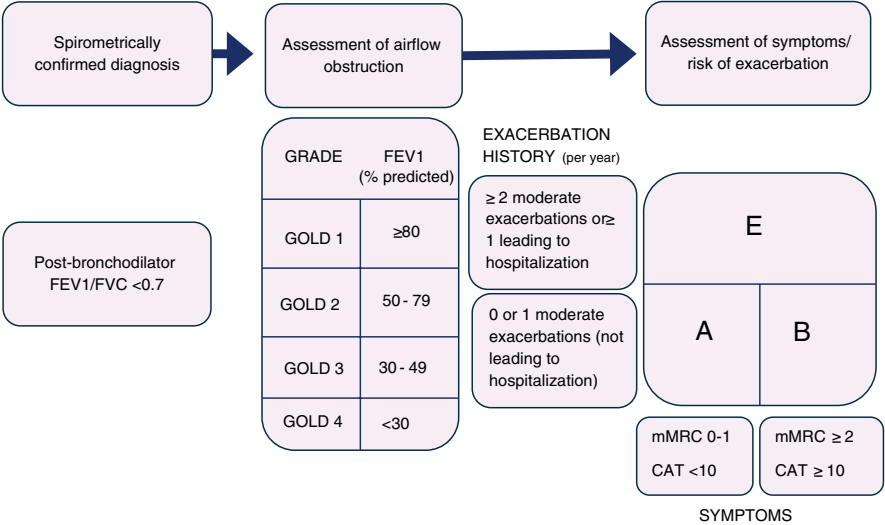


Fig. 2.45 GOLD ABE assessment tool. (© 2024, 2025, Global Initiative for Chronic Obstructive Lung Disease, available from www.goldcopd.org, published in Deer Park, IL, USA. Used with permission)

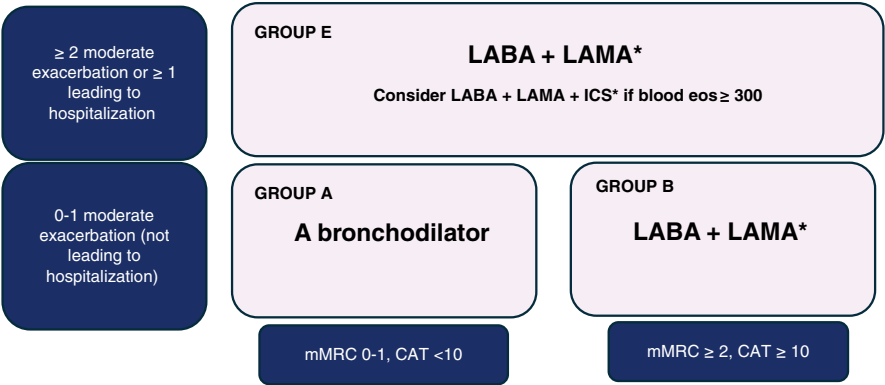


Fig. 2.46 Initial pharmacological treatment. LABA = long-acting beta2 agonist, LAMA = long-acting muscarinic antagonist, ICS = inhaled corticosteroid, eos = eosinophil count in cells per microliter, exacerbations refer to the number of exacerbations per year. *Single inhaler therapy may be more convenient and effective than multiple inhalers. (© 2024, 2025, Global Initiative for Chronic Obstructive Lung Disease, available from www.goldcopd.org, published in Deer Park, IL, USA. Used with permission)

Nebulizers:

- Short-acting beta 2 (β_2) agonist (SABA): salbutamol 2.5–5 mg
- Short-acting anti-muscarinic (SAMA): ipratropium bromide 500 mic

Systemic steroid: methylprednisolone or prednisolone.

Antibiotic: in case of pneumonia, critical illness, and need of mechanical ventilation, or if two or more of the following exist:

- Increased dyspnea
- Increased sputum volume
- Increased purulence of the sputum

Interventions Which Can Improve COPD Outcomes

Multiple interventions showed improvement of survival and other favorable outcomes in COPD patients:

- Smoking cessation.
- Influenza/pneumococcal/COVID vaccinations.
- Long-term oxygen therapy (LTOT): it is indicated in patients who have partial pressure of arterial oxygen (PaO_2) < 55 mmHg or <60 mmHg with evidence of core pulmonale or secondary polycythemia.
- Noninvasive positive pressure ventilation.
- Pulmonary rehabilitation.

Acute Respiratory Distress Syndrome (ARDS)

Definition of ARDS

ARDS is an acute, diffuse, inflammatory lung injury characterized by increased pulmonary vascular permeability, hypoxemia, bilateral radiographic opacities, increased physiological dead space, and decreased lung compliance.

Pathophysiology of ARDS

ARDS has three stages:

- Exudative stage (day 1–7): it is characterized by diffuse alveolar damage (DAD) with injury to alveolar epithelium and capillary endothelium, increased vascular permeability leading to protein-rich edema in alveolar spaces and inflammatory cell infiltration (neutrophils dominate).
- Proliferative stage (day 7–21): proliferation of type II pneumocytes and fibroblast activation, with alveolar fibrin deposition.
- Fibrotic stage (>21 days): fibrosis of lung tissue and global damage to underlying lung structure.

Diagnosis of ARDS

The diagnostic criteria for ARDS have changed over time. The *Berlin* definition, published in 2012, improved diagnostic accuracy and addressed limitations of earlier definitions. The updated criteria include the following:

- Timing: acute onset of lung disease within 7 days of a known clinical insult or new/worsening respiratory symptoms.
- Origin of edema: respiratory failure not fully explained by cardiac failure or fluid overload, confirmed by echocardiography or other objective assessments if needed.
- Chest imaging: bilateral pulmonary infiltrates not fully explained by pleural effusion, lobar/lung collapse, or pulmonary nodules.
- Oxygenation ($\text{PaO}_2/\text{FiO}_2$ ratio with PEEP or CPAP ≥ 5 cmH₂O):
 - Mild: $200 < \text{PaO}_2/\text{FiO}_2 \leq 300$ mmHg
 - Moderate: $100 < \text{PaO}_2/\text{FiO}_2 \leq 200$ mmHg
 - Severe: $\text{PaO}_2/\text{FiO}_2 \leq 100$ mmHg

PaO_2 = partial pressure of arterial oxygen, FiO_2 = fraction of inspired oxygen, PEEP = positive end expiratory pressure, CPAP = continuous positive airway pressure.²²

Causes of ARDS

Causes are summarized in Table 2.8.

Investigations of ARDS

- Complete blood count (CBC): leukocytosis in bacterial infection, pancreatitis, burn. Leucopenia and/or thrombocytopenia in viral illness and certain forms of vasculitis.
- Chemistry, renal and liver function test: to rule out end organ damage or associated pathology, e.g., pulmonary renal syndrome.
- Chest X-ray or computed tomography (CT): bilateral infiltrates as required for diagnosis of ARDS.
- Electrocardiogram (ECG), cardiac enzymes, brain natriuretic peptide (BNP/pro-BNP), echocardiography: to rule out cardiogenic cause of pulmonary edema.

Table 2.8 Causes of ARDS

Pulmonary causes	Extrapulmonary causes
Pneumonia	Sepsis
Pulmonary contusion	Severe burns
Aspiration pneumonitis	Major trauma
Inhalational injury	Transfusion associated lung injury
Pulmonary vasculitis	Severe acute pancreatitis

- Blood gas: to assess hypoxemia and its severity. Other possible findings include hypercapnia and high lactate.
- Investigations for etiology: septic screen, vasculitis workup, viral serology, polymerase chain reaction (PCR) for influenza, COVID-19, etc.

Management of ARDS

As in any critical case, ARDS must be approached with ABC and management of each step accordingly.

The patient must be connected to oxygen, two large peripheral cannulas, and a monitor.

If the patient is not severely hypoxemic and does not require urgent intubation, a trial of high-concentration oxygen therapy can be initiated. Options include high flow nasal cannula (HFNC), noninvasive positive pressure ventilation (NIPPV), or non-rebreather mask. The *FLORALI trial* [1] compared the three modalities of oxygenation in patients with acute noncardiogenic respiratory failure, and it has shown better survival in HFNC use without difference in rate of intubation. If the patient has severe hypoxemia or cannot tolerate conventional oxygen therapy, intubation should not be delayed.

Isolation of patients if suspected of having viral etiology.

Treatment should target the underlying cause. Use antibiotics for community-acquired (CAP) and hospital-acquired pneumonia (HAP). Give antivirals for influenza, COVID-19, or other viral infections. Adjust therapy based on the identified causative agent and local guidelines.

The patient should follow a conservative fluid management strategy, avoiding fluid overload. Evidence from the *FACTT trial* showed this approach reduces ICU length of stay (LOS) and duration of mechanical ventilation (MV) [25].

Multiple modalities have been studied and used in ventilated patients with ARDS including ventilatory strategies, pharmacological agents and other specific interventions as outlined below:

Ventilatory Strategies

- *Lung protective strategy*: it aims to maintain a low tidal volume (TV) of approximately 6 mL/kg of ideal body weight (IBW), while avoiding high airway pressures, specifically keeping plateau pressure (Pplat) < 30 cmH₂O. The *ARDSNet trial* [5] demonstrated a significant mortality benefit with low tidal volume ventilation compared to traditional higher volumes.
- *Adjustment of PEEP*: illustrated in the section “[Mechanical Ventilation](#).”
- *Recruitment maneuver*: it has been studied as a method to improve oxygenation in ARDS. The *Kacmarek trial* [26] evaluated recruitment maneuvers combined with a decremental PEEP approach, showing improvement in oxygenation and reduction in peak inspiratory pressure (PIP). In contrast, the *ART trial* [27] compared recruitment with PEEP titration to a low PEEP strategy and found an increased mortality rate in the recruitment group. In clinical practice, recruitment maneuvers remain controversial and should be used based on individual patient characteristics and severity of ARDS.

- *Airway pressure release ventilation (APRV): APRV-ARDS meta-analysis* [28] demonstrated that this ventilation mode reduces hospital mortality, duration of mechanical ventilation, and ICU LOS. APRV also improves lung compliance, oxygenation index, and mean airway pressure (MAP) compared to low tidal volume ventilation. Details on APRV adjustment are discussed in the section “[Mechanical Ventilation](#).”
- *High frequency oscillatory ventilation (HFOV)*: Two major trials in 2013 evaluated HFOV in ARDS patients. The *OSCAR trial* [29] found no mortality benefit or improvement in ventilator-free days compared to conventional ventilation. The *OSCILLATE trial* [30] showed a higher mortality rate in the HFOV group compared to low tidal volume ventilation. Consequently, HFOV is not recommended for routine use in ARDS management.

Pharmacological Agents

- *Neuromuscular blockers (NMB)*: ventilation, lung compliance, and airway resistance may improve with paralysis of the ventilated patients. The *ACURASYS trial* [31] randomized patients with severe ARDS ($\text{PaO}_2/\text{FiO}_2$ ratio < 150 mmHg) to receive either a cisatracurium infusion or placebo for 48 h and demonstrated a 90-day mortality benefit for patients who received cisatracurium. In contrast, the *ROSE trial* [32] studied cisatracurium in patients with ARDS with a similar degree of hypoxemia but did not demonstrate any significant benefit.
- *Steroids*: they are among the pharmacological agents studied for the treatment of ARDS. Multiple trials have evaluated their role and timing. The *Meduri trial* [33] investigated methylprednisolone in early ARDS and showed improvements in pulmonary function, duration of MV, ICU LOS, and survival. The *DEXA-ARDS* [34] assessed early administration of dexamethasone (20 mg daily for 5 days, followed by 10 mg for another 5 days), demonstrating improvements in survival and MV duration. In contrast, the *LaSRS trial* [35] evaluated late administration of methylprednisolone (after >14 days of ARDS onset) and found an increased mortality rate. Based on these findings, early steroid use in ARDS may offer clinical benefits, while late administration may worsen outcomes.
- *Nitric oxide (NO)*: Inhaled NO reduces ventilation/perfusion (V/Q) mismatch by causing localized vasodilation in pulmonary capillaries adjacent to ventilated lung units. There is a transient improvement in oxygenation, although this has not been shown to translate into a reduction in mortality [36].

Other Interventions

- *Prone position*: is one of the most effective interventions that has shown improvement in mortality, oxygenation, duration of MV, and ICU stay. The *PROSEVA trial* [37] studied patients with moderate to severe ARDS ($\text{PaO}_2/\text{FiO}_2 < 150$ mmHg) who were placed in the prone position for 16 h/day and demonstrated significant results in this group.

Mechanism of prone position:

- It shifts the heart ventrally and the diaphragm caudally, these can improve the pulmonary functional residual capacity (FRC).

- Transpulmonary pressure can improve in ventral and dorsal parts of the chest as the overdistention decreases ventrally, and the collapse decreases dorsally resulting in improvement of the V/Q mismatch.

When to start prone position:

For any patient who failed to improve after starting the lung protective strategy and has moderate to severe ARDS ($\text{PaO}_2/\text{FiO}_2 < 150$ mmHg and needs $\text{PEEP} \geq 5$ cmH₂O and $\text{FiO}_2 \geq 0.6$).

How to apply prone position:

Prone positioning is typically applied for 16–20 h/day. During this period, close monitoring of oxygenation and hemodynamics is essential. Regular blood gas analysis should be performed to assess response. A minimum of four blood gas samples is recommended:

- 1 h before starting prone positioning
- 1 h after starting
- Immediately before returning to supine (de-proning)
- 4 h after de-proning

These measurements help guide assessment of the patient's response and determine the need for continued prone therapy on subsequent days.

When to stop prone position:

Prone positioning can be discontinued when the patient meets the following criteria, maintained for at least 4 h after de-proning:

- $\text{PaO}_2/\text{FiO}_2 \geq 150$ mmHg
- $\text{FiO}_2 \leq 60\%$
- $\text{PEEP} \leq 10$ cmH₂O

Another indication for stopping is prone failure, defined as no improvement in the $\text{PaO}_2/\text{FiO}_2$ ratio after two consecutive prone sessions.

Complications of prone: summarized in Table 2.9.

Contraindications of prone: summarized in Table 2.10.

- *Veno-venous extracorporeal membrane oxygenation (VV-ECMO)* [38]: VV-ECMO is considered in cases of severe ARDS, particularly for patients with a $\text{PaO}_2/\text{FiO}_2 < 80$ mmHg or a Murray score of 3–4 (see Table 2.11), who have failed maximal conventional therapy and have been mechanically ventilated for less than 7 days.

Two major trials have evaluated the role of ECMO in ARDS. The CESER trial [40] showed improved survival in patients transferred to specialized ECMO centers, compared to those managed with conventional ventilation. The EOLIA trial [41] assessed early ECMO in patients with severe ARDS, defined by at least one of the following:

Table 2.9 Complications of prone position

Nerve compression (e.g., brachial plexus injury)
Crush injury
Venous stasis (e.g., facial edema)
Dislodging endotracheal tube
Pressure sores (e.g., facial)
Dislodging vascular catheters or drainage tubes
Retinal damage
Transient reduction in arterial oxygen saturation
Vomiting
Transient arrhythmias

Table 2.10
Contraindications of prone position

Acute bleeding (e.g., hemorrhagic shock, massive hemoptysis)
Multiple fractures or trauma (e.g., unstable fractures of femur, pelvis, face)
Spinal instability
Pregnancy
Raised intracranial pressure >30 mmHg or cerebral perfusion pressure <60 mmHg
Tracheal surgery or sternotomy within 2 weeks

Table 2.11 Murray score, the final score is obtained by dividing the sum of the points by the number of the components

Parameter/score	0	1	2	3	4
PaO ₂ /FiO ₂	≥300 mmHg >40 kPa	225–299 30–40	175–224 23–30	100–174 13–23	<100 <13
CXR	Normal	1 point per quadrant infiltrated			
PEEP	<5	6–8	9–11	12–14	≥15
Compliance (mL/cmH ₂ O)	≥80	60–79	40–59	20–39	≤19

As proposed by Murray et al. [39]
CXR chest X-ray, *PEEP* positive end expiratory pressure, *PaO₂* partial pressure of arterial oxygen, *FiO₂* fraction of inspired oxygen

- PaO₂/FiO₂ < 50 mmHg for ≥3 h
- PaO₂/FiO₂ < 80 mmHg for ≥6 h
- pH < 7.25 with PaCO₂ ≥ 60 mmHg for ≥6 h

While the EOLIA trial did not show a statistically significant survival benefit, results were limited by crossover, as 28% of patients in the conventional therapy group eventually received ECMO.

A key principle of lung protection during ECMO is that gas exchange is primarily supported by the extracorporeal circuit, not the native lungs, and thus ventilator settings should be chosen to limit ventilator-induced lung injury (resting lung strategy).

Contraindications of VV-ECMO:

- End-stage organ failure, which is not amenable for recovery or transplantation, e.g., cirrhosis, chronic lung disease, and end-stage malignancy.
- Central nervous system (CNS) catastrophe, e.g., severe traumatic brain injury.
- MV >7 days with Pplat >30 cmH₂O and FiO₂ > 90%.

Causes of hypoxemia on VV-ECMO:

- Low flow rate
- Low fraction of delivered oxygen (FdO₂)
- Membrane oxygenator failure
- Recirculation: defined as post-oxygenator blood returning to the drainage cannula, typically due to a short distance (<15 cm) between the drainage and return cannulae.

Causes of hypercapnia on VV-ECMO:

- Low flow rate
- Membrane failure
- Low sweep gas flow

Weaning of VV-ECMO:

The ECMO flow can be decreased to 1–1.5 LPM/ or FdO₂/sweep gas can be weaned, patient should tolerate low sweep gas flow (<2 LPM), and the following criteria should be met:

- Oxygenation: FiO₂ ≤ 60%, PEEP ≤ 10 cmH₂O, PaO₂ ≥ 70 mmHg
- Ventilation: TV ≤ 6 mL/kg/IBW, Pplat ≤ 28 cmH₂O, respiratory rate (RR) ≤ 28 bpm, normal blood gas
- Radiology: Chest radiograph demonstrates improvement in appearance

Figure 2.47 [42] summarizes the ARDS management protocol based on the severity of the disease.

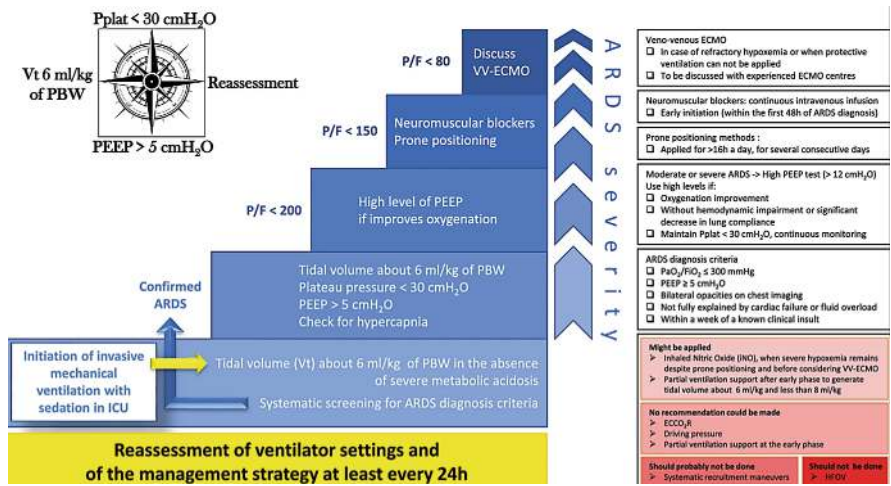


Fig. 2.47 Summary for ARDS management recommendations. ECMO = extracorporeal membrane oxygenation, PEEP = positive end expiratory pressure, PBW = predicted body weight, PaO₂ = partial pressure of arterial oxygen, FiO₂ = fraction of inspired oxygen, ECCO₂R = extracorporeal carbon dioxide removal, HFOV = high frequency oscillatory ventilation. (Sourced from: Papazian et al. [42])

Pleural Effusion

Causes of Pleural Effusion

Pleural effusion results from various pathophysiological mechanisms. Increased pulmonary capillary wedge pressure (PCWP); which raises hydrostatic pressure, and decreased oncotic pressure both lead to transudative effusion. In contrast, increased pleural permeability causes exudative effusion. Table 2.12 summarizes the causes of both types.

Pleural Fluid Analysis

Pleural fluid analysis is indicated in cases of significant effusion, typically assessed by ultrasound or lateral decubitus chest X-ray. If the effusion is >1 cm, it should be tapped.

The fluid is analyzed to determine the etiology (transudate vs. exudate), followed by specific tests to identify the exact pathology. Samples are typically sent for lactate dehydrogenase (LDH), total protein, albumin, cholesterol, glucose, pH, culture, cytology, tuberculosis polymerase chain reaction (TB-PCR), adenosine deaminase (ADA), cell count, triglycerides, brain natriuretic peptide (BNP or Pro-BNP), and amylase.

Light’s criteria are the initial approach for pleural fluid analysis, exudative effusion is diagnosed if any of the three criteria was found: (P: Pleural, S: Serum)

Table 2.12 Causes of pleural effusion

Transudate	Congestive heart failure
	Nephrotic syndrome
	Liver cirrhosis
	Pulmonary embolism (can also be exudative)
	Hypoalbuminemia (e.g., malnutrition, malabsorption)
Exudate	Infections (pneumonia, TB)
	Malignancy
	Connective tissue diseases
	Abdominal diseases (pancreatitis, esophageal rupture)
	Chylothorax

TB tuberculosis

- P LDH/S LDH > 0.6
- P total protein/S total protein > 0.5
- P LDH > 2/3 of the upper limit of normal value

Light’s criteria may have false positive exudative results in patients who are using diuretics; other criteria were added for confirmation of exudative effusion if any was found:

- P cholesterol > 55 mg/dL
- P cholesterol > 45 mg/dL + P LDH > 200 U/L
- Serum Pleural Albumen Gradient < 1.2 g/dL
- Serum Pleural Protein Gradient < 3.1 g/dL

Complicated effusion: is defined if any of the following is found:

- Positive gram stain or culture of the pleural effusion
- Empyema
- Radiological finding of loculated effusion (Fig. 2.48)
- Pleural fluid PH < 7.2
- Pleural glucose < 60 mg/dL

Disease-specific pleural fluid investigations:

Heart failure: a pleural Pro-BNP >1500 pg/mL is highly sensitive and specific.
Tuberculosis: acid fast bacilli (AFB) has <10% sensitivity, PCR has up to 50% sensitivity, pleural biopsy has 70% sensitivity, ADA <40 excludes TB and >70 highly suggests TB [43].
Malignant effusion: cytology is sensitive if an adequate sample is obtained, Glucose often <60 mg/dL.
Pancreatitis/esophageal rupture: amylase is elevated.
Rheumatoid arthritis: glucose is <60 mg/dL.

Fig. 2.48 Loculated effusion seen by ultrasound



Empyema: LDH > 1000 U/L, pH < 7.2, glucose < 60 mg/dL, culture is often positive.
 Chylothorax: triglycerides > 110 mg/dL.

Management of Pleural Effusion

Management depends on the underlying cause and the presence of symptoms.

Symptomatic patients: indicated for therapeutic thoracentesis.

Specific interventions:

- Complicated effusion: tube thoracostomy is indicated.
- Loculated effusion: tube thoracostomy, video-assisted thoracoscopic surgery (VATS), intrapleural tissue plasminogen activator (TPA) [44], or deoxyribonuclease (DNase).
- Malignancy: serial thoracentesis, tube thoracostomy, or pleurodesis depending on the clinical scenario.
- Hepatic hydrothorax: frequent thoracentesis, pleurodesis, or VATS for closure of diaphragmatic defect.

Hemoptysis

Causes of hemoptysis: Table 2.13.

Investigations in Patients with Hemoptysis

- *CBC and coagulation profile:* possible findings are leukocytosis (sepsis), leukopenia (viral or SLE), and coagulopathy.
- *Renal function, urine analysis, and microscopic exam:* to rule out acute kidney injury (AKI) related to pulmonary renal syndrome.

Table 2.13 Causes of hemoptysis

System	Examples
Pulmonary	Tuberculosis (TB), viral bronchitis, fungal infection, e.g., aspergilloma, lung cancer
Cardiac	Mitral stenosis, pulmonary embolism (PE)
Vasculitis	Goodpasture's syndrome (anti-GBM), ANCA vasculitis, systemic lupus erythematosus (SLE)
Coagulopathy	Congenital or acquired including adverse effect of the antithrombotic drugs

GBM glomerular basement membrane, *ANCA* anti-neutrophil cytoplasmic antibodies

- *Chest X-ray/CT chest*: possible findings are diffuse alveolar hemorrhage (DAH), cavitory lesion, and malignancy.
- *Electrocardiogram (ECG) and echocardiography*: to rule out cardiac causes.
- *Blood gases*: to assess the level of hypoxemia.
- *Bronchoscopy*: for diagnosis, performing bronchoalveolar lavage (BAL), obtaining biopsies, and controlling bleeding, if feasible.
- *Vasculitis workup*: ANCA-C, ANCA-P, antinuclear antibodies (ANA), complement levels (C3, C4), anti-GBM antibodies.
- *Viral workup, TB, and septic screen*: to rule out infectious causes.

Management of Hemoptysis

- As in any critical case, hemoptysis is approached with ABC and management of each step accordingly.
- Infection control:
 - Isolate the patient until infectious causes (e.g., TB) are ruled out.
 - Apply airborne/droplet precautions as appropriate.
- Supportive care:
 - Ensure adequate oxygenation and ventilation.
 - If acute respiratory distress syndrome (ARDS) develops, apply lung-protective strategies as outlined in the section “[Acute Respiratory Distress Syndrome](#).”
- Bronchoscopy:
 - Performed for diagnostic and therapeutic purposes.
 - Helps identify causes such as DAH, infection, or tumors.
 - Enables BAL, biopsy, and control of localized bleeding.
- Pharmacologic interventions:
 - Trial of inhaled tranexamic acid or epinephrine [45].
- If bleeding is massive and unilateral, consider inserting a double-lumen endotracheal tube (DLT) to isolate the affected lung (Figs. 2.49 and 2.50).
- Definitive interventions:
 - Computed tomography angiography (CTA) with embolization and/or surgical intervention in persistent or uncontrolled bleeding.

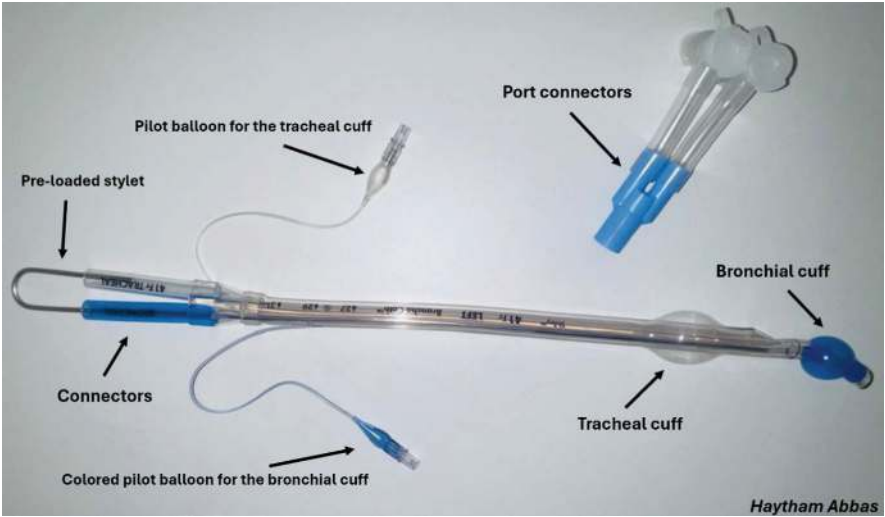
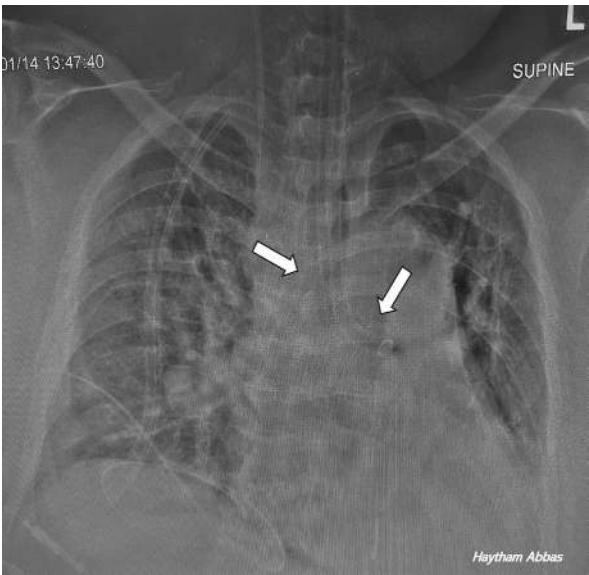


Fig. 2.49 Double-lumen endotracheal tube structures

Fig. 2.50 Double-lumen endotracheal tube in the chest X-ray



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Chapter 3

Neurology



Haytham Abbas  and Abdullah Elhosiny

Introduction

Neurology and neurocritical care is a crucial chapter with rich scientific content essential for ICU practitioners. On a daily basis, intensivists encounter neurological conditions requiring urgent intervention and a precise approach, such as ischemic stroke, intracranial hemorrhage, status epilepticus, traumatic brain injury, and delirium. Critical neurological skills, including the assessment of intracranial pressure through various modalities, must also be mastered. This chapter equips ICU practitioners with the knowledge and tools needed to manage these conditions effectively.

Intracranial Pressure (ICP) Monitoring

Introduction

The total intracranial volume is around 1400–1500 mL that is divided into three components:

- Brain parenchyma 80%
- Cerebrospinal fluid (CSF) 10%
- Blood 10%

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The *Monro-Kellie* doctrine or hypothesis states that the sum of volumes of brain, CSF, and intracerebral blood is constant. An increase in one should cause a reciprocal decrease in either one or both of the remaining two.

Indications for ICP Monitoring

- Nontraumatic: pathology that could raise the patient's ICP with Glasgow coma scale (GCS) ≤ 8 and further deterioration is expected.
- Traumatic: GCS ≤ 8 with abnormal computed tomography (CT) of the brain. If the CT is normal, two or more of the following must be present: systolic blood pressure < 90 mmHg, abnormal posturing, and age > 40 .

Methods of ICP Monitoring

Non-invasive:

- Ocular sonography for optic sheath diameter
- Measurement of intra-ocular pressure (pupillometry)
- Trans-cranial Doppler (TCD): using pulsatility index

Invasive: ICP monitoring using a microsensor placed in one of four locations:

- Intraparenchymal (least invasive)
- Intraventricular (gold standard as it allows therapeutic intervention)
- Subarachnoid
- Epidural

Assessment of ICP Waveform

For patients with a pressure microsensor or external ventricular drain (EVD), ICP can be assessed frequently using the following steps (Fig. 3.1):

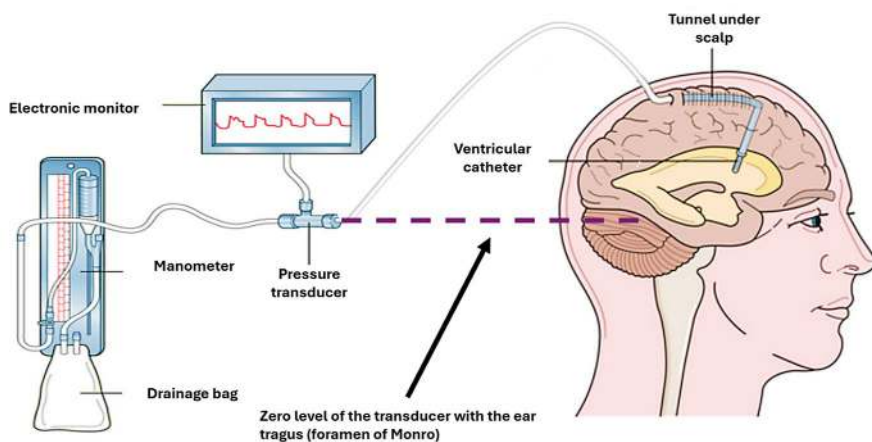


Fig. 3.1 Intracranial pressure monitoring system using ventricular catheter. (Adapted from original source: Morton and Ellenbogen [1], Neupsy Key, used with permission)

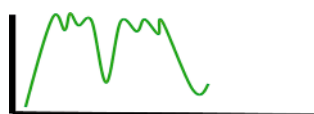
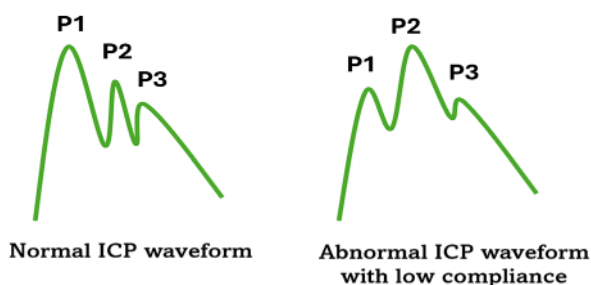
- Connect the ICP probe to a transducer.
- Level the transducer with the ear tragus, which anatomically corresponds to the foramen of Monro.
- Connect the transducer to the monitor via a pressure line.
- Open the transducer valve to atmospheric pressure, zero the ICP waveform on the monitor, then close the valve to begin ICP monitoring.

The waveform has three Ps:

- P1 is percussion wave reflects the arterial phase.
- P2 is tidal wave reflects the intracranial compliance.
- P3 is dirotic notch reflects the aortic valve closure.

Normally $P1 > P2 > P3$ and if ICP is increasing, P2 will be larger than P1 as the intracranial compliance is affected. Figures 3.2 and 3.3 show different ICP waveforms.

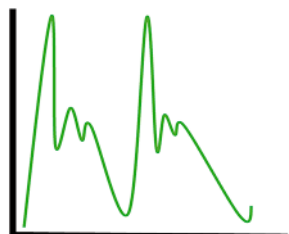
Fig. 3.2 Normal and abnormal ICP waveform related to increased intracranial pressure. ICP = intracranial pressure



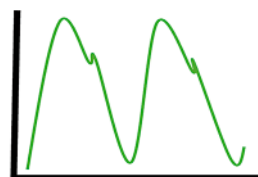
Diminished P1 due to low systolic blood pressure



Flat wave due to catheter blockage or dislodgement



Prominent P1 due to high systolic blood pressure



Rounded waveform due to critically high ICP

Fig. 3.3 Different ICP waveform morphologies related to different clinical cases. ICP = intracranial pressure

Lundberg waveforms are another method to assess ICP and include three types of waves (Fig. 3.4) [2]:

- Lundberg A (always abnormal): a sustained elevation of ICP that exceeds 20 mmHg for more than 5 min; this represents reduced cerebral compliance and increased ICP.
- Lundberg B: Brief elevations in ICP, typically up to 20 mmHg and lasting less than 5 min. These waves can appear in normal conditions but may also indicate unstable ICP. If observed, the patient should be monitored closely and assessed frequently.
- Lundberg C (always normal): rapid oscillation with pressure that does not reach 20 mmHg, it is related to cardiac and respiratory cycles.

Common Complications of Invasive ICP Monitoring

- Bleeding
- Infection
- Hydrocephalus

Assessing ICP by Ultrasound Through Optic Sheath Diameter

Using a linear ultrasound probe placed over the closed eyelid, elevated ICP can be estimated when the optic nerve sheath diameter (ONSD) exceeds 5 mm. The measurement is taken 3 mm of the lower reflection point (Figs. 3.5 and 3.6).

Fig. 3.4 Lundberg waveforms for assessment of the intracranial pressure

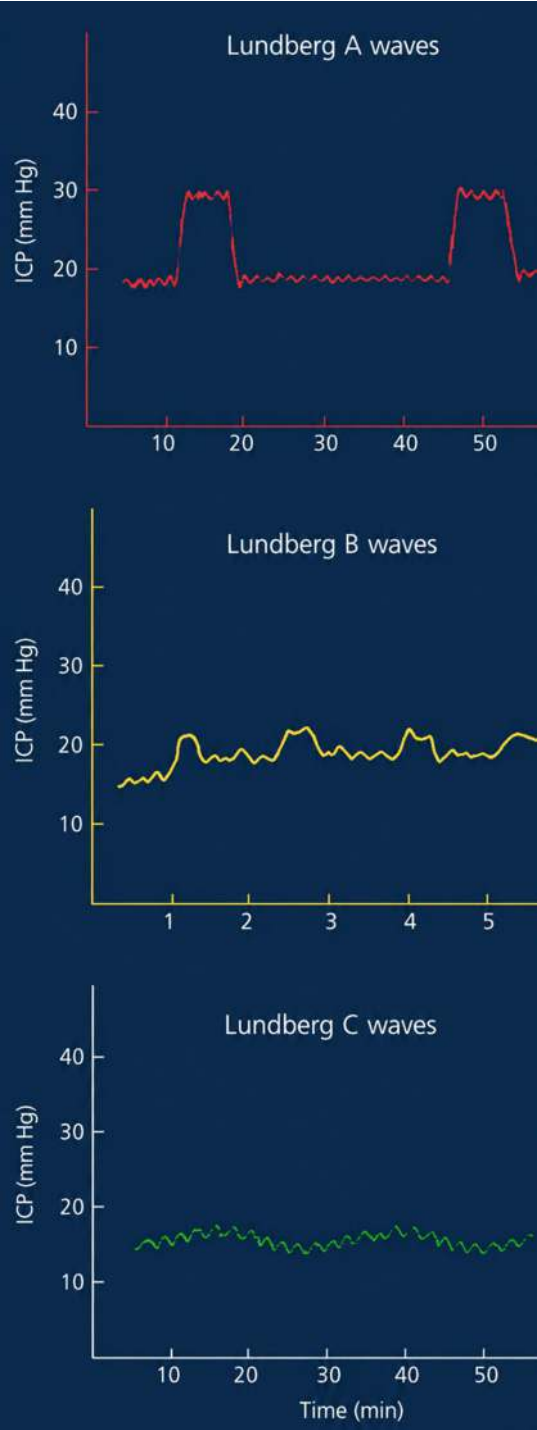
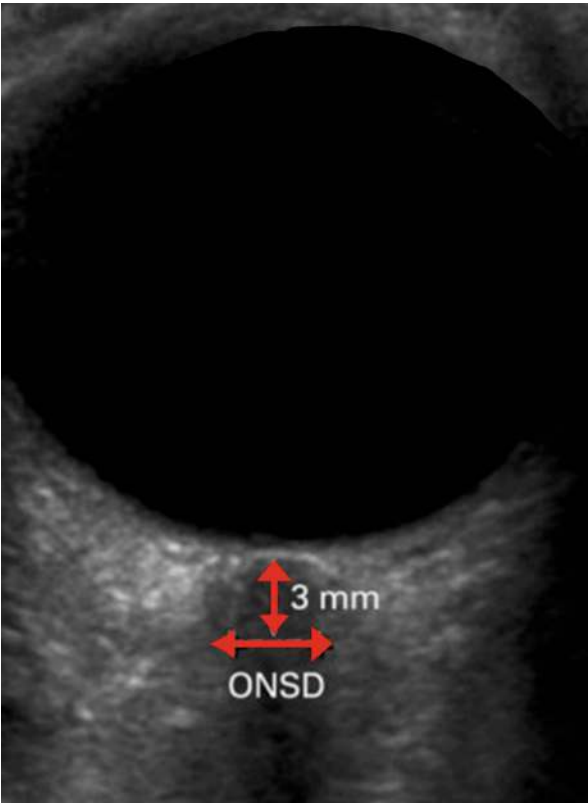


Fig. 3.5 Using the linear ultrasound probe placed over the closed eyelid to assess the intracranial pressure



Fig. 3.6 Assessment of intracranial pressure by measuring optic nerve sheath diameter (ONSD) using ultrasound



Ischemic Stroke

Clinical Manifestations of Ischemic Stroke (Table 3.1)

Investigations for Patients with Ischemic Stroke

- Electrocardiogram (ECG): assessing for ischemic changes or arrhythmia (atrial fibrillation/flutter).
- Computed tomography (CT)/magnetic resonance imaging (MRI) diffusion of the brain: to localize the site of stroke.
- CT angiography: for major artery involvement (e.g., MCA, internal carotid) and identifying candidates for mechanical thrombectomy.
- Echocardiography: to detect thrombi, vegetations, or other embolic sources.
- Carotid Doppler ultrasound: to rule out carotid stenosis.
- Diabetic and lipid profile: as risk factors for atherosclerosis.
- Complete blood count (CBC) and coagulation profile: to exclude coagulopathy before thrombolysis.

Management of Patients with Acute Ischemic Stroke

As in any critical case, acute ischemic stroke must be approached with ABC and management of each step accordingly.

In any neurocritical case, a neuroprotective strategy must be implemented. This includes the following:

- Normotension: maintain normal blood pressure, avoid hypotension to preserve cerebral perfusion pressure (CPP)
- Normocapnia: target PaCO₂ of 35–40 mmHg
- Normoxia: target SpO₂ >94%
- Normothermia: keep temperature normal; treat hyperthermia promptly
- Normoglycemia: target blood glucose 140–180 mg/dL
- Head elevation: to promote venous drainage and reduce intracranial pressure (ICP)

Table 3.1 Clinical manifestations of ischemic stroke according to the effected vessel

Site of infarction	Clinical feature
Anterior cerebral artery (ACA)	Weakness and sensory loss in the lower limbs > upper limbs, behavioral changes, and loss of inhibitory impulses on bladder (urinary incontinence)
Middle cerebral artery (MCA)	Contralateral facial weakness (CN VII), possible tongue deviation (CN XII), sensory and motor loss (upper limb > lower limb), aphasia, neglect, and homonymous hemianopia
Posterior cerebral artery	Visual field defect and blindness
Vertebro-basilar	Ophthalmoplegia, pseudo-bulbar symptoms (dysarthria, dysphagia, etc.), and ataxia
Cerebral vein thrombosis	Headache and altered mental status

CN cranial nerve

If SpO₂ <94%, provide oxygen. Attach the patient to a monitor and insert two large-bore peripheral cannulas for investigations and treatment.

Hypertension is treated only if the blood pressure exceeds 220/120 mmHg, or 185/110 mmHg in patients eligible for thrombolytic therapy. Blood pressure should be maintained below 180/105 mmHg for at least the first 24 h after thrombolytic therapy. It should also be maintained at ≤180/105 mmHg during mechanical thrombectomy and for 24 h afterward.

On emergency arrival, management must be time-targeted following the advanced cardiac life support (ACLS) protocol as following [3]:

- 10 min: stabilization and general assessment.
- 20–25 min: neurological assessment (history, focal deficits, thrombolysis contra-indications) and clinical exam, followed by transfer for CT brain.
- 45 min: obtain CT brain results and confirm ischemic stroke diagnosis.
- 60 min: initiate thrombolytic therapy if no contraindications.

Thrombolysis [4]

Thrombolysis should be provided for reperfusion in any patient with a disabling ischemic stroke who presents within the therapeutic window and has no contraindications to treatment. Table 3.2 summarizes the contraindications to tissue plasminogen activator (tPA).

The therapeutic window for disabling ischemic stroke is up to 4.5 h, regardless of the National Institutes of Health Stroke Scale (NIHSS) score. This window may be extended in patients with stroke of unknown onset or in those presenting 4.5–9 h

Table 3.2 Contraindications to the use of intravenous tPA for acute ischemic stroke

Ischemic stroke within the past 3 months
Severe head trauma within the past 3 months
Intracranial or intraspinal surgery within the past 3 months
History of intracranial hemorrhage
Intra-axial intracranial neoplasm
GI malignancy
GI bleeding in the last 21 days
Active internal bleeding
Coagulopathy defined as platelets <100,000 platelets/ μ L, INR >1.7, aPTT >40 s, or PT >15 s
Full treatment dose of LMWH in the previous 24 h
Use of Factor Xa inhibitors and direct thrombin inhibitors in the previous 48 h
Aortic arch dissection
Clinical presentation of infective endocarditis
CT brain showing intracranial hemorrhage or extensive hypodensity suggesting irreversible injury

Powers et al. [5]

aPTT activated partial thromboplastin time, *CT* computed tomography, *GI* gastrointestinal, *INR* international normalized ratio, *LMWH* low-molecular-weight heparin, *PT* prothrombin time

from onset, based on advanced imaging criteria (e.g., diffusion-weighted imaging–fluid-attenuated inversion recovery mismatch or perfusion-based mismatch).

The choices of thrombolytic therapy include the following:

- Alteplase: administered at a dose of 0.9 mg/kg intravenously, with 10% given as an initial bolus over 1 min and the remaining dose infused over 60 min. The total dose should not exceed 90 mg.
- Tenecteplase: administered at a dose of 0.25 mg/kg intravenously as a single bolus, with a maximum dose of 25 mg.

Thrombolysis has been supported by multiple clinical trials, including the following:

The *NINDS trial* [6] evaluated alteplase administration within 3 h of ischemic stroke and showed improved neurological outcomes, despite an increased risk of minor bleeding and intracranial hemorrhage (ICH).

The *ECASS III trial* [7] evaluated alteplase administration between 3 and 4.5 h after stroke onset (excluding patients with a prior history of stroke and diabetes mellitus, NIHSS score >25, or age >80 years) and showed favorable neurological outcomes, with an increased risk of ICH.

The *TRACE III trial* [8] evaluated tenecteplase administration in patients with stroke onset 4.5–24 h who cannot receive endovascular thrombectomy and have specific CT/MRI criteria and showed reduction in the risk of long-term disability with a numerical increase in the risk of symptomatic intracranial hemorrhage.

Mechanical Thrombectomy

In patients with proximal large-vessel occlusion (e.g., proximal MCA or internal carotid artery), mechanical thrombectomy can be used as a reperfusion therapy and is indicated within up to 24 h of symptom onset. It can also be considered in patients with basilar artery occlusion presenting within 24 h of symptom onset and have a NIHSS score ≥ 10 [4]. Mechanical thrombectomy has been supported by multiple clinical trials including the following:

The *MR CLEAN trial* [9] evaluated mechanical thrombectomy within 6 h after alteplase administration and demonstrated improved neurological outcomes compared to alteplase alone.

The *DEFUSE-3 trial* [10] evaluated thrombectomy 6–16 h after stroke onset and showed favorable neurological outcomes.

The *DAWN trial* [11] extended the window to 6–24 h and also demonstrated positive results.

Decompressive Craniotomy

Indicated in malignant MCA infarction with cytotoxic brain edema, when the following criteria are met:

- Presentation within 48 h of stroke onset
- Patient's age <60 years
- >50% of MCA territory on the CT is affected

Three trials, *DESTINY*, *DECIMAL*, and *HAMLET* [12], evaluated decompressive craniectomy in patients with malignant MCA infarction. The inclusion criteria included age <60 years and presentation within 48 h of symptom onset. The procedure was associated with improved survival and functional outcomes.

Post-Stroke Medical Management

- *Antiplatelets*: single or dual therapy depending on stroke size; initiated 24 h after thrombolysis.
- *Statin*: high intensity statin (e.g., atorvastatin 80 mg daily).
- *Venous thromboembolism (VTE) prophylaxis*: should not be started within the first 24 h after thrombolytic therapy.
- *Therapeutic anticoagulant*: indicated in specific conditions:
 - Atrial fibrillation or flutter
 - Cardiac thrombi
 - Thrombophilia
 - Bridging therapy in carotid endarterectomy

In cases of large infarcts or hemorrhagic transformation, anticoagulation should be delayed for 14 days to reduce the risk of bleeding.

Intracranial Hemorrhage (ICH)

Causes and Sites of ICH

The most common cause of ICH is uncontrolled hypertension. Hypertensive bleeding sites are as follows:

- Putamen (portion of basal ganglia)
- Thalamus
- Pons
- Cerebellum

Other causes include trauma, vasculitis, amyloidosis, vascular malformation, and coagulopathy.

Investigations of Patients with ICH

- Complete blood count (CBC) and coagulation profile: identify and correct coagulopathy.
- Blood gas: assess and maintain normoxia and normocapnia.
- Toxicology screen: especially in young patients with drug use history.
- CT brain: identifies hematoma site and size.

- CT angiography: excludes vascular malformation, especially in young patients without risk factors (e.g., sympathomimetic use).
- Digital subtraction angiography (DSA): detects suspected vascular malformations and may have therapeutic role.

Management of ICH

As in any critical case, ICH is approached with ABC and management of each step accordingly.

Neuroprotective strategy: maintain normotension, normocapnia, normoxia, normothermia, normoglycemia, and head elevation (details in the section “[Ischemic Stroke](#)”).

ICH management is mostly conservative and rarely needs surgical intervention.

The management should focus on blood pressure (BP) control and coagulopathy correction.

Hypertension management:

- Target systolic blood pressure (SBP) >130 to <140 mmHg.
- If SBP >150 mmHg, initiate intravenous (IV) antihypertensives (e.g., labetalol, nicardipine) for rapid BP control.
- Multiple trials have evaluated target blood pressure in ICH and its impact on neurological outcomes. The *INTERACT2 trial* showed that targeting SBP <140 mmHg resulted in improved neurological outcomes compared to <180 mmHg [13]. The *ATACH-2 trial* showed that targeting SBP of 129 mmHg has no significant benefit over 141 mmHg and was associated with increased renal adverse events [14].

Correction of coagulopathy:

- Target platelets $>100 \times 10^9/L$, and international normalized ratio (INR) <1.4.
- Anticoagulation reversal should be initiated based on the type of anticoagulant used (Table 3.3).

Surgical evacuation of the hematoma:

- Usually, surgical intervention is not required in ICH and depends on the hematoma's size and location.
- Surgery is classically indicated in cerebellar hemorrhage >3 cm with clinical deterioration, brain stem compression, or obstructive hydrocephalus.
- The *STICH I and II trials* evaluated surgical evacuation in spontaneous ICH and found no significant benefit in survival or neurological outcomes compared to conservative management [15, 16].

Table 3.3 Anticoagulation agents with their recommended antidotes

Anticoagulant	Antidote
Heparin	Protamine sulphate 1 mg for every 100 units of heparin
Enoxaparin	Andexanet Or Protamine sulphate
Dabigatran	Idarucizumab 5 gm
Rivaroxaban	Andexanet
Edoxaban	Or
Apixaban	4 factors prothrombin complex concentrate (PCC)
Warfarin	4 factors PCC + IV vitamin K 10 mg

IV intravenous

Subarachnoid Hemorrhage (SAH)

Causes of SAH

There are multiple causes of SAH which include the following:

- Intracranial aneurysm: it is the etiology of 80–85% of SAH cases and the most common sites are as follows:
 - Anterior cerebral artery (ACA)/and anterior communicating artery (30–40%)
 - Middle cerebral artery (MCA) bifurcation (20–25%)
 - Posterior communicating artery (20%)
 - Basilar artery bifurcation (5–15%)
- Arteriovenous (A-V) malformation
- Trauma

Clinical Manifestations of SAH

The classical presentation of SAH is thunderclap headache, defined as a sudden, severe headache reaching the peak within 1 min. The differential diagnosis of thunderclap headache is summarized in Table 3.4.

Other manifestations include vomiting, photophobia, altered mental status, seizure, and focal deficit.

Two common grading systems are used for clinical assessment of SAH, Hunt and Hess, and World Federation of Neurosurgeons (Table 3.5).

Investigations of SAH

- Electrocardiogram (ECG), cardiac enzymes, echocardiography: assess cardiac complications post-SAH.
- Complete blood count (CBC), electrolytes (e.g., sodium and glucose): detect anemia and metabolic disturbances.
- Chest X-ray, blood gas: evaluate for pulmonary complications post SAH, maintain normoxia and normocapnia.

Table 3.4 Causes of thunderclap headache

Sub-arachnoid hemorrhage (SAH) due to ruptured aneurysm
Reversible cerebral vasoconstriction syndromes (RCVS)
Cerebral venous thrombosis
Cervical artery dissection
Infections: meningoen­cephalitis, complicated sinusitis
Intracerebral hemorrhage
Posterior reversible encephalopathy syndrome
Pituitary apoplexy

Table 3.5 World Federation of Neurosurgeons and Hunt and Hess grading systems in SAH

Grade	World Federation of Neurosurgeons	Hunt and Hess
1	GCS 15 No motor deficit	Asymptomatic, minimal headache, slight nuchal rigidity
2	GCS 13–14 No motor deficit	Moderate-severe headache, nuchal rigidity, only cranial nerve palsy, no other deficits
3	GCS 13–14 With motor deficit	Drowsiness, confusion, mild neurological deficit
4	GCS 7–12 +/- motor deficit	Stupor, moderate-severe hemiparesis, early decerebrate rigidity, and vegetative disturbance
5	GCS ≤6 +/- motor deficit	Deep coma, decerebrate, rigidity, moribund appearance

Adapted from Hunt and Hess [17] and WFNS Committee Report [18]
GCS Glasgow coma scale

- Computed tomography (CT) of the brain: the diagnosis of choice in SAH; >93% sensitivity in the first 24 h (Fig. 3.7). Also used to grade vasospasm risk via Modified Fisher Scale (Table 3.6).
- Lumbar puncture: xanthochromia may occur 12 h after the insult, indicated when CT brain is normal, but SAH is still suspected.
- CT angiography: identifies aneurysm, defines location, and detects complications like vasospasm.
- Cerebral angiography: digital subtraction cerebral angiography (DSA) is gold standard for aneurysm detection and vasospasm assessment. It also offers therapeutic options.
- Transcranial Doppler (TCD): monitors vasospasm. Diagnostic if:
 - Mean flow velocity (MFV) >120 cm/s
 - Increased velocity for >50%
 - Lindegaard ratio of >3; ratio of mean flow velocities in middle cerebral artery and internal carotid artery (MCA/ICA) (Table 3.7).

Fig. 3.7 CT image showing diffuse subarachnoid hemorrhage



Table 3.6 Modified Fisher Scale, the higher grade the higher risk of vasospasm

Modified Fisher Scale	
Grade 1	Thin SAH (<1 mm) No IVH
Grade 2	Thin SAH (<1 mm) IVH present
Grade 3	Thick SAH (>1 mm) No IVH
Grade 4	Thick SAH (>1 mm) IVH present

Adapted from Frontera et al. [19]
SAH subarachnoid hemorrhage, IVH intraventricular hemorrhage

Table 3.7 Transcranial Doppler criteria for vasospasm

Severity of vasospasm	MFV cm/s	MFV ratio of MCA/ICA (Lindagaard ratio)
Normal	<80	<3
Mild	<120	<3
Moderate	120–150	3–5.9
Severe	150–200	>6
Critical	>200	>6

Adapted from Park et al. [20]
MCA middle cerebral artery, MFV mean flow velocity, ICA internal carotid artery

Management of SAH

As in any critical case, SAH must be approached with ABC and management of each step accordingly.

Brain protective strategy, as described in section “[Ischemic Stroke](#)”.

Target systolic blood pressure (SBP) before aneurysm securing is 140–160 mmHg. Hypotension must be avoided, and SBP should remain >110 mmHg.

Nimodipine 60 mg every 4 h for 21 days is initiated to improve survival and neurological outcomes in patients with cerebral vasospasm, as shown in the *Allen trial* [21].

Aneurysm securing can be achieved by endovascular coiling or surgical clipping. The *ISAT trial* compared both methods in patients with aneurysmal SAH and found better survival and neurological outcomes in the coiling group [22]. Surgical clipping may be preferred over coiling in the following situations:

- Wide neck to body ratio aneurysm
- MCA aneurysms or distal aneurysms

Neurological Complications of SAH

- *Rebleeding*: usually occurs in the first 72 h especially after rapid reduction of intracranial pressure (ICP), e.g., after external ventricular drainage (EVD) insertion. Posterior SAH is more likely to re-bleed compared to anterior.
- *Obstructive hydrocephalus*: usually in the first 72 h, particularly in patients with intraventricular hemorrhage (IVH) and large thickness SAH.
- *Seizure*: should be treated aggressively, but routine prophylaxis is not recommended especially phenytoin due to association with worse neurological outcomes [23].
- *Cerebral vasospasm*: it may occur after 3–4 days of the insult; the peak is after 7–10 days, and the risk remains up to 21 days. The patient should be monitored closely for sudden mental status changes. Diagnosis can be confirmed with cerebral angiography or TCD.
- Management of vasospasm:
 - Keep the blood pressure in higher normal, maintain euvolemia, and avoid hypovolemia.
 - Continue nimodipine for a total of 21 days.
 - Use inotropic support, e.g., milrinone as it can induce cerebral vasodilation [24].
 - Traditionally, triple H (hypertension, hypervolemia, and hemodilution) was used, but currently it is not recommended [25].
 - For refractory cases, balloon angioplasty or intra-arterial vasodilators administration can be tried.

Non-neurological Complications of SAH

Cardiac complications:

- Myocardial stunning with ECG changes
- Takotsubo cardiomyopathy
- Long QT interval

Respiratory complications:

- Acute respiratory distress syndrome (ARDS)
- Neurogenic pulmonary edema
- Cardiogenic pulmonary edema
- Aspiration pneumonia

NB: in ARDS, lung protective strategy should not be associated with permissive hypercapnia, as hypercapnia may worsen neurological outcomes.

Metabolic:

- Anemia
- Hyperglycemia
- Hyperthermia
- Sodium disorders:
 - Central diabetes insipidus: polyuria and hypernatremia, treated with desmopressin.
 - Cerebral salt waste: hyponatremia with hypovolemia, treated with normal saline and fludrocortisone if refractory.
 - Syndrome of inappropriate antidiuretic hormone secretion (SIADH): hyponatremia with normovolemia, symptomatic cases treated with hypertonic saline. Avoid fluid restriction as volume depletion may increase the risk of vasospasm.

Status Epilepticus (SE)

Definition and Causes of Status Epilepticus

Status epilepticus is defined as a seizure lasting more than 5 min, or recurrent episodes of seizure without regaining consciousness.

Subtypes of status epilepticus [26]:

- *Established status epilepticus*: ongoing seizure after administration of an appropriately dosed benzodiazepine.
- *Refractory status epilepticus*: persistent seizure despite benzodiazepines and an appropriately dosed non-benzodiazepine anti-seizure medication (ASM); typically fosphenytoin, valproic acid, or levetiracetam.
- *Super refractory status epilepticus*: seizure that continues for more than 24 h despite general anesthesia or recurs upon anesthetic weaning.

Causes are as follows:

- Drugs: sympathomimetics, alcohol withdrawal, and epileptogenic drugs, e.g., Imipenem.
- Infections: central nervous system (CNS) infections and systemic infections in epileptic patients.
- Metabolic: electrolyte disturbances (sodium, glucose, calcium, magnesium), uremia, and liver failure.
- CNS: new epilepsy, missed or low doses of ASM, brain insult, e.g., stroke, traumatic brain injury (TBI), and vasculitis.

Investigations of Status Epilepticus

- Complete blood count (CBC)/coagulation profile: leukocytosis in bacterial meningitis, leukopenia in viral encephalitis, coagulopathy causing intracranial hemorrhage (ICH).
- Renal, liver, electrolytes: to exclude metabolic causes.
- Toxicology screen and ASM serum level.
- Chest X-ray: to exclude aspiration post seizure.
- Computed tomography (CT) of brain: to exclude acute CNS insult.
- Electroencephalogram (EEG): for confirmation of epileptic activities.
- Lumbar puncture: if CNS infection or vasculitis is suspected.

Management of Status Epilepticus

As in any critical case, status epilepticus must be approached with ABC and management of each step accordingly.

The airway must be protected by placing the patient in the lateral position and using an oropharyngeal airway to prevent tongue bite.

Administer 100% oxygen, attach to a monitor, and insert two large-bore intravenous (IV) cannulas.

Extract random blood sugar, CBC, basic metabolic profile, toxicology, and ASM level.

Arrange for CT brain when seizure is controlled.

If the patient is hypoglycemic, administer 50% dextrose and add thiamine (100 mg IV) to prevent Wernicke encephalopathy.

Initiate IV benzodiazepine. If IV access is not available, use alternative routes as outlined in Fig. 3.8.

The *RAMPART trial* demonstrated that intramuscular (IM) midazolam is more effective than attempting IV access for lorazepam in terminating seizures during pre-hospital status epilepticus [27].

If the seizure continues, start a non-benzodiazepine ASM such as fosphenytoin, levetiracetam, or valproic acid.

If the seizure continues despite one or two doses of benzodiazepine and one or two non-benzodiazepine ASM, initiate rapid sequence intubation (RSI), general anesthesia, continuous EEG monitoring, and urgent neurology consultation (Fig. 3.8).

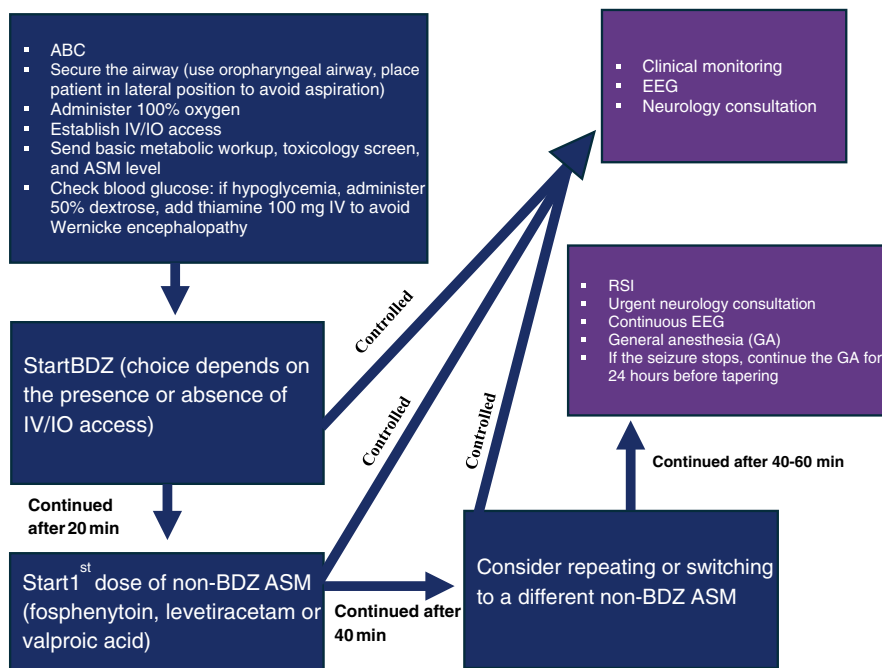


Fig. 3.8 Management of status epilepticus. IV = intravenous, IO = intraosseous, ASM = antiseizure medications, BDZ = benzodiazepine, RSI = rapid sequence intubation, EEG = electroencephalogram. BDZ with IV/IO access: lorazepam 0.1 mg/kg, maximum 2 mg/min and 4 mg/dose. Diazepam 0.2 mg/kg, maximum 5 mg/min and 10 mg/dose (doses may be repeated once). BDZ with no IV/IO access: midazolam 10 mg intramuscular, diazepam rectal or intranasal 0.2 mg/kg maximum 20 mg. Non-BDZ ASM: fosphenytoin 20 mg/kg, maximum 150 mg/min and 1500 mg/dose. Valproic acid 40 mg/kg, maximum 10 mg/kg/min and 3000 mg/dose. Levetiracetam 60 mg/kg over 15 min and maximum of 4500 mg/dose (all are given as a single dose). General anesthesia (GA) for refractory status epilepticus: midazolam 0.2 mg/kg bolus with infusion of 0.1–3 mg/kg/h, propofol 1–2 mg/kg bolus with infusion of 20–200 mcg/kg/min, phenobarbital: 5 mg/kg bolus, followed by 1–5 mg/kg/h. Adapted from: Glauser et al. [66]

Other ASMs may be used in SE, though they are not routinely recommended due to limited evidence or potential adverse effects. Lacosamide (200–400 mg IV) is generally well tolerated and may have comparable efficacy to other ASMs in treating SE [28, 29].

However, it has rare but serious adverse events including second-degree and complete atrioventricular (AV) block. An electrocardiogram (ECG) should be obtained prior to initiation and during maintenance therapy to monitor for PR interval prolongation.

If the seizure is controlled with a general anesthetic agent, it should be gradually weaned after 24 h to prevent relapse. Burst suppression also can be considered.

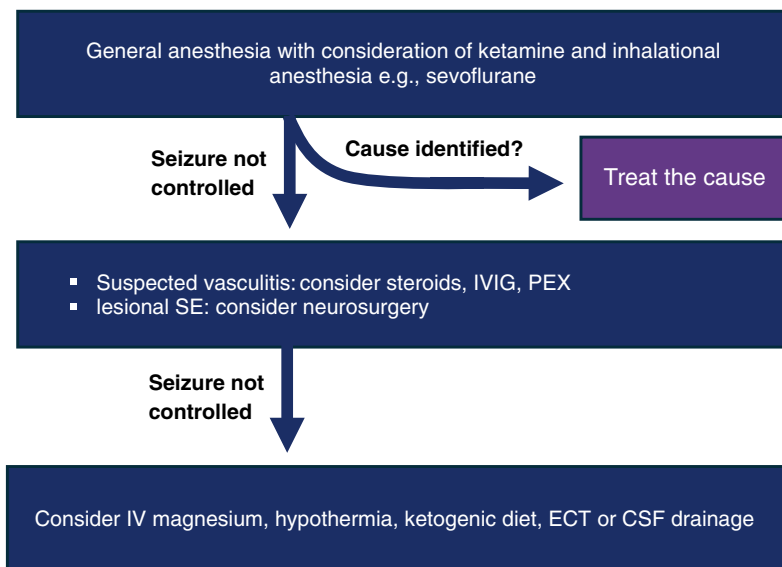


Fig. 3.9 Management of super-refractory SE. PEX = plasma exchange, IVIG = intravenous immunoglobulin, SE = status epilepticus, ECT = electro-convulsive therapy, CSF = cerebrospinal fluid. (Adapted from: Shorvon and Ferlisi [30])

If seizures persist beyond 24 h despite general anesthesia and trials of multiple anesthetic infusions, the patient is considered to have super-refractory status epilepticus, and appropriate management should be initiated (Fig. 3.9). Management often begins with ketamine, an N-methyl-D-aspartate (NMDA) receptor antagonist.

Other agents such as sevoflurane (inhalational anesthesia) may also be considered.

In suspected autoimmune or vasculitic causes, initiate pulse steroids, plasma exchange, and/or intravenous immunoglobulin (IVIG).

Additional options include the following:

- Magnesium sulfate infusion
- Focal resection neurosurgery
- Cerebrospinal fluid (CSF) drainage
- Therapeutic hypothermia
- Ketogenic diet

Analgesia Sedation and Delirium

ICU patients are at high risk for pain, agitation, and delirium. Therefore, each facility must implement a clear protocol to manage these conditions. The primary goal is to ensure comfort and control pain and agitation without causing over-sedation.

Assessment of Pain

Different tools are used to assess pain, depending on whether the patient is awake or sedated.

Two common tools are used for awake patients:

- Numerical rating scale (0 indicates no pain, 10 indicates worst pain ever).
- Wong-Baker visual scale depends on facial expression, smiling face indicates no pain, crying indicates worst pain (Fig. 3.10).

For sedated patients, pain is assessed using scales such as:

- Behavioral pain scale (BPS), which evaluates three factors: facial expression, upper limb movements, and compliance with the mechanical ventilator (Table 3.8). A total score of 3 indicates no pain, while 12 indicates severe pain.
- Critical care pain observation tool (CPOT) is another scale which assesses four domains: facial expression, movements, muscle tension, and ventilator compliance.

Management of Pain

- *Nonpharmacological strategies*: involve simple interventions such as adjusting the patient's position, eliminating potential sources of physical discomfort (e.g., tubes or lines causing irritation), and applying thermal therapy like warm or cold compresses.
- *Pharmacological agents*: are essential, especially in ICU patients who often experience severe pain due to invasive lines and procedures. Analgesics are mandatory in such cases. The most commonly used agents are opioids (Table 3.9). Other analgesics include non-opioid options such as paracetamol, ketamine, regional analgesia (e.g., peripheral nerve block) and medications used for neurogenic pain (e.g., gabapentin).
- *Dosing strategy*: Intermittent boluses are typically used. However, if more than three boluses per hour are required, consider switching to a continuous infusion.



Fig. 3.10 Wong-Baker faces pain rating scale

Table 3.8 Behavioral Pain Scale

Item	Description	Score
Facial expression	Relaxed	+1
	Partially tightened (e.g., brow lowering)	+2
	Fully tightened (e.g., eyelid closing)	+3
	Grimacing	+4
Upper limb movements	No movement	+1
	Partially bent	+2
	Fully bent with finger flexion	+3
	Permanently retracted	+4
Compliance with mechanical ventilation	Tolerating movement	+1
	Coughing but tolerating ventilation for most of the time	+2
	Fighting ventilator	+3
	Unable to control ventilation	+4
Total score		3–12

Sourced from: Payen et al. [31]

Table 3.9 Types of opioids commonly used in ICU

Opioid	Dose	Duration of analgesia	Half-life	Comments
Fentanyl	50–100 mcg IV boluses 50–200 mcg/h IV infusion	30–60 min	2–4 h	100× potency > morphine No active metabolites
Morphine	10–15 mg orally every 3–4 h 2–5 mg IV boluses every 3–4 h	3–5 h	2–4 h	Active metabolites which accumulate in renal or hepatic dysfunction Histamine release
Hydromorphone	1–3 mg orally every 3–4 h 0.2–0.5 mg IV boluses every 3–4 h 0.5–2 mg/h IV infusion	3–4 h	2–3 h	10× potency > morphine Reduce dose in renal impairment
Remifentanyl	1 mcg/kg IV bolus followed by 0.05–0.2 mcg/kg/min	5–10 min	3–10 min	Ultrashort half life
Tramadol	50–100 mg orally every 4–6 h	4–6 h	6–9 h	Reduce the dose in renal and hepatic impairments

Assessment for Agitation

Multiple scales are used to assess agitation; one commonly used tool is the Richmond Agitation-Sedation Scale (RASS) (Table 3.10).

Control of Sedation

- Analgesia alone may control agitation.
- If sedation is needed, start with boluses.
- If >3 boluses/hour are required, consider continuous infusion.
- Titrate dose to maintain appropriate sedation (e.g., RASS = 0; avoid over/under-sedation).
- Bispectral Index (BIS) is an alternative tool to assess sedation depth (Fig. 3.11) [33].
- Perform daily sedation vacations which had shown to reduce ventilation duration [34] and is part of the ventilator-associated pneumonia (VAP) prevention bundle.

Common sedative agents used in ICU are summarized in Table 3.11.

Multiple trials have compared the effects of various sedative agents:

- The *MENDS trial* found that dexmedetomidine resulted in more coma-free days compared to lorazepam, but with a higher incidence of bradycardia [35].
- The *SEDCOM trial* compared dexmedetomidine to midazolam, showing similar levels of sedation, but midazolam was associated with a higher rate of delirium [36].
- The *MENDS2 trial* compared dexmedetomidine with propofol and found no significant difference in the rate of delirium or coma duration [37].
- The *PRODEX/MEDEX trial* compared dexmedetomidine with both midazolam and propofol. Dexmedetomidine resulted in more coma-free days but was associated with more hypotension and bradycardia compared to midazolam. There was no difference between dexmedetomidine and propofol in terms of sedation levels or duration of mechanical ventilation (MV) [38].

Table 3.10 Richmond agitation-sedation scale (RASS)

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

Sourced from: Sessler et al. [32]. Used with permission from Virginia Commonwealth University

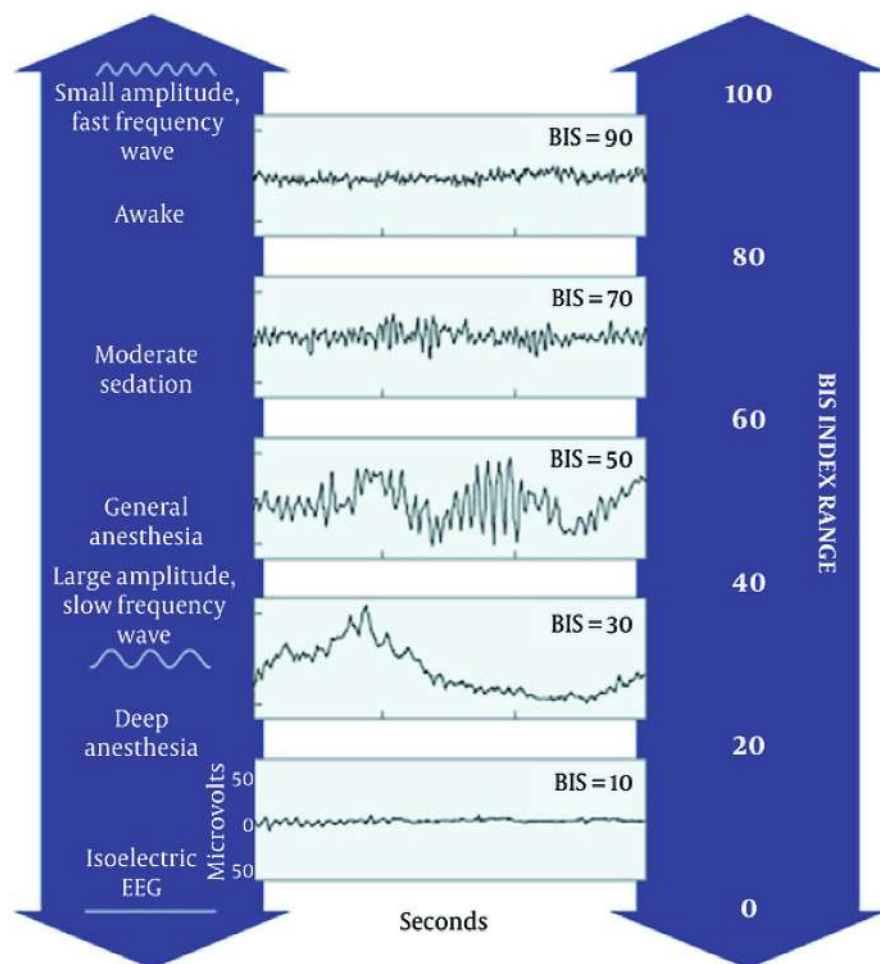


Fig. 3.11 Bispectral Index (BIS). (Sourced from Yousefi-Banaem et al. [33])

Definition, Types, and Risk Factors for Delirium

- Delirium is defined as acute confusional status over a short duration.
- Types of delirium: hyperactive (19–26%), hypoactive (46–54%), and mixed type (24–31%) [39].
- Risk factors:
 - Patient factors: old age, comorbidities, baseline cognitive dysfunction, alcoholism.
 - Acute illness factors: sepsis, shock, metabolic dysfunction, hypoxia.
 - Iatrogenic: disturbed sleep pattern, sedation (benzodiazepine), invasive lines.

Table 3.11 Types of sedative agents commonly used in ICU

Drug	Mechanism of action	Half life	Comment
Propofol	Gamma-aminobutyric acid (GABA)- α agonist	40 min	Side effects: hypotension, respiratory depression, green urine, propofol infusion syndrome (bradycardia, ST changes, lactic acidosis, rhabdomyolysis).
Dexmedetomidine	α 2 agonist	2–3 h	It has an analgesic effect, does not cause respiratory depression (used for weaning and in agitation). Side effects: hypotension and bradycardia.
Ketamine	N-methyl-D-aspartate (NMDA) receptor blocker	20 min	Bronchodilator, used in status epilepticus, does not cause hypotension and it has an analgesic effect. Side effects: demand ischemia with hypertension and tachycardia, may increase intracranial pressure and intra-ocular pressure.
Midazolam	GABA- α agonist	2–6 h	Side effects: delirium and respiratory depression.
Lorazepam	GABA- α agonist	14–18 h	Side effects: delirium, at high dose it might cause propylene glycol toxicity with increased risk of high anion gap metabolic acidosis.

α alpha

Diagnosis of Delirium

Delirium is diagnosed by the confusion assessment method for the intensive care unit (CAM-ICU) approach (Fig. 3.12).

Management of Delirium

- *Nonpharmacological:*
Sleep hygiene, hearing and vision aids, removal of unnecessary lines, early mobilization, and family support.
- *Pharmacological:*
No medication has been proven effective for all subtypes of delirium.
- *For hyperactive delirium:*
 - *Dexmedetomidine* can decrease the risk of delirium.
 - *Antipsychotics* (e.g., haloperidol, quetiapine, olanzapine, and risperidone) are dopamine receptor blockers. Adverse effects include long QT interval, neuroleptic malignant syndrome (NMS), and extrapyramidal manifestations.
 - Benzodiazepine for alcohol withdrawal.

Figures 3.13 and 3.14 summarize analgesia, sedation, and delirium approaches.

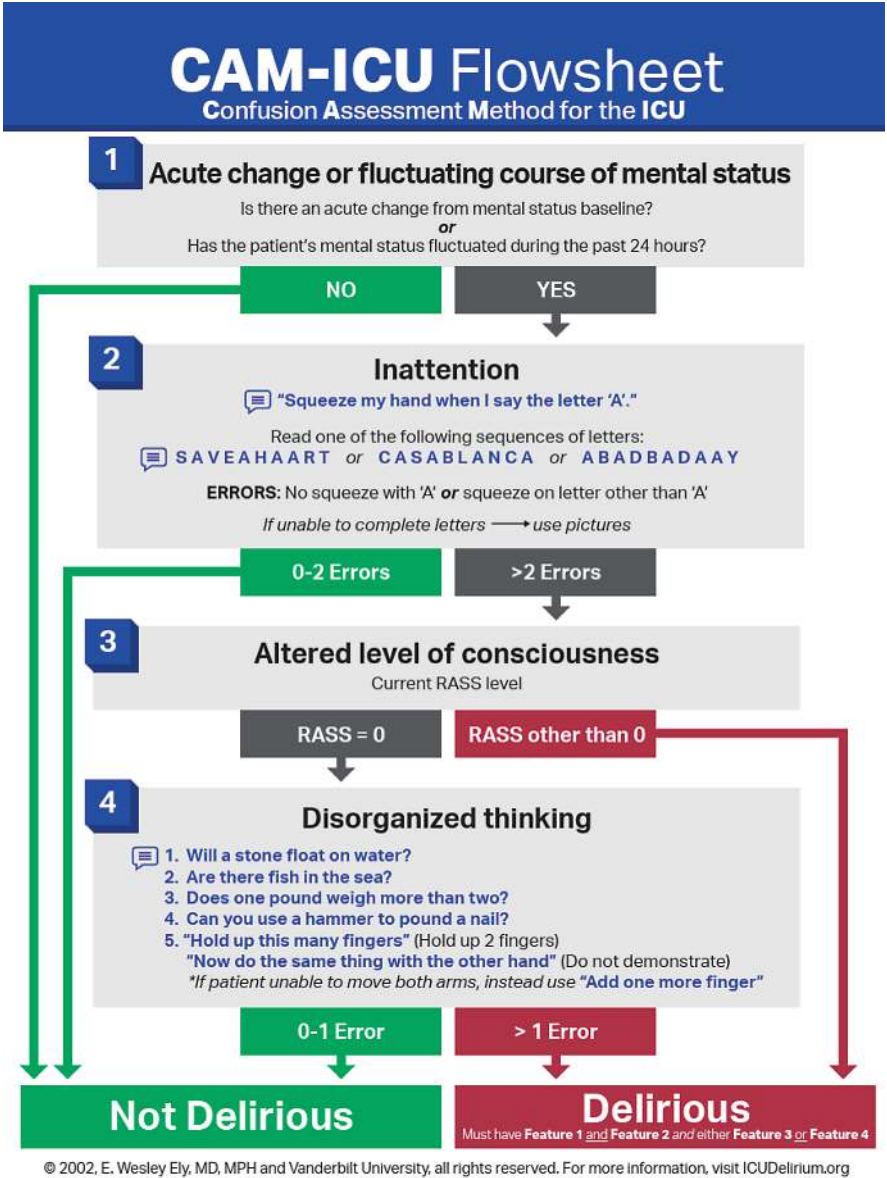


Fig. 3.12 CAM-ICU approach. (Used with permission)

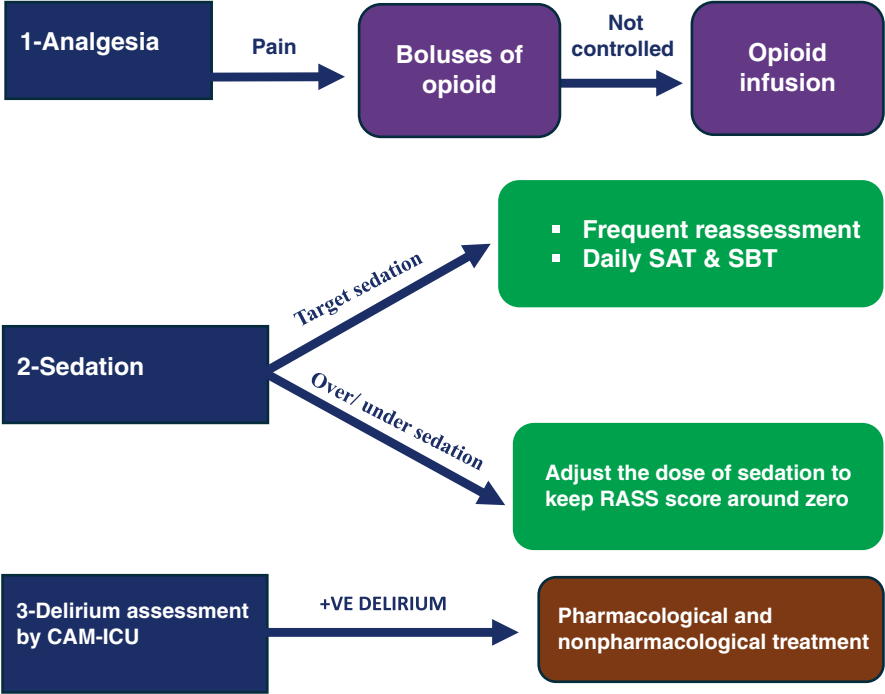


Fig. 3.13 Summary for the approach to analgesia, sedation, and delirium. SAT = spontaneous awaking trial, SBT = spontaneous breathing trial

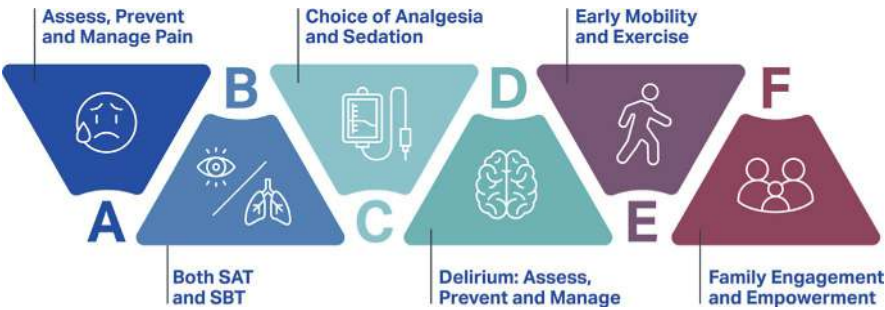


Fig. 3.14 ABCDEF bundle for analgesia, sedation, and delirium. SAT = spontaneous awaking trial, SBT = spontaneous breathing trial. (Sourced from [ICUDelirium.org](https://www.icudelirium.org). Mart et al. [40]. Used with permission)

Alcohol Withdrawal

Subtypes and Clinical Presentation of Alcohol Withdrawal

- *Minor withdrawal*: Occurs 6–48 h after the last alcohol intake; symptoms may include mild anxiety, tremor, sweating, headache, palpitations, poor appetite, and gastrointestinal discomfort, but mental status remains intact.
- *Withdrawal seizures*: Usually occur within 48 h after cessation, typically generalized tonic-clonic seizure.
- *Alcoholic hallucinosis*: Characterized by isolated visual hallucinations, sometimes auditory or tactile, developing 12–48 h after stopping alcohol.
- *Delirium tremens (DT)*: A severe withdrawal syndrome starting 48–96 h after the last drink, lasting up to 5–7 days. Features are disorientation, agitation, hallucinations, tachycardia, hypertension, hyperthermia, and diaphoresis.

Differential Diagnosis of Alcohol Withdrawal

Sympathomimetic toxicity, benzodiazepine/opioid withdrawal, and central nervous system (CNS) infection.

Assessment of Alcohol Withdrawal

Clinical Institute Withdrawal Assessment for Alcohol revised (CIWA-Ar) score is used for assessment and management of alcohol withdrawal (Table 3.12).

Management of Alcohol Withdrawal

As in any critical case, alcohol withdrawal is approached with ABC and management of each step accordingly.

If the patient is actively seizing, initiate status epilepticus management as outlined in the section “[Status Epilepticus \(SE\)](#)”.

Insert two large-bore cannulas, start resuscitation with crystalloid, administer thiamine before dextrose to prevent Wernicke encephalopathy, and send basic metabolic workup.

Table 3.12 CIWA-Ar score is made by giving a point for each one of the 10 components

Clinical Institute Withdrawal Assessment for Alcohol revised	
Symptoms	Range of scores
Nausea or vomiting	0 (no nausea, no vomiting)–7 (constant nausea and/or vomiting)
Tremor	0 (no tremor)–7 (severe tremors, even with arms not extended)
Paroxysmal sweats	0 (no sweat visible)–7 (drenching sweats)
Anxiety	0 (no anxiety, at ease)–7 (acute panic states)
Agitation	0 (normal activity)–7 (constantly trashes about)
Tactile disturbances	0 (none)–7 (continuous hallucinations)
Auditory disturbances	0 (not present)–7 (continuous hallucinations)
Visual disturbances	0 (not present)–7 (continuous hallucinations)
Headache	0 (not present)–7 (extremely severe)
Orientation/clouding of sensorium	0 (orientated, can do serial additions)–4 (disorientated for place and/or person)

Adapted from: Sullivan et al. [41]

Benzodiazepine: The drug of choice for DT. Start with diazepam 10–15 mg intravenous (IV) every 10–15 min or lorazepam 2–4 mg IV every 15–20 min until appropriate sedation achieved, then titrate to CIWA-Ar scale with aim of <10.

Monitoring frequency: evaluate CIWA-Ar score every 1–4 h for the first 24 h, every 4–8 h for the next 24 h then every 24 h thereafter. For CIWA-Ar score >10, administer additional benzodiazepine dose.

For refractory cases, consider intubation and starting sedative agents like phenobarbital or propofol.

Post ROSC Neurological Assessment and Brain Death

Neurological Assessment and Prognostication Post ROSC

Post-return of spontaneous circulation (ROSC) care follows the ABCD approach; “D” stands for disability, managed with targeted temperature management (TTM) for 24–48 h, as outlined in the section “[Advanced Cardiac Life Support \(ACLS\)](#)”, Chap. 1. Neurological function is then assessed to identify poor prognostic factors. Prognostic tools are applied 72 h after ROSC; these tools are illustrated in Table 3.13 and Fig. 3.15.

Definition and Assessment for Brain Death

Brain death is defined as irreversible loss of consciousness, all brain stem functions, and the capacity to breathe.

Requirements before brain death assessment:

Table 3.13 Prognosticating tools post return of spontaneous circulation (ROSC)

Tools	Detail	Comment
EEG	EEG features suggesting poor outcome ≥ 72 h post-ROSC are as follows: Absence of EEG reactivity to external stimuli Burst suppression Status epilepticus	Facilitates evaluation of consciousness in patients under sedation Detects non-convulsive status epilepticus
Blood tests	Neuron-specific enolase (NSE) S-100B	Hemolysis causes false positive result Not affected by sedatives
Imaging	MRI brain CT brain	Useful in ruling out other causes of coma They should be used only combined with the other tools
SSEPs	Bilateral absence of SSEP N20 wave ≥ 72 h suggests poor outcome	Not affected by sedatives, NMBAs, or metabolic derangement Affected by hypothermia

SSEPs somatosensory evoked potentials, *NMBAs* neuromuscular blocking agents, *EEG* electroencephalogram, *CT* computed tomography, *MRI* magnetic resonance imaging

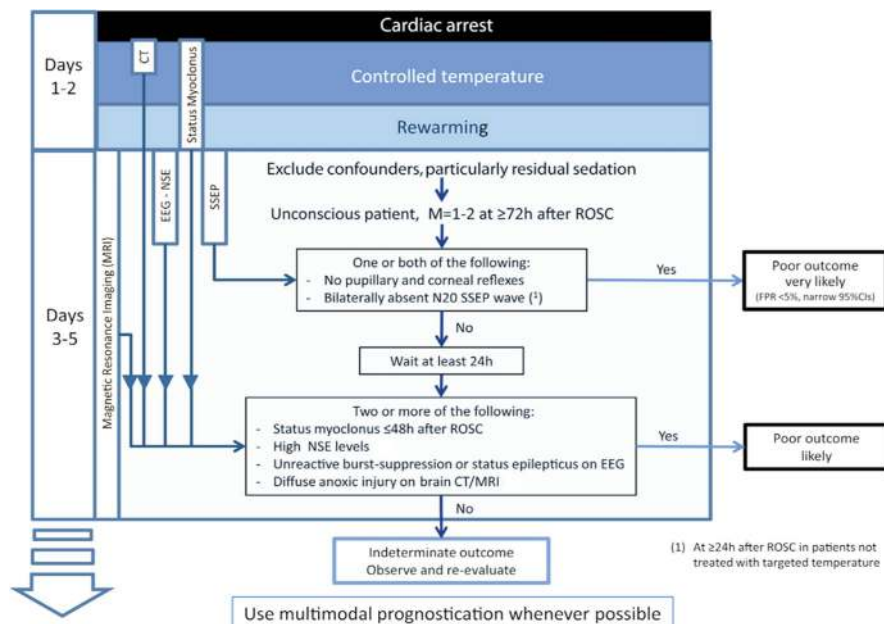


Fig. 3.15 Prognostication algorithm post ROSC [42]. (Sourced from: Sandroni et al. [43])

- Notify the organ donation committee.
- Confirm a catastrophic CNS event consistent with brain death, e.g., intracranial hemorrhage (ICH), subarachnoid hemorrhage (SAH), traumatic brain injury (TBI).
- If the patient has been sedated, all sedative agents must be discontinued for an appropriate duration.
- Exclude drug intoxication (e.g., alcohol, barbiturates); barbiturate levels should be <10 mcg/mL.
- In post-ROSC patients, wait at least 72 h before proceeding with brain death determination.
- Correct any metabolic disturbances, including acid-base imbalance, electrolyte abnormalities (sodium, glucose, calcium, magnesium), thyroid, renal, or hepatic dysfunction.
- Ensure hemodynamic stability, with systolic blood pressure >90 mmHg and core temperature >36 °C.

Once all the required conditions are met, the brain death examination can be performed and the diagnosis confirmed. The diagnosis is primarily based on the clinical examination, but ancillary tests may be used when the clinical exam cannot be fully completed or is inconclusive. In such cases, ancillary tests become mandatory. Brain death criteria include the following:

- Deep coma with Glasgow coma scale (GCS) of 3/15
- Loss of all brain stem reflexes (Table 3.14):
- Positive apnea test:

The test begins with confirming the patient's stability; core temperature must be above 36 °C, and systolic blood pressure above 90 mmHg. The patient is pre-oxygenated with 100% oxygen targeting an initial arterial blood gas with a pH of 7.35–7.45, partial pressure of arterial oxygen (PaO₂) >200 mmHg, and partial pressure of arterial carbon dioxide (PaCO₂) between 35 and 45 mmHg. Once these values are achieved, the patient is disconnected from the ventilator while receiving oxygen via a catheter or T-piece to maintain oxygenation. The patient is observed for 8–10 min for any signs of spontaneous respiratory effort. At the end of this period, a repeat arterial blood gas is obtained. The test is considered positive if no respiratory movement is observed and the PaCO₂ has increased by ≥20 mmHg from baseline or has reached ≥60 mmHg. If the patient becomes unstable during the test (e.g., hypotension, arrhythmia, or hypoxia), the procedure should be aborted and repeated later. A modified apnea test may be used in case of apnea test failure. This involves keeping the patient connected to the ventilator with oxygen delivery via continuous positive airway pressure (CPAP) or using low minute ventilation, allowing a controlled rise in PaCO₂ to the diagnostic threshold while monitoring for absence of respiratory effort [44].

- Ancillary tests for brain death confirmation are summarized in Table 3.15.

Care of organ donor: (see Table 3.16)

Table 3.14 Brain stem reflexes

Brain stem reflex	Finding	Afferent nerve supply	Efferent nerve supply
Corneal reflex	No eyelid movement in response to corneal touch by a swab	V (trigeminal)	VII (facial)
Pupillary light reflex	Fixed pupils with no constriction in response to light	II (optic)	III (oculomotor)
Gag reflex	No gag when posterior oropharynx is touched	IX (glossopharyngeal)	X (vagus)
Cough reflex	No cough in deep tracheal suction	X (vagus)	X (vagus), phrenic and intercostal nerves
Oculocephalic reflex	No eye movement with brisk lateral head movement Normally, eyes move in direction opposite to the head (doll's eyes) Contraindicated in cervical spine fracture	VIII (vestibular)	III (oculomotor) IV (trochlear) VI (abducent)
Oculovestibular reflex	No eye movement with ice-water flushing to the external auditory canal Normally, eyes move involuntarily toward the flushing side	VIII (vestibular)	III (oculomotor) IV (trochlear) VI (abducent)

Table 3.15 Ancillary tests for brain death confirmation

Tool	Comment
Electroencephalogram (EEG)	Most used modality Results are affected by metabolic derangement and drug intoxication
Somatosensory evoked potential (SSEP)	A peripheral stimulus is applied, and the response is recorded at the contralateral primary sensory cortex
Cerebral angiography	A confirmatory test reveals absence of intracerebral blood flow
Transcranial Doppler	Complete absence of flow may be unreliable if acoustic windows are inadequate
Nuclear medicine scan (cerebral blood flow scan)	Intravenous rapid bolus injection of radionuclide isotope such as Tc99m Absence of radionuclide detection in blood pools in the distribution of large vessels and brain parenchyma confirms the diagnosis

Table 3.16 Care of organ donor

<i>Lines and vital signs</i>
Monitor temperature, heart rate, rhythm, SpO ₂ , blood pressure, mean arterial pressure (MAP). Insert peripheral and central venous catheters. Insert arterial line for hemodynamic monitoring and frequent blood gas sampling. Insert urinary catheter for strict urine output monitoring. Consider insertion of PAC particularly in depressed cardiac function and/or hemodynamic instability (LVEF<45%, MAP<60 mm Hg or requiring dopamine >10 mcg/kg/min or equivalent).
<i>Investigations and targets</i>
CBC, renal function/electrolytes, liver function, blood gases, random blood sugar, ECG, chest X-ray, hormonal profile, septic screen (cultures), viral serology. Maintain serum Na >135 and <155 mEq/dl. Maintain serum K >3.5 and <5 mEq/dl. Correct metabolic and respiratory acidosis or alkalosis aiming to keep arterial pH 7.35–7.45. Maintain hemoglobin >7 g/dL and transfuse packed RBC accordingly.
<i>Hemodynamics and cardiac management</i>
Goals of hemodynamics: MAP ≥60 mmHg. CVP 6–12 mmHg. PAOP ≤12 mmHg. SVR 800–1200 dynes/s/cm ⁵ . Dopamine dosage <10 mcg/kg/min. Urine output ≥1 mL/kg/h. LVEF >45%. Maintain euvolemia: assess frequently volume status by using different modalities (e.g., PPV, SVV, CVP, PAOP) and replace fluid accordingly. Use isotonic crystalloid for resuscitation. If MAP <60 mmHg, despite achieving euvolemia, assess if shock is related to decreased SVR or cardiac output. Infuse arginine vasopressin for decreased SVR. If MAP remains <60 mmHg with LVEF >45%, add vasopressor agent (e.g., norepinephrine, phenylephrine). If MAP remains <60 mmHg with LVEF <45%, add inotropic agent (e.g., dobutamine, dopamine, epinephrine). If hemodynamic goals are not met and LVEF remains less than 45%, HRT may be required.

(continued)

Table 3.16 (continued)

<i>Pulmonary and ventilatory care</i>
Tidal volume (TV): 6–8 mL/kg of the ideal body weight.
Titrate TV and respiratory rate to keep PaCO ₂ 35–45 mmHg.
PEEP: 8–10 cm H ₂ O.
PIP <35 mmHg.
FiO ₂ : 100%, then titrate down as tolerated aiming to keep PaO ₂ 80–100 mmHg.
Early flexible bronchoscopy for inspection and airway clearance.
<i>Hormonal replacement</i>
Arginine vasopressin: start at dose of 0.01–0.04 units/min, adjust it to maintain MAP >60 mmHg and urinary output 0.5–1 mL/kg/h. It should be considered in:
Hypotension despite adequate volume resuscitation.
Presence of DI (polyuria, hypernatremia, high serum osmolarity, low urine osmolarity).
Desmopressin: for cases of DI without hypotension.
Hydrocortisone 300 mg IV/day, or methylprednisolone.
Insulin: the target blood sugar is controversial but generally:
Keep blood sugar <180 mg/dL.
Avoid the use of glucose-containing intravenous fluids.
Thyroid hormones: should be considered for hemodynamically unstable donors with LVEF <45%. Both T3 and T4 are acceptable for use as a component of replacement.
<i>General care</i>
Maintain normothermia by warmer.
Venous thromboembolism prophylaxis.
Stress ulcer prophylaxis.
Mouth and eye care.
Scheduled turning to prevent pressure sores.

Adapted from: Kotloff et al. [45], Copeland et al. [46], and Tanim Anwar and Lee [47]
SpO₂ oxygen saturation, *PAC* pulmonary artery catheter, *CBC* complete blood count, *ECG* electrocardiogram, *Na* sodium, *K* potassium, *RBC* red blood cells, *CVP* central venous pressure, *PAOP* pulmonary artery occlusion pressure, *SVR* systemic vascular resistance, *PPV* pulse pressure variation, *SVV* stroke volume variation, *LVEF* left ventricular ejection fraction, *PEEP* positive end expiratory pressure, *PIP* peak inspiratory pressure, *FiO₂* fraction of the inspired oxygen, *PaCO₂* partial pressure of arterial carbon dioxide, *PaO₂* partial pressure of arterial oxygen, *HRT* hormonal replacement therapy, *DI* diabetes insipidus, *T3* triiodothyronine, *T4* thyroxine

Traumatic Brain Injury (TBI)

TBI cases are managed according to advanced trauma life support (ATLS) guidelines for general trauma, as detailed in the Chap. 5. In this topic, our focus will be solely on TBI, with an aim to understand the appropriate care strategy and potential interventions that may be beneficial.

Investigations for TBI

- Blood gas: assess lactate, base deficit, hypoxemia, and hypercapnia; all must be corrected in TBI.
- Complete blood count (CBC) and coagulation profile: rule out coagulopathy, which may worsen hemorrhagic brain injury.

- Chemistry, renal and liver function test: exclude metabolic encephalopathy, and monitor during hyperosmolar therapy.
- Computed tomography (CT) of brain: evaluate anatomical injury during secondary survey.
- Magnetic resonance imaging (MRI) of brain: for stable patients; more sensitive than CT.
- Electroencephalogram (EEG): for seizures or suspected non-convulsive seizures.

Management of TBI [48]

As in any trauma case, TBI is approached with primary survey (ABCDE) aiming to stabilize the patients, followed by secondary survey aiming to do a full assessment.

Brain protective strategy (as detailed in section “[Ischemic Stroke](#)”) includes maintaining normoxia, normocapnia, normotension, normoglycemia, normothermia, providing deep sedation in severe intubated cases, and elevating the head unless a cervical spine fracture is suspected.

Airway management includes drug-assisted intubation for patients with severely altered mental status, such as Glasgow Coma Scale (GCS) ≤ 8 . Other indications include hypoventilation, severe hypoxia, foreign body obstruction, or profound circulatory collapse.

Breathing must be stabilized to ensure adequate oxygenation by assessing respiratory rate, signs of respiratory distress, oxygen saturation, and identifying life-threatening chest complications such as tension pneumothorax or hemothorax, which require immediate intervention.

Circulatory management includes securing two large-bore peripheral lines; sending a basic metabolic profile; initiating resuscitation with crystalloids, blood, and blood products with or without inotropic support; and aiming to maintain systolic blood pressure (SBP) >110 mmHg in patients younger than 50 or older than 69 years, and SBP >100 mmHg in those aged 50–70 years [49].

Intracranial pressure (ICP) monitoring: It must be considered in any patient with TBI who has a GCS ≤ 8 with positive CT brain findings. If the CT brain is normal, consider ICP monitoring in 2 out of 3 criteria: age >40 years, SBP <90 mmHg or motor posturing. The target is to keep ICP <20 mmHg and cerebral perfusion pressure (CPP) to be 60–70 mmHg. CPP = mean arterial pressure (MAP) – ICP.

Seizure prophylaxis: Such as phenytoin, may be used to reduce the risk of early post-traumatic seizures within the first 7 days, as supported by evidence [50].

Hyperosmolar therapy: It is used in case of vasogenic edema or high ICP.

- Hypertonic saline: can be given as either intermittent doses or continuous infusion with regular monitoring of serum sodium (Na) and osmolarity (Osm). The target serum sodium is 145–155 mmol/L; it should be discontinued when serum Na exceeds 160 mmol/L or S.Osm >320 mOsm/kg. Side effects include hypernatremia and volume overload.

- Mannitol: 0.5–1 g/kg three times daily; use with caution in renal impairment and discontinue if serum osmolality exceeds 320 mOsm/kg or osmolar gap exceeds 18 mOsm/kg.

Hyperventilation: A temporary measure used until surgical management of life-threatening neurological emergencies, aiming to keep partial pressure of arterial carbon dioxide (PaCO_2) between 28 and 35 mmHg; prolonged hyperventilation may reduce cerebral blood flow and worsen outcomes.

Decompressive craniotomy: It is indicated for persistent high ICP in severe TBI; two trials were conducted to study its effect. The *DECRA trial* showed no mortality benefit and worse neurological outcomes [51], while the *RESCUE-ICP trial* demonstrated improved survival but with poorer neurological outcomes [52].

Other indications for neurosurgical interventions are as follows:

- Epidural hematoma: surgical evacuation is indicated if the hematoma size is >3 cm with consciousness deterioration, midline shift >0.5 cm, or if located in the posterior fossa causing 4th ventricle compression.
- Sub-dural hematoma: surgical evacuation is indicated if the hematoma size is >1 cm, midline shift >0.5 cm, or with deteriorating consciousness.

Steroid: Not recommended; it was evaluated and showed increased mortality in TBI (*CRASH-I*) [53].

Tranexamic acid: It is evaluated and showed no significant clinical benefit in TBI (*CRASH-III*) [54].

Spinal Cord Injury (SCI)

Neurogenic and Spinal Shock

Neurogenic shock: a type of distributive shock characterized by the triad of hypotension, bradycardia, and hypothermia. Caused by disruption of the sympathetic chain and unopposed vagal tone, leading to decreased systemic vascular resistance (SVR).

Spinal shock: loss of all reflexes below the affected spinal level. The most sensitive one is the bulbocavernosus reflex, defined by absence of involuntary anal contraction in response to genital stimulation (Fig. 3.16).

ASIA (American Spinal Injury Association) impairment scale is a simplified scale to classify severity of SCI (Table 3.17) [55].

Spine Imaging

Spinal imaging is indicated in trauma patients who meet any one of the national emergency X radiography utilization study (NEXUS) criteria (Fig. 3.17) [56].

Fig. 3.16 The bulbocavernosus reflex examination in spinal shock. (Courtesy of Dr. Nabil Ebraheim, used with permission)

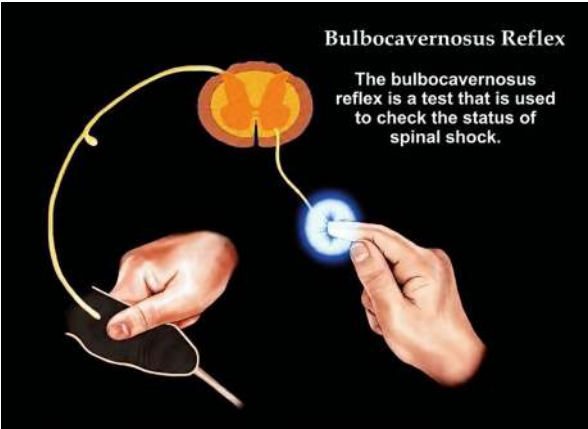


Table 3.17 The American Spinal Injury Association (ASIA) Impairment Scale to classify the severity of spinal cord injuries

A	Complete	No motor or sensory function preserved at segments S4–S5
B	Sensory incomplete	Sensory but no motor function preserved below injury level, including S4–S5
C	Motor incomplete	Some motor function preserved below injury level; more than half of muscles below level have muscle grade <3
D	Motor incomplete	Motor function preserved below injury level; at least half of muscles below level have muscle grade ≥ 3
E	Normal	Normal motor and sensory function

Management of SCI

As in any trauma case, patients with SCI are approached with primary survey followed by secondary survey as per advanced trauma life support (ATLS) recommendations [57]. In severe trauma, a cervical collar should be maintained until SCI is ruled out.

As a part of airway management and when the patient needs urgent intubation, it should be performed with the following sequence: drug-assisted induction, removal of the neck collar, in-line stabilization followed by laryngoscope-guided intubation (direct or video).

For breathing management, monitor respiratory rate (RR), forced vital capacity (FVC), and blood gases to assess for impending respiratory failure, especially in trauma at C5 level or above.

For circulatory management, insert two large-bore peripheral cannulas for sampling and drug administration, connect the patient to a cardiac monitor, and maintain hemodynamics with mean arterial pressure (MAP) >80 mmHg. If hypotensive, give 1–2 L of crystalloids and initiate vasopressors early, such as norepinephrine or dopamine if severe bradycardia is present.

Steroids were traditionally used in spinal cord injury, but are no longer recommended, as evidence from the *Bracken I, II, and III trials* showed no significant benefit and an increased risk of hospital-acquired infections [58–60].

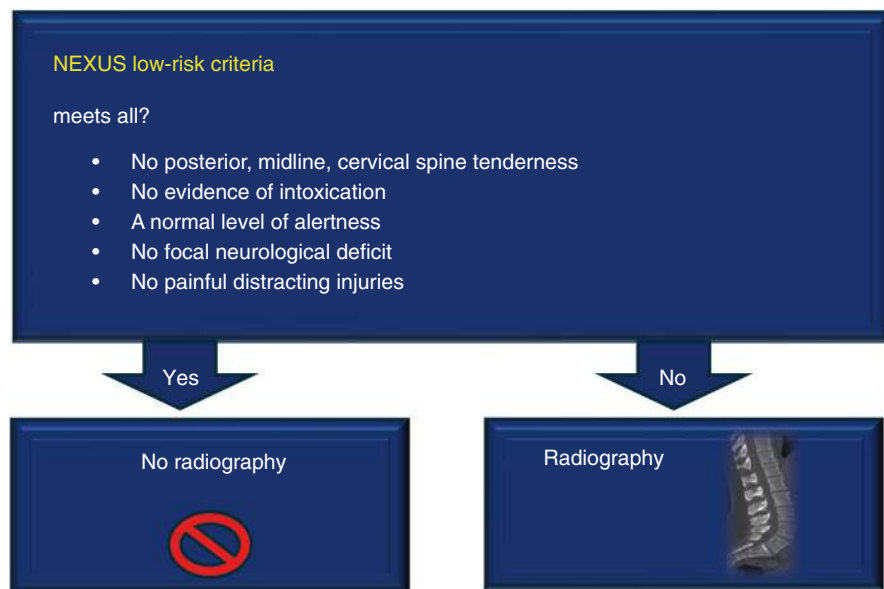


Fig. 3.17 National emergency X radiography utilization study (NEXUS) criteria. (Hoffman et al. [56])

Late Management of SCI

- Airway and breathing: for patients likely to be ventilator-dependent, consider early tracheostomy. Implement regular chest physiotherapy and ventilator-associated pneumonia (VAP) prevention bundles to reduce VAP risk.
- Physiotherapy: essential to prevent muscle wasting and maintain mobility.
- Urinary and gastrointestinal care: patients are at risk for neurogenic bladder, urinary tract infections (UTIs), and stool incontinence.
- Skin care: reposition patients every 2 h to prevent or limit bed sore development.
- Venous thromboembolism (VTE) prophylaxis: ensure appropriate measures to prevent VTE.

Tetanus

Pathophysiology of Tetanus

Clostridium tetani, an anaerobic, Gram-positive, spore-forming bacillus, enters the body through skin injuries and releases a toxin (tetanospasmin) that is disseminated via the bloodstream to the spinal cord, where it inhibits neurotransmitters, causing uncontrolled motor neuron activity.

Clinical Manifestations of Tetanus

- Rigidity and muscle spasm
- Autonomic dysfunction

The incubation period of tetanus is typically 7–10 days. It begins with muscle spasms and rigidity, and patients may exhibit clinical signs such as lockjaw and opisthotonos (Fig. 3.18). As the disease progresses, autonomic dysfunction may develop, including hypertension, hyperthermia, tachycardia, and arrhythmias. The severity of clinical manifestations can be assessed using the Ablett classification (Table 3.18).

Differential Diagnosis of Tetanus

- Neuroleptic malignant syndrome
- Serotonin syndrome
- Meningoencephalitis

Prevention of Tetanus

Any patient with a cut or puncture wound should be evaluated by a medical team to assess the wound and review the tetanus vaccination history. Based on this assessment, tetanus toxoid, tetanus immunoglobulin, both, or neither may be administered (Fig. 3.19).

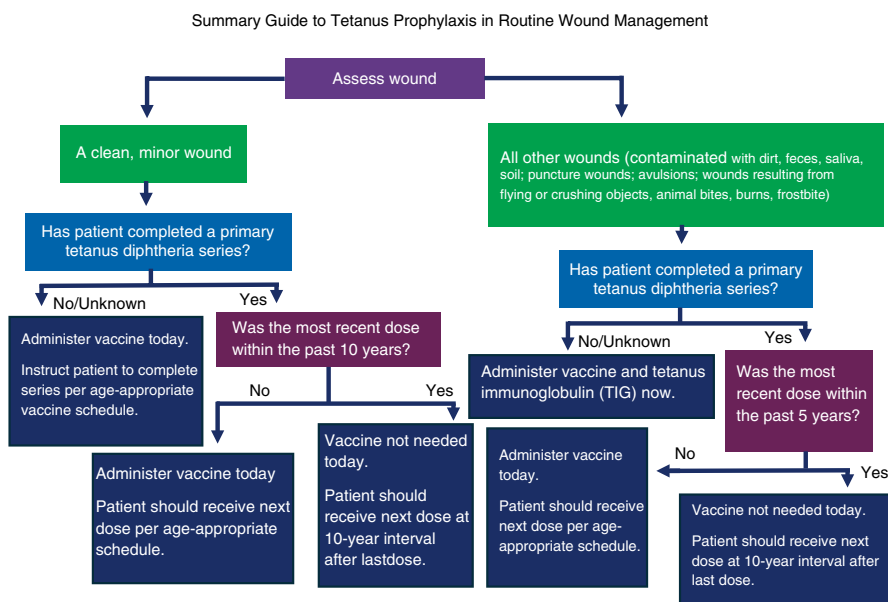


Fig. 3.18 Clinical signs of tetanus: lockjaw (left) and opisthotonos (right). (Courtesy of Centers for Disease Control and Prevention (CDC))

Table 3.18 Ablett classification for the severity of tetanus

Grade	Clinical features
I (mild)	Mild trismus, general spasticity, no respiratory compromise, no spasm, no dysphagia
II (moderate)	Moderate trismus, rigidity, short spasm, mild dysphagia, moderate respiratory involvement, respiratory rate >30 bpm
III (severe)	Severe trismus, generalized rigidity, prolonged spasm, severe dysphagia, apneic spells, pulse >120 bpm, respiratory rate >40 bpm
IV (very severe)	Grade 3 with severe autonomic instability (hypertension and tachycardia alternating with hypotension and bradycardia)

Ablett [61]

**Fig. 3.19** Tetanus prophylaxis in wound management. (Adapted from Centers for Disease Control and Prevention (CDC) [62])

Management of Tetanus

As in any critical case, tetanus is approached with ABC and management of each step accordingly.

Cases must be reported to the Ministry of Health.

Early intubation should be considered, particularly in patients with severe rigidity or compromised airway protection.

Sedation including midazolam and/or propofol, fentanyl, neuromuscular blockers (NMB), e.g., rocuronium, all should be considered.

Surgical debridement of the infected injury.

Tetanus toxoid and immunoglobulin.

Antibiotic to cover *Clostridium tetani*, e.g., intravenous metronidazole 500 mg four times daily.

For persistent cases, intrathecal baclofen can be used.

For autonomic instability, magnesium sulphate, clonidine, and/or selective beta-blockers (BB), e.g., esmolol can be used (non-selective BB is contraindicated as it increases the mortality mostly due to hypotension) [63].

Recovery might take long time, and long-term management should be applied, which includes early tracheostomy, aggressive physiotherapy, preventive strategies for ventilator-associated pneumonia (VAP), urinary tract infection (UTI), bed sores, and venous thromboembolism (VTE).

Guillain-Barre Syndrome (GBS)

Pathogenesis and Causes of GBS

It is an acute inflammatory demyelinating polyneuropathy, most likely of autoimmune origin, typically triggered by a preceding infection. The most common cause is gastroenteritis due to *Campylobacter jejuni*. Other associated infections include upper respiratory tract infections, Cytomegalovirus (CMV), Epstein-Barr virus (EBV), and Herpes simplex virus (HSV).

Clinical Presentation and Types of GBS (Table 3.19)

Investigations for Patient with GBS

- Neuroimaging (brain and spine): performed to exclude alternative causes of neurological deficits.
- Nerve conduction studies (NCS): typically show findings consistent with a demyelinating polyneuropathy.
- Lumbar puncture (LP): reveals albuminocytologic dissociation; elevated cerebrospinal fluid (CSF) protein with a normal white cell count.
- Spirometry: used to monitor forced vital capacity (FVC) for early detection of respiratory compromise or impending respiratory failure.

Table 3.19 Common types of Guillain-Barre syndrome

Type	Autoantibodies	Clinical features
Acute inflammatory demyelinating polyneuropathy	Anti-GM2	Pain and numbness are usually the first clinical feature Ascending symmetrical paralysis Hyporeflexia Sensory loss Autonomic dysfunction (tachycardia, arrhythmia)
Miller Fisher syndrome	Anti-GQ1b	Ophthalmoplegia, ataxia, areflexia

GM2 monosialotetrahexosylganglioside 2, GQ1B disialosylganglioside Q1b

Differential Diagnosis of GBS

- Botulism
- Myasthenia gravis
- ICU-acquired weakness
- Transverse myelitis

Management of GBS

As in any critical case, GBS patient is approached with ABC and management of each step accordingly. For airway and breathing, the patient should be assessed for signs of impending respiratory failure, including inability to maintain the airway, respiratory distress, respiratory acidosis on blood gas, or spirometry findings such as forced vital capacity (FVC) <20 mL/kg, maximum inspiratory pressure (MIP) <30 cmH₂O, or maximum expiratory pressure (MEP) <40 cmH₂O; any of which warrants intubation and mechanical ventilation.

In circulation management, the patient should be connected to a cardiac monitor due to the risk of autonomic dysfunction, and two large-bore intravenous cannulas should be inserted for fluid resuscitation and blood sampling.

Treatment includes intravenous immunoglobulin (IVIG) at a dose of 1 g/kg daily for 2 days or 400 mg/kg daily for 5 days, or plasma exchange in five sessions, which may lead to a faster onset of action and shorter recovery time. However, there is no evidence that either modality is superior to the other [64].

Myasthenia Gravis (MG)

Pathogenesis and Causes of Relapse of MG

Myasthenia gravis is an autoimmune disorder characterized by the production of autoantibodies against postsynaptic acetylcholine receptors (AChRs) at the nicotinic neuromuscular junction. This impairs acetylcholine binding and receptor activation, leading to reduced neuromuscular transmission and progressive muscle weakness, particularly with repetitive use. Exacerbations or relapses can be triggered by various factors, including infections, surgical procedures, and certain medications such as calcium channel blockers, beta-blockers, macrolides, fluoroquinolones, and magnesium.

Clinical Features of MG

- Weakness worsening with repetitive movement.
- Cranial nerves involvement:
 - Ocular nerves: diplopia and ptosis, the ptosis may occur after 45 s of upward gaze and improve with ice over the eyes.
 - Bulbar symptoms: dysphagia, dysarthria, and choking.

- Myasthenic crisis: characterized by impending respiratory failure and should be assessed clinically by observing signs of respiratory distress, respiratory acidosis on arterial blood gas, inability to count from 1 to 10 or 1 to 20 in a single breath, or spirometry findings such as forced vital capacity (FVC) <20 mL/kg, maximum inspiratory pressure (MIP) <30 cmH₂O, or maximum expiratory pressure (MEP) <40 cmH₂O.
- Cholinergic crisis: results from excessive dosing of cholinesterase inhibitors and presents with muscarinic symptoms such as salivation, lacrimation, polyuria, diarrhea, and other signs of parasympathetic overactivity.

Differential Diagnosis

- Lambert-Eaton myasthenic syndrome (LEMS): Table 3.20 illustrates the difference between MG and LEMS
- Guillain-Barre syndrome (GBS)
- Botulism

Investigations for MG

- Blood gas: to rule out respiratory acidosis as a marker for respiratory failure.
- Autoantibodies: AChR and muscle-specific tyrosine kinase antibodies (MuSK).
- Electromyography (EMG): shows a decreased response to repetitive stimuli.
- Computed tomography (CT) of the chest: to rule out thymoma.

Management of Myasthenic Crisis

As in any critical case, patient with myasthenic crisis is approached with ABC and management of each step accordingly.

For airway and breathing management, assess the patient for signs predicting impending respiratory failure and manage properly with intubation and mechanical ventilation if needed.

Treatment includes intravenous immunoglobulin (IVIG) at a dose of 1 g/kg daily for 2 days or 400 mg/kg daily for 5 days, or plasma exchange in five sessions, which may lead to a faster onset of action and shorter recovery time. However, there is no evidence that either modality is superior to the other [65].

Table 3.20 Comparison between myasthenia gravis and Lambert-Eaton myasthenic syndrome

	Myasthenia gravis (MG)	Lambert-Eaton myasthenic syndrome (LEMS)
Common malignancy	Thymoma	Small cell lung cancer
Autoantibodies	Acetylcholine receptor antibodies (AChR)	Voltage-gated calcium channel
Effected neuromuscular junction (NMJ) site	Postsynaptic	Presynaptic
Ocular and bulbar symptoms	Common	Uncommon
Autonomic dysfunction	None	Common
Deep tendon reflexes	Normal	Reduced
Repetitive movement	Worsens the weakness	Improves the weakness

Chronic Management of MG

- Cholinesterase inhibitors, pyridostigmine to improve symptoms of weakness.
- Immunosuppression: steroid plus azathioprine or cyclosporine.
- Thymectomy.

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Chapter 4

Gastroenterology



Haytham Abbas  and Wail Tashkandi

Introduction

In the chapter of gastroenterology, ICU trainees will become familiar with common critical cases such as GI bleeding and hepatic diseases. The chapter also covers nutritional assessment, focusing on mastering assessment tools and providing appropriate feeding.

Gastrointestinal (GI) Bleeding

Causes of Upper and Lower GI Bleeding

GI bleeding is classified as upper or lower based on whether it is proximal or distal to the ligament of Treitz. Upper GI bleeding (UGIB) can present with melena, hematemesis, or coffee ground vomiting, while lower GI bleeding (LGIB) typically presents with haematochezia. However, massive UGIB can also present with haematochezia.

Causes of UGIB

- Peptic ulcer disease (PUD) (20%–60%)
- Erosive gastropathy

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- Esophagitis
- Oesophageal varices
- Other causes: malignancy, vascular cause, e.g. angiodysplasia, Mallory Weiss tear, etc.

Causes of LGIB

- Diverticular haemorrhage (30%)
- Vascular, e.g. angiodysplasia, haemorrhoid, ischemia, etc.
- Polyps/tumour
- Colitis

Obscure GI bleeding It is a GI bleeding which not seen in the upper and lower endoscopy; it might be related to small bowel bleeding. Causes are:

- Small bowel angiodysplasia
- Crohn's disease
- Cancer
- Dieulafoy's lesion

Management of Massive GI Bleeding

As in any critical case, upper and lower GI bleeding are approached with ABC and management of each step accordingly.

If bleeding is massive and presents as hematemesis with airway compromise, urgent intubation is required to secure the airway.

Insert two large-bore intravenous (IV) cannulas for resuscitation and initiate an IV crystalloid bolus while preparing packed red blood cells (PRBCs) and other blood products. Send blood samples for CBC, crossmatch, coagulation profile, blood gas, liver function tests, and basic metabolic panel.

If the patient is in haemorrhagic shock, activate the massive transfusion protocol, administering PRBCs, fresh frozen plasma (FFP), and platelets.

Start IV proton pump inhibitor (PPI) therapy (e.g. omeprazole 80 mg loading dose, then 8 mg/h infusion) for suspected peptic ulcer disease (PUD) [1].

In cirrhotic patients, start octreotide (50 mcg loading dose, then 50 mcg/h infusion) for suspected variceal bleeding.

Consult the GI team for urgent endoscopy. If the procedure is inconclusive or bleeding persists, further management depends on patient stability and whether the bleeding is from the upper or lower GI tract (see Figs. 4.1 and 4.2).

Scoring System in GI Bleeding

Multiple scores were designed to predict the outcome of acute GI bleeding AIMS 65 and Glasgow Blatchford scores are examples, see Fig. 4.3 and Table 4.1.

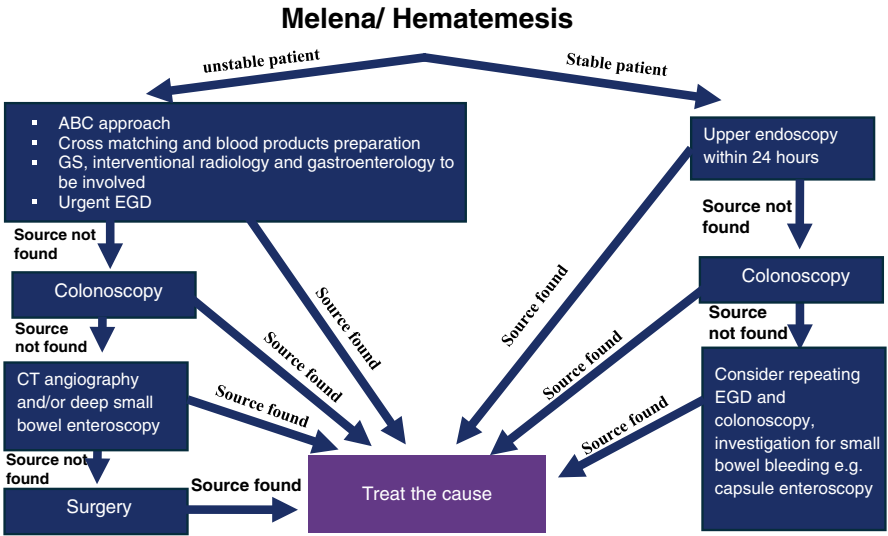


Fig. 4.1 Management of upper GI bleeding. GS = general surgery, EGD = Esophagogastroduodenoscopy, CT = computed tomography

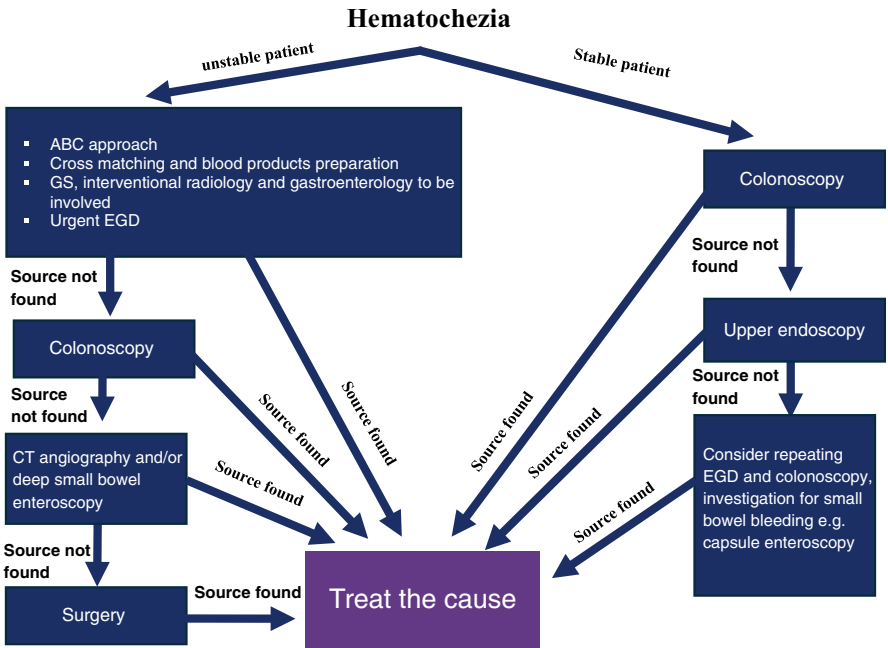


Fig. 4.2 Management of lower GI bleeding. GS = general surgery, EGD = Esophagogastroduodenoscopy, CT = computed tomography

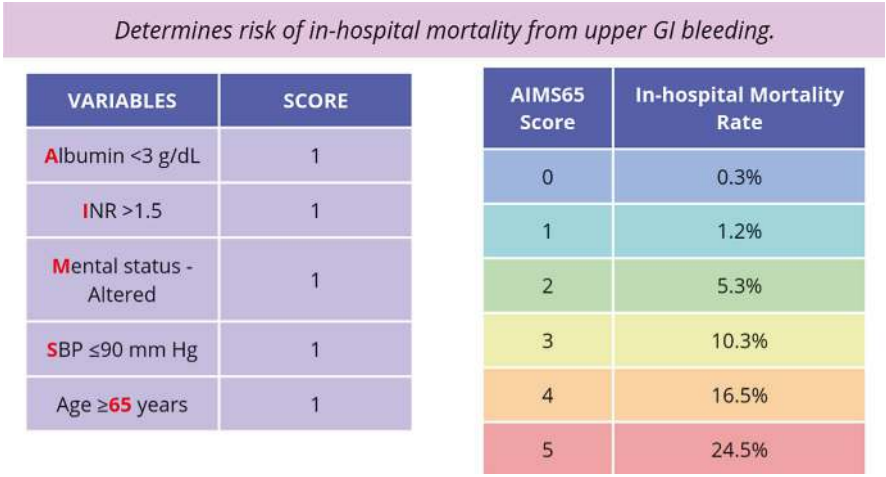


Fig. 4.3 AIMS 65 score for upper GI bleeding. (Sourced from www.openmed.co.in)

Table 4.1 Glasgow-Blatchford score helps identify which patients with upper GI bleeding (UGIB) may be safely discharged from the emergency room

Glasgow-Blatchford Bleeding Score (GBS)		
Parameter	Range/finding	Score
Blood urea nitrogen (mg/dL)	18.2 to <22.4	2
	22.4 to <28.0	3
	28.0 to <70.0	4
	≥70.0	6
Haemoglobin (g/dL)	12.0 to <13.0 (men); 10.0 to <12.0 (women)	1
	10.0 to <12.0 (men)	3
	<10.0	6
Systolic blood pressure (mmHg)	100–109	1
	90–99	2
	<90	3
Heart rate (beats per minute)	≥100	1
Other markers	Melena	1
	Syncope	2
	Hepatic disease ^a	2
	Cardiac failure ^a	2

Blatchford et al. [2]

Scores range from 0 to 23, with higher scores corresponding to increasing acuity and mortality
A score of 0 suggests low risk of complications, and these patients may not need to be admitted
Scores ≥6 are associated with >50% risk of needing intervention

^aThe patient must be known clinically and by the investigations to have chronic liver or cardiac diseases

Liver Cirrhosis

Definition and Clinical Findings of Cirrhosis

Cirrhosis is a liver disease characterized by fibrosis and formation of regenerative nodules causing distortion of the hepatic architecture. When the liver loses its function, complications begin to occur. At this stage, the condition is called decompensated liver cirrhosis. The pathophysiology of decompensated cirrhosis is summarized in Table 4.2.

Aetiology of Liver Cirrhosis: See Table 4.3

Scoring System Using for Liver Cirrhosis

Multiple scores were designed for patients with cirrhosis aiming to identify the prognosis and the survival expectations for those patients; Child-Turcotte-Pugh score and MELD scores (Model for End Stage Liver Disease) are common examples (Fig. 4.4 and Table 4.4).

Investigations of Liver Cirrhosis

CBC and coagulation profile: Pancytopenia due to hypersplenism and coagulopathy with high international normalized ratio (INR) and partial thromboplastin time (PTT).

Liver function test: Aspartate transaminase (AST) > alanine transaminase (ALT) in advanced cirrhosis, high bilirubin level.

Renal function test: Rule out hepatorenal syndrome (HRS), electrolyte disturbances as it can worsen the hepatic encephalopathy.

Table 4.2 Complications of liver cirrhosis

Pathophysiology	Complications	
Portal hypertension	Oesophageal varices Ascites Hepatic hydrothorax Splenomegaly	
Decrease the metabolism of toxins	Ammonia	Hepatic encephalopathy
	Nitric oxide	Systemic hypotension Hepato-renal syndrome (HRS) Hepato-pulmonary syndrome
	Oestrogen	Loss of libido Gynecomastia
Hypersplenism, decreased coagulation factors production (vitamin K dependent factors)	Pancytopenia Coagulopathy	
Decreased production of protein C, S and Antithrombin III	Thrombosis, e.g. deep venous thrombosis (DVT) and portal vein thrombosis	
Others	Hepato-cellular carcinoma (HCC)	

Table 4.3 Causes of liver cirrhosis

Infectious	Chronic viral hepatitis (hepatitis B, C)
Metabolic	Alcoholic liver disease Nonalcoholic fatty liver disease Hemochromatosis Alpha-1 Antitrypsin deficiency Wilson disease
Autoimmune	Autoimmune hepatitis Primary and secondary biliary cirrhosis Primary sclerosing cholangitis Celiac disease
Congestion	Right-sided heart failure Veno-occlusive disease
Medication	Methotrexate and amiodarone

MELD Score = $9.57 \times \log_e \text{Serum Cr (mg/dL)} + 3.78 \times \log_e \text{Serum Bilirubin (mg/dL)} + 11.2 \times \log_e \text{INR} + 6.43$ ▪ If any value is <1, the MELD assumes the score is equal to 1. ▪ If hemodialysis, value for Creatinine is set at 4 mg/dL.	3 months mortality %	MELD score
	1.9–3.7	<9
	6–20	10–19
	19.6–45.5	20–29
	52.6–74.5	30–39
	71–100	>40
MELD-Na = MELD Score - Na - $0.025 \times \text{MELD} \times (140 - \text{Na}) + 140$ Sodium values are restricted to the range of 125–140 mmol/L; any value outside this range is adjusted to the nearest limit.	MELD-Na Score	90-Day Mortality
	<17	<2%
	17-20	3-4%
	21-22	7-10%
	23-26	14-15%
	27-31	27-32%
	≥32	65-66%

Fig. 4.4 MELD and MELD-Na scores for prognostication of cirrhosis. Cr = creatinine, INR = international normalized ratio, Na = sodium [3, 4]

Blood gas: To assess lactate level and metabolic acidosis.

Ultrasound abdomen with Doppler: To assess for presence of ascites, hepatic focal lesions in hepatocellular carcinoma (HCC), biliary tract, portal and hepatic vasculature, and ruling out structural renal disease in HRS.

Triphasic computed tomography (CT) of liver: To confirm HCC.

Table 4.4 Child-Turcotte-Pugh score for prognostication of cirrhosis

Child-Turcotte-Pugh (CTP) Score			
Variable	1 Point	2 Points	3 Points
Serum Bilirubin (mg/dL)	≤ 2.0	2–3	> 3.0
Serum Albumin (g/dL)	> 3.5	2.8–3.5	< 2.8
Prothrombin Time (Prolongation, s)	1–4	5–6	> 6
Hepatic Encephalopathy	None	Minimal	Advanced
Ascites	None	Slight	Moderate
One- and Two-Year Survival Based on CTP Score			
Class	Points	1-year survival	2-year survival
A	5–6	100%	85%
B	7–9	80%	60%
C	10–15	45%	35%

Pugh et al. [5]

Fibroscan: To assess the level of fibrosis.

Investigations for the aetiology of cirrhosis: Viral hepatitis serology (Hepatitis B, C, D), autoimmune profile (ANA: antinuclear antibody, ASMA: anti-smooth muscle antibody, AMA: antimitochondrial antibody, anti-LKM: antibody to liver kidney microsome), metabolic profile (ferritin, transferrin, ceruloplasmin, 1α antitrypsin level, lipid and diabetes mellitus profile).

Variceal Haemorrhage Management

It is one of the complications which correlates to the severity of the disease and occurs due to portal hypertension.

Patient who has an acute upper gastrointestinal bleeding (UGIB) due to variceal haemorrhage must be approached with ABC and management of each step accordingly.

The approach is similar to other UGIB cases, with specific interventions for variceal haemorrhage.

Airway: Intubate if airway is compromised (e.g. hypoxemia, shock, severe encephalopathy).

Circulation: Insert two large-bore cannulas for resuscitation, labs, and crossmatch.

Transfusion: Prepare for massive transfusion based on bleeding severity or haemorrhagic shock.

Medications:

- Start intravenous octreotide: 50 mcg bolus, then 50 mcg/h infusion.
- Antibiotics (e.g. ceftriaxone or ciprofloxacin) have been shown to reduce sepsis and mortality [6]

Endoscopy: Involve gastroenterology immediately for endoscopic intervention (band ligation or sclerotherapy), based on variceal site and accessibility.

Balloon tamponade using a Sengstaken-Blakemore tube (Fig. 4.5): It is a temporary measure to control variceal bleeding until definitive intervention can be performed. The tube has three main ports: a gastric inflation port, an oesophageal inflation port and a gastric aspiration port. After inflating the gastric balloon, traction is applied to occlude the gastroesophageal junction, followed by inflation of the oesophageal balloon to tamponade the bleeding. Inflation should not exceed 6 h to avoid the risk of oesophageal necrosis, and 15-min deflation intervals should be applied between inflation periods.

Positioning can be confirmed by chest radiograph (Fig. 4.6) [8].

Fig. 4.5 Sengstaken-Blakemore tube insertion

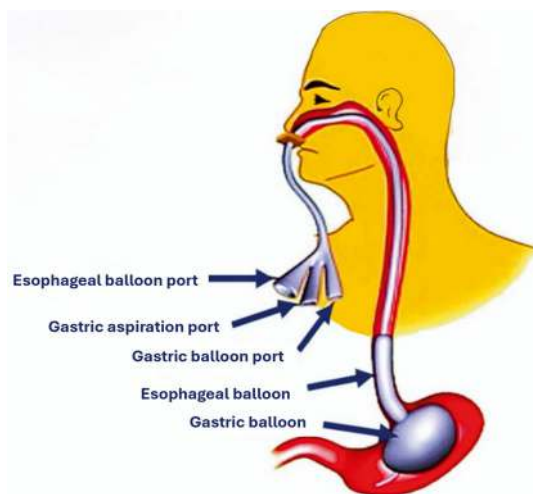
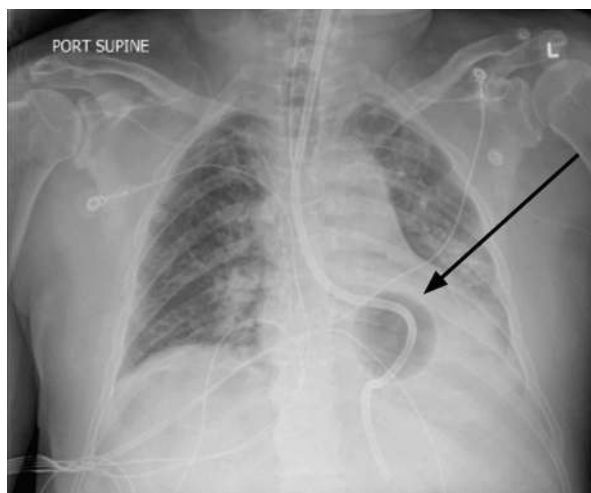


Fig. 4.6 Chest x-ray showing malpositioned Blakemore catheter [7]



Transjugular intrahepatic portosystemic shunt (TIPS): If bleeding cannot be controlled with endoscopic or medical measures, TIPS should be considered. It reduces the risk of rebleeding by lowering portal hypertension.

Liver transplantation: definitive treatment for end-stage liver disease.

Spontaneous Bacterial Peritonitis (SBP)

Cirrhotic patients have risk of ascites due to portal hypertension and hypoalbuminemia. Ascites may be complicated with SBP especially in those patients who have ascites with low protein <1 g/dL, having gastrointestinal bleeding or previous history of SBP.

The causative organism is usually gram-negative rods, e.g. *Escherichia coli* or *Klebsiella*, but gram-positive bacteria also can be the causative agent, e.g. *Enterococcus faecalis*.

Diagnosis of SBP is made by ascitic tapping and analysis which shows neutrophilic count >250 cells/ μ L; this ascitic sample has a classical picture of cirrhotic patient with high serum ascites albumin gradient (SAAG) >1.1 g/dL and low total protein <2.5 g/dL. Culture from the ascitic fluid also should be sent.

SBP with septic shock is approached with ABC and management of each step accordingly.

Definitive treatment includes antibiotic, e.g. ceftriaxone, piperacillin tazobactam or meropenem according to the bacterial resistance history and results.

Human albumen must be added as evidence showing better survival. The dose is 1.5 g/kg on day one and 1 g/kg on day 3 [9].

Hepatic Encephalopathy (HE)

Hepatic encephalopathy is a reversible spectrum of neuropsychiatric abnormalities in cirrhosis and/or portosystemic shunting, primarily due to impaired ammonia detoxification. However, serum ammonia levels poorly correlate with severity.

Categorization and Grading

Type A: Hepatic encephalopathy occurs in the setting of acute liver failure.

Type B: Hepatic encephalopathy occurring in the setting of portal-systemic bypass with no intrinsic hepatocellular disease.

Type C: Hepatic encephalopathy occurs in the setting of cirrhosis with portal hypertension or systemic shunting.

There are four clinical grades for HE as follows:

Grade I: changes in behaviour, mild confusion, slurred speech and disordered sleep

Grade II: lethargy and moderate confusion

Grade III: marked confusion (stupor), incoherent speech, sleeping but arousable

Grade IV: coma and unresponsive to pain

Table 4.5 Precipitating factors for hepatic encephalopathy

Medications	Benzodiazepines
	Narcotics
	Alcohol
Ammonia related	Gastrointestinal bleeding
	Infection
	Hypokalaemia
	Constipation
Volume depletion	Haemorrhage
	Diarrhoea
	Vomiting
	Diuretics
	Large volume paracentesis
Portosystemic shunting	

Precipitating factors for HE: Summarized in Table 4.5.

Treatment of HE

Severe HE is approached with ABC and management of each step accordingly.

Airway: consider intubation in case of severe encephalopathy, hypoxia or hypoventilation.

Correction of the precipitating factors, e.g. gastrointestinal bleeding, SBP or hypokalaemia.

Medications:

- Lactulose 30–40 mL, 2–4 times daily, aiming for 2–3 soft stools per day. If oral administration is not possible, it can be given as an enema.
- Rifaximin 550 twice daily or 400 three times daily.

Hepato-Renal Syndrome (HRS)

Pathogenesis

Due to systemic hypotension in cirrhotic patients, which is related to high nitric oxide levels, systemic vascular resistance (SVR) decreases. This reduction in SVR results in minimization of renal perfusion, which stimulates the renin angiotensin aldosterone system (RAAS), leading to renal vasoconstriction and ascites formation.

Types of HRS

Type 1: shows at least twofold increase in serum creatinine during a short period (less than 2 weeks).

Type 2: less severe than type 1 disease. The major clinical feature is ascites that is resistant to diuretics.

Table 4.6 Criteria to diagnose hepatorenal syndrome

<i>Diagnosis of cirrhosis with ascites</i>
<i>Diagnosis of acute kidney injury (AKI)</i>
Increase in serum creatinine (SCr) ≥ 0.3 mg/dL within 48 h
Or
$\geq 50\%$ increase in SCr from baseline (known or presumed to have occurred within the past 7 days)
<i>No improvement in kidney function after:</i>
2 days of diuretic withdrawal
Volume expansion with IV albumin: 1 g/kg/day, up to 100 g/day
<i>Absence of shock</i>
<i>No current or recent use of nephrotoxic drugs</i>
<i>No evidence of structural kidney injury</i>
Proteinuria ≤ 500 mg/day
<50 red blood cells per high-power field (RBC/HPF)
Normal renal ultrasonography

Adapted from: Angeli et al. [10]

Diagnosis of HRS

Table 4.6 summarizes criteria for HRS diagnosis.

Treatment of HRS

Management of acute kidney injury (AKI) as outlined in the Chap. 7.

For critically ill patient with shock: use norepinephrine or vasopressin to maintain the hemodynamics.

For stable patient: terlipressin is given as intravenous boluses (1–2 mg every 4–6 h) [11], or Midodrine is given orally three times daily (starting at 7.5 to a maximum dose of 15 mg), and octreotide is either given as a continuous intravenous infusion (50 mic/h) or subcutaneous (100–200 mic three times daily).

Albumen is given for 2 days as intravenous boluses (1 g/kg per day, 100 g maximum), followed by 25–50 g per day until the other agents are stopped.

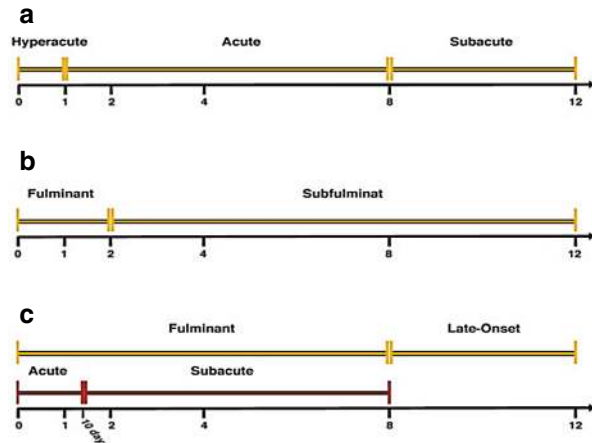
Acute Liver Failure (ALF)

Definition of ALF

It is an acute liver injury, hepatic encephalopathy and coagulopathy in a patient without cirrhosis or preexisting liver disease. While the onset varies between reports, a commonly used cutoff is an illness duration of <26 weeks.

Multiple classification systems used to define the ALF based on the time between jaundice to encephalopathy (see Fig. 4.7) [12].

Fig. 4.7 classification and subtypes of ALF based on the time between jaundice to encephalopathy. (a) corresponds to O'Grady's, (b) to Bernau's and (c) to Mochida's classifications [12]



Causes of ALF

- Drugs: acetaminophen (the most common drug), mushroom poisoning, sympathomimetics, phenytoin, valproic acid, antitubercular drugs.
- Viral hepatitis: hepatitis A, B, E (especially in pregnancy) and D, *Cytomegalovirus* (CMV), *Epstein Barr virus* (EBV), *Herpes simplex virus* (HSV), *Varicella zoster virus* (VZV).
- Metabolic: alcoholic, Wilson disease
- Autoimmune hepatitis
- Ischemic: shock, sepsis, Budd-Chiari syndrome, veno-occlusive disease
- Pregnancy related: acute fatty liver of pregnancy, HELLP
- Malignant infiltration

Clinical Manifestations of ALF

- Fatigue/malaise
- Lethargy
- Nausea and/or vomiting
- Right upper quadrant pain
- Jaundice
- Mental status changes (e.g. lethargy, difficulty sleeping, coma)

Complications of ALF

- CNS: encephalopathy which has four grades:
 - Grade 1: attention deficit, disordered sleep
 - Grade 2: asterixis, confusion
 - Grade 3: somnolence, rigidity
 - Grade 4: coma; increased intracranial pressure (ICP) with respiratory depression, bradycardia and hypertension
- Cardiovascular: hypotension and distributive shock
- Pulmonology: hypoxia, acute respiratory distress syndrome (ARDS)

- Renal: oliguria, acute kidney injury (AKI) due to prerenal, acute tubular necrosis (ATN), or hepato-renal syndrome (HRS)
- Gastrointestinal (GI) : increased risk of GI bleeding and stress ulcer
- Haematology: coagulopathy and bleeding tendency
- Infections: immunocompromised status and increased risk of sepsis
- Endocrine: hypoglycaemia

Investigations of ALF

- Complete blood count (CBC) and coagulation profile: rule out coagulopathy.
- Liver function test: monitor transaminases and bilirubin.
- Renal function test and blood gas: rule out AKI, metabolic acidosis, and high lactate.
- Abdominal ultrasound with Doppler: assess liver parenchyma, vasculature, biliary tract and abnormalities in renal parenchyma in AKI.
- ALF aetiology workup: viral serology, acetaminophen level, toxicology screen, ceruloplasmin, autoimmune profile (ANA: antinuclear antibody, ASMA: anti-smooth muscle antibody, anti-LKM: antibody to liver kidney microsome).
- Liver biopsy: if aetiology is unclear.

Management of ALF

As in any critical case, ALF is approached with ABC and management of each step accordingly.

Airway: consider intubation in patients with grade 3 or 4 encephalopathy to maintain airway.

Urgent referral to liver transplant centre.

Circulation: insert two large bore cannulas, connect to a cardiac monitor, administer a resuscitation fluid and extract basic workup.

Hepatic Encephalopathy: it is the most common cause of death in patients with ALF, management include:

- Brain protective strategy: normotension, normocapnia, normoxia, normothermia, normoglycemia and head elevation (illustrated in section “[Ischemic Stroke](#)”, Chap. 3).
- Hyperosmolar therapy: hypertonic saline or mannitol (illustrated in the section “[Traumatic Brain Injury \(TBI\)](#)”, Chap. 3).
- ICP monitoring can be considered in grade 4 or progressing grade 3 encephalopathy.
- Hyperventilation: a transient intervention in case of impending herniation until a lifesaving procedure to be performed like decompressive craniotomy.
- Barbiturate coma by using phenobarbital or thiopental in refractory high ICP.

Management of other complications:

- Shock: volume assessment and resuscitation +/- vasopressors.
- AKI: STOP approach (illustrated in the section “[Acute Kidney Injury \(AKI\)](#)”, Chap. 7), assess for the cause of AKI and treat accordingly including HRS management and haemodialysis if indicated.
- GI: ulcer prophylaxis.

- Infections: send for septic screen, start broad spectrum antibiotic if sepsis is diagnosed or highly suspected.
- Haematology: correct coagulopathy in case of bleeding or need for surgical procedure.
- Endocrine: regular check-up for serum glucose and correct hypoglycaemia.

Definite Treatment

- Paracetamol: N-acetylcysteine
- HSV: Acyclovir
- Hepatitis B: Tenofovir, entecavir
- Bud Chiari syndrome: Anticoagulation and transjugular intrahepatic portosystemic shunt (TIPS)
- Pregnancy related: Delivery
- Wilson: Plasma exchange, penicillamine, zinc

Liver transplantation: indications are summarized in Table 4.7.

Table 4.7 Indications of liver transplantation in acute liver failure

King’s College Criteria for Liver Transplantation
ALF due to acetaminophen toxicity:
(a) pH <7.30 (irrespective of grade of encephalopathy) or
(b) All three following conditions:
Prothrombin time >100 s
Serum creatinine >300 µmol/L
Grade III or IV encephalopathy
ALF due to non-acetaminophen:
(a) Prothrombin time >100 s (irrespective of grade of encephalopathy) or
(b) Any three of the following variables (irrespective of grade of encephalopathy):
Age <10 or >40 years
Aetiology-non-A, non-B hepatitis, halothane hepatitis, idiosyncratic drug reactions
Duration of jaundice before onset of encephalopathy >7 days
Prothrombin time >50 s
Serum bilirubin >300 µmol/L

O’Grady et al. [13]

Acute Pancreatitis

Causes of acute pancreatitis: See Table 4.8.

Scoring System in Acute Pancreatitis

Multiple scores were designed for evaluation and prognostication of acute pancreatitis such as:

- Glasgow score (Table 4.9).
- Ranson’s criteria (Table 4.10).
- Balthazar score: depends on CT scan findings (Table 4.11).
- APACHE II score (Acute Physiology and Chronic Health Evaluation II).
- BISAP; simple 5-point scoring system, blood urea nitrogen (BUN) >25 mg/dL, impaired mental status, systemic inflammatory response syndrome (SIRS), age >60 years, and pleural effusion. It is used within the first 24 h, score ≥3 predicts high risk of organ failure and mortality [17].

Table 4.8 Causes of acute pancreatitis

Obstructive	Systemic	Mechanical
Gallstones	Drugs, e.g. steroids, furosemide, azathioprine, valproic acid	Trauma
Neoplasm (e.g. head of pancreas)	Alcohol	Post ERCP
Cystic fibrosis	Metabolic: hypercalcemia, hyperparathyroidism, hypertriglyceridemia	
Congenital anomalies	Viruses: HIV, CMV, mumps, etc.	
	Scorpion bites	
	Autoimmune	

HIV human immunodeficiency virus, *CMV* cytomegalovirus, *ERCP* endoscopic retrograde cholangiopancreatography

Table 4.9 Glasgow criteria for acute pancreatitis, score ≥3 indicate severe pancreatitis

<i>P</i> — $PaO_2 < 8$ kPa (60 mmHg)
<i>A</i> —Age >55 years
<i>N</i> —WBC >15,000 cells/ μ L (<i>neutrophils</i>)
<i>C</i> —Calcium <2 mmol/L
<i>R</i> —Urea >16 mmol/L (<i>renal</i>)
<i>E</i> —LDH >600 or ALT/AST >200 units/L (<i>enzymes</i>)
<i>A</i> —Albumin <32 g/L
<i>S</i> —Glucose >10 mmol/L (<i>sugar</i>)

Blamey et al. [14]
PaO₂ partial pressure of arterial oxygen, *WBC* white blood cells, *LDH* lactate dehydrogenase, *ALT* alanine transaminase, *AST* aspartate transferase

Table 4.10 Ranson’s criteria for acute pancreatitis

At admission or diagnosis:
Age over 55 years
White blood count (WBC) >16,000 cells/ μ L
Blood glucose >200 mg/dL
Serum Lactic dehydrogenase (LDH) >350 U/L
Serum aspartate aminotransferase (AST) >250 U/L
During initial 48 h:
Haematocrit fall >10%
Blood urea nitrogen rise >5 mg/dL
PaO ₂ <60 mmHg
Serum calcium <8 mg/dL
Base deficit >4 meq/L
Estimated fluid sequestration >6 L
Ranson [15]
PaO ₂ partial pressure of arterial oxygen

Table 4.11 Balthazar score for acute pancreatitis

Grading of Pancreatitis (Balthazar Score)				
Grade	Description	Points	% Necrosis	Necrosis Points
A	Normal pancreas	0	–	–
B	Enlargement of pancreas	1	0	0
C	Inflammatory changes in pancreas or peripancreatic fat	2	<30	2
D	One pancreatic fluid collection	3	30–50	4
E	≥ 2 peripancreatic fluid collections	4	>50	6
Prognostic Scoring (CT Grade + Necrosis Points)				
Points Scored	% Mortality			
0–3	3			
4–6	6			
7–10	17			

Balthazar et al. [16]

Investigations in Acute Pancreatitis

- Complete blood count (CBC) and coagulation profile: exclude leucocytosis, low haematocrit and/or disseminated intravascular coagulation (DIC).
- Liver function test: rule out cholestasis and acute hepatitis.
- Chemistry and renal function: assess for acute kidney injury (AKI), electrolyte disturbances, e.g. hypocalcaemia.
- Blood gas: assess lactate level, base deficit and respiratory failure.
- Amylase and/or lipase: diagnostic if $\geq 3\times$ normal level.
- Aetiology workup: e.g. triglycerides and calcium levels.

- Chest imaging: assess for pleural effusion and acute respiratory distress syndrome (ARDS).
- Abdominal ultrasound: assess for biliary obstruction, ascites and pancreatic changes (enlargement, collections, necrosis, abscess).
- Computed tomography of the abdomen: not indicated in acute setting. It provides better visualization for the pancreas and the surrounding structures.
- Magnetic resonance cholangiopancreatography (MRCP): for highly suggested biliary obstruction when ultrasound is inconclusive.
- Endoscopic ultrasound: assess pancreatic structure, detect microlithiasis, and enable therapeutic drainage.

Management of Acute Pancreatitis [18, 19]

As in any critical case, acute pancreatitis is approached with ABC and management of each step accordingly. The main lines of management include:

- Aggressive intravenous hydration: crystalloid fluids, preferably Ringer's lactate, remain the fluid of choice. Monitor renal function, lactate, and urine output [20].
- Analgesia: e.g. opioids and paracetamol for pain control.
- Enteral feeding: start as soon as tolerated; no significant difference between nasogastric and nasojejunal routes [21].
- Antibiotics: only indicated for infectious complications, such as acute calculous cholecystitis, ascending cholangitis, abscess formation or infected necrosis.
- Endoscopic retrograde cholangiopancreatography (ERCP): perform in cases of biliary obstruction or ascending cholangitis.
- Hypertriglyceridemia-induced pancreatitis: treat with intravenous insulin with glucose to maintain euglycaemia, fenofibrate +/- plasma exchange [22, 23].
- Management of local complications:
 - Pseudocyst: typically forms ≥ 4 weeks after onset. Management is conservative if asymptomatic, drainage (radiology, endoscopy, or surgery) if symptomatic.
 - Walled off pancreatic necrosis: also occurs ≥ 4 weeks after onset. Management is conservative if asymptomatic, drainage if symptomatic, antibiotic + drainage if infected.
 - Necrosis: management is conservative if not infected. If infected, antibiotic + drainage by radiology, endoscopy or surgery.

Nutritional Assessment

ICU patients require careful nutritional assessment and individualized support. Nutritional status, underlying disease and comorbidities should be evaluated to guide optimal nutrient provision.

Up to 30%–50% of hospitalized patients are malnourished. Severe illness often induces a catabolic state, which can be worsened by inadequate protein and energy intake, leading to poorer outcomes.

Nutritional Assessment Tools

Nutritional status is best assessed through a combination of medical history, physical examination and laboratory investigations. Multiple assessment tools were designed for that purpose which include:

- Subjective Global Assessment (SGA)
- Anthropometric data; weight, height, triceps skinfold thickness (Fig. 4.8)
- Nutritional Risk Score (NRS) and Nutrition Risk in the Critically Ill (NUTRIC) (see Table 4.12) [25]

SGA classifies the patients into well nourished (SGA-A), moderately malnourished (SGA-B) or severely malnourished (SGA-C).

Laboratory Investigations in Nutritional Assessment

- Pre-albumin
- Transferrin
- Retinol binding protein
- Albumin: levels may decrease with chronic malnutrition
- C-reactive protein (CRP): an acute phase reactant that increases in inflammation and decreases in malnutrition
- Chemistry: magnesium, phosphorus, calcium, blood urea nitrogen, liver function and creatinine assays
- Micronutrient deficiencies: iron studies, vitamin B12 and folate, vitamin D, zinc, copper, selenium levels

Fig. 4.8 Triceps skinfold thickness



Table 4.12 Nutritional risk screening and NUTRIC

<i>(A) Nutritional risk screening 2002</i>		
<i>Score</i>	<i>Impaired nutritional status</i>	<i>Severity of disease</i>
0. Absent	Normal nutritional status	Normal nutritional requirements
1. Mild	Weight loss >5% in 3 months Or Food intake <50%–75% of normal requirement in the preceding week	Hip fracture Chronic diseases (cirrhosis, COPD, haemodialysis, diabetes, oncology)
2. Moderate	Weight loss >5% in 2 months Or BMI 18.5–20.5 kg/m ² + impaired general condition Or Food intake 25%–50% of normal requirement in the preceding week	Major abdominal surgery, stroke, severe pneumonia, hematologic malignancy
3. Severe	Weight loss >5% in 1 month Or BMI <18.5 kg/m ² + impaired general condition Or Food intake 0%–25% of normal requirement in the preceding week	Head injury Bone marrow transplant ICU patient (APACHE score >10)
<i>(B) NUTRIC score</i>		
<i>Score variables</i>	<i>Range</i>	<i>Points</i>
Age (years)	<50	0
	50–<75	1
	≥75	2
APACHE II score	<15	0
	15–<20	1
	≥20	2
SOFA score	<6	0
	6–<10	1
	≥10	2
Number of comorbidities	0–1	0
	≥2	1
Days from hospital to ICU admit	0–<1	0
	≥1	1

Mundi et al. [24]

Note: To calculate the total score, first, find the score (0–3) for impaired nutritional status and severity of disease; second, add the two scores for a total score; third, if age is ≥70 years, add one point to the total score to correct for the frailty of the elderly; and fourth, if age-corrected total is ≥3, start nutritional therapy

Abbreviations: *APACHE* acute physiology and chronic health evaluation, *BMI* body mass index, *COPD* chronic obstructive pulmonary disease, *NUTRIC* nutrition risk in critically ill, *SOFA* sequential organ failure assessment

Nutritional Requirement Assessment

Determining energy expenditure is essential for planning the feeding regimen and estimating nutritional requirements. Energy expenditure can be measured or estimated in different ways:

- *Indirect calorimetry*: it is the gold standard and utilizes measurement of carbon dioxide production (VCO_2) and oxygen consumption (VO_2) [26].
 R/Q ratio which = VCO_2/VO_2 is the main equation that is used in indirect calorimetry to determine the energy expenditure:
 - Hypermetabolism >100% of predicted energy expenditure
 - Normo-metabolism = 90%–100% of predicted energy expenditure
 - Hypometabolism <90% of predicted energy expenditure
- *Harris-Benedict equation*: basal energy expenditure (BEE) is estimated by specific equations targeting the patients according to their gender.
 - BEE (Males): $66 + 13.7 (\text{weight in kg}) + 5 (\text{height in cm}) - 6.8 (\text{age in years})$
 - BEE (Females): $655 + 9.6 (\text{weight in kg}) + 1.8 (\text{height in cm}) - 4.7 (\text{age in year})$
- *Simplified basal energy expenditure*: $BEE = 25 \times \text{body weight Kcal/day}$.
 Generally, this equation can be changed according to the comorbidities and the form of acute illness, for example:
 - Septic patients need $BEE \times 1.5$
 - Burn with large body surface area needs $BEE \times 2$

Protein diet must be preserved in malnutrition, acute illness, e.g. sepsis, and comorbidities, e.g. renal or hepatic failure. However, no difference in the clinical outcomes was identified among high vs low protein intake [27]. Nitrogen balance estimates the status of protein diet; positive nitrogen balance indicates anabolic, and negative nitrogen balance indicates catabolic status.

Current evidence also does not show significant differences in clinical outcomes between full and partial nutritional support. Several trials have investigated this; the *EDEN trial* compared trophic feeding (10 mL/kg/day) to full enteral feeding in critically ill patients and found no significant difference in clinical outcomes [28]. The *PermiT trial* evaluated permissive underfeeding (with adequate protein intake) versus full feeding and also reported no difference in mortality or other clinical endpoints [29].

Enteral and Parenteral Nutrient [26, 27]

Enteral feeding is the preferred method for providing nutritional support. It is cost-effective, helps maintain gut mucosal integrity, reduces the risk of bacterial translocation, and supports gastrointestinal immune function.

If no contraindications, early enteral feeding is suggested to be started within 48 h.

If enteral feeding is contraindicated such as in intestinal obstruction, mesenteric ischemia, perforated viscus, colitis or hemodynamic instability, total parenteral nutrition (TPN) can be considered.

Despite the controversy about the ideal time to start the TPN, it is suggested to be after 3–7 days when enteral feeding is contraindicated. It should be considered earlier in severe malnourishment.

Several clinical trials have compared enteral vs parenteral nutrition, as well as early vs late initiation of feeding in critically ill patients; the *CALORIES trial* found no significant difference in clinical outcomes between total enteral and parenteral nutrition [30]. The *NUTRIREA2 trial* studied early parenteral nutrition in mechanically ventilated ICU patients and similarly reported no significant difference compared to early enteral nutrition [31].

The *Early-PN trial* found no clinical benefit of early versus late total parenteral nutrition (TPN) in patients unable to receive enteral feeding [32]. The *EPaNIC trial* showed that early TPN was associated with longer hospital stays and a higher rate of infections compared to late initiation [33].

TPN Calculation

- Calories calculation per gram of macronutrient (Fat = 9.4 kcal/g, Protein = 4.1 kcal/g, Carbohydrate = 3.4 kcal/g).

Fluid requirement can be estimated by *Holliday-Segar method* which is: 100 cc/kg for the 1st 10 kg, 50 cc/kg for the 2nd 10 kg then 20 cc/kg for each remaining kgs.

- Total protein needs = 1.0 (g/d) × weight (kg).
- Total caloric needs = 25 (kcal) × weight (kg).
- Determine of lipid emulsion 20%–30% of caloric intake.
- Carbohydrate 70%–80% of caloric intake.
- Determine standard electrolytes, multivitamins and trace elements.

Example for 80 kg patient who needs TPN:

- The total fluid requirement is $(100 \times 10 + 50 \times 10 + 20 \times 60) = 1000 + 500 + 1200 = 2700$ mL.
- The Protein dose is 1.0 g/kg = 80 g/day so if the solution is 5% amino acid, he will need $80 \times 100/5 = 1600$ mL.
- The caloric requirement is 25 kcal/kg = $25 \times 80 = 2000$ kcal.
- The carbohydrate dose is 70% = $70 \times 2000/100 = 1400$ kcal, $1400/3.4 = 411$ g so if the solution is D50%, the patient will need $411 \times 100/50 = 822$ mL.
- The lipid dose is 30% = $30 \times 2000/100 = 600$ kcal, $600 \text{ kcal}/9 = 67$ g, so if the solution is 20% fatty acid, the patient will need $67 \times 100/20 = 333$ mL.
- Multivitamins and trace elements need to be added.

Gastric Residual Assessment

Routine monitoring of gastric residual volume (GRV) is not recommended, as evidence does not support a reduced risk of ventilator-associated pneumonia (VAP),

and it may increase the risk of vomiting. The *NUTRIREA-1 trial* found no benefit of routine GRV checks in preventing VAP [34], while the *REGANE trial* showed that GRV up to 500 mL can be safely tolerated without increasing gastrointestinal complications or VAP risk [35]. Therefore, enteral feeding should not be interrupted for $\text{GRV} \leq 500 \text{ mL}$.

Refeeding Syndrome

It is a clinical condition that results from reinstitution of nutrition to patients who have been starving. Chronic malnutrition leads to protein catabolism with total body phosphate depletion despite normal serum phosphate. The sudden introduction of carbohydrates leads to an anabolic state, unmasking total body phosphate depletion and leading to a precipitous drop in serum phosphate. The release of insulin results in marked uptake of phosphate, potassium and magnesium into cells.

It may manifest as severe electrolyte derangement. Hypophosphatemia, hypomagnesaemia and hypocalcaemia are typical. Thiamine deficiency can also occur, leading to Wernicke encephalopathy.

Clinical Manifestations of Refeeding Syndrome

Cardiovascular: arrhythmia, heart failure

Respiratory: respiratory depression, ventilator dependency

Gastrointestinal: vomiting, constipation

Renal: electrolyte disturbances

Musculoskeletal: weakness

CNS: encephalopathy, ataxia, delirium

Risk Factors for Refeeding Syndrome

- Low body mass index (BMI)
- Chronic malnutrition
- Recent poor oral intake for several days
- Chronic malabsorption
- Alcoholism

Management and Prevention of Refeeding Syndrome

- Recognition of the high-risk patients.
- Daily correction and follow-up of serum electrolytes and vitamin supplements, e.g. thiamine.
- Trophic feeding to be started with level of 5–10 mL/kg/h with gradual increase in the rate of feeding until reaching the full requirement after 4–7 days.

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Chapter 5

Surgery



Haytham Abbas  and Wail Tashkandi

Introduction

In the surgery chapter, ICU practitioners will learn how to manage surgical emergencies in collaboration with various surgical teams. General trauma is among the most critical conditions requiring a structured approach and effective multidisciplinary teamwork with surgical staff.

General Trauma

Trauma is a major cause for mortality and disability worldwide, and death distribution can be immediate, early, or late. For every death due to trauma, three patients suffer permanent disability.

Management of trauma cases follows the advanced trauma life support (ATLS) guidelines and requires a multidisciplinary team with clearly defined responsibilities.

The process involves two phases:

- Primary survey: focuses on patient stabilization using the ABCDE approach.
- Secondary survey: conducted after stabilization; includes a thorough head-to-toe examination.

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Management of Trauma Case [1]

Following a code trauma announcement, all relevant subspecialties must be immediately available. The multidisciplinary team proceeds with the primary survey, followed by the secondary survey.

Primary survey: using the ABCDE approach (Airway, Breathing, Circulation, Disability, and Exposure).

- *Airway:* Assess the patient's ability to maintain a patent airway. Drug-assisted intubation (DAI), the preferred term over rapid sequence intubation (RSI), should be considered in the following cases:

- Low Glasgow Coma Scale (GCS) ≤ 8
- Hypoventilation
- Respiratory distress
- Circulatory shock or arrest
- Airway obstruction or facial swelling

If the patient is suspected of having neck spine fracture, the intubation process must be initiated by induction of sedation, removal of neck collar, in-line stabilization, then using laryngoscope (direct or video) for the intubation.

- *Breathing:* Initial assessment includes respiratory rate (RR), oxygen saturation (SpO_2), chest auscultation, and evaluation for signs of respiratory distress. Extended Focused Assessment with Sonography in Trauma (E-FAST) can aid in identifying life-threatening thoracic injuries.

Common life-threatening complications include tension pneumothorax, open pneumothorax, hemothorax, pericardial tamponade, circulatory arrest, foreign body airway obstruction, and tracheobronchial injury. Specific interventions are recommended to manage these complications as follows:

- *Tension pneumothorax:*

- Needle decompression at the 5th intercostal space, mid-axillary line
- Thoracostomy tube insertion with a tube size of 28–32 Fr

- *Open pneumothorax:* triple side dressing with thoracostomy tube insertion.
- *Hemothorax:* thoracostomy tube with monitoring of blood collection. Urgent thoracic surgery is recommended if the collected blood is >1500 mL or >200 mL/h for 4 h.
- *Pericardial tamponade:* cardiac surgery.

- *Circulation:* Establish two large-bore peripheral intravenous lines. Administer up to 1 L of crystalloid for rapid infusion. Assess for hemorrhagic shock (see Table 5.1). Obtain initial laboratory workup, including blood gas, crossmatch, complete blood count (CBC), coagulation profile, electrolytes, renal, and liver function tests.

Table 5.1 Classes of hemorrhage in trauma

Parameter	Class I	Class II	Class III	Class IV
Approximate blood loss	<15%	15–30%	31–40%	>40%
Heart rate (bpm)	<100	100–120	120–140	>140
Blood pressure	Normal	Normal	Decreased	Decreased
Pulse pressure	Normal	Decreased	Decreased	Decreased
Respiratory rate	Normal	Normal	Increased	Increased
Urine output	Normal	Slightly decreased	Decreased	Markedly decreased/anuric
Consciousness	Mild anxiety	Mild anxiety	Anxiety and confusion	Confusion and lethargy
Metabolic acidosis	No acidosis	Mild acidosis	Moderate acidosis	Severe acidosis
Resuscitation	Crystalloid	Crystalloid +/- blood	Blood	Massive transfusion

Adapted from: Mutschler et al. [2]. Used with permission

- *Massive transfusion protocol*: defined as the need for >4 units of packed red blood cells (PRBCs) within 1 h or >10 units within 24 h. Transfusion should include other blood products to reduce the risk of coagulopathy. While the optimal ratio of PRBCs to fresh frozen plasma (FFP) and platelets remains controversial, several trials have evaluated this strategy. The *PROMMTT trial* demonstrated that early administration of FFP and platelets with PRBCs improves survival [3]. The *PROPPR trial* compared a 1:1:1 ratio of PRBCs: FFP: platelets to a 2:1:1 ratio, showing no significant difference in overall mortality but improved hemostasis with the 1:1:1 ratio [4].
- *Tranexamic acid*: typically administered as a 1-g intravenous dose over 10 min, followed by a 1-g infusion over 8 h. The *CRASH II trial* investigated its use in trauma patients and showed an association with improved survival [5].
- *Thromboelastogram (TEG)/Rotational Thromboelastometry (ROTEM)*: commonly used to guide blood product administration by assessing coagulation status in trauma patients (Fig. 5.1).
- *Permissive hypotension*: may help control bleeding until definitive management is initiated. However, it is contraindicated in traumatic brain injury, as hypotension can worsen neurological outcomes. The *Morrison trial* demonstrated that targeting a mean arterial pressure (MAP) of 50 mmHg improved postoperative coagulopathy and survival compared to a MAP of 65 mmHg [6].
- *Damage control surgery (DCS)*: is a surgical approach focused on stabilizing the patient, with planned re-exploration after hemodynamic stabilization. In trauma settings, the primary goal of DCS is early control of bleeding sources.

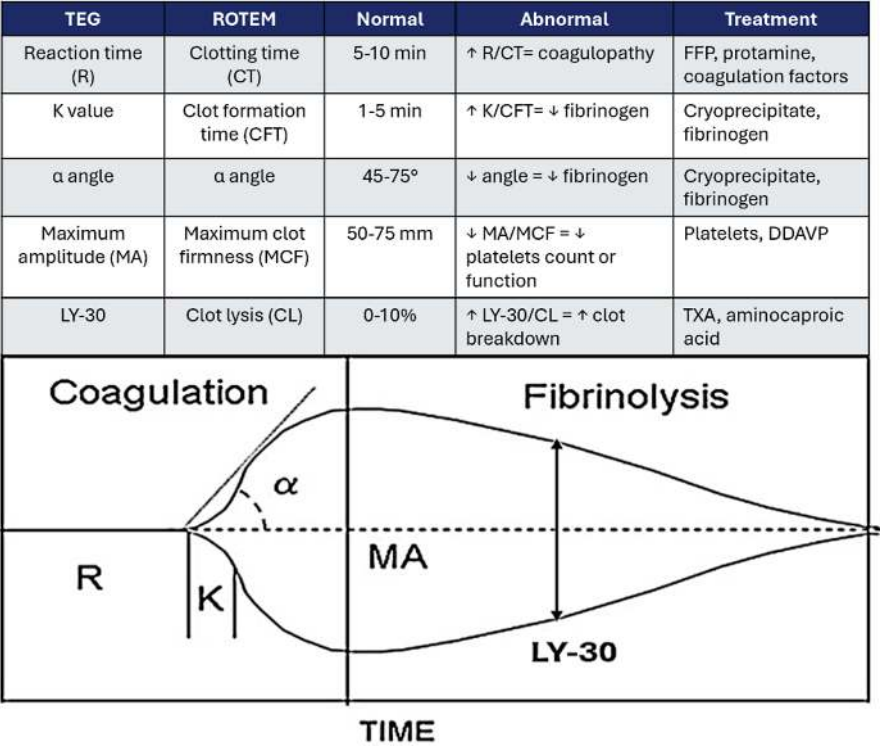


Fig. 5.1 Thromboelastogram (TEG) and Rotational Thromboelastometry (ROTEM) for assessment of coagulopathy. FFP = fresh frozen plasma, DDAVP = desmopressin, TXA = tranexamic acid

- *Disability*: assessment and management of patients with traumatic brain injury (TBI) and spinal cord injury (SCI) are illustrated in the Chap. 3.
- *Exposure*: involves fully exposing the patient from head to toe to identify any additional injuries. A log roll maneuver can aid in examining the posterior aspect while maintaining spinal precautions. After assessment, the patient should be promptly covered and warmed to prevent hypothermia, which is part of the lethal triad along with acidosis and coagulopathy.

Adjuncts to primary survey: After completing the ABCDE assessment, additional measures include connecting the patient to a cardiac monitor, inserting a Foley catheter (unless urethral injury is suspected), and placing a nasogastric tube (NGT) as indicated.

Secondary survey: consists of:

- History taking: using the AMPLE mnemonic (Allergies, Medications, Past illnesses/Pregnancy, Last meal, Events/Environment related to injury)
- Head-to-toe clinical examination
- Adjuncts to the secondary survey: includes radiological investigations, such as whole-body CT, to assess injured organs

Abdominal Compartment Syndrome

Definition of Intra-Abdominal Hypertension (IAH) and Abdominal Compartment Syndrome (ACS)

IAH is defined as increasing of the abdominal pressure for a level of >12 mmHg.

ACS is defined as increasing of the abdominal pressure for a level of >20 mmHg with evidence of end organ damage.

Types and Causes of ACS

Primary ACS: resulting from direct injury or disease of intra-abdominal organs (e.g., pancreas, colon, abdominal aorta).

Secondary ACS: arising from extra-abdominal causes such as burns, sepsis, or volume overload.

Recurrent ACS: occurs after surgical treatment of primary or secondary ACS.

Organs damage in ACS: summarized in Table 5.2.

Measurement of Intra-Abdominal Pressure (IAP) (Fig. 5.2) [7]

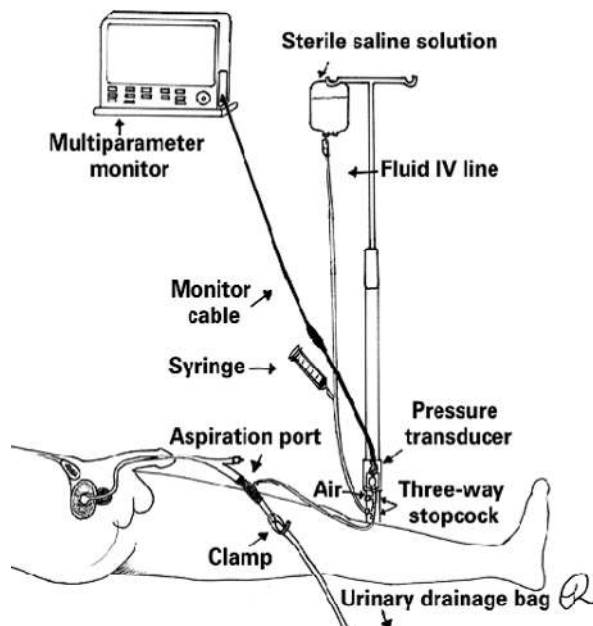
1. Attachment: clamp the Foley catheter and inject 20 mL of saline into the bladder.
Attach the catheter to a pressure transducer.
2. Leveling: position the transducer at the level of the symphysis pubis.
3. Zeroing: connect the transducer to the monitor and zero it before closing the system to obtain accurate IAP readings.
4. Positioning: all measurements should be performed with the patient in the supine position, head flat, and at end-expiration.

Table 5.2 Systemic complications of ACS

System	Pathophysiology	Clinical finding
CVS	Compression of IVC → ↓ preload Compression of diaphragm → ↑ SVR and ↓ cardiac contractility All → ↓ CO	↑ CVP Hypotension
Pulmonology	Compression of the diaphragm → ↓ FRC and ↓ compliance	Hypoxia Hypercapnia ↑ PIP and ↑ P plat
Renal	Compression of renal vein ↓ renal perfusion → RAAS stimulation	AKI Oliguria
CNS	Impaired venous drainage from cerebral outflow	↑ ICP ↓ Cerebral perfusion pressure
GIT	Compression of portal and mesenteric veins Bacterial translocation	Sepsis Lactic acidosis Jaundice

CVS cardiovascular system, IVC inferior vena cava, SVR systemic vascular resistance, CO cardiac output, CVP central venous pressure, FRC functional residual capacity, PIP peak inspiratory pressure, P plat plateau pressure, RAAS renin angiotensin aldosterone system, AKI acute kidney injury, CNS central nervous system, ICP intracranial pressure, GIT gastrointestinal tract

Fig. 5.2 Intra-abdominal pressure monitoring system. (Sourced from Milanesi et al. [7])



Management of ACS

As in any critical case, ACS is approached with ABC and treatment of each step accordingly.

Management strategies aimed at reducing intra-abdominal pressure include:

- GIT evacuation: nil per os (NPO), nasogastric tube (NGT) for drainage, and laxatives.
- Avoid hypervolemia: minimal fluid intake, diuresis, ultrafiltration in renal failure.
- Sedation and neuromuscular blockers.
- Reversed Trendelenburg position and removal of tight clothes.
- Ascitic tapping if marked ascites is present.
- Surgical decompression for persistent cases.

Burn

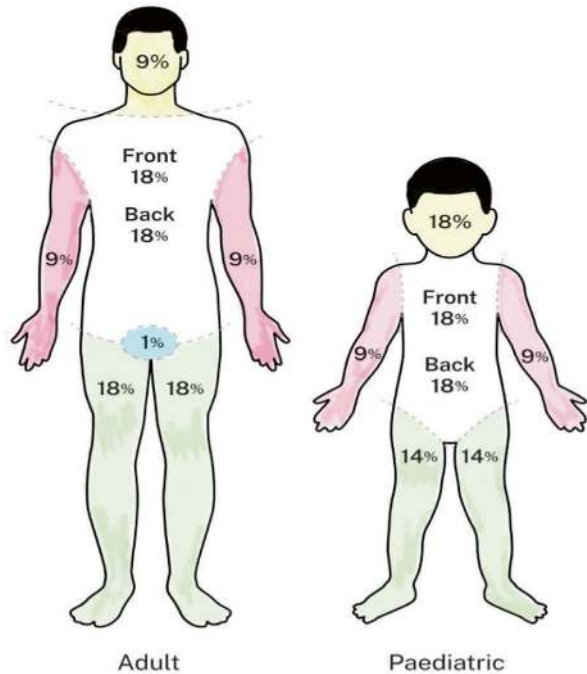
Estimation of Burn Severity

Burn severity depends on the body surface area (BSA) and the depth of the effected limbs.

BSA is estimated by rule of 9 (summarized in Fig. 5.3).

Burn depth is classified as follows:

- *Superficial*: Involves the epidermis only; lesions are erythematous and painful without blistering.

Fig. 5.3 Rule of 9 for burn

- *Partial thickness*: Extends into the dermis; lesions are erythematous, painful, and blistered.
- *Full thickness*: Involves the subcutaneous layer; lesions are white, painless, and lack capillary refill.

Management of Burn

Burn management follows the advanced trauma life support (ATLS) approach and starts with ABCDE [1].

History from surrogates should include details such as presence of additional trauma (e.g., road traffic accident, fall), duration of exposure, signs of inhalational injury, environmental context (indoor vs. outdoor), and presence of explosions.

- *Airway*: Anticipate a difficult airway; ensure expert presence and prepare all necessary difficult airway equipment. Assess the patient for signs suggesting inhalational injury:
 - Stridor
 - Carbon-stained sputum
 - Head and neck burn
 - Burned nasal hair
 - Horsiness of the voice or oropharyngeal edema

Drug-assisted intubation should be considered in inhalational burn, hypoxemia, hypoventilation, low Glasgow coma scale (GCS), or shock.

- *Breathing*: assess for respiratory distress and administer 100% oxygen if there is a high risk of carbon monoxide (CO) poisoning, regardless of oxygen saturation. For ventilated patients, use lung-protective strategies due to the increased risk of acute respiratory distress syndrome (ARDS) resulting from inhalational injury. Early bronchoscopy may be performed to evaluate mucosal injury and perform bronchoalveolar lavage (BAL).
CO poisoning is diagnosed via blood gas with co-oximetry. Management includes 100% oxygen administration. Although hyperbaric oxygen therapy is not part of primary resuscitation, it may be considered later for end-organ damage such as encephalopathy, myocardial ischemia, or carboxyhemoglobin (COHb) levels >25% (>15% in pregnancy).
- *Circulation*: Establish two large peripheral intravenous cannulas and obtain initial laboratory workup, including arterial blood gas, to exclude metabolic acidosis and elevated lactate levels suggestive of cyanide toxicity. Immediate fluid resuscitation is essential, particularly in patients with deep partial or full-thickness burns or burns involving more than 20% of total body surface area (TBSA). Traditionally, fluid requirements are calculated using the Parkland formula [8]:

$$\text{Volume} = 4 \text{ mL} \times \% \text{TBSA} \times \text{Weight (kg)}$$

Half of the volume is administered in the first 8 h, and the remaining half over the next 16 h. Recent consensus guidelines recommend a reduced resuscitation volume using $2 \text{ mL} \times \text{weight (kg)} \times \% \text{TBSA}$.

If cyanide toxicity is suspected, administer the antidotes including hydroxocobalamin and sodium thiosulfate.

- *Analgesia*: titrate opioids and non-opioid analgesics to control pain.
- *Escharotomy*: should be considered early in circumferential burn to avoid limb compartment.

Complications of Burn

- *Respiratory*: airway obstruction and ARDS
- *Cardiovascular*: shock (distributive, cardiogenic, or hypovolemic) and myocardial ischemia
- *Renal*: acute kidney injury (AKI) due to pre-renal, acute tubular necrosis (ATN), abdominal compartment, or rhabdomyolysis
- *Gastrointestinal*: malnutrition, stress ulcer
- *Hematology*: venous thromboembolism
- *Infectious*: sepsis and nosocomial infection
- *Musculoskeletal*: limb compartment

Acute Mesenteric Ischemia (AMI)

Definition and Causes of Mesenteric Ischemia

Mesenteric ischemia is defined as a reduction or complete absence of blood supply to the small intestine. It is most commonly caused by arterial occlusion, particularly involving the superior mesenteric artery (SMA) or its branches. Other causes include hypoperfusion (e.g., shock status) and venous occlusion. Causes are:

- *Arterial embolism*: the most common cause of mesenteric ischemia, typically due to embolic occlusion of the SMA. Often associated with cardiac conditions such as atrial fibrillation, valvular disease, or atherosclerotic plaques.
- *SMA thrombosis*: commonly results from atherosclerotic disease at the origin of the SMA. Additional risk factors include vascular injury and dissection.
- *Nonocclusive mesenteric ischemia*: due to hypoperfusion (e.g., shock state).
- *Mesenteric venous thrombosis (MVT)*: due to hypercoagulable state.

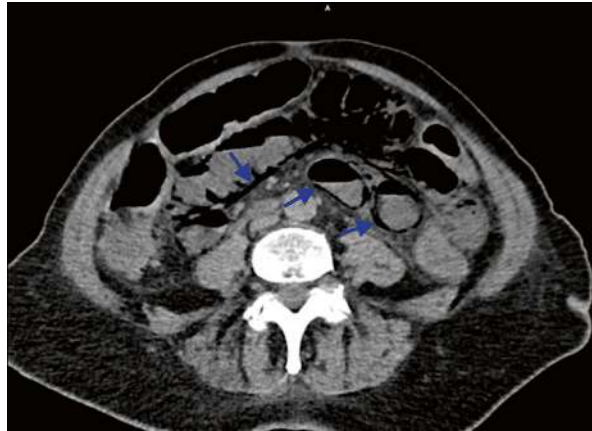
Clinical Presentation of AMI

- **Arterial occlusion**: sudden onset of severe abdominal pain out of proportion to physical examination findings.
- **Venous occlusion**: typically presents with slower onset, intermittent abdominal pain.
- **Nonocclusive**: may present with abdominal distention, pain, nausea, vomiting, or lower gastrointestinal (GI) bleeding. Patients often exhibit signs and symptoms related to systemic hypoperfusion, such as hypotension, altered mental status, or oliguria.
- **Abdominal examination**: often unremarkable in early stages but may reveal distention. In advanced or complicated cases, signs of an acute abdomen, including peritonitis due to bowel gangrene, may be present.

Investigations of AMI

- *Complete blood count (CBC) and coagulation profile*: may reveal leukocytosis with neutrophilia and coagulopathy.
- *Blood gas and lactate*: may reveal metabolic acidosis and high lactate.
- *Amylase*: may increase.
- *Renal/ liver function*: rule out end organ damage due to sepsis or hypoperfusion.
- *Electrocardiogram (ECG), echocardiography*: rule out cardioembolic causes.
- *Thrombophilia workup*: in case of MVT.
- *Computed tomography (CT) of the abdomen*: may show thumbprinting or ileus in early stage and pneumatosis intestinalis in late stage (Fig. 5.4) [9].
- *CT angiography*: the noninvasive test of choice for diagnosis of AMI.
- *Angiography*: the gold standard for diagnosis and potentially therapeutic.

Fig. 5.4 Pneumatosis intestinalis. (Sourced from Erdem et al. [9])



Management of AMI

As in any critical case, AMI is approached with ABC and management of each step accordingly.

Generally, management includes hemodynamic stabilization, anticoagulation, antibiotic coverage, nil per os (NPO), and monitoring of intra-abdominal pressure to rule out abdominal compartment syndrome (ACS).

Complicated course such as gangrenous bowel or peritonitis needs urgent surgery for bowel resection.

Specific management according to the etiology:

- SMA thrombosis: percutaneous stenting or surgical revascularization.
- SMA embolism: embolectomy (catheter-based aspiration vs. surgical).
- Nonocclusive: correct underlying cause and shock.
- Mesenteric vein thrombosis: prolonged anticoagulation, tailored to the underlying cause of thrombophilia. In severe or refractory cases, thrombectomy may be considered.

Necrotizing Fasciitis

Definition of Necrotizing Fasciitis

Necrotizing fasciitis is a severe and potentially fatal soft tissue infection that mainly targets the superficial fascia. It is frequently mistaken for cellulitis in clinical settings, which makes early recognition crucial. The condition has a sudden onset and advances rapidly, causing extensive tissue damage. Delayed diagnosis and treatment significantly increase the risk of death. While it most commonly affects the lower limbs, it can also involve the upper limbs, abdominal wall, or, in cases involving the perineal and genital regions, is known as Fournier's gangrene.

Fig. 5.5 Necrotizing fasciitis of the lower limb. (Courtesy of Dr. Wajdi Nassier. Used with permission)



Types and Causes of Necrotizing Fasciitis

Type I (polymicrobial): the most common type and polymicrobial in origin due to anaerobic, gram positive (Gm +ve), and gram negative (Gm -ve) bacteria. A common example is Fournier's gangrene.

Type II (monomicrobial): due to Beta-hemolytic *Streptococcus* group A (*Streptococcus pyogenes*) and *Staphylococcus aureus*. It primarily affects the limbs.

Type III (Clostridium species and Gm -ve bacteria): caused by organisms such as *Vibrio* spp. It affects the limbs, trunk, and perineum.

Type IV (Fungal): caused by *Candida* species, it affects the limbs, trunk, and perineum. This type progresses rapidly, particularly in immunocompromised patients.

A second classification can be simplified to monomicrobial or polymicrobial necrotizing fasciitis.

Risk Factors for Necrotizing Fasciitis

- Immunocompromised state (diabetes mellitus, use of steroid, renal/ liver failure)
- Intravenous drug use
- Alcoholism
- Trauma (penetrating trauma such as animal bites or post-surgery)

Clinical Presentation of Necrotizing Fasciitis

Symptoms include severe pain out of proportion to the clinical exam, redness, and hotness.

Early signs include erythema, swelling and tenderness.

Advanced stages may show skin blisters, bullae and/or crepitus (Fig. 5.5) [10].

Patients may also present with disseminated, fulminant disease characterized by signs and symptoms of hypoperfusion resulting from septic shock and multi-organ failure.

Fig. 5.6 Necrotizing fasciitis of the abdominal wall post exploration. (Sourced from Falconi et al. [11])



Investigations and Diagnosis of Necrotizing Fasciitis

The most definitive method for diagnosing necrotizing fasciitis is early surgical exploration in cases with high clinical suspicion, allowing direct assessment of subcutaneous tissue, fascia, and muscle (Fig. 5.6) [11].

- *Complete blood count (CBC) and coagulation profile:* may show leukocytosis with neutrophilia and coagulopathy.
- *Septic screen including blood culture.*
- *Inflammatory markers:* e.g., C reactive protein (CRP) and procalcitonin.
- *Renal/ liver function, blood gas and lactate:* rule out end organ damage and hypoperfusion related to sepsis/septic shock.
- *Creatine kinase (CK):* rhabdomyolysis may occur as a complication due to muscle necrosis.
- *Xray:* may show gas formation (Fig. 5.7) [12].
- *Computed tomography (CT)/ magnetic resonance imaging (MRI):* can show the extent of fascial necrosis (Fig. 5.8).

Management of Necrotizing Fasciitis

As in any critical case, necrotizing fasciitis is approached with ABC and management of each step accordingly.

Early management of sepsis/septic shock, i.e., intravenous fluid, antibiotic, vasopressors, and source control (illustrated in section “[Sepsis and Septic Shock](#)”, Chap. 8).

Empirical antibiotic treatment must be broad-spectrum to cover Gm +ve, Gm –ve and anaerobic bacteria. Examples include vancomycin combined with meropenem and/or piperacillin tazobactam.

Clindamycin has an antitoxic effect, and it is added for this advantage [13, 14].

Early and extensive surgical debridement is essential and may need to be repeated. The use of a vacuum-assisted wound closure device (VAC) may also be considered to aid healing.

Additional therapies that may be considered include hyperbaric oxygen therapy and intravenous immunoglobulin (IVIG) [15, 16].



Fig. 5.7 Lower limb X ray showing gas formation. (Radhi and Clements [12])

Fig. 5.8 CT pelvis showing fascial necrosis and gas formation in patient with Fournier's gangrene



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Chapter 6

Toxicology



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Introduction

Toxicology is a key aspect of critical care practice and requires a solid understanding to manage poisoned patients effectively. This chapter provides a structured approach to common toxicological emergencies in the ICU. Focus areas include identification of major toxins, use of specific antidotes, indications for hemodialysis, and other critical management strategies.

Approach to Toxicology

Initial Presentation of an Intoxicated Patient

Managing patients in the field of toxicology has unique challenges, and their approach differs significantly. They are assessed by ABCDEF approach, which stands for Airway, Breathing, Circulation, Decontamination, Elimination, and Finding an antidote.

The patient's history is often incomplete, unreliable, or unobtainable. The primary goals are to determine what was ingested, the quantity, and the timing. It is

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also important to know what the patient was doing at the onset of illness and to gather any relevant past medical history. Such a history is usually obtained from family or friends.

In the toxicology field, patient examination typically focuses on identifying the group of toxins and their side effects. Key clinical signs to examine those patients are vital signs, level of consciousness, pupil reaction, and whether patient is dry or wet, and subsequently, they are assessed if they fit a particular toxidrome. Rapid recognition of a toxidrome (if present) can help in quick management if that class of toxin is involved (see Fig. 6.1). Immediate electrocardiogram (ECG), blood glucose level, and exposure of the patient completely all are also necessary actions.

Airway: consider drug-assisted intubation in patients with severe encephalopathy, hypoventilation, severe hypoxemia, or shock.

Toxidrome	HR & BP Hypertension vs hypotension Tachycardia vs bradycardia	Respiratory Rate Tachypnea vs Bradypnea	Temperature Hyperthermic vs Hypothermic	Pupils Miosis vs Mydriasis	Bowel sounds Hyperactive vs Silent	Diaphoresis Sweaty vs Dry	CNS Agitated vs Somnolent
Anticholinergic: e.g., atropine, tricyclic anti- depressant			Hyperthermic 	Mydriasis 	Silent 	Dry 	Agitated 
Cholinergic: e.g., organophosphate, insecticides		 Others: bronchorrhea & bronchospasm		Miosis 	Hyperactive 	Sweaty 	Both  
Sedative agents: e.g., benzodiazepine, propofol			Hypothermic 		Silent 	Dry 	Somnolent 
Opioid: e.g., morphine, fentanyl, tramadol and heroin			Hypothermic 	Miosis 	Silent 	Dry 	Somnolent 
Sympathomimetic: e.g., cocaine, amphetamine, methamphetamine			Hyperthermic 	Mydriasis 	Hyperactive 	Sweaty 	Agitated 

Fig. 6.1 Toxidromes. HR = heart rate, BP = blood pressure, CNS = central nervous system

- Special considerations for the central nervous system (CNS) manifestations:
- Encephalopathy: the administration of certain agents can treat encephalopathy, such as thiamine if thiamine deficiency is suspected (e.g., in alcoholic patients), glucose in cases of hypoglycemia, and naloxone in opioid toxicity.
 - Seizure: generally, best treated with benzodiazepines, followed by barbiturates if necessary. Phenytoin is typically not recommended for controlling seizures in poisoned patients as it blocks sodium channels which can exacerbate the efficacy of other sodium channels blocker toxins, in addition that it has a low efficacy to control seizure in this field.
 - Agitation: effectively treated with benzodiazepine.

Breathing: treat hypoxia, hypoventilation, and respiratory failure by adding supplemental oxygen, positive pressure ventilation if needed, and consider naloxone if suspected opioid toxicity.

Circulation: keep the patient on two large bore cannulas for resuscitation and extraction of the workup which includes complete blood count (CBC), renal/liver function tests, electrolytes, glucose, coagulation profile, blood gas with anion gap and osmolar gap calculation, creatine kinase (CK), toxicology screen, and Paracetamol level. It is important to do serum levels of certain toxins to guide in management, such as levels of toxic alcohols, paracetamol, salicylates, digoxin, iron, and others. However, urine toxicology screening or testing results seldom directly influence patient management in the initial acute stage as results are usually delayed, and toxicology screening has limitations (Table 6.1). Toxicologic screening may be appropriate for medicolegal reasons, or when there is doubt about the diagnosis [1].

- Management of the cardiac complications:
- Hypotension: is treated with boluses of intravenous (IV) fluid, inotropes and vasopressors for persistent hypotension.
 - Hypertension: often it is related to sympathomimetic toxicity, and it usually responds to benzodiazepine. For persistent hypertension, alpha blockers or cal-

Table 6.1 Limitations of drug screen in toxicology

<i>Timing</i>	Drugs may be detected after days to weeks of exposure
<i>Noninclusive</i>	A negative screen does not rule out some exposure
<i>Sample error</i>	Assay may be negative in diluted urine
<i>Nonspecific</i>	Most tests use enzyme-immunoassays that only detect classes such as opioids, cannabinoids, benzodiazepines, cocaine, amphetamines, and barbiturates Opioid screens do not detect meperidine Benzodiazepine screens do not detect flunitrazepam
<i>Cross-reactivity</i>	Selegiline, methylphenidate, and pseudoephedrine come positive in amphetamine toxicity Carbamazepine, cyproheptadine, and chlorpromazine come positive in tricyclic antidepressant toxicity

cium channel blockers (CCB) can be given. Beta blockers (BB) alone are absolutely contraindicated as it worsens the blood pressure due to unopposed alpha-adrenergic stimulation.

- Ventricular tachycardia: treat it with sodium bicarbonate for possible tricyclic anti-depressant (TCA) toxicity. Class Ia, Ic, and III are absolutely contraindicated as they may worsen the arrhythmia. For digoxin toxicity, administer specific Fab fragments.
- Bradyarrhythmia: it is treated as per advanced cardiac life support (ACLS) bradycardia algorithm, and by administration of antidotes for the causative toxins, e.g., BB, CCB, or digoxin.

Decontamination [2]: multiple agents are used for decontamination of toxins including:

- Activated charcoal
- Whole bowel irrigation
- Gastric lavage
- Endoscopy/surgery

Activated charcoal (AC): it should be given within 1 h and up to 4 h from ingestion of the toxins.

Contraindications include:

- Depressed mental status without airway protection.
- Presence of intestinal obstruction.
- If endoscopy is needed, it likely will impair visibility.

It should be given for toxins likely to be decontaminated by AC. Use the mnemonic “*The yellow ABCD*” to remember:

- Theophylline
- Yellow oleander
- Antimalarial- quinine
- Barbiturate- phenobarbital
- Carbamazepine
- Dapsone

However, activated charcoal is not effective for:

- Acids
- Alkalis
- Alcohol
- Metals (lead, iron, arsenic, mercury)
- Ions (sodium, potassium, magnesium, calcium)
 - Gastric lavage: No proven benefit even if it is performed within 1 h.
 - Whole bowel irrigation: Involves administration of polyethylene glycol to induce diarrhea. There is no proven benefit from its use, but it has potential benefits in asymptomatic body packers.

Elimination: agents to induce toxins elimination include:

- Multiple doses of activated charcoal (MDAC)
- Saline diuresis
- Urinary alkalization
- Hemodialysis

– Alkalization of the urine:

It is used to counteract the effect of weak acid toxins, e.g., salicylate.

Technique: administer an IV bolus of 1–2 mEq/kg of sodium bicarbonate (NaHCO_3), followed by a continuous infusion of 150 mEq NaHCO_3 + 850 mL dextrose 5% (D5W) at a rate of 200–250 mL/h.

Goal: maintain urine pH of 7.5 or higher. Serum pH should not exceed 7.55–7.60.

Monitoring: close monitoring of blood pH, urine pH, and serum electrolytes is essential.

Complications include hypokalemia and volume overload.

- Hemodialysis: several medications are dialyzable, and hemodialysis should be considered for each, use “C- BLAST” mnemonic to remember them [3]:

- Carbamazepine
- Barbiturate
- Lithium
- Alcohol-Atenolol
- Salicylate—Sodium valproate
- Theophylline

Find antidote [2]: Table 6.2 summarizes each toxin and its antidote.

Table 6.2 Common toxins with the antidotes

Poison	Antidote	Poison	Antidote
Acetaminophen	N-acetylcysteine	Isoniazid	Pyridoxin
Digoxin	Immune fab	Organophosphate	Atropine, pralidoxime
Carbon mono-oxide	100% oxygen, hyperbaric oxygen	Salicylate	Sodium bicarbonate (NaHCO_3)
Calcium channel blocker (CCB), beta blocker (BB)	Calcium, glucagon, insulin, intralipid	Opioids	Naloxone
Methemoglobin	Methylene blue, ascorbic acid	Anticholinergic	Physostigmine
Iron	Deferoxamine	Sympathomimetic, e.g., cocaine	BDZ, alpha blockers for HTN +/- BB (but not BB alone)
Cyanide	Hydroxocobalamin, sodium thiosulfate	Tricyclic antidepressant (TCA)	NaHCO_3

(continued)

Table 6.2 (continued)

Poison	Antidote	Poison	Antidote
Arsenic, mercury, lead	Dimercaprol	Serotonin syndrome, e.g., MAOI	BDZ and cyproheptadine
Methanol, ethylene glycol	Ethanol, fomepizole	Neuroleptic malignant syndrome, e.g., antipsychotics	Dantrolene
Benzodiazepine (BDZ)	Flumazenil (avoid in chronic use of BDZ, TCA use, history of seizure)	Malignant hyperthermia, e.g., succinylcholine	Dantrolene

HTN hypertension, *MAOI* monoamine oxidase inhibitors

Management of Specific Toxic Exposures

Opioid Toxicity

Diagnosis is mainly made clinically.

Most opiates appear in urine toxicology.

Management includes:

General toxicology approach: ABCDEF.

Airway protection and ventilatory management: bag-valve mask and naloxone may prevent need for intubation.

Naloxone:

- It is indicated for respiratory depression or depressed level of consciousness.
- If the patient is apneic or near apneic, the dose will be 2 mg; may repeat the dose every 3 min up to 10 mg total. If no response, it is unlikely to be opioid overdose.
- If opioid naïve with minimal respiratory depression, the dose will be 0.4 mg.
- If opioid dependent with minimal respiratory depression, the dose will be 0.05 mg.
- In long-acting opioid overdose, patient might require infusion of naloxone.

Cholinergic Toxicity

It occurs most commonly secondary to organophosphate and carbamate exposure. Organophosphate is rapidly absorbed from skin, gastrointestinal (GI) tract, and lungs. It binds to acetylcholinesterase to block its function.

Clinical features: the mnemonic *SLUDGE + killer Bs* aids to remember the clinical manifestations of the drugs with cholinergic effect (salivation, lacrimation, urination, diarrhea, GI upset, and emesis) and killer Bs are bradycardia, bronchospasm, and bronchorrhea (Fig. 6.2).

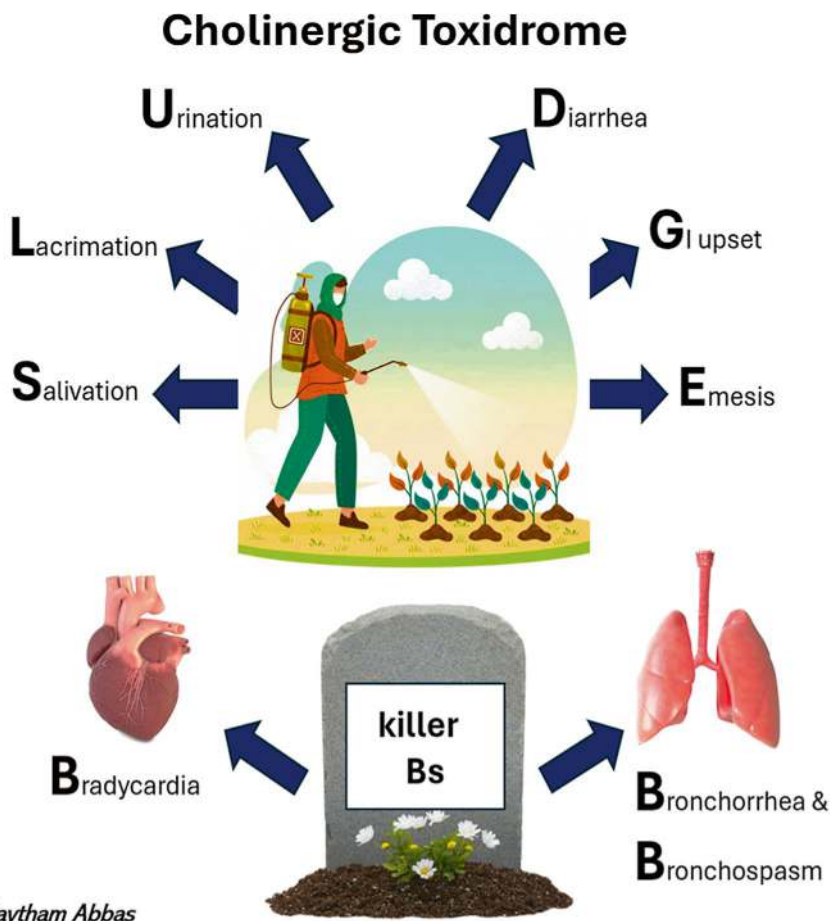


Fig. 6.2 Cholinergic toxidrome

Management:

General toxicology approach: ABCDEF.

Self-protection with personal protective equipment (PPE).

Remove clothing and decontamination with water and soap.

Consider intubation and mechanical ventilation if airway protection is compromised or consciousness is severely depressed. If neuromuscular blockade is required, use rocuronium and avoid succinylcholine due to prolonged paralysis from acetylcholinesterase inhibition.

Atropine: 2–4 mg IV every 5 min titrate aiming to dry the respiratory secretions. Note that patient might need >100 mg of atropine total dose.

Pralidoxime to restore acetylcholinesterase activities (it prevents aging of the acetylcholine receptors).

Sympathomimetic Toxicity

Clinical features: mydriasis, tachycardia, hypertension, fever, profuse sweating, confusion, and agitation.

Possible complications: rhabdomyolysis, seizures, intracranial hemorrhage, acute coronary syndrome, and multiorgan failure. Administration of sodium channel blockers with cocaine toxicity may cause wide QRS.

Management:

General toxicology approach: ABCDEF.

Benzodiazepines are the first line management for agitation, hypertension, and hyperthermia.

If hypertension remains uncontrolled, use phentolamine, nicardipine, or nitroprusside.

Avoid beta-blockers due to risk of hypertensive crisis from unopposed alpha-adrenergic stimulation.

Wide QRS due to sodium channel blockade with cocaine toxicity requires sodium bicarbonate.

Anticholinergic Toxicity

Exposure to anticholinergics is quite common due to anticholinergic effects in a lot of medications such as antihistamines, antidepressants, antipsychotics, and antiparkinsonians. Some plants also have anticholinergic effects such as Jimson weed (found in Arabian desert) and amanita mushroom.

Clinical features include blurred vision, urinary retention, hyperthermia, dry mouth and skin, and absent bowel sounds (Fig. 6.3).

Management:

General toxicology approach: ABCDEF.

Benzodiazepines for agitation.

Intravenous hydration.

Physostigmine may be considered for agitation or delirium unresponsive to benzodiazepines.

Contraindicated if non-anticholinergic toxicity is suspected (e.g., QRS >100 ms, TCA overdose) due to risk of bradycardia, atrioventricular (AV) block, or cardiac arrest. Toxicology consultation is strongly recommended prior to use.

Metabolic toxins: examples include:

- Salicylate
- Alcohol
- Cyanide

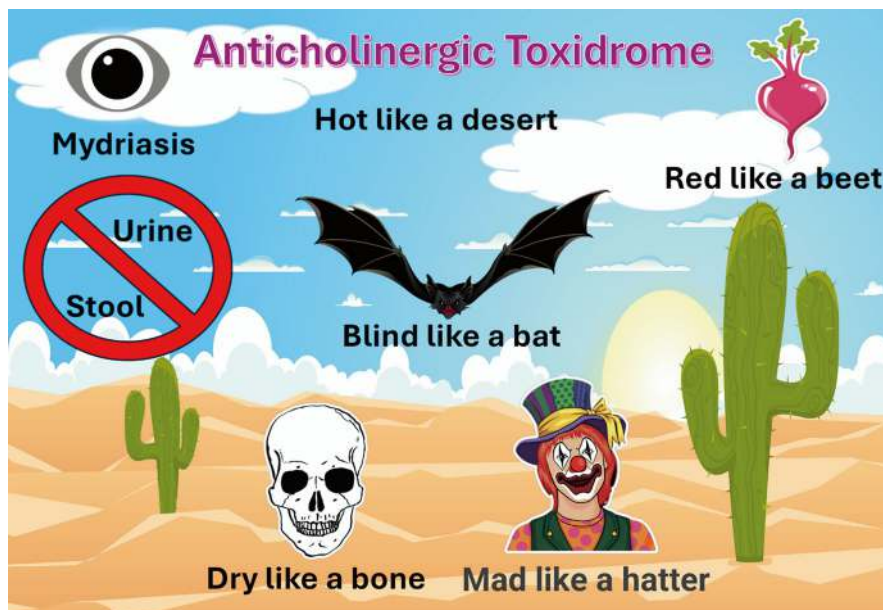


Fig. 6.3 Anticholinergic toxidrome

Salicylate Toxicity

Mechanism of action: Salicylate stimulates the chemoreceptor trigger zone in the medulla, causing nausea and vomiting. It also activates the respiratory center of the medulla, resulting in hyperventilation, respiratory alkalosis, and increasing renal elimination of bicarbonate. It interferes with cellular metabolism, inhibition of tri-carboxylic acid cycle, leading to metabolic acidosis and hyperthermia.

Clinical manifestations: summarized in Fig. 6.4.

Management of Salicylate Toxicity

General approach: ABCDEF.

Intubation: If needed, minimize the apnea time after induction of sedation as prolonged apnea can worsen acidemia.

Decontamination: Use AC if presented early.

Elimination: Salicylate can be eliminated with urine alkalization using NaHCO_3 or through hemodialysis.

Administer sodium bicarbonate at 1–2 mEq/kg as bolus dose followed by an infusion of 150 mEq NaHCO_3 + 850 mL D5W at a rate of 150–250 mL/h.

Monitoring: Target the urine pH to be 7.5–8, check urine pH, blood gas, and serum salicylate level every 1–2 h, and stop treatment when salicylate level is

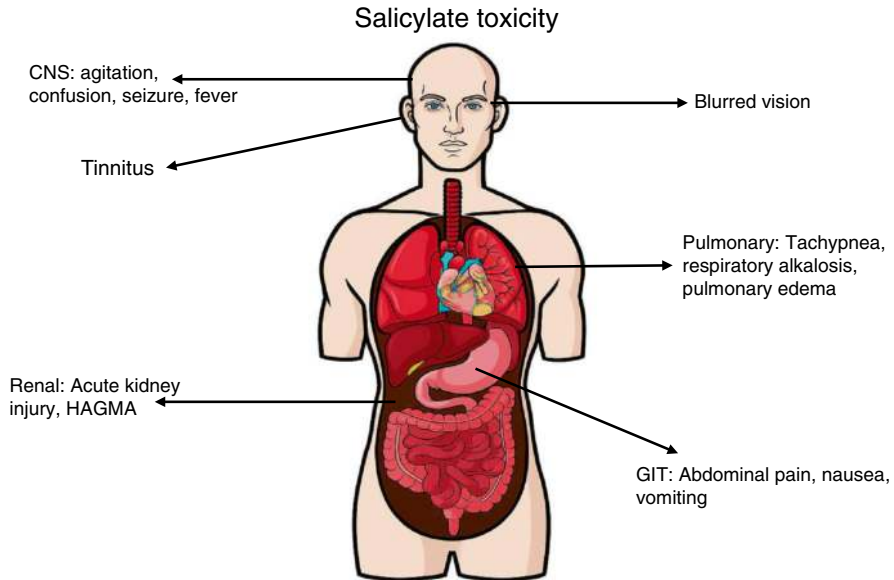


Fig. 6.4 Manifestations of salicylate toxicity. CNS = central nervous system, HAGMA = high anion gap metabolic acidosis, GIT = gastrointestinal tract

<40 mg/dL, metabolic acidosis has resolved, and patient is asymptomatic with normal respiratory rate and effort.

Indications of hemodialysis [3]:

- Encephalopathy or seizure
- Flash pulmonary edema
- Acute kidney injury (AKI)
- Persistent acidemia
- Salicylate level >90 mg/dL with normal renal function
- Salicylate level >80 mg/dL with impaired renal function

Toxic Alcohol

Common toxic alcohols include ethylene glycol and methanol, which present clinically with high anion gap metabolic acidosis (HAGMA) and a high osmolar gap (OG).

Metabolism: They are metabolized by alcohol dehydrogenase (ADH) into toxic metabolites, formic acid from methanol, and glycolic acid from ethylene glycol.

Formate toxicity (from methanol) can end by retinal damage and sudden visual loss or basal ganglia hemorrhage.

Glycolic acid (from ethylene glycol) can manifest with AKI and calcium oxalate crystal deposition in renal tubules (depicted in Figs. 6.5 and 6.6) [3].

Management of Alcohol Toxicity

General approach: ABCDEF.

Fomepizole or ethanol can inhibit ADH if administered early.

AC is not effective in alcohol toxicity.

NaHCO_3 may be used to correct severe acidemia.

Folinic acid can be given in methanol toxicity as it decreases the formate.

Pyridoxine and thiamine can be given for ethylene glycol as they decrease glycolic acid.

Indications for hemodialysis in alcohol toxicity:

- Late presentation (HAGMA)
- AKI
- Visual abnormalities
- Encephalopathy

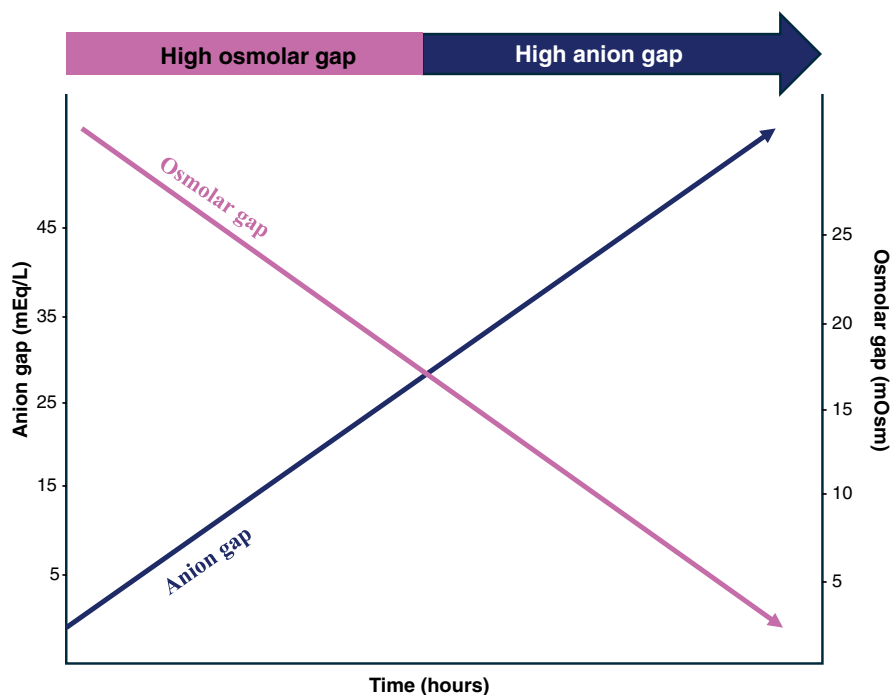


Fig. 6.5 The relation between osmolar gap and anion gap in toxic alcohol metabolism

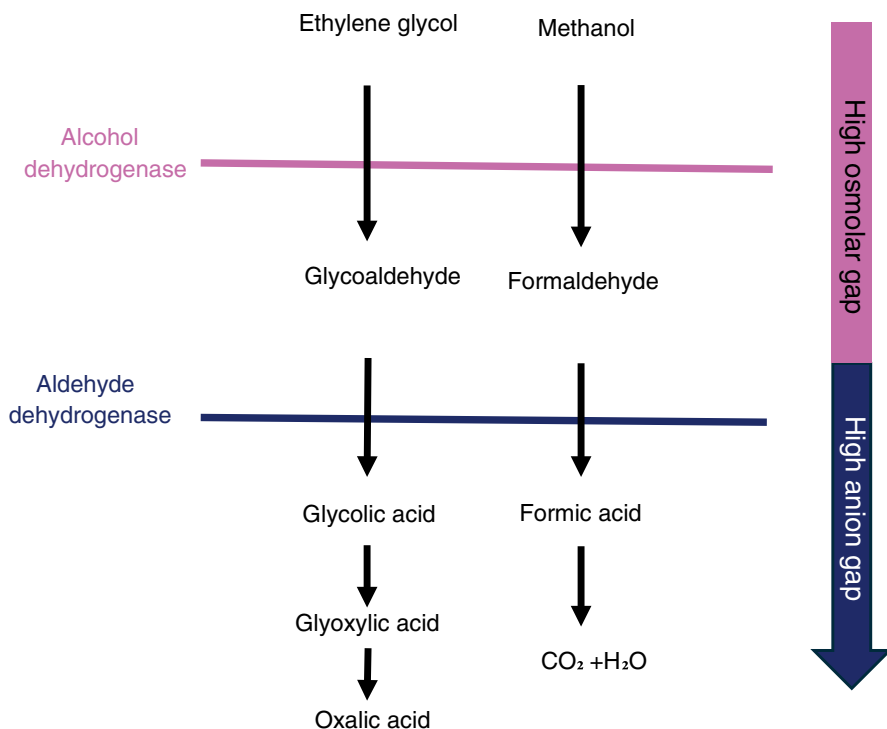


Fig. 6.6 Metabolism of toxic alcohols

Cyanide Toxicity

Pathogenesis and Etiology

Cyanide inhibits mitochondrial activity, leading to anaerobic metabolism and lactic acidosis. Sources of cyanide toxicity include inhalational injury (e.g., house fires) or as a side effect of certain drugs (e.g., sodium nitroprusside).

Arterial and venous blood gases, if taken together, may show similar oxygen level in both samples due to lack of oxygen consumption by tissues.

Treatment of Cyanide Toxicity

General approach: ABCDEF.

Hydroxocobalamin +/- sodium thiosulfate.

Cardiac toxins: common examples include:

- Calcium channel blockers (CCB) and beta-blockers (BB)
- Tricyclic anti-depressants (TCA)
- Digoxin

Calcium Channel Blockers (CCB) and Beta-Blockers (BB)

Clinical Manifestations

- Hypotension
- Bradycardia
- AV block
- Nausea and vomiting
- Low Glasgow coma scale (GCS)
- Hyperglycemia with CCB and hypoglycemia with BB

Management of CCB and BB Toxicity

General approach: ABCDEF.

For hypotension and bradycardia, follow the ACLS bradycardia algorithm (atropine, dopamine, epinephrine, and pacing).

Activated charcoal in the first 4 h.

Direct antidotes:

- Calcium: Calcium gluconate 3–6 g or Calcium chloride 1–2 g.
- Glucagon: 3–10 mg/h.
- High dose insulin euglycemia: 1–10 unit/kg infusion until improvement in heart rate (HR) >60 bpm and contractility function. Monitor serum glucose and potassium level frequently.
- Intralipid emulsion.

Tricyclic Antidepressant (TCA) Toxicity

Clinical Manifestations

- CNS manifestations: Decreased level of consciousness and seizure
- Cardiac manifestations: ECG changes (wide QRS, long QT, R wave in AVR >3 mm) (Fig. 6.7)
- Anticholinergic effect
- QRS >100 ms has a 30% risk of seizures.
QRS >160 ms has a 50% risk of arrhythmias.

Management of TCA Toxicity [4]

General approach: ABCDEF.

AC administration in the first 4 h.

Benzodiazepine is the best treatment for seizure in TCA toxicity.

Sodium bicarbonate (NaHCO₃): Initiate when ECG shows QRS >100 or arrhythmia.

Dose: 1–2 mEq/kg IV bolus, followed by 150 mEq + D5W 850 mL at a rate of 150–250 mL/h. Aim to maintain a serum pH of 7.45–7.55. Continue treatment until QRS is <100, arrhythmia is resolved, and the R wave in AVR is decreasing.

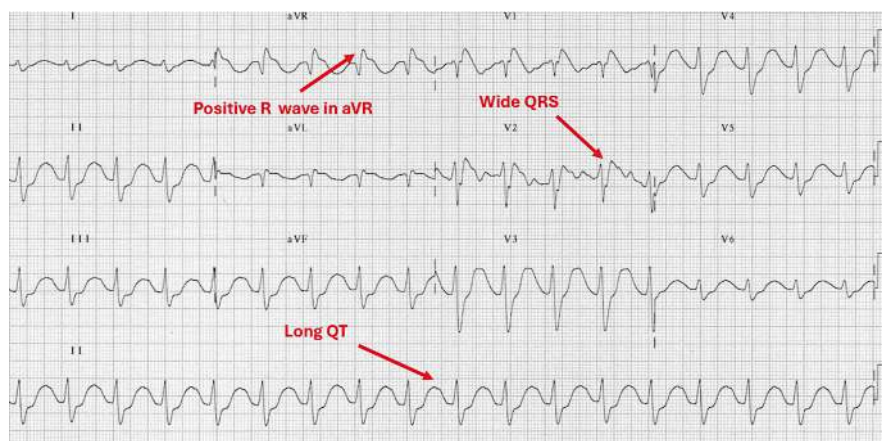


Fig. 6.7 ECG changes in tri-cyclic antidepressant toxicity

Table 6.3 Clinical manifestations of digoxin toxicity

<i>Digestive</i>	Vomiting, nausea, anorexia, diarrhea
<i>Neurologic</i>	Fatigue, headache, disorientation, delirium, confusion
<i>Visual</i>	Blurred or double vision, altered color perception, greenish-yellow halos around images or lights
<i>Cardiac arrhythmia</i>	PVCs (the most common), atrial tachyarrhythmias with AV block, bradycardia, ventricular bigeminy, junctional rhythms, VT and VF

AV atrioventricular, PVCs premature ventricular contractions, VT ventricular tachycardia, VF ventricular fibrillation

Digoxin Toxicity

Clinical manifestations of digoxin toxicity: summarized in Table 6.3.

Management of Digoxin Toxicity [5]

General approach: ABCDEF.

AC in the first 4 h.

Serial ECGs and serum potassium, renal function, and digoxin level (at presentation and after 6 h of ingestion) must be obtained.

Immune FAB is indicated in the following:

- Life-threatening or hemodynamically unstable arrhythmia (ventricular tachycardia; ventricular fibrillation; asystole; complete heart block; Mobitz II heart block; symptomatic bradycardia)
- Hyperkalemia (serum potassium >5 to 5.5 mEq/L)
- Evidence of end-organ dysfunction from hypoperfusion (e.g., renal failure, altered mental status).

Gastrointestinal Toxins

Paracetamol Toxicity

Pathogenesis: Paracetamol is mainly metabolized to sulphate and glucuronide metabolites. A small amount is metabolized by cytochrome P450 system to the toxic metabolite N-acetyl- benzoquinone-imine (NAPQI). Normally, NAPQI is detoxified by binding to glutathione, and the compound is then renally excreted. In overdose, metabolism to sulphate and glucuronide is overwhelmed. Metabolism via the P450 system increases and NAPQI production rises. If NAPQI production exceeds available glutathione, hepatic NAPQI levels rise and toxicity ensues.

Toxic dose

>10 g or >200 mg/kg as single ingestion or over 24 h period.

>6 g or >150 mg/kg per 24 h period over 2 days.

Risk Factors for Toxicity Include

- Pre-existing glutathione depletion, e.g., features of eating disorders, chronic alcoholism, cystic fibrosis, and human immunodeficiency virus (HIV)
- Pharmacological induction of the cytochrome P450 system, e.g., phenytoin, rifampin, and carbamazepine

Management of Paracetamol Toxicity [6, 7]

General approach: ABCDEF.

AC in the first 4 h.

Monitoring: In acute toxicity, check paracetamol levels between 4 and 24 h post-ingestion and assess using the *Rumack-Matthew* nomogram (Fig. 6.8). The *Rumack-Matthew* nomogram is useful only for single acute ingestion. It is not reliable for multiple ingestions or chronic supratherapeutic dosing.

Direct antidote: N-acetylcysteine (NAC)

- IV regimen: Loading dose: 150 mg/kg over 1 h, then: 50 mg/kg over 4 h, then: 100 mg/kg over 16 h.
- Oral regimen: Loading dose: 140 mg/kg, then: 70 mg/kg every 4 h $\times$ 17 doses.
- NAC is very effective and mostly prevents toxicity if administered within 8 h post-ingestion.
- NAC for chronic or multiple supratherapeutic ingestions is indicated if:
 - Paracetamol level >20 mcg/mL or
 - Abnormal liver function tests (LFTs)
- Urgent NAC + liver transplant referral are indicated If:
 - Creatinine >3.3 mg/dL
 - Prothrombin time (PT) >100 s
 - pH <7.3 or
 - Altered mental status

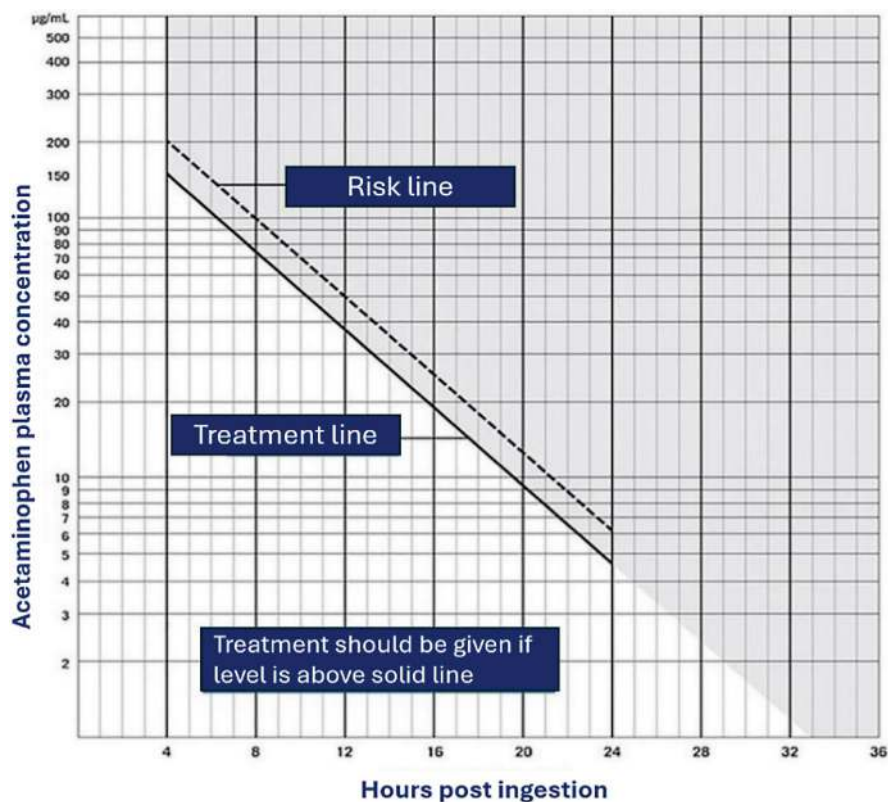


Fig. 6.8 Rumack-Matthew nomogram for paracetamol toxicity monitoring. (Adapted from Haider et al. [10])

- NAC is not indicated if:
 - Paracetamol level <10 mcg/mL and
 - Normal LFTs
- Stop NAC if:
 - Paracetamol level <10 mcg/mL.
 - Aminotransferases are clearly decreasing.
 - International normalized ratio (INR) <2.
 - If not, give additional 100 mg/kg over 16 h, then reassess.

Neurotoxins

- Lithium
- Isoniazid (INH)
- Carbon monoxide (CO)
- Sedations

Table 6.4 Manifestations of acute lithium toxicity

<i>Neurological</i>	Tremor, hyperreflexia, clonus Ataxia Confusion, delirium, agitation, coma Seizure
<i>Non-neurological</i>	Nausea, vomiting, diarrhea Tachycardia, arrhythmia Hyperthermia Shock

Lithium Toxicity

Lithium toxicity can occur with acute ingestion, an increased dose, or worsening renal function.

Primary toxicity is neurological dysfunction (see Table 6.4), but cardiac effects like arrhythmia can also occur.

Chronic toxicity may result in hyperparathyroidism, nephrogenic diabetes insipidus, or hypothyroidism.

Management of Lithium Toxicity

General approach: ABCDEF

Poor response to AC

Volume expansion with crystalloid

Hemodialysis is indicated in these conditions [3]:

- Serum level >5 mEq/L or >4 mEq/L with renal impairment
- End-organ damage like seizure, encephalopathy, or AKI

NB: Serum lithium level has a poor correlation with the degree of toxicity.

Carbon Monoxide (CO) Toxicity

CO poisoning is common and usually caused by inhalation of smoke or gases. It should be suspected in high-risk patients, as it can be missed due to falsely normal oxygen saturation. This occurs because CO binds to hemoglobin with 200 times greater affinity than oxygen and carboxyhemoglobin (COHb) absorbs light of pulse oximeters similarly to oxyhemoglobin.

Methemoglobinemia is another cause of impaired oxygen delivery, but in contrast, it shows signs of hypoxemia despite normal oxygen content. Table 6.5 compares CO poisoning and methemoglobinemia.

Table 6.5 Comparison between carbon mono-oxide and methemoglobinemia

	Methemoglobinemia	CO toxicity
Pathophysiology	Conversion of ferrous (Fe^{2+}) to ferric (Fe^{3+})/low affinity to oxygen	CO highly binds to hemoglobin
Causes	Congenital, nitrites, local anesthesia, sulphonamide, antimalaria	Burn (charcoal, house fire), gases
Clinical presentation	Cyanosis	Flushing, red mucosa, headache
Oxygen saturation	Low	Normal
Blood gas	Normal PaO_2	Low SaO_2
Investigation	Co-oximeter	Co-oximeter
Management	Stop the causative agent, methylene blue and ascorbic acid	100% oxygen +/- hyperbaric oxygen (if CO >25% or >15% in pregnancy, or in case of end organ damage)

PaO_2 partial pressure of arterial oxygen, SaO_2 arterial oxygen saturation

Hyperthermia

Difference Between Hyperthermia and Fever

Fever is an increase in body temperature due to resetting of the temperature center in the hypothalamus. Usually, it responds well to antipyretics. Common examples of conditions causing fever are infection, malignancy, and vasculitis.

Hyperthermia is an increase in body temperature due to an imbalance between heat production and heat loss.

Increased heat production can occur in neuroleptic malignant syndrome (NMS), serotonin syndrome (SS), thyroid storm, and malignant hyperthermia (MH). Decreased heat loss can occur in cases of heat stroke. Usually, such conditions do not respond to the regular antipyretics, and they need cooling methods like iced water and fans.

Differences Between NMS, SS and MH

- *Etiology:*
 - NMS: a delayed presentation which occurs as an adverse effect of antipsychotics [8].
 - SS: an acute presentation which occurs due to exposure to a serotonin-enhancing drugs, e.g., monoamine oxidase inhibitors (MAOI), selective serotonin reuptake inhibitors (SSRI) [9].
 - MH: an acute presentation which occurs after exposure to inhalational anesthesia or Succinylcholine, often due to a genetic defect in the ryanodine receptor.
- *Clinical presentation:* Table 6.6

Table 6.6 Clinical presentation of serotonin syndrome (SS), neuroleptic malignant syndrome (NMS), and malignant hyperthermia (MH)

	SS	NMS	MH
Onset	Abrupt	Gradual	Abrupt
Course	Rapid	Prolonged	Rapid
CNS exam	Myoclonus, tremors, and hyperreflexia	Diffused rigidity and hyporeflexia	Diffused rigidity and hyporeflexia
Pupils	Mydriasis	Normal	Normal
Others			Marked increase of CO ₂ production

CO₂ carbon dioxide

Management of the Three Conditions

General approach: ABCDEF

Patients with MH need hyperventilation

Cooling measures: cold intravenous fluids, cold blankets, ice, and fans. For persistent cases, consider extracorporeal membrane oxygenation (ECMO)

Volume expansion with crystalloid

Discontinue the causative agent

Treatment of the complications: disseminated intravascular coagulation (DIC), rhabdomyolysis, AKI

Antidote:

- For MH and NMS: dantrolene
- For SS: benzodiazepine, and in severe cases cyproheptadine

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Chapter 7

Nephrology



Haytham Abbas , Fahmi Aldhaheeri, and Majed Fakeeh

Introduction

Nephrology is an essential part of ICU practice, involving a range of critical conditions and skills that ICU staff must master. These include blood gas analysis, assessment and correction of electrolyte disturbances, and initiating continuous renal replacement therapy (CRRT). Acute kidney injury (AKI) is a common and serious complication in the ICU, requiring a structured and effective management approach, which will be discussed in this chapter.

Arterial Blood Gas (ABG)

Five key components must be identified when interpreting blood gas results:

1. Primary disorder
2. Compensation

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- 3. Anion gap (AG) calculation
- 4. Extra-metabolic disorder
- 5. Osmolar gap (OG)

Primary Disorder

It can be interpreted by the rule of 4 (Fig. 7.1).

Compensation

Compensation can be assessed using either a numerical method or specific formulas such as Winter’s formula for metabolic acidosis.

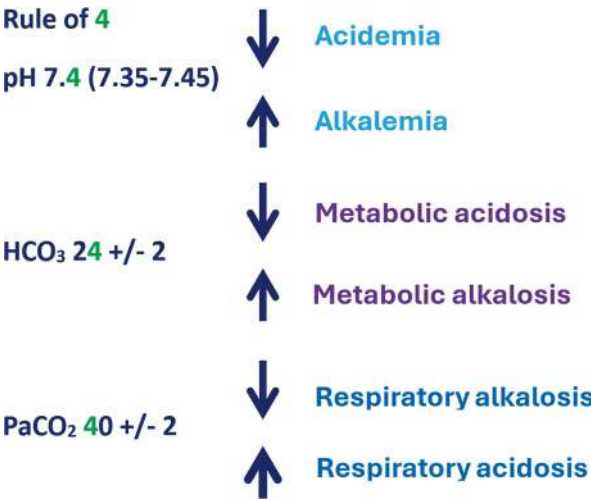
Numerical Method

1 2 4 5 7 10

HCO₃ = bicarbonate, PaCO₂ = partial pressure of arterial carbon dioxide.

In metabolic acidosis: For every ↓1 mmol/L in HCO₃, PaCO₂ decreases by 1 mmHg.
In metabolic alkalosis: For every ↑10 mmol/L in HCO₃, PaCO₂ increases by 7 mmHg.

Fig. 7.1 Primary disorder detection by rule of 4.
HCO₃ = bicarbonate,
PaCO₂ = partial pressure of arterial carbon dioxide



In acute respiratory acidosis: For every $\uparrow 10$ mmHg in PaCO_2 , HCO_3 increases by 1 mmol/L.

In chronic respiratory acidosis: For every $\uparrow 10$ mmHg in PaCO_2 , HCO_3 increases by 4 mmol/L.

In acute respiratory alkalosis: for every $\downarrow 10$ mmHg in PaCO_2 , HCO_3 decreases by 2 mmol/L.

In chronic respiratory alkalosis: for every $\downarrow 10$ mmHg in PaCO_2 , HCO_3 decreases by 5 mmol/L.

Equations

- Winter's Formula: expected PaCO_2 (mmHg) in metabolic acidosis =

$$1.5 \times \text{HCO}_3 (\text{mmol/L}) + 8 \pm 2$$

- Expected PaCO_2 (mmHg) in metabolic alkalosis =

$$0.9 \times \text{HCO}_3 (\text{mmol/L}) + 16 \pm 2$$

Anion Gap (AG) Calculation

$$\text{AG} (\text{mmol/L}) = \text{Na} (\text{mmol/L}) - [\text{Cl} (\text{mmol/L}) + \text{HCO}_3 (\text{mmol/L})]$$

Na = sodium, Cl = chloride.

Normally, it is ≤ 12 mmol/L.

In hypoalbuminemia (albumen < 4 g/dL), add 2.5 to the AG for every 1 g/dL of the reduced albumin.

Extra-Metabolic Disorder

In case of high anion gap metabolic acidosis (HAGMA), extra-metabolic disorders should be discovered by using the equation of: $(\text{calculated AG} - \text{normal AG}) / (\text{normal HCO}_3 - \text{measured HCO}_3) = \delta \text{AG} / \delta \text{HCO}_3$

$$= (\text{Calculated AG} - 12) / (24 - \text{HCO}_3)$$

Osmolar Gap (OG)

If the result is 1–2 = no added abnormality, >2 = metabolic alkalosis, <1 = non anion gap metabolic acidosis (NAGMA)

Osmolar gap is the difference between measured and calculated serum osmolality.

$$\begin{aligned} \text{Calculated Osmolality (mOsm / kg)} &= 2 * \text{Na (mmol / L)} \\ &+ \text{glucose (mg / dL)} / 18 + \text{BUN (mg / dL)} / 2.8 \end{aligned}$$

Na = sodium, BUN = blood urea nitrogen

If the OG is >10 mOsm/kg, it will suggest external ingestion of specific substances.

ABG interpretation example:

Na 149 mmol/L, Cl 105 mmol/L, HCO_3^- 17 mmol/L, blood urea nitrogen (BUN) 28 mg/dL, creatinine 2.3 mg/dL, albumin 4.0 g/dL, pH 7.3, PaCO_2 24 mmHg, PaO_2 90 mmHg, random blood sugar (RBS) 120 mg/dL, serum osmolality 350 mOsm/kg.

1. Primary disorder: metabolic acidosis (low pH and low HCO_3^-).
2. Compensation: Winter's formula $\text{PaCO}_2 = 1.5 \times 17 + 8 = 33.5$ mmHg so, the patient also has respiratory alkalosis.
3. AG: $\text{NA} - (\text{HCO}_3^- + \text{Cl}) = 27$ mmol/L (albumen is normal so, no correction for the AG).
4. Extra-metabolic disorder: $\Delta \text{AG} / \Delta \text{HCO}_3^- = 15/7 = 2.14$ so, the patient has metabolic alkalosis.
5. OG: measured Osm – calculated Osm
 $\text{Calculated Osm} = 2\text{Na} + \text{glucose}/18 + \text{BUN}/2.8 = 314$ mOsm/kg.
 $\text{OG} = 36$ mOsm/kg which is high.

So, the patient has HAGMA, respiratory alkalosis, metabolic alkalosis, and high OG.

Example for that, methanol toxicity with vomiting and hyperventilation for compensation.

Causes of HAGMA: it is summarized in Fig. 7.2.

Causes of NAGMA: Fig. 7.3.

In NAGMA, urine anion gap can help to differentiate between renal vs gastrointestinal causes.

$$\text{Urine anion gap (mEq / L)} = \text{urine} [\text{K (mEq / L)} + \text{Na (mEq / L)}] - \text{Cl (mEq / L)}$$

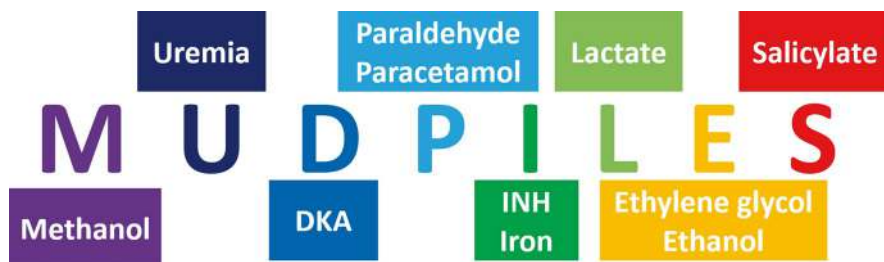


Fig. 7.2 Causes of HAGMA. DKA = diabetic ketoacidosis, INH = isoniazid



Fig. 7.3 Causes of NAGMA. RTA = renal tubular acidosis

Na = sodium, K = potassium, Cl = chloride

Chloride reflects ammonium (NH_4) secretion in the urine.

If the result is positive $\rightarrow$ renal cause

If the result is negative $\rightarrow$ gastrointestinal cause

Causes of high OG: summarized in Table 7.1.

Causes of Metabolic Alkalosis

Approaching metabolic alkalosis cases must involve assessment of urine chloride [$\text{UCl} > 20$ (mEq/L) = saline resistant, $\text{UCl} < 20$ (mEq/L) = saline responsive] and blood pressure assessment [renin angiotensin aldosterone system (RAAS) related or nonrelated] (Fig. 7.4).

Treatment of metabolic alkalosis:

- Saline-responsive type: Treat with normal saline and stop diuretics.
- Saline-resistant type: Treat the underlying cause.
- If volume overload: Use potassium-sparing diuretics or acetazolamide.
- If hypokalemia: Give potassium replacement and potassium-sparing diuretics.

Table 7.1 Causes of high anion gap (AG) and osmolar gap (OG)

AG	OG	Example
High	High	Methanol, ethanol, ethylene glycol, propylene glycol
Normal	High	Isopropyl alcohol
High	Normal	Salicylate, paracetamol

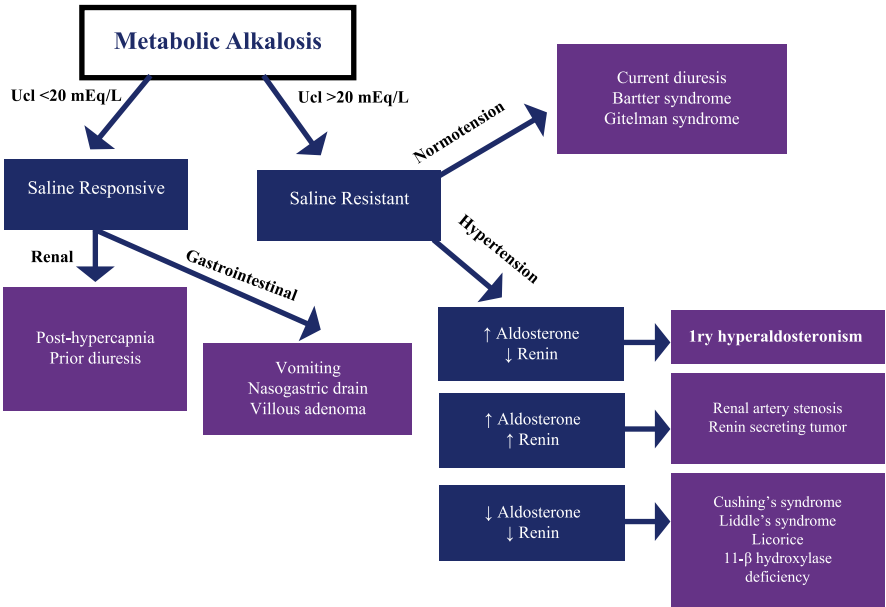


Fig. 7.4 Approach and causes of metabolic alkalosis

Sodium Homeostasis

Sodium homeostasis depends mostly on the water content in the body; when the body’s water increases, sodium starts to decrease. Antidiuretic hormone (ADH) is the most hormone to control the body’s water content and therefore the sodium level. Aldosterone is another hormone, which can play a role in sodium homeostasis in response to renin angiotensin aldosterone system (RAAS) in case of hypoperfusion as it acts on distal tubules to enhance sodium reabsorption.

Approach to Hyponatremia (Fig. 7.5)

Hyponatremia is evaluated clinically using history, physical examination, and investigations to determine the etiology and volume status. Management is guided accordingly.

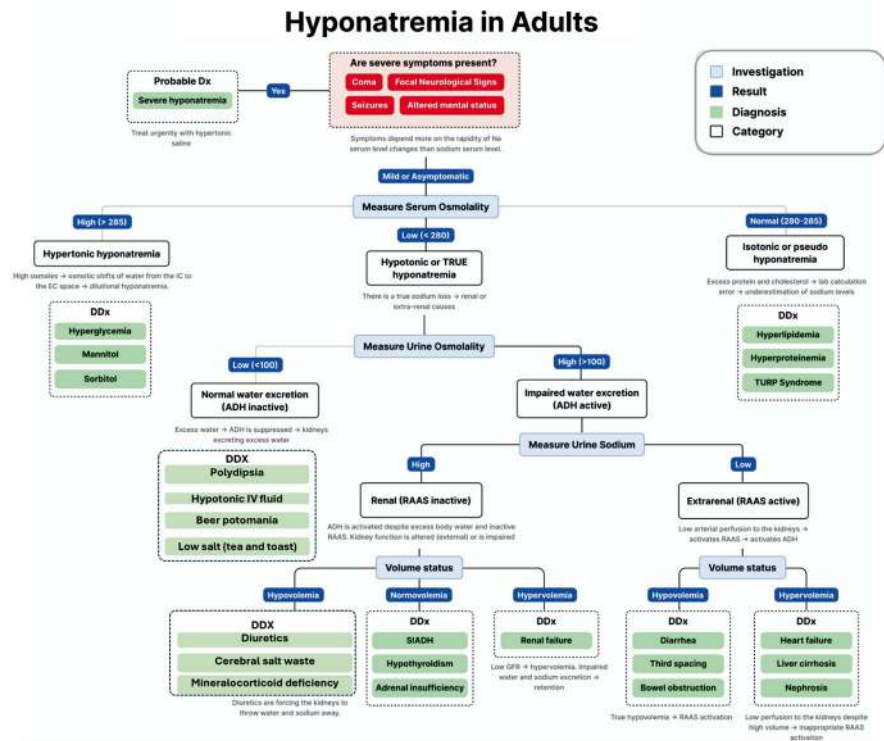


Fig. 7.5 Approach to hyponatremia. IC = intracellular, EC = extracellular, TURP = transurethral resection of the prostate, SIADH = syndrome of inappropriate antidiuretic hormone secretion, IV = intravenous, ADH = antidiuretic hormone, RAAS = renin angiotensin aldosterone system, GFR = glomerular filtration rate. (Adapted from the original source, courtesy of Khudhur M., used with permission)

History: Assess clinical presentation (e.g., altered consciousness, weakness, seizures), symptom duration (<48 h or >48 h), precipitating factors (poor intake, vomiting, diarrhea, diet, medications such as diuretics, antipsychotics, antidepressants), and comorbidities (central nervous system [CNS], thyroid, adrenal, cardiac, pulmonary, liver, and renal disease).

Clinical examination: Aims to address the volume status of the patient (hypervolemic, hypovolemic, or euvolemic), neurological signs, e.g., level of consciousness and signs of chronic disease (cardiac, pulmonary, CNS, thyroid, adrenal, hepatic, or renal diseases).

Investigations of Hyponatremia

- Serum osmolality, urine osmolality, and urine sodium.
- Renal function and other electrolytes: exclude other metabolic derangement.
- Random blood sugar (RBS): each 100 mg/dL increases in RBS, and sodium decreases by 2 mEq/L.

- Complete blood count (CBC): exclude anemia of chronic disease.
- Liver Function Test (LFT).
- Blood gas: assess for metabolic acidosis, metabolic alkalosis and measure anion gap.
- Cardiac enzymes, electrocardiogram (ECG), and echocardiography.
- Thyroid Function Test (TFT).
- Cortisol level.
- Chest X-ray: rule out pulmonary disease.
- Abdominal ultrasound: assess liver and kidneys.

Management of Hyponatremia

Management aims to correct serum sodium and address the underlying cause, including discontinuation of offending drugs. This requires thorough assessment to identify the etiology and frequent monitoring of serum sodium during correction. Five key factors to consider:

- Severity of hyponatremia (severe if <120 mEq/L)
 - Duration: acute (<48 h) vs. chronic (>48 h)
 - Symptoms: symptomatic vs. asymptomatic
 - Volume status: hypovolemic, euvolemic, or hypervolemic
 - Serum osmolality: hypo-osmolar, iso-osmolar, or hyperosmolar
- In acute hyponatremia (<48 h), correction to normal sodium levels is acceptable due to a low risk of osmotic demyelination syndrome (ODS). In chronic hyponatremia (>48 h), unknown duration, or no previous sodium baseline:

- Limit correction to $\leq 6-8$ mEq/L/day in high-risk patients for ODS
- Limit to $\leq 10-12$ mEq/L/day in low-risk patients

Risk factors for ODS are:

- Serum sodium <105 mEq/L
- Hypokalemia
- Liver disease
- Malnutrition
- Alcoholism

In symptomatic hyponatremia (e.g., unconsciousness, agitation, seizures), initiate hypertonic saline with hourly serum sodium monitoring until an increase of 4–6 mEq/L is achieved or symptoms resolve.

In cases of hyponatremia with CNS pathology (e.g., stroke, traumatic brain injury), treatment with hypertonic saline is also indicated.

In asymptomatic hyponatremia, management is guided by volume status:

- Hypovolemic: Treat with normal saline, encourage oral intake, and discontinue thiazide diuretics.
- Euvolemic: address and treat the cause:
 - Syndrome of inappropriate antidiuretic hormone secretion (SIADH): Implement fluid restriction, discontinue offending drugs (e.g., antipsychotics, antidepressants), and treat underlying CNS or pulmonary disease.

- Hypothyroidism or adrenal insufficiency: hormone replacement.
- Psychogenic polydipsia: water restriction.
- Beer potomania/tea and toast diet: increase salt intake.
- Hypervolemia: Use loop diuretics (e.g., furosemide) and manage underlying cardiac, renal, or hepatic disease.

If rapid correction of hyponatremia occurs, consider D5W (5% dextrose in water) $\pm$ desmopressin to prevent or limit further overcorrection.

Correction of serum sodium by giving 1 L of fluid can be estimated by the following equation:

$$\begin{aligned} & (\text{Infusate Na} - \text{serum Na}) / \text{total body water (TBW)} \\ & (\text{sodium content in the IVF} : 3\% \text{NaCl} = 513 \text{ mEq / L}, 0.9\% \text{NaCl} = 154 \text{ mEq / L}) \\ & (\text{TBW} = 60\% \text{ of weight in kg in males}, 50\% \text{ of weight in kg in females}). \end{aligned}$$

Example: 70 kg female patient with serum sodium of 110 mEq/L and planned to be started on 1 L of 3%NaCl, the expected increase in serum sodium = $(513 - 110) / (70/50) = 11.5 \text{ mEq/L}$.

Approach to Hypernatremia

Like hyponatremia, approach to hypernatremia requires assessment of volume status and underlying causes. History, examination, and investigations guide appropriate management.

History: includes symptoms (confusion, weakness, coma) and precipitating factors (poor oral intake, diarrhea, vomiting, hypertonic solution use, CNS diseases, drug history such as lithium and furosemide).

Clinical examination: focuses on volume status and assessment of comorbidities, such as CNS disease.

Investigations of hypernatremia: include serum osmolarity, urine osmolarity, urine sodium, basic metabolic profile, and other electrolytes (Fig. 7.6).

Management of Hypernatremia

Depends on whether hypernatremia is acute or chronic and involves treating the underlying cause. In volume depletion, correction is done with hypotonic fluids, e.g., dextrose, hypotonic saline ($\frac{1}{2}$ NS, $\frac{1}{4}$ NS), or plain water.

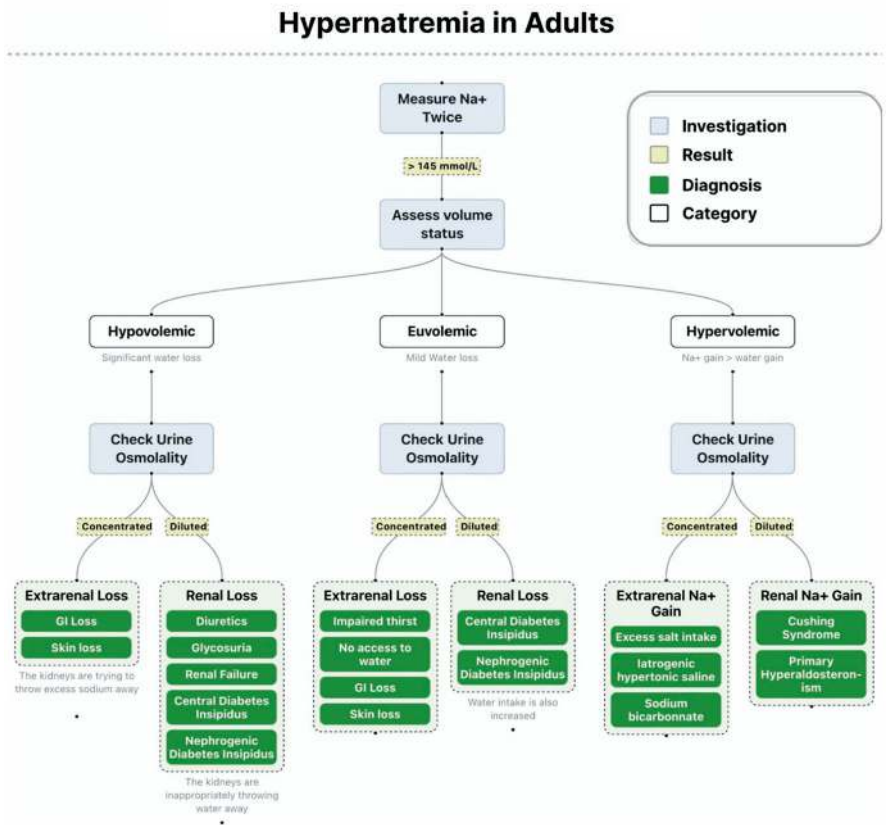


Fig. 7.6 Approach and causes of hypernatremia. GI = gastrointestinal. (Courtesy of Khudhur M., used with permission)

Water deficit (WD) is estimated using:

$$\text{Water Deficit} = \left[\frac{(\text{serum Na} - 140)}{140} \right] \times \text{TBW}$$

Total body water (TBW) = 60% of wt in kg in males, 50% of wt in kg in females.

Example: 80 kg male patient with serum Na of 160 mEq/L, $\text{WD} = (160 - 140)/140 \times (80 \times 0.6) = 6.8 \text{ L}$

In acute setting, correction can be safe as there is low risk of brain edema. In chronic setting, correction of serum sodium must be slow, not to exceed 10 mEq/L/24 h.

Hypervolemia with hypernatremia is managed by discontinuation of the hypertonic solution, starting hypotonic solutions like dextrose and diuresis.

Diabetes insipidus (DI) is managed with desmopressin for central DI, correction of the etiology, and thiazide for nephrogenic DI.

Potassium Homeostasis

Potassium (K) homeostasis is regulated by multiple mechanisms:

- Renal system: K excretion is regulated in the distal tubules by renin angiotensin aldosterone system (RAAS), where aldosterone increases sodium reabsorption and excretion of potassium and hydrogen.
- Transcellular shift: Various factors influence K movement between intracellular and extracellular compartments.
- Gastrointestinal (GI): A high-potassium diet increases GI absorption, while some medications reduce potassium availability by limiting its absorption.

Approach to Hypokalemia

Understanding potassium homeostasis helps guide the approach to hypokalemia.

Key factors include:

- Blood pressure: Hypertensive vs normotensive
- Urine potassium: Renal vs extrarenal losses
- Acid-base status: Metabolic alkalosis vs acidosis
- Other contributing factors: Hypomagnesemia and conditions causing intracellular shift (e.g., insulin, beta agonists, metabolic alkalosis, hypokalemic periodic paralysis) (Fig. 7.7)

Investigations of Hypokalemia

Urine K/Creatinine ratio, 24 h urine K, blood gas, serum magnesium, and renin/aldosterone in case of hypertension.

Electrocardiogram (ECG): assess QT interval, U wave, ST, T wave changes (Fig. 7.8).

Management of Hypokalemia

As in any critical case, severe hypokalemia must be approached with ABC and management of each step accordingly.

Direct management involves potassium replacement, correction of the underlying cause (e.g., stopping causative drugs), and addressing associated electrolyte abnormalities such as hypomagnesemia.

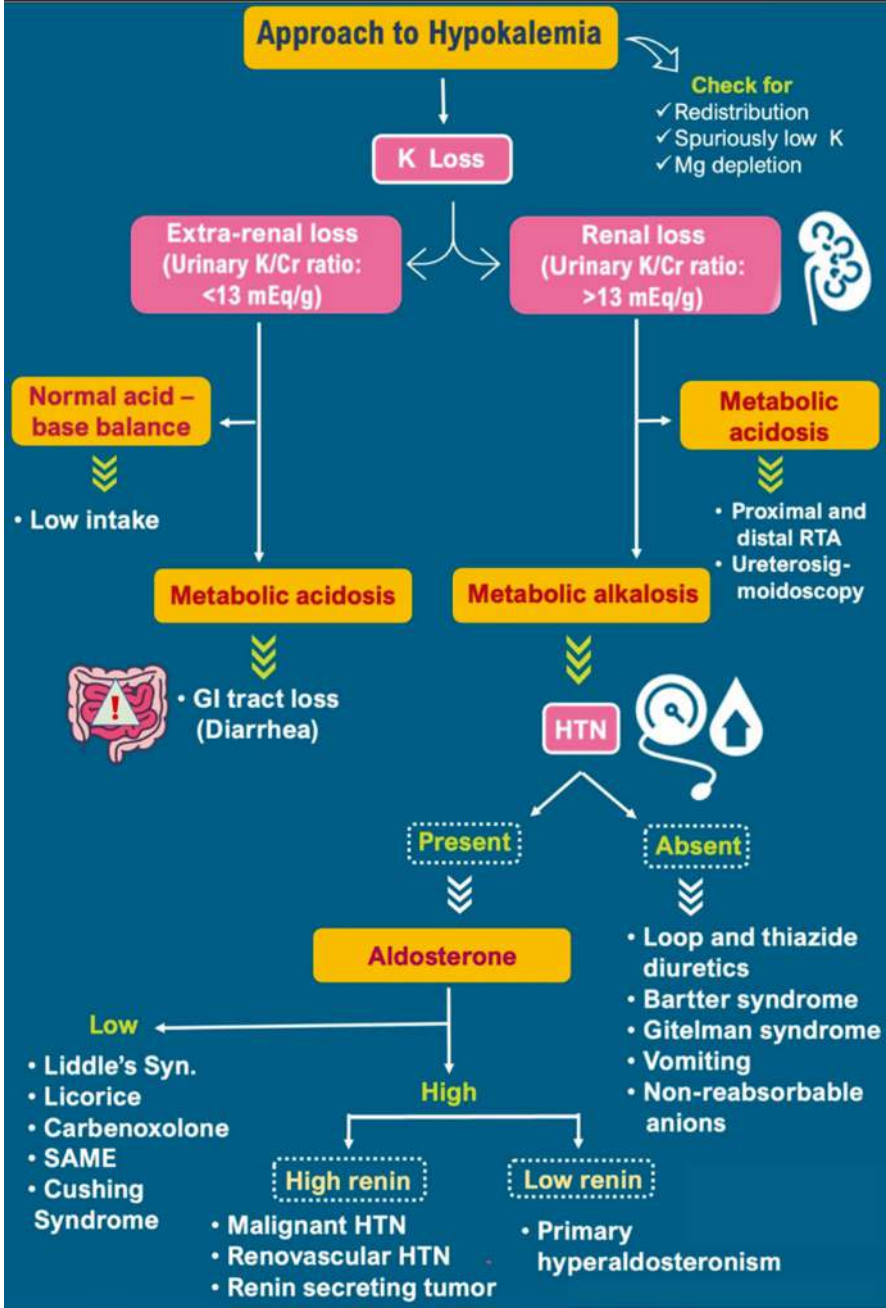


Fig. 7.7 Approach and causes of hypokalemia, RTA = renal tubular acidosis, SAME = syndrome of apparent mineralocorticoid excess, HTN = hypertension, K = potassium, Mg = magnesium, Cr = creatinine, GI = gastrointestinal. (Courtesy of Priti Meena M.D, used with permission)

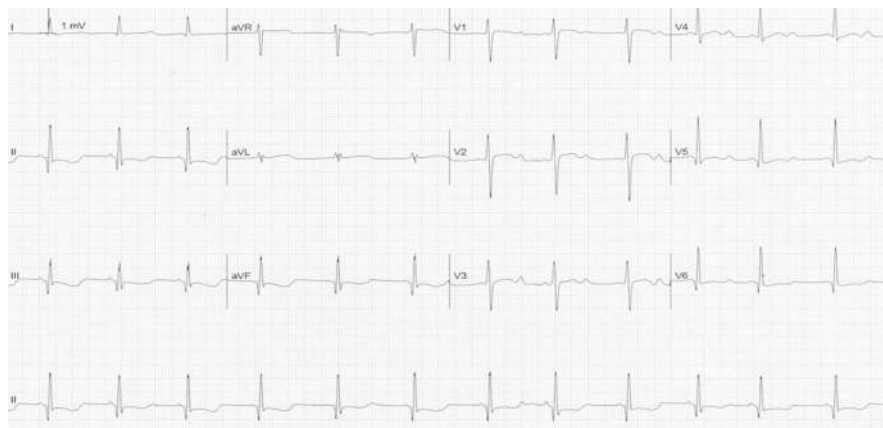


Fig. 7.8 U wave, flat T wave, ST depression in case of hypokalemia

Potassium chloride can be administered at a rate of 10 mEq/h peripherally. If rapid correction is needed, it can be given through a central line at a rate of up to 40 mEq/h. Oral potassium and potassium sparing diuretics can also be considered.

Approach to Hyperkalemia

As with hypokalemia, understanding potassium homeostasis is key. Hyperkalemia may result from decreased renal excretion of potassium or increased extracellular shift. Other mechanism is increased potassium production after an acute insult like rhabdomyolysis, tumor lysis syndrome (TLS), or hemolysis. In some situations, potassium level can be falsely high due to technical problem or pseudohyperkalemia as in the case of thrombocytosis and leukocytosis (Fig. 7.9).

Investigations of Hyperkalemia

Renal function and other electrolytes, urine potassium, and blood gas.

Complete blood count (CBC): rule out hemolysis and pseudohyperkalemia due to leukocytosis or thrombocytosis.

Creatine kinase (CK): for suspected rhabdomyolysis.

Uric acid: for suspected TLS.

Cortisol level.

Abdominal ultrasound: assess renal status.

ECG: assess for changes of hyperkalemia; tented T waves, PR prolongation, wide QRS, flattening of P wave and sine waves (Fig. 7.10).

Management of Hyperkalemia

As in any critical case, hyperkalemia is approached with ABC and management of each step accordingly.

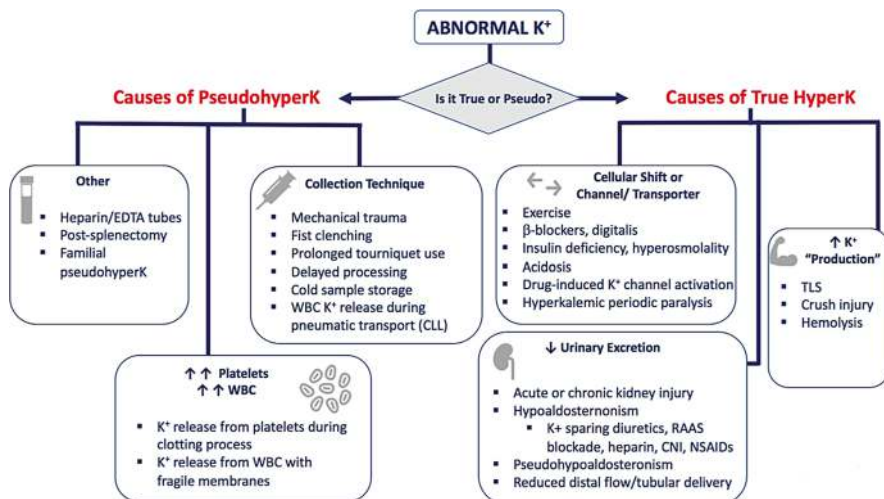
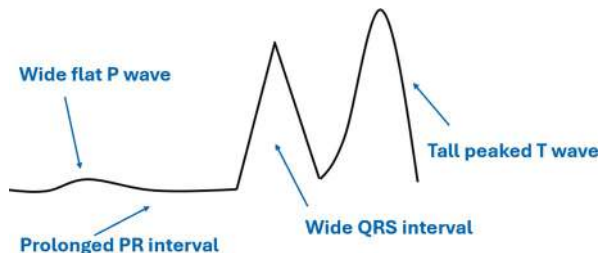


Fig. 7.9 Approach and causes of hyperkalemia. TLS = tumor lysis syndrome, β = beta, RAAS = renin angiotensin aldosterone system, CNI = calcineurin inhibitors, NSAIDs = nonsteroidal anti-inflammatory drugs, WBC = white blood cells, CLL = chronic lymphocytic leukemia, EDTA = Ethylenediaminetetraacetic Acid. (Courtesy of NephSim, used with permission)

Fig. 7.10 ECG changes in hyperkalemia



Treatment of the underlying etiology is essential.

Anti-hyperkalemic agents can be classified as the following:

- Cardiac stabilizers in case of ECG changes, including calcium gluconate 1–3 g or calcium Chloride 1 g.
- Lowering agents acting by inducing intracellular shifting: intravenous insulin with dextrose, e.g., 10 units insulin + 50 mL of dextrose 50%, salbutamol nebulization 20 mg, and sodium bicarbonate 50–200 mEq.
- Lowering agents acting on the renal system: furosemide (if overloaded), intravenous fluid (if hypovolemic), and hemodialysis.
- Lowering agents decreasing GI potassium absorption: patiromer or sodium zirconium.

Magnesium Homeostasis

Uses of Magnesium in the ICU

- *Asthma exacerbation*: magnesium avoids smooth muscle contraction and inhibits acetylcholine release and therefore induces bronchodilation.
- *Super-refractory status epilepticus*: it depresses the central nervous system (CNS) and may control seizure.
- *Preeclampsia/eclampsia*: the drug of choice for prevention and treatment of seizure.
- *Torsade de points*: polymorphic ventricular tachycardia because of long QT syndrome.

Complications of Hypermagnesemia

- *Cardiovascular*: hypotension, bradycardia, prolonged PR, wide QRS, atrioventricular block, and cardiac arrest.
- *Pulmonary*: respiratory depression; respiratory rate (RR) should be monitored periodically.
- *CNS*: coma, hyporeflexia, muscle weakness; deep tendon reflexes should be examined periodically.

Management of Hypermagnesemia

Magnesium toxicity should be approached with ABC and management of each step accordingly.

- Stop magnesium administration.
- Calcium chloride or calcium gluconate with a dose of 1 g can be administered especially if cardiac complications happen.
- Remove magnesium from the body: diuretics or hemodialysis in severe cases.
- Monitoring serum magnesium regularly.
- Repeated examination of deep tendon reflexes, RR, and continuous electrocardiogram (ECG) to monitor clinical response to treatment.

Acute Kidney Injury (AKI)

Scoring System for AKI

Multiple systems were designed to diagnose and classify AKI; Kidney Disease Improving Global Outcomes (KDIGO) and RIFLE are common examples (Tables 7.2 and 7.3).

Causes of AKI

- *Pre-renal*: due to ischemia, sepsis, shock, cardiorenal syndrome, hepatorenal syndrome (HRS), abdominal compartment syndrome (ACS), renal artery thrombosis, nonsteroidal anti-inflammatory drugs (NSAIDs), contrast induced nephropathy (CIN).

Table 7.2 KDIGO staging system

Stage	Creatinine criteria	Urine output criteria
1	Cr 1.5–1.9 times baseline, OR Cr increase >0.3 mg/dL	<0.5 mL/kg/h × 6–12 h
2	Cr 2–2.9× baseline	<0.5 mL/kg/h for >12 h
3	Cr >3× baseline, OR Cr >4 mg/dL, OR Initiation of RRT	<0.3 mL/kg/h for >24 h, OR Anuria >12 h

Sourced from: Khwaja [13]

RRT renal replacement therapy, Cr creatinine

Table 7.3 RIFLE classification system

Stage	Creatinine criteria	Urine output criteria
Risk	Cr 1.5 times baseline	< 0.5 mL/kg/h × 6 h
Injury	Cr 2 times baseline	<0.5 mL/kg/h for >12 h
Failure	Cr >3× baseline OR Cr >4 mg/dL	<0.3 mL/kg/h for >24 h, OR Anuria >12 h
Loss	Complete loss of kidney function for >4 weeks	
ESRD	Complete loss of kidney function for >3 months	

Sourced from: Bellomo et al. [14]

Cr creatinine, ESRD end stage renal disease

- *Renal:*

- Acute tubular necrosis (ATN):

- Ischemia: due to the same causes of prerenal
- Drugs: vancomycin, aminoglycoside, foscarnet, amphotericin, cisplatin, hydroxyethyl starch (HES)
- Pigments: myoglobin (rhabdomyolysis) and hemoglobin (intravascular hemolysis)
- Crystals: due to uric acid, acyclovir
- Monoclonal immunoglobulin light chains (in multiple myeloma)
- Contrast induced nephropathy

- Acute interstitial nephritis (AUN):

- Allergic: beta lactams, sulfa drugs, NSAIDs, proton pump inhibitors (PPIs)
- Infection: pyelonephritis, viral, legionella, tuberculosis
- Infiltrative: sarcoidosis, lymphomas, leukemias
- Autoimmune: Sjögren's, tubulointerstitial nephritis and uveitis (TINU) and systemic lupus erythematosus (SLE)

Table 7.4 Laboratory findings in pre-renal and acute tubular necrosis AKI

Pre-renal	ATN
Blood urea nitrogen (BUN)/creatinine >20	BUN/ creatinine <20
Bland sediment	Granular cast (muddy brown) see Fig. 7.11
Fractional excretion of sodium (FENa) <1% ^a	FENa >2%
Fractional excretion of urea (FEUN) <35% ^a	FEUN >50%
Urine sodium <10–20 mEq/L	Urine sodium >20–40 mEq/L
Urine osmolality >500 mOsm/kg	Urine osmolality <350 mOsm/kg

^aFENa = (UNa/PNa)/(UCr/PCr), if the patient is on diuretic use FEUN = (UUN/PUN)/(UCr/PCr), (UNa = urine sodium, PNa = plasma sodium, UCr = urine creatinine, PCr = plasma creatinine, UUN = urine urea, PUN = plasma urea)

- Glomerulonephritis (GN):
 - Nephritic syndrome: post-infection GN, endocarditis, lupus nephritis, membranoproliferative, cryoglobulinemia, IgA nephropathy, anti-neutrophil cytoplasmic antibodies (ANCA) vasculitis
 - Nephrotic syndrome: membranous, minimal change, focal segmental glomerulosclerosis, diabetes mellitus, amyloidosis, SLE, and cryoglobulinemia
- Thrombotic micro-angiopathy (TMA): thrombotic thrombocytopenic purpura (TTP), hemolytic uremic syndrome (HUS), and catastrophic anti-phospholipid syndrome (APL).
- *Post renal*: obstruction due to stone, bladder cancer.

Investigations for AKI

Complete blood count (CBC) and coagulation profile: assess for TMA, anemia.

Chemistry, renal function, and blood gases.

Urine analysis, microscopy, osmolality, electrolytes (sodium, urea, and creatinine).

Autoimmune profile, complement levels (C3, C4): for suspected GN.

Renal ultrasound.

Kidney biopsy: if diagnosis is unclear.

Pre-Renal vs ATN

Table 7.4 explains the laboratory findings in each one.

Management of AKI

As in any critical case, AKI is approached with ABC and management of each step accordingly.

Treatment of the causative agent is essential.

STOP approach for AKI:

- *Sepsis* and hypoperfusion: administer fluids, maintain hemodynamics and euvolemia.

Fig. 7.11 Granular cast (muddy brown) in ATN. (Courtesy of NephSim, used with permission)

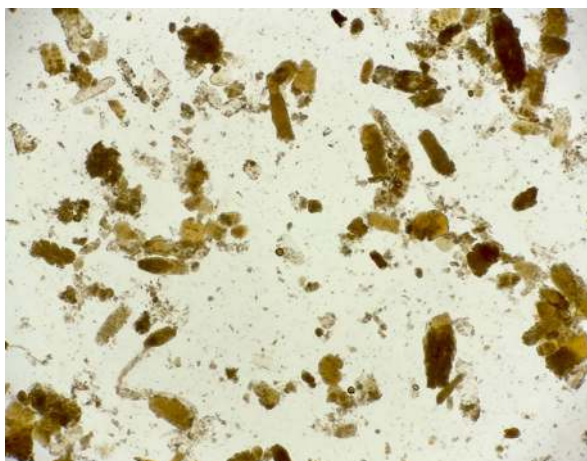
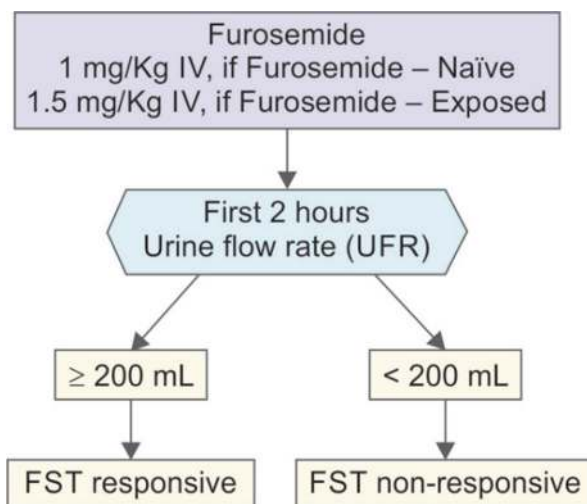


Fig. 7.12 Furosemide Stress Test [1]



- *Toxins*: avoid nephrotoxic agents.
- *Obstruction*: insert Foley's catheter and rule out obstruction via ultrasound.
- *Primary renal disease*: Perform full workup; treat underlying cause.

Volume Overload and Furosemide Stress Test (FST)

Start diuretics in volume overload. If oliguria persists, perform FST (Fig. 7.12). A positive response indicates intact tubular function and likely short-term recovery. A negative response suggests ongoing dysfunction and possible need for dialysis [1].

Renal replacement therapy (RRT): Initiate continuous or intermittent hemodialysis if absolute indications are present:

- Persistent acidemia
- Persistent hyperkalemia

- Refractory overload
- Uremic pericarditis
- Uremic encephalopathy
- Dialyzable drug intoxication (illustrated in Chap. 6)

Multiple trials, including *IDEAL-ICU* and *AKIKI* trials, compared early vs late initiation of RRT. No significant differences in mortality or major outcomes were observed between the groups [2, 3].

Contrast-Induced Nephropathy (CIN)

Mechanism of Nephrotoxicity

Iodine contrast can induce nephrotoxicity with multiple mechanisms:

- Pre-renal vasoconstriction
- Acute tubular necrosis
- Contrast induced diuresis

Risk Factors for CIN

- Old age
- Diabetes mellitus
- Acute illness, e.g., sepsis or shock
- Pervious chronic kidney disease (CKD) with GFR <30 mL/min
- Use of nephrotoxic medication, e.g., NSAIDs

Prevention of CIN

- Avoid contrast if not essential.
- If needed, use low volume and low concentration; avoid repeated doses.
- Avoid other nephrotoxic drugs.
- Optimize hemodynamics and administer intravenous crystalloid [4].
- Sodium bicarbonate may be administered [4–6].
- N-acetylcysteine: no strong evidence for its efficacy [4, 6, 7].
- Hold metformin >48 h before contrast to reduce lactic acidosis risk.

Rhabdomyolysis

A syndrome of muscle necrosis with myoglobin release into circulation. Myoglobin can obstruct renal tubules and cause volume depletion, leading to kidney injury.

Causes of Rhabdomyolysis

- Trauma: crush injury, burn, prolonged immobility, surgery, compartment syndrome.
- Exertional: heat stroke, seizure, malignant hyperthermia (MH), neuroleptic malignant syndrome (NMS).

- Non-exertional: electrolyte disturbances, e.g., hypokalemia, drug, e.g., statin, propofol, and cocaine.

Investigations for Rhabdomyolysis

Chemistry and renal function: AKI, hyperkalemia, hypocalcemia, and hyperphosphatemia are expected.

Urine analysis: positive blood with no red blood cells due to pigments of myoglobin.

Creatine kinase (CK): usually >5000 units/L.

Treatment of Rhabdomyolysis

Follows standard AKI management approach.

Treat underlying cause.

Aggressive intravenous hydration with crystalloids; target urine output 2–3 mL/kg/h [8].

Sodium bicarbonate (NaHCO_3) +/- diuresis can be considered despite having no strong evidence [8–10].

Correct electrolyte abnormalities (e.g., hyperkalemia, hyperphosphatemia).

Renal Replacement Therapy (RRT)

Renal Replacement Therapy (RRT) is a modality that replaces the normal blood-filtering function of the kidneys. It is used when the kidneys lose their function in case of acute or chronic renal failure.

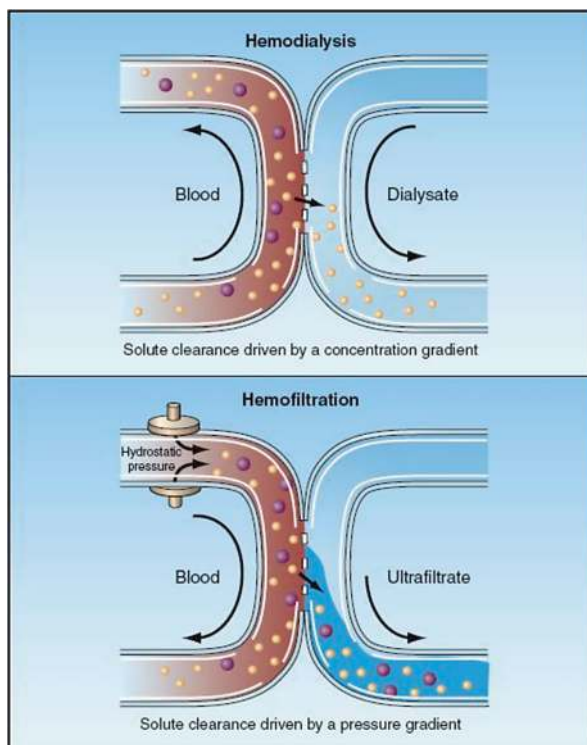
RRT Modalities

- Intermittent renal replacement therapy (IRRT)
 - Intermittent hemodialysis (IHD)
 - Peritoneal dialysis (PD)
- Continuous renal replacement therapy (CRRT).
 - Continuous veno-venous hemodialysis (CVVHD)
 - Continuous veno-venous hemofiltration (CVVH or CVVHF)
 - Continuous veno-venous hemodiafiltration (CVVHDF)
- Other modalities of dialysis:
 - SCUF → slow continuous ultrafiltration
 - SLED → sustained low-efficiency dialysis
- Renal transplant

Mechanisms of Action of RRT (Fig. 7.13)

Blood passes through a semi-permeable membrane, allowing solute and water removal via:

Fig. 7.13 Mechanisms of solute clearance by hemodialysis and hemofiltration. (Courtesy of Anesthesia Key, 34-3, used with permission)



Diffusion → Hemodialysis

Convection → Hemofiltration

Hemodialysis (Diffusion, CVVHD)

- Solutes move across the membrane via a concentration gradient.
- Effective for removing small solutes (e.g., urea, creatinine, electrolytes).

Hemofiltration (Convection, CVVHF)

- Water and solutes move across the membrane via a pressure gradient.
- Requires replacement fluid, given pre- and post-filter.
- Pre-filter: reduces clotting risk.
- Post-filter: improves convective clearance.
- Removes larger solutes, e.g., inflammatory mediators.

Hemodiafiltration (CVVHDF)

Both diffusion and convection

Intermittent vs. continuous RRT:

see Table 7.5

Table 7.5 Comparison between intermittent hemodialysis (IHD) and continuous renal replacement therapy (CRRT)

	Advantages	Disadvantages
IHD	Short duration Less anticoagulation (less bleeding) Better in hyperkalemia	Technically difficult Requires trained personnel Requires a fresh water supply Requires hygienic removal of effluent More hemodynamic instability More electrolyte disequilibrium
CRRT	Hemodynamic stability compared to IHD (however not translated into reduced mortality) Easy to operate Superior solute and volume control Adequate nutritional support is possible	Urea clearance is limited by exchange volume and interruptions Requires anticoagulation Mobilization of patients is difficult Not good in hyperkalemia as IHD More hypothermia More infection due to manipulation of dialysate and replacement bags

Writing Order for CRRT

Consists of the following data:

1. Type of CRRT and duration
2. Dialysis dose: divided to
 - Dialysate flow rate (DFR) (mL/h)
 - Replacement fluid (RF) (mL/h) pre- and post-filter
 - Ultrafiltration (UF) (mL/h)
3. Blood flow rate (mL/min)
4. Use of anticoagulants
5. Measuring filtration fraction

1. Type of CRRT and duration

The choice of CRRT modality depends on the clinical assessment of the patient and whether convection (e.g., CVVHF), diffusion (e.g., CVVHD), or a combination of both (e.g., CVVHDF) is most appropriate.

It usually extends for 24–72 h.

2. Dialysis dose

Optimal dose of renal replacement therapy (RRT) is controversial.

High-dose (40 mL/kg) versus low-dose (25 mL/kg) CRRT showed no significant difference in major outcomes, but high dose was linked to increased hypophosphatemia and more frequent filter changes (*RENAL trial* [11]).

The dose is divided into dialysate flow rate, replacement fluid (pre-/post-filter), and ultrafiltration.

The common usable dose of CRRT is 25–30 mL/kg/h.

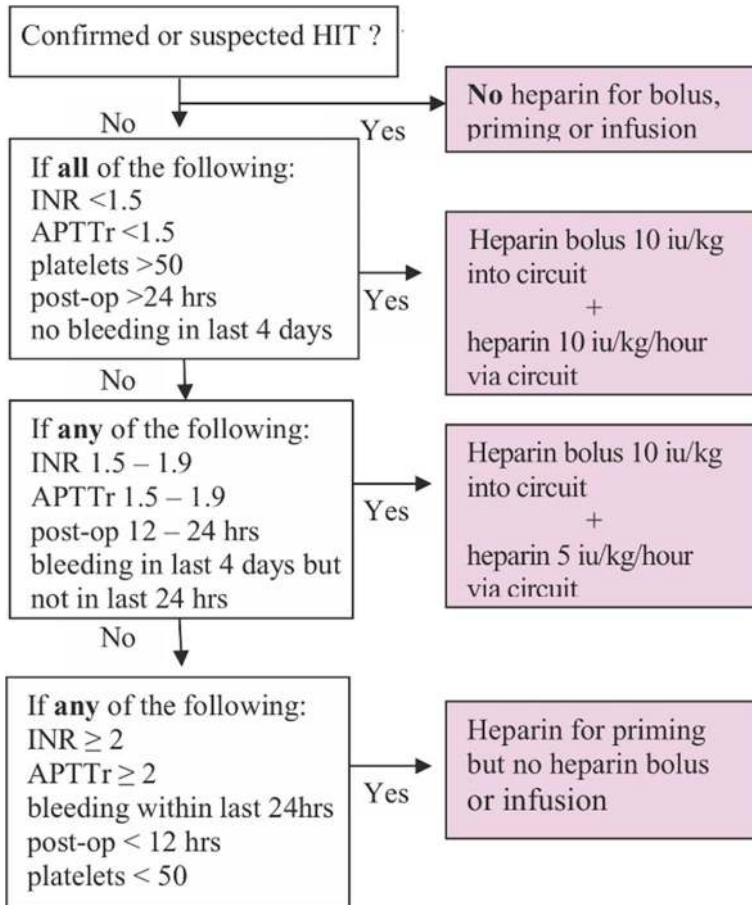


Fig. 7.14 Heparin anticoagulation during continuous renal replacement therapy. HIT = heparin induced thrombocytopenia, INR = international normalized ratio, APTTr = activated partial thromboplastin time ratio [12]. (Used with permission)

3. Blood flow rate

Higher blood flow reduces the risk of circuit clotting. If anticoagulated, set blood flow at 150–200 mL/min; if not anticoagulated, increase to 200–300 mL/min.

4. Anticoagulation (AC): heparin vs citrate or no AC

If normal coagulation profile → heparin (Fig. 7.14) [12]

If coagulopathic → citrate or no AC

Monitor for citrate toxicity:

- Hypocalcemia (ionized calcium)
- Metabolic alkalosis
- Avoid in liver failure due to risk of metabolic acidosis

5. Filtration fraction (FF)

Filtration fraction is the volume of plasma removed from the dialyzed blood by ultrafiltration.

Filter clotting occurs with $FF > 20\text{--}25\%$.

$FF = \text{total ultrafiltration rate} / (\text{plasma flow rate} + \text{the prefilter replacement fluid flow rate})$

$\text{Total ultrafiltration rate (mL/h)} = \text{pre filter replacement fluid rate (mL/h)} + \text{post filter replacement fluid rate (mL/h)} + \text{fluid removal rate (mL/h)}.$

$\text{Plasma flow rate (mL/h)} = \text{blood flow rate (mL/min)} \times 60 \text{ (min/h)} \times (1 - \text{hematocrit})$

$$\text{So, } FF = \frac{\left(\begin{array}{l} \text{pre-filter replacement fluid rate} \\ + \text{post-filter replacement fluid rate} + \text{fluid removal rate} \end{array} \right)}{\left[\begin{array}{l} \text{Blood flow rate} \times 60 \times (1 - \text{hematocrit}) \\ + \text{the prefilter replacement fluid flow rate} \end{array} \right]}$$

Example: 60 years old male, 70 kg, a case of septic shock with multi-organ failure including acute kidney injury with anuria since 24 h, blood urea nitrogen is 150 mg/dL, potassium 6 mEq/L (persistent despite receiving medical treatment), he is on high dose noradrenaline and vasopressin, his hematocrit is 30%, has normal coagulation profile, we decided to start him on CRRT, write the order with calculation of filtration fraction.

- CVVHDF for 24–72 h.
- Dialysis dose is 25 mL/kg/h which is approximately 1800 mL/h.
 - Dialysate flow rate (DFR): 900 mL/h
 - Replacement fluid (RF): prefilter 500 mL/h, post filter 300 mL/h
 - Ultrafiltration (UF): 100 mL/h
- Blood flow rate: 200 mL/min.
- Heparin 10 IU/kg bolus, then 10 IU/Kg/h.
- $FF = (\text{pre-filter replacement} + \text{post-filter replacement} + \text{fluid removal}) / \text{Blood flow rate} \times 60 \times (1 - \text{hematocrit}) + \text{the prefilter replacement} = (500 + 300 + 100) / [200 * 60 * (1 - 0.3) + 500] = 0.1 = 10\%$.

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Chapter 8

Infectious Diseases



Haytham Abbas  and Ans Ahmed

Introduction

Infectious diseases are critical in ICU practice. Sepsis and septic shock are major conditions, representing a large portion of ICU cases, requiring proper approach and management as illustrated in this chapter. This chapter also covers antibiotic selection and key antimicrobial agents. Common fungal, viral, and protozoal infections are also discussed.

Uses of Antibiotics

Types of bacteria: (Fig. 8.1)

Types of resistant bacteria: (Fig. 8.2)

Common examples: Vancomycin-resistant *Enterococcus faecalis* (VRE), methicillin-resistant *Staphylococcus aureus* (MRSA), *Pseudomonas*, extended spectrum beta-lactamase (ESBL), carbapenem-resistant *Enterobacteriaceae* (CRE), and *Acinetobacter*.

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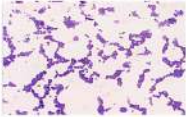
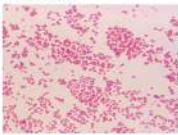
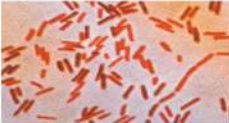
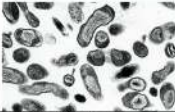
Morphologies and types of bacteria	Examples
GM +ve cocci in chains 	Alpha hemolysis: <i>Streptococcus pneumoniae</i> , <i>Streptococcus viridans</i> Beta hemolysis group A: <i>Streptococcus pyogenes</i> Beta hemolysis group B: <i>Streptococcus agalactiae</i> <i>Enterococcus faecalis</i>
GM +ve cocci in clusters 	Coagulase negative: <i>Staphylococcus epidermidis</i> Coagulase positive: <i>Staphylococcus aureus</i>
GM -ve cocci 	<i>Neisseria gonorrhoeae</i> & <i>Neisseria meningitidis</i>
GM +ve bacilli 	Mnemonic: ABCD-L A ctinomycetes B acillus cereus or anthrax C lostridium D iphtheria L isteria
GM –ve bacilli 	Most bacteria are GM -ve If you encounter a species not commonly known, it is likely GM -ve Examples include: ▪ <i>Enterobacteriaceae</i> (e.g., <i>Escherichia coli</i>, <i>Salmonella</i>, <i>Klebsiella</i>, <i>Shigella</i>, <i>Enterobacter</i>, <i>Proteus</i>). ▪ <i>Pseudomonas</i> ▪ <i>Acinetobacter</i>
Spirochetes 	<i>Treponema pallidum</i> <i>Leptospira</i> <i>Borrelia</i>
Coccobacilli 	<i>Haemophilus influenzae</i> <i>Chlamydia</i> <i>Bordetella pertussis</i> <i>Yersinia pestis</i> <i>Coxiella burnetii</i> <i>Brucella</i>
Atypical bacteria: No color with gram-staining (no cell wall)	<i>Chlamydia</i> , <i>Legionella</i> , and <i>Mycoplasma</i>
Anaerobic bacteria	<i>Bacteroid Fragilis</i> , <i>Clostridium</i> , <i>Fusobacterium</i>

Fig. 8.1 Types and morphologies of bacteria. GM +ve = gram positive, GM –ve = gram negative. (The microscopic pictures are sourced from Centers for Disease Control and Prevention (CDC) Public Health Image Library collection)

Definitions for Multidrug-Resistant (MDR), extensively Drug-Resistant (XDR) and Pandrug-Resistant (PDR) bacteria			
Bacterium	MDR	XDR	PDR
S. aureus	The isolate is non-susceptible to at least 1 agent in ≥ 3 antimicrobial categories	The isolate is non-susceptible to at least 1 agent in all but 2 or fewer antimicrobial categories	Non-susceptibility to all agents in all antimicrobial categories for each bacterium
Enterococcus spp.			
Enterobacteriaceae			
P. aeruginosa			
Acinetobacter spp.			

Fig. 8.2 Types of resistant bacteria. S = *Staphylococcus*, P = *Pseudomonas*. (Courtesy of [Fadic.net](#), used with permission)

Table 8.1 Bactericidal versus bacteriostatic modes of action of the antibiotics

Bactericidal	Bacteriostatic
Beta lactams	Tetracyclines
Glycopeptides	Macrolides
Aminoglycosides	Clindamycin
Quinolones	Cotrimoxazole
Metronidazole	Linezolid

Mechanism of action of the antibiotics: (Table 8.1, Fig. 8.3)

Time vs. concentration-dependent activities of antibiotics: (Fig. 8.4) [1]

Antibiotic classes and their coverage: (GM +ve = gram positive, GM –ve = gram negative)

- *Penicillin*
 - *Benzylpenicillin (Penicillin G)*:
 - Used for syphilis treatment.
 - Secondary prophylaxis for rheumatic fever, 1.2 million unit/month.
 - *Nafcillin, Oxacillin, and Flucloxacillin*: for methicillin-sensitive *Staphylococcus aureus* (MSSA) coverage.

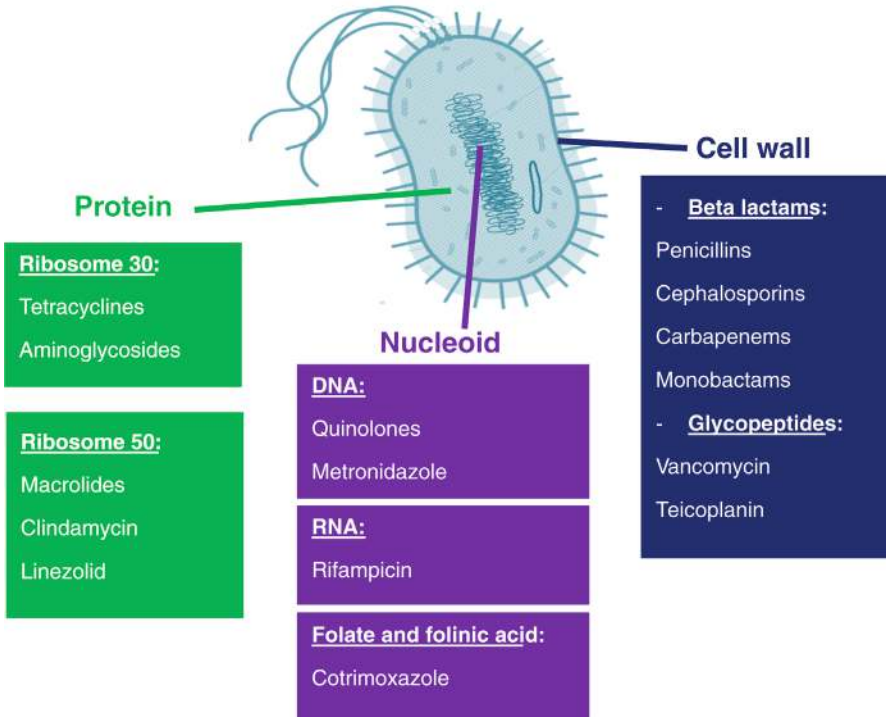


Fig. 8.3 Mechanism of action of the antibiotic groups. DNA = Deoxyribonucleic acid, RNA = Ribonucleic acid

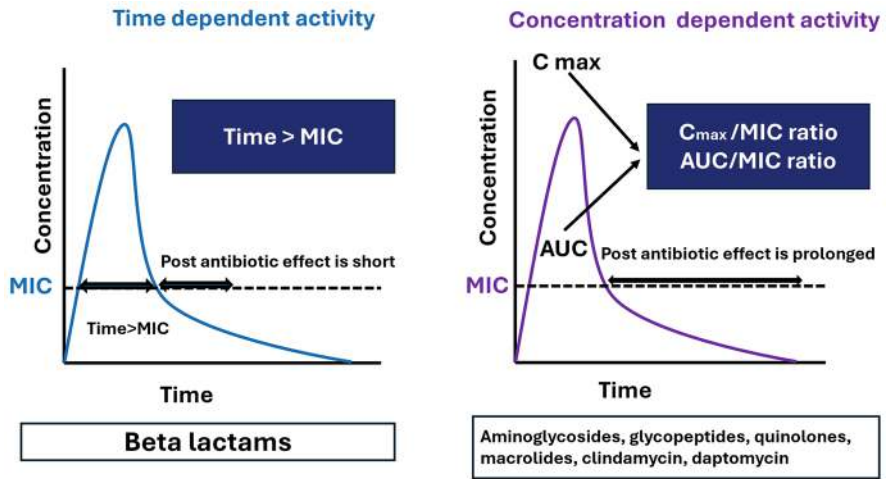


Fig. 8.4 Time- versus concentration-dependent antibiotics. AUC = area under curve, MIC = minimum inhibitory concentration, C_{max} = maximal concentration

Table 8.2 Comparison between ceftriaxone and ceftazidime coverage

Coverage	Ceftriaxone	Ceftazidime
Gram positive	Yes	No
Gram negative	Yes	Yes
<i>Pseudomonas</i>	No	Yes

- *Combination therapy:*
 - *Amoxicillin + Clavulanic acid* → covers GM +ve, GM –ve, and anaerobes.
 - *Ampicillin + Sulbactam* → GM +ve including *Enterococcus*, *Listeria*, GM –ve including *Acinetobacter* if sensitive, and anaerobes.
 - *Piperacillin + Tazobactam* → GM +ve, GM –ve including *Pseudomonas*, and anaerobes.
- *Cephalosporin*
 - *1st generation: e.g., Cefazolin:*
Covers GM +ve including MSSA. Clinically, used as prophylactic for surgeries.
 - *2nd generation: e.g., Cefuroxime:*
Covers mostly GM –ve, good choice for urinary tract infection (UTI).
 - *3rd generation: Ceftriaxone and Ceftazidime (Table 8.2)*
 - *4th generation: Cefepime:* covers GM +ve, GM –ve including *Pseudomonas*.
 - *Ceftaroline:* covers MRSA.
 - *Cefiderocol:* one of the most potent antimicrobials covering GM –ve bacteria including the resistant groups (e.g., *Pseudomonas*, CRE, and *Acinetobacter*), proven for UTI and pneumonia.
 - *Combination of Cephalosporine + beta-lactamase inhibitors:*
 - *Ceftazidime-Avibactam:*
Covers GM –ve organisms including CRE and the highly resistant *Pseudomonas*, proven for UTI, intra-abdominal infection, and pneumonia.
 - *Ceftolozane-Tazobactam:*
Covers GM –ve organism including highly resistant *Pseudomonas*, proven for UTI, intra-abdominal infection, and pneumonia.
- *Carbapenem:*
Covers GM +ve, anaerobic, and GM –ve organisms including ESBL.
 - *Meropenem and Imipenem:*
Both are effective against infections caused by ESBL-producing organisms and *Pseudomonas*. However, meropenem is preferred in central nervous system (CNS) infections due to its better brain penetration, also has lower risk of inducing seizures compared to imipenem.
 - *Ertapenem:*
Administered once daily via intramuscular injection; however, it is not recommended for the treatment of bacteremia, CNS infections, or infections caused by *Pseudomonas* species due to limited efficacy.

- *Combination of Carbapenem + beta-lactamase inhibitors:*
 - *Imipenem-Cilastatin-Relebactam:*
Covers GM –ve organisms (e.g., CRE and the highly resistant *Pseudomonas*), proven for UTI, intra-abdominal infection and pneumonia.
 - *Meropenem-Vaborbactam:*
Covers GM –ve organism including CRE, proven for UTI treatment.
- *Monobactam:*
 - *Tazobactam, Sulbactam:* beta-lactamase inhibitors used in combination with other beta lactams to enhance their activity.
 - *Aztreonam:* covers GM –ve organisms including *Pseudomonas*, and has no cross allergy with penicillin.
- *Polymyxin E (Colistin):*
 - Effective against highly resistant GM –ve organisms, including CRE, *Pseudomonas*, and *Acinetobacter*.
 - Although combination therapy is often used based on expert opinion, there is no conclusive data supporting its superiority over monotherapy.
 - Side effects: nephrotoxicity and neurotoxicity.
- *Glycopeptides:*
A group of antibiotics that target GM +ve bacteria including MRSA.
 - *Vancomycin:*
 - The first choice for MRSA.
 - The first choice in penicillin-resistant *Enterococcus faecalis*.
 - Good bioavailability in the blood and CNS.
 - Side effects: nephrotoxicity and red man syndrome (Fig. 8.5) [2].
 - If red man syndrome happened, the rate of infusion should be decreased.
 - The trough level should be sent before the 4th or 5th dose with a target level of 15–20 mg/L and AUC/MIC should be ≥ 400 , with the MIC of ≤ 1 mg/L.
 - It is the first choice to treat *Clostridium difficile* and administered orally.
 - *Teicoplanin:*
Has a similar spectrum of activity to vancomycin, but it does not cross the brain and is less likely to cause red man syndrome or nephrotoxicity.
- *Daptomycin:*
 - A lipopeptide antibiotic with potent activity against GM +ve bacteria, especially vancomycin-resistant strains such as VRE and MRSA.
 - It has been proven for bacteremia and soft tissue infection.
 - Not effective in pulmonary infection.



Fig. 8.5 Red man syndrome as a side effect of vancomycin. (Rubinstein and Keynan [2])

- *Tetracycline*
 - *Doxycycline*:
 - Covers GM +ve, GM –ve, anaerobes, and atypical bacteria.
 - Also active against *Actinomyces*, *Borrelia*, *Brucella*, *Cholera*, and *Coxiella*.
 - Combined with quinine for treatment of *Malaria falciparum*.
 - Side effects: gastrointestinal (GI) upset, photosensitivity, benign intracranial hypertension, and teratogenicity.
 - *Tigecycline*:
 - Covers GM +ve including MRSA, GM –ve including CRE and *Acinetobacter*, anaerobes, and atypical bacteria.
 - Does not cover the 3Ps (*Pseudomonas*, *Proteus*, and *Providencia*).
 - Associated with increased mortality in critically ill patients [3].
 - Not effective for bacteremia or poor blood supply, e.g., diabetic foot.
- *Aminoglycosides*:
 - Cover GM –ve organisms including *Pseudomonas* (gentamycin and amikacin).
 - Provide a synergistic effect in the treatment of infective endocarditis (gentamycin).
 - Second-line treatment for tuberculosis (TB) (streptomycin, kanamycin, or amikacin).
 - Used also in the treatment of *Brucella* (gentamycin).
 - Side effects: ototoxicity (irreversible), nephrotoxicity, neuromuscular paralysis, and teratogenicity.

- *Macrolides*:
 - Cover GM +ve and atypical bacteria (azithromycin and clarithromycin).
 - Erythromycin is not commonly used nowadays like the other macrolides but used sometimes as a prokinetic for GI intolerance.
 - Fidaxomicin: one of the best choices for *Clostridium difficile*.
 - Azithromycin and clarithromycin are used in the treatment of community-acquired pneumonia (CAP).
 - The drugs of choice for *pertussis*.
 - Side effect: long QT interval.
- *Clindamycin*:
 - Covers GM +ve and anaerobes.
 - Has antitoxic effect (good choice for diabetic foot and necrotizing fasciitis).
 - Used in combination with quinine in the treatment of *Falciparum malaria*, with pyrimethamine for *toxoplasmosis* and with primaquine for *Pneumocystis jirovecii* pneumonia (PJP).
 - Primarily treats infections above the diaphragm (e.g., head and chest) but also some below the diaphragm (e.g., lower limbs and genitalia).
 - Side effect: *Clostridium difficile* infection.
- *Linezolid*:
 - Covers GM +ve bacteria including MRSA.
 - The best choice for MRSA pneumonia, especially if resistant to vancomycin or in severe necrotizing pneumonia.
 - Not proven for bacteremia.
 - Side effects: thrombocytopenia and lactic acidosis.
- *Quinolones*:
 - *Old generation*: Ciprofloxacin:
 - Covers GM –ve bacteria including *Pseudomonas*.
 - Good choice for UTI, prostatitis, typhoid fever, traveler's diarrhea, osteomyelitis, brucellosis, and prophylaxis for meningococcal meningitis.
 - *New generation*: respiratory quinolones (moxifloxacin and levofloxacin):
 - Cover GM +ve, GM –ve and atypical bacteria.
 - Good choice for CAP.
 - Used as a second line therapy for tuberculosis.
 - Levofloxacin covers UTI and *Pseudomonas* while moxifloxacin doesn't.
 - Side effects: long QT interval, tendinitis, and cartilage damage.
- *Metronidazole*:
 - Effective against anaerobic bacteria, especially infections below the diaphragm (e.g., intra-abdominal, diabetic foot, genitalia), and also used for CNS infections.
 - Treats certain protozoal infections such as amebiasis and giardiasis.

- *Co-trimoxazole*:
 - Covers GM –ve and GM +ve including MRSA, but not *Streptococci*.
 - The drug of choice for *PJP* pneumonia.
 - Side effects: renal impairment, i.e., acute interstitial nephritis, decreased creatinine excretion, and renal tubular acidosis (RTA) type 4.
- *Rifampin*:
 - One of the first-line treatments of TB.
 - Provides a synergistic effect against MRSA in case of prosthetic valve or prosthetic joint.
 - Used in the treatment of brucellosis.
 - Used also as a prophylaxis for meningococcal meningitis.
 - Side effects: hepatitis, pancytopenia, red color body fluid.

Combination Therapy of Antibiotics

- *CAP*: ceftriaxone + macrolides or respiratory quinolones used alone (levofloxacin or moxifloxacin).
- *Meningitis*: ceftriaxone + vancomycin, add steroid (showed favorable survival and neurological outcomes) [4] and add ampicillin to cover listeria in age >50 or in immunocompromised patients.
- *Highly resistant GM –ve bacteria*: such as *Pseudomonas* and CRE, which are resistant to ceftazidime-avibactam and imipenem-cilastatin-relebactam, can be treated with a combination of ceftazidime-avibactam plus aztreonam or with cefiderocol alone.
- *Endocarditis*:
 - *Native valve*: vancomycin + ceftriaxone/or gentamycin.
 - *Prosthetic valves*: vancomycin, gentamycin, and rifampin.
 - *Enterococcus faecalis*:
 - For penicillin sensitive, a combination of ampicillin + ceftriaxone.
 - For penicillin resistant, a combination of vancomycin + ceftriaxone/or gentamycin.
 - For VRE, a combination of daptomycin+ ampicillin.

Fungal Infections

Morphology of fungal infections: (Fig. 8.6)

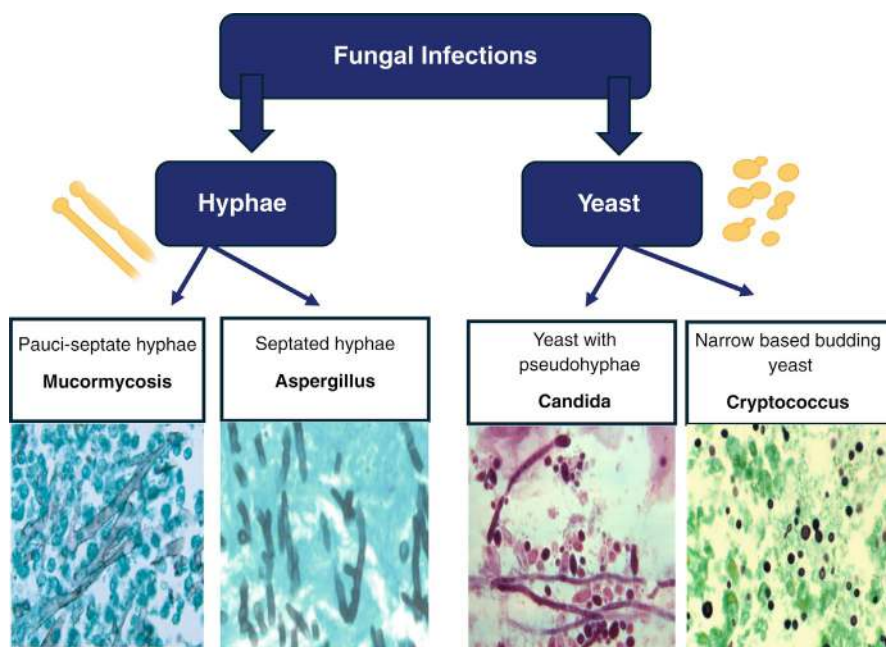


Fig. 8.6 Morphology of fungal infections. (The microscopic pictures are sourced from Centers for Disease Control and Prevention (CDC) Public Health Image Library collection)

Candida Infections

- *Risk factors:*
 - Neutropenia
 - Diabetes mellitus
 - Parenteral nutrition
 - Vascular catheter
 - Multiple colonization
 - Prolonged use of antibiotics
- *Candida species:*
 - *Candida albicans*
 - Non-*Albicans*: *Krusei*, *Glabrata*, *Tropicalis*, *Auris*
- *Common forms of Candida infection:*
 - Candidemia
 - *Candida* endocarditis
 - *Candida* endophthalmitis
 - Candiduria
 - Esophageal candidiasis

Table 8.3 Candida score

Components	Score if present	Score if absent
Clinical sepsis	2	0
Total parenteral nutrition (TPN)	1	0
Surgery	1	0
Multifocal colonization	1	0

Adapted from León et al. [5]

Candida Score

Candida score may be used to assess the likelihood of *Candida* infection (Table 8.3). In ICU patients with sepsis or septic shock, early antifungal therapy is more beneficial when the *Candida* score >3 , compared to patients with a score ≤ 3 , in whom invasive candidiasis is less likely.

Management of Candidemia

- Start echinocandin: anidulafungin, caspofungin, or micafungin.
- Removal of invasive lines.
- Echocardiography to rule out endocarditis.
- Fundus exam to rule out endophthalmitis.
- Repeat the blood culture to confirm eradication and to continue the management for 14 days after the negative culture result.

Management of Candida Endocarditis

- Echinocandins
- Cardiac surgery (illustrated in section “[Infective Endocarditis](#)”, Chap. 1)

Management of Candida endophthalmitis: Fig. 8.7 [6]

- Chorioretinitis due to *C. albicans*:
intravenous (IV) fluconazole + consider intravitreal amphotericin.
- Chorioretinitis due to *C. Krusei* or *C. Glabrata*:
IV amphotericin B + flucytosine + consider intravitreal amphotericin.
- Chorioretinitis + vitritis:
Systemic therapy as above + intravitreal amphotericin + consider vitrectomy.

Management of Candiduria

Asymptomatic patients: No antifungal treatment required. Remove or replace Foley catheter, if present.

Symptomatic, neutropenic, or undergoing urologic procedures (e.g., cystoscopy):

- Initiate fluconazole.
- If resistant *Candida* species: consider amphotericin B or flucytosine.

Management of esophageal candidiasis: (Fig. 8.8) [8]

Usually occurs in immunocompromised patients, particularly patients with acquired immunodeficiency syndrome (AIDS).

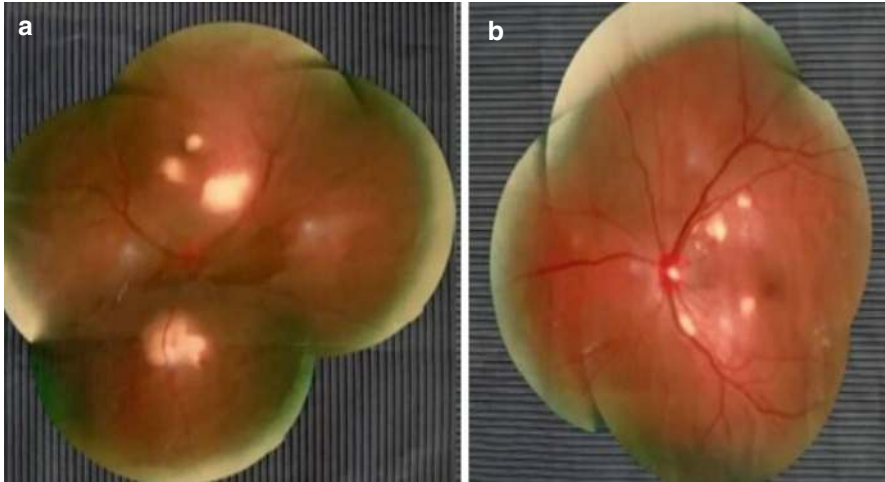


Fig. 8.7 Color fundus photography of the (a) right and (b) left eyes showing diffuse yellowish-white patches in retina involved macula. (Hakamifard et al. [6])

Fig. 8.8 Endoscopy showing esophageal candidiasis. (Sourced from: Narang et al. [7]. Used with permission)



Symptoms Include the Following

- Dysphagia
- Odynophagia
- Vomiting
- Chest pain

Treatment: fluconazole orally or intravenously.

Cryptococcosis

Cryptococcosis is an opportunistic pathogenic yeast, causing serious infections, most commonly meningitis.

It targets immunocompromised patients, mostly patients with AIDS.

Investigations

- Lumbar puncture (LP): shows increased opening pressure, elevated white blood cells (WBCs) and protein.
- Indian ink stain: positive for *Cryptococcus* in the cerebrospinal fluid (CSF).
- Cryptococcal antigen: Detectable in blood and CSF.
- Cryptococcal culture: isolated from blood and CSF.

Treatment

Amphotericin B + flucytosine for 1–2 weeks followed by fluconazole for 10 weeks.

Invasive Aspergillosis

Invasive aspergillosis targets immunocompromised patients mostly neutropenic patients.

Investigations

- *Biomarkers:*
 - 1,3-beta-D-glucan antigen test: can give false positive results in patients with *Candida* or *Pneumocystis jirovecii* pneumonia (PJP) infections and in patients on hemodialysis.
 - Serum galactomannan antigen test: false-positive results may be shown in patients taking beta lactam antibiotics.
- *Radiology:*
 - Computed tomography (CT) chest: might show invasive infiltrates with halo sign (Fig. 8.9).

Fig. 8.9 Halo sign on chest CT due to invasive aspergillosis. (Kedar et al. [9])



Management

Voriconazole: The drug of choice. Side effect includes long QT interval.

Mucormycosis

Mucormycosis is a serious fungal infection, usually in patients who are immuno-compromised, and the most common risk factor is diabetic ketoacidosis (DKA). Other risk factors include glucocorticoid treatment, hematologic malignancy, hematopoietic or solid organ transplantation, iron overload, and recent coronavirus-2019 (COVID-19) infection [10].

This infection most commonly involves the nasal cavity, paranasal sinuses, orbits, and brain (Fig. 8.10).

Other sites may include the lungs, gastrointestinal tract (stomach and intestines), and skin.

Diagnosis

- Clinical examination
- Radiologic imaging: brain, chest, and sinuses
- Tissue biopsy and fungal culture

Treatment

- Intravenous amphotericin B for ≥ 3 weeks, followed by oral posaconazole
- Surgical debridement of necrotic tissue
- Glycemic control (especially in diabetic patients)

Fig. 8.10 Mucormycosis infiltration to the nose, sinuses, and eyes



Sepsis and Septic Shock

Definition of Sepsis and Septic Shock

- *Old definitions:*
 - Sepsis: a systemic manifestation of infection; systemic inflammatory response syndrome (SIRS) criteria + suspected infection (Table 8.4).
 - Severe sepsis: sepsis + end-organ damage.
 - Septic shock: severe sepsis + hypotension not reversed with fluid resuscitation.
- *New definitions:*
 - SIRS and severe sepsis are no longer used.
 - Sepsis: life-threatening organ dysfunction caused by dysregulated host response to infection. It is identified by acute change in the sequential organ failure assessment (SOFA) of ≥ 2 (Fig. 8.11).
 - Septic Shock: is a subset of sepsis with circulatory and cellular/metabolic dysfunction associated with higher risk of mortality. The patients can be clinically identified by a vasopressor requirement to maintain a mean arterial pressure (MAP) ≥ 65 mmHg with serum lactate > 2 mmol/L in the absence of hypovolemia.

Scoring System in Sepsis and Septic Shock

Multiple scoring systems have been developed to assess disease severity and predict mortality in patients with sepsis and septic shock. Commonly used tools include the quick Sequential Organ Failure Assessment (qSOFA), National Early Warning Score (NEWS), NEWS2 (Fig. 8.12), and Modified Early Warning Score (MEWS).

The qSOFA criteria include a respiratory rate ≥ 22 breaths/min, altered mentation, and systolic blood pressure ≤ 100 mmHg. It is a simple bedside tool used to identify adult patients with suspected infection who are at increased risk of poor outcomes [13]. On the other hand, according to the latest guidelines, the use of NEWS, NEWS2, MEWS, or SIRS is recommended over qSOFA as a single screening tool for sepsis [14].

Table 8.4 Systemic inflammatory response syndrome (SIRS) criteria

The systemic inflammatory response syndrome (SIRS)
Criteria: Meet two or more of the following:
Temperature: $< 36^{\circ}\text{C}$ or $> 38^{\circ}\text{C}$
Heart rate: > 90 beats/ minute
Respiratory rate: > 20 breaths/ minute
White blood cell count: < 4000 cells per mm^3 , $> 12,000$ cells per mm^3 or $> 10\%$ immature (band) forms

Adapted from Bone et al. [11]

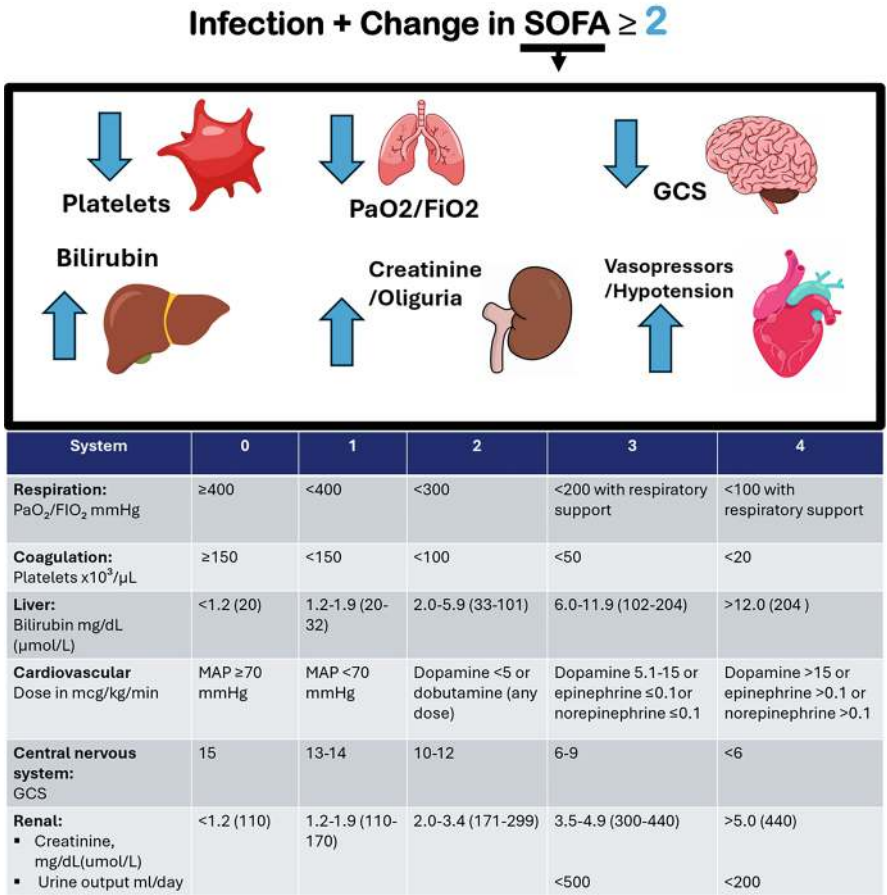


Fig. 8.11 SOFA score. PaO₂ = partial pressure of arterial oxygen, FiO₂ = fraction of inspired oxygen, MAP = mean arterial pressure, GCS = Glasgow coma scale. (Adapted from: Vincent et al. [12])

Investigations of Sepsis and Septic Shock

- Complete blood count (CBC), coagulation profile, renal function, hepatic function, blood gas, chest X-ray, electrocardiogram (ECG), and cardiac enzymes: assess for end-organ damage and SOFA score criteria.
- Serum lactate: assess the level of tissue hypoperfusion.
- C-reactive protein (CRP) and procalcitonin: inflammatory markers increasing with sepsis.
- Septic screen and cultures: blood (at least two sets of blood culture and if central line is present, one central and one peripheral sample), urine, sputum, bed sore.
- Imaging: selected based on clinical presentation and suspected site of infection to identify any source requiring control.

Physiological parameter	Score						
	3	2	1	0	1	2	3
Respiratory rate (per minute)	≤8		9-11	12-20		21-24	≥25
Oxygen saturation scale 1 (%)	≤91	92-93	94-95	≥96			
Oxygen saturation scale 2 (%)	≤83	84-85	86-87	88-92 ≥93 on air	93-94 on oxygen	95-96 on oxygen	≥97 on oxygen
Air or oxygen?		Oxygen		Air			
Temperature (C°)	≤35.0		35.1-36.0	36.1-38.0	38.1-39.0	≥39.1	
Systolic blood pressure (mmHg)	≤90	91-100	101-110	111-219			≥220
Heart rate (per minute)	≤40		41-50	51-90	91-110	111-130	≥131
Level of consciousness				A			C, V, P or U

Fig. 8.12 National Early Warning Score 2 (NEWS 2), 0–4 = low risk, red score (score of 3 in any individual parameter) = low-moderate risk, 5–6 = moderate risk, ≥7 = high risk. A = alert, C = confused, V = responds to voice, P = responds to pain, U = unresponsive. (Reproduced from: Royal College of Physicians. National Early Warning Score (NEWS) 2, 2017)

Management of Sepsis and Septic Shock [15]

As in any critical case, septic shock is approached with ABC and management of each step accordingly.

Management of sepsis and septic shock should be started immediately as delays are associated with worse outcomes. Core components of the management plan include the following:

- Fluid resuscitation
- Antimicrobials
- Vasoactive drugs
- Source control
- General supportive measures

Fluid Resuscitation

- Fluid resuscitation must be initiated at a dose of 30 mL/kg of crystalloids, administered within the first 3 h. Smaller doses may be considered based on comorbidities and volume status.
- Balanced crystalloids may be preferred over normal saline (NS). The *SMART trial* compared balanced crystalloids (Plasma-Lyte or Ringer's lactate) to NS in critically ill patients and found improved survival and renal outcomes with balanced fluids [16]. The *SALT-ED trial* conducted in non-critically ill patients also demonstrated better renal outcomes with balanced crystalloids compared to NS [17].
- Albumin may be used in patients who have received large volumes of crystalloids, if hemodynamic targets are not achieved.
- Hydroxyethyl starches (HESs) are not recommended for intravascular volume replacement. In the *6S trial*, HES was associated with increased mortality and renal complications compared to lactated Ringer's [18]. The *CHEST trial* also showed increased risk of renal injury with HES compared to NS [19].

Mean Arterial Pressure and Hemodynamic Targets

- The initial target MAP should be 65 mmHg. Higher MAP targets did not show improved outcomes (*SEPSISPAM trial*) [20].
- Dynamic variables are preferred over static measures to assess fluid responsiveness [21].
- Lactate clearance and capillary refill time are both acceptable markers of tissue perfusion; the *ANDROMEDA-SHOCK trial* found no significant difference in outcomes between the two markers [22]. Additional clinical indicators include urine output, mental status, and other signs of organ perfusion.

Antimicrobial Therapy

- Intravenous (IV) antimicrobials should be administered as soon as possible, ideally within the first hour of recognizing sepsis or septic shock. The *Kumar study* demonstrated that each hour of delay is associated with a 7.6% increase in mortality [23].
- Methicillin-resistant *Staphylococcus aureus* (MRSA) coverage should be considered in patients at high risk, including those who are immunocompromised, recently hospitalized, have invasive lines, known MRSA colonization, IV drug use, infection at typical anatomical sites (e.g., skin, soft tissue, central line), or exposure to high-risk community.
- For suspected multidrug-resistant (MDR) gram-negative infections, empirical coverage is recommended, with de-escalation once culture results are available.
- Early antifungal therapy is suggested for patients at high risk of invasive fungal infection, particularly those who are immunocompromised (e.g., neutropenia), have prolonged use of invasive vascular devices, receive total parenteral nutrition, have had recent major surgery (especially abdominal), prolonged hospitalization, recent fungal infection, or multisite fungal colonization.
- Anaerobic infection coverage is suggested for patients at high risk of anaerobic infection. Risk factors include intra-abdominal or deep gynecological sources of

infection, necrotizing soft tissue infections, head and neck infections, and central nervous system abscesses or empyema [14].

- A prolonged infusion strategy is recommended for maintenance doses of beta lactam antibiotics after the initial bolus to optimize pharmacodynamic targets [24].

Source Control

- The source of infection should be identified promptly, and once apparent, definitive source control (e.g., drainage, debridement, removal of infected devices) must be performed as soon as possible.
- After adequate source control, if the optimal duration of antibiotic therapy is unclear, it is reasonable to use procalcitonin levels in combination with clinical assessment to guide the decision to discontinue antibiotics.

Vasoactive Medications (Fig. 8.13)

- Norepinephrine is recommended as the first-line vasopressor for septic shock.
- If the target MAP is not achieved with norepinephrine alone (dose >0.25 mcg/kg/min), vasopressin (up to 0.03 units/min) may be added, rather than further increasing the norepinephrine dose. The *VASST trial* showed no overall mortality benefit from adding vasopressin to norepinephrine, but a survival benefit was observed in a subgroup requiring lower vasopressor doses [25]. The *VANISH trial* compared vasopressin to norepinephrine and found no significant difference in clinical outcomes [26].

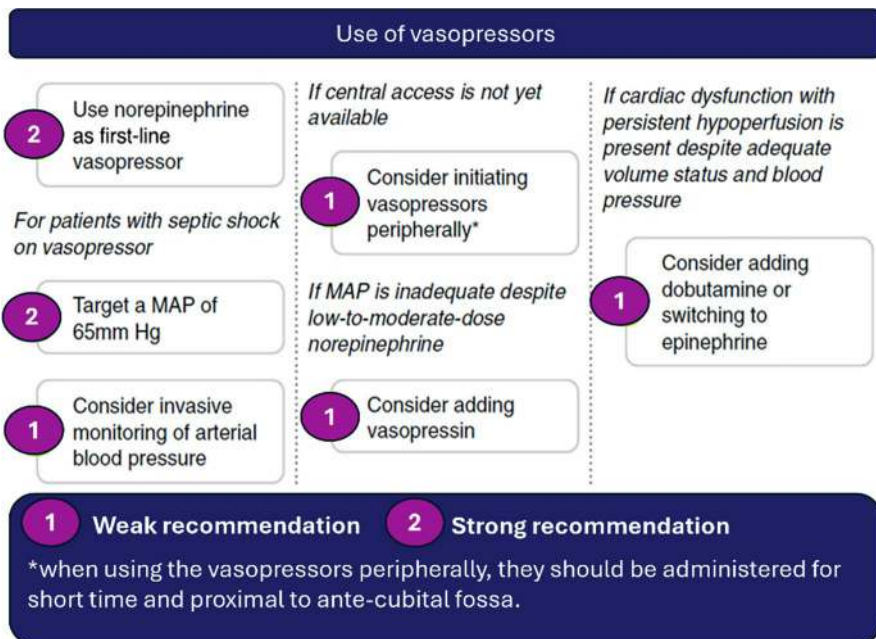


Fig. 8.13 Vasoactive drugs use in septic shock. MAP = mean arterial pressure. (Adapted from Evans et al. [15]. Used with permission)

- In patients with persistent hypoperfusion despite adequate fluid resuscitation and norepinephrine use, consider adding dobutamine, or using epinephrine alone, particularly when cardiac dysfunction is suspected.

Steroids

Corticosteroids are suggested for use in septic shock, particularly in patients requiring high doses of vasopressors or with refractory shock despite adequate fluid resuscitation and vasopressor support. Multiple studies have evaluated the role of steroids in septic shock:

The *ANNANE 2002* [27] and the *APROCCHSS 2018* [28] trials studied the combination of hydrocortisone and fludrocortisone, showing improved survival and reduced vasopressor requirements. The *CORTICUS 2008* trial found that hydrocortisone did not improve survival, but it significantly reduced vasopressor dependency [29]. The *ADRENAL 2018* also showed no mortality benefit, but hydrocortisone use was associated with shorter ICU and hospital stay, lower vasopressor requirements, and improved MAP [30].

Early Goal-Directed Therapy (EGDT)

EGDT is no longer recommended, as major clinical trials failed to show significant improvement in outcomes (illustrated in section “[Hemodynamic Assessment](#)”, Chap. 1).

General Supportive Measures

- Acute respiratory distress syndrome (ARDS): Patients with septic shock who develop ARDS should be managed with a lung-protective ventilation strategy, prone positioning, neuromuscular blocking agents, and other interventions as indicated by evidence-based ARDS protocols.
- Transfusion of blood products:
 - Packed red blood cells (PRBCs): if hemoglobin <7.0 g/dL unless there is myocardial ischemia, severe hypoxemia, or acute hemorrhage.
 - Fresh frozen plasma (FFP): only in coagulopathy with bleeding or planned invasive procedures.
 - Platelets: $<10,000/\mu\text{L}$ (transfuse regardless of bleeding), $<20,000/\mu\text{L}$ (if high bleeding risk), $<50,000/\mu\text{L}$ (in cases of active bleeding, surgery, or invasive procedures).
- Enteral feeding should be initiated early, ideally within 72 h, unless contraindicated.
- Stress ulcer prophylaxis is recommended for patients at high risk.
- Venous Thromboembolism (VTE) Prophylaxis: pharmacological prophylaxis is preferred over mechanical methods unless contraindicated.
- Renal Replacement Therapy (RRT): avoid early initiation of RRT unless strongly indicated. No clear benefit has been shown between intermittent and continuous RRT in terms of outcomes.

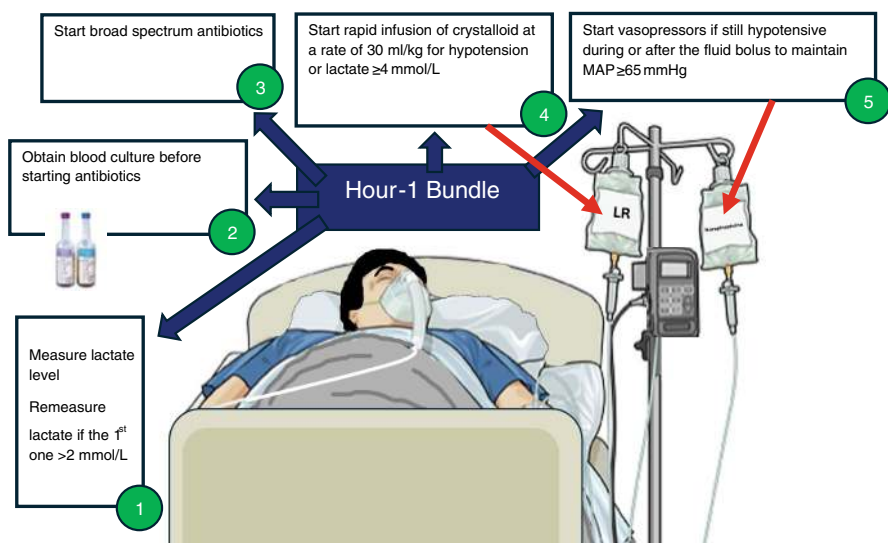


Fig. 8.14 Hour 1 surviving sepsis campaign bundle of care. MAP= mean arterial pressure. (Adapted from Levy et al. [32]. Used with permission)

- Glycemic Control: initiate IV insulin therapy when random blood glucose >180 mg/dL.
- Sodium Bicarbonate (NaHCO_3): routine use of sodium bicarbonate to correct hyperlactatemia is not recommended. It may be considered when pH <7.2, but evidence is limited. The *BICAR-ICU trial* found no significant benefit in using bicarbonate to maintain pH >7.3 in acidotic ICU patients [31].

One hour bundle in the management of septic shock patient: (Fig. 8.14) [33]

Human Immunodeficiency Virus (HIV)

Common Definitions and Presentations of HIV Patients

- *Acute HIV*: 2–6 weeks post-infection; symptoms include fever, sore throat, myalgia, lymphadenopathy, and rash.
- *Acquired Immunodeficiency Syndrome (AIDS)*: HIV with CD4 (cluster of differentiation 4) <200 cells/mm³ or presence of AIDS-defining opportunistic infections or malignancies.

Investigations to confirm HIV: Fig. 8.15 [35]

- *HIV-1/HIV-2/P24 antigen compo test*: Initial screening test; may be positive within 1–12 weeks post-infection. Requires confirmatory testing.
- *HIV1 and HIV2 serology*: Confirms the specific type of HIV.

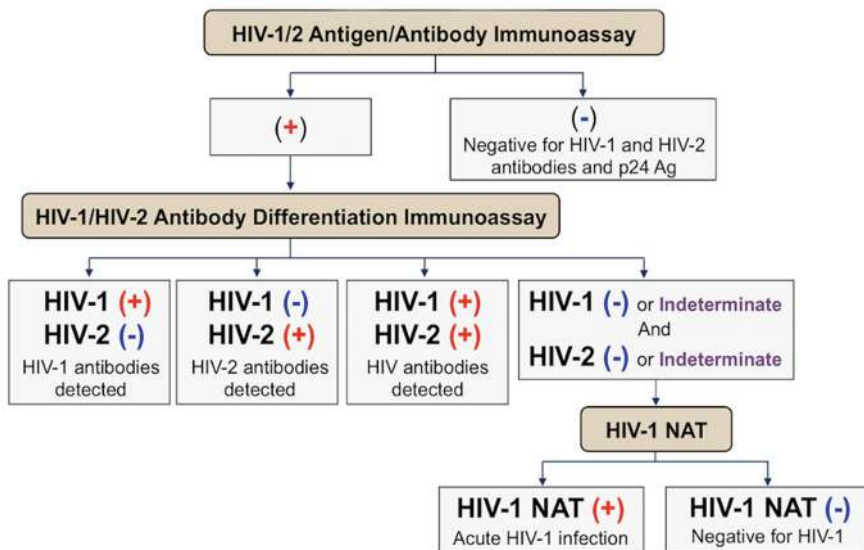


Fig. 8.15 Laboratory testing algorithm for the diagnosis of HIV infection. HIV = human immunodeficiency virus, Ag = antigen, NAT = nucleic acid test. (Sourced from: Centers for Disease Control and Prevention and Association of Public Health Laboratories [34])

- *HIV polymerase chain reaction (PCR)*: Detects viral PCR; levels are typically high during acute infection.
- *CD4*: Used to assess immune status and risk of opportunistic infections.

Types of Opportunistic Infections, Diseases, and Malignancies in Relation to CD4

- *CD4 < 500*:
 - Seborrheic dermatitis
 - Psoriasis
 - Oral hairy leukoplakia: due to *Epstein-Barr virus* (EBV)
- *CD4 < 200*:
 - *Pneumocystis jirovecii* pneumonia (PJP)
 - Toxoplasmosis
 - Progressive multifocal leukoencephalopathy (PML): due to John Cunningham virus (JC virus)
 - Cryptococcosis
 - *Candida*: e.g., oral thrush and *Candida* esophagitis
- *CD4 < 100–50*
 - Mycobacterium avium complex (MAC)
 - Cytomegalovirus (CMV): retinitis, encephalitis, hepatitis, colitis, esophagitis
 - CNS Lymphoma: due to EBV

- Any CD4:
 - Tuberculosis (TB)
 - Kaposi sarcoma: due to human herpesvirus-8 (HHV8)
 - Varicella zoster virus (VZV)
 - Human papilloma virus (HPV) complications

HIV-Related Pulmonary Diseases

Multiple pulmonary diseases, including opportunistic infections and malignancies, commonly affect patients with HIV. These conditions often present with characteristic radiological patterns. Table 8.5 summarizes the typical radiological findings associated with various pathogens.

Pneumocystis jirovecii Pneumonia (PJP)

- Symptoms: fever, night sweating, dyspnea on exertion, and dry cough.
- Investigations:
 - Chest X-ray: may be normal early; typically shows bilateral interstitial infiltrates; pneumothorax may occur.
 - Blood gas: low partial pressure of arterial oxygen (PaO₂) with high A-a gradient.
 - Positive 1,3-beta-D-glucan antigen.
 - Positive PJP sputum with silver stain.
- Treatment:
 - Trimethoprim/sulfamethoxazole (TMP-SMX) 15–20 mg of TMP/kg divided three times daily.
 - Corticosteroids: indicated if PaO₂ <70 mmHg or A–a gradient >35 mmHg, shown to reduce mortality and respiratory failure [36].

Table 8.5 Radiological findings associated with pulmonary diseases in HIV

Chest imaging	Causing diseases
Normal	Early <i>Pneumocystis jirovecii</i> pneumonia (PJP)
Bilateral interstitial infiltrates	PJP, tuberculosis (TB), viral diseases
Lobar consolidation	Bacterial, TB
Cavitary lesion	TB, <i>Nocardia</i> , <i>Staphylococcus aureus</i> , Non-tuberculous mycobacterium (NTM)
Miliary shadow	TB
Pleural effusion	Lymphoma, Kaposi sarcoma, TB, bacterial

HIV-Related Central Nervous System (CNS) Diseases

- ***Meningoencephalitis:***

- *Cryptococcosis*: illustrated in section “**Fungal Infections**”.
- *Bacterial meningitis*: cerebrospinal fluid (CSF) exam shows elevated white blood cells (WBC) predominantly polymorphonuclear, high protein, and low glucose. Management is illustrated in section “**Uses of Antibiotics**”.
- *TB*: CSF exam shows elevated WBC (predominantly lymphocytes), high protein, low glucose, positive TB-PCR, and adenosine deaminase (ADA) [37]. Management should involve an infectious diseases expert. Typically, treatment includes first-line anti-TB drugs: isoniazid, rifampin, ethambutol, and pyrazinamide (same as pulmonary TB). In comparison to the duration of treatment in pulmonary TB which extends for almost 6 months, TB meningitis has longer duration of management for 9–12 months. Also, steroids are added in TB meningitis as the evidence showed improvement of survival [38].
- *Viral meningitis/encephalitis*: causes are *Cytomegalovirus* (CMV), *Herpes simplex virus* (HSV), and others. CSF shows elevated WBC mostly lymphocytic, high protein, normal glucose, and positive PCR test for the causative virus.

Treatment targets the causative virus:

- CMV: Ganciclovir or valganciclovir; foscarnet for refractory cases.
- HSV: Acyclovir.

- ***Space-occupying lesions with radiological findings:***

- *Ring enhancement brain lesions* (Fig. 8.16):
 - *Toxoplasmosis*: blood test is positive for toxoplasma immunoglobulin G (IgG). Treatment includes pyrimethamine + sulfadiazine/or clindamycin.
 - *Tuberculoma*: diagnosed by biopsy sent for culture and TB-PCR.
 - *Brain abscess*: diagnosed by sample sent for culture. Empirical treatment includes ceftriaxone and metronidazole or meropenem alone.
 - *Primary CNS Lymphoma*: diagnosed by positron emission tomography (PET) scan, and biopsy sent for histopathology.
- *Progressive Multifocal Leukoencephalopathy (PML)* (Fig. 8.17): Caused by JC virus; CSF sample should be sent for JC virus PCR.

Anti-retroviral therapy (ART) should be initiated under the guidance of an infectious disease's expert for HIV patients. However, it should not be started during an active opportunistic infection (e.g., tuberculosis or cryptococcosis) due to the risk of immune reconstitution inflammatory syndrome (IRIS), which may worsen the patient's condition.

Fig. 8.16 Ring enhancement lesions in brain imaging. (Sourced from: Bhiraju et al. [39])

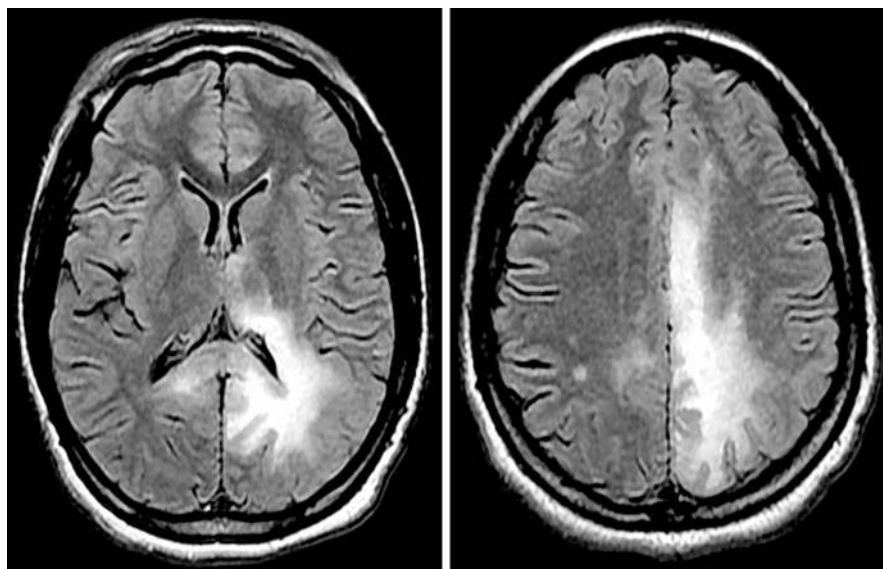
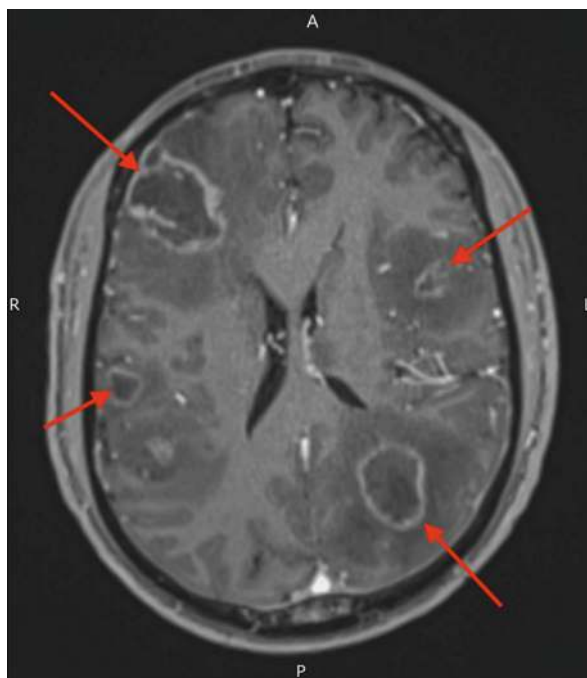


Fig. 8.17 Progressive multifocal leukoencephalopathy (PML) in brain imaging. (Sourced from: Aung et al. [40])

Malaria

Types of Plasmodium Species

- *Plasmodium falciparum*: Most clinically aggressive; associated with severe malaria.
- *Plasmodium vivax*: Forms hypnozoites in hepatocytes; risk of reactivation.
- *Plasmodium ovale*: Also forms hypnozoites; similar relapse potential as *P. vivax*.
- *Plasmodium malariae*: Causes chronic, low-grade parasitemia. It may cause proteinuria and membranoproliferative glomerulonephritis.
- *Plasmodium knowlesi*: Zoonotic; can cause severe, rapidly progressing malaria.

Pathogenesis of Malaria

Malaria is transmitted by the bite of an infected female *Anopheles* mosquito, which injects sporozoites into the human host. The parasite undergoes a complex life cycle involving hepatic and erythrocytic stages, as illustrated in Fig. 8.18.

Symptoms and Signs of Malaria

- Fever: classically, periodic and associated with chills.
- Flu-like symptoms.
- Headache and body aches.

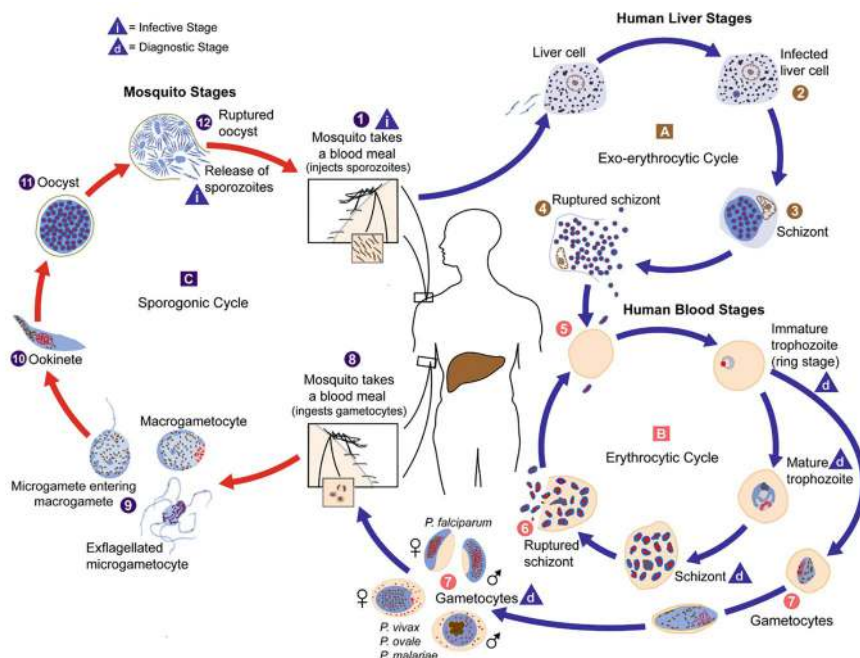


Fig. 8.18 Life cycle of malaria parasites. (Courtesy of Centers for Disease Control and Prevention (CDC))

- Severe disease may be associated with symptoms related to end-organ damage, e.g., altered mental status, seizure, respiratory distress, dark urine, bleeding tendency.
- Hepatosplenomegaly.
- Jaundice.

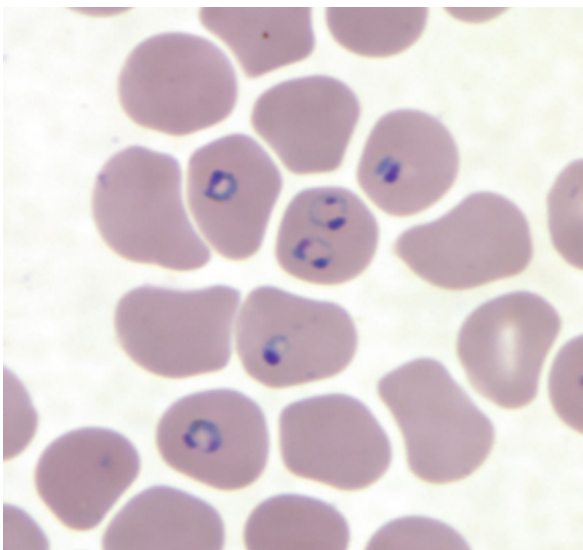
Investigations of Malaria

- Blood film (malaria test): detects *Plasmodium* trophozoites (see Fig. 8.19).
- Complete blood count (CBC) and coagulation profile: assess for anemia and disseminated intravascular coagulation (DIC).
- Renal function and electrolytes: identify acute kidney injury and electrolyte imbalances.
- Blood gas: may reveal metabolic acidosis and elevated lactate.
- Liver function test (LFT): may reveal elevated transaminases and bilirubin.
- Random blood sugar (RBS): exclude hypoglycemia.
- Chest imaging: evaluate for acute respiratory distress syndrome (ARDS).
- Lumbar puncture and brain imaging: rule out other causes of encephalopathy.

Features of Severe Malaria

- Cerebral malaria: altered mental status, seizure
- ARDS
- Shock
- Coagulopathy
- Hypoglycemia; RBS <40 mg/dL
- Acidosis; bicarbonate <15 mEq/L, lactic acidosis
- Hyperbilirubinemia; bilirubin >5 mg/dL
- Anemia; hemoglobin <5 g/dL
- Parasitemia >5–10%
- Renal failure

Fig. 8.19 Blood film showing *Plasmodium falciparum* trophozoites. (Courtesy of centers for disease control and prevention (CDC))



Management of Severe Malaria [41]

As in any critical case, malaria is approached with ABC and management of each step accordingly.

Definite treatment: artesunate 2.4 mg/kg at 0, 12, and 24 h then every 24 h if parasitemia is >1%. When parasitemia drops to <1%, shift to oral regimen like atovaquone/proguanil (Malarone).

Exchange transfusion: Previously used in severe malaria, but current guidelines no longer recommend it, despite occasional expert use.

Treatment of end-organ damage:

- Shock: maintain hemodynamics with intravenous fluid +/- vasopressors.
- Cerebral malaria: control seizure, brain protective strategy.
- ARDS: lung protective strategy.
- Acute kidney injury: STOP approach (illustrated in section “[Acute Kidney Injury \(AKI\)](#)”, Chap. 7), dialysis if needed, correction of acidosis and electrolyte disturbances.
- Anemia and coagulopathy: blood product transfusion if needed.
- Hypoglycemia: dextrose and regular RBS checkup.

Fever in the ICU

The most common cause of fever in ICU patients is infection, typically of bacterial origin. Etiology may be community-acquired in newly admitted patients or nosocomial in long-stay cases. Common infectious sources include the following:

- Pneumonia
- Pyelonephritis
- Bacteremia/catheter-related blood stream infection (CRBSI)
- *Clostridium difficile*
- Soft tissue infections
- Intra-abdominal infections (e.g., cholecystitis, ascending cholangitis, peritonitis)
- Osteomyelitis
- Sinusitis
- Fungal infections
- Viral infections

If the septic workup is negative and infectious causes are excluded, consider non-infectious causes:

- Venous thromboembolism (VTE): pulmonary embolism (PE) and deep venous thrombosis (DVT).
- Neurological causes: stroke, subarachnoid hemorrhage (SAH) and other neurological catastrophes.
- Intra-abdominal: acalculous cholecystitis, pancreatitis.
- Endocrinopathy: adrenal insufficiency, thyrotoxicosis.
- Drug related: phenytoin, sympathomimetics, alcohol withdrawal, antipsychotics (neuroleptic malignant syndrome), serotonergic agents (serotonin syndrome).

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Chapter 9

Rheumatology



Mohamed Cheikh and Haytham Abbas 

Introduction

Although critical rheumatologic cases are rare, they are highly challenging, require prompt intervention, and necessitate a multidisciplinary approach. This chapter outlines key management strategies for such cases.

Pulmonary Renal Syndrome

Pulmonary-renal syndrome refers to a group of diseases characterized by diffuse alveolar hemorrhage (DAH) combined with acute kidney injury (AKI) due to glomerulonephritis. It is most commonly caused by vasculitis; however, other differential diagnoses, such as viral infections or septicemia with multiorgan failure, must be ruled out.

Investigations for Pulmonary-Renal Syndrome

- *Complete blood count (CBC) and coagulation profile:* detect leukocytosis (e.g., bacterial infection), leukopenia (e.g., viral infection or lupus), and coagulopathy.
- *Renal function, electrolytes and blood gas:* assess kidney function and the need for dialysis.
- *Renal ultrasound:* rule out chronic kidney disease (CKD) and other causes of AKI.

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- *Urinalysis and urine microscopy*: detect hematuria, proteinuria, red blood cells (RBC) cast, and acanthocytes.
- *Renal biopsy*: for confirmation and prognostication of glomerulonephritis.
- *Chest imaging*: assess for pulmonary infiltrates consistent with DAH.
- *Bronchoscopy*: for diagnosis, bronchioalveolar lavage (BAL), and control of bleeding if possible.
- *Vasculitis workup*: including antineutrophil cytoplasmic antibodies (ANCA-C, ANCA-P), antinuclear antibody (ANA), complement levels (C3, C4), anti-double-stranded deoxyribonucleic acid (anti-dsDNA), anti-Smith antibody, and anti-glomerular basement membrane (anti-GBM) antibody.
- *Viral panel and septic screen*: rule out infectious etiologies.

Management of Pulmonary Renal Syndrome

As in any critical case, pulmonary renal syndrome is approached with ABC and treatment of each step accordingly.

Multidisciplinary care: Early involvement of pulmonology, nephrology, rheumatology, and infectious disease specialists.

Diffuse alveolar hemorrhage:

- Maintain oxygenation.
- Acute respiratory distress syndrome (ARDS): apply lung-protective ventilation strategies and follow ARDS protocols.
- Bronchoscopy: for confirmation of DAH, BAL, and control bleeding if focused.
- Consider a trial of inhaled tranexamic acid and epinephrine.

Acute Kidney Injury:

- Monitor renal function and basic metabolic profile.
- Initiate dialysis if indicated.
- Perform kidney biopsy for diagnosis and staging.

Vasculitis:

- Conduct workup to rule out systemic lupus erythematosus (SLE), anti-glomerular basement membrane (anti-GBM) disease, and ANCA-associated vasculitis.
- Start pulse corticosteroids and cyclophosphamide or rituximab. Consider plasma exchange as adjunct therapy [1, 2].

Infection:

- Isolate the patient if viral pneumonia is suspected.
- Perform viral panel and septic screen.
- Start broad-spectrum antibiotics and adjust antivirals based on results.

Rheumatology Emergencies

Systemic Lupus Erythematosus (SLE)

Diagnosis of SLE: Figure 9.1 outlines the European league against rheumatism (EULAR) and American college of rheumatology (ACR) criteria for the classification of SLE.

Lupus Emergencies

- Pulmonary renal: outlined in the section “Pulmonary Renal Syndrome”.
- Lupus cerebritis: symptoms include psychosis, delirium, seizure or coma. Investigations to confirm the diagnosis include brain magnetic resonance imaging (MRI) showing signs of cerebritis and vasculitis, and lumbar puncture (LP) that may reveal high protein level. Management includes pulse steroid and cyclophosphamide [3].
- Cytopenia: Severe anemia and thrombocytopenia is treated with pulse steroid and rituximab for refractory thrombocytopenia [3].

Clinical domains			Immunologic domains		
Domain	Criteria	Points	Domain	Criteria	Points
Constitutional domain	Fever(> 38° C)	2	Antiphospholipid antibody domain	Anticardiolipin IgG > 40 GPL or anti-β2GP1 IgG > 40 units or lupus anticoagulant	2
Cutaneous domain	Non-scarring alopecia	2	Complement proteins domain	Low C3 or low C4	3
	Oral ulcers	2		Low C3 and low C4	4
	Subacute cutaneous or discoid lupus	4	Highly specific antibodies domain	Anti-dsDNA antibody	6
	Acute cutaneous lupus	6		Anti-Smith antibody	6
Arthritis domain	Synovitis or tenderness in at least 2 joints	6	✓ Classification criteria are not diagnosis criteria		
Neurologic domain	Delirium	2	✓ All patients classified as having SLE must have ANA ≥ 1:80 (entry criterion)		
	Psychosis	3	✓ Patients must have ≥ 10 points to be classified as SLE		
	Seizure	5	✓ Items can only be counted for classification if there is no more likely cause		
Serositis domain	Pleural or pericardial effusion	5	✓ Only the highest criterion in a given domain counts		
	Acute pericarditis	6	✓ SLE classification requires points from at least one clinical domain		
Hematologic domain	Leukopenia (< 4000/mcL)	3	REFERENCE: <i>Aringer et al. Abstract #2928. 2018 ACR/ARHP Annual Meeting</i> Figure 9.1: EULAR/ACR criteria for classification of systemic lupus erythematosus (SLE). ANA= antinuclear antibody, C= complements (C3, C4), Anti-dsDNA= Anti-double stranded deoxyribonucleic acid, Anti-Smith, β2GP1= beta 2 glycoprotein 1, IgG= immunoglobulin G. <i>Courtesy of Laurent ARNAUD, used with permission.</i>		
	Thrombocytopenia (platelet count < 100,000/mcL)	4			
	Autoimmune hemolysis	4			
Renal domain	Proteinuria > 0.5 g/24 hr	4			
	Class II or V lupus nephritis	8			
	Class III or IV lupus nephritis	10			

Fig. 9.1 EULAR/ACR criteria for classification of systemic lupus erythematosus (SLE), ANA = antinuclear antibody, C = complements (C3, C4), Anti-dsDNA = Anti-double stranded deoxyribonucleic acid, Anti-Smith = Anti-Smith, β2GP1 = beta 2 glycoprotein 1, IgG = immunoglobulin G. (Courtesy of Laurent ARNAUD, used with permission [12])

Catastrophic Antiphospholipid Syndrome (CAPS)

Criteria for diagnosis of antiphospholipid syndrome (APS) and CAPS (Table 9.1)

Management of CAPS [4]

As in any critical case, CAPS is approached with ABC and treatment of each step accordingly.

- Involvement of rheumatology and hematology experts.
- Pulse steroid, anticoagulation, intravenous Immunoglobulin (IVIG) and/or plasma exchange.
- Rituximab for refractory cases.

Rheumatoid Arthritis (RA)

- *Atlantoaxial subluxation [5]:* All patients with RA should be evaluated for atlantoaxial subluxation prior to intubation. A cervical spine X-ray (in flexion and extension) should be obtained. If there is high clinical suspicion, a computed tomography (CT) or MRI of the cervical spine is indicated. If subluxation is confirmed, a difficult airway should be anticipated, and neurosurgical consultation is required due to the risk of cervical spine instability or dislocation.
- *Cardiovascular [6]:* Patients with RA are at increased risk for cardiovascular disease such as myocardial infarction (MI), atherosclerosis, endocarditis, myo-

Table 9.1 Criteria for diagnosis of APS and CAPS

<i>Diagnostic criteria for antiphospholipid syndrome (APS)</i>
Clinical criteria:
Vascular thrombosis: ≥ 1 arterial, venous, or small vessel thrombosis.
Pregnancy morbidity:
1. ≥ 1 fetal death (at or beyond the 10th week of gestation)
2. ≥ 1 premature birth before the 34th week of gestation because of eclampsia, severe preeclampsia, or placental insufficiency
3. ≥ 3 consecutive (pre) embryonic losses (before the 10th week of gestation)
Laboratory criteria:
Lupus anticoagulant positivity on ≥ 2 occasions at least 12 weeks apart.
Anticardiolipin antibody (IgG and/or IgM) in medium or high titer (i.e., >40 , or above the 99th percentile), on two or more occasions at least 12 weeks apart.
Anti- $\beta 2$ -glycoprotein-I antibody (IgG and/or IgM) in medium or high titer (i.e., above the 99th percentile) on two or more occasions at least 12 weeks apart.
<i>Definite APS is present if at least one of the clinical criteria and one of the laboratory criteria are met</i>
<i>Diagnosis of catastrophic antiphospholipid syndrome (CAPS)</i>
History of APS or presence of antiphospholipid antibody
Involvement of three organs, systems, or tissues
Manifestations appear at the same time or over the course of 1 week
Microvascular thrombosis on histopathology

Adapted from: Miyakis et al. [13] and Siniscalchi et al. [14]
 β beta, IgG and IgM immunoglobulin (G and M)

carditis and pericarditis. In ICU cases, treat these disorders as per standard of care, pay attention for presence of tumor necrosis factor inhibitors (Anti-TNF) in patient with advanced heart failure as they are contraindicated in decompensated heart failure.

- *Pulmonary:*
 - *Lung fibrosis:* Patient with RA and lung fibrosis at increased risk for respiratory failure, that might need ICU admission, consider CT chest for follow up and pulmonary function test (PFT) if tolerable. Consult rheumatology and pulmonology to consider the appropriate immunosuppressive/biologic therapy as well as anti-fibrotic agents such as nintedanib.
 - *Pulmonary hypertension (PHTN):* Consider right side heart catheter to confirm group 1 PHTN, rule out other causes, and to consider treatment as standard of care if it is confirmed.

Systemic Sclerosis [7]

- *Hypertensive emergency due to scleroderma renal crisis [8]:* This is a life-threatening complication characterized by acute kidney injury (AKI), abrupt onset of moderate to severe hypertension, and normal urine sediment without heavy proteinuria. Microangiopathic hemolytic anemia may also be present. The gold standard therapy is angiotensin-converting enzyme inhibitors (ACEi), preferably short-acting agents administered every 6 h. The target is a gradual reduction in systolic blood pressure (SBP) by 20 mmHg over 24 h. If the ACEi is maxed out (e.g., captopril 450 mg/24 h), additional antihypertensives should be considered, such as calcium channel blockers (CCBs) or vasodilators.
- *Pulmonary:*
 - *Lung fibrosis [9]:* Beside standard of care ICU management, consider addition of immunosuppressives such as mycophenolate (MMF) or cyclophosphamide after discussion with rheumatology and pulmonology.
 - *Pulmonary hypertension (PHTN):* Standard therapy of group 1 PHTN, involving pulmonology and rheumatology experts, and consideration of right side heart catheterization.

Ankylosing Spondylitis

- *Cardiovascular:* Common complications are aortic dissection and atrioventricular (AV) block. They need standard of care management, and rheumatology follow up to optimize disease control (remission).
- *Pulmonary:* Apical lung fibrosis is common. Management include standard of care, rheumatology and pulmonology follow up to optimize disease control.

Inflammatory Myositis

- *Respiratory muscles involvement* [10]:
 - Diagnosis is supported by PFT showing reduced forced vital capacity (FVC), maximum inspiratory pressure (MIP), or maximum expiratory pressure (MEP). Arterial blood gas may show type II respiratory failure.
 - Start pulse corticosteroids (methylprednisolone 500–1000 mg/day for 3–5 days) and IVIG (2 g/kg divided over 2–5 days).
 - Consider rituximab for refractory cases.
 - Conduct swallowing assessment, as gastrointestinal or respiratory muscle involvement are indications for IVIG therapy.
- *Lung fibrosis*: Manage according to standard care and consult rheumatology and pulmonology to optimize disease control.
- *Cardiovascular* [11]: Myocarditis and AV block can occur in inflammatory myositis. In addition to standard care of management, myocarditis is treated with pulse steroid (500–1000 mg/day for 3–5 days) and immunosuppressive agents such as methotrexate, MMF or rituximab for refractory cases. Cardiac MRI vs positron emission tomography (PET) scan (cardiac study) is recommended to confirm the myocarditis.

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Chapter 10

Endocrinology



Haytham Abbas , Khaled Bayamin, and Riyadh Alghamdi

Introduction

Endocrine emergencies are common and require appropriate management in the ICU. The most frequent are diabetic, thyroid, adrenal, and calcium disorders, each needing a focused strategy and co-management with an endocrinology expert, as outlined in this chapter.

Diabetic Emergency

Diabetic Ketoacidosis (DKA)

Patients diagnosed with type I and, occasionally, type II diabetes mellitus (DM) are at risk of developing diabetic ketoacidosis (DKA), an emergency condition requiring hospitalization and close monitoring. Risk factors for DKA include the following:

- Insulin non-compliance

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- Recent infection
- Surgery
- Ischemia: e.g., myocardial infarction (MI), stroke, and mesenteric ischemia

Pathogenesis of DKA

Under normal circumstances, glucose is metabolized for energy production. In the absence or deficiency of insulin, the usual glycolysis mechanism is disrupted. Energy production shifts to the utilization of fatty acids, culminating in the formation of ketone bodies.

Clinical Features and Diagnosis

Patients may exhibit various symptoms such as nausea, vomiting, abdominal pain, polyuria, polydipsia, rapid shallow breathing, lethargy, confusion, and symptoms related to precipitating factors like fever and chest pain.

Diagnosis involves three key findings [1]:

- High blood sugar (>200 mg/dL; note that it can be normal in some situations like in pregnancy and if the patient is on sodium-glucose transport protein 2 (SGLT2) inhibitors like empagliflozin and canagliflozin).
- High anion gap metabolic acidosis (HAGMA) with pH <7.3 and/or bicarbonate <18 mmol/L.
- Ketosis: The predominant ketone is beta hydroxybutyrate (BOHB), detected in blood with a concentration of >3 mmol/L, acetoacetate can also be identified in urine analysis with $+2$ or greater.

Other findings may include hyponatremia; $\uparrow$ glucose by 100 mg/dL = $\downarrow$ sodium (Na) by 2 mEq/L, and hyperkalemia (extracellular shift with acidosis).

Management of DKA [1]

As in any critical case, DKA must be approached with ABC, with each step managed accordingly.

The primary direct therapy involves intravenous fluids (IVF), intravenous (IV) insulin, and potassium correction.

- *IVF*: DKA patients are volume-depleted and require aggressive hydration. Initiate with normal saline (NS or 0.9% NaCl) or balanced crystalloid solutions (like ringer lactate) at a rate of 500–1000 mL/h during the first 2–4 h. After restoration of intravascular volume, the subsequent choice for fluid replacement depends on the volume state, serum glucose, and sodium levels:
 - If random blood sugar (RBS) >250 mg/dL, no dextrose is added.
 - If RBS <250 mg/dL, dextrose is added to the fluid.
 - In euglycemic DKA (glucose <200 mg/dL and positive BOHB), 5% or 10% dextrose needs to be started alongside 0.9% NaCl/crystalloid at the start of the insulin treatment.
 - If serum Na is in the higher range (>135 – 140 mEq/L), use 1/2 NS (0.45%NaCl).
 - If the serum Na is in the lower range (<135 mEq/L), use NS.
- *Intravenous Insulin*: Administer an initial bolus of 0.1 units/kg, followed by an infusion of 0.1 units/kg/h. The subsequent infusion rate depends on RBS

readings, and a clear protocol, typically established by endocrinology experts in each medical facility, should be followed.

Note that IV insulin should not be started until serum potassium (K) reaches 3.5 mEq/L and above (insulin causes hypokalemia).

- *Potassium Chloride*: Monitor serum potassium regularly and correct if necessary:
 - If serum K >5 mEq/L, no correction is needed.
 - If K 3.5–5 mEq/L, add 10–20 mEq with each liter to keep serum K 4–5 mEq/L.
 - If K <3.5 mEq/L, stop insulin immediately until potassium is corrected.
- *Sodium Bicarbonate (NaHCO₃)*: It is not recommended for DKA treatment, except if serum pH <7.0. It can induce tissue hypoxia, carbon dioxide (CO₂) narcosis, and cause volume overload which disturbs volume assessment.
- *Subcutaneous (SC) Insulin*: Once the patient is out of DKA, which is defined by plasma ketone <0.6 mmol/L, plasma glucose <11.1 mmol/L (<200 mg/dL), serum bicarbonate ≥18 mmol/L, and venous pH ≥7.3, and when patient is able to eat, SC insulin can be initiated by using rapid-acting agent (like lispro or glulisine) and long-acting agent (like glargine) with bridging time of 1–2 h before discontinuing IV insulin. Avoid bridging by using ultra-long-acting insulin.

Hyperosmolar Hyperglycemia State (HHS)

Patients experiencing HHS present with a markedly elevated blood sugar levels (>600 mg/dL) with calculated effective serum osmolality (S.Osm) >300 mOsm/kg, calculated as $[2 \times \text{Na (mmol/L)} + \text{glucose (mmol/L)}]$, OR total serum osmolality >320 mOsm/kg $[2 \times \text{Na (mmol/L)} + \text{glucose (mmol/L)} + \text{urea (mmol/L)}]$. Those patients typically exhibit a normal pH and an absence of ketosis [1].

Risk Factors of HHS

In addition to severe dehydration, HHS shares similar risk factors with diabetic ketoacidosis.

Clinical Manifestations of HHS

Clinical manifestations of HHS include severe dehydration, altered mental status, polyuria, polydipsia, and the potential for hyperosmolality-related complications such as thrombosis (e.g., MI and stroke).

Management of HHS [1]

The management approach parallels that of DKA. Bridging with subcutaneous (SC) insulin is considered once the patient shows clinical improvement, is able to eat, and has a measured or calculated serum osmolality below 300 mOsm/kg and blood glucose <250 mg/dL.

Figure 10.1 summarizes the management of DKA and HHS.

Complications of DKA/HHS Management

- Cerebral edema
- Hypokalemia

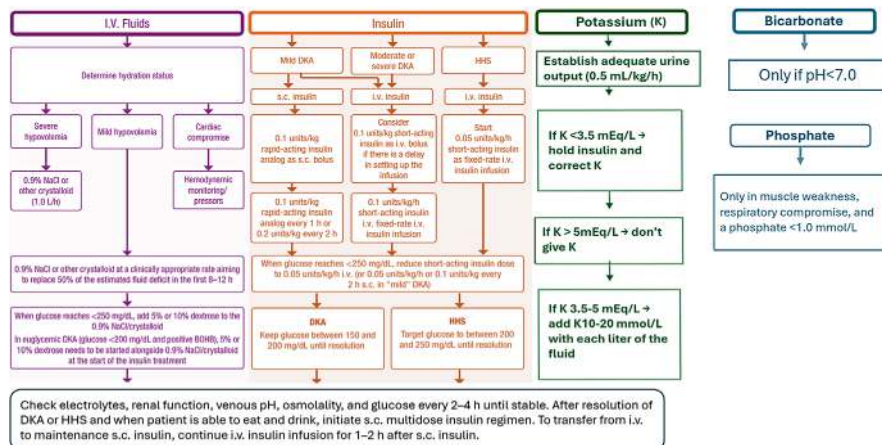


Fig. 10.1 Algorithm for management of diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemia state (HHS). BOHB beta hydroxybutyrate, NaCl sodium chloride, iv intravenous, sc subcutaneous. (Adapted from: Umpierrez, et al. [1]. Used with permission)

- Hypoglycemia
- Volume overload
- Hyperchloremic non-anion gap metabolic acidosis

These potential complications emphasize the importance of careful monitoring and adjustment of the treatment regimen to mitigate adverse effects during the management of HHS and DKA.

Thyroid Emergency

Interpretation of thyroid function test (TFT) results: Table 10.1.

Myxedema Coma

Clinical Presentation

In addition to general manifestations of hypothyroidism (e.g., cold intolerance, sleepiness, periorbital edema, and weight gain), myxedema coma patients may exhibit the following findings:

- Altered mental status
- Hypotension
- Bradycardia
- Hypothermia

Table 10.1 Thyroid function test abnormalities

TSH	FT3 and FT4	Disease
↑	↑	Central hyperthyroidism, TSH-secreting adenoma
	Normal	Subclinical hypothyroidism
	↓	Primary hypothyroidism
↓	↑	Primary hyperthyroidism
	Normal	Subclinical hyperthyroidism
	↓	Central hypothyroidism, sick euthyroid
Normal	↓	Sick euthyroid

TSH thyroid stimulating hormone, *FT3* Free triiodothyronine, *FT4* free thyroxine

- Respiratory depression
- Metabolic derangement (hyponatremia and hypoglycemia)

Investigations of Myxedema Coma

- Complete blood count (CBC): exclude macrocytic anemia and thrombocytopenia related to hypothyroidism.
- Blood gas: detect type II respiratory failure.
- Electrolytes: rule out hyponatremia and hypoglycemia.
- Lipid profile: assess for dyslipidemia.
- Thyroid Function Tests (TFT): TSH, FT3, FT4 to confirm the diagnosis.

Management of Myxedema Coma

As in any critical case, myxedema coma is approached with ABC and management of each step accordingly.

- Treat hypoventilation with non-invasive ventilation (NIV) or mechanical ventilation if needed.
- Manage symptomatic bradycardia following the advanced cardiac life support (ACLS) protocol.
- Correct hypoglycemia with regular blood sugar monitoring.

Direct Therapy Includes the Following [2, 3]

- Initial thyroid hormone replacement for myxedema coma should be levothyroxine given intravenously. A loading dose of 200–400 mcg of levothyroxine may be given. Subsequent doses include a daily oral replacement with 1.6 mcg/kg of body weight. Triiodothyronine can also be started at a dose of 5–20 mcg intravenously, followed by 2.5–10 mcg every 8 h.
- Empiric glucocorticoid coverage should be employed as part of the initial therapy for myxedema coma, with intravenous glucocorticoid preceding levothyroxine administration to avoid adrenal crisis. Use hydrocortisone 50 mg intravenously every 6 h.

Thyroid Storm

Thyroid storm represents the severe form of hyperthyroid status, typically occurring in patients with hyperthyroidism experiencing stressful conditions like acute infection or surgery.

Clinical Manifestations of Thyroid Storm

In addition to general symptoms and signs of hyperthyroidism (e.g., heat intolerance, lack of sleep, weight loss, staring look, and goiter), thyroid storm manifests as acute and severe symptoms affecting multiple body systems:

- Hyperthermia
- Tachycardia (sinus tachycardia, atrial fibrillation)
- Central nervous system: confusion, restlessness, delirium
- Gastrointestinal tract: diarrhea, vomiting
- Cardiovascular system: high cardiac output failure

Investigations of Thyroid Storm

- TFT: Hyperthyroid picture
- Electrocardiogram (ECG): tachyarrhythmias
- Creatine kinase (CK), renal function, and chemistry: rule out rhabdomyolysis, acute kidney injury (AKI), or electrolyte disturbances

Management of Thyroid Storm [4]

- As in any critical case, thyroid storm is approached with ABC and treatment of each step accordingly.
- Secure the airway and maintain oxygenation.
- Tachyarrhythmia is treated as per ACLS protocol.
- Treat the precipitating factor.
- Direct therapy includes the following:
 - Propylthiouracil or methimazole; propylthiouracil is given as 500–1000 mg load, then 250 mg every 4 h, it blocks new hormone synthesis and T4-to-T3 conversion. Methimazole is given at a dose of 20 mg every 4–6 h, it blocks new hormone synthesis.
 - Beta-blockers: propranolol is given at a dose of 60–80 mg every 4 h, consider invasive monitoring in congestive heart failure patients. An alternate drug is esmolol infusion.
 - Iodine (saturated solution of potassium iodide) 5 drops (0.25 mL or 250 mg) orally every 6 h. It blocks new hormone synthesis and thyroid hormone release. Do not start it until 1 h after antithyroid drugs. Alternative drug is Lugol's solution.
 - Steroids: hydrocortisone 300 mg intravenous load, then 100 mg every 8 h. It may block T4-to-T3 conversion, and it is also used as a prophylaxis against relative adrenal insufficiency. Alternative drug is dexamethasone.
 - Cholestyramine: it decreases the gastrointestinal absorption of thyroid hormones.

- Cooling measures: e.g., cold saline and iced water.
- Plasma exchange: sometimes can be used in refractory cases.

Adrenal Crisis

Adrenal insufficiency may arise from primary causes when it is called Addison's disease, with etiologies including autoimmune origin, infectious factors, e.g., tuberculosis and viral illness, hemorrhage, or metastasis. Alternatively, it can be secondary, linked to pituitary disease, or iatrogenic due to external steroid intake.

Clinical Presentation of Adrenal Crisis

In addition to the clinical features of adrenal insufficiency (e.g., weight loss, fatigue, and hyperpigmentation in Addison's disease), patients experiencing an adrenal crisis may present with nausea, vomiting, shock, and confusion.

Predisposing factors include stressful conditions such as sepsis, surgery, or acute illness.

Investigations

Laboratory findings may reveal:

- Hyponatremia
- Hypoglycemia
- Hyperkalemia
- Non-anion gap metabolic acidosis (NAGMA)
- Low serum cortisol level which is confirmed by the cosyntropin stimulation test

Management of Adrenal Crisis

As in any critical case, adrenal crisis is approached with ABC and treatment of each step accordingly.

Maintain the hemodynamics if the patient is shocked by intravenous fluid $\pm$ vasopressors.

Correct the hypoglycemia and electrolyte disturbances.

Direct therapy: Initiate hydrocortisone at 50 mg every 6 h.

Pheochromocytoma

Pheochromocytoma is a neuroendocrine disease characterized by excessive catecholamine secretion by the adrenal gland.

Clinical Presentation of Pheochromocytoma

Patients may present with headache, tremor, palpitation, sweating, tachycardia, hypertension, or hypertensive emergency.

Investigations

- Electrocardiogram (ECG).
- Serum and urine metanephrines and normetanephrines.
- Abdominal imaging, e.g., computed tomography (CT) to localize the adrenal mass.
- Additional investigations for hypertensive emergencies depend on the clinical presentation and aim to exclude end-organ damage.

Management of Pheochromocytoma [5, 6]

- ABC: Ensure patient stability.
- Manage hypertensive emergencies with an alpha-blocker (e.g., phenoxybenzamine) $\pm$ beta-blocker. Beta-blockers should not be administered alone or before alpha-blockers as it may worsen the hypertension.
- Surgical excision of the tumor: Control blood pressure with alpha-blocker $\pm$ beta-blocker before surgery.
- Post-surgery: Closely monitor blood pressure and serum glucose and provide fluid $\pm$ inotropic support as needed.

Calcium Disorders

Causes of calcium disorders: Table 10.2.

Clinical Presentation of hypercalcemia

The mnemonic “stones, bones, groans, and psychic moans” aids in recalling the clinical manifestations of hypercalcemia:

Table 10.2 Calcium disorders

Ca	PTH	PO4	1–25(OH)2D	Clinical condition
↑	↑	↓	N	Primary hyperparathyroidism
		↑	N	Tertiary hyperparathyroidism
		N	N	Familial hypocalciuric hypercalcemia
				Lithium side effect
	↓	↑	↑	Vitamin D excess (intake or granulomatous diseases)
		N	N	Malignancy (bone turnover or PTHrP)
				Medications: thiazide, milk alkali
				Endocrine: thyrotoxicosis, Addison’s
↓	↓	↑	N	Hypoparathyroidism
	↑	↑	N	Secondary hyperparathyroidism
				Pseudohypoparathyroidism
		↓	↓	Vit-D deficiency

Ca calcium, PTH parathyroid hormone, PO4 phosphate, 1–25(OH)2D 1,25 dihydroxy-vitamin D, PTHrP parathyroid hormone-related protein

- Renal: Kidney stones, polyuria (nephrogenic diabetes insipidus), and acute kidney injury (AKI).
- Bone: Bone pain and osteoporosis.
- Gastrointestinal tract: Constipation, pancreatitis, peptic ulcer disease, and vomiting.
- Neurological: Confusion, depression, and coma.
- Cardiovascular: Shortening of the QT interval and arrhythmias.

Investigations of Hypercalcemia

Calcium (Ca), parathyroid hormone (PTH), phosphate (PO₄), and vitamin D (25-OH-D, and 1,25-OH₂-D) are primary investigations to determine the etiology of hypercalcemia.

Electrocardiogram (ECG): exclude arrhythmias and short QT interval.

Subsequent investigations depend on these results, exploring possibilities such as malignancy and primary hyperparathyroidism.

Additional investigations aim to rule out complications like pancreatitis and renal stones.

Management of Hypercalcemia

Severe hypercalcemia (Ca level >15 mg/dL) is a medical emergency that requires to be approached by ABC with management of each step accordingly.

Treatment of the etiology and complications must be initiated.

Direct therapies for hypercalcemia include the following [7]:

- Hydration with crystalloids like normal saline is the first and the most important intervention [8].
- Gentle diuresis with furosemide if signs of volume overload are present.
- Bisphosphonate (e.g., zoledronic acid): Useful in malignancy-induced hypercalcemia.
- Steroids: Beneficial in certain malignancies, vitamin D intoxication, and granulomatous diseases.
- Calcitonin: Rapid and short-acting, may develop tachyphylaxis.
- Denosumab: Used in malignancy.
- Hemodialysis: If other measures are ineffective.

Clinical Presentation of Hypocalcemia

- *Neuromuscular:*
 - Tetany
 - Paresthesia (perioral, extremities)
 - Muscle twitching
 - Carpopedal spasm
 - Trousseau's sign: defined as induction of carpopedal spasm by inflation of a sphygmomanometer above systolic blood pressure for 3 min (Fig. 10.2).
 - Chvostek's sign: defined as contraction of the facial muscles triggered by tapping the facial nerve just anterior to the ear (Fig. 10.2) [9]
 - Seizures

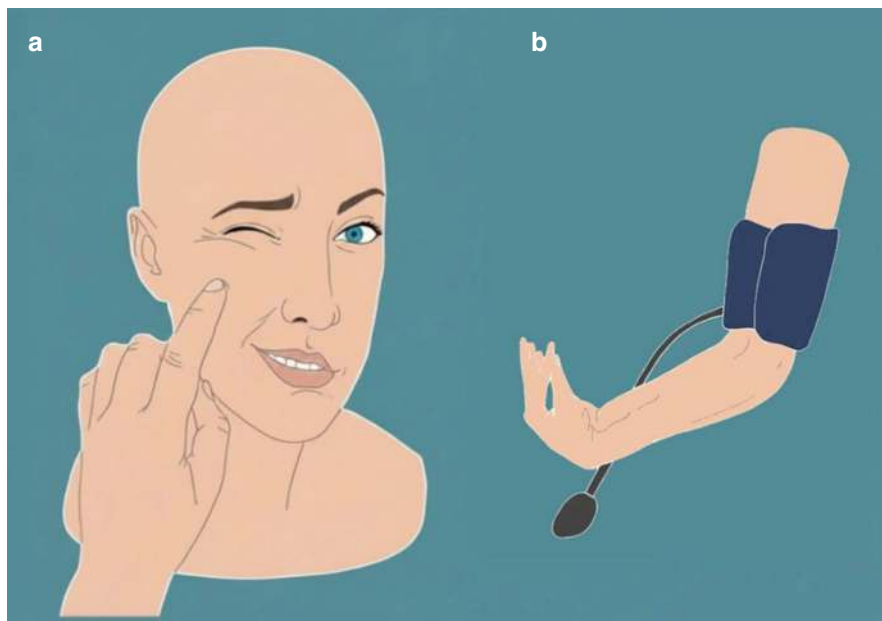


Fig. 10.2 (a) Chvostek (b) Trousseau signs of hypocalcemia

- *Cardiac*
 - Prolonged QT interval
 - Hypotension
 - Arrhythmias
- *Pulmonary:*
 - Laryngospasm
 - Bronchospasm

Investigations of Hypocalcemia

Ca, PTH, PO₄, and vitamin D are the primary investigations to determine the etiology of hypocalcemia.

Serum magnesium (Mg): Hypomagnesemia causes hypocalcemia by inducing PTH resistance or deficiency.

ECG: exclude arrhythmias and long QT interval.

Management of Hypocalcemia

Severe hypocalcemia with acute reduction of serum corrected calcium to ≤ 7.5 mg/dL (≤ 1.9 mmol/L) or ionized calcium to ≤ 3 mg/dL, or in the form of symptomatic cardiac, neurological, or pulmonary manifestations, is an emergency which must be approached with ABC and treatment of each step accordingly.

Airway and breathing must be supported with ventilation (non-invasive or mechanical ventilation), and oxygenation when the patient is complicated with laryngospasm or bronchospasm.

Arrhythmias are treated as per advanced cardiac life support (ACLS) protocol.

Seizure is treated as in status epilepticus approach (*status epilepticus* topic/neurology chapter).

The core management is intravenous calcium; 1 or 2 g of calcium gluconate, in 50 mL of 5% dextrose or normal saline to be infused over 10–20 min. The bolus may be repeated after 10–60 min, if needed to resolve symptoms.

Treatment of the etiology including correction of serum magnesium in case of hypomagnesemia is essential.

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Chapter 11

Hematology and Oncology



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Introduction

Hematological emergencies are common and must be well understood by ICU practitioners. Life-threatening causes of anemia and thrombocytopenia require prompt recognition and targeted management. Blood product transfusion is a key intervention, and intensivists should be familiar with the evidence-based guidelines supporting its use. The second part of this chapter addresses oncology emergencies, each requiring specific diagnostic and therapeutic approaches.

Anemia

Causes and Pathogenesis of Anemia

Anemia results from either bone marrow failure or increased blood loss/destruction. Reticulocyte count serves as a marker of bone marrow activity; elevated in peripheral causes (e.g., hemolysis, hemorrhage) and decreased in marrow suppression or failure. Based on pathogenesis, anemia is classified as follows:

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Bone marrow related:

- Deficiency of essential components: iron, vitamin B12, folate, erythropoietin.
- Bone marrow suppression: chemotherapy, radiotherapy, chronic diseases.
- Bone marrow infiltration: malignancy (leukemia, lymphoma, metastases), infection, fibrosis.

Blood loss/destruction:

- Hemorrhage.
- Hemolysis causes are as follows:
 - Congenital
 - Hemoglobinopathy: sickle cell disease (SCD) and thalassemia.
 - RBCs wall pathology: spherocytosis and elliptocytosis.
 - Enzymes deficiency: G6PD (glucose-6-phosphate-dehydrogenase) and pyruvate kinase.
 - Mechanical: prosthetic valve, splenomegaly.
 - Microangiopathy: disseminated intravascular coagulation (DIC), thrombotic thrombocytopenic purpura (TTP), hemolytic uremic syndrome (HUS).
 - Toxins: snake venom, lead poisoning.
 - Autoimmune: cold and warm.
 - Infection: malaria.
 - Paroxysmal nocturnal hemoglobinuria (PNH).

Mean corpuscular volume (MCV) is a blood test that measures the average size of red blood cells (RBCs). Based on MCV, anemia is classified into microcytic, normocytic, or macrocytic types. Common causes for each category include the following:

- *Microcytic (MCV < 80 fL)*
 - Iron deficiency anemia (IDA)
 - Anemia of chronic disease
 - Thalassemia
 - Sideroblastic anemia
 - Lead poisoning
- *Normocytic (MCV 80–95 fL)*
 - Hemolytic anemia
 - Acute bleeding
 - Anemia of chronic diseases
 - Aplastic anemia
- *Macrocytic (MCV > 95 fL)*
 - Megaloblastic anemia (due to vitamin B12 and folate deficiency)
 - Hypothyroidism

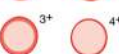
RBC Morphologies					
Sizes	Hemoglobin concentration	Inclusions	Shapes		Distribution
Normal 	Hypochromia 	Howell-Jolly body 	Acanthocyte 	Sickle cell 	Rouleaux 
Microcyte 			Burr cell 	Spherocyte 	
Macrocyte 	Polychromasia (reticulocyte) 	Basophilic stippling 	Schistocyte 	Ovalocyte 	Agglutination 
			Target cell 	Tear drop 	

Fig. 11.1 Different red blood cell morphologies

- Liver disease
- Alcohol
- Myelodysplastic syndrome (MDS)

Investigations of Anemia

Complete blood count (CBC) with differential: hemoglobin, white blood cells (WBCs), platelets, MCV, mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), and red cell distribution width (RDW).

Coagulation profile: to rule out coagulopathy.

Renal function: impaired kidney function with anemia may be seen in multiple medical conditions such as chronic kidney disease (CKD), thrombotic microangiopathy (TMA), and vasculitis.

Blood formation components: IDA (↓ serum iron, ↑ total iron binding capacity [TIBC], ↓ ferritin, ↓ transferrin), vitamin B12 deficiency (↓ vitamin B12, ↑ methylmalonic acid, ↑ homocysteine), folate deficiency (↓ folic acid, ↑ homocysteine).

Reticulocyte index: >2% → good bone marrow proliferation, <2% → low proliferation.

Hemolytic workup: ↑ reticulocytes, ↑ total bilirubin, ↑ lactate dehydrogenase (LDH), ↓ haptoglobin, Coombs test (positive in autoimmune hemolytic anemia).

Blood film for morphology: Fig. 11.1 [1].

Further workup depends on the primary investigations, e.g., hemoglobin electrophoresis, and bone marrow biopsy.

Sickle Cell Disease (SCD)

Pathogenesis of SCD

SCD is a recessive condition characterized by beta-globin mutation leading to structurally abnormal hemoglobin which is called hemoglobin-S (Hb-S).

Diagnosis of SCD

Patients typically present with hemolytic anemia. Peripheral blood smear may show sickled RBCs and Howell-Jolly bodies, indicating functional asplenia. Definitive diagnosis is confirmed by hemoglobin electrophoresis, which identifies the presence of Hb-S.

Clinical Manifestations of SCD and Crises

- *Anemia*: by multiple mechanisms:
 - Acute/chronic hemolytic anemia.
 - Aplastic crisis: due to Parvo virus B19 infection.
 - Sequestration crisis: a life-threatening complication in which RBCs are sequestered in the spleen, leading to shock. It typically occurs in young children before repeated splenic infarctions result in functional asplenia or auto-splenectomy.
- *Infection*: Due to hyposplenism or auto-splenectomy, patients with SCD are at increased risk for infections, particularly with encapsulated organisms such as *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae*, which may cause pneumonia, meningitis, and sepsis. Chronic infections like osteomyelitis are also common, often caused by *Salmonella* spp. and *Staphylococcus aureus*.
- *Vaso-occlusive crisis*:
 - Neurological: stroke
 - Pulmonary: acute chest syndrome (ACS) and pulmonary hypertension
 - Musculoskeletal: painful crisis, avascular necrosis, dactylitis (hand-foot syndrome)
 - Splenic infarction
 - Renal papillary necrosis
 - Priapism
- Other complications: gallstones, growth retardation, and delayed puberty.

Acute Chest Syndrome (ACS)

ACS is a serious complication of sickle cell disease, defined as a new pulmonary infiltrate on chest imaging accompanied by fever and/or at least one respiratory symptom such as chest pain, cough, dyspnea, wheezing, hypoxia, or respiratory distress.

Management of ACS [2, 3]

As in any critical case, ACS is approached with ABC and management of each step accordingly.

Maintain oxygenation: conventional oxygen, noninvasive ventilation (NIV), or mechanical ventilation.

Intravenous fluid for hydration.

Analgesia: such as opioids and paracetamol.

Antibiotics to cover community acquired pneumonia (CAP).

Other measures: venous thromboembolism (VTE) prophylaxis, bronchodilators, and incentive spirometry.

Simple vs. exchange transfusion:

- Simple transfusion is recommended to maintain hemoglobin around 10 g/dL. It is indicated in cases with mild symptoms such as oxygen saturation (SpO_2) <95%, radiological infiltrates without respiratory failure, as a temporary measure before initiating exchange transfusion, or when hemoglobin is <5 g/dL.
- Exchange transfusion aims to keep HB-S < 30% and is indicated in the following settings: SpO_2 <85%, multilobar pneumonia (>1 lobe), respiratory distress and progression of ACS despite simple transfusion.

Ischemic Stroke [2, 4]

Management follows standard ischemic stroke protocols, including thrombolysis, mechanical thrombectomy, and antiplatelet therapy (as detailed in the section “Ischemic Stroke”, Chap. 3). In addition, periodic exchange transfusions are essential, targeting Hb-S <30% and hemoglobin around 10 g/dL to reduce the risk of recurrence.

Thrombocytopenia

Etiology of Thrombocytopenia

The most common causes of new-onset thrombocytopenia in hospitalized patients are sepsis and drug-induced thrombocytopenia. Similar to anemia, thrombocytopenia is classified as either due to bone marrow suppression or peripheral destruction:

Bone marrow–related causes:

- Nutritional deficiency: Vitamin B12, folate.
- Bone marrow suppression: chemotherapy, radiotherapy, infection (sepsis, viral).
- Bone marrow infiltration: malignancy (leukemia, lymphoma, metastasis), fibrosis.

Peripheral destruction causes:

- Immune mediated: causes include heparin-induced thrombocytopenia (HIT) and immune thrombocytopenia (ITP). ITP can be primary or secondary to infectious causes (e.g., human immunodeficiency virus (HIV), hepatitis C virus (HCV)), vasculitis (e.g., systemic lupus erythematosus (SLE), anti-phospholipid

syndrome (APS)), *Helicobacter pylori*, hypothyroidism, and malignancy, e.g., chronic lymphocytic leukemia (CLL).

- Non-immune mediated: causes include microangiopathy, mechanical destruction, e.g., from prosthetic valve and hypersplenism.

Investigations of Thrombocytopenia

- Complete blood count (CBC): assess for other cytopenias and determine if thrombocytopenia is isolated.
- Citrated platelet count: confirm true thrombocytopenia and rule out pseudo-thrombocytopenia due to platelet clumping.
- Coagulation profile: exclude coagulopathy.
- Renal function and chemistry panel: impaired kidney function with thrombocytopenia may indicate thrombotic microangiopathy (TMA) or vasculitis.
- Vitamin B12 and folate levels: identify nutritional deficiencies affecting bone marrow production.
- Thyroid function tests, *Helicobacter pylori* testing, autoimmune profile, viral serology: evaluate for secondary causes of ITP.
- Peripheral blood film: assess platelet morphology and detect abnormal or immature blood cells.
- Bone marrow examination: indicated when the diagnosis is unclear or if hematological malignancy or marrow failure is suspected.

Heparin-Induced Thrombocytopenia (HIT)

Types of HIT: Table 11.1.

4Ts score is used to assess the probability of HIT (Table 11.2).

In cases of intermediate or high suspicion of HIT, the following steps should be taken: discontinue all forms of heparin, confirm the diagnosis with laboratory testing for antibodies to the heparin–platelet factor 4 (PF4) complex, and initiate a non-heparin anticoagulant.

Choices of anticoagulation include argatroban, bivalirudin, danaparoid, fondaparinux, or direct oral anticoagulants (DOAC), e.g., dabigatran and apixaban.

Thrombotic Microangiopathy (TMA)

Causes and Etiology of TMA: Table 11.3 [7].

Clinical Presentation of TMA

- *Thrombotic thrombocytopenic purpura (TTP)*: pentad of thrombocytopenia, hemolytic anemia, renal impairment, altered mental status, and fever.

Table 11.1 Types of heparin-induced thrombocytopenia (HIT)

	HIT type 1	HIT type 2
Severity	Typically, mild and transient	A severe and potentially life-threatening reaction to heparin with an increased risk of thrombosis
Mechanism	Non-immune mediated, direct platelet activation by heparin	Antibody-mediated, with heparin-induced formation of antibodies against heparin-PF4 complexes
Platelet count	Mild to moderate decrease	Moderate to severe decrease
Onset	Within the first 2 days of heparin therapy	It occurs 5–10 days after heparin exposure
Thrombotic complications	Rare, usually asymptomatic	Common, including DVT, PE, DIC
Diagnostic tests	Clinical suspicion and laboratory tests (SRA and ELISA)	Clinical suspicion and laboratory tests (SRA and ELISA)
Treatment	Discontinue heparin	Discontinue heparin and initiate alternative anticoagulation
Prognosis	Excellent. Platelet count returns to normal within a few days without complications	Poor, with a high risk of thrombotic complications and mortality without appropriate treatment

PF4 platelet factor 4, *DVT* deep vein thrombosis, *PE* pulmonary embolism, *DIC* disseminated intravascular coagulation, *SRA* serotonin-release assay, *ELISA* enzyme-linked immunosorbent assay

Table 11.2 The 4Ts score for predicting the probability of heparin-induced thrombocytopenia (HIT)

Category	2 points	1 point	0 point
Thrombocytopenia	>50% fall, or nadir $\geq 20 \times 10^9/L$	30–50% fall, or nadir $10-19 \times 10^9/L$	<30% fall, or nadir $<10 \times 10^9/L$
Timing of the decrease in platelet count	Clear onset between days 5 and 10 OR Platelet count fall at ≤ 1 day if prior heparin exposure within the last 30 days	Consistent with fall at 5–10 days but unclear (e.g., missing platelet counts) OR Onset after day 10 OR Fall ≤ 1 day with prior heparin exposure within 30–100 days	Platelet count fall at <4 days without exposure within past 100 days
Thrombosis or other sequelae	Proven thrombosis, skin necrosis, or acute systemic reaction after heparin bolus	Progressive or recurrent thrombosis; non-necrotizing (erythematous) skin lesions; suspected thrombosis (not proven)	None
Other causes of thrombocytopenia	None apparent	Possible	Definite

0–3 points: Low probability

4–5 points: Intermediate probability

6–8 points: High probability

Lo et al. [5]. Used with permission

Table 11.3 Causes of thrombotic microangiopathy (TMA)

Conditions associated with TMA
<i>ADAMTS13 deficiency</i> : Thrombotic thrombocytopenic purpura
<i>Complement-mediated</i> : Atypical hemolytic uremic syndrome
<i>Infection-associated TMA</i>
Bacterial: Shiga toxin–producing <i>Escherichia coli</i> –associated hemolytic uremic syndrome (STEC-HUS), <i>Streptococcus pneumoniae</i> , <i>Campylobacter jejuni</i> , <i>Klebsiella pneumoniae</i>
Viral: influenza, HIV, EBV, CMV, BK virus, parvovirus B19, SARS-CoV-2
Fungal: histoplasmosis
<i>Autoimmune diseases</i> : Systemic lupus erythematosus, antiphospholipid syndrome (APS) including catastrophic APS, scleroderma renal crisis, primary glomerulonephritis and vasculitis
<i>Malignancy-associated TMA</i>
Solid: Breast, gastric, lung, ovarian, prostate, and urothelial cancers
Hematologic: Myelo and lymphoproliferative, monoclonal gammopathies
<i>Pregnancy-associated</i> : In preeclampsia/HELLP
<i>Metabolic</i> : Defects of cobalamin metabolism
<i>Transplantation-associated TMA</i> :
Solid organ
Hematopoietic stem cell transplant
<i>Drug-induced</i> :
Immune mediated
Via drug-triggered antibodies against platelets/neutrophils: gemcitabine, oxaliplatin, trimethoprim-sulfamethoxazole, quinine, vancomycin
Via autoantibodies against ADAMTS13: ticlopidine
Non-immune mediated
Chemotherapy: alemtuzumab, gemcitabine, mitomycin C, vincristine, doxorubicin, pentostatin, tyrosine kinase inhibitors, proteasome, and check point inhibitors
Immunosuppressive therapy: calcineurin inhibitor, sirolimus, interferon β
Antibiotics: ciprofloxacin, levofloxacin, metronidazole, nitrofurantoin, penicillin
Other: cocaine, ecstasy, estrogen/progesterone, anti-inflammatories, oxymorphone, simvastatin
<i>Hypertensive emergency</i>

Adapted from: Genest et al. [6]. Used with permission

ADAMTS13 a disintegrin and metalloprotease with a thrombospondin type1 motif, member 13, *HIV* human immunodeficiency virus, *EBV* Epstein-Barr virus, *CMV* cytomegalovirus, *SARS-CoV-2* severe acute respiratory syndrome coronavirus 2, *HELLP* hemolysis-elevated liver enzymes and low platelets

- *Hemolytic uremic syndrome (HUS)*: triad of thrombocytopenia, hemolytic anemia, and renal impairment. Renal impairment is typically more prominent in HUS than in TTP.

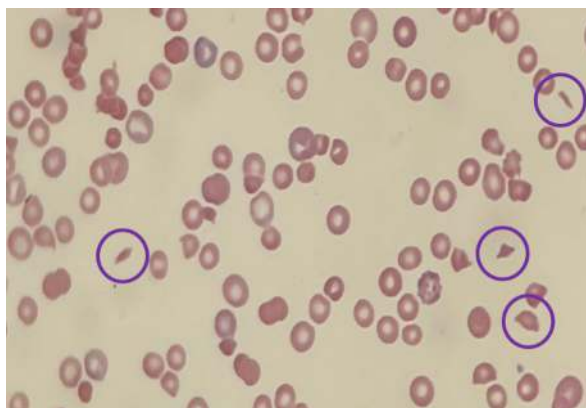
Investigations and Results of TMA

CBC, hemolytic workup: Coombs negative hemolytic anemia and thrombocytopenia.

Renal function: acute kidney injury (AKI).

Blood film: fragmented red blood cells (RBCs) (schistocytes), see Fig. 11.2.

Fig. 11.2 Fragmented red blood cells (schistocytes)



Investigations to Confirm the Etiology

- ADAMTS13 activity: To diagnose TTP; severe deficiency (<10%) is highly suggestive.
- Complement studies: Assessment of the hereditary complement pathway and acquired antibodies to complement factor H in suspected atypical HUS.
- Shiga toxin testing: To confirm Shiga toxin producing *Escherichia coli*-associated hemolytic uremic syndrome (STEC-HUS).
- Autoimmune workup, viral serologies, malignancy screening.

Management of TMA

As in any critical case, TMA must be approached with ABC and management of each step accordingly.

Treatment of AKI: STOP approach (section “[Acute Kidney Injury](#)”, Chap. 7) +/- dialysis.

Treatment of the causative agents is essential:

- Drug induced → discontinuation
- Pregnancy related → delivery
- Treatment of infectious causes, malignancy, and autoimmune diseases

Directed therapy:

- Plasmapheresis is the first-line treatment and the management of choice for TTP. The PLASMIC score can be used to estimate the likelihood of TTP and guide the initiation of plasma exchange while awaiting confirmatory ADAMTS13 results (Table 11.4).
- Complement C5 inhibitors such as eculizumab or ravulizumab are the treatments of choice for atypical HUS. These patients typically do not respond to plasma exchange, making early differentiation from TTP essential [9, 10].

Table 11.4 PLASMIC score

Criteria	Points
Platelet count $<30 \times 10^9/L$	1
Hemolysis variables (reticulocyte count elevation, undetectable haptoglobin, or bilirubin—indirect >2.0 mg/dL)	1
No active cancer	1
No history of solid-organ or stem-cell transplant	1
MCV <90 fL	1
INR <1.5	1
Creatinine <2.0 mg/dL	1

Bendapudi et al. [8]

High risk = 7 points, Intermediate risk = 5–6 points, Low risk = 0–4 points

INR international normalized ratio, MCV mean corpuscular volume

Disseminated Intravascular Coagulation (DIC)

Definition of DIC

DIC is a life-threatening condition marked by widespread activation of the coagulation cascade, leading to both excessive clot formation and severe bleeding. It results from an underlying disease or condition, causing systemic clotting that depletes the body's clotting factors and platelets.

Pathogenesis of DIC

1. *Trigger*: DIC starts due to an underlying condition (e.g., sepsis, trauma, malignancy) that causes widespread activation of clotting pathways.
2. *Widespread clotting*: Systemic coagulation results in the formation of microvascular thrombi that block small blood vessels.
3. *Consumption of platelets and coagulation factors*: The body rapidly uses up clotting factors and platelets to form clots, leading to their depletion.
4. *Bleeding phase*: As coagulation factors are consumed, the body loses its ability to clot effectively, leading to severe bleeding.
5. *Organ failure*: Microthrombi obstruct blood flow to organs, causing ischemia and organ damage, while hemorrhage further complicates the situation.

Causes of DIC

- Sepsis (most common cause)
- Severe trauma (especially head trauma)
- Malignancy (e.g., acute promyelocytic leukemia)
- Obstetric complications (e.g., amniotic fluid embolism, placental abruption)
- Viral or bacterial infections
- Severe liver disease
- Snake bites
- Severe allergic reactions
- Vascular disorders (e.g., aneurysms)

Table 11.5 ISTH scoring system for DIC

ISTH scoring system for DIC	
Platelet count ($\times 10^9/L$)	Score
>100	0
<100	1
<50	2
Fibrin-related marker, e.g., D-dimer	Score
No increase	0
Moderate increase	1
Strong increase	2
Prothrombin time prolongation (s)	Score
<3	0
3–6	1
>6	2
Fibrinogen (g/L)	Score
>1.0	0
<1.0	1

Taylor [13]

Score <5: non-overt DIC (low probability of overt DIC), Score ≥ 5 : overt DIC

Diagnosis [11, 12]

Diagnosis is made based on clinical presentation (bleeding and clotting signs) and laboratory tests. DIC is confirmed by assessing the following:

- *Prolonged PT (prothrombin time) and aPTT (activated partial thromboplastin time)*: Suggests consumption of clotting factors.
- *Elevated D-dimers*: A marker of excessive clot formation and breakdown.
- *Low platelets*: Due to consumption during clot formation.
- *Low fibrinogen levels*: Due to consumption during clotting (hypofibrinogenemia).
- *Schistocytes on a blood smear*: Fragmented red blood cells from mechanical destruction in microthrombi.

Scoring System for DIC

The International Society on Thrombosis and Hemostasis (ISTH) has developed a scoring system based on laboratory results to help diagnose and track DIC severity (Table 11.5).

Management of DIC [11, 12, 14]

1. *Treat the underlying cause*: The primary focus is to address and treat the root cause (e.g., sepsis, and trauma).
2. *Supportive care*:
 - *Hemodynamic support*
 - *Blood product replacement in case of bleeding or invasive procedures*:
 - *Platelet transfusion* to maintain target platelet levels.
 - *Fresh frozen plasma (FFP)* for restoring clotting factors.
 - *Cryoprecipitate or fibrinogen concentrate* to replenish fibrinogen levels.

- *Anticoagulation*: In some cases (e.g., chronic DIC with thrombosis predominance), low-dose heparin may be used to prevent further clotting.
3. *Monitoring*: Regular monitoring of CBC, coagulation profile, fibrinogen levels, and D-dimers to guide ongoing treatment and transfusion needs.

Transfusion of Blood Components

Packed red blood cells (PRBCs): Indications of transfusion are as follows [15]:

- Hemorrhagic shock.
 - Anemia with hemoglobin <7 g/dL.
 - Anemia with hemoglobin <8 g/dL in myocardial ischemia or pericardiac surgery.
- The aim is to keep hemoglobin >8–10 g/dL [16].

Multiple trials have compared liberal vs. restrictive transfusion strategies. The *TRICC trial* compared hemoglobin targets of 7–9 g/dL (restrictive) vs. 10–12 g/dL (liberal), showing that the restrictive strategy was as effective, and possibly superior, in critically ill patients except those with acute myocardial infarction or unstable angina [17]. The *TRISS trial*, conducted in septic shock patients, found no significant difference between strategies [18]. The *Villanueva trial*, in patients with upper gastrointestinal bleeding, showed improved survival with a restrictive strategy (Hgb >7 g/dL) compared to a liberal one (Hgb >9 g/dL) [19].

Platelets: Indications for transfusion are summarized in Table 11.6 [15].

Table 11.6 Indications for platelets transfusion

Transfusion indications	Platelet count ($\times 10^9/L$)
<i>Thrombocytopenia and procedures</i>	
Ocular surgery or neurosurgery with no active bleeding	<100
Major surgery with no active bleeding	<50
Diagnostic lumbar puncture	<50
Central venous catheter placement	<20
<i>Bleeding</i>	
Non-CNS active bleeding	<50
CNS active bleeding	<100
Hemorrhage requiring massive transfusion	Regardless of platelets count, transfuse red blood cells, plasma, and platelets in ratios of 1: 1: 1 to 2: 1: 1
<i>Thrombocytopenia without bleeding</i>	
General	<10
Body temperature > 38 °C, sepsis	<20

Adapted from: Sharma et al. [15]; Raval et al. [20]

CNS central nervous system

Other hematological indications:

- Acute promyelocytic leukemia if platelets $<30\text{--}50 \times 10^9/\text{L}$.
- In platelets consumption disorders, e.g., thrombotic thrombocytopenic purpura (TTP), immune thrombocytopenia (ITP), heparin-induced thrombocytopenia (HIT), and disseminated intravascular coagulation (DIC), platelet transfusion is indicated only in cases of active bleeding or prior to invasive procedures.

Fresh frozen plasma (FFP): Indicated only for bleeding due to coagulopathy, such as in DIC or liver disease.

Cryoprecipitate: Contains von Willebrand factor (vWF), factor VIII, factor XIII, and fibrinogen. Indicated in:

- Bleeding due to dysfibrinogenemia (e.g., post-thrombolytic therapy, DIC).
- Factor XIII deficiency with bleeding.
- von Willebrand disease with bleeding.

Fibrinogen: Indicated in bleeding due to dysfibrinogenemia (e.g., post-thrombolytic therapy, DIC).

Complications of Transfusion

- *Transfusion-associated circulatory overload (TACO):* Presents with signs of volume overload. Management includes stopping transfusion, providing oxygen or positive pressure ventilation, and administering diuretics.
- *Transfusion-related acute lung injury (TRALI):* Typically occurs within 6 h of transfusion. Management includes oxygen therapy and a lung-protective ventilation strategy.
- *Coagulopathy:* Commonly occurs with massive transfusion. Prevention includes transfusing FFP and platelets alongside RBCs.
- *Citrate toxicity:* Can cause hypocalcemia, metabolic alkalosis, and lactic acidosis, especially in patients with liver dysfunction.
- *Infections:* Rare complication caused by bacterial or viral contamination of donor blood.
- *Acute hemolysis:* Caused by ABO incompatibility. Symptoms include fever and flank pain; may lead to acute kidney injury (AKI). Treatment: intravenous fluids $\pm$ diuretics to maintain urine output, and antipyretics.
- *Delayed hemolysis:* Usually less severe than acute hemolysis; occurs 5–7 days post-transfusion. Treatment: supportive care.
- *Febrile nonhemolytic reaction:* Presents with fever and rigors, usually within 6 h post-transfusion. Caused by antibodies against donor white blood cells and cytokines in blood products. Treatment: supportive care.
- *Allergic reaction:*
 - Urticaria: Treat with antihistamines
 - Anaphylaxis (rare): Treat with epinephrine, steroids, and standard management of anaphylaxis.

Oncology Emergencies

Febrile Neutropenia

Definition of Febrile Neutropenia

Fever $>38.3^{\circ}\text{C}$ once or $>38.0^{\circ}\text{C}$ for >1 h in a neutropenic patient with an absolute neutrophil count (ANC) $<0.5 \times 10^9/\text{L}$, or $<1.0 \times 10^9/\text{L}$ with a predicted decline to $<0.5 \times 10^9/\text{L}$.

Sources of Infection

Most common: gastrointestinal (e.g., neutropenic typhlitis, anorectal infections, bacterial translocation).

Other sources: catheter-related infections, mucositis, etc.

Common organisms: Gram-negative (especially *Pseudomonas aeruginosa*), gram-positive (e.g., *Staphylococcus aureus*), and fungal pathogens.

Clinical Evaluation of Febrile Neutropenia

Requires thorough head-to-toe examination to identify infection sources: skin/soft tissue, pulmonary, abdominal, central nervous system (CNS), cardiac, and catheter sites.

Laboratory Investigations: complete blood count (CBC), inflammatory markers, basic metabolic panel, blood cultures (including from central lines), and urine and sputum cultures. Additional tests based on symptoms (e.g., stool culture and *Clostridium difficile* toxin assay if diarrhea; cerebrospinal fluid [CSF] analysis if meningitis suspected).

Radiological investigations: chest X-ray. Further imaging (e.g., imaging of abdomen, sinuses, brain, or chest) based on clinical findings.

Management of Febrile Neutropenia [21]

As in any critical case, febrile neutropenia is approached with ABC and management of each step accordingly.

Pseudomonas coverage should be started immediately, e.g., cefepime, piperacillin/tazobactam, meropenem.

Coverage for methicillin-resistant *Staphylococcus aureus* (MRSA) is recommended in high-risk patients, including those with:

- Suspected gram-positive infections (e.g., mucositis, soft tissue infections, pneumonia, invasive catheter).
- Hemodynamic instability.
- Positive MRSA colonization.

Initiate antifungal (e.g., echinocandin) if fever persists >4 days despite appropriate antibacterial treatment. Consider early initiation in patients with septic shock.

Granulocyte colony stimulating factor (GCSF) is proven to improve neutropenia and hospitalization but has no impact on mortality [22].

Tumor Lysis Syndrome (TLS)

Occurs in patients with highly proliferative tumors (e.g., high-grade lymphomas, leukemias), often after chemotherapy. Rapid cell turnover leads to transcellular electrolyte shifts, causing potentially life-threatening electrolyte disturbances.

Clinical Presentation and Scoring of TLS

Cairo-Bishop classification is used to diagnose cases of TLS (Table 11.7) [24].

Management of TLS [25]

As in any critical case, TLS is approached with ABC and management of each step accordingly.

Aggressive hydration with crystalloid and monitoring of urine output.

Trial of diuresis in case of volume overload.

Correction of hyperphosphatemia, hyperkalemia, and only symptomatic hypocalcemia.

Uric acid–lowering agents include allopurinol and rasburicase, with rasburicase reserved for severe cases. Rasburicase should be avoided in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency due to the risk of hemolysis.

Management of seizures (as illustrated in section “[Status Epilepticus](#)”, Chap. 3), arrhythmia, and cardiac arrest (as per advanced cardiac life support protocols).

Acute kidney injury (AKI): STOP approach (illustrated in the section “[Acute Kidney Injury](#)”, Chap. 7) and consider dialysis. Indications of dialysis are same as in other causes of AKI in addition to:

- Hyperphosphatemia induced symptomatic hypocalcemia
- A calcium phosphate product $>70 \text{ mg}^2/\text{dL}^2$

Hypercalcemia

Illustrated in the section “[Calcium Disorders](#)”, Chap. 10.

Table 11.7 Cairo-Bishop criteria used in diagnosis of tumor lysis syndrome (TLS)

Cairo-Bishop TLS syndrome classification	
Laboratory TLS	Clinical TLS
Uric acid ≥ 8.0 mg/dL (hyperuricemia)	Acute kidney injury defined as serum creatinine $>1.5 \times$ the upper limit of normal for the patient's age and sex Cardiac arrhythmia or sudden cardiac death Seizure, tetany, or other symptomatic hypocalcemia
Potassium ≥ 6.0 mEq/dL (hyperkalemia)	
Phosphorus ≥ 4.6 mg/dL (hyperphosphatemia)	
Calcium ≤ 7.0 mg/dL (hypocalcemia)	
Patients must meet more than two of four laboratory criteria in the same 24-h period within 3 days before or 7 days after initiation of chemotherapy.	

Adapted from: Cairo and Bishop [23]

Spinal Cord Compression

Occurs due to vertebral metastasis which can be related to prostate, breast, or lung cancers. Other causes include multiple myeloma and lymphomas.

Clinical Presentation of Cord Compression

Patients may complain of back pain, sensory/motor loss below the level of compression, and autonomic dysfunction (neurogenic bladder and stool incontinence).

Magnetic resonance imaging (MRI) of the spine is the diagnostic tool of choice; computed tomography (CT) may be considered if MRI is unavailable.

Management of Cord Compression

Management should be initiated immediately without delay.

Steroids: dexamethasone 10 mg loading dose followed by 4 mg every 6 h.

Urgent neurosurgical intervention for decompression.

Radiotherapy also can be considered.

Superior Vena Cava (SVC) Syndrome

SVC obstruction occurs in some malignancies, primarily lung cancer and non-Hodgkin lymphoma (NHL).

Clinical Presentation: May include facial and upper limb edema, dyspnea, CNS manifestations, and upper airway complications (e.g., stridor). On examination, patients may exhibit a positive Pemberton's sign, defined as facial congestion following arm elevation for approximately 1 min (Fig. 11.3).

Diagnosis: Made by Doppler ultrasound and confirmed with CT venography.

Management of SVC Syndrome

- As in any critical case, SVC syndrome is approached with ABC and management of each step accordingly.
- Secure the airways in case of stridor and laryngeal edema.
- In severe cases (e.g., encephalopathy or laryngeal edema), endovascular intervention is the treatment of choice for stenting or thrombus removal.
- Steroids may be added to reduce edema progression and are indicated for steroid-sensitive tumors such as lymphoma.
- In non-severe cases, treatment options include endovascular intervention, radiotherapy, or chemotherapy for chemo-sensitive tumors, based on oncology expert opinion.



Fig. 11.3 Clinical photograph of patient showing a left-sided neck swelling (a). The “Pemberton’s sign” is seen in (b). (Sourced from: Sriramka et al. [26]. Used with permission)

Hyperleukocytosis and Leukostasis

Hyperleukocytosis is defined as a white blood cell (WBC) count $>100 \times 10^9/L$, though complications may occur at lower levels. It is common in acute myeloid leukemia (AML) and is associated with increased mortality. Leukostasis refers to tissue hypoperfusion caused by very high WBC counts. In patients with hyperleukocytosis, respiratory failure and intracranial hemorrhage are the leading causes of death, often complicated by disseminated intravascular coagulation (DIC) or TLS.

Pathophysiology of Hyperleukocytosis and Leukostasis

Hyperleukocytosis: uncontrolled blast proliferation with reduced affinity for the bone marrow.

Leukostasis: leads to end-organ hypoperfusion through microvascular occlusion, hemorrhage, infarction, and edema at the tissue level.

Clinical Manifestations of Leukostasis

- Neurologic manifestations: altered level of consciousness, delirium, coma, headache, vision changes, focal deficits, intracranial hemorrhage.

- Pulmonary manifestations: hypoxemia, shortness of breath, respiratory failure.
- Other manifestations: myocardial infarction, arrhythmias, right ventricular failure, acute kidney injury, bowel or limb ischemia, priapism.

Investigations of Leukostasis

- *CBC and coagulation profile*: WBC is $>100 \times 10^9/L$, DIC can be present.
- *Blood gas*: oxygen may be falsely low due to cellular metabolism in vitro, lactic acidosis due to anerobic glycolysis.
- *Electrolytes and renal function*: it may show pseudohyperkalemia, and TLS.
- *Other investigations*: depend on the clinical presentation, e.g., electrocardiogram, cardiac enzymes, and brain and chest imaging.

Management of Leukostasis [27]

As in any critical case, leukostasis is approached with ABC and management of each step accordingly.

Fluids for hydration should be administered to reduce blood viscosity, but caution must be taken to avoid volume overload leading to pulmonary edema and worsening respiratory failure.

If possible, avoid therapies that may increase blood viscosity, e.g., red blood cells and diuretics.

Emergent cytoreductive therapy with induction chemotherapy should be initiated as directed by the hematologist.

Other temporizing measures include the following:

- Hydroxyurea: may be useful in cases of diagnostic uncertainty or when induction chemotherapy is considered high risk.
- Leukapheresis [28, 29]: rapidly lowers WBC in a single session but has not demonstrated reduced mortality or complications; contraindicated in acute promyelocytic leukemia.

Frequent monitoring of blood tests is essential to detect complications such as TLS and DIC.

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Chapter 12

Obstetrics and Gynecology



Haytham Abbas , Shadi Halasa, and Mohammed Almuashi

Introduction

Obstetric and gynecologic emergencies are critical due to the dual focus of resuscitation for both the mother and the fetus. Effective management requires a multidisciplinary approach involving obstetrics, intensive care, neonatology, and other relevant specialties to ensure optimal outcomes. This chapter outlines common emergencies and their management strategies.

Physiological Changes of Pregnancy

Airway

- Progesterone-mediated hyperemia and edema of mucosal surfaces.
- Difficulty and a higher incidence of failure to intubate.

Breathing

- Higher oxygen consumption.
- Increased aspiration risk.
- Increased risk of pulmonary edema (increased blood volume and lower oncotic pressure).

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- Difficult to implement protective ventilation as hypercapnia produces fetal acidosis.
- Total lung capacity (TLC) decreases by 5%.
- Functional residual capacity (FRC) decreases by 20%.
- Minute volume increases by 50% from an increase in tidal volume (TV) and respiratory rate (RR). This leads to chronic respiratory alkalosis (pH 7.4–7.47, with PaCO₂ 30–32 mmHg), kidneys excrete bicarbonate (HCO₃) to compensate the respiratory alkalosis and HCO₃ is usually found to be 18–21 mmol/L.

Circulation

- Tachycardia, lower blood pressure from decreased systemic vascular resistance (SVR).
- Aortocaval compression.
- Maternal blood volume increases by 40%.
- Normal ejection systolic murmur and third heart sound.
- Normal echocardiography with non-significant changes like increases in all cardiac chamber dimensions, increased left ventricular thickness, small pericardial effusions, mild tricuspid regurgitation (TR), and mild mitral regurgitation (MR).

Hematology

- Increase in venous thromboembolism (VTE) risk up to five times.
- Dilutional anemia (hemoglobin level is <11 g/dL in first trimester, and <10.5 g/dL in second and third trimesters).
- Gestational thrombocytopenia (GT): diagnosed with the following criteria: no history of thrombocytopenia before the pregnancy, platelets count should not be <50 × 10⁹/L and no schistocytes are seen in the blood smear.

Gastrointestinal

- Gastro-esophageal reflux disease (GERD), which increases the risk of aspiration.
- Hypoalbuminemia from hemodilution.
- Increase in alkaline phosphatase (ALP).

Renal

- Glomerular filtration rate (GFR) increases by 50%, with lower serum creatinine and urea.

Pre-Eclampsia/Eclampsia

Pre-eclampsia is defined as hypertension with blood pressure >140/90 mmHg after 20 weeks of gestation, associated with proteinuria (>2 + or >300 mg/day) or end-organ damage related to severe presentation of the disease.

The severe manifestations of pre-eclampsia are as follows:

- Systolic blood pressure (SBP) >160 mmHg and/or diastolic blood pressure (DBP) >110 mmHg

- Central nervous system (CNS) manifestations, e.g., encephalopathy, blurred vision, or severe headache
- Acute kidney injury (AKI) with creatinine >1.1 mg/dL
- Pulmonary edema
- Two to three times increase of aminotransferases or severe upper abdominal pain
- Thrombocytopenia with platelets $<100 \times 10^9/L$

Investigations of Pre-Eclampsia

- *Complete blood count (CBC), coagulation profile, hemolytic workup:* rule out hemolysis, thrombocytopenia, and coagulopathy.
- *Chemistry/renal function:* exclude AKI.
- *Liver function test:* assess for transaminitis.
- *Urine analysis, protein creatinine ratio:* assess for proteinuria.
- *Chest X-ray:* rule out pulmonary edema.

Other investigations depend on the clinical presentation:

- Abdominal pain $\rightarrow$ abdominal ultrasound (exclude subcapsular hemorrhage), liver function, amylase, lipase, glucose, ammonia.
- Severe neurological manifestations: brain imaging to exclude complications, e.g., intracranial hemorrhage (ICH) or posterior reversible encephalopathy syndrome (PRES) (Fig. 12.1).
- In thrombocytopenia, a blood film must be sent to rule out thrombotic thrombocytopenic purpura (TTP).

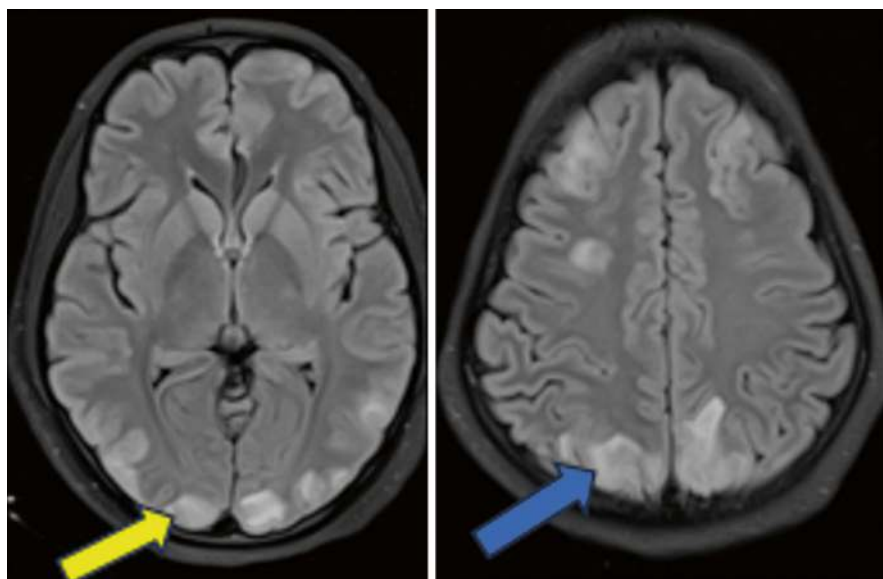


Fig. 12.1 Posterior reversible encephalopathy syndrome (PRES) is shown in the brain MRI. (Paladi et al. [1])

Management of Pre-Eclampsia [2, 3]

As in any critical case, pre-eclampsia is approached with ABC and management of each step accordingly.

Multidisciplinary management involving an obstetrician and relevant subspecialties based on clinical presentation is essential.

Blood pressure control should be achieved as soon as possible using safe antihypertensives (e.g., labetalol, nifedipine, hydralazine, nicardipine). It is reasonable to target a SBP of 130–150 mmHg and a DBP of 80–100 mmHg.

Urgent delivery of the fetus.

Seizure prophylaxis: recommended in severe cases (e.g., severe hypertension and end-organ damage) and for secondary prevention after eclamptic seizures.

Magnesium sulfate (MgSO_4) is the drug of choice:

- Intravenous (IV): 4 g bolus over 20–30 min → maintenance 1–2 g/h infusion.
- Intramuscular (IM) (if no IV access): initial 10 g (5 g in each buttock, deep IM) → maintenance 5 g IM every 4 h in alternate buttocks.

Monitoring: hemodynamics, respiratory rate, deep tendon reflexes (to detect magnesium toxicity):

- Reflexes present with a magnesium level of 2–3.5 mmol/L
- Loss of reflexes with magnesium level of 4–5 mmol/L
- Respiratory depression with magnesium level of >6 mmol/L

Eclampsia [4] defined as a seizure complicating pre-eclampsia.

It is approached the same as status epilepticus cases with ABC and attention to securing the airway, oxygenation, and keeping the patient on two large-bore IV canulas for extraction and treatment.

Directed therapy includes IV magnesium sulfate with a bolus of 4–6 g followed by infusion at a rate of 1–2 g/h.

Benzodiazepine (lorazepam 0.1 mg/kg, maximum of 2 mg/min, or diazepam 0.2 mg/kg, maximum of 5 mg/min) can also be started immediately. For recurrent seizures, consider reloading with magnesium and use of antiseizure drugs, including the benzodiazepine and other agents like phenytoin, levetiracetam, or fosphenytoin, but not sodium valproate, which is preferably avoided.

HELLP Syndrome

It is a severe condition during pregnancy and characterized by the presence of hemolytic anemia, thrombocytopenia, and transaminitis.

Clinical presentation: patients with HELLP syndrome might have severe right upper quadrant (RUQ) pain, nausea/vomiting, and RUQ tenderness. Other symptoms and signs of pre-eclampsia can be present.

Investigations show anemia with positive hemolytic workup ($\uparrow$ lactate dehydrogenase [LDH], $\uparrow$ total bilirubin, $\downarrow$ haptoglobin), thrombocytopenia, and transaminitis with $>$ two times increase of alanine transaminase (ALT) and aspartate transaminase (AST).

Abdominal ultrasound should be requested to exclude complications like subcapsular hematoma or rupture.

It is managed as in pre-eclampsia with frequent monitoring of CBC and liver function tests.

Acute Fatty Liver of Pregnancy (AFLP)

As with other causes of acute liver failure, AFLP may present with encephalopathy, coagulopathy, renal impairment, hypoglycemia, and multiorgan failure.

Management requires urgent delivery and a multidisciplinary approach, involving gastroenterology and referral to a liver transplant center (see section “[Acute Liver Failure](#)”, Chap. 4).

Table 12.1 outlines the differential diagnosis of AFLP.

Table 12.1 Differential diagnosis of acute fatty liver of pregnancy (AFLP)

Findings	HELLP syndrome	AFLP	TTP	HUS
Neurologic symptoms/signs	Headache and blurred vision	Confusion (hepatic encephalopathy)	Confusion, seizure	Rare (unless atypical)
Fever	Rare	Rare	Possible	Rare
Hypertension	Common (with pre-eclampsia)	Rare	Possible	Rare
Thrombocytopenia platelets count $\times 10^9/L$	>20	>20	<20	>20
Hemolysis	Prominent	Rare	Prominent	Prominent
Anemia	Common	Rare	Prominent	Prominent
DIC	Rare	Common	Rare	Rare
Hypoglycemia	Absent	Common	Absent	Absent
Impaired renal function	Possible	Common	Possible	Prominent
LDH (international units/L)	>600	Variable	>1000	>1000
Elevated ammonia	Rare	Common	Absent	Absent
Elevated transaminases	Prominent	Prominent	Mild	Mild

HELLP hemolysis, elevated liver enzymes, low platelets, *TTP* thrombotic thrombocytopenic purpura, *HUS* hemolytic uremic syndrome, *DIC* disseminated intravascular coagulation, *LDH* lactate dehydrogenase

Air Embolism

Clinical Presentation

Diaphoresis, restlessness, chest pain, dyspnea, tachypnea, hypoxemia, tachycardia, hypotension, encephalopathy, or cardiac arrest. On auscultation, patients may have “mill wheel murmur.”

Electrocardiogram (ECG) may show ST-segment changes.

Treatment

- As in any critical case, air embolism should be approached by ABC, with management of each step accordingly.
- Administer 100% oxygen to enhance nitrogen washout from air bubbles.
- Provide cardiovascular and ventilatory support as needed.
- Position the patient in left lateral decubitus with Trendelenburg to prevent air from obstructing the right ventricular outflow.
- If a central venous catheter is present, attempt air aspiration.
- Hyperbaric oxygen therapy should be considered for cerebral air embolism.

Amniotic Fluid Embolism (AFE)

Pathogenesis and Risk Factors

AFE is a rare but catastrophic pregnancy complication with high maternal mortality. Its exact pathophysiology is unclear, but is likely immune-mediated, triggered by amniotic fluid entry into maternal circulation. This results in direct myocardial depression and cytokine release (e.g., histamine, prostaglandins, and serotonin), leading to shock and an anaphylactoid reaction. Risk factors of AFE include the following:

- Induction of labor
- Multiple pregnancy
- Advanced maternal age
- Operative delivery (vaginal and cesarean section)
- Eclampsia
- Polyhydramnios
- Cervical laceration
- Uterine rupture

Clinical Presentation

Restlessness, confusion, seizure, hypoxia, hypotension, cardiac arrest, and coagulopathy, e.g., disseminated intravascular coagulation (DIC).

Differential Diagnosis

- Pulmonary embolism (PE)
- Congestive heart failure

- Sepsis
- Anaphylaxis

Management

- As in any critical case, AFE should be approached by ABC and management of each step accordingly.
- Supportive management.
- Oxygenation: noninvasive ventilation (NIV)/mechanical ventilation.
- Vasoactive agents +/- mechanical support, e.g., extracorporeal membrane oxygenation (ECMO) for persistent shock.
- Correction of coagulopathy.
- Treat the associated post-partum hemorrhage (PPH).

Ovarian Hyperstimulation Syndrome (OHSS)

OHSS is an exaggerated ovarian response to ovulation induction, leading to fluid shift from the intravascular space to third spaces, primarily the abdominal cavity.

Clinical Presentation of OHSS: see Table 12.2.

Table 12.2 Classification of OHSS based on clinical severity

Class	Clinical findings
Mild	Abdominal distention/discomfort Mild nausea/vomiting
Moderate	Moderate abdominal pain Nausea/vomiting Ultrasonographic evidence of ascites
Severe	Severe abdominal pain Intractable nausea and vomiting Significant ascites +/- pleural effusion Rapid weight gain Oliguria Serum creatinine 1–1.5 mg/dL Creatinine clearance ≥ 50 mL/min Hyponatremia ($\text{Na} < 135$ mEq/L) Elevated Hct $> 45\%$ Elevated WBC $> 15,000$ cells/ μL Liver dysfunction
Critical	Tense ascites +/- pleural effusion Thromboembolism ARDS Oliguria/anuria Serum creatinine ≥ 1.6 mg/dL Creatinine clearance < 50 mL/min Elevated Hct $> 55\%$ Elevated WBC $> 25,000$ cells/ μL

Adapted from: Navot et al. [5]

Hct hematocrit, *WBC* white blood cells, *Na* sodium, *ARDS* acute respiratory distress syndrome

Management of OHSS [6]

- Severe cases of OHSS should be approached by ABC, with management of each step accordingly.
- Intravenous hydration with crystalloids and/or colloids.
- Gentle diuresis in case of hypervolemia.
- Daily weight and abdominal circumference measurements.
- Venous thromboembolism (VTE) prophylaxis.
- Analgesia.
- Abdominal paracentesis of tense ascites and thoracentesis of massive effusion.
- Daily assessment of chemistry/renal function, and CBC.

Tocolytic-Induced Pulmonary Edema

It may occur as a complication of sympathomimetic therapy, specifically a beta-2 agonist like terbutaline [7].

Clinical Presentation

Symptoms: Dyspnea, tachypnea, hypoxemia, cough, tachycardia, chest pain.

Signs: Bibasilar crackles on auscultation.

Chest X-ray: Bilateral diffuse interstitial opacities consistent with pulmonary edema.

Echocardiography: Normal findings for pregnancy; no structural cardiac abnormality.

Treatment

- As a critical case, it should be approached by ABC and managed at each step accordingly.
- The offending agent should be discontinued and another tocolytic considered if needed.
- Supplemental oxygen/ventilation.
- Diuresis.

Peripartum Cardiomyopathy (PPCM)

PPCM is defined as heart failure occurring during the peripartum period without other identifiable cardiac causes.

Management follows standard heart failure and/or cardiogenic shock protocols, including the following:

- Cardioprotective agents, inotropes, and mechanical support as needed.
- Avoid teratogenic drugs during pregnancy, e.g., angiotensin-converting enzyme inhibitors (ACEi), angiotensin II receptor blockers (ARBs), and spironolactone.

These medications can be used safely after delivery (see section “[Cardiogenic Shock](#)”, Chap. 1).

- Safe medications during pregnancy: beta-blockers (BB), digoxin, nitrate, hydralazine, and diuretics.
- Anticoagulation: should be considered if ejection fraction (EF) < 35%.
- Patients with severe or refractory cardiomyopathy should be evaluated for advanced therapies, including left ventricular assist device (LVAD) or cardiac transplantation.

Advanced Cardiac Life Support (ACLS) in Pregnancy

ACLS is performed as in non-pregnant patients, with specific pregnancy-related considerations:

- Anticipate a difficult airway; involve anesthesia or airway experts early.
- Immediate involvement of obstetrics for potential perimortem cesarean delivery within 5 min of cardiac arrest onset.
- In addition to high-quality cardiopulmonary resuscitation (CPR), uterus should be pushed laterally to relieve aortocaval compression.
- If on magnesium sulfate (MgSO_4), discontinue infusion and administer calcium gluconate or calcium chloride to reverse toxicity.
- The potential causes of cardiac arrest must be reviewed and excluded (ABCDEFGH):
 - Anesthesia: failed intubation, aspiration, drug reaction
 - Bleeding: peripartum hemorrhage
 - Cardiac: peripartum cardiomyopathy and non-pregnancy-related cardiac conditions
 - Drugs: MgSO_4 , tocolytic, anaphylaxis
 - Embolism: pulmonary embolism (PE), air embolism, amniotic fluid embolism
 - Fever: sepsis
 - General: 5Hs, 5Ts
 - Hypertension: pre-eclampsia, eclampsia, HELLP

Figure 12.2 summarizes the approach by using the mnemonic WOMAN (W = what is the cause? O = offset the uterus, M = magnesium and multidisciplinary team, A = airway and ACLS, N = neonate). The standard approach was illustrated in section “[Advanced Cardiac Life Support](#)”, Chap. 1 [8].

ACLS In Pregnancy

WOMAN approach:

W = What is the cause? (ABCDEFGH) Anesthetic complications, Bleeding, Cardiac, Drugs, Embolism, Fever, General: 5Hs, 5Ts, Hypertension
O = Offset the uterus Manual left uterine displacement (LUD) to reduces aortocaval compression and improves venous return
M = Magnesium & Multidisciplinary Team ▪ Hold magnesium and administer calcium gluconate as an antidote ▪ Multidisciplinary team: Involve obstetrics, anesthesia, neonatology early
A = Airway & ACLS ▪ Anticipate difficult airway due to anatomical/physiological changes, call for expert help ▪ ACLS: Follow standard ACLS protocols
N = Neonatal delivery (Perimortem Cesarean) Deliver the neonate within 5 minutes of arrest

Fig. 12.2 Advanced cardiac life support (ACLS) in pregnancy (WOMAN approach)

Post-Partum Hemorrhage (PPH)

PPH has various definitions globally. The traditional definition is ≥ 500 mL blood loss after vaginal delivery or ≥ 1000 mL after cesarean birth. However, this can be inaccurate due to hidden bleeding or dilution with amniotic fluid. The American College of Obstetricians and Gynecologists (ACOG) revised the definition as:

Cumulative blood loss ≥ 1000 mL, OR
Bleeding with signs or symptoms of hypovolemia within 24 h of delivery.

Etiology: 4Ts (Table 12.3).

Management of PPH [10]

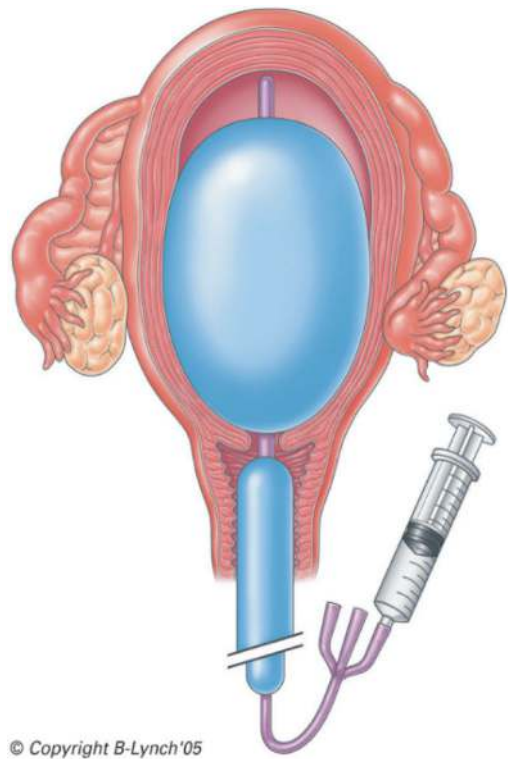
- Severe cases must be approached with ABC and management of each step accordingly.
- Establish two large-bore peripheral IV cannulas.
- Initiate fluid resuscitation and send blood for crossmatch and basic labs (CBC, coagulation profile, metabolic panel).
- Apply massive transfusion protocol (MTP) in severe cases.
- Correct coagulopathy with appropriate blood products and tranexamic acid. Tranexamic acid has been shown to improve survival (*WOMAN trial* [11]).
- Identify and control the obstetric source of bleeding (e.g., lacerations, hematomas, retained tissue).

Table 12.3 4Ts causes of post-partum hemorrhage

4Ts	Cause	Incidence (%)
Tone	Atonic uterus	70
Trauma	Lacerations, hematomas, inversion, rupture	20
Tissue	Retained tissue, invasive placenta	10
Thrombin	Coagulopathies	1

Evensen et al. [9]

Fig. 12.3 Uterine balloon tamponade in post-partum hemorrhage. (Courtesy of Danso and Reginald [12]. Used with permission)



- Uterine atony management:
 - Fundal massage and compression.
 - Increase oxytocin infusion.
 - Add other uterotonics if bleeding persists, e.g., Carboprost tromethamine, misoprostol, and methylergometrine.
 - Uterine tamponade (Fig. 12.3) [12].
 - For refractory bleeding, consider angiography with embolization or hysterectomy.

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Chapter 13

General ICU



Haytham Abbas , Assad Bafarag, and Mohammad Jawish

Introduction

This general ICU chapter outlines standard care practices and various clinical bundles used to improve patient outcomes and reduce complications. It also addresses ethical considerations and communication skills essential in ICU settings. Additionally, this chapter covers key statistical concepts and numerical data relevant to clinical practice and research analysis.

FAST HUGS BID

ICU patients need assessment in a more holistic and wider approach in comparison to other patients. The FAST HUGS BID method aims to improve outcomes and overall quality of life for ICU patients. It is designed to contain multiple care points which help ICU patients to achieve this goal. These care points include the following:

- Fluid and Food
- Analgesia

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- Sedation
- Thromboembolic risk assessment
- Head up
- Ulcer prophylaxis
- Glycemic control
- Spontaneous breathing trial
- Bowel motion/Bed sores
- Indwelling catheters
- De-escalation of antibiotics

Fluid

ICU patients require frequent assessment of volume status as part of hemodynamic monitoring. For patients needing volume expansion, evidence does not show a clear superiority of colloids over crystalloids. The *SAFE trial* compared albumin with normal saline (NS) for ICU resuscitation and found no significant difference in outcomes; however, albumin may benefit patients with septic shock, while NS may be preferable in traumatic brain injury (TBI) [1]. The *ALBIOS trial* evaluated albumin replacement in sepsis or septic shock patients with hypoalbuminemia and also showed no significant benefit [2].

While the choice of crystalloid remains debated, balanced crystalloids such as Ringer's lactate (LR) or Plasma-Lyte may be preferable in aggressive resuscitation due to the high chloride content of NS, which can worsen acidemia. Clinical trials such as *SMART* and *SALT-ED* have shown improved outcomes with balanced crystalloids compared to NS.

Food

Nutritional assessment and feeding (enteral/parenteral) are outlined in section “[Nutritional Assessment](#)”, Chap. 4.

Analgesia/Sedation

Outlined in section “[Analgesia, Sedation, and Delirium](#)”, Chap. 3.

Thromboembolic Risk Assessment

Venous thromboembolism (VTE) is the most common cause of preventable in-hospital death worldwide. Every medical institution should implement a standardized VTE risk assessment tool.

In the absence of contraindications (e.g., active bleeding), pharmacological VTE prophylaxis should be initiated. If pharmacologic measures are contraindicated, mechanical prophylaxis (e.g., intermittent pneumatic compression) must be used.

Combination therapy with both pharmacological and mechanical prophylaxis is generally not recommended, as evidence from the *PREVENT trial* showed no added benefit over pharmacological prophylaxis alone [3].

Head Up

Head elevation is a key component of the ventilator-associated pneumonia (VAP) prevention bundle. Evidence from the *Drakulovic trial* demonstrated a reduced risk of VAP in patients maintained in a semi-recumbent position [4]. All ventilated patients should be positioned semi-recumbently unless contraindicated (e.g., spinal cord injury).

Ulcer Prophylaxis

ICU patients are at increased risk of gastrointestinal (GI) bleeding due to stress-related mucosal damage. The primary risk factors include mechanical ventilation and coagulopathy. Additional risk factors are hypotension, renal impairment, liver disease, burns, trauma, and central nervous system (CNS) injury.

For high-risk patients, intravenous proton pump inhibitors (PPIs) are recommended for prophylaxis. The *PEPTIC trial* compared PPIs with histamine-2 receptor blockers (H2 blockers) in mechanically ventilated patients and found that PPIs reduced the risk of GI bleeding [5]. Similarly, the *SUP-ICU trial* demonstrated a significant reduction in clinically important GI bleeding with IV PPI compared to placebo [6]. However, PPI use may increase the risk of *Clostridium difficile* infection and pneumonia. In patients without risk factors for GI bleeding, prophylaxis may be de-escalated to oral PPI, H2 blocker, or discontinued altogether.

Glycemic Control

Hypoglycemia in ICU patients has been associated with increased mortality, as demonstrated in the *NICE-SUGAR trial* (2009) [7]. Conversely, hyperglycemia can lead to complications such as infections and ICU-acquired weakness.

Current guidelines recommend maintaining blood glucose levels between 140 and 180 mg/dL in critically ill patients. If blood glucose exceeds 180 mg/dL on more than one occasion, insulin therapy (typically using a sliding scale) should be initiated.

Spontaneous Breathing Trial

Outlined in section “[Weaning of Ventilation](#)”, Chap. 2.

Bowel Motion

Bowel dysfunction is common in ICU patients, with both constipation and diarrhea frequently encountered.

Constipation is often multifactorial, associated with malnutrition, opioid use, ileus, and electrolyte disturbances. It can contribute to complications such as delirium, pain, agitation, and prolonged ICU stay. Management includes identifying and treating underlying causes, along with the use of appropriate laxatives.

Diarrhea may result from overfeeding, nutritional intolerance, *Clostridium difficile* infection, or bowel ischemia. A thorough evaluation of these potential causes is essential, and management should be tailored accordingly.

Bed Sores

Prolonged pressure over bony prominences compromises capillary blood flow, leading to tissue ischemia and injury. This process can result in the development of pressure ulcers (bedsores) within 2–6 h if unrelieved.

Stages: (see Fig. 13.1).

Risk factors: (see Table 13.1).

Risk assessment should be performed on admission using a standardized scoring system such as the Braden or Norton Scale, with daily reassessment thereafter (Fig. 13.2 shows Braden scale) [8].

Key interventions to reduce the risk of pressure ulcers include the following:



Fig. 13.1 Stages of pressure ulcer. (Sourced from www.openmed.co.in. Used with permission)

Table 13.1 Risk factors for bed sores

Risk factors for pressure ulcer development
<i>External factors:</i>
Pressure
Friction (skin against external surface)
Moisture
<i>Patient factors:</i>
Immobility
Hypoperfusion (e.g., hypotension and hypovolemia)
Malnutrition
Incontinence
Sensory loss (no detection for tissue injury)
Microcirculatory impairment (e.g., diabetes and peripheral vascular disease)

- Minimize immobility: Limit sedation and initiate early, aggressive physical therapy.
- Regular repositioning: Reposition patients at least every 2 h, ensuring pressure is relieved from bony prominences.
- Prophylactic dressings: Apply protective dressings to high-risk areas.
- Nutritional support: Ensure adequate caloric intake with optimal protein levels.
- Moisture and incontinence management: Keep the skin clean and dry to prevent maceration.
- Hemodynamic stability: Maintain adequate blood pressure and oxygenation to support tissue.

BRADEN SCALE					
PREDICTING PRESSURE INJURIES					
Patient's Name _____		Evaluator's Name _____		Date of Assessment _____	
SENSORY PERCEPTION ability to respond meaningfully to pressure-related discomfort	1. Completely Limited Unresponsive (does not moan, flinch, or grasp) to painful stimuli, due to diminished level of consciousness or sedation. OR limited ability to feel pain over most of body	2. Very Limited Responds only to painful stimuli. Cannot communicate discomfort except by moaning or restlessness. OR has a sensory impairment which limits the ability to feel pain or discomfort over 1/3 of body.	3. Slightly Limited Responds to verbal commands, but cannot always communicate discomfort or the need to be turned. OR has some sensory impairment which limits ability to feel pain or discomfort in 1 or 2 extremities.	4. No Impairment Responds to verbal commands. Has no sensory deficit which would limit ability to feel or voice pain or discomfort.	
MOISTURE degree to which skin is exposed to moisture	1. Constantly Moist Skin is kept moist almost constantly by perspiration, urine, etc. Dampness is detected every time patient is moved or turned.	2. Very Moist Skin is often, but not always moist. Linen must be changed at least once a shift.	3. Occasionally Moist Skin is occasionally moist, requiring an extra linen change approximately once a day.	4. Rarely Moist Skin is usually dry, linen only requires changing at routine intervals.	
ACTIVITY degree of physical activity	1. Bedfast Confined to bed.	2. Chairfast Ability to walk severely limited or non-existent. Cannot bear own weight and/or must be assisted into chair or wheelchair.	3. Walks Occasionally Walks occasionally during day, but for very short distances, with or without assistance. Spends majority of each shift in bed or chair.	4. Walks Frequently Walks outside room at least twice a day and inside room at least once every two hours during waking hours.	
MOBILITY ability to change and control body position	1. Completely Immobile Does not make even slight changes in body or extremity position without assistance.	2. Very Limited Makes occasional slight changes in body or extremity position but unable to make frequent or significant changes independently.	3. Slightly Limited Makes frequent though slight changes in body or extremity position independently.	4. No Limitation Makes major and frequent changes in position without assistance.	
NUTRITION usual food intake pattern	1. Very Poor Never eats a complete meal. Rarely eats more than 1/3 of any food offered. Eats 2 servings or less of protein (meat or dairy products) per day. Takes fluids poorly. Does not take a liquid dietary supplement. OR is NPO and/or maintained on clear liquids or IV's for more than 5 days.	2. Probably Inadequate Rarely eats a complete meal and generally eats only about 1/3 of any food offered. Protein intake includes only 3 servings of meat or dairy products per day. Occasionally will take a dietary supplement. OR receives less than optimum amount of liquid diet or tube feeding.	3. Adequate Eats over half of most meals. Eats a total of 4 servings of protein (meat, dairy products) per day. Occasionally will refuse a meal, but will usually take a supplement when offered. OR is on a tube feeding or TPN regimen which probably meets most of nutritional needs.	4. Excellent Eats most of every meal. Never refuses a meal. Usually eats a total of 4 or more servings of meat and dairy products. Occasionally eats between meals. Does not require supplementation.	
FRICTION & SHEAR	1. Problem Requires moderate to maximum assistance in moving. Complete lifting without sliding against sheets is impossible. Frequently slides down in bed or chair, requiring frequent repositioning with maximum assistance. Spasticity, contractures or agitation leads to almost constant friction.	2. Potential Problem Moves feebly or requires minimum assistance. During a move skin probably slides to some extent against sheets, chair, restraints or other devices. Maintains relatively good position in chair or bed most of the time but occasionally slides down.	3. No Apparent Problem Moves in bed and in chair independently and has sufficient muscle strength to lift up completely during move. Maintains good position in bed or chair.		
Total Score					

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Fig. 13.2 Braden scale for predicting risk of pressure ulcers

Indwelling Catheters

ICU patients are frequently connected to multiple invasive devices, including endotracheal tubes (ETT), Foley catheters, central venous catheters (CVC), nasogastric tubes (NGT), and others. Each device should be assessed daily for continued necessity to minimize the risk of device-related complications.

All procedures involving insertion, maintenance, and removal must follow standardized protocols to ensure patient safety and reduce the risk of infections, thrombosis, and other device-associated complications.

Central Venous Catheter (CVC)

- Needs standardized education (indications for CVC use, proper sterile technique for placement, site maintenance).
- CVC checklist is used during catheter insertion to assure proper sterility.
- Observer executing checklist must be empowered to stop the procedure if violations are observed.
- Complications monitoring and data should be regularly reviewed by ICU and hospital leadership.

- The femoral vein (FV) site should generally be avoided, as it limits patient mobilization. Although traditionally thought to carry a higher risk of infection, evidence does not show a significant difference in catheter-related bloodstream infection (CRBSI) rates between the FV and internal jugular vein (IJV). The *3SITES* trial compared the risks of CRBSI, thrombosis, and pneumothorax among central lines placed in the subclavian vein (SCV), FV, and IJV. The SCV was associated with the lowest rates of CRBSI and thrombosis but had a higher risk of pneumothorax. No significant differences in outcomes were observed between the IJV and FV sites [9].
- Use ultrasound guidance for IJV and FV catheter insertion.
- Maximum sterile technique during the CVC insertion as following:
 - Hand hygiene (alcohol hand rub or antiseptic soap).
 - Chlorhexidine-based skin prep.
 - Maximum sterile barrier precautions for all operators (hat, mask, sterile gloves, sterile gown).
 - Full body sterile drape.
 - Sterility of the equipment.
 - Placement of proper transparent dressing with chlorhexidine biopatch.
- CVC maintenance:
 - Daily bathing of patients with chlorhexidine.
 - Transparent dressing to be changed every 5–7 days with chlorhexidine skin prep.
 - Immediate change of the dressing if not intact or soiled.
 - Hubs are to be disinfected with alcohol or chlorhexidine as per standard protocol prior to accessing them.
 - Assess the patient daily for catheter removal.
- Practices that did not decrease infection rate and should not be routinely employed:
 - Antimicrobial ointment at CVC insertion site.
 - Placement of peripherally inserted central catheter (PICC) rather than CVC (infection rate is same in inpatients) [10].
 - Systemic antimicrobial prophylaxis.
 - Routine catheter replacement.
 - Routine blood culture.

Endotracheal Tube (ETT)

- Standardized education and training on lung-protective ventilation strategies and the VAP prevention bundle must be implemented for all ICU staff.
- VAP rates should be continuously monitored, with data regularly reviewed by ICU teams and hospital leadership to guide quality improvement initiatives.
- Bundles of VAP include the following:
 - Hand hygiene compliance.
 - Daily spontaneous awakening trial and spontaneous breathing trial.

- Daily assessment of readiness to extubate.
- Oral care compliance.
- Head elevation compliance ($>30^\circ$).
- Maintain ETT cuff pressure of at least 20 cmH₂O.
- ETT with supraglottic suction ports.
- Venous thromboembolism (VTE) prophylaxis.
- Peptic ulcer prophylaxis.

Urinary Catheter

- Catheter associated urinary tract infection (CAUTI) is one of the most common nosocomial infections in ICU settings. Its incidence can be reduced through the following measures:
 - Development of processes to decrease catheter insertion rates.
 - Daily assessment for catheter removal.
 - Sterile insertion (hand hygiene, sterile gloves and drape, antiseptic cleaning of urethral meatus).
 - Maintain sterile closed drainage system.
 - Conduct routine surveillance of CAUTI rates and feedback to local leadership.
- Practices not recommended for CAUTI prevention:
 - Routine use of antimicrobial impregnated catheters.
 - Routine urine cultures in asymptomatic patients.
 - Treatment of asymptomatic bacteriuria.
 - Prophylactic use of systemic antibiotics.
 - Scheduled catheter changes without indication.
 - Continuous bladder irrigation with antimicrobials for prevention.

De-Escalation of Antibiotics

Antibiotic resistance is a growing global concern, with antibiotic misuse and over-use being among the most significant contributing factors. To combat this, implementing a robust antibiotic stewardship program within medical facilities is essential.

Communication Skills

The core principles of medical ethics are as follows:

- Beneficence: restoring health and relieving suffering.
- Non-maleficence: not to harm.
- Autonomy: respect the patient's choice and wishes.
- Justice: fair allocation of medical resources.

General Skills of Communication

- Environment:
 - Appropriate timing (if no emergency).
 - Calm, supportive setting.
 - Private space (closed door).
 - Basic comforts (e.g., water, tissue).
- People involved in communication:
 - Patient (if competent).
 - Closest relative (if patient is not competent).
 - Primary caregiver (if multiple relatives).
 - Ask caregiver about involving other relatives.
 - Involve others if message is not understood.
- Body language:
Facial expressions appropriate to the situation:
 - Sympathetic (bad news)
 - Confident (management plan, consent)
 - Honest and apologetic (medical errors)
- Tone of voice:
 - Low, sympathetic tone with pauses (for bad news)
 - Clear, steady voice with slower pace (for management plan and consent)
- Good listening:
 - Builds trust and rapport
 - Helps uncover hidden information
- Checking knowledge:
Assess prior knowledge to determine starting point.
- Taking feedback:
Confirm understanding; offer clarification if needed.
- Communication tools:
Functional phone and email for follow-up questions.

Breaking Bad News

Delivering bad news is common in the ICU and needs skills to be mastered, steps of breaking bad news are as follows:

- The general skills as described.
- Giving time for the patient or the relatives to absorb the shock.

- Explaining the medical plan.
- Explaining the role of subspecialties.
- Arrangement of other meetings with the subspecialties.
- Providing support to have power, faith, and hope.

Do Not Resuscitate (DNR)

DNR or palliative care management is also common in the ICU, steps of DNR discussion are as follows:

- The general skills as described.
- The unresolvable medical situation must be understood.
- Checking the knowledge and familiarity of DNR.
- Explaining the process and the law of the DNR as it is a three expert physician's opinion.
- Explaining the importance of palliative care management.
- Providing support to have power and faith.

Medical Errors

Communicating medical errors is a challenging skill due to unpredictable reactions. It requires proper training and includes the following steps:

- Be fully honest.
- Avoid making excuses.
- Emphasize that responsibility is shared by the team.
- Expect emotional reactions; remain calm and express sincere regret.
- Acknowledge the patient's or family's right to complain.
- Once emotions are managed, explain how the issue was addressed.

Informed Consent

The voluntary agreement to a medical intervention by the patient or relatives after full disclosure of the procedure's nature, risks, benefits, and alternatives by the physician.

It is a legal authorization that must be documented in a consent form.

Difficulties with informed consent in the ICU:

- Physician related:
 - Use of medical language.
 - Undiscovered risks and benefits of the interventions.
 - Limited time.
 - Unclear how the patient or the relatives are receiving the information, and how to deliver the information to not frighten them.
 - Deciding if the patient is competent to consent or who acts as surrogate decision-maker.
 - Time-sensitive procedures which require immediate consent.
- Patient or relatives related:
 - Limited understanding.
 - Selective hearing and comprehension.
 - Fear and denial which affect decision-making ability.

Five Elements of Informed Consent

- Competence
- Disclosure
- Understanding
- Voluntariness
- Consenting

Competence

- Ability to understand a procedure's major risks and benefits to make an informed decision.
- Identify factors impairing decision-making (e.g., dementia, delirium).
- Use assessment tools, e.g., the Richmond Agitation-Sedation Scale (RASS), Confusion Assessment Method for the ICU (CAM-ICU).
- Involve psychiatry if assessment is difficult.
- If patient is not competent, involve relatives.
- If no relatives or surrogate, hold a multidisciplinary team meeting.

Disclosure

- The general skills to be used as described.
- Assess patient's understanding of the procedure.
- Explain benefits and necessity of the procedure.
- Describe contraindications, side effects, complications, and their likelihood.
- Discuss benefits, risks, and chances of alternative therapies.
- For non-emergency interventions, allow time for decision-making and consultation with other experts.

Understanding

- Demonstrate understanding of the procedure, risks, and benefits.
- Recognize the right to refuse the intervention.
- Encourage questions and offer answers.

Voluntariness

Free decision-making without pressure or coercion (patient's right).

If the patient or surrogate refuses the procedure, refusal must be documented by signature (physician's right).

Consenting

- Documentation of the procedure.
- Risks and benefits.
- Full patient's information.

Statistics

Healthcare practitioners should be familiar with multiple statistical indices, as they play an important role in evidence-based practice and the interpretation of clinical trials. Examples of these indices include the following:

- Mean, median and mode: (see Fig. 13.3)
- Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV): (Fig. 13.4)
- Type I and II errors: (see Fig. 13.5)
- Types of studies: (see Figs. 13.6 and 13.7)

Mean: The average value in a data set

To find the mean, all values must be summed then divided by the number of those values

Example: The mean for this set of numbers 13,18,13,14,13,16,14,21,13 =
 $(13 + 18 + 13 + 14 + 13 + 16 + 14 + 21 + 13) / 9 = 15$

Median: The middle value in list of numbers

For an odd number of values, median will be a single value, e.g., 1, 2, 5, 7, 8

Median = 5

For an even number of values, median will be 2 values e.g., 1, 2, 5, 7, 8, 10

Median = 5 and 7

Mode: The value that occurs most often

If no number is repeated then there is no mode e.g., 13,18,13,14,13,16,14,21,13

Mode = 13

Fig. 13.3 Calculation of mean, median, and mode

Positive test result	True positive (TP)	False positive (FP)	PPV= TP/ (TP + FP)
Negative test result	False negative (FN)	True negative (TN)	NPV= TN/(TN+FN)
	Sensitivity= TP/(TP+FN)	Specificity= TN/(TN+FP)	

Fig. 13.4 Calculation of sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV)

		Reality	
		True	False
Result	True		Type I error False positive
	False	Type II error False negative	

Fig. 13.5 Type I and II errors

P-Value

P-value is the probability of obtaining the observed results, or more extreme results, assuming that there is no real difference or effect.

A lower *p*-value indicates greater statistical significance.

A *p*-value ≤ 0.05 is generally considered statistically significant.

Odds Ratio (OR) and 95% Confidence Interval (CI): see Fig. 13.8.

A 95% CI is the range of values that is likely to contain the true effect.

Significant results:

- Have a narrow (smaller) confidence interval (more precise estimate)
- The 95% CI does not cross or include 1 for an OR
- 1 is the null value, meaning no difference or effect

Number Needed to Treat (NNT): see Fig. 13.9.

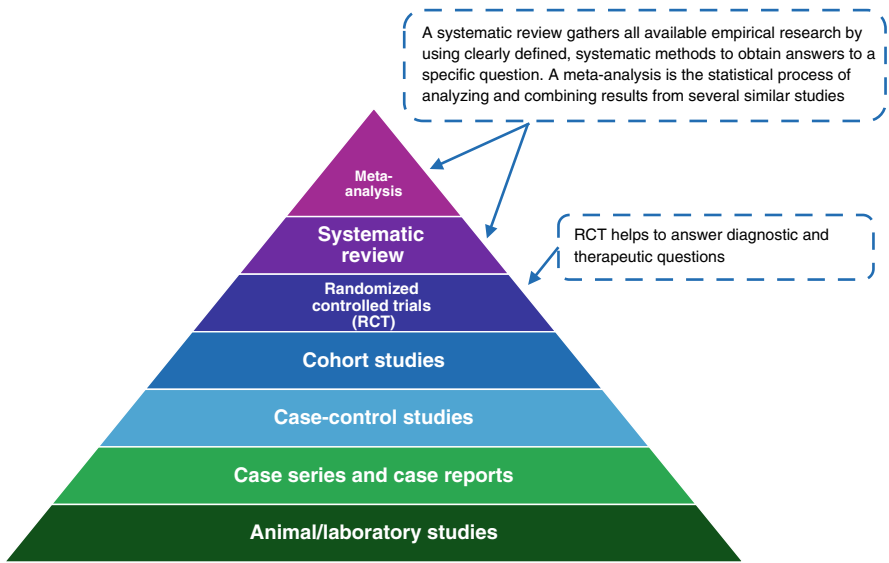


Fig. 13.6 Pyramid of studies and levels of evidence; the higher the position in the pyramid, the stronger the level of evidence

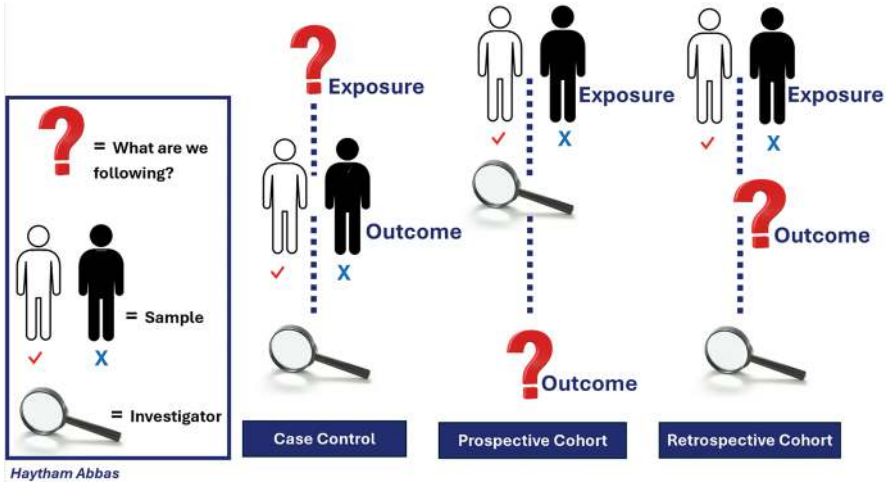


Fig. 13.7 The differences between case control, prospective cohort, and retrospective cohort studies

Fig. 13.8 95% Confidence interval

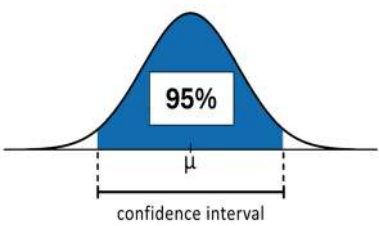


Fig. 13.9
EER = experimental event rate, CER = control event rate, ARR = absolute risk reduction, NNT = number needed to treat

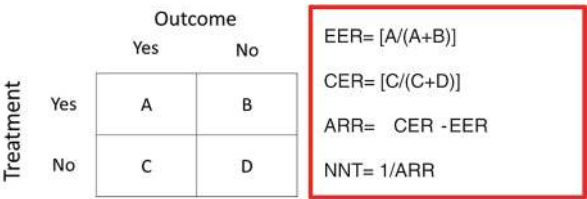
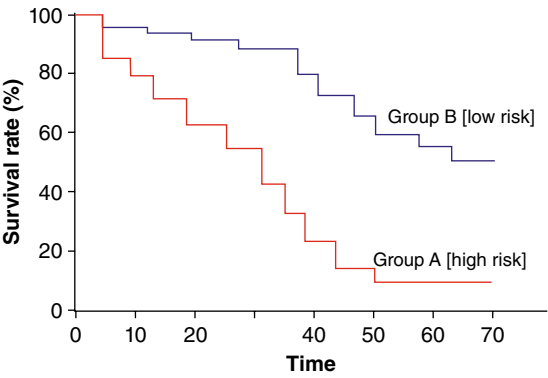


Fig. 13.10 The Kaplan–Meier chart



The result reflects the number of individuals who should receive the intervention to get one beneficial outcome.

Charts

- The Kaplan–Meier chart: used to estimate survival (Fig. 13.10).
- Forest plot: used in meta-analysis (Fig. 13.11).

Equations Used in ICU

Cardiovascular

- Fick equation: cardiac output (CO) = $VO_2/[10 \times Hb(g/dL) \times 1.34 \times (SaO_2 - ScvO_2)] \times 100$ ($VO_2 = 125 \times BSA$)
- Systemic Vascular Resistance (SVR) = $(MAP - CVP)/CO \times 80$
- Pulmonary Vascular Resistance (PVR) = $(MPP - PCWP)/CO \times 80$

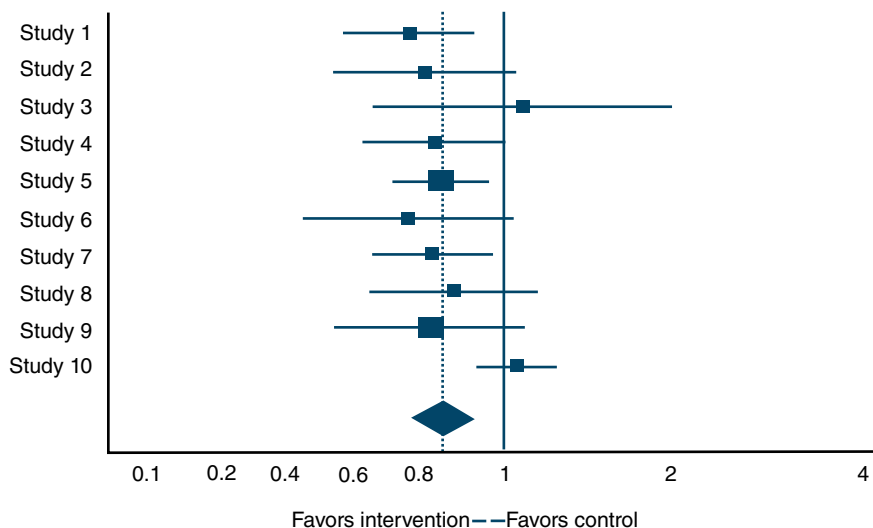


Fig. 13.11 Forest plot

- Arterial oxygen Contents (CaO_2) = $1.34 \times \text{Hb (g/dL)} \times \text{SpO}_2 + 0.003 \times \text{PaO}_2$
- Oxygen Delivery (DO_2) = $\text{CaO}_2 \times \text{CO}$
- Oxygen Consumption (VO_2) = $(\text{CaO}_2 - \text{CvO}_2) \times \text{CO}$
- Collapsibility index of IVC = $(\text{diameter maximum} - \text{diameter minimum}) / \text{diameter maximum} \times 100 \rightarrow >50\% = \text{volume responsive, used in spontaneously breathing patient.}$

Distensibility index of IVC = $(\text{diameter maximum} - \text{diameter minimum}) / \text{diameter minimum} \times 100 \rightarrow >18\% = \text{volume responsive, used in mechanically ventilated patient.}$

- Pulse Pressure Variation (PPV) = $(\text{PP maximum} - \text{PP minimum}) / \text{PP mean} \times 100 \rightarrow \text{PPV} >13\% = \text{volume responsive}$
 - Stroke Volume Variation (SVV) = $(\text{SV maximum} - \text{SV minimum}) / \text{SV mean} \times 100 \rightarrow \text{SVV} >13\% = \text{volume responsive}$
 - Mean Arterial Pressure (MAP) = $(\text{SBP} + 2\text{DBP}) / 3$
 - Blood Pressure (BP) = $\text{CO} \times \text{SVR}$
 - Cardiac Output (CO) = $\text{SV} \times \text{HR}$
 - Cardiac Index (CI) = CO / BSA
 - Stroke volume can be estimated by echocardiography, and = $\text{LVOT VTI} \times \text{CSA}$
- [$\text{CSA} = (\text{LVOTd})^2 \times 0.785$]

Respiratory System

- A-a gradient: $\text{A} = \text{alveolar oxygen} = \text{FiO}_2 \times (\text{Patm} - \text{PH}_2\text{O}) - (\text{PaCO}_2 \times 1.25)$
 $\text{Patm} = 760, \text{PH}_2\text{O} = 47, 760 - 47 = 713, \text{a} = \text{arterial oxygen (from ABG)}$
 A-a gradient normally = $\text{age} / 4 + 4$

- ↑ A-a gradient:
 - V/Q mismatch, e.g., pneumonia
 - Shunt: anatomical (intracardiac shunt, pulmonary AV malformation, hepatopulmonary) or physiological, e.g., ARDS
 - Diffusion: e.g., lung fibrosis
- Normal A-a gradient:
 - Hypoventilation
 - High altitude
- $\text{PaCO}_2 = \text{VCO}_2 / (\text{MV} - \text{VD})$
 MV (minute ventilation) decreases with hypoventilation.
 VD (dead space) can be anatomical related to any pathology from nose to alveoli or alveolar related to hypoperfusion, e.g., in heart failure, pulmonary embolism or hypovolemia.
- Static Compliance = $\text{TV} / (\text{Pplat} - \text{PEEP})$
- Dynamic Compliance = $\text{TV} / (\text{PIP} - \text{PEEP})$
- Airway Resistance = $(\text{PIP} - \text{Pplat}) / \text{flow}$
- Mean Airway Pressure (MAP) = $(T_{\text{ins}} / T_{\text{cyc}}) \times (\text{PIP} - \text{PEEP}) + \text{PEEP}$
- Airway pressure gradient = $\text{flow} \times \text{resistance} + (\text{TV} / \text{compliance})$
- Driving Pressure = $\text{Pplat} - \text{PEEP}$ (in ARDS, keep it <15 cmH₂O)
- Rapid Shallow Breathing Index (RSBI) = RR / TV (if <105, patient is weanable)

Nephrology

- Winter's formula: $\text{PaCO}_2 = \text{HCO}_3 \times 1.5 + 8 \pm 2$
- In metabolic alkalosis, expected $\text{PaCO}_2 = 0.9 \times \text{HCO}_3 + 16 \pm 2$
- In acute respiratory acidosis, change of pH = $0.008 \times [\text{PaCO}_2 (1) - \text{PaCO}_2 (2)]$
- In chronic respiratory acidosis, change of pH = $0.003 \times [\text{PaCO}_2 (1) - \text{PaCO}_2 (2)]$
- Anion Gap (AG) = $\text{NA} - (\text{CL} + \text{HCO}_3)$
- Urine AG = $\text{NA} + \text{K} - \text{CL}$
- Osmolar gap = $\text{measured osmolality} - \text{calculated osmolality}$
- Serum osmolality (S.Osm) = $2 \text{ Na (mEq/L)} + \text{glucose (mg/dL)} / 18 + \text{BUN (mg/dL)} / 2.8$
- Glomerular Filtration Rate (GFR) = $(140 - \text{age}) \times \text{weight (in kg)} / 72 \times \text{creatinine (mg/dL)}$
- Correction of serum sodium in hyponatremia by giving 1 L of IVF can be estimated by the following: $\text{Infusion Na} - \text{serum Na} / \text{TBW}$
 (infusion Na is: 3% NaCl = 513 mEq/L, 0.9% NaCl = 154 mEq/L) (TBW = 60% of the weight in kg in males, 50% of weight in kg in females)
- Water deficit = $[(\text{serum Na} - 140) / 140] \times \text{TBW}$
- $\text{FENa} = (\text{UNa} / \text{PNa}) / (\text{UCr} / \text{PCr})$. If on diuretic use $\text{FEUN} = (\text{UUN} / \text{PUN}) / (\text{UCr} / \text{PCr})$
- In CRRT, filtration fraction (FF) = $\text{total ultrafiltration rate} / \text{plasma flow rate} + \text{the prefilter replacement fluid flow rate}$

$$= (\text{pre-filter replacement fluid rate} + \text{post-filter replacement fluid rate} + \text{fluid removal rate}) / [\text{blood flow rate} \times 60 \times (1 - \text{hematocrit}) + \text{the prefilter replacement fluid flow rate}]$$

Other Equations

- Cerebral Perfusion Pressure (CPP) = MAP – ICP
- Cerebral Blood Flow (CBF) = CPP/CVR
- Basal Energy Expenditure (BEE) = 25 × body weight
- Parkland formula for burn resuscitation = 4 mL × %TBSA × weight in kg (half the dose to be given in the first 8 h, and the second half to be given in the next 16 h). The last guidelines recommended to minimize the dose (2 mL × %TBSA × weight in kg)

VO₂ = oxygen consumption, Hb₂ = hemoglobin, SaO₂ = arterial oxygen saturation, ScvO₂ = central venous oxygen saturation, BSA = body surface area, CVP = central venous pressure, MPP = mean pulmonary pressure, PCWP = pulmonary capillary wedge pressure, SpO₂ = oxygen saturation, PaO₂ = partial pressure of arterial oxygen, CvO₂ = venous oxygen content, IVC = inferior vena cava, PP = pulse pressure, SV = stroke volume, SBP = systolic blood pressure, DBP = diastolic blood pressure, HR = heart rate, LVOT = left ventricular outflow tract, LVOTd = LVOT diameter, CSA = cross sectional area, VTI = velocity time integral, FiO₂ = fraction of inspired oxygen, Patm = atmospheric pressure at sea level, PH₂O = water pressure, PaCO₂ = partial pressure of arterial carbon dioxide, ABG = arterial blood gas, V/Q = ventilation perfusion, AV = arterio-venous, ARDS = acute respiratory distress syndrome, VCO₂ = carbon dioxide production, TV = tidal volume, Pplat = plateau pressure, PEEP = positive end expiratory pressure, PIP = peak inspiratory pressure, T_{ins} = inspiratory time, T_{cy} = respiratory cycle time, RR = respiratory rate, Na = sodium, Cl = chloride, HCO₃ = bicarbonate, K = potassium, BUN = blood urea nitrogen, TBW = total body water, FENa = fraction excretion of sodium, FEUN = fraction excretion of urea nitrogen, UNa = urine sodium, PNa = plasma sodium, UCr = urine creatinine, PCr = plasma creatinine, UUN = urine urea nitrogen, PUN = plasma urea nitrogen, ICP = intracranial pressure, CVR = cerebral vascular resistance, TBSA = total body surface area.

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