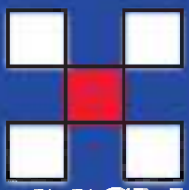
Rajesh Chawla
Subhash Todi *Editors*

ICU Protocols

A Stepwise Approach



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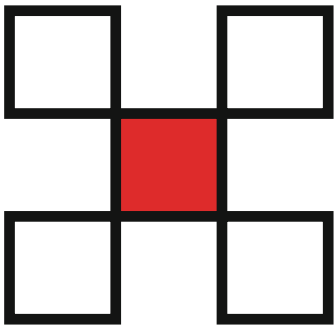

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An endeavour of Indian College of Critical Care Medicine under the auspices of Indian Society of Critical Care Medicine.

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To my parents, wife Renu, and daughters Aakanksha and Aakriti for their unconditional love and support. Special thanks to all my students, residents, fellows, and colleagues who inspire and educate me.

–Rajesh Chawla

To my mother, my wife Shailja, and daughter Suchira for their understanding, tolerance, and patience shown during the gestational period of this manual.

–Subhash Todi

Preface

It gives us great pleasure to present to you the first edition of "ICU protocol Book – a stepwise approach" under the auspices of Indian Society of Critical Care Medicine (ISCCM). The goal of this book is to provide residents, fellows, critical care practitioners, and allied health care professionals with a current and comprehensive stepwise algorithm for bedside diagnosis and management of the most frequently encountered problems in the intensive care unit (ICU).

This book is neither a condensed text book as some of the current hand books are nor an elementary primer. Although it is small enough to carry around, yet it is big enough to contain all essential elements of ICU care. The management of various conditions has been described in a stepwise fashion to avoid missing any important step in both the workup and treatment.

It is a multiauthor book, written by well-known practitioners in the field of critical care in India. We have included contributions from other specialties that bring a complementary perspective to the multidisciplinary management of critically ill patients. We have avoided the didactic style of writing and have made it more algorithmic with bulleted points to highlight important steps. Each chapter starts with a typical case scenario followed by stepwise management of diagnostic workup and treatment of that condition. Flow sheet, tables, charts, figures, and illustrations have been added at appropriate places. Each chapter ends with current authoritative references with annotations to guide the reader about more in-depth reading and important web resources. To prevent the manual from becoming voluminous, we have not gone into the details of the pathophysiology of each condition. We have included an appendix that has drug doses, ICU formulae, normal values, and ICU syllabus for the trainees.

The chapters of this book follow a uniform format and are divided on the basis of organ system and special topics (trauma, toxicology, metabolic problems, and procedures). It is important to understand that the field of critical care, like everything else, is not static but changes constantly. This book does not purport to define standard of care but is only a guide to current clinical practice in intensive care medicine. It is generally presumed that multiauthor books are only superficially edited and their chapters reflect the styles of its authors. In this book, we have tried to give a uniform format to all the chapters reflecting the purpose of the book. We have both worked together as a team for more than a year and reviewed each chapter to ensure the authenticity of the information.

This is an important educational venture of ISCCM, and we hope the book will be read not only in India but also regionally and internationally. Last but not the least, we sincerely hope that this manual will be used by the residents, wherever they are, for better bedside care of critically ill patients.

Rajesh Chawla
Subhash Todi

Acknowledgments

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Special thanks to editorial team of Springer who have supported this medical project. We particularly thank Dr. Naren Aggarwal for multiple helpful suggestions and support to the process of finalization of this book.

Also, we would like to give our special thanks to Mr. Vijay Prakash, Mr. Tapas Kayal, and Mr. Bhagwan Dass for their assistance in the office work and completing the manuscript.

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Part I

Respiratory System

Rajesh Chawla and Gopi Chand Khilnani

Airway Management

1

Sheila Nainan Myatra and Jigeeshu V. Divatia

A 60-year-old morbidly obese diabetic male patient with a left lobar pneumonia was shifted from the ward to the intensive care unit (ICU). He had history of progressive breathlessness and altered mental status for 6 h. He was drowsy but arousable, and had a respiratory rate of 33 breaths/min. SpO_2 was 92% with facemask using 6 L of oxygen per min. Heart rate was 110/min and blood pressure was 90/60 mmHg.

Tracheal intubation is one of the most commonly performed procedures in the ICU. In the ICU, unlike in the operating room with controlled conditions, a significant proportion of these procedures can be associated with life-threatening complications. This chapter gives a stepwise approach to airway management in the ICU, along with a detailed description of the preparation, assessment, procedure, precautions, maintenance, and complications associated with tracheal intubation.

Step 1: Be prepared for advanced airway management before arrival

- History from the treating team will give you some idea of the equipment and expertise needed for airway management (e.g., mental state, respiratory and hemodynamic status, time of last feeding, comorbidities that might complicate airway management, and contraindications to succinylcholine/other drugs).
- Check oxygen source, properly working suction, airway tray/cart, monitors, drugs, and personal protection equipment are ready.

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Step 2: Initial assessment, preoxygenation, and ventilation

Remember, failure to intubate will not harm a patient but failure to oxygenate/ventilate will. Ensure adequate oxygenation at all times.

- Critically ill patients may have oxygen transport limitation and time-consuming airway management. During apnea, the time for oxyhemoglobin desaturation below 85% is much faster in these patients. Thus, maximal preoxygenation (at least 3 min) is recommended to buy adequate time to tolerate apnea during intubation.
- Instead of a simple facemask, give high-flow oxygen (12–15 L per min) using the mask and AMBU bag with a reservoir bag. This way you will be ready to ventilate if required and can give higher oxygen concentration (provide 100% oxygen).
- Check breathing, with the airway open (head-tilt/chin-lift/jaw-thrust maneuver), look for adequate chest expansion and rate of breathing, listen for audible breath sound (also auscultate chest), and feel for airflow.
- If the patient is not breathing adequately with airway open, perform bag-mask ventilation with a reservoir bag attached. Ensure adequate chest rise. Hold the mask with both hands if ventilation is difficult.
- Bag-mask ventilation may be difficult in the following cases: obesity, presence of a beard, facial deformity/dressing, massive/heavy jaw, large tongue, edentulousness, any airway pathology, poor neck extension, history of snoring, and obstructive sleep apnea.
- Clear upper airway obstruction if present:
  - Snoring, gurgling sound, paradoxical movement of the chest wall (inward movement during inspiration) and abdomen and inadequate/absent chest rise during ventilation may suggest upper airway obstruction.
  - Perform an oral or nasal (with soft malleable catheter) suctioning for no more than 10 s at a time and resume oxygenation soon after.
  - Use an oropharyngeal or nasopharyngeal airway if obstruction is not cleared by suctioning. The airway should have a length equivalent to distance from the tip of the nose/angle of the mouth to the tragus. Nasopharyngeal airway diameter should be less than the patient's nostril. It should be avoided if the patient has risk of nasal trauma/bleeding or cerebrospinal fluid rhinorrhea.
- Currently it is recommended to preoxygenate using noninvasive positive pressure ventilation in case of acute respiratory failure whenever possible. Use pressure support ventilation with FiO_2 of 1.0, inspiratory pressure support from 5 to 15 cmH_2O, to obtain an expiratory tidal volume between 6 and 8 mL/kg and positive end-expiratory pressure of 5 cmH_2O.
- Attach the cardiac monitor, noninvasive blood pressure, and pulse oximeter and secure the intravenous line. These setups should not hamper/delay ventilation and oxygenation.

Step 3: Assess the need for tracheal intubation

- Look for clinical signs of acute respiratory failure: anxiousness, sweating, restlessness, cyanosis, shortness of breath, rapid breathing and air hunger, use of accessory muscles of ventilation, paradoxical abdominal breathing, exhaustion, confused state or drowsiness.

Table 1.1 Mallampati classification[a] (modified by Samsoon and Young)

Mallampati class	Intraoral structures visible
Class I	Soft palate, fauces, uvula, pillars
Class II	Soft palate, fauces, portion of uvula
Class III	Soft palate, base of uvula
Class IV	Hard palate only (later added by Samsoon and Young)

[a]By S. Rao Mallampati
Mallampati classification is based on the structures seen with maximal mouth opening and tongue protrusion without phonation in the sitting position. The observer's eye should be at the level of the patient's mouth. This classification correlates with intubation difficulty

- Arterial blood gas analysis may help measure disease severity. However, it should not replace clinical evaluation or delay need for airway intervention.
- Common indication of endotracheal intubation are as follows:
  - Facilitation of invasive mechanical ventilation (inadequate oxygenation/ventilation, shock, cardiac arrest, avoidance of hypercarbia, controlled hyperventilation, need for neuromuscular paralysis, postoperative elective ventilation)
  - Protection of the respiratory tract from aspiration of gastric contents
  - Tracheobronchial toilet
  - Relief of upper airway obstruction

Step 4: Assessment for difficult intubation

- Several methods are available; however, they are often impractical to use and also difficult to assess in the ICU unlike in the operating room, especially during emergency airway management.
- Generally accepted, independent predictors of difficult airway in controlled setting which can be quickly and easily assessed are as follows:
  - Length of upper incisor—relatively long
  - Interincisor distance—less than two fingers (3 cm)
  - Overbite—maxillary incisors override mandibular incisors
  - Temporomandibular joint translation—cannot place mandibular incisors anterior to maxillary incisors
  - Mandibular space compliance—small, stiff, indurated, or occupied by mass
  - Thyromental distance—less than three fingers (6 cm)
  - Mallampati class—III and IV (Table 1.1 and Fig. 1.1)
  - Neck—short, thick
  - Limited neck mobility—cannot touch chin to chest or cannot extend neck
- Despite outward appearances, a history of difficult intubation may be the most reliable predictor of future difficult intubation.
- Call for help in advance if difficulty in oxygenation, ventilation or intubation is anticipated.

Step 5: Checklist before intubation

Providing adequate ventilation is a priority over intubation. Hence, do not attempt intubation until everything is ready. Before intubation, check the following:

- Fasting status
- Oxygen source and working suction

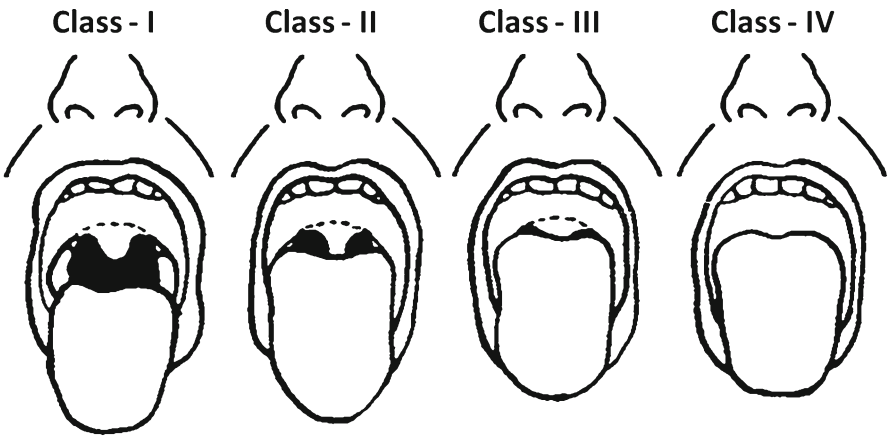

Fig. 1.1 Mallampati classification (modified by Samsoon and Young)

- Monitoring present (cardiac monitor, noninvasive blood pressure, pulse oximeter). Intra-arterial pressure monitoring is preferable and may be considered prior to nonemergency intubations especially in patients with shock.
- The intravenous line is secured. Fluid loading is recommended (isotonic saline 500 mL or colloid 250 mL) in absence of cardiogenic pulmonary edema. Be prepared to treat hypotension.
- All airway equipment are at hand (Table 1.2) and checked.
  - Working laryngoscopes (two blades—one standard blade and one long blade): Check light.
  - Endotracheal tubes (ETTs): Keep appropriate size tube ready (at least two). Check cuff for leaks and apply jelly on the cuff. The ETT with subglottic suction should preferably be used for all patients in whom prolonged intubation is anticipated.
- All the appropriate drugs are drawn up and ready (Table 1.3).
- Personal protection is adequate (gloves, mask, and eye protection) and expert help is available in case of anticipated difficult airway.
- If the patient is to be ventilated, set up the ventilator and prepare drugs for long-term sedation.

Step 6: Proceed with tracheal intubation

- *Proper positioning* (refer to Fig. 1.2)
  - Remove the head board and position the patient's head at the edge of the bed resting on a pillow of at least 10 cm thickness, with the forehead at the level of operators xiphisternum.
  - Flex the patient's neck and extend the head (sniffing position). This aligns the oral, pharyngeal, and laryngeal axes making pathway from lips to glottis nearly in a straight line.

Table 1.2 Intubation tray/portable intubation cart—basic equipment

The contents of the intubation cart may be modified as per the need of the ICU and airway skills of the users
1. *Preoxygenation and Ventilation*
Self-inflating ventilating bag with a reservoir bag attached /anesthesia circuit (for positive pressure ventilation)
Face masks various sizes
Oropharyngeal and nasopharyngeal airway
2. *Endotracheal Intubation*
Laryngoscope—At least 2 blades (assortment of Miller and Macintosh blades)
Endotracheal Tube—Appropriately sized (at least 2) size 7.5–8.5 in adult males and 6.5–7.5 in adult females. ETT with subglottic suction should be preferably used for all patients in whom prolonged intubations is anticipated
Lignocaine jelly
10 ml. syringe for inflating tube cuff
Magill's
Stylet
Bougie
Tube fixator/tapes and ties
3. *End-tidal CO_2 monitor/disposable CO_2 detector device*
4. *Drugs*
Induction agents and muscle relaxants (refer to Table 1.3)
Topical anesthetics and vasoconstrictors
Vasopressors to treat hypotension
5. *Fiberoptic Bronchoscope*
6. *Rescue Devices*—LMA/ILMA and cricothyroidotomy set

  - In patients with suspected cervical spine injury, maintain the head in neutral position and give manual in-line cervical stabilization. Use the cervical collar at all times during airway manipulations.
- *Drug therapy (preintubation)*: The choice of agents (Table 1.3) will depend on the hemodynamic status of the patient and the anticipated nature of difficulty in intubation.
  - Patients may be given intravenous fentanyl, morphine, or midazolam. Physicians with appropriate experience may choose to use anesthetic induction agents such as ketamine, thiopentone sodium, propofol, or etomidate. These drugs should be given slowly to effect with or without muscle relaxants. Intravenous ketamine, unless contraindicated, is the preferred induction agent, especially in hemodynamically unstable patients.
  - Etomidate is cardiostable, but there are concerns of adrenal insufficiency following even a single dose.
  - Propofol can cause profound hypotension and myocardial depression and should be used with extreme caution.

Table 1.3 Drugs used to facilitate intubation

Name	Usual intravenous dose	Advantages	Disadvantages
Anesthetic, amnesic, and analgesic drugs			
Midazolam	0.02–0.2 mg/kg	Relatively cardiostable	Optimum intubation condition may not be obtained when used alone
		Better amnesia	
		Sedation	
Fentanyl	0.05–0.4 mg	Fast-acting	Optimum intubation condition may not be obtained when used alone
		Relatively cardiostable	
		Analgesia	
		Cough suppression	
		Useful in combination with midazolam	
Morphine	0.05–0.2 mg/kg	Analgesia	Optimum intubation condition may not be obtained when used alone
		Cough suppression	
		Useful in combination with midazolam	Hypotension
Ketamine	1–2 mg/kg	Cardiostable	Increased intracranial/introcular pressure
		Bronchodilator	Does not suppress airway reflexes
		Potent analgesic	Hypertension and tachycardia
		Safe induction of anesthesia	
Propofol	1–2.5 mg /kg	Bronchodilatation useful in COPD/asthma	Can cause profound hypotension and bradycardia
		Suppression of airway reflexes	
		Reduces ICP	
Etomidate	0.2–0.6 mg/kg	Cardiostable	Adrenal suppression
Thiopentone sodium	5–7 mg/kg	Rapid induction	Hypotension
		Reduces ICP	Can precipitate laryngospasm and bronchospasm

Neuromuscular blocking agents			
Succinylcholine	0.5–2 mg/kg	Rapid action (1 min) and short duration (up to 10 min) hence ideal for RSI	Hyperkalemia and cardiac arrest
			Contraindicated in severe acidosis, acute or chronic neuromuscular disease, burn patients and cervical spine trauma (upto 6 months),lower motor neuron disease
			Malignant hyperthermia
Rocuronium bromide	0.4–2.0 mg/kg	Rapid action (60–90 s) hence ideal for RSI	Long acting (30–90 min)
		No complications associated with Scoline	
Vecuronium bromide	0.05–0.1 mg/kg	Cardiostable	Long acting (30–60 min)
		Delayed action	
Atracurium besylate	0.4–0.5 mg/kg	Not metabolized by liver or kidney	Long acting (20–30 min)
		Delayed action	Histamine release
			Hypotension

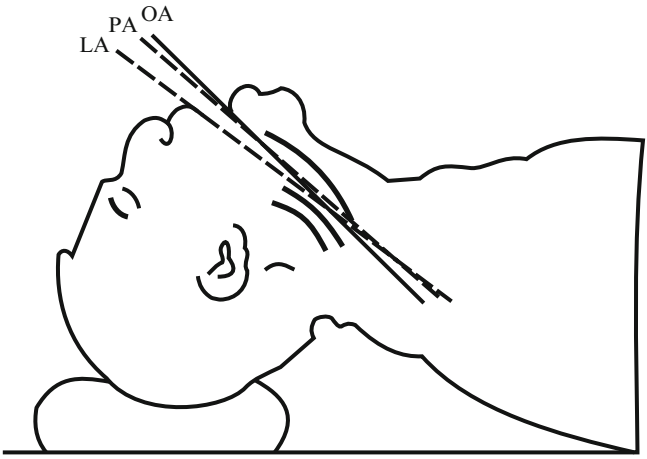

Fig. 1.2 Ideal head and neck position during intubation showing alignment of the oral, pharyngeal, and laryngeal axes (OA, PA, LA)

  - Rapidly acting muscle relaxants such as succinylcholine/rocuronium may be used for rapid sequence intubation. Succinylcholine is used only in absence of hyperkalemia, severe acidosis, acute or chronic neuromuscular disease, extensive burn, and cervical trauma.
  - Longer-acting muscle relaxants (e.g., atracurium and vecuronium) should be given only after confirming that ventilation is possible.
  - Note that in sick, fatigued patients, very small drug doses may be sufficient. Inject drugs very slowly and until effect (do not give calculated/standard induction doses).
- *Rapid sequence intubation (RSI)*: As most ICU patients are at a risk of aspiration, this sequence should preferably be performed during all intubations.
  - After giving adequate preoxygenation and proper position, cricoid pressure is given just before the beginning of induction. As soon as the patient is asleep, increase the pressure.
  - Use only rapidly acting muscle relaxants (suxamethonium or rocuronium) while maintaining cricoid pressure.
  - Only if saturation is not maintained, give gentle positive pressure ventilation (modified RSI).
  - Perform laryngoscopy and intubation. Hold the laryngoscope handle in the left hand. Open the mouth of the patient with the thumb and the index finger of the right hand. Insert the laryngoscope blade gently into the mouth from the right-side angle of the mouth and move it to the left side taking the tongue along with the blade as it is inserted further inside the mouth. When the epiglottis is visualized, insert the curved blade into the vallecula and pull the laryngoscope forward and upward to expose the glottis (Fig. 1.3). Now, insert the ETT using the right hand between the vocal cords under direct vision.

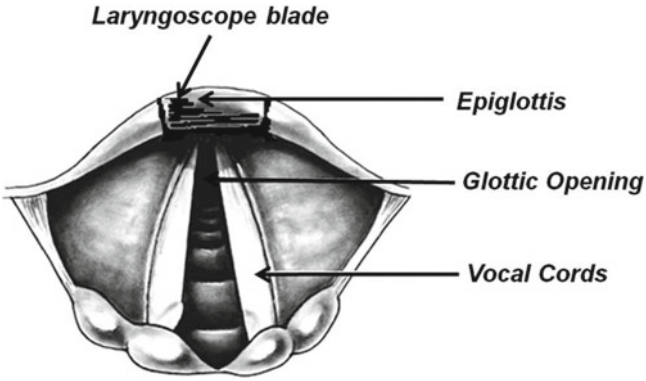

Fig. 1.3 Glottic view during laryngoscopy

  - For nasal intubation, use prior nasal mucosal vasoconstrictors and lubrication; Magill's forceps may be used to guide the tube into the trachea.
  - Optimal external laryngeal manipulation (OELM) with the right hand or by an assistant by quickly pressing in both cephalad and posterior direction over the thyroid, cricoids or hyoid cartilage may be used to further optimize laryngoscopic view.
  - Use of stylet in ETT, bougie (a thin long plastic/rubber cylinder with a bent tip that is passed through the partially visible glottic opening and then the ETT is guided over it), or other airway adjunct can aid oral intubation.
  - After intubation, inflate the ETT cuff just enough (usually 4–6 mL) to avoid pharyngeal leak during ventilation.
  - Release cricoid pressure only after intubation, cuff inflation, and confirmation of tube placement.
- *Confirm tracheal tube placement* (clinically by auscultation over the stomach and lungs (5-point auscultation): The gold standard to confirm correct tube placement is by using end-tidal CO_2 with a portable capnograph (wait to see five to six waveforms before confirmation). Disposable calorimetric CO_2 detectors devices may be used instead. If in doubt, confirm by direct visualization of the tube between cords. If still in doubt, take it out and continue bag-mask ventilation.
- *Proper tube positioning* (ideally 2.5–4 cm above carina): Confirm bilaterally equal chest expansion and air entry in the lungs by auscultation. Using depth of tube insertion (i.e tube fixation at 20 cm. mark for females and 22 cm. mark for males at the incisor level) is most superior method to determine proper tube position in adults. When all above 3 methods are combined, the sensitivity is 100% and the specificity is 95%. Make a note of the exact distance of the ETT at the lips/nose on the case notes and ICU chart. This position should be noted daily during every nursing shift.
- *Tube fixation*: Secure the ETT with two tube tapes and preferably also a tube tie or use a commercial ETT fixator. Insert an oro/nasogastric tube under direct vision.
- Anticipate and treat hypotension with vasopressors and colloids.

Step 7: Steps after tracheal intubation

- Initiate mechanical ventilation if required.
- Give analgesia and sedation as required.
- Obtain chest radiograph to confirm tube position, bilateral lung expansion, and oro/nasogastric tube position.
- Do not start feeding until position of oro/nasogastric tube is confirmed on chest radiograph.
- Check the ETT cuff pressure using the cuff pressure machine and maintain it below 20 mmHg at all times.

Step 8: Management of a difficult airway

- *Anticipated difficult airway*
  - Ensure that expert airway help is available before attempting tracheal intubation.
  - If ventilation is not possible, avoid the use of muscle relaxants.
  - An awake fiber optic intubation with the flexible fiberscope is the gold standard for an anticipated difficult airway and can be used for both oral and nasal intubations. It should be considered as the first option rather than the last resort in such a situation.
  - Videolaryngoscopes may be used if available and will give an optimum view, making intubation easier, especially in a difficult airway setting.
- *Unanticipated difficult airway* (Fig. 1.4)

Step 9: Watch for and treat immediate complications of endotracheal intubation

- Esophageal intubation/endobronchial intubations/accidental ETT disconnections—atelectasis formation/collapse in the unventilated lung and hyperinflation and barotrauma with development of pneumothorax of the intubated lung (in endobronchial intubations) can cause profound hypoxemia manifesting as bradycardia and even progressing to cardiac arrest
- Hypertension, tachycardia, raised intracranial pressure, and myocardial ischemia due to stimulation from laryngoscopy and intubation
- Hypotension due to loss of sympathetic tone from drugs for intubation or dynamic hyperinflation due to hyperventilation or relative dehydration
- Aspiration of gastric contents
- Airway trauma, bleeding
- Negative pressure pulmonary edema after sudden relief of severe airway obstruction
- Cardiac arrest

Step 10: Follow a protocol for airway maintenance

- Proper maintenance of the airway will reduce the incidence of accidental extubations, disconnections, tube blockage, and nosocomial pneumonia.
- Keep the head elevated at 30–45°.
- All ETT and tracheostomy tubes (TT) should be checked for position at incisor teeth/alae nasi, adequate fixation, patency, tracheal cuff pressure (<20 mmHg), and pharyngeal leak during each shift and should be documented.

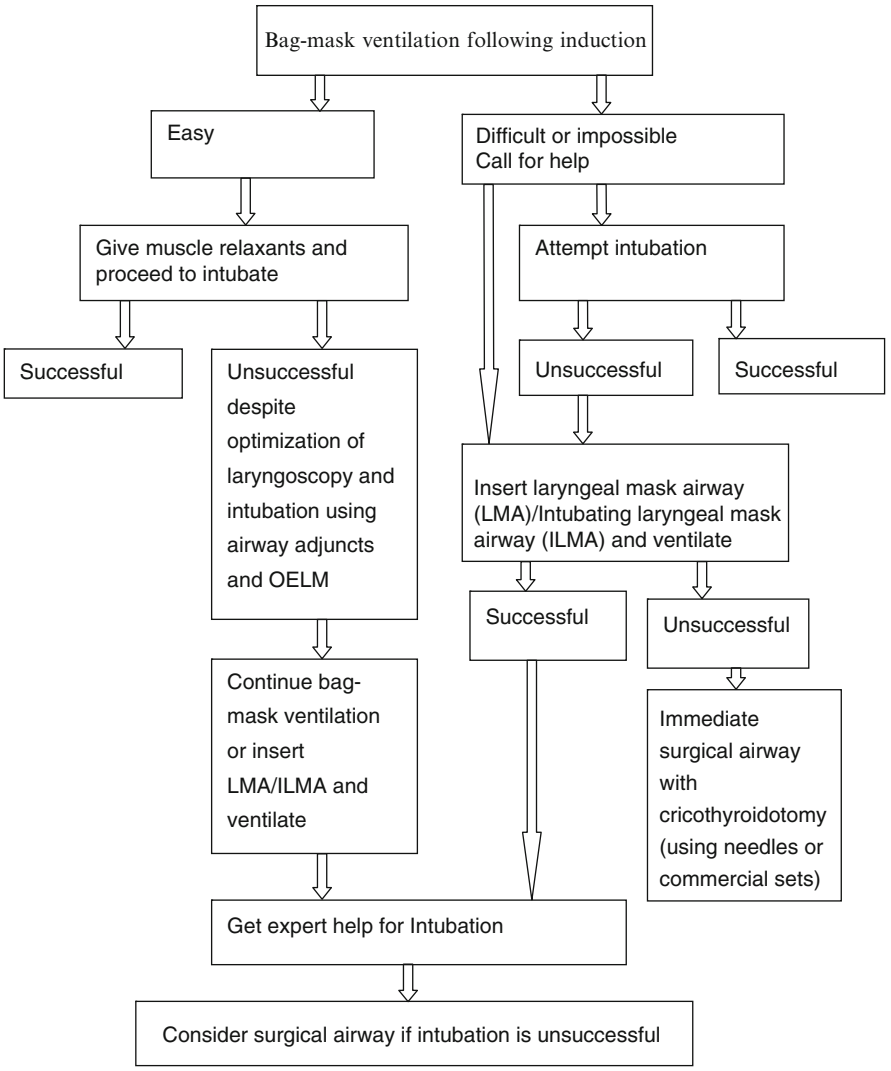

Fig. 1.4 Unanticipated difficult airway management

- In case of oral ETTs, secure firmly at the angle of the mouth and change position preferably every 24 h to avoid sores/ulcers.
- Oral ETTs (without subglottic suction) should be cut 2–3 cm from the angle of the mouth.
- The universal connector should be pushed right down to its shoulder to avoid accidental disconnections.
- Confirm correct positioning of ETTs above the carina on the X-ray and document in the case notes.

- All ventilated patients should receive humidification (with HME (Heat and Moisture Exchanger) filter or using a heated humidifier circuit).
- ETT/TT suction should be done only when required and preferably using a closed suction system.
- Sedate patients well when they need to remain intubated. Do not allow them to get restless.
- Start weaning the patient off sedation, only in the daytime when ICU staff is in adequate strength.
- Do not leave the patient unattended when sedation has been turned off and the patient is just about waking up. Reassure patients as they wake up from sedation.
- Apply boxer gloves/bandages to those patients who appear agitated. Refrain from tying patient's limbs.
- Report any airway accident as a "critical incident."

Step 11: Extubation of the airway (refer to Chap. 7)

- Perform a good oral and endotracheal suction prior to extubation.
- Keep all equipment ready for reintubation/noninvasive ventilation if required.
- Do a cuff-leak test (especially after prolonged intubations)—deflate the ETT cuff and check for air leak around the cuff. If absent, suspect laryngeal edema. Consider the use of steroids and plan extubation at a later date over a tube exchanger.
- Intravenous methylprednisolone started 12 h before a planned extubation has been shown to substantially reduce the incidence of postextubation laryngeal edema and reintubation in patients intubated for more than 36 h and having absent cuff leak.
- In a patient with a difficult airway, ensure that expert airway help is available prior to extubation and extubate preferably over a tube exchanger. Oxygenate the patient through the exchanger and remove it only when you are sure that the airway is not compromised/obstructed. If in doubt, pass the ETT back inside over the tube exchanger and secure in place.

Step 12: Continue to watch for and treat complications of tracheal intubation (days to months after extubtion)

- Sore throat
- Airway edema
- Airway infections/pneumonia
- Laryngeal damage/granuloma
- Tracheal stenosis, tracheomalacia, trachea-esophageal fistula

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   Ketamine is a safe and valuable alternative to etomidate for endotracheal intubation in critically ill patients and should be considered in those with sepsis.

Acute Respiratory Failure

2

Randeep Guleria and Jaya Kumar

Case scenario 1

A 30-year-old male patient presented with acute onset of breathlessness, dry cough, fever, myalgia, and malaise for 4 days. On examination, he was found to be febrile and restless, with respiratory rate of 46/min and pulse rate of 124/min. His oxygen saturation was 80% on room air, and chest skiagram showed bilateral parenchymal infiltrate.

Case scenario 2

A 60-year-old male patient with chronic obstructive airway disease presented with increasing shortness of breath, cough, and expectoration for 5 days and drowsiness with confusion for 1 day. On examination, he was found to be drowsy, cyanosed with respiratory rate of 30/min, tachycardia, and flapping tremors. His oxygen saturation was 80% on initial evaluation, and a chest radiograph showed hyperinflated lung fields and right lower zone infiltrates.

Case scenario 3

A 30-year-old female patient with anxiety disorder presented to the emergency department in a comatosed condition with history of ingestion of some unknown tablets. On examination, she was found to be E2M4V1, with pulse rate of 64/min, respiratory rate of 14/min, and blood pressure of 90/60 mmHg.

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Acute respiratory failure results from the failure of respiratory system in one or both of its gas exchange functions—oxygenation and carbon dioxide elimination. It is a major cause of morbidity and mortality in intensive care units (ICUs). There are two types—type 1 hypoxic respiratory failure and type 2 hypercapnic respiratory failure.

Step 1: Initiate cardiopulmonary resuscitation

All patients should be resuscitated as mentioned in Chap. 78.

- *Airway*: In all patients with altered sensorium, a secure airway should be the first priority. This includes clearing the upper airway and keeping it patent. If the patient cannot maintain an airway, endotracheal intubation should be performed to keep the airway patent.
- *Breathing*: Once the airway is patent, the breathing has to be assessed. If it does not result in adequate gas exchange, oxygen supplementation and assisted ventilation may be required.
- *Circulation*: An intravenous access should be established and intravenous fluids should be started.

Step 2: Clinical assessment including history and detailed physical examination

- Take appropriate history and do detailed examination to distinguish whether the etiology is pulmonary or extrapulmonary and to know whether it is type 1 or type 2 respiratory failure (Tables 2.1 and 2.2). Assess the severity and find out the underlying cause and/or precipitating cause. Specific focus should be on the following:
  - A detailed respiratory system and neurological assessment.
  - Look for clinical features of hypoxia and hypercapnia (Tables 2.1 and 2.2).
  - Signs of pulmonary hypertension and right ventricular failure.
  - Clinical features of drug overdose.
  - Chest wall deformity, obesity.

Step 3: Check pulse oximetry and do arterial blood gas analysis

Pulse oximetry and arterial blood gases are the mainstay of diagnosis and essential to decide on the therapeutic intervention.

- Oximetry is a rapid technique to know if there is significant hypoxia, but it gives no clue about the presence or absence of hypercapnia. Also, the severity of hypoxia on pulse oximetery should be interpreted cautiously if the patient is already on oxygen.

Table 2.1 Hypoxia-related clinical features

Restlessness, anxiety
Irritability, impaired intellectual functioning, and consciousness
Cyanosis
Tachycardia, hypertension
Bradycardia, arrhythmia
Shock, hypotension
Convulsions, coma, death

Table 2.2 Hypercapnia-related clinical features

Headache
Drowsiness, confusion
Warm extremities, flushing, sweating
Bounding pulse, tachycardia
Tremors, myoclonic jerks, asterixis, seizures
Papilledema, coma

- Arterial blood gas analysis is essential for both diagnostic and therapeutic decisions.
  - Type 1 respiratory failure is recognized by hypoxemia (PaO_2 < 60 mmHg). With or without widening of alveolar-arterial oxygen gradient, $PaCO_2$ is either low or normal.
  - Type 2 respiratory failure is diagnosed when a PaO_2 of less than 60 mmHg is associated with a $PaCO_2$ of more than 45 mmHg and respiratory acidosis.
- This needs to be followed by an assessment of the pH and HCO_3 to decide whether the type 2 respiratory failure is acute, acute on chronic, or chronic.
- Type II acute respiratory failure presents with low pH, high $PaCO_2$, and normal HCO_3; acute on chronic presents with low pH, high $PaCO_2$, and high HCO_3; while chronic respiratory failure presents with normal pH along with raised $PaCO_2$ and HCO_3.
- This should be followed by an assessment of alveolar-arterial oxygen gradient, which helps to narrow down the cause of respiratory failure (see appendix 2).

$$PaO_2 = PiO_2 - PaCO_2 / R$$

Step 4: Differentiate between type 1 and type 2 respiratory failures

Type 1 respiratory failure occurs when the gas exchange is inadequate at rest or during exercise, leading to hypoxemia, and PaO_2 is less than 60 mmHg (Table 2.3).

Type 2 respiratory failure occurs as a result of alveolar hypoventilation, which can be due to a pulmonary or extrapulmonary cause. Chronic obstructive pulmonary disease is the commonest cause of type 2 respiratory failure, but various other conditions listed below can also lead to hypercapnia and respiratory failure (Table 2.4).

An approach to a patient with acute hypoxemic respiratory failure is summarized in Fig. 2.1.

Step 5: Send investigations

- Complete hemogram and biochemistry
- Lung function tests (if possible) that helps to differentiate between obstructive, restrictive, and mixed ventilatory defects
- Chest radiograph that may help to identify hyperinflation, pulmonary edema, pneumonia, pneumothorax, neoplasm and others to give a clue to the underlying etiology
- Electrocardiogram to identify cardiac disorders

Table 2.3 Causes of hypoxemic respiratory failure

1. Ventilation/perfusion mismatch
Airways disease
Chronic obstructive pulmonary disease
Asthma
Cystic fibrosis
Bronchiolitis obliterans
Alveolar filling
Cardiogenic Pulmonary edema
Mitral valve stenosis
Acute respiratory distress syndrome
Pneumonia
Alveolar hemorrhage
Partial atelectasis
Alveolar proteinosis
Transfusion related acute lung injury (TRALI)
Acute interstitial pneumonia
Cryptogenic organizing pneumonia
Aspiration, near-drowning
Pulmonary vascular disease—thromboembolism, fat embolism
2. Shunt
Alveolar filling—see the above causes
Atelectasis
Intrapulmonary shunts—pulmonary AVM (Arterio Venous Malformation)
Intracardiac shunt—PFO, ASD, VSD
3. Hypoventilation—refer to type 2 respiratory failure for causes of hypoventilation
4. Low inspired pressure of oxygen—high altitude

- Computed tomography (CT) or magnetic resonance imaging (MRI) if indicated for interstitial lung disease, neoplasm, stroke, and other neurological disorders
- Two-dimensional echocardiography for identification of cor pulmonale, intracardiac shunt, patent ductus arteriosus, and pulmonary embolism

Step 6: Initiate specific treatment

The primary aim is to maintain oxygenation and adequate alveolar ventilation and treatment for the underlying etiology. The key principles in the management of respiratory failure are as follows:

- Optimized oxygen therapy
- Identification of the underlying cause and adequate treatment for the same
- Clinical assessment and arterial blood gases to help decide the severity
- Treatment for any precipitating cause
- Appropriate pharmacological treatment
- Ventilatory support—noninvasive and invasive
  Oxygen therapy (see Chap. 14)

Table 2.4 Causes of type 2 respiratory failure

Central nervous system depression/decreased ventilatory drive
Respiratory center (medulla) dysfunction
Drug overdose
Hypothyroidism
Sleep apnea
Central nervous system (CNS) causes— stroke, tumor
Neuromuscular diseases
Guillain–Barré syndrome
Poliomyelitis
Myasthenia gravis
Amyotrophic lateral sclerosis
Cervical cord lesions
Polyneuropathies
Muscle diseases like muscular dystrophy, polymyositis
Chest wall/pleural diseases
Kyphoscoliosis
Morbid obesity
Pneumothorax

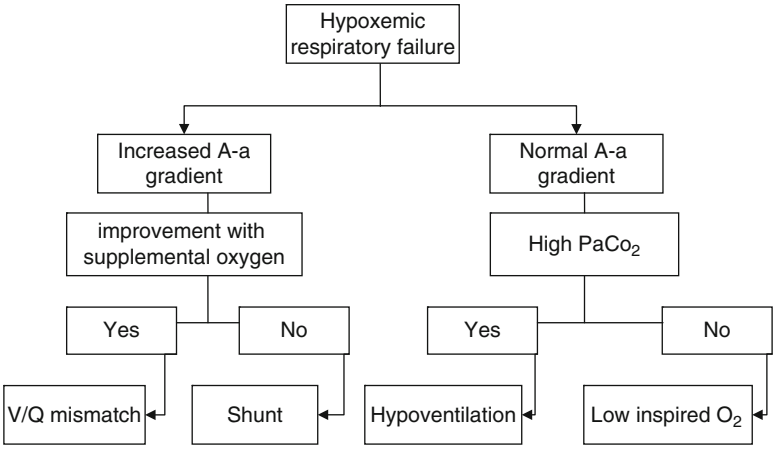

Fig. 2.1 An approach to hypoxemic respiratory failure to know the etiology

- The primary goal is to correct the hypoxemia to maintain adequate tissue oxygenation.
- Oxygen has to be given cautiously with monitoring as uncontrolled high-flow oxygen can lead to respiratory depression and worsening hypercapnia in type 2 respiratory failure. Oxygen saturation around 90% should be maintained.

- Supplemental oxygen can be provided through nasal prongs at a flow rate of 1–3 L/min or through a Venturi mask to deliver 24–28% oxygen in hypercapnic failure.
- Nasal prongs are better tolerated but provide less predictable oxygen concentration in comparison to the Venturi mask.
- The aim is to maintain oxygen saturation above 90%, PaO_2 more than 60 mmHg, and pH more than 7.35.

  Assisted ventilation
- Assisted ventilation, either noninvasive or invasive, is indicated if there is clinical deterioration or if respiratory acidosis persists despite optimum oxygen and medical therapy. Refer to specific Chaps. 3 and 4 for further details.

Step 7: Further management

- Optimum treatment for the underlying etiology must be undertaken simultaneously.

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Noninvasive Positive-Pressure Ventilation

3

Rajesh Chawla and Subhash Todi

A 56-year-old male patient, a known case of chronic obstructive pulmonary disease (COPD), presented with acute breathlessness, cough with increase in expectoration, and low-grade fever. On examination, he was found to be in acute respiratory distress, with respiratory rate (RR) of 28/min. He was using his accessory muscles, was slightly drowsy, and breath sounds were diminished on both sides.

Noninvasive positive-pressure ventilation (NIPPV) augments spontaneous ventilation using the tight-fitting nasal or oronasal mask without endotracheal intubation. This can be used in a large number of conditions if there is no contraindication. The application of NIPPV should not delay clinically indicated endotracheal intubation.

Step 1: Initial resuscitation

- The patient should be resuscitated as mentioned in Chap. 78.
- The first step after resuscitation would be to quickly examine the patient in detail.
- Look for hemodynamic instability, sensorium, and oxygenation by pulse oximetry.
- If SpO_2 is low, give oxygen—not more than 1–2 L/min. Titrate oxygen to minimum flow to keep SpO_2 at 87–92%.

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- Check arterial blood gas (ABG) and initiate other investigations as mentioned below:
  - Hemogram, blood urea, serum creatinine, and serum electrolytes
  - Blood and sputum culture if infection is suspected
  - Chest skiagram
  - Electrocardiogram (ECG) and Echocardiogram (Echo)

Disease-specific treatment such as bronchodilators (salbutamol and ipratropium nebulization), antibiotics, corticosteroids should be started.

Step 2: Assess the need of NIPPV

- In addition to the rest of the treatment, NIPPV should be applied simultaneously to a patient in acute respiratory failure (ARF), based on the clinical criteria (Table 3.1), provided there is no contraindication.
- There are no absolute contraindications for the use of NIPPV. Some contraindications have, however, been suggested (Table 3.2).
- NIPPV is indicated in patients with appropriate diagnosis and proven evidence of effectiveness of NIPPV if any two of the clinical criteria are fulfilled (Table 3.1).

Table 3.1 Clinical criteria

Moderate to severe respiratory distress
Tachypnea (respiratory rate >25/min)
Accessory muscle use or abdominal paradox
Blood gas derangement pH < 7.35, $PaCO_2$ > 45 mmHg
PaO_2/FiO_2 < 300 or SpO_2 < 92% with FiO_2 0.5

Table 3.2 Contraindications

Nonavailability of trained medical personnel
Inability to protect the airways—comatose patients, patients with cerebrovascular accident or bulbar involvement, confused and agitated patients, upper airway obstruction
Hemodynamic instability—uncontrolled arrhythmia, patients on very high doses of inotropes, recent myocardial infarction
Inability to fix the interface—facial abnormalities, facial burns, facial trauma, facial anomaly
Severe gastrointestinal symptoms—vomiting, obstructed bowel; recent gastrointestinal surgery, upper gastrointestinal bleeding
Life-threatening hypoxemia
Copious secretions
Conditions in which NIPPV has not been found to be effective
NIPPV should only be applied in ARF if there is evidence for its efficacy in that disease state (Table 3.3)

Table 3.3 Effectiveness for NIPPV in ARF from different causes

Causes of ARF	Level of evidence
Acute exacerbation of COPD (AECOPD)	A
Weaning (AECOPD)	A
Cardiogenic pulmonary edema (CPE)	A
Immunocompromised patient	A
Postoperative respiratory failure	B
Preintubation oxygenation	B
Endoscopy	B
Asthma exacerbations	C
Acute respiratory distress syndrome (ARDS)	C
Postextubation respiratory failure	C
Do-not-intubate status	C
Pneumonia	C

A strong, *B* intermediate, *C* weak

Step 3: Application of NIPPV

Protocol for application of NIPPV: For successful NIPPV, it is important to fine-tune the patient, interface, and ventilator.

- Patient interface—nasal or oronasal mask.
- Mode of ventilation:
  - Bilevel positive airway pressure—spontaneous or spontaneous/timed mode in portable pressure ventilators or NIPPV option on conventional ventilators.
  - Pressure support/pressure control/volume control—conventional ventilators.

Explain the therapy and its benefit to the patient in detail. Also, discuss the possibility of intubation.

- Choose the correct size interface. The oronasal mask is preferred in ARF.
- Set the NIPPV portable pressure ventilator in spontaneous or spontaneous/timed mode.
- Start with very low settings, low inspiratory positive airway pressure (IPAP) of 6–8 cm H_2O with 2–4 cm H_2O of expiratory positive airway pressure (EPAP). The difference between IPAP and EPAP should be at least 4 cm H_2O at all times.
- To start with administer oxygen at 2 L/min.
- Hold the mask with the hand over the face. Do not fix it.
- Increase EPAP by 1–2 cm increments until the patient's inspiratory efforts are able to trigger the ventilator.
- If the patient is making inspiratory effort and the ventilator does not respond, it indicates that the patient has not generated enough respiratory effort to counter auto-PEEP and trigger the ventilator (in COPD patients). Increase EPAP further until this happens. Most of the patients require EPAP of about 4–6 cm H_2O. Patients who are obese or have obstructive sleep apnea require higher EPAP to trigger the ventilator.
- When the patient's effort is triggering the ventilator, leave EPAP at that level.

- Now, start increasing IPAP in increments of 1–2 cm up to a maximum pressure, which the patient can tolerate without discomfort and there is no major mouth or air leak.
- In some NIPPV machines, inspiratory time (T_i) can be adjusted. Setting the T_i at 1 s is a reasonable approach.
- Now, secure interface with head straps. Avoid excessive tightness. If the patient has a nasogastric tube, put a seal connector in the dome of the mask to minimize air leakage.
- After titrating the pressure, increase oxygen to bring oxygen saturation to around 90%.
- As the settings may be different in wakefulness and sleep, readjust them accordingly.

When NIPPV is being initiated for ARF, close monitoring and the capability to initiate endotracheal intubation and other resuscitation measures should be available in the same setup. Start NIPPV preferably in the intensive care unit or in the emergency room in ARF.

Application of NIPPV using a critical care ventilator

- The first step is to select a ventilator, which is capable of fulfilling the needs of the patient.
- Explain the therapy to the patient.
- Choose the appropriate mode. Usually, pressure support or pressure control modes are preferred. Standard critical care ventilators using flow-by system (noninvasive mode option) allow the patient to breathe without expending effort to open valves. In selected patients, such as those suffering from neuromuscular diseases, volume assist or volume control mode may be used.
- Choose an appropriate interface.
- Silent ventilator alarms.
- Keep FiO_2 at 0.5.

Using pressure support/control approach

- Start with low settings such as inspiratory pressure support at 5–6 cm H_2O and PEEP at 4 cm H_2O.
- Initiate NIPPV while holding the mask in place and confirm optimum fit. If it is big or small or loose, change it.
- Hold the mask. Do not fix the headgear.
- Now, increase PEEP until inspiratory efforts are able to trigger the ventilator.
- If the patient is making inspiratory effort and the ventilator does not respond, it indicates that the patient has not generated enough respiratory effort to counter auto-PEEP and trigger the ventilator (in COPD patients). Increase PEEP further until this happens.
- Once the patient's inspiratory efforts trigger the ventilator, start increasing pressure support further, keeping the patient's comfort in mind. (Reduced respiratory rate, reduced use of respiratory accessory muscle, etc.) Ensure that there are no major leaks.

Table 3.4 Monitoring of NIPPV in ARF

Mask comfort
Tolerance of ventilator settings
Respiratory distress
Respiratory rate
Sensorium
Accessory muscle use
Abdominal paradox
Ventilator parameters
Air leaking
Adequacy of pressure support
Adequacy of PEEP
Tidal volume (5–7 mL/kg)
Patient–ventilator synchrony
Continuous oximetry (until stable)
ABG, baseline and 1–2 h, then as indicated

- When there is significant mouth leak, there may be asynchrony. In that case, pressure control will be the preferred mode of NIPPV and the T_i can be set to avoid asynchrony.
- Increase fraction of oxygen concentration to maintain oxygen saturation more than 90% at all times.
- Secure interface with the headgear. It should be tight, but not overtight. Small leaks are acceptable.
- A peak inspiratory pressure of more than 25 cm is rarely required in COPD, but higher pressures can be used when using NIPPV for other indications. PEEP is usually titrated between 5 and 10 cm H_2O to improve triggering and oxygenation.

Step 4: Patient must be monitored very closely

- The patient must be monitored very closely clinically (Table 3.4). All this must be documented every 15 min for the first hour in the clinical notes.
- The patient will show improvement in parameters if NIPPV is effective.
- ABG sample should be sent after 30 min to 1 h after the application of noninvasive ventilation.
- In ventilator setting, look for air leaks, triggering and patient–ventilator interaction.

Step 5: Continuously look for complications and manage them

- Monitor carefully the worsening respiratory distress, sensorium, tachypnea, and deteriorating blood gases, and intervene early because delay in intubation is a very common major complication of NIPPV.
- Most complications are minor that can be managed very easily, and so every attempt should be made to continue NIPPV.

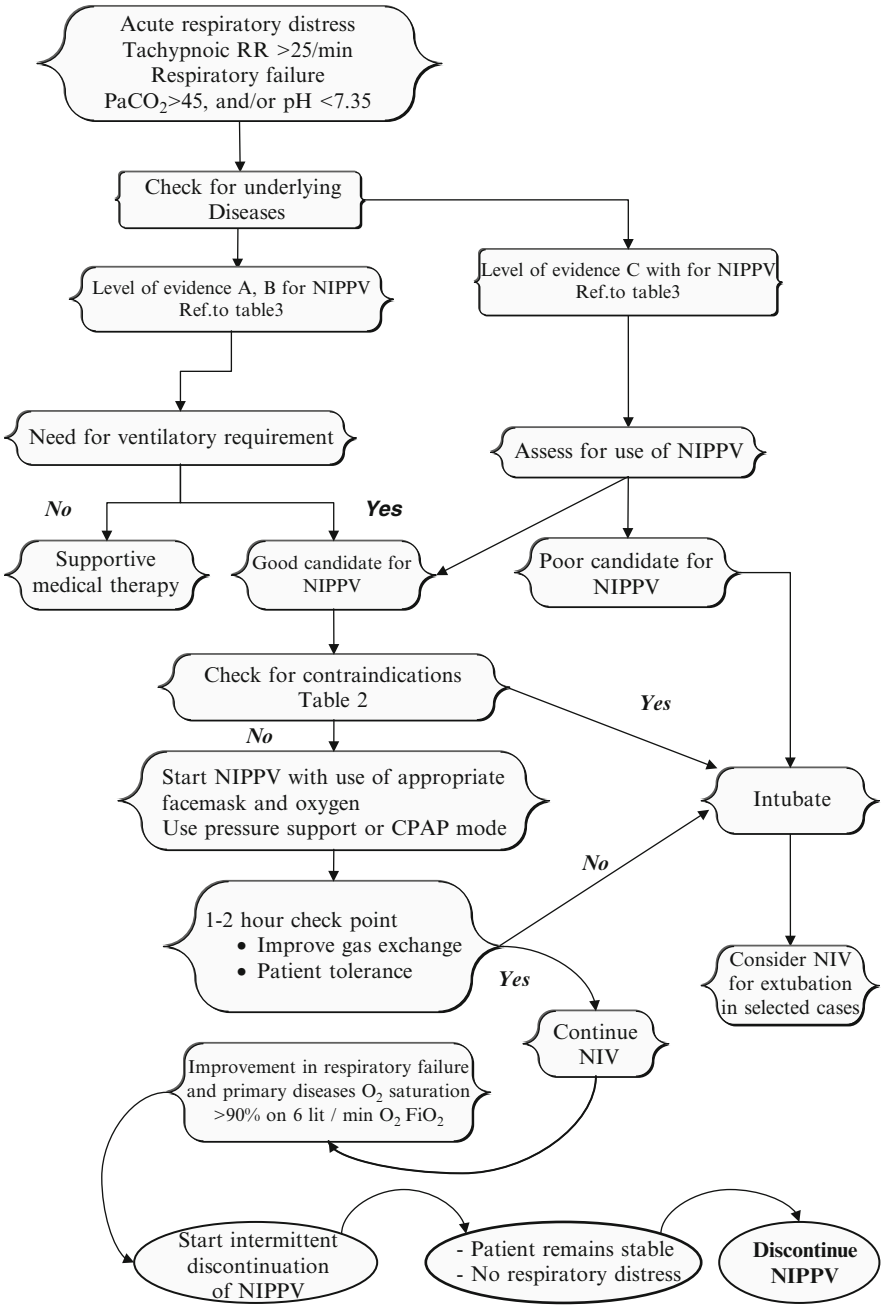

Fig. 3.1 Application of NIPPV

- It is extremely important for the air seal to be tight. Ulceration and pressure necrosis related to local skin effects commonly occur at the bridge of the nose. Protective synthetic coverings may help prevent skin breakdown and ulceration on the bridge of the nose.
- Eye irritation and pain or congestion of the nasal sinuses may occur. Put some decongestant nasal drops.
- Distension of the stomach due to aerophagia and aspiration can occur secondary to vomiting. A nasogastric tube can be used to relieve the distension while still allowing the mask to seal.
- Adverse hemodynamic effects from NIPPV are unusual, although preload reduction and hypotension may occur. Give intravenous fluids.

Step 6: Discontinuation of NIPPV

It is very important to know when to discontinue NIPPV and intubate and ventilate the patient.

- NIPPV failure
  - Worsening mental status
  - Deterioration of pH and $PaCO_2$ after 1–3 h of therapy
  - Refractory hypoxemia—when even a brief discontinuation of NIPPV leads to significant fall in oxygen saturation
- Intolerance to NIPPV
- Hemodynamic instability.
- Inability to clear secretions.

Step 7: Weaning

- Initially, give NIPPV continuously as long as possible.
- Once the patient is tolerating periods off NIPPV, start discontinuing during daytime and give during nighttime. In 2–3 days, the patient can be weaned off the NIPPV.
- A brief outline of the application of NIPPV is shown in Fig. 3.1.

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4. Schönhofer B, Sortor-Leger S. Equipment needs for noninvasive mechanical ventilation. Eur Respir J. 2002;20(4):1029–36.
   A review of the equipment, location, and troubleshooting during the use of noninvasive ventilation in ARF

Website

1. http://www.isccm.org/edu_guidelines.htm
   ISCCM Guidelines—comprehensive guidelines dealing with every aspect of NIPPV

Basic Mechanical Ventilation

4

Gopi Chand Khilnani and Vijay Hadda

A 30-year-old male patient came to the emergency department with history of fever, shortness of breath for 3 days, and alteration in sensorium since morning. He was in respiratory distress with respiratory rate of 34/min. He was drowsy (Glasgow coma score 8) and febrile (102°F). His pulse was 110/min, blood pressure was 116/78 mmHg, and JVP was normal. He was immediately intubated and put on assisted ventilation.

Mechanical ventilation is indicated in patients with acute respiratory failure when they are unable to maintain adequate oxygenation and/or remove carbon dioxide. None of the ventilatory mode can cure the disease process. However, it supports ventilation till you address the reversible primary problem. Mechanical ventilation should not be started without thoughtful consideration as tracheal intubation and ventilation are associated with significant complications.

Step 1: Initial resuscitation (refer to Chap. 78)

- Any patient coming to the emergency department should be examined quickly to assess oxygenation and hemodynamic status. Resuscitation should be started without delay.
- All patients with respiratory distress require immediate attention to airway.
- They should be put on high-flow oxygen except patients with chronic obstructive pulmonary disease where low flow oxygen can be started to increase SpO_2 to

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Table 4.1 Indications and objectives of mechanical ventilation

To overcome the mechanical problem
Rest/unloading of the fatigued/overloaded inspiratory muscles
Prevention or treatment of the lung atelectasis
An adjunct to anesthetic or neuromuscular blockade
Treatment for flail chest
To regulate gas exchange
Reverse hypoxemia in patients with respiratory failure
Keep $PaCO_2$ lower than normal in patients with raised intracranial pressure
Normalize the $PaCO_2$ in patients with muscle fatigue or neuromuscular disease
To increase the lung volume
During end inspiration—minimize V/Q mismatch and intrapulmonary shunting, improve hypoxemia, and treat atelectasis
During end expiration (positive end-expiratory pressure [PEEP]), keep alveoli open at the end of expiration and improve gas exchange in acute respiratory distress syndrome (ARDS) and other causes of alveolar collapse

90%. If the patient requires assisted ventilation, he/she should be intubated and ventilated (Table 4.1).

- Circulation needs to be maintained by fluid infusion. If clinically evidence of cardiac impairment is present, fluids should be given cautiously.

Step 2: Choose the mode of mechanical ventilation

- Once it has been decided that patient requires mechanical ventilation, the next step is to choose the appropriate mode of mechanical ventilation.
- The characteristics of commonly used modes of mechanical ventilation are summarized in Table 4.2. Assist-control mechanical ventilation (ACMV) is the most widely used method.
- Assist-control mode can be volume-controlled (more commonly used) or pressure-controlled. The differences between two are summarized in Table 4.3.
- The ventilatory support can be controlled mandatory ventilation (CMV) or assisted controlled mandatory ventilation (ACMV) depending on the use of patients' effort for triggering the ventilator.
- The patient's ventilation is totally controlled by the ventilator and the patient cannot trigger the ventilator during CMV, while ACMV delivers controlled breaths as well as assists patient-triggered breath.
- ACMV is the most commonly used mode of mechanical ventilation and can be used to deliver either volume-preset or pressure-preset ventilation.
- In volume-preset ACMV, a preset tidal volume (VT) is delivered, irrespective of inspiratory pressure.
- In pressure-preset ACMV, a fixed inspiratory pressure (Pinsp) is applied to the respiratory system. The VT is determined by lung and chest wall compliance and airway resistance.
- Although both volume-set and pressure-set ACMVs can achieve the same levels of ventilation, volume-preset ACMV is more frequently used.

Table 4.2 Characteristics of commonly used modes of mechanical ventilation

Mode	Type of breath	Triggering mechanism	Cycling mechanism	Comments
CMV	Each breath delivers a preset mechanical tidal volume or pressure	Time	Inspiration is terminated by delivery of preset tidal volume or by time in pressure-controlled	Used in patients who have no respiratory effort
ACMV	Each breath, assist or control, delivers a preset mechanical tidal volume or pressure	Either patient-triggered (assist) or time-triggered (controlled)	Inspiration is terminated either by delivery of preset tidal volume (volume controlled) or by high pressure limit or by time in pressure-controlled	Alveolar hyperventilation may be a potential hazard
SIMV	Mechanical tidal breath at preset rate and the patient may breathe spontaneously between mandatory breaths	Mandatory breath may be time-triggered or patient-triggered	Mandatory breaths are volume- or time-cycled; patient controls spontaneous rate and volume	It provides an interval (synchronization window) just prior to triggering during which the ventilator is responsive to patient's effort and supports spontaneous breath
PSV	Pressure-support breaths are considered as spontaneous	Patient-triggered	The breaths are flow cycled by a set flow threshold, which is generated by the patient	This a commonly used mode for weaning

CMV controlled mandatory ventilation, *ACMV* assist-control mechanical ventilation, *IMV* intermittent mandatory ventilation, *SIMV* synchronized intermittent mandatory ventilation, *PSV* pressure-support ventilation

Table 4.3 Comparison between volume-controlled and pressure-controlled breaths

	Type of breath	
Variable	Volume-controlled	Pressure-controlled
Tidal volume	Set by the operator; remains constant	Variable with changes in patients' effort and respiratory system impedance
Peak inspiratory pressure	Variable with changes in patients' effort and respiratory system impedance	Set by the operator; remains constant
Inspiratory time	Set by the operator or as a function of respiratory rate and flow settings	Set by the operator; remains constant
Inspiratory flow	Set by the operator or as a function of respiratory rate and tidal volume	Variable with changes in patients' effort and respiratory system impedance
Inspiratory flow waveforms	Set by the operator; remains constant; can use constant, sine, or decelerating flow waveforms	Flow waves are always decelerating

Table 4.4 Initial ventilatory setting

Mode—assist/control (volume or pressure)	
Plateau pressure	<30 cm H_2O
Tidal volume	8 mL/Kg ideal body weight (see formula in Appendix 2)
Inspiratory time	0.7–1.2 s
Rate	10–12 breaths/min
PEEP	4 cm H_2O
FiO_2	1.0
Once the patient is stabilized	
FiO_2	To maintain PaO_2 more than 60 mmHg
PEEP	Set according to FiO_2 requirements (predetermined according to the degree of hypoxemia)
Plateau pressure	Recheck in an attempt to keep plateau pressure below 30 cm H_2O
Tidal volume	Maintain 6 mL per kg of ideal body weight

Step 3: Set the ventilator setting

The various initial ventilatory settings for a patient with the normal lung are given in Table 4.4.

Step 4: Set alarms

The following alarms need to be set:

- Peak pressure—high/low—10–15 cm above or below the peak inspiratory pressure generated on constant basis
- Minute ventilation—high/low—50% above or below the set volume
- Low exhaled tidal volume—50% of the delivered tidal volume
- High respiratory rate
- Set apnea ventilation parameters

Step 5: Connect the ventilator to the patient

- Connect the patient to the ventilator.

Step 6: Monitoring and adjustments during mechanical ventilation

- Patients should be closely monitored. Plateau pressure should be measured at least every 4 h and after any changes in tidal volume and PEEP.
- The ventilatory setting should be adjusted as described in mechanical ventilation in ARDS and obstructive airway diseases in Chaps. 5 and 6.
- A few patients are difficult to rest on the ventilator and continue to demonstrate a high work of breathing.
- Auto-PEEP may be responsible for this, and addition of extrinsic PEEP to nearly counterbalance the auto-PEEP improves the patient's comfort dramatically. The external PEEP should be set approximately 80% of auto-PEEP.
- Another approach is to increase minute ventilation though this worsens auto-PEEP and bicarbonate loss.
- If the problem still persists, then a careful search should be made for processes that might drive the patient to a respiratory rate higher than is desirable (e.g., hypoperfusion, pleural effusion, and pain).
- If the patient continues to make significant inspiratory efforts after these, then judicious sedation is advised.
- If there is frequent high-pressure alarm, then look for bronchospasm, pneumothorax, atelectasis, blockade of endotracheal tube with secretions, right main bronchus intubation, etc.
- Once the patient improves and the respiratory muscles are adequately rested, the patient should assume some of the work of breathing and be evaluated for weaning from the mechanical ventilation. The patients fulfilling the weaning criteria are extubated.

Step 7: Monitor and manage complications

Ventilation is never without complications. They should be diagnosed and managed (Table 4.5).

Step 8: Weaning from the ventilator (Chap. 7)

- Patients who have recovered considerably from the underlying diseases should be assessed daily for readiness of weaning (Table 4.6), and those satisfying criteria should be given a spontaneous breathing trial (SBT).
- Patients may be given SBT for 30–120 min and patients are monitored for signs of SBT failure (Table 4.7). Those who successfully tolerate this can be extubated.

Step 9: Monitoring during postextubation period

- Once the patient is extubated, he/she should be monitored for any appearance of respiratory distress/failure because some patients may develop weaning failure and may require reintubation.

Table 4.5 Complications of intubation and mechanical ventilation

Equipment
Malfunction or disconnection
Incorrect settings
Pulmonary
Airway intubation (e.g., damage to teeth, vocal cords, and trachea)
Ventilator-associated pneumonia (e.g., reduced lung defense)
Ventilator-associated lung injury (e.g., diffuse lung injury due to regional overdistension or tidal recruitment of alveoli)
Overt barotraumas (e.g., pneumothorax)
O_2 toxicity
Patient–ventilator asynchrony
Circulation
↓ Right ventricular preload → ↓ cardiac output
↑ Right ventricular afterload (if the lung is overdistended)
↓ Splanchnic blood flow with high levels of PEEP or mean Paw
↑ Intracranial pressure with high levels of PEEP or mean Paw
Fluid retention due to ↓ cardiac output → ↓ renal blood flow
Other
Gut distension (air swallowing, hypomotility)
Mucosal ulceration and bleeding
Peripheral and respiratory muscle weakness
Sleep disturbance, agitation, and fear (which may be prolonged after recovery)
Neuropsychiatric complications

Table 4.6 Criteria for assessing readiness of patients for weaning

Some evidence of reversal of the underlying cause of respiratory failure
Adequate oxygenation (e.g., $PaO_2/FiO_2 > 200$, requiring PEEP < 5–8 cm H_2O, $FiO_2 < 0.4–0.5$, and pH > 7.25)
Hemodynamic stability, no active myocardial ischemia, no clinically significant hypotension or use of vasopressors (dopamine or dobutamine in a lower dose, <5 μg/kg/min, acceptable)
The capability to initiate an inspiratory effort

Table 4.7 Criteria for defining failure of SBT—various parameters monitored during SBT

$SpO_2 \leq 90\%$ and/or $PaO_2 \leq 60$ mmHg
Spontaneous tidal volume ≤4 mL/kg ideal body weight
Respiratory rate ≥35/min
pH ≤ 7.30 if measured
Respiratory distress
Two or more of the following:
Heart rate ≥120/min or ≥20% increase from the baseline
Marked use of accessory muscles
Abdominal paradox
Diaphoresis
Marked subjective dyspnea

Suggested Reading

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   Source material

Mechanical Ventilation in Acute Respiratory Distress Syndrome

5

Farhad N. Kapadia and Umakant Bhutada

A 25-year-old female patient presented with fever with chills and vomiting. The following day, she noted increased difficulty in breathing. The chest X-ray showed extensive bilateral infiltrates, and she needed supplemental oxygen to keep the saturation at more than 90%. Echocardiography showed normal cardiac function. She was getting progressively fatigued and increasingly drowsy and was intubated.

Acute respiratory distress syndrome (ARDS) is characterized by a brief precipitating event followed by rapidly developing dyspnea. These patients have markedly impaired respiratory system compliance and reduced aerated lung volume. The hypoxemia is refractory to low fraction of oxygen concentration and low positive end expiratory pressure (PEEP). The mortality from ARDS is around 35–40%. Current therapy of ARDS revolves around treatment of underlying cause, lung protective ventilatory strategy, and appropriate fluid management.

Step 1: Initiate resuscitation and identify the reason for deterioration.

- Initial resuscitation should be done, as mentioned in Chap. 78.
- Take history, perform quick physical examination, and initiate basic investigation such as arterial blood gas and the chest X-ray to arrive at a probable cause for deterioration in respiratory status.

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Table 5.1 Conditions associated with ARDS

Pulmonary (*primary*)
Pneumonia
Aspiration
Smoke inhalation
Lung contusion
Near-drowning
Venous air embolism
Extrapulmonary (*secondary*)
Sepsis
Pancreatitis
Blood transfusion
Fat emboli
Major burn
Poly trauma
Amniotic fluid embolism
Neurogenic pulmonary edema
Cardiopulmonary bypass
Drug reactions (aspirin, nitrofurantoin)

- Acute respiratory distress syndrome (ARDS) used to be diagnosed when a patient fulfilled the following criteria:
  - Acute onset
  - Presence of a predisposing condition (Table 5.1)
  - Bilateral infiltrates on the chest skiagram
  - PaO_2/FiO_2 less than 200 for ARDS
  - PaO_2/FiO_2 less than 300 for ALI
  - Pulmonary arterial occlusion pressure less than 18 mmHg or no clinical evidence of the left-sided heart failure

The definition of ARDS has been revised recently .The new definition of ARDS is called "Berlin ARDS definition" (Table 5.2).

Step 2: Assess the need for continuous positive airway pressure (CPAP) or noninvasive ventilation (NIV)

- NIV/CPAP has a very limited role in a patient developing ARDS.
- It may be used in selected patients who are immunosuppressed, with close monitoring to help improve oxygenation and decrease the work of breathing.
- A minority of patients show a marked improvement, and they may be taken off this cautiously after a few days of stabilization.
- Most of the patients show very little or transient improvement, and it is important not to persist with NIV and instead proceed to tracheal intubation before a major deterioration occurs (see Chap. 3).

Table 5.2 The Berlin definition of Acute Respiratory Distress Syndrome

Acute Respiratory Distress Syndrome	
Timing	Within 1 week of a known clinical insult or new or worsening respiratory symptoms
Chest imaging[a]	Bilateral opacities- not fully explained by effusion, lobar/lung/collapse, or nodules
Origin of edema	Respiratory failure not fully explained by cardiac failure or fluid overload Need objective assessment (eg, echocardiography) to exclude hydrostatic edema if no risk factor present
Oxygenation[b]	
Mild	200 mg Hg <Pao_2/FiO_2 <300 mm Hg with PEEP or CPAP > 5 cm H_2O[c]
Moderate	100 mg Hg <PaO_2/FiO_2 < 200 mm Hg with PEEP > 5 cm H_2O
Severe	PaO_2/FiO_2 < 100 mg Hg with PEEP >5 cm H_2O

Abbrevations: CPAP, continous positive airway pressure; FiO_2, fraction of inspired oxygen; PaO_2, partial pressure of arterial oxygen; PEEP, positive end-expiratory pressure.
[a]Chest radiograph or computed tomograph scan.
[b]If altitude is higher than 1000 m, the correction factor should be calculated as follows: [PaO_2/FiO_2X (barometric pressure/760)].
[c]This may be delivered noninvasively in the mild acute respiratory distress syndrome group.

Step 3: Assess the need for mechanical ventilation

- In the following situations of ARDS, mechanical ventilation should be initiated electively. To avoid complications of emergent intubation, it is improper to wait till the patient deteriorates further.
  - Persistent hypoxemia (SpO_2 < 90%) on non-rebreathing facemask oxygen or NIV
  - Excessive work of breathing and high minute ventilation, which is often a subjective assessment
  - Hemodynamic instability

Step 4: Understand principles of ventilation in ARDS

- The major principle is to keep the patient stable and cause minimal iatrogenic damage till such time the underlying disease resolves.
- In ARDS, mechanical ventilation is primarily used to reverse hypoxemia and decrease the work of breathing.
- Positive-pressure ventilation is unphysiological, and adverse effects of this must be prevented or rapidly reversed.
- Initially, there may be a significant hemodynamic deterioration, which mandates adequate monitoring and reversal with fluids and appropriate inotrope and vasopressor agents.
- High volumes, high airway pressures, and repeated opening and closing of collapsed alveoli may further damage the lung, worsen the ARDS, and contribute to systemic inflammation.
- These patients are prone to ventilator-associated pneumonia due to prolonged ventilation required and occasionally due to use of corticosteroid.

- The mechanical ventilation protocol for a patient with ARDS is based on the concept that the lung is largely consolidated, and may be viewed as a "baby lung" with only about a third of the alveoli remaining open. This "consolidation" primarily results from the alveolar wall becoming stiff and shutting down, rather than the alveoli actually being fluid-filled.
- The concept of a "sponge lung" implies the gravitational effect of lung injury and the appropriate ventilatory strategy can open up or recruit these shut alveoli. This is demonstrated in imaging studies that show that changes of position of the patient cause changes in the patterns of aeration of the lung, with the lowest or most dependent areas shutting down due to the weight of the lung above, the alveoli in the highest part remaining mostly open. On the basis of these concepts, one of the strategies of mechanical ventilation is to "open up the lung and keep it open."

Step 5: Decide on the initial settings on the ventilator

- A protocol should be followed for initiating ventilator setting, which may be customized according to the patient's need.
- Initially the following setting needs to be decided:
  - Mode—volume control ventilation (ARDS network protocol) or pressure control as the starting mode
    - Tidal volume (in volume control mode)
      - Calculate ideal body weight (IBW): Male IBW = 50 + 2.3 [height (inches) − 60]; female IBW = 45.5 + 2.3 [height (inches) − 60].
      - Set initial tidal volume (TV) to 8 mL/kg IBW.
      - Reduce TV by 1 mL/kg intervals every 2 h until TV = 6 mL/kg IBW.
    - Inspiratory pressure (pressure control)
      - Inspiratory airway pressure should be limited to less than 30 cm H_2O.
    - FiO_2 and positive end-expiratory pressure (PEEP)
      - Initial FiO_2 should be kept high and PEEP 5–10 cm H_2O to keep oxygen saturation more than 90%.
      - FiO_2 should be titrated down subsequently if oxygen saturation is more than 90%. Titrate PEEP as per ARDSnet table.
    - Minute ventilation
      - Adjust respiratory rate (maximum up to 35/min) to achieve a minute ventilation commensurate with patients' demand.
    - Inspiratory flow or inspiratory time or I:E ratio (depending on the ventilator type)
      - Set the inspiratory flow rate above patients' demand (usually >80 L/min); adjust flow rate to achieve goal of inspiratory–expiratory ratio of 1:1.0–1.3.

Step 6: Try to achieve goals of ventilation

- After initial ventilator setup, the patient should be monitored for safety and efficacy of ventilator settings and an attempt should be made to ventilate within certain goals.

– *Oxygenation goal:* $PaO_2 = 55–80$ mmHg or $SpO_2 = 88–95\%$
  - Use these incremental FiO_2–PEEP combinations to achieve oxygenation goal:

FiO_2	0.3	0.4	0.4	0.5	0.5	0.6	0.7	0.7
PEEP	5	5	8	8	10	10	10	12

FiO_2	0.7	0.8	0.9	0.9	0.9	1.0	1.0	1.0
PEEP	14	14	14	16	18	20	22	24

– Plateau pressure (Pplat) goal = 30 cm H_2O
  - Keep inspiratory pressure in pressure control below 30 cm H_2O.
  - In volume assist control, check Pplat (use 0.5-s inspiratory pause), SpO_2, total RR, TV, and arterial blood gases.
  - If Pplat is more than 30 cm H_2O, decrease TV by 1 mL/kg steps (minimum 4 mL/kg IBW).
  - If Pplat is less than 25 cm H_2O and TV is less than 6 mL/kg, increase TV by 1 mL/kg until Pplat is more than 25 cm H_2O or TV is 6 mL/kg.
  - If Pplat is less than 30 cm H_2O and breath stacking occurs, one may increase TV in 1 mL/kg IBW increments (to a maximum of 8 mL/kg) as long as Pplat is less than 30 cm H_2O.
  - In patients with obesity and stiff chest wall or high Intraabdominal pressure (IAP) a higher plateau pressure may be tolerated.
– pH goal: 7.30–7.45
  Acidosis management: pH less than 7.30
  - If pH is 7.15–7.30, increase RR until pH is more than 7.30 or $PaCO_2$ is less than 25 mmHg (maximum RR = 35); if RR is 35 and $PaCO_2$ is less than 25 mmHg, $NaHCO_3$ may be given.
  - If pH is less than 7.15 and $NaHCO_3$ is considered or infused, TV may be increased in 1 mL/kg steps until pH is more than 7.15 (Pplat goal may be exceeded).

  Alkalosis management: if pH is more than7.45, decrease RR if possible.

Step 7: Management strategy for life-threatening hypoxemia

- Rescue strategies need to be implemented in patients who remain persistently hypoxemic in spite of maximum F_iO_2 and PEEP combination. The following strategies are used:
  – Recruitment maneuver.
  – Airway pressure release ventilation (APRV)/inverse ratio ventilation (IRV).
  – Prone positioning.
  – High-frequency ventilation.
  – Extracorporeal membrane oxygenation.
  – Inhaled nitric oxide.
    1. *Recruitment maneuver*

Table 5.3 Recruitment maneuvers

Indications
1. As rescue measure to improve oxygenation
2. After disconnections in ventilator circuit (if responsive to recruitment maneuvers)
3. Postintubation to assess recruitability
Steps
1. The patient should be well sedated/paralyzed
2. The patient should be adequately hydrated
3. The patient should be hemodynamically stable and no arrhythmias
4. Avoid in patients with severe chronic respiratory disease, intracranial hypertension, morbid obesity, and pregnancy
Method 1:
Keep the patient in CPAP mode and deliver 40 cm H_2O pressure for up to 30 s at FiO_2 of 1.0
Method 2:
Put patient in pressure control mode
FiO_2 of 1.0
Inspiratory pressure 40–50 cm H_2O
PEEP 20–30 cm H_2O
Rate 8–20/min
Inspiratory time 1–3 s
Duration 1–2 min
Start with lower inspiratory pressure (40) and PEEP (20) and if there is no response go to higher pressure
Complications
1. Hypotension (mean arterial pressure <60 mmHg)
2. Desaturation (SpO_2 < 85%)
3. Cardiac arrhythmias
4. Barotrauma (pneumothorax, pneumomediastinum, new air leak)

Recruitment maneuver is to apply a high level of sustained airway pressure to open up the collapsed alveoli and then high PEEP to prevent recollapse (Table 5.3).

2. *IRV/APRV* (Inverse Ratio Ventilation/Airway Pressure Release Ventilation)
   - IRV and APRV may be considered in difficult-to-manage ARDS patients.
   - IRV, during which the ratio of inspiratory time to expiratory time exceeds one, can be achieved using either volume or pressure modes of ventilation. Prolongation of the inspiratory time results in increased mean airway pressures, often improving oxygenation.
   - APRV uses high continuous airway pressure to promote alveolar recruitment and to maintain adequate lung volume, and a time-cycled release phase to a lower pressure in supplementing spontaneous minute ventilation. By allowing unrestricted spontaneous breathing throughout the ventilator cycle, APRV allows for better ventilation of dependent lung regions; spontaneous breathing reduces atelectasis.

- These modes of ventilation may lead to ventilation with a low tidal volume leading to hypercapnia, which is termed "permissive hypercapnia" as it is a necessity for safe ventilation.
- Permissive hypercapnia is usually safe but may have some harmful effects, which include pulmonary vasoconstriction and pulmonary hypertension, proarrhythmic effects due to increased discharge of the sympathetic nervous system, and cerebral vasodilation leading to increased intracranial pressure.
- Permissive hypercapnia should probably be used with caution in patients with heart disease and is relatively contraindicated in those with elevated intracranial pressure.

3. *Prone position*
   - Prone position can be considered if the patient has any of the following:
     - Severe hypoxemia: $PaO_2/FiO_2 < 140$ mmHg.
     - $PaO_2 < 55$ with $FiO_2 \geq 0.7$ or plateau pressure >30 cm H_2O.
   - Contraindications:
     - Life-threatening shock (mean arterial pressure <65 mmHg with or without vasopressors).
     - Raised intracranial pressure more than 30 mmHg, or cerebral perfusion pressure less than 60 mmHg.
     - Spinal instability or any unstable fracture.
     - Recent thoracoabdominal surgery.
     - Open wound or burns on ventral body surface.
     - Massive hemoptysis.
     - Arrhythmias.
   - Steps to proning:
     - Proning needs trained staff; it requires 4–6 persons.
     - Have a central and arterial line in place.
     - Arrange for cushions.
     - Fix tube and lines well.
     - Empty the nasogastric tube.
     - Sedate well and paralyze if required.
     - Cover eyes.
     - Place electrocardiograph (ECG) electrodes on the back.
     - One person stands at the head end and holds the ETT with one hand and the head with the other.
     - Disconnect monitoring.
     - Bring the patient on the edge of the bed.
     - Turn the patient by three persons and place on supporting cushions under chest and lower pelvis.
     - Immediately reconnect monitors and take BP, SpO_2.
     - Auscultate chest.
     - Make sure abdomen is free (for respiration).One should be able to pass hands between abdomen and mattress.

  - Extracushion pads for genitalia, axilla, ears, breasts, knees, foot.
  - Check ABG within 30 min.
  - Turn the head alternately to right and left every 2 h.
- Duration—two methods used:
  - Intermittent: 8–20 h/day
  - Continuously for longer duration till patient shows improvement
- Complications:
  - Pressure ulcers
  - Displacement of endotracheal tubes, thoracotomy tubes, and vascular catheters

4. *High-frequency ventilation*
   - Consider high-frequency ventilation, which implies application of mechanical ventilation with a respiratory rate that exceeds 100 breaths/min.
   - HFOV supports pulmonary gas exchange by entraining gas from a bias flow circuit and delivering subnormal tidal volumes to the lungs at rates between 3 and 15 cycles per second (Hz).
   - Smaller tidal volume is delivered, which limits alveolar overdistension.
   - Higher mean airway pressure is attained, so there is more alveolar recruitment.
   - Constant airway pressure is applied during both inspiration and expiration, which prevents end-expiratory alveolar collapse.
   - Oxygenation can be adjusted independently of CO_2 removal by adjusting the mean pressure and FiO_2.
   - CO_2 removal is increased by increasing the oscillation pressure amplitude, decreasing the frequency, increasing percent inspiratory time, and causing intentional cuff leak.
   - To maximize lung protection, emphasis is placed on achieving frequency as high as possible in combination with the lowest amplitude.
   - HFOV can be considered under the following circumstances:
     - Oxygenation failure: FiO_2 equal to or more than 0.7 and PEEP more than 14 cm H_2O
     - or
     - Ventilation failure: pH less than 7.25 with tidal volume equal to or more than 6 L/kg predicted body weight and plateau airway pressure equal to or more than 30 cm H_2O.
     - It may be considered for patients with ARDS who are failing conventional ventilation. In the absence of studies showing improved clinical outcomes, it remains an investigational tool for routine management of ARDS.
   - Contraindications:
     - Known severe airflow obstruction.
     - Intracranial hypertension
   - Target
     - Oxygenation target: SpO_2 88–95% or PaO_2 55–80 mmHg
     - Ventilation target pH: 7.25–7.35

- Initial HFOV settings
  - Bias flow = 40 L/min
  - Inspiratory time = 33%
  - mPaw = 34 cm H_2O
  - FiO_2 = 1.0
  - Amplitude (ΔP) = 90 cm H_2O
  - Initial frequency based on most recent arterial blood gas:
    - pH more than 7.10 = 4 Hz
    - pH 7.10–7.19 = 5 Hz
    - pH 7.20–7.35 = 6 Hz
    - pH > 7.35 = 7 Hz
- Oxygenation can be improved by increasing the airway pressure and FiO_2.
- Recruitment maneuver, prone position, and nitric oxide can be used as adjuncts.
- Ventilation goals are achieved using frequency as the primary adjustment, rather than the oscillation pressure amplitude.
- Higher frequencies are emphasized, which will result in smaller TV.
- Transition to conventional ventilation.
  - When patients have reached at FiO_2 of 0.4 and mPaw of 22 cm H_2O and remained on those settings for at least 12 h.
  - Initial settings:
    - VT = 6 mL/kg predicted body weight
    - FiO_2 = 0.5
    - PEEP = 16 cm H_2O
    - RR = 25
- Check arterial blood gas in 30–60 min.
- Revert to HFOV if the patient again meets criteria for oxygenation or ventilation failure.

Step 8: Evaluate effects on oxygenation, static compliance, and dead-space ventilation

- $$\text{Static lung compliance} = \frac{\text{VT}}{\text{Plateau pressure} - (\text{PEEP} + \text{autoPEEP})}$$
- Normal value of static compliance is 100 mL/cm H_2O.
- If there is significant improvement, then continue with therapy. If there is no significant improvement, then proceed to the next intervention.

Step 9: Consider administration of glucocorticoids

- Weigh the risks and benefits for individual patients. It should be avoided in patients with active infection.
- It is used within 2 weeks of onset.
- Dose should be methylprednisolone 1 mg/kg bolus followed by 1 mg/kg/day infusion.

- Use only when paralytic agents are discontinued.
- Response is seen within 5 days. If there is no response, it may be discontinued.
- If favorable response, continue for 14 days or until extubation, thereafter half dose for 7 days followed by one-fourth dose for another 7 days, and then stop.
- The safety profile is proven including no added risk of infection.

Step 10: Administer fluids conservatively
- Monitoring fluid status with the central line is required. Pulmonary artery catheter is not recommended.
- Conservative fluid management strategy should be adopted but not at the risk of organ perfusion.
- Hemodynamics is maintained with fluids, vasopressors, and dobutamine for low cardiac index.

Step 11: Consider immunonutrition

Present guidelines recommend to initiate enteral immunonutrition with formulation containing antiinflammatory lipid profile, that is, eicosapentenoic acid, gamalinoleic acid (GLA) (omega-3 fish oil, borage oil), and antioxidants. There has been a recent study casting doubt on enteral immune nutrition.

Step 12: Decide on need for tracheostomy
- Tracheostomy should be performed once the patient is off high FiO_2 and PEEP support but still needs continuing ventilator support due to high minute ventilation. (See Chap. 96 on Percutaneous Tracheostomy)

Step 13: Consider weaning (see Chap. 7)
- Weaning attempts should be started once FiO_2 and PEEP support decrease and minute ventilation requirement comes down.

Step 14: Initiate aggressive mobilization regimen

In order to prevent long-term neuromuscular disability, early aggressive physiotherapy should be started from the initial days.

Suggested Reading

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Clinical outcomes are similar whether lower or higher peep levels are used, with a tidal volume goal of 6 mL/kg of predicted body weight and an end-inspiratory plateau-pressure limit of 30 cm H_2O.
8. The Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. N Engl J Med. 2000;342(18):1301–08.
Mortality is lower in the group treated with lower tidal volumes than in the group treated with traditional tidal volumes (31.0% vs. 39.8%, $P = 0.007$).

Websites

1. http://www.ardsnet.org
The official website of the ARDS Network, initiated by National Heart, Lung, and Blood Institute and National Institutes of Heath to carry out multicenter clinical trials of ARDS treatments.

Mechanical Ventilation in Obstructive Airway Diseases

6

Raj Kumar Mani

A 23-year-old female patient, known to be asthmatic since childhood and on regular inhalers, developed breathlessness at work. Several puffs of salbutamol failed to relieve the symptoms, and she rapidly went on to have wheezing and restlessness followed by air hunger. She was brought to the emergency department.

Obstructive pulmonary diseases are a major cause of mortality and morbidity. Acute respiratory failure in chronic obstructive pulmonary disease (COPD) is one of the common reasons for admission to the intensive care unit (ICU). Use of noninvasive ventilation has revolutionized the treatment and outcome of COPD patients.

Step 1: Initiate resuscitation

- The patient should be resuscitated as mentioned in Chap. 78.
- All the patients admitted with respiratory distress require immediate attention to the airway. This assessment is done mainly by clinical means.

They should be put on oxygen flow to increase SpO_2 to more than 90%. For chronic obstructive pulmonary disease (COPD) patient, use controlled inhaled oxygen through the venturi mask to keep SpO_2 88–90%. Patients who have increased work of breathing and seem to be getting exhausted may require assisted ventilation.

Step2: Assess severity

It is done based on the following:

- Able to speak full sentences.
- Restlessness.

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- Respiratory rate and pattern of respiration.
- Use of accessory muscles.
- Pulse rate and pulsus paradoxus (inspiratory decrease in systolic blood pressure by > 10 mmHg).
- Sensorium, fatigue.
- Auscultation: Wheezes and crackles; silent chest signifies very severe airflow obstruction.
- Peak expiratory flow rate is an objective measure of airflow obstruction: less than 30% of baseline/predicted would indicate likelihood of respiratory failure. Initially, check every 30 min to assess response to the therapy.
- SpO_2: Hypoxia is usually correctable with supplemental oxygen. Refractory hypoxia should trigger search for pneumothorax, atelectasis, pneumonia, or occult sepsis.
- Arterial blood gases: In asthma, normal or elevated $PaCO_2$ signifies respiratory failure due to respiratory muscle fatigue. pH of less than 7.28 would indicate the need for ventilatory support. Hyperlactatemia may occur due to muscle fatigue or adrenergic agents.

Step 3: In the absence of imminent respiratory or circulatory failure, start immediate medical management of asthma

- Nebulized salbutamol 2.5 mg (0.5 mL of 5% solution in 2.5 mL saline) or levosalbutamol should be repeated every 20 min for three doses and then less frequently, dictated by the patient's clinical response. More frequent and even continuous nebulization of salbutamol at a dosage of 10–15 mg can be used in acute bronchial asthma within limits of toxic effects such as tachycardia and tremors.
- Nebulized ipratropium (0.5 mg every 20 min) should be included in initial treatment concomitantly with salbutamol for better bronchodilatation.
- If the nebulizer is not available, use four puffs of salbutamol meter dose inhalers (MDI) through a spacer device.
- Corticosteroids should be initiated at the earliest to prevent respiratory failure. The usual doses are as follows: Hydrocortisone injection 100 mg every 6 h or methylprednisolone 60–125 mg every 6–8 h. Oral prednisolone 60 mg is equally effective especially in COPD.
- Oxygen supplementation is continued to keep SpO_2 more than 90%.
- Methylxanthines: Aminophylline may be used as a second-line agent, although its role is much debated. A loading dose of 5–6 mg/kg is followed by a continuous infusion of 0.6 mg/kg/h. Avoid loading dose in case the patient has been on oral theophyllines earlier.
- Magnesium sulfate (2 g infusion) over 20 min can also be tried in refractory cases of asthma, although its role is unproven.
- Antibiotics are not required routinely in bronchial asthma exacerbation and should be given only if there is evidence of infection.
- Quinolones or macrolides may be used for COPD exacerbation and should be given only if there is evidence of infection, although most of these are viral in origin.

Step 4: Assess need for respiratory support

- Noninvasive ventilation (NIV): For a fatiguing patient, struggling to breathe in spite of medical treatment, NIV may be tried. Inspiratory positive airway pressure reduces work of breathing and expiratory positive airway pressure overcomes auto-positive end-expiratory pressure (auto-PEEP). Extended trials of NIV may be warranted if the sensorium and patient comfort are improving (see Chap. 3).
- Noninvasive positive pressure ventilation is more useful in patients with COPD; there are limited data on its use in acute severe asthma.
- Continuously monitor the heart rate, respiratory rate, SpO_2, blood pressure, and sensorium. Reassess every 30 min until the patient is stable and comfortable. Nursing attendance should be continuous.

Step 5: Assess the need for intubation and mechanical ventilation (MV)

- Impending respiratory arrest.
- Circulatory failure.
- Altered sensorium: progressive drowsiness, agitation, or severe restlessness.
- In a conscious patient, no improvement or deterioration after 3–4 h of optimal medical therapy and NIV support.
- In asthma, PCO_2 of more than 55 mmHg and pH less than 7.28.
- In COPD, more severe hypercarbia and acidosis are well tolerated. However, the general appearance and the degree of distress and fatigue of the patient are more important than the absolute values. NIV is initially used in these patients. MV is used only if there are contraindications or failure of NIV.

Step 6: Initiate MV

Principles: Because of severe airway obstruction, dynamic hyperinflation or air trapping takes place. Progressive inflation leads to equilibrium of inflow and outflow of air in the lungs to take place at a high resting lung volume. MV aimed at normalizing blood gas values would further overdistend the lungs with its attendant barotrauma and circulatory consequences.

- *Orotracheal intubation*: Follow the steps of rapid sequence intubation. As far as possible, a tube size of 8 or more is used, and therefore orotracheal route is preferred.
- *Sedation and paralysis*: At the time of intubation, short-acting sedatives (midazolam) and short-acting neuromuscular blocking agents (succinylcholine) are used. For maintenance of sedation to assist MV, midazolam/propofol infusion can be used. Neuromuscular blocking agents should be avoided as infusion to prevent critical illness neuropathy.
- Avoid delivering high rate and tidal volume with bag ventilation.
- *Initial ventilator settings*: Controlled mechanical ventilation (CMV) mode; tidal volume 8–10 mL/kg or less; respiratory rate 10–15 breaths/min; minute ventilation 6–8 L/min or less; peak flow rate 100 L/min or more; FiO_2 of 1.0, I:E ratio at least 1:3; PEEP should be set to zero to avoid overinflation in control ventilation (Table 6.1).

Table 6.1 Initial ventilator settings in status asthmaticus and COPD

Setting	Recommendation
Respiratory rate	10–15 breaths/min
Tidal volume	8–10 mL/kg
Minute ventilation	6–8 L/min
PEEP	0 cm H_2O
Inspiratory flow	≥100 L/min
I:E ratio	≥1:3
FiO_2	1.00

- When the patient is on assist control mode of ventilation, PEEP may be titrated cautiously to counteract auto-PEEP for easier triggering.

Aerosolized bronchodilator therapy should be used properly during MV as mentioned below:

- Always do proper suctioning before starting nebulization.
- Heat and moisture exchangers, if used, should be removed.
- Water in circuit reduces delivery of aerolized bronchodilators, and therefore remove this before starting bronchodilators.
- Change alarm limits and other settings on the ventilator to suit the use of nebulizers, and do not forget to reset them back to the original settings after nebulization is over.
- Nebulizers and pressurized meter dose inhalers (PMDIs) are equally effective.
- Higher dose of bronchodilators is required in MV than in ambulatory patients.
- PMDIs should be used with adaptors and synchronized with inspiration of the ventilatory cycle.
- The nebulizer should be attached in inspiratory line of the ventilator 46 cm away from the Y-piece.
- Nebulizer gas flow should be kept at 6–8 L/min.
- The ultrasonic nebulizer can also be used to give nebulizer therapy.

Monitor:

- Pplat (plateau pressure) reflects intrinsic PEEP (PEEPi) or dynamic hyperinflation and should be kept at less than 30 cm H_2O.
- Peak airway pressure reflects only proximal airway pressure and is generally high.
- Avoid overventilation. The risk of barotrauma generally correlates with end-expiratory lung volume, not with the pressure. Hypotension is usual after MV due to dynamic hyperinflation, intrinsic PEEP, dehydration, and use of sedatives. It should be managed by giving fluid challenge.

Step 7: Liberation from MV (see Chap. 7)

Once the airway resistance decreases as reflected by improvement in Pplat and hypercarbia, larger minute ventilation becomes possible without increase in dynamic hyperinflation (DHI).

- Spontaneous breathing is then allowed by discontinuing paralysis and deep sedation.
- The patient is given spontaneous breathing trials with a T-piece or low continuous positive airway pressure (≤8 cm H_2O).
- After 30–120 min, if the trial is successful, the ventilator is withdrawn. In the event of failure of the trial, the patient is placed on assist-control or pressure support modes.
- While on spontaneous breathing, a PEEP of 5–8 cm H_2O may be applied to reduce inspiratory threshold load imposed by PEEPi.
- Additional attempts at liberation are carried out after 24 h to allow for the return of diaphragmatic function.

Step 8: Supportive therapy

Adequate deep vein thrombosis prophylaxis and stress ulcer prophylaxis are mandatory in these patients. In COPD patients, adequate nutrition support with less carbohydrate proportion to decrease CO_2 production is desirable.

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Weaning

7

Rajesh Chawla, Vishakh Varma, and Rakesh Sharma

A 50-year-old smoker, a known case of chronic obstructive pulmonary disease (COPD) with dilated cardiomyopathy, was admitted to the intensive care unit (ICU) with altered sensorium and acute respiratory distress. His arterial blood gases showed severe hypoxemia and acute respiratory acidosis. He was intubated and put on controlled mechanical ventilation (CMV). He improved in 2 days. Spontaneous breathing trial (SBT) was tried and the patient was extubated after successful SBT. After 5 h, the patient again developed severe respiratory distress and had to be reintubated. He failed several trials of SBT. Tracheostomy was done on the ninth day of ventilation.

Weaning from mechanical ventilation means the transition from total ventilatory support to spontaneous breathing. It is usually a rapid and smooth process in most of the patients however this can become a progressive and prolonged process in 20–25% of the cases. These patients require a systematic approach for successful liberation from the ventilator. It should be started early once the patients fulfils the criteria for weaning. This weaning has two components: liberation from the ventilator and extubation. The sooner the patient is liberated from the ventilator,

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the lesser are the chances of ventilator-associated pneumonias, ventilator-induced lung injury, decreased ICU length of stay, and overall reduced mortality.

Step 1: Identify readiness for weaning

- Weaning should never be hurried as it can be successful only when the patient is ready both physically and mentally. At the same time, it should also not be delayed as it is associated with complications. Any patient on MV should be considered for weaning if he/she fulfils the readiness criteria as mentioned below.
  1. Prerequisites "readiness criteria"
     - The underlying reason for MV has been stabilized and the patient is improving.
     - The patient is hemodynamically stable on minimal-to-no pressors.
     - Oxygenation is adequate (e.g., $PaO_2/FiO_2 > 200$, PEEP < 5–8 cm H_2O, $FiO_2 < 0.5$).
     - The patient is able to initiate spontaneous inspiratory efforts.
     - Besides these criteria, the patient should be afebrile (temperature <38°C), have stable metabolic status (pH ≥ 7.25), adequate hemoglobin (e.g., Hb > 8–10 g/dL), and adequate mentation (e.g., arousable, Glasgow coma scale >13).
  2. Understand the predictors of successful weaning
     The predictors of successful weaning have been designed from physiologic parameters to help the decision-making process. However, none of the tests alone are particularly powerful, and clinical judgment is of paramount importance.
     - Rapid shallow breathing index (RSBI) is assessed by putting patient on T-piece for 2 min
       - F (frequency)/V_t (tidal volume in litres) less than 100 is predictor of successful weaning.
       - The threshold of 100 is not binding and can be relaxed by 10–20 in patients with endotracheal tube size less than 7 and in women.
     - Minute ventilation less than 10 L/min.
     - Respiratory rate (RR) less than 35 breaths/min.
     - Maximum inspiratory pressure more negative than −30 cm H_2O.

Step 2: Prepare for weaning

Stop continuous infusion of sedation daily to awaken the patient to do spontaneous awakening trial(SAT)

- Communicate with patient, explain the procedure, and calm them.
- Record baseline parameters and keep flow sheet at the patient's bedside.
- Keep a calm peaceful environment and have the nurse or physician remain at the bedside to offer encouragement and support.
- If patient fails SAT (Table 7.1), restart sedation on half of the previous dose.
- If patient passes the SAT after stopping sedation, assess the patient for spontaneous breathing trial (SBT) based on the prerequisites criteria mentioned in step 1.

Table 7.1 Clinical criteria of SAT Failure

SAT failure
Anxiety, agitation, or pain
Respiratory rate >35/min
SpO_2 <88%
Respiratory distress
Acute cardiac arrhythmia

Step 3: Do spontaneous breathing trial (SBT)

Whenever possible, position the patient upright in bed.

Thoroughly suction the endotracheal tube and ensure patency.

Any of the following modes can be chosen for SBT:

A. T-piece:
- Patients are disconnected from the ventilator and made to breathe humidified oxygen—air mixture through a T-piece connected to the endotracheal/tracheostomy tube for 30–120 min.
- Increased respiratory load is offered by the endotracheal tube. Dyspnea and fatigue should be carefully avoided.

B. Pressure support:
- The pressure support level is to be gradually reduced, titrated to RR and patient comfort.
- A level of 6–8 cm H_2O pressure support is considered to overcome the tube resistance.
- Put the patient on PS of 6–8 cm H_2O and PEEP of 4 cm H_2O.

Table 7.2 Failure of SBT

Objective measurements	$PaO_2 \leq 50$–60 mmHg on $FiO_2 \geq 0.5$ or $SaO_2 \leq 90\%$
	$PaCO_2 > 50$ mmHg or an increase in $PaCO_2 > 8$ mmHg
	pH < 7.32 or a decrease in pH > 0.07 pH unit
	Rapid shallow breathing index >105
	RR > 35 or an increase of >50%
	Heart rate >140 or an increase of >20%
	Systolic blood pressure >180 or an increase of >20%
	Systolic blood pressure <90
	Cardiac arrhythmias
Subjective clinical assessments	Agitation and anxiety
	Depressed mental status
	Diaphoresis
	Cyanosis
	Evidence of increasing effort
	Increased accessory muscle activity
	Facial signs of distress
	Dyspnea

Duration:
The duration should be 30–120 min—shorter time for the patients on the ventilator for less than 1 week and longer for the patients on prolonged MV.

Step 4: Monitor closely
- Patient comfort, dyspnea, and all vital and respiratory parameters should be closely monitored. SBT should be terminated if it fails (Table 7.2).
- SBT should be tried at least once in 24 h. More frequent SBTs do not help.
- At the end of the trial, if it succeeds, the patient is considered for extubation.

Step 5: Extubate the patient
After undergoing a successful SBT, a few more criteria should be fulfilled before deciding about extubation:
- Adequate cough reflex—spontaneously or while suctioning.
- Patient should be able to protect airways, and they should follow simple commands.
- Secretions should not be copious.
- A cuff leak of less than 110 mL measured during assist-control ventilation helps to identify patients who are at high risk of developing postextubation stridor/obstruction of airway.
- No radiological or surgical procedure is being planned in the near future.
- Extubation should not be done at the end of the day.

Step 6: Monitor for extubation failure
After extubation, the patient should be observed closely for signs of extubation failure as mentioned below:
- RR more than 25/min for 2 h
- Heart rate more than 140 beats/min or sustained increase or decrease of more than 20%
- Clinical signs of respiratory muscle fatigue or increased work of breathing
- SaO_2 less than 90%; PaO_2 less than 80 mmHg, on FiO_2 more than 0.50
- Hypercapnia ($PaCO_2 > 45$ mmHg or >20% from preextubation), pH < 7.33

Step 7: Try noninvasive ventilation (NIV)
- If the signs of extubation failure are present, the physician should try NIV particularly in conditions where its role is proved; for example, in COPD, postoperative failure after lung resection surgery, or decompensated obstructive sleep apnea.
- NIV has the advantage of reduced complications and better patient interactions. However, it is important to keep in mind that it should not delay reintubation (if required), and every hour that a patient spends on NIV when intubation is clearly required increases mortality and delays recovery.
- NIV is used in three clinical settings:
  - As an alternative weaning technique for the patients who failed SBT: Extubate and put on NIV—well-documented role in COPD patients without significant comorbidities and in centers with expertise in NIV use.

- As a prophylactic measure for the patients with a high risk of reintubation: Studied in postoperative patients. Start NIV electively after successful SBT and extubation.
- As the treatment of respiratory insufficiency after extubation (postextubation failure): Useful in COPD.

In conditions where role of NIV is not proved, the patients should be reintubated.

Reintubation carries higher mortality either because of underlying medical condition or because of possible complications such as aspiration or ventilator-associated pneumonia.

Step 8: Identify difficult weaning

Weaning success is defined as extubation and the absence of ventilator support 48 h following extubation.

- *Weaning failure* is defined as one of the following:
  - Failed SBT
  - Reintubation and/or resumption of ventilator support following successful extubation
  - Death within 48 h following extubation
- The term *weaning in progress* is used for the patients who are extubated, but remain supported by NIV.
- *Difficult weaning*—Patients who fail initial weaning and require up to three SBT or as long as 7 days from the first SBT to achieve successful weaning.
- *Prolonged weaning*—Patients who fail at least three weaning attempts or require more than 7 days of weaning after the first SBT.

Step 9: Ascertain the cause of weaning difficulty

- Carry out a detailed examination of the patient, and look for the cause of difficult weaning.
- Make a checklist based on pathophysiologic mechanisms:

I. Inadequate respiratory drive
   - Nutritional deficiencies
   - Excess of sedatives
   - Central nervous system abnormality
   - Sleep deprivation

II. Inability of the lungs to carry out gas exchange effectively
   - Unresolving pneumonia
   - Unresolved pulmonary edema/fluid overload
   - Undiagnosed pulmonary embolism
   - The splinting effect of obesity, abdominal distension, or ascites

III. Respiratory muscle fatigue/weakness
   - Nutritional and metabolic deficiencies
   - Critical illness polyneuropathy/myopathy
   - Hypokalemia
   - Hypomagnesemia

- Hypocalcemia
- Hypophosphatemia
- Hypoadrenalism
- Hypothyroidism
- Corticosteroids: myopathy, hyperglycemia
- Chronic renal failure
- Systemic disease sepsis: impaired diaphragmatic force generation
- Refractory hypoxemia and hypercapnia
- Persistently increased work of breathing
- Ineffective triggering, auto-PEEP
- Increased resistance due to ventilator tubings or humidification devices
- Poor cardiac performance
- Neuromuscular dysfunction/disease
- Drugs

IV. Anxiety
It is difficult to distinguish anxiety from ventilatory failure. If in doubt, always presume it to be ventilatory failure.

V. Psychological dependency in difficult weaning

Step 10: Treat all the reversible causes identified

- Provide good nutrition, but avoid overfeeding.
- Have good glycemic control (110–140 mg/dL).
- Correct metabolic factors (especially metabolic alkalosis).
- Maintain hemoglobin above 7–8 g/dL.
- Maintain adequate cardiac output and tissue perfusion.
- Treat arrhythmia.
- Treat hypothyroidism and steroid deficiency or excess.
- Control the patient's underlying illness.
- Abolish ventilator dysynchrony with appropriate inspiratory flow and trigger settings.
- Change of the mode of ventilation may help improve patient–ventilator interactions.
- Reverse bronchospasm as much as possible and reduce dynamic hyperinflation.
- Drain out significant pleural effusions and ascites.
- Treat intraabdominal hypertension.
- Treat pulmonary edema aggressively.
- Discontinue the use of steroids, aminoglycosides, colistin, and statins, if possible.
- Avoid fluid overload in renal failure and cardiac failure—do dialysis if indicated.
- Make the patient comfortable.
- Aggressive physiotherapy and mobilization.
- Reverse oversedation.
- Treat anxiety: Improve patient communication, use relaxation techniques, and give low-dose benzodiazepines.
- Diagnose and treat narcotic/benzodiazepine withdrawal.
- Treat delirium and depression.
- Ensuring nighttime sleep may be helpful.

Step 11: Plan the weaning process in difficult weaning

1. Select the mode of ventilation
   The mode of ventilation used should provide adequate respiratory support and prevent diaphragmatic atrophy.
   - Pressure support ventilation: It is most commonly used, and has been shown to be better than SIMV for weaning.
   - Continuous positive airway pressure (CPAP): Besides the usual benefits of improved oxygenation and improved left ventricular function, it has beneficial role in selected patients with hypoxemic respiratory failure.
   - Automatic tube compensation: It may be helpful in narrow endotracheal tubes to overcome tube resistance.
   - Proportional assist ventilation: It has been studied with CPAP and shown to improve respiratory mechanics.
   - Adaptive support ventilation: It has been shown to be better than SIMV in postcardiac surgery patients.
   - Control Mechanical Ventilation (CMV): It has logical use in patients showing respiratory fatigue on spontaneous mode. So it is recommended to use this mode in cases of difficult weaning at night to give rest to the muscles.
2. Plan tracheostomy.
   - Percutaneous tracheostomy has been shown to have fewer complications than surgical tracheostomy and to be more cost-effective (see Chap. 96).
   - Potential benefits of using tracheostomy in difficult-to-wean patients are as follows:
     – Decreased work of breathing
     – Reduced requirement of sedation and improved patient comfort and cooperation
     – Earlier reinstitution of oral feeding
     – Less chances of accidental extubation
   - In spite of the above-mentioned benefits, tracheostomy has not been consistently shown to decrease mortality. It has resulted in a number of dependent survivors. It facilitates easier bedside management of such patients.
3. Do aggressive physiotherapy and mobilization
   Physiotherapy and mobilization are prerequisites for successful weaning. Early institution of physiotherapy in a protocol-driven approach and daily assessment to achieve maximum mobility is now an integral part of ICU management.
4. Select proper place for weaning
   Cost-effective care has been shown to be provided in respiratory intermediate care units and specialized regional weaning centers. It requires team effort and expertise.

Step 12: Choose a weaning protocol

Protocol-driven weaning has more chances of success, reduced costs, and probably reduced mortality. Two basic weaning protocols are used for a prolonged weaning patient:

- Progressive reduction of ventilator support
- Progressively longer periods of SBTs

No significant difference in weaning success and mortality rate, duration of ventilatory assistance, or total hospital length of stay is reported between these two weaning techniques in the difficult-to-wean patients. A combination of both the protocols can also be used.

Step 13: Decide about home ventilation

Indications:

- An inability to be completely weaned from ventilatory support including NIV
- A progression of disease etiology that requires increasing ventilatory support

Patients should have stable physiology and proper resources, personnel, and motivation.

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Massive Hemoptysis

8

Avdhesh Bansal and Viny Kantroo

A 36-year-old chronic alcoholic male patient presented to the emergency department with history of a large amount of blood being coughed out for the past 24 h. He had had three such episodes, the last one just about 1 h ago. There was no history of such previous episodes in the past. Although there was no history of fever, he had been feeling weak for the past 2 weeks.

Hemoptysis is defined as coughing of blood from the respiratory system. Hemoptysis is one of the important symptoms of cardiopulmonary disease. It can be mild or severe requiring admission to the intensive care unit (ICU). If massive hemoptysis is not treated aggressively, it is associated with significant mortality.

Step 1: Initiate resuscitation

Take history of the patient and find out the approximate amount of hemoptysis. Severe hemoptysis is defined as hemoptysis of more than 400–600 mL/24 h. After a quick physical examination of the patient, initiate resuscitation.

Airway:

- Maintaining an open airway should be the first priority in the management. The main objective is to prevent asphyxiation.
- Intubate with single-lumen endotracheal tube in cases of severe and diffuse endobronchial bleeding. It may achieve immediate control of the airways to allow

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adequate suctioning and diagnostic and therapeutic fiber-optic bronchoscopy. It may also be helpful in cases of nonavailability of the double-lumen tube or expertise.
- Double-lumen endotracheal tube can be helpful to isolate and ventilate the lungs separately if the bleeding is lateralized. The double-lumen tubes are, however, easily obstructed by clots and do not permit passage of bronchoscopes of adequate size to allow bronchial toilet under unobstructed vision. It may still, however, be possible to confirm the tube position. Be careful as it can result in tube displacement.

Breathing:
- Large amount of blood in the tracheobronchial tree may be a major impediment to gas exchange. Maintain oxygen saturation above 94% by administering oxygen. Position the patient in lateral decubitus toward the site of bleeding as it spares the contralateral lung from aspiration.

Circulation:
- All patients should be admitted to the intensive care unit. Vital signs should be monitored continuously.
- The intra-arterial line should be inserted for continuous blood pressure monitoring.
- Two large-bore intravenous lines or a central venous catheter should be inserted and intravenous fluids should be started.
- If the condition is rapidly deteriorating, O-positive blood (O-negative in case of women of childbearing age) should be transfused while waiting for blood grouping and crossmatching. Meanwhile, determine the blood type, crossmatch, and request for red cell units, depending on the requirement. Assess the severity of volume loss (see Chap. 64).

Step 2: Clinical assessment and localization of bleeding site
- The first step in diagnosing hemoptysis is to determine the bleeding source: respiratory tract versus a nasopharyngeal or gastrointestinal source. Querying the patient identifies the correct source in 50% of cases.
- Hemoptysis is characterized by cough with frothy sputum, which is alkaline when tested with litmus paper. In contrast, hematemesis is accompanied by nausea and vomiting, and is frequently acidic. Epistaxis is usually traumatic and may be localized by anterior rhinoscopy and examination of the oropharynx. Aspirated blood or swallowed blood from any of the sites can make it difficult to initially identify the origin of bleeding.

Step 3: Find out the etiology
Take a detailed history and perform physical examination, keeping in mind the various causes of severe hemoptysis (Table 8.1).

Physical examination: The amount, color, and character of bleeding should be noted. On examination, look for specific signs that can point to a specific diagnosis as mentioned in Table 8.2.

Table 8.1 Causes of severe hemoptysis

Bronchiectasis	Pulmonary tuberculosis
Fungal infections in cavities—aspergilloma	Bronchogenic carcinoma
Severe mitral stenosis	Coagulopathies
Foreign bodies	Trauma
Vasculitis	Pulmonary embolism

Table 8.2 Focused physical examination

Digital clubbing—bronchiectasis or lung carcinoma
Stridor—tracheal tumors or a foreign body
Oral and aphthous ulcers, genital ulcers, and uveitis—Behcet's disease in which pulmonary arteriovenous malformations (AVM) are responsible for hemoptysis
Cutaneous purpura or ecchymosis—coagulation disorders
Diastolic murmur—mitral stenosis
Saddle nose with rhinitis and septal perforation—Wegener's granulomatosis

Step 4: Plan investigations

The following investigations should be ordered in all patients:

- Hemoglobin, hematocrit, platelets count, coagulation studies (prothrombin time including international normalized ratio, partial thromboplastin time).
- Renal function tests.
- Liver function tests.
- Arterial blood gas analysis.
- D-dimer, urinalysis.
- Chest skiagram: Chest radiography helps in localizing the bleeding source in 60% of cases and identifying possible etiology such as a lung mass, cavitary lesion, or alveolar hemorrhage.
- Further investigations will depend on the possible diagnosis.
- Sputum/bronchoalveolar lavage should be tested for bacteria including mycobacteria, fungi, and malignant cells.
- Multidetector computed tomography (MDCT) has proved to be of considerable diagnostic value in localizing the site of bleeding. Contrast-enhanced MDCT produces high-resolution angiographic studies with a combination of multiplanar reformatted images. Therefore, MDCT angiography is able to identify the source of bleeding and underlying pathology with high sensitivity. This is of particular importance to the interventional radiologist planning for arterial embolization.
- If MDCT is not available, contrast-enhanced single-detector spiral CT can be performed to detect bronchial and nonbronchial systemic arterial vascular lesions such as thoracic aneurysm and AV malformation. Except for life-threatening situations, thoracic CT scans should be performed prior to bronchoscopy.

Step 5: Bronchoscopy

- Diagnostic bronchoscopy is the primary method for diagnosis and localization of hemoptysis. Rigid bronchoscopy is ideally recommended in cases of massive hemoptysis because of its ability to maintain airway patency.

- Flexible bronchoscopy (FOB) is used more widely, considering the ease of performance at the patient's bedside without the use of general anesthetic and operating theatre suite. Vasoactive drugs can be instilled directly into the bleeding source. The overall diagnostic accuracy of bronchoscopy in localizing the site of bleeding is 50%, but it is less useful in identifying the underlying cause. Further disadvantages include nonvisualization during active hemoptysis, and ineffectiveness of endobronchial therapies in most cases. The ideal time for bronchoscopy is controversial, but the consensus is to perform urgent bronchoscopy in patients with massive hemoptysis.
- In case plug of blood clot is seen in a segment, it is recommended not to remove it as it may restart massive hemoptysis.
- *Administer local therapy*: The following therapeutic measures can be tried through the fiber bronchoscope to control bleeding.
  - Iced saline bronchial lavage in the involved lung
  - Iced saline lavage of up to 1,000 mL in 50 mL aliquots at the bleeding site
  - Administration of topical hemostatic agents, such as epinephrine (1:20,000) or thrombin-fibrinogen
  - Tamponade therapy, using oxidized regenerated cellulose mesh
- Another alternative site-specific therapy that can be tried using the flexible bronchoscope includes endobronchial tamponade using a balloon tamponade catheter to prevent aspiration to the unaffected contralateral lung and preserve gas exchange.
- A bronchus-blocking balloon catheter has been designed to be used through the working channel of the flexible bronchoscope which has a second channel that is used to instill vasoactive hemostatic agents, such as iced saline, epinephrine, vasopressin, or thrombin-fibrinogen, to control bleeding.

Step 6: Start pharmacotherapy

- Antibiotics and steroids, depending on the underlying condition, are necessary to control the precipitating cause.
- Intravenous vasopressin has not been shown to improve the outcome, and therapies such as vitamin K supplements and tranexamic acid have a doubtful role.
- Correct coagulation abnormalities with appropriate platelet, fresh frozen plasma, and cryoprecipitate.
- Recombinant activated factor VII (rFVIIa) can be tried as it has been reported as an effective temporizing measure in unstable patients with hemoptysis due to community-acquired pneumonia, when conventional treatment is not immediately available in the setting of a regional hospital.

Step 7: Bronchial artery embolization (BAE)

- Bronchial artery angiography is highly effective in localizing the source of bleeding and identifying a vessel for embolization. The bronchial circulation (a high-pressure circuit with systolic pressure of 120 mmHg) is the most common source of massive hemoptysis, accounting for 95% of all cases. Less than 5% of

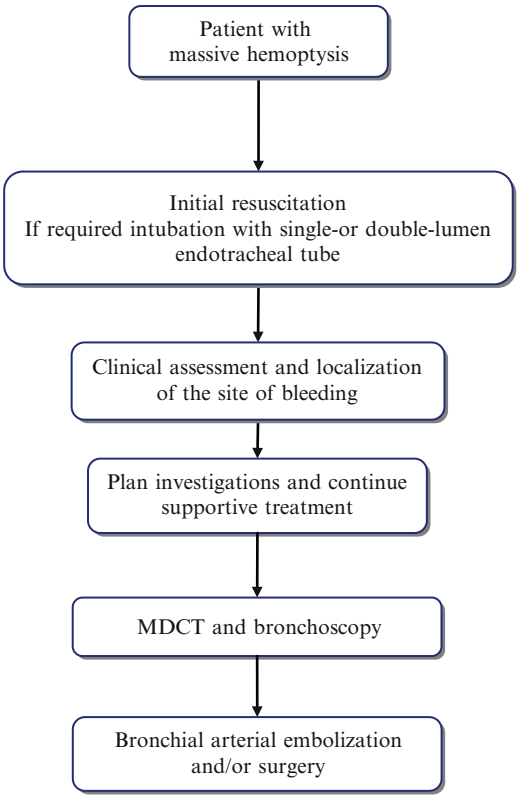

Fig. 8.1 The management of severe hemoptysis

bleeding arises from the pulmonary circulation (a low-pressure circuit with a systolic pressure of 15–20 mmHg).

- Once the bleeding bronchial artery is located, particles (polyvinyl alcohol foam, absorbable gelatin, pledgets of Gianturco steel coils) are infused into the artery. BAE achieves immediate control of the bleeding in 75–90% of cases. Postembolization recurrence of hemoptysis has been observed in 20% of cases.
- Remember that this is a temporizing procedure while every effort is being made to make a clear diagnosis and treat accordingly, except in AV malformations in which this could be the definitive treatment.
- If bronchial artery angiography does not reveal a bleeding vessel, a pulmonary angiogram is required to investigate the pulmonary circulation.

Step 8: Surgical resection (segmentectomy, lobectomy, and pneumonectomy)
Surgery is indicated in the following conditions:

- BAE is unavailable or technically unfeasible, or bleeding or aspiration of blood continues despite embolization.

- Surgical resection of the bleeding site is possible if the lesion can be localized and the patient is fit for surgery.
- Surgery is also preferable when the acuity (rate and amount of bleeding) of hemoptysis precludes safe BAE.
- More specific indications for surgery in massive hemoptysis include persistent bleeding from a mycetoma resistant to medical management, bronchial adenoma, iatrogenic pulmonary artery rupture, leaking aortic aneurysm, hydatid cysts, and selected AV malformations.

Step 9: Endobronchial brachytherapy

This therapy serves well in treating residual or recurrent carcinoma. It can be effective for the patients who have been treated with maximal doses of external beam radiation. However, it can be potentially dangerous. Massive hemoptysis and mediastinal fistulae are the most common complications. A brief summary of management is described (Fig. 8.1).

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Pulmonary Thromboembolism

9

Rajesh Chawla and Subhash Todi

A 67-year-old male patient was admitted to hospital with severe community-acquired pneumonia and acute respiratory failure. He was treated with antibiotics and mechanical ventilation. He improved with the treatment and was extubated on day 4. On day 7, he suddenly developed acute severe breathlessness and chest pain.

Pulmonary embolism (PE) is the most common preventable cause of hospital death. PE should be suspected in all patients who present with new or worsening dyspnea, chest pain, or sustained hypotension without any other obvious cause. High index of suspicion and prompt management can improve survival in these patients. Mortality of acute PE is approximately 30%, which can be reduced to 2.5% by appropriate management

Step 1: Initiate resuscitation

- Provide oxygen to maintain saturation at more than 90% in suspected case of PE, and resuscitate as mentioned in Chap. 78.
- If the patient is hypotensive, administer 500–1,000 mL isotonic crystalloid. Any more volume resuscitation should be given with caution as it may increase right ventricle (RV) wall tension and cause ischemia and worsening of shock.
- Record a detailed medical history and perform physical examination.

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Table 9.1 Revised Geneva Score

The revised Geneva score:
Older than 65 years (1 point)
Previous DVT or PE (3 points)
Surgery or fracture within 1 month (2 points)
Active malignant condition (2 points)
Unilateral lower limb pain (3 points)
Hemoptysis (2 points)
Heart rate
75–94 beats/min (3 points) or
95 beats/min or more (5 points)
Pain on lower limb deep venous palpation and unilateral edema (4 points)
The probability is assessed as follows:
Low probability (0–3 points)
Intermediate probability (4–10 points)
High probability (≥11 points)

Step 2: Assess the risk factors

Assess the risk factors for PE and deep venous thrombosis (DVT) from medical history as mentioned below:

- Prior venous thromboembolism
- Immobility for more than 48 h—congestive heart failure, septic shock, surgery with general anesthesia, mechanical ventilation
- Abdominal or lower extremity surgery or trauma
- Hypercoagulable states
- Malignancy
- Spinal cord injury
- Heparin-induced thrombocytopenia
- Pregnancy or use of oral contraceptives
- Indwelling central venous catheters
- Obesity
- Congestive heart failure

Step 3: Assess clinical probability of PE

Clinical probability of PE is based on either clinical judgment or clinical decision rules (Revised Geneva Score) as mentioned in Table 9.1.

Step 4: Initiate treatment

- While diagnostic confirmation is awaited, anticoagulant treatment with subcutaneous low-molecular-weight heparin (LMWH), fondaparinux, or intravenous unfractionated heparin (UFH) should be initiated as soon as possible in patients with clinical probability of PE, if there are no contraindications.
- UFH is preferred in hemodynamically unstable patients in whom thrombolytic therapy is being planned. Patients are considered to be hemodynamically unstable if they are in shock or have a systolic blood pressure of less than 90 mmHg

Table 9.2 Weight-based nomogram of heparin infusion

APTT(s)	Dose change
<35 (1.2×control)	80 U/kg bolus, increase drip by 4 U/kg/h
35–45 (1.2–1.5×control)	40 U/kg bolus, increase drip by 2 U/kg/h
46–70 (1.5–2.3×control)	No change
71–90 (2.3×control)	Reduce drip by 2 U/kg/h
>90 (>3×control)	Hold heparin for 1 h, reduce drip by 3 U/kg/h

or a drop in systolic pressure of more than 40 mmHg for more than 15 min in the absence of new-onset arrhythmia, hypovolemia, or sepsis.

- UFH is also preferred in the critically ill patients in the intensive care unit (ICU) with PE, requiring numerous procedures or in the patients suffering from renal failure.
- Dose adjustment for LMWH is required for patients with renal failure, obesity, pregnancy, and thrombophilias should ideally be titrated with antifactor Xa levels.

Most of the patients with acute PE are candidates for initial anticoagulant treatment with subcutaneous LMWH or fondaparinux or intravenous UFH. LMWH and fondaparinux are preferred over UFH.

The usual doses of anticoagulation for PE are mentioned below:

A. UFH:

- Give the bolus of 80 units IU/kg or 5,000 IU followed by infusion at 18 units IU/kg/h, keeping activated partial thromboplastin time (APTT) between 1.5 and 2.5 times normal.
- Obtain stat APTT 6 h after heparin bolus and after 6 h of dose change.
- When two consecutive APTT levels are in therapeutic range, order APTT (and readjust heparin drip as needed) every 24 h.

Adjust heparin infusion based on the sliding scale mentioned in Table 9.2 .

B. Enoxaparin:

- 1 mg/Kg s/c twice a day.

C. Dalteparin 5,000 units s/c twice daily.

D. Fondaparinux:

- Weight <50 kg—5 mg s/c once a day.
- Weight 50–100 kg—7.5 mg s/c once a day.
- Weight >100 kg—10 mg s/c once a day.

Step 5: Order investigations

- Electrocardiogram, X-ray chest (posteroanterior view), and arterial blood gas analysis should be ordered in all these patients. Although these tests are nonspecific, they do increase the index of suspicion.
- Baseline prothrombin time (PT), partial thromboplastin time (PTT), and platelet count.
- Renal functions test.

- Choice of further investigations will depend on:

(a)	Index of suspicion of PTE
(b)	Hemodynamic stability of the patient
(c)	Availability of tests at the center
(d)	Sensitivity, specificity, and positive predictive value of the test

- If the patient has a high probability of PE clinically or on the basis of a high probability score, and can be safely moved to computed tomography (CT) room and is in a position to cooperate with breath holding, he/she should undergo multidetector CT (MDCT) for CT pulmonary angiography, irrespective of his/her hemodynamic status.
- If the patient is hemodynamically unstable and has a high probability of PE clinically or on the basis of a high probability score, and is critically ill and cannot be shifted, he/she should be subjected to echocardiography preferably transesophageal echocardiography (TEE) and lower extremity ultrasonography. His/her blood sample should be sent for a D-dimer level. A negative echo and venous Doppler, however, do not rule out clinically significant PE. Efforts should be made to stabilize the patient hemodynamically, and once the patient stabilizes, he/she should be sent for MDCT pulmonary angiography, if doubt still remains about the diagnosis.
- If the patient is hemodynamically stable and has a low or medium probability score, then order a high-sensitivity D-dimer level (enzyme-linked immunosorbent assay).
- If high-sensitivity D-dimer is positive (level more than 500 ng/mL) in low or medium probability, further testing with MDCT pulmonary angiography is indicated.
- If high-sensitivity D-dimer is negative in low or medium probability, the risk of PTE is very low (0.14%) and no further testing is required.
- Remember that the specificity of an increased D-dimer level is reduced in patients with cancer, in pregnant women, and in hospitalized and elderly patients. A value less than 500 ng/ml is rarely seen in most hospitalized patients in the ICU because they have a high fibrin turnover during critical illness, thus limiting its value in these patients. A negative high-sensitivity D-dimer rules out PE in low and medium probability, and a negative moderate sensitivity D-dimer rules out PE only in low probability cases.
- A ventilation/perfusion scan may be done in patients with a high probability of PE and where there is a contraindication for CT such as renal failure or if CT scan is not available.
- In pregnant women with clinical findings suggestive of PE, an MDCT chest should be done. The concern about radiation is overcome by the hazard of missing a potentially fatal diagnosis or exposing the mother and fetus to unnecessary anticoagulant treatment. MDCT delivers a higher dose of radiation to the mother, but a lower dose to the fetus than ventilation/perfusion scanning. Venous ultrasonography of legs and 2-D echocardiography can be done in these patients before MDCT.

Table 9.3 Risk stratification of patients with PE also has potential clinical implications for triage

Absence of right ventricular dysfunction and normal troponin level—admit in ward
Hemodynamically stable with right ventricular dysfunction or injury—admit the patient in High Dependency Unit (HDU)
Hemodynamically unstable and right ventricular dysfunction and injury—admit to the ICU

Table 9.4 Thrombolytic therapy regimens for acute PE

Drug	Protocol
Streptokinase	250,000 U IV (loading does during 30 min; then 100,000 U/h for 24 h)
Urokinase	2,000 U/lb IV (loading does during 10 min; then 2,000 U/lb/h for 12–24 h)
Tissue-type plasminogen activator	100 mg IV during 2 h

Step 6: Identify the risk of adverse outcome for triage

- Risk stratification should be done promptly because fatal PE generally occurs early after hospital admission (Table 9.3).
- It is based on clinical features and markers of myocardial dysfunction or injury.
- If the patient is hemodynamically stable, then order TEE, troponin, and brain natriuretic peptide (BNP) levels.
- Myocardial dysfunction (right ventricular dilatation, hypokinesia, and ventricular septal bowing) based on echo and injury markers (elevated troponin and BNP) is useful and helps decide about thrombolysis, as mentioned below (Table 9.3).

The risk of adverse outcome is more in the following situations:
Shock (systolic blood pressure <90 mmHg) and/or BP drop ≥40 mmHg for >15 min and sustained hypotension
Immobilization due to neurological disease
Age 75 years or more
Cardiac, renal, or respiratory disease or cancer

Step 7: Consider thrombolysis

(a) If the patient is hemodynamically unstable
  - Admit to the ICU
  - Start anticoagulation, preferably intravenous UFH. Keep APTT time 1.5–2.5 to normal.
  - Administer thrombolytic therapy (Table 9.4) if there are no contraindications (Table 9.5). Discontinue heparin during thrombolysis.
  - Give other supportive measures to stabilize the patient.

(b) Hemodynamically stable patients with right myocardial dysfunction and injury suggested by TEE and markers (raised troponin and BNP) may also be considered for thrombolytic therapy if there are no contraindications (Table 9.5).

Table 9.5 Contraindication for thrombolytic therapy

Absolute contraindications
Prior intracranial hemorrhage
Known structural cerebral vascular lesion
Known malignant intracranial neoplasm
Ischemic stroke within 3 months
Suspected aortic dissection
Active bleeding or bleeding diathesis (excluding menses), significant closed-head trauma or facial trauma within 3 months
Relative contraindications
History of chronic, severe, poorly controlled hypertension
Severe uncontrolled hypertension on presentation (systolic blood pressure >180 mmHg or diastolic blood pressure >110 mmHg)
Traumatic or prolonged (>10 min) CPR or major surgery less than 3 weeks
Recent (within 2–4 weeks) internal bleeding
Noncompressible vascular punctures
For streptokinase/anistreplase—prior exposure (more than 5 days ago) or prior allergic reaction to these agents
Pregnancy
Active peptic ulcer
Current use of anticoagulant (e.g., warfarin sodium) that has produced an elevated international normalized ratio (INR) > 1.7 or PT > 15 s

Step 8: Hemodynamically stable patients with PE without myocardial dysfunction or injury

- Admit to the ward.
- Anticoagulate with LMWH or fondaparinux or UFH.
- Closely watch for vitals and respiratory distress. Consider early mobilization.

Step 9: Consider invasive treatment

Patients in whom thrombolytic therapy is contraindicated and whose hemodynamic status does not improve with medical treatment, the following should be considered:

- Percutaneous mechanical thrombectomy (thrombus fragmentation and aspiration)
- Surgical embolectomy

Step 10: Initiate vitamin K antagonist therapy

- Vitamin K antagonist (warfarin) should be initiated as soon as possible, preferably on the first treatment day, and heparin should be continued.
- Heparin should be discontinued when INR reaches a level of 2.0 or higher for at least 24 h. Duration of treatment is usually for 3–6 months.
- LMWH is preferred over warfarin in cancer and in pregnant women for long-term treatment.

Step 11: Inferior vena caval filters

They are indicated in the following conditions:

- Contraindication to anticoagulation therapy
- Recurrent thromboembolism despite anticoagulant therapy
- Bleeding while on anticoagulants

Step 12: Long-term treatment

Patients should be started on lifelong anticoagulant treatment in the following conditions:

- Recurrent PE
- Cancer

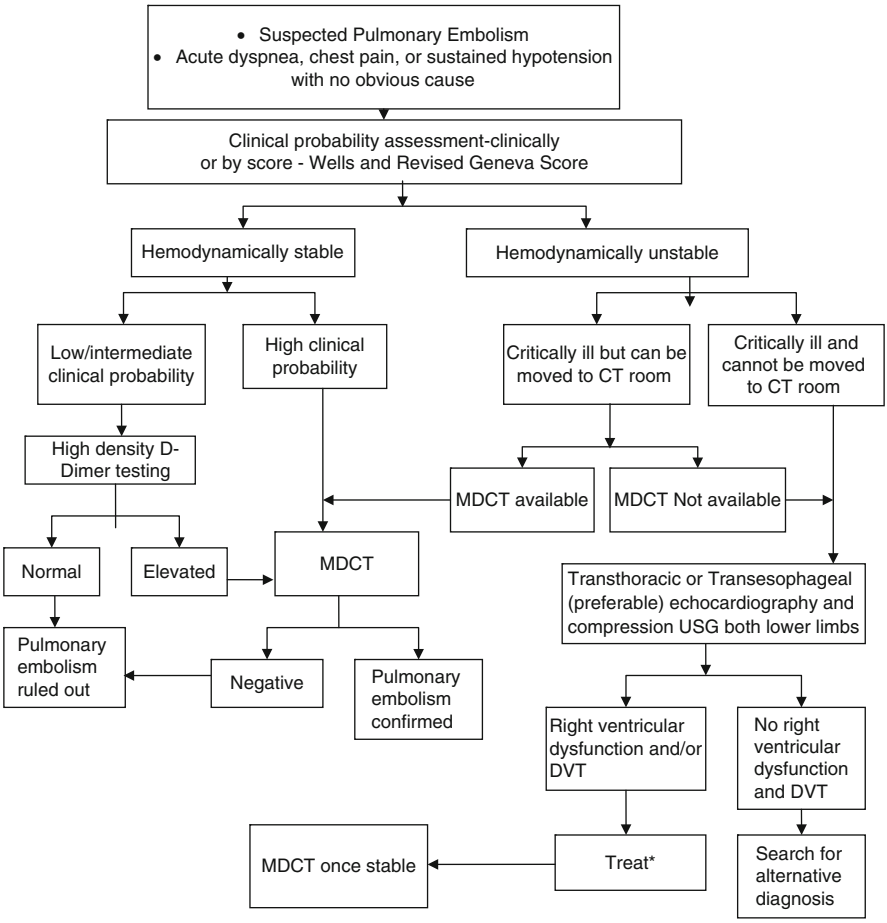

Fig. 9.1 Approach to a patient of suspected acute pulmonary embolism. *MDCT* Multidetector CT with pulmonary angiography, *Please refer to text

Step 13: Prevent venous thromboembolism

Approximately 90% of PEs originate from DVT of proximal leg veins, which are preventable with adequate prophylaxis. See the Chap. 79 on comprehensive ICU care.

Summary of management of suspected pulmonary embolism is given in Fig. 9.1.

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Severe Community-Acquired Pneumonia

10

Subhash Todi and Rajesh Chawla

A 50-year-old male smoker presented to the emergency department with fever and acute shortness of breath for the past 2 days. He had a respiratory rate of 30/min, blood pressure of 140/90, pulse 110/min regular, and SpO_2 88% on 2 L nasal cannula. He was alert and communicating. He had a history of hypertension and diabetes. He had brought a chest X-ray, which showed left lower zone opacity.

Community-acquired pneumonia is a common illness affecting 2–3 million patients each year in the USA. Only about 20% of patients require hospitalization, of which approximately 10–20% require intensive care unit (ICU) care. Mortality in hospitalized patients can be up to 30%, of which majority occur in patients admitted to the ICU.

Step 1: Initiate resuscitation
The patient should be resuscitated as described in Chap. 78.

Step 2: Assessment of severity
Many scoring systems have been suggested to assess the severity of community-acquired pneumonia (CAP). This is best done by a simple CURB-65 score. The CURB-65 score is based on five easily measurable factors (score 1 for each factor).

- Confusion
- Urea (>20 mg/dL)
- Respiratory rate more than 30 breaths/min

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- Blood pressure (systolic <90 mmHg or diastolic <60 mmHg)
- Age more than 65 years

The patient with a score of 3 or more should be assessed for intensive care unit (ICU) care. The simplified version of CURB -65 is CRB-65 which has similar predictability of severity and mortality in hospital settings.

Step 3: Start empiric antibiotics

- While initial resuscitation is going on, the cornerstone of the therapy for suspected infection is prompt and empiric antibiotics at the earliest.
- Ideally, one should send blood and sputum culture prior to starting antibiotics, but if these are delayed beyond 1 h for logistic reasons, antibiotics should be given without delay. The initial choice of antibiotics is of utmost importance because an inappropriate choice can increase mortality.
- A detailed history should be taken to identify patients who are at a high risk of drug-resistant infection, as mentioned below.
  - Previous hospitalization in 9 months
  - Previous antibiotics in 3 months
  - Comorbidity—liver failure, renal failure, chronic obstructive pulmonary disease (COPD), heart failure, diabetes, asplenia
  - Steroid use, immunosuppressive drugs
  - Details of the antibiotics used recently
- Principles of choosing an antibiotic (Tables 10.1, 10.2 and 10.3):
  - Cover common organisms responsible for pneumonia: both typical and atypical.

Table 10.1 Common organisms responsible for severe pneumonia, requiring ICU admission

Streptococcus pneumoniae 17%
Legionella 10%
Staphylococcus aureus (methicillin-sensitive *S. aureus*) 5%
Gram-negative bacilli (non-ESBL) 5%
Haemophilus influenzae 3%
Respiratory viruses 4%
Gram-negative bacilli (ESBL)
Pseudomonas
Community-acquired methicillin-resistant *S. aureus* (MRSA)
Unknown 41%

Table 10.2 Antibiotic choices in patients with no risk factors

A beta-lactam (cefotaxime, ceftriaxone, or ampicillin-sulbactam) plus azithromycin
Or
A beta-lactam (cefotaxime, ceftriaxone, or ampicillin-sulbactam) plus a respiratory fluoroquinolone (levofloxacin,moxifloxacin)
Or
For penicillin-allergic patients, a respiratory fluoroquinolone and aztreonam

Table 10.3 Antibiotic choice in a patient at risk of drug-resistant infection

1. If ESBL or pseudomonas is a concern
An antipneumococcal, antipseudomonal beta-lactam (piperacillin-tazobactam, cefepime, imipenem, or meropenem) plus either ciprofloxacin or levofloxacin (750 mg)
Or
The above beta-lactam plus an aminoglycoside and azithromycin
Or
The above beta-lactam plus an aminoglycoside and an antipneumococcal fluoroquinolone (for penicillin-allergic patients, substitute aztreonam for beta-lactam)
2. If MRSA is a concern
Add vancomycin or linezolid

- Cover resistant organisms such as extended-spectrum beta-lactamases (ESBL), in patients at risk.
- Avoid the antibiotic class to which patients have recently been exposed.
- Use parenteral antibiotics.
- Use antibiotics in adequate dose and frequency (see Chap. 49).
- Follow antibiotic policy of your unit/hospital for severe pneumonia.

Step 4: Order investigations

While initial resuscitation and empirical antibiotics are being given, basic diagnostic workup should be performed. The workup should include the following:

- Complete blood cell count
- Blood culture—two sets
- C-reactive protein
- Urea, creatinine
- Liver function test, prothrombin time
- Serum electrolytes
- Arterial blood gas, lactate
- Urine for microscopy
- Chest X-ray, electrocardiogram
- Echocardiogram; optional if patient is in septic shock
- Sputum sample should be a representative one and should reach the laboratory without delay
- Sputum—Gram stain, aerobic culture and sensitivity (C&S)
- Sputum cytology
- Urine for Legionella antigen, pneumococcal antigen (if available)

Step 5: Further supportive therapy needs to be instituted simultaneously

- Severe pneumonia with septic shock and multiorgan failure should be treated according to sepsis guidelines (Chap. 50).
- Aerosolized nebulization of bronchodilators should be routinely used especially if a patient has a history of COPD or asthma.

Table 10.4 Noninfectious causes

Heart failure
Cryptogenic organizing pneumonia
Malignancy
Pulmonary embolism
Pulmonary eosinophilic pneumonia
Hypersensitivity pneumonitis
Vasculitis—Wegner's granulomatosis

- *Noninvasive ventilation*: For patients with increased work of breathing, especially in COPD with acute exacerbation, a trial of noninvasive ventilation is worthwhile. These patients should be closely monitored for subjective improvement and an improving blood gas at 2 h. If there is no improvement, they should be intubated and ventilated without delay.
- *Steroids*: Continue equivalent dose of intravenous steroids if the patient is receiving it for asthma or COPD and give low-dose intravenous steroids in patient with vasopressor-resistant septic shock.
- Other general supportive ICU measures should be instituted (see Chap. 78).

Step 6: Consider the following for a patient not responding to initial therapy

With appropriate antibiotic therapy, some improvement in patient's clinical course should be seen within 48–72 h. This should be assessed clinically, as radiographic resolution takes more time.

For nonresponders the following conditions should be considered:

- Organisms not covered by empiric choice of antibiotics.
- Atypical organisms—tuberculosis, strongyloidosis, melioidosis, H1N1 influenza, etc.
- Complicated pneumonia—lung abscess, Empyema, intrabronchial obstruction, resistant organisms.
- Nosocomial problem—secondary infection.
- Alternative diagnosis—look for noninfectious causes in nonresponding patients and investigate appropriately (Table 10.4).

Step 7: Further investigations

Further diagnostic workup should be undertaken judiciously keeping the cost factor in mind to differentiate the possibilities in nonresponders.

- Bronchoscopy with bronchoalveolar lavage.
- In intubated patients, endotracheal suction or nonbronchoscopic lavage may be sent for quantitative culture.
- Serology for HIV1 and II, H1N1, antinuclear factor, antineutrophil cytoplasmic antibodies, *Legionella*
- Nasal swab for MRSA, viral panel
- Pro-brain natriuretic peptide (BNP) levels
- D-dimer, leg venous Doppler
- Ultrasonogram (USG) chest/computed tomographic scan (CT) chest
- Procalcitonin

Step 8: Give antibiotics for adequate duration

- Duration of antibiotics should be individualized based on clinical response, type of organisms, biomarker response, development of complications, and comorbidities.
- Minimum 5 days of antibiotic is recommended.
- Prolonged antibiotics up to 2 weeks should be considered in selected cases such as slow responders, *Pseudomonas*, and *Staphylococcus* infection, lung abscess, empyema, and metastatic infection.

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Ventilator-Associated Pneumonia

11

Rajesh Pande

A 50-year-old diabetic male patient was admitted to the hospital with ischemic stroke (GCS = E1V1M3). He was put on invasive positive-pressure ventilation support. On the fourth day of ICU stay, he developed fever (38.6°C), a rise in total leukocyte count (15.6, N 93%), and heterogeneous, ill-defined shadows in the right lower zone in the chest X-ray. Chest auscultation revealed bronchial breathing in the right infra-axillary area, and the nurse reported an increase in amount and purulence of secretions requiring frequent suctioning. The patient needed 5 mcg/min noradrenaline to maintain systolic blood pressure of more than 100 mmHg.

When a patient on ventilatory support develops new infiltrate in the chest X-ray along with fever and leukocytosis after 48 h of intubation, it is suggestive of ventilator-associated pneumonia (VAP). This occurs in 9–27% of intubated patients. The risk increases with the duration of mechanical ventilation.

Step 1: Initiate resuscitation
The patient should be resuscitated, as mentioned in Chap. 78.

Step 2: Rule out noninfectious cause of chest infiltrate
There are various noninfectious conditions that can result in pulmonary shadows, which must be ruled out:

- Atelectasis: It is common in postoperative period following upper abdominal surgery due to hypoventilation. Left lower lobe atelectasis is very common following coronary artery bypass grafting. Radiological signs include displaced

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Table 11.1 The modified CPIS

CPIS points	0	1	2
Tracheal secretions	Rare	Abundant	Abundant + purulent
Chest X-ray infiltrates	No infiltrate	Diffused	Localized
Temperature (°C)	≥36.5 and ≤38.4	≥38.5 and ≤38.9	≥39 or ≤36
Leukocytes count (per mm^3)	≥4,000 and ≤11,000	<4,000 or>11,000	<4,000 or >11,000+ band forms ≥500
P_{aO2}/F_{IO2} (mm Hg)	>240 or ARDS		≤240 and no evidence of ARDS
Microbiology	Negative		Positive

fissures; crowded bronchovascular markings and shifts in the positions of the hila, diaphragm, and mediastinum; and increased density or radiopacity of the lung tissue. Fever and leukocytosis may not always be present.

- Aspiration: Right lower lobe is commonly involved. Infiltrates may take up to 12 hrs to appear in the chest x-ray after the event. History of vomiting or bile-colored endotracheal secretions on suctioning is a good clue to the diagnosis. It may be a purely chemical pneumonitis initially, caused by acidic gastric contents.
- Pulmonary embolism: It is generally acute onset in the background of risk factors for deep venous thrombosis and pulmonary embolism (PE).
- Pulmonary hemorrhage may resemble dense alveolar consolidation. Generally, endotracheal (ET) secretions are bloodstained. Coagulation profiles or other immunological markers may be deranged.
- Cardiogenic pulmonary edema.
- Acute respiratory distress syndrome (ARDS).
- Fluid overload.
- Drug reactions.
- Cryptogenic organizing pneumonia.

Scoring systems such as the clinical pulmonary infection score (CPIS) (Table 11.1) or National Nosocomial Infections Surveillance (NNIS) and biomarkers are a great help in differentiating the pulmonary infiltrate as VAP or noninfectious.

The modified CPIS at baseline is calculated from the first five variables. For positive Gram stain and culture, two points are added to the CPIS baseline score. A score of more than six at baseline or after incorporating the Gram stain or culture result is considered suggestive of pneumonia.

Step 3: Send cultures and initiate empiric antibiotics

- While initial resuscitation is going on, the cornerstone of therapy in suspected infection is prompt and empiric antibiotic therapy.
- Ideally, one should send blood and endotracheal aspirate or do fiberoptic bronchoscopy with bronchoalveolar lavage for Gram stain and quantitative aerobic culture prior to starting antibiotics.
- If there is delay in obtaining samples for logistic reasons beyond an hour, antibiotics should be given without delay.

Table 11.2 Microoragnisms causing early and late VAP

Early-onset VAP	Late-onset VAP
Within 4 days of ventilation	≥5 days
Pathogens: *S. aureus* (usually methicillin-sensitive *S. aureus* (MSSA)), *Streptococcus pneumoniae*, *Haemophilus influenza*, and Gram-negative enteric bacilli	MDR pathogens: MRSA, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and *Stenotrophomonas maltophilia*
Risk of MDR pathogens similar to late onset if previous hospitalization or exposure to antibiotics is present	Mortality 33–50%

- The initial choice of antibiotics is of utmost importance. An inappropriate initial choice increases mortality.
  1. Selection of empiric antibiotic therapy should be based on the following:
     (a) Patient risk factors
     (b) Early- or late-onset pneumonia (Table 11.2)
     (c) Recent exposure to specific antibiotic classes
     (d) Local epidemiology of infection and antibiogram
     (e) Previous antibiotic therapy
  2. Detailed history should be taken to identify patients who are at high risk of drug-resistant infection as mentioned below:
     - Antimicrobial therapy in preceding 90 days
     - Current hospitalization of 5 days or more
     - High frequency of antibiotic resistance in the community or in the specific hospital unit
     - Presence of risk factors for health care-associated pneumonia (HCAP)
       - Hospitalization for 2 days or more in preceding 90 days
         – Residence in a nursing home or extended care facility
         – Home infusion therapy (including antibiotics)
         – Chronic dialysis within 30 days
         – Home wound care
         – Family member with multidrug-resistant pathogen
         – Immunosuppressive disease and/or therapy
  3. Principles of choosing an antibiotic:
     - Cover common organisms responsible for pneumonia depending on the epidemiology of infection and their sensitivity in your ICU.
     - Cover resistant organisms like ESBL in patients at risk.
     - Avoid the antibiotic class to which the patient has been recently exposed.
     - Use parenteral antibiotics.
     - Use antibiotics in adequate dose and frequency (see Chap. 49).
  4. Follow the antibiotic policy of your unit/hospital.
     A. Limited-spectrum antibiotic therapy is appropriate in patients with suspected VAP with no risk factors for multidrug-resistant (MDR) pathogens (early-onset pneumonia).

- Recommended antibiotics for early-onset pneumonia as per the guidelines are ceftriaxone or fluoroquinolone, or ampicillin/sulbactam or ertapenem.

B. Late-onset VAP (Table 11.2)
- Gram-negative bacteria (GNB) including ESBL-producing Klebsiella, *Escherichia coli*, MDR Acinetobacter, MDR *Pseudomonas aeruginosa*, methicillin-resistant *Staphylococcus aureus* (MRSA), and rarely Enterococcus (vancomycin-resistant enterococci) are the common organisms causing late-onset pneumonia.
- These ESBL bugs are resistant to the third- and fourth-generation cephalosporins and show an inoculum effect to beta-lactam/beta-lactamase inhibitor (BL/BLI) combinations.
- The suggested recommendation is to use carbapenems as empirical therapy in late-onset VAP. In less critically ill patients, BL/BLI combinations may be used.
- For Pseudomonas infections, two antipseudomonal agents should be used. The treatment should be started on the basis of local epidemiology of the ICU. Many of the Pseudomonas species are MDR and are sensitive only to colistin or polymyxin B (use adequate dosage).
- Vancomycin is the preferred choice for Gram-positive organisms (MRSA). Teicoplanin or Linezolid can also be used.
- MDR Acinetobacter strains are currently sensitive only to colistin, high doses of sulbactam, and tigecycline.

Step 4: Send further investigations

While initial resuscitation and empirical antibiotics are being given, basic diagnostic workup should be sent. These should include the following:
- Complete blood count
- CRP, urea, creatinine
- Liver function test
- Prothrombin time, Na, K
- Blood culture—two sets if not sent earlier
- Endotracheal aspirates or fiberbronchoscopy with protected specimen brush (PSB) or bronchoalveolar lavage (BAL)
- Arterial blood gas, lactate
- Procalcitonin
- Urine for microscopy
- Chest X-ray
- ECG or echocardiogram optional if the patient is in septic shock

Step 5: De-escalate antibiotics
- Clinical improvement usually takes 2–3 days, and therapy should not be changed during this time unless the condition deteriorates.
- If protected specimen brush (PSB) or bronchoalveolar lavage (BAL) culture results are negative in a patient who is clinically improving and hemodynamically

stable, antibiotic therapy should be discontinued or given for a short duration (5 days).

- If the culture is negative for MRSA, linezolid or vancomycin can be safely stopped, and if the culture is positive for MRSA, other antibiotics can be stopped.
- If no organism is found, one should try to look for other causes of lung shadows, that is, atelectasis, collapse, aspiration, pulmonary embolism, and hemorrhage. It decreases unnecessary exposure to antibiotics and helps to reduce resistance to antibiotics.
- Change to oral therapy once the patient accepts orally and is hemodynamically stable.
- The initial antibiotics should be given intravenously with changeover to oral therapy in responsive patients with an intact gastrointestinal function. The organism should be sensitive to oral antibiotics.
- Fluoroquinolones and linezolid are equally bioavailable in either intravenous or oral preparations.
- All patients with VAP (except the patients with VAP due to non-fermenting Gram-negative bacilli) should receive antibiotics for not more than 8 days.
- Patients with VAP due to *P. aeruginosa* or Acinetobacter species may be given a 2-week therapy to prevent the risk of recurrence.
- Antibiotic dosing should be adjusted in patients with impaired renal or hepatic function (Fig. 11.1).

Step 6: Prevention of VAP in the ICU

Evidence-based guidelines have recommended a number of measures that may affect the development of VAP (labeled as VAP bundles)

Pharmacological methods	Non-pharmacological methods
1. Hand hygiene with alcohol based solution	1. Use of noninvasive mask ventilation
2. Oral care with chlorhexidine	2. Avoid reintubation
3. Short course of antibiotic therapy (when clinically applicable)	3. Orotracheal and orogastric intubation
4. Sedation control and weaning protocol	4. Use of heat moisture exchanger
5. Restricted blood transfusion	5. Closed endotracheal suction
6. Vaccines (influenza and pneumococcal)	6. Subglottic secretion drainage
	7. Change of ventilator circuit only for each new patient
	8. Semirecumbent positioning
	9. Shortening duration of mechanical ventilation
	10. Rotational beds
	11. Adequate intensive care staffing
	12. Use of protocol bundles
	13. Education and training

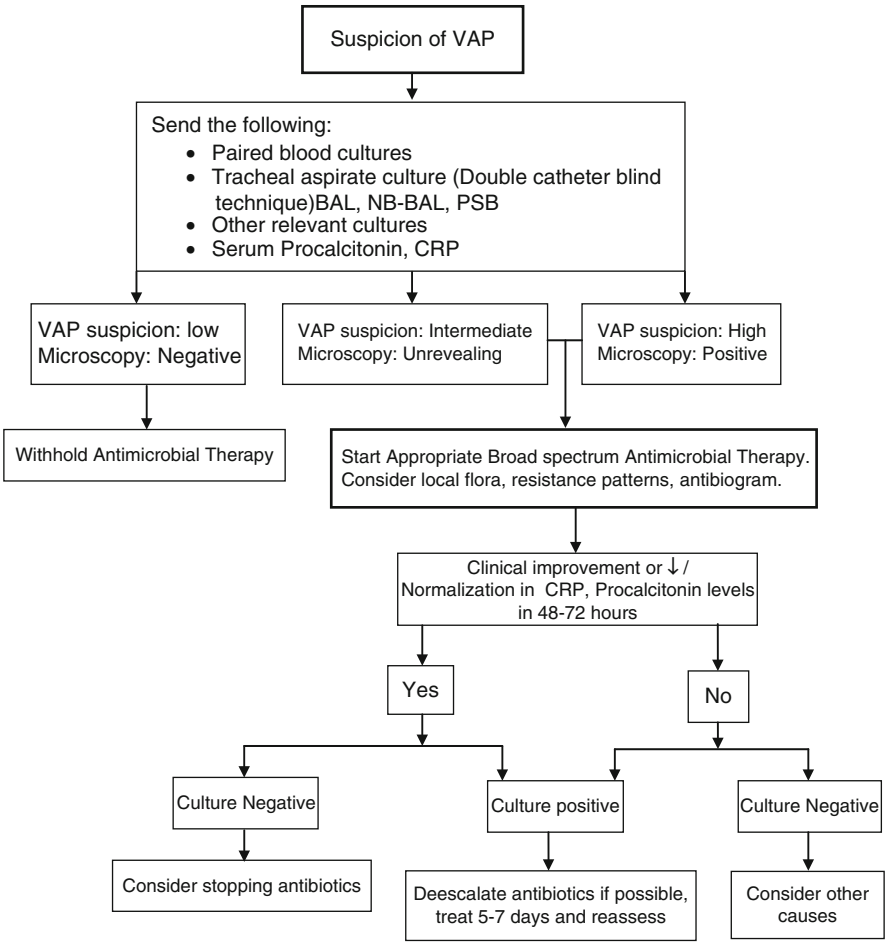

Fig. 11.1 Management of ventilator-associated pneumonia

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Pleural Diseases

12

Sudha Kansal and Rajesh Chawla

A 65-year-old chronic male smoker, with a known case of coronary artery disease with history of congestive heart failure, presented with increasing shortness of breath. He had right-sided pleuritic chest pain. He was afebrile, tachycardic, tachypneic, and hypoxemic on room air. Chest skiagram done in triage showed bilateral pleural effusion, with more pleural fluid on the right side than on the left side. The patient was shifted to the ICU.

Pleural effusion is a relatively uncommon cause for admission to intensive care unit; however, it occurs during stay in the ICU due to complications of diseases and procedures performed in these patients. It may be difficult to detect pleural effusion and pneumothorax in critically ill patients in supine chest X-ray.

Step 1: Initiate resuscitation and take history

- After initial resuscitation, take a detailed history of chest pain, palpitation, fever, cough with expectoration, hemoptysis, decrease in urine output, edematous feet, distension of abdomen, right hypochondrial pain, and weight loss.
- Also, inquire about medication and other relevant history, keeping in mind the common causes of pleural effusion in the ICU (Table 12.1).

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Table 12.1 Common causes of pleural effusion in the ICU

Causes	Types of fluid
Congestive heart failure (36%)	Transudate
Pneumonia (22%)	Exudate
Malignancy (14%)	Exudate
Pulmonary embolism (11%)	Both
Viral disease	Exudate
Postcoronary artery bypass graft	Exudate
Cirrhosis with ascites	Transudate
Fluid overload/renal failure	Transudate
Acute respiratory distress syndrome	Transudate
Severe hypoalbuminemia	Transudate
Tuberculosis	Exudate

Step 2: Perform the examination

- Perform a thorough examination to establish the diagnosis. Check vital signs, JVP, cyanosis, SpO_2, pallor, edematous feet, lymphadenopathy, and any evidence of deep venous thrombosis (DVT).
- Systemic examination should be carried out for S3, asymmetric breath sounds, crepitations, bronchial breathing, hepatomegaly, right hepatic tenderness, and ascites.

Step 3: Plan investigations

- Hemogram.
- Renal function tests.
- Liver functions tests, prothrombin time/partial thromboplastin time (PT/PTT).
- ECG.
- 2D echo.
- Cardiac enzymes—BNP.
- Relevant cultures—depending on the suspected etiology.
- Chest X-ray—chest skiagram shows obliteration of the costophrenic angle. Supine portable chest X-ray may not show classical features of pleural effusion. Subtle features such as haziness over entire hemithorax and loss of diaphragm outline may only be noted.
- Ultrasonography (USG) of the chest—one may do USG of the chest for evaluation and quantification of fluid. This helps to know whether fluid is free or loculated. USG may also help to know the character of fluid depending on the echogenicity.
- A contrast-enhanced CT (CECT) of the thorax is useful in a case of undiagnosed effusion as it helps to evaluate underlying lung, pleural, and mediastinal pathologies.
- CT pulmonary angiography should be done if there is suspicion of pulmonary embolism.

Step 4: Pleurocentesis

- One need not do pleurocentesis if the cause of pleural fluid is obvious. Indications of pleurocentesis could be diagnostic or therapeutic (Table 12.2).

Table 12.2 Indications of pleurocentesis

Diagnostic
Clinically significant pleural effusion
Pleural fluid of more than 10 mm on lateral decubitus X-ray
If undiagnosed effusion persists despite >3 days of diuresis or is unilateral in patients with congestive heart failure
An air-fluid level in pleural space
Suspicion of empyema
Therapeutic
If the patient has shortness of breath at rest

- Aspiration can be done with or without USG guidance (depends on the experience of the operator and amount of effusion). However, in mechanically ventilated patients, it is advisable to do aspiration under the USG guidance.
- Chest skiagram, postprocedure—this is not required routinely. Do it after the procedure if air is obtained during thoracocentesis or the patient complains of cough, chest pain, dyspnea, and in all mechanically ventilated patients.

Step 5: Send pleural fluid investigations

- pH
- Protein, albumin
- Glucose
- Lactate dehydrogenase (LDH)
- Adenosine deaminase (ADA)
- Amylase if indicated
- Total cell count, differential cell count
- Cytology
- Microbiological investigations depending on the suspected illness

It is important to differentiate between exudate and transudate to diagnose the etiology of pleural effusion (Tables 12.3 and 12.4).

Table 12.3 Differentiating exudates from transudate

Fluid is exudate if any of the following is present:
(a) Pleural fluid/serum protein ratio—>0.5
(b) Pleural fluid/serum LDH ratio—>0.6
(c) Pleural fluid LDH—>2/3 upper limit of serum LDH
(d) Pleural fluid protein—>2.9 g/dL
(e) Serum albumin–pleural fluid albumin—<1.2
(f) Serum protein–pleural fluid protein gradient—<3.1
(g) Pleural fluid cholesterol—>60 mg/dL

Table 12.4 Investigations of exudative pleural effusion

If infectious effusion—Gram stain and C/S
If malignant—cytology
If TB—ADA, PCR
If chylothorax—triglyceride cholesterol, chylomicron estimation
If clinical suspicion of pulmonary embolism—multidetector row CT (MDCT) pulmonary angiography

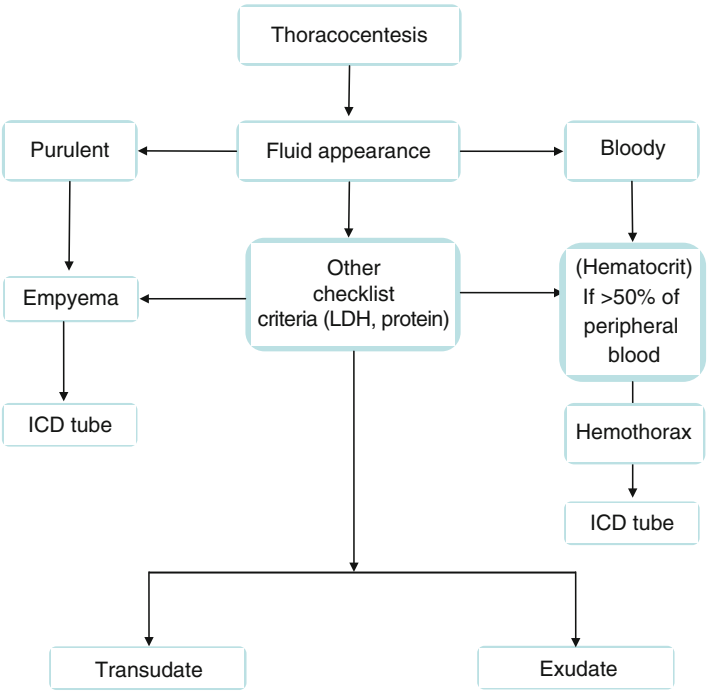

Fig. 12.1 The workup plan for the diagnosis of pleural effusion

The workup plan for the diagnosis of pleural effusion is described in Fig. 12.1.

Step 6: Disease-specific Management

The management of pleural effusion in special situations is described as follows:

A. *Parapneumonic effusion*

When the patient develops parapneumonic effusion, the main treatment consists of antibiotics. A parapneumonic effusion is aspirated only if it fulfills the criteria mentioned above for indication of pleurocentesis. It is important to differentiate between complicated and uncomplicated effusions.

(a) Place the ICD tube in parapneumonic effusion only if it is complicated.

- It is loculated effusion or fills more than half of hemithorax, or an air-fluid level is seen.

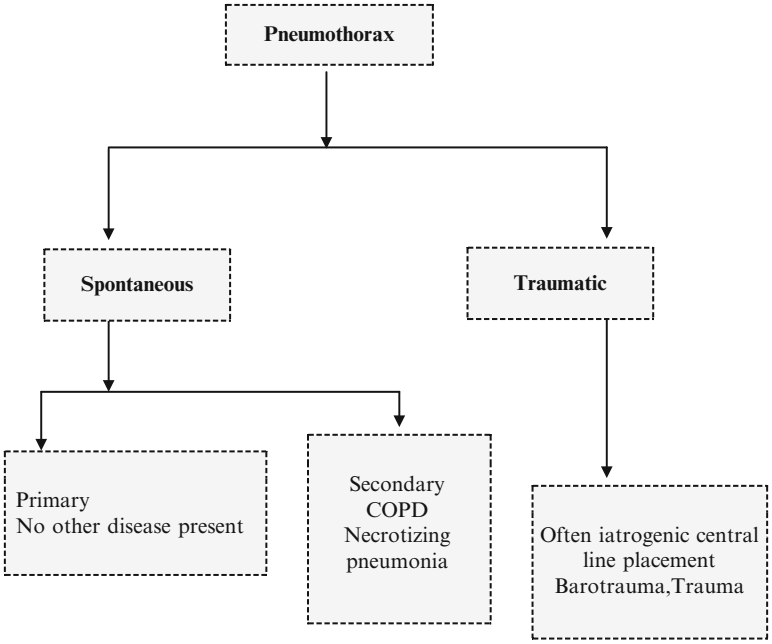

Fig. 12.2 Etiology of pneumothorax

- Pus on aspiration, Gram stain, or culture positive.
- pH less than 7.2, glucose less than 60 mg%.

(b) Remove the tube when:
- The patient has improved or drain is less than 50 mL/day.

(c) If parapneumonic effusion does not improve:
- Consider fibrinolysis with streptokinase, thoracoscopy, or thoracotomy.

B. Malignant effusion
- Often large and symptomatic.
- Common in lung cancer, breast cancer and lymphoma, gastrointestinal tract malignancy, and unknown primary.
- If recollects in less than 3 weeks and the patient is symptomatic—do tube thoracostomy and pleurodesis.

C. Pleural effusion associated with pulmonary embolism

If there is high clinical suspicion in appropriate setting, investigate and treat them (see Chap. 9).

D. Undiagnosed pleural effusion
- In 20% effusion, despite extensive investigation, cause may not be found.
- If clinically stable, continue conservative treatment.
- If deterioration in condition, plan thoracoscopy.

Pneumothorax
- Air in pleural space can be a medical emergency in ICU patients and requires immediate attention.

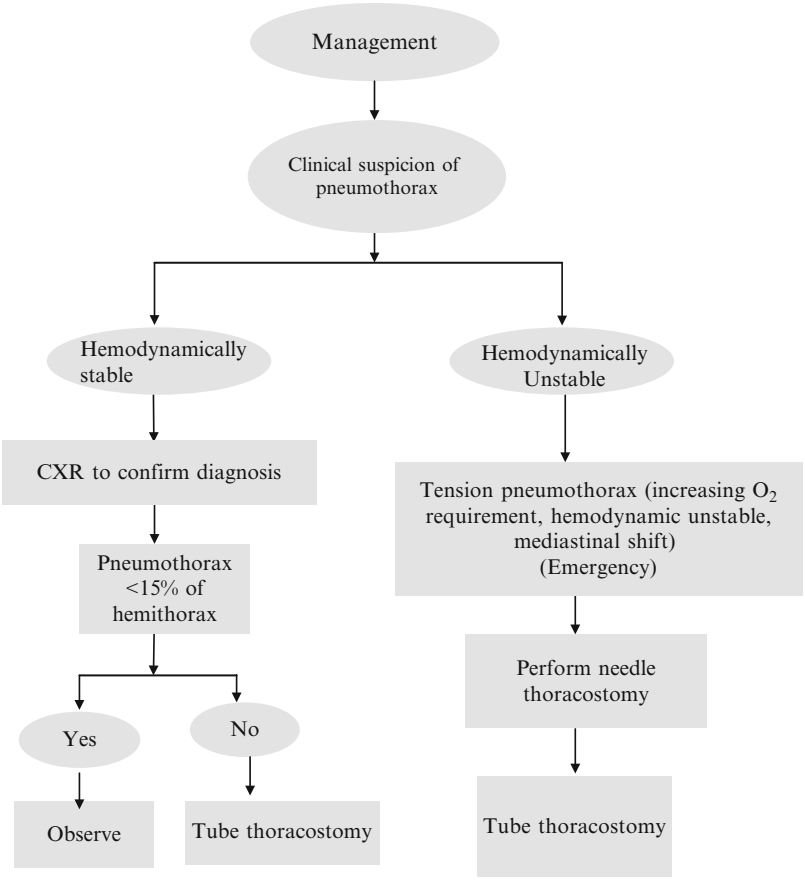

Fig. 12.3 Management of pneumothorax

- Pneumothorax can be spontaneous or traumatic. Spontaneous pneumothorax can be primary when no cause is identified or secondary if there is underlying disease.
- Traumatic pneumothorax also includes iatrogenic pneumothorax (central line, barotrauma) (Fig. 12.2).
  A brief outline of management of pneumothorax is described in Fig. 12.3.
- However, if the patient is on mechanical ventilation, any degree of pneumothorax must be drained by tube thoracostomy.

Step 7: Remove ICD

- Pneumothorax resolved.
- No air leak for 24 h and lung remains expanded after clamping chest tube for 6–12 h.
- Lung fully expanded for 24 h.

- However, if lungs are extensively affected in patients on mechanical ventilation who require high positive end-expiratory pressure (PEEP), then better to remove ICD only when the patient improves and off positive-pressure ventilator.

Suggested Reading

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Websites

1. www.winfocus.org
A website on lung ultrasound by a dedicated group
2. www.criticalecho.com
A comprehensive site for ICU sonography

Sleep-Disordered Breathing

13

Jagdish Chander Suri

A 52-year-old obese male patient was admitted to the intensive care unit (ICU) with history of fever, increased cough with sputum, and gradually progressive breathlessness for 7 days. On examination he was observed to be drowsy. He had history of snoring and excessive daytime sleepiness. His arterial blood gases were suggestive of acute on chronic respiratory acidosis with type 2 respiratory failure. He was treated in the ICU with antimicrobials, bronchodilators, and mechanical ventilation.

Sleep-disordered breathing (SDB) has been increasingly recognized as an independent cause or an important factor contributing to the development of acute respiratory failure in the ICU. Appropriate and timely treatment can change the outcomes in these patients.

Step 1: Initiate resuscitation

- Initiate resuscitation as described in Chap. 78.
- It is important to suspect the presence of SDB and obesity hypoventilation syndrome (OHS) in every case of hypercapnic respiratory failure so that an early and effective treatment can be initiated.
- Apply noninvasive ventilation (NIV) immediately as these patients with SDB and hypercarbic respiratory failure respond very well to this modality.

The goals of treatment are to reverse sleep-induced hypoventilation and upper airway obstruction and to optimize oxygenation. The algorithm for titration of NIV is shown in Fig. 13.1.

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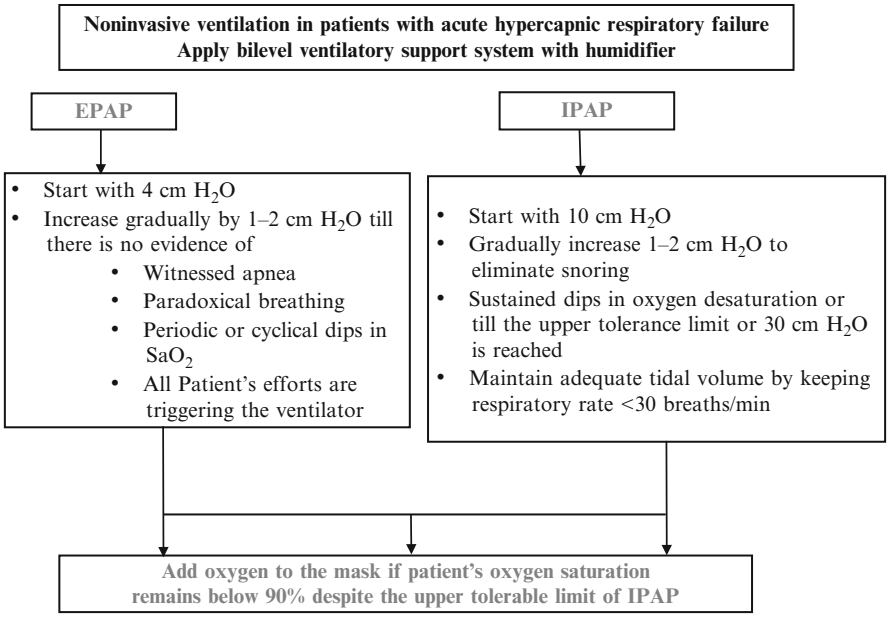

Fig. 13.1 Suggested guidelines for titration of NIV

Step 2: Take a detailed history and do physical examination

Identify symptoms and signs of obstructive sleep apnea–hypopnea syndrome and obesity hypoventilation syndrome.

In all obese patients with hypercapnic respiratory failure, SDB should be considered a possible cause. The common symptoms are as follows:

- Fatigue
- Breathlessness on minimal exertion
- Mood disorders
- Morning headaches
- Loud interrupted snoring
- Hypersomnolence
- Choking attacks during sleep
- Witnessed apneas
- Awakening, snorting, or gasping
- Unrefreshing sleep
- Large neck circumference
- Poorly controlled hypertension
- Craniofacial abnormalities (micrognathia, retrognathia, macroglossia)

Step 3: Admit to the ICU

The patient should be admitted to the ICU if any of the following criteria are met:

- Acute acidemia—pH less than 7.30
- Decreased level of consciousness or coma

- Hemodynamic instability
- Refractory hypoxemia
- Intolerance to continuous positive airway pressure (CPAP) therapy

Step 4: Understand respiratory failure in SDB

- SDB constitutes a spectrum of disorders of various severities with intermittent snoring as the mildest form at one end and OHS as the most severe form at the other end of the spectrum. Heavy snoring and upper airway resistance syndrome and mild, moderate, and severe sleep apnea lie in between these two extremes.
- The patients commonly encountered in the ICUs generally suffer from severe obstructive sleep apnea syndrome (OSAS) and/or OHS or those with overlap syndrome, that is, when OSAS occurs simultaneously with chronic obstructive pulmonary disease (COPD).

Respiratory failure in sleep occurs because of the following reasons:

- Increased airflow resistance due to partial or complete obstruction of the upper airway.
- Decreased ventilatory response to hypoxic and hypercapnic stimuli.
- Marked hypotonia of accessory muscles of respiration, particularly during rapid eye movement (REM) sleep leading to severe hypoventilation.
- Altered lung mechanics due to obesity result in decreased functional residual capacity (FRC), expiratory reserve volume (ERV), vital capacity (VC), and forced expiratory volume in 1 s (FEV1).
- The consequences of untreated SDB include hypertension, stroke, cardiac failure, and excessive daytime sleepiness.

Respiratory failure is usually precipitated by complicating respiratory illnesses such as infections, acute exacerbation of asthma, COPD, and congestive cardiac failure.

Step 5: Perform relevant laboratory investigations

- Complete blood counts
- Blood glucose (fasting and postprandial)
- Lipid profile
- Thyroid function test
- Serum electrolytes
- Arterial blood gases
- ECG
- Chest X-ray
- Echocardiography
- Spirometry

Step 6: Monitor closely during NIV

The following parameters should be monitored during treatment:

- The level of consciousness
- Vital signs

- Respiratory rate
- Use of accessory muscles
- SaO_2, end-tidal CO_2
- Triggering
- Patient–ventilator synchrony
- Esophageal pressure monitoring (selected cases)
- Arterial blood gas frequently

Precautions
- In patients with overlap syndrome, expiratory positive airway pressure (EPAP) higher than auto-positive end-expiratory pressure (auto-PEEP) may worsen the hyperinflation, leading to increase in respiratory rate and work of breathing.
- There may be worsening of blood gases in the first few days due to intense hypoventilation caused by rebound increase in delta and REM sleep.

Step 7: Intubate if indicated

Indication of intubation and mechanical ventilation
- NIV failure.
  - Worsening mental status
  - Deterioration of pH and $PaCO_2$ after 1–3 h of therapy
  - Refractory hypoxemia
  - Intolerance to NIV
- Hemodynamic instability.
- Inability to clear secretions.
- Intubation of the patient with severe OSAS or OHS is associated with significant difficulties and complications due to limited mouth opening and neck mobility.
- The pharynx is anatomically small with large tongue. The ability to withstand apnea or hypopnea is poor due to low oxygen reserves associated with decreased FRC.
- The intubation should be done by an experienced intensivist preferably with the help of a fiberoptic bronchoscope.

Indications of Tracheostomy
It was the main treatment before the development of NIV. Now, it is used occasionally in patients who cannot tolerate NIV or have poor compliance to NIV or who cannot be successfully extubated after a period of mechanical ventilation.

Step 8: Manage comorbid medical conditions
- Most patients of SDB and OHS have concomitant respiratory, cardiac, and metabolic comorbidities such as COPD, asthma, congestive heart failure, and diabetes.
- In addition to NIV and oxygen, the appropriate treatment of these conditions should also be instituted.

Step 9: Plan a sleep study (polysomnography) before discharge

- Although some patients may already have the diagnosis, majority of the patients presenting to the ICU with acute respiratory failure had no prior diagnosis.
- If the diagnosis of OSAS or OHS is suspected, a bedside sleep study may be performed for both diagnostic and titration purposes. However, if the bedside sleep laboratory is not available, the patient can be treated empirically with NIV with the help of a pulse oximeter, as shown in Fig. 13.1.

Diagnostic Criteria for SDB

- The newly revised International Classification of Sleep Disorders defines obstructive sleep apnea–hypopnea syndrome (OSAHS) as when a patient has a respiratory distress index (RDI) (apneas + hypopneas + respiratory effort-related arousals + flow limitations) of five or more than five per hour of sleep with the appropriate clinical presentation such as excessive daytime sleepiness, unrefreshing sleep, fatigue, insomnia, mood disorders, or other neurocognitive disturbances.
- The severity of SDB is assessed by the number of abnormal breathing events per hour of sleep, the degree of sleepiness, and the degree of oxygen desaturation during sleep.

Mild	AHI or RDI	5–15/h
Moderate	AHI or RDI	16–30/h
Severe	AHI or RDI	>30/h AHI

AHI apnea–hypopnea index, *RDI* respiratory disturbance index

Diagnostic Criteria for OHS

- BMI more than 30 kg/m^2
- Awake arterial hypercapnia ($PaCO_2 > 45$ mmHg)
- Exclusion of other causes of hypoventilation
- Polysomnography revealing sleep hypoventilation with nocturnal hypercapnia with or without obstructive apnea–hypopnea events

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   The objective of this study was to alert critical care physicians to the syndrome of obstructive sleep apnea with respiratory failure ("near miss" death) and to elucidate characteristics that might allow earlier recognition and treatment of such patients.

Websites

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   Postoperative complications in patients with obstructive sleep apnea
2. http://Chestjournal.chestpubs.org/content/118/3/591.full
   Cardiac rhythm disturbances in the obstructive sleep apnea syndrome

Oxygen Therapy

14

Surinder K. Jindal and Ashutosh Nath Aggarwal

A young female patient presented to the emergency department with history of sore throat, high-grade fever, and cough with minimal hemoptysis for the past 5 days. On examination, she was found to be in respiratory distress. Her chest examination report was normal. The chest skiagram showed bilateral infiltrates and SpO_2 was 80%.

Oxygen is the commonest drug used in patients admitted in Intensive Care Unit. There are various methods available for delivering oxygen. Overzealous treatment with oxygen should be avoided due to the risk of oxygen toxicity.

Step 1: Assess the need for oxygen therapy

- The need for oxygen therapy in the intensive care unit (ICU) depends on the presence of documented hypoxia and/or inadequate oxygenation.
- Presence of nonspecific symptoms and signs suggestive of hypoxia should be evaluated with objective measurements of oxygenation.
- Arterial blood gas analysis with measurement of oxygen (PaO_2) and carbon dioxide ($PaCO_2$) partial pressures remains the gold standard for hypoxia demonstration.
- Pulse oximetry is a noninvasive method, which provides arterial oxygen saturation (SpO_2) as a substitute for PaO_2 for routine monitoring. The reading of pulse oximetry could be inconsistent (see Chap. 15).

Oxygen is applied if any of the following is present:

- Hypoxia (i.e., PaO_2 <60 mmHg) due to any cause.

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- Respiratory failure due to
  - Acute respiratory distress syndrome
  - Acute exacerbation of chronic obstructive pulmonary disease (COPD) or asthma
  - Pneumonia
- In emergency situations (e.g., cardiorespiratory arrest, acute cardiogenic pulmonary edema, or stroke), oxygen administration may be initiated empirically, pending detailed clinical and laboratory evaluation. Blood gas analysis should be made available as early as possible.
- Normoxemic hypoxia (i.e., normal PaO_2) but presence of tissue hypoxia in the following conditions:
  - Severe anemia
  - Low cardiac output state
  - Hypotension
  - Severe sepsis
  - Vascular (arterial) occlusion
- Failure of tissues to utilize oxygen (e.g., poisoning)—histotoxic hypoxia.

Step 2: Initiate oxygen administration

- Before giving oxygen, one needs to ensure patency of the airways. This might require endotracheal intubation or tracheostomy.
- It is generally customary to start with a high FiO_2—100% for cardiorespiratory arrest and 50–100% for acute hypoxemic respiratory failure.
- The FiO_2 can be increased or decreased after the assessment of clinical and laboratory response to the initial administration.
- Relatively lower concentrations are used in patients with hypercapnic respiratory failure (such as COPD) with the preexisting chronic hypoventilation.
- High concentration of oxygen may worsen CO_2 retention and cause CO_2 narcosis by abolishing the hypoxic respiratory stimulation. However, optimum FiO_2 must be ensured since hypoxia is always more deleterious than hypercapnia. Various devices can be used for applying oxygen.

Administration Devices

1. *Source*: Most well-equipped ICUs have continuous pressurized oxygen and air supply available at each bed. In this fashion, both oxygen and air can be simultaneously fed into an oxygen blender to control the output FiO_2. Oxygen cylinders and concentrators are required as a backup source in case of failure of central supply.
2. *Oxygen delivery*: Oxygen is delivered either alone noninvasively or along with assisted respiratory support.
   A. *Stand-alone oxygen*
      - The ICU patients are sicker with high ventilatory requirements than the general ward patients. Higher concentrations of oxygen are required, which are provided with high-flow systems.

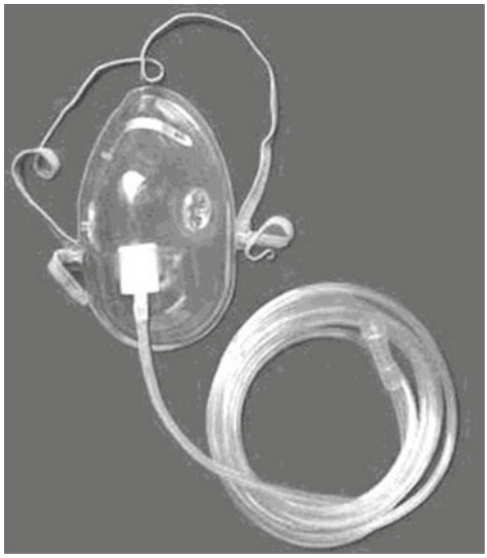

Fig. 14.1 Simple face mask

Nasal cannulation is usually insufficient in severe hypoxemic respiratory failure. The nasal cannula is a low-flow, low-oxygen device and cannot deliver tracheal FiO_2 more than 0.4–0.5. High flow rates do not result in high FiO_2 and have a drying and irritating effect on nasal mucosa.

Simple face mask is a low-flow delivery system which provides FiO_2 from 0.4 to 0.6 at flow rate of 5–8 L/min. This mask does not need tight seal (Fig. 14.1).

Venturi masks are preferred for precise titration of oxygen being administered. FiO_2 can be more precisely controlled from 0.24 to 0.5 at high flow rates simply by changing the jet nozzle and adjusting oxygen flow rates. This is particularly helpful in patients with acute exacerbation of COPD where controlled oxygen supplementation is quite critical (Fig. 14.2).

- Oxygen delivery is also provided through a mask with a reservoir, which is a high-oxygen, high-flow device. A high FiO_2 of up to 0.6–0.9 can be delivered through these masks (Figs. 14.3 and 14.4).

B. *O_2 supplementation during noninvasive positive-pressure ventilation (NIPPV)*

- NIPPV in ICUs is administered either through conventional mechanical ventilation or through a portable system.
- Supplemental oxygen is delivered by simply adding it to the mask or the circuit.
- Oxygen should be added into the circuit distal to the exhalation port.
- The highest concentration is achieved with O_2 added to the mask, with the leak port in the circuit, and with the lowest setting of inspiratory and expiratory pressures. Unfortunately, the delivered FiO_2 with NIPPV portable systems remains unpredictable.

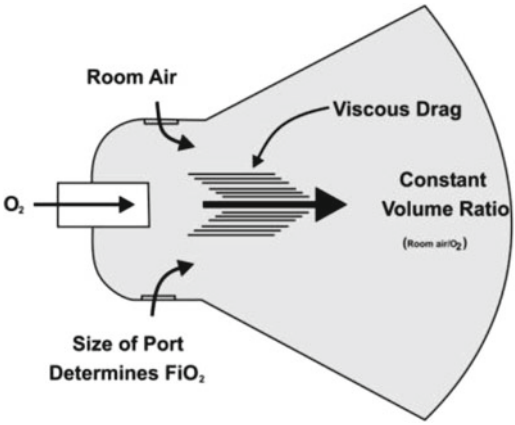

Fig. 14.2 Schematic diagram showing the principle involved in the venturi mask

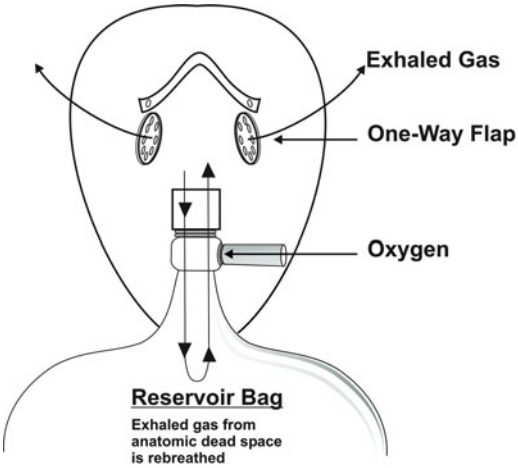

Fig. 14.3 Schematic diagram showing the principle of partial non-rebreather mask

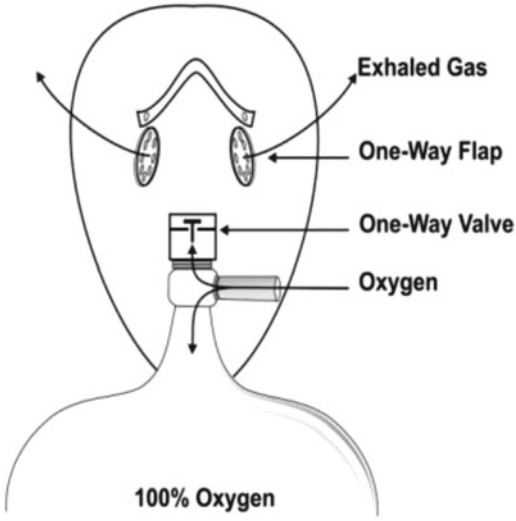

Fig. 14.4 Schematic diagram showing the principle of non-rebreather face mask

- In case there is a need for precise oxygen delivery, it is better to use a conventional ventilator with an integrated oxygen blender.

C. *O2 supplementation through conventional mechanical ventilation*

- Most of the currently available mechanical ventilators are capable of delivering tightly controlled and high levels of FiO_2 to intubated patients.
- The integrated microprocessor-controlled gas blenders allow blending of compressed oxygen and air and precise delivery of a preset FiO_2 for continued and long periods.
- It is also possible to deliver high FiO_2 and even 100% oxygen through such systems.
- This is the reason that mechanical ventilation remains the cornerstone of management of severe hypoxia to improve oxygenation to a satisfactory level in most severe forms of respiratory failure.

Step 3: Monitor adequacy of oxygenation

Tissue oxygenation is a better method of assessment for the need of oxygen therapy. This can be determined through the following:

- Mixed venous oxygen saturation (SvO_2) can be measured by taking blood sample from the proximal pulmonary artery. This reflects the amount of oxygen "leftover" in the venous blood after body tissues have removed (used) whatever oxygen they needed.
- The pulmonary artery catheter is required for measuring SvO_2, which is associated with many complications.
- $ScvO_2$, the central venous oxygen saturation measured by the placement of a catheter in the superior vena cava, can be taken as a surrogate for SvO_2.
- A low SvO_2/$ScvO_2$ suggests that the cardiac output and the level of oxygenation are insufficient to meet the metabolic demands of body tissues.

Step 4: Understand risks of oxygen therapy in ICUs

Oxygen administration is not without risks and toxicities.

- Oxygen toxicity is likely in an ICU patient when high concentration (>0.5 FiO_2) is needed for longer periods (≥36 h).
- Oxygen toxicity in such a situation causes symptoms of restlessness, nausea, dyspnea, retrosternal discomfort, and paresthesia; later, lung injury and fibrosis may occur.
- The following precautions are therefore important:
- Use the lowest possible FiO_2 but maintain the adequate and required oxygenation.
- Use judicious levels of positive end-expiratory pressure to reduce the overall FiO_2 requirement.
- Regularly monitor manifestations of oxygen toxicity.

Suggested Reading

1. Jindal SK, Agarwal R. Oxygen therapy. 2nd ed; 2008. New Delhi: Jay Pee Brothers.
This book gives a detailed description of different aspects of oxygen therapy in all clinical conditions.

2. Huang YC. Monitoring oxygen delivery in the critically ill. Chest. 2005;128(5 Suppl. 2):554S–60S.
This article reviews the basic principles of DO(2) and the abnormal oxygen supply–demand relationship seen in patients with shock. It also discusses approaches for monitoring DO(2), including clinical symptoms/signs, acid–base status, and gas exchange, which provide global assessment, as well as gastric tonometry, which may reflect regional DO(2).
3. Kallstrom TJ. AARC clinical practice guideline: oxygen therapy for adults in the acute care facility—2002 revision and update. Respir Care. 2002;47:717–20.
4. Leach RM, Treacher DF. The pulmonary physician in critical care. 2. Oxygen delivery and consumption in the critically ill. Thorax. 2002;57:170–7.
Early detection and correction of tissue hypoxia is essential if progressive organ dysfunction and death are to be avoided. However, hypoxia in individual tissues or organs caused by disordered regional distribution of supplemental oxygen may be lifesaving in some situations but cannot correct inadequate oxygen delivery caused by a low cardiac output or impaired ventilation.
5. Schwartz AR, Kacmarek RM, Hess DR. Factors affecting oxygen delivery with bi-level positive airway pressure. Respir Care. 2004;49:270–275.
Delivered oxygen concentration during BiPAP is a complex interaction between the leak port type, the site of oxygen injection, the ventilator settings, and the oxygen flow.

Pulse Oximetry and Capnography

15

Deepak Govil and Sachin Gupta

A 50-year-old male patient, a known case of chronic obstructive pulmonary disease (COPD), was admitted to the hospital with acute exacerbation. He was drowsy and cyanotic. His respiratory rate was 26/min. He was admitted for the management of COPD.

Pulse oximetry and capnography are essential components of respiratory monitoring in the intensive care unit.

Step 1: Examine the patient in detail and do pulse oximetry

- Presence of nonspecific symptoms and signs, which are suggestive of hypoxia, should be evaluated with objective measurements of oxygenation.
- Standard blood gas analyzer calculates oxygen saturation by partial pressure of oxygen plotted against the oxyhemoglobin dissociation curve for varying pH. Blood gas analyzer fitted with CO-oximeter directly measures oxygen saturation in the arterial blood sample (SaO_2).
- The pulse oximeter is a medical device that indirectly monitors the oxygen saturation of patients' blood and the changes in blood volume in the skin, producing a photoplethysmograph (SpO_2).

Step 2: Understand the principle of pulse oximetry

- The fundamental physical property that allows the pulse oximeter to measure the oxygen saturation of hemoglobin is based on Beer–Lambert law, which relates to the concentration of a solute to the intensity of light transmitted through a solution.

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- The pulse oximetry is based on two physical principles:
  - The light absorbance of the oxygenated hemoglobin is different from that of the reduced hemoglobin, at the oximeter's two wavelengths, which include red and near-infrared light.
  - The absorbance of both wavelengths has a pulsatile component, which is due to the fluctuations in the volume of arterial blood between the source and the detector.
- Typically, a pulse oximeter has a pair of small light-emitting diodes (LEDs) facing a photodiode through a translucent part of the patient's body, usually a fingertip or an earlobe.
- One LED is red, with the wavelength of 660 nm, and the other is infrared, with the wavelength of 905, 910, or 940 nm. Absorption at these wavelengths differs significantly between oxyhemoglobin and its deoxygenated form; therefore, the oxy-/deoxyhemoglobin ratio can be calculated from the ratio of the absorption of the red and infrared light.
- The microprocessor filters the extraneous signals or noises so that accurate oxygen saturation can be calculated.
- The arterial signal is pulsatile and it can be distinguished from nonpulsatile signals. The microprocessor can select out the absorbance of the pulsatile fraction of the blood, that is, due to arterial blood (AC), from the constant absorbance by nonpulsatile venous or capillary blood and other tissue pigments (DC), thus eliminating the effect of tissue absorbance to measure the oxygen saturation of arterial blood.

Step 3: Understand pitfalls and limitations

1. Dyshemoglobinopathies
   - Pulse oximetry is considered to be accurate when oxygen saturation is between 70% and 100% provided that oxygenated hemoglobin and reduced hemoglobin are the only measured species of hemoglobin. But if methemoglobin and carboxyhemoglobin (COHb) increase in concentration, then the reliability of pulse oximetry becomes doubtful.
   - Meth-Hb absorbs equal amount of red and infrared light, and the ratio is equal to 1 at 85% saturation. So even if the patient is hypoxic, the pulse oximeter will read 85%. Vice versa, if oxygen saturation is 100%, then the pulse oximeter will also read 85%.
   - COHb absorbs very little light at 940 nm, while at 660 nm, its extinction coefficient is very similar to oxyhemoglobin. Thus, the presence of significant COHb will resemble the curve of oxyhemoglobin in the red range, with no effect on the infrared, and "look like" oxyhemoglobin, causing the pulse oximeter to overread.
   - When these dyshemoglobins are suspected, then pulse oximetry should be supplemented by in vitro multiwavelength CO-oximetry.
2. Poor perfusion
   - Poor perfusion leads to poor arterial pulse waveform, and so the pulse oximeter fails to detect the correct oxygen saturation. This can happen during

cardiopulmonary bypass (CPB), cold extremities, hypovolemia, low cardiac output, and peripheral vascular disease.

3. Arrhythmias
   The pulse oximeter may not be able to detect the correct saturation during rapid atrial fibrillation or during intra-aortic balloon pump application.
4. Miscellaneous
   - Black, blue, and green nail polishes give lower saturation.
   - Values lower than 70% are not considered to be completely accurate.
   - The movement of the patient like shivering or seizure will not give accurate measurements as the pulse oximeter fails to detect normal arterial pulsations.
   - The hyperemic limb may show lower readings as capillary and venous flow becomes pulsatile.
   - It cannot detect hypoventilation or hypercarbia despite good saturation.

Despite a few limitations, the pulse oximeter remains a useful tool in the ICU as it can be read continuously and gives a reliable estimation of oxygen saturation of the patient.

Capnography

Step 1: Understand the principle of capnography

- Capnography is the graphic display of instantaneous CO_2 concentration versus time (time capnogram) or expired volume (volume capnogram) during a respiratory cycle.
- The usefulness of capnography lies in checking the position of the endotracheal tube, ventilation, and perfusion status of the lung.

Principle

- The intensity of infrared radiation projected through a gas mixture containing CO_2 is diminished by absorption.
- Expired air can be either analyzed as an inline device (mainstream) or sampled outside (sidestream).

Basic Physiology of Capnogram

- Assuming complete inspiration, there will be no CO_2 in the large airways at the end of inspiration. As the patient starts exhaling, initially the CO_2 sensor will not detect any CO_2 as the exhalation comes from dead space.
- As the exhalation continues, CO_2 increases and reaches its peak and is detected at the sensor. After exhalation, as the patient starts inspiring, CO_2 falls back to the zero baseline as he or she inspires CO_2-free air. This gives rise to a typical waveform called capnogram (Fig. 15.1).

Phase I: At the start of exhalation, anatomical and physiological dead space is expired, so no CO_2
Phase II: Exhalation continues, so CO_2 rises
Phase III: CO_2 plateau
Phase IV: Inspiration

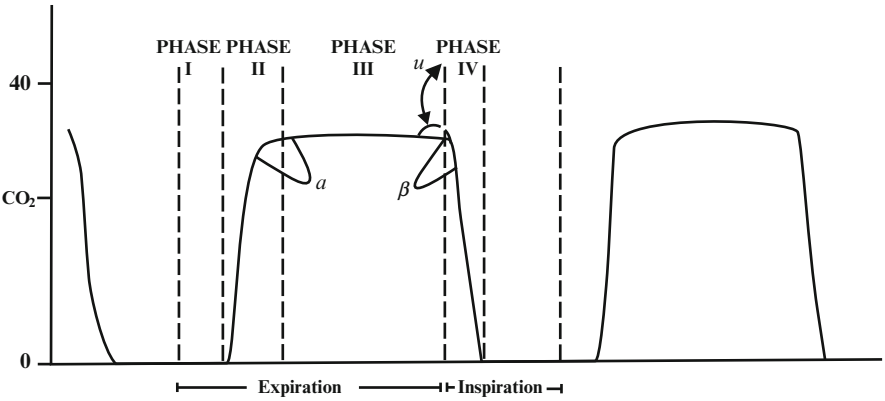

Fig. 15.1 Normal Capnogram

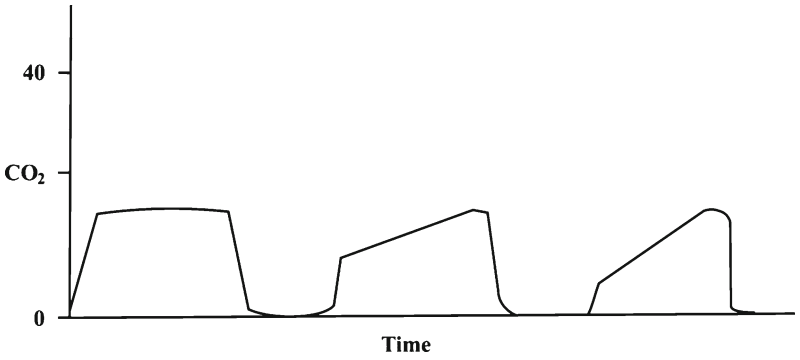

Fig. 15.2 Capnogram showing obstruction in the respiratory pathway

Step 2: Understand clinical applications of capnography

- Slanting and prolongation of expiratory phase is indicative of obstruction in the respiratory pathway, that is, either obstruction in the endotracheal tube or obstructive lung disease (Fig. 15.2).
- The elevation of the baseline is indicative of rebreathing, insufficient gas flows (Fig. 15.3).
- Contamination of the expired sample by fresh gas flows or sampling site too near to fresh gas (Fig. 15.4).
- Low $EtCO_2$ indicates hyperventilation (Fig. 15.5).
- High $EtCO_2$ indicates hypoventilation (Fig. 15.6).
- Sudden fall in $EtCO_2$ can be due to asystole, hypotension, or massive pulmonary embolism (Fig. 15.7).
- This type of capnogram is observed when sudden CO_2 is released after unclamping a major blood vessel or release of tourniquet (Fig. 15.8).

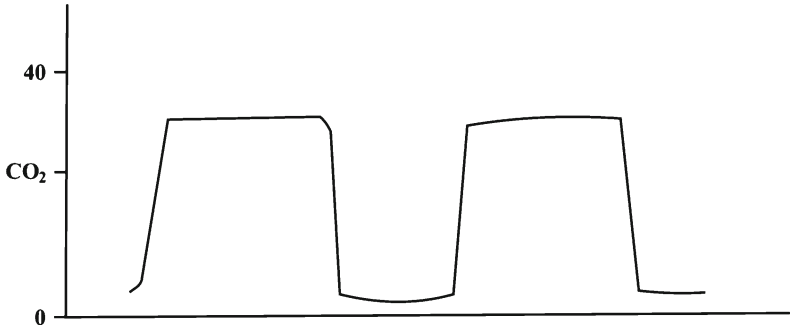

Fig. 15.3 Capnogram showing elevation of the baseline is indicative of rebreathing, insufficient gas flows

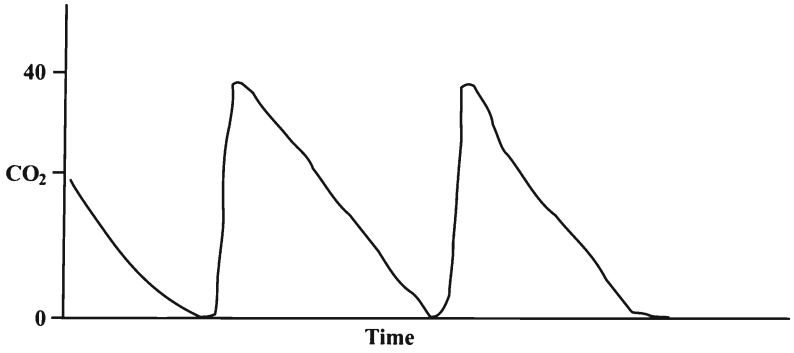

Fig. 15.4 Capnogram showing contamination of the expired sample by fresh gas flows or sampling site too near to fresh gas

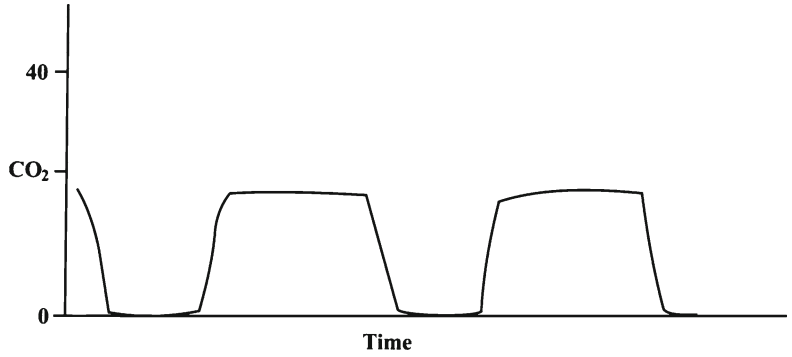

Fig. 15.5 Capnogram showing Low $EtCO_2$ indicates hyperventilation

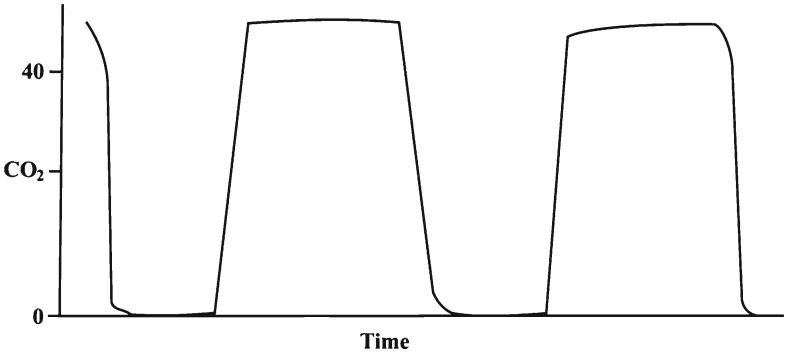

Fig. 15.6 Capnogram showing high $EtCO_2$ indicates hypoventilation

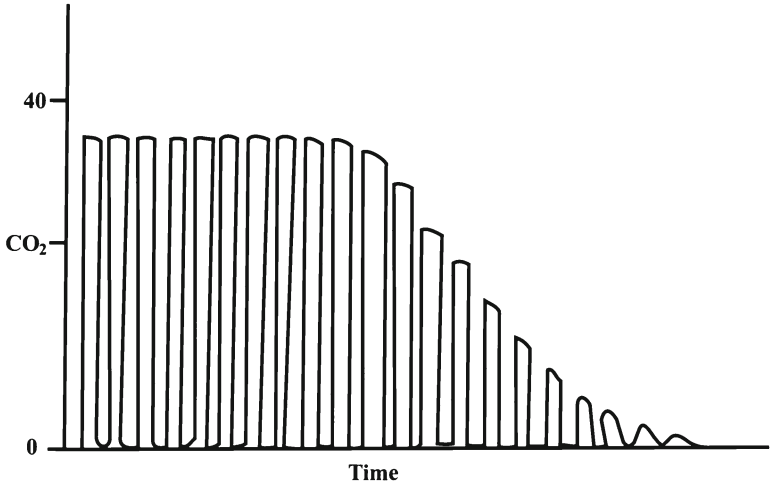

Fig. 15.7 Capnogram showing sudden fall in $EtCO_2$ can be due to asystole, hypotension, or massive pulmonary embolism

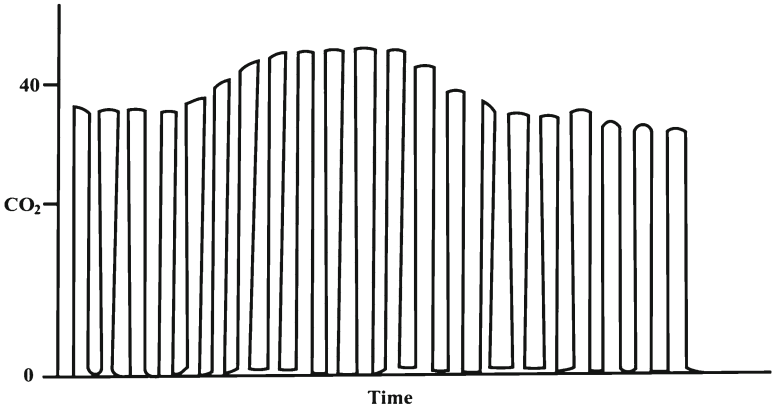

Fig. 15.8 Capnogram showing sudden rise in CO_2 after unclamping a major blood vessel or release of tourniquet

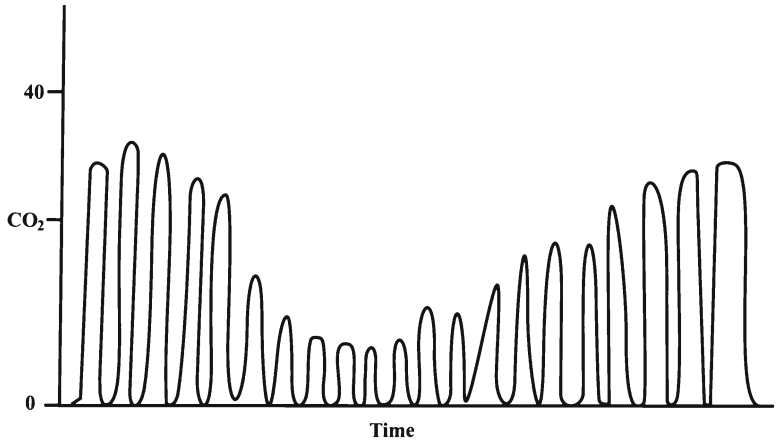

Fig. 15.9 Capnogram showing sudden fall and rise of $EtCO_2$ is due to small air embolus

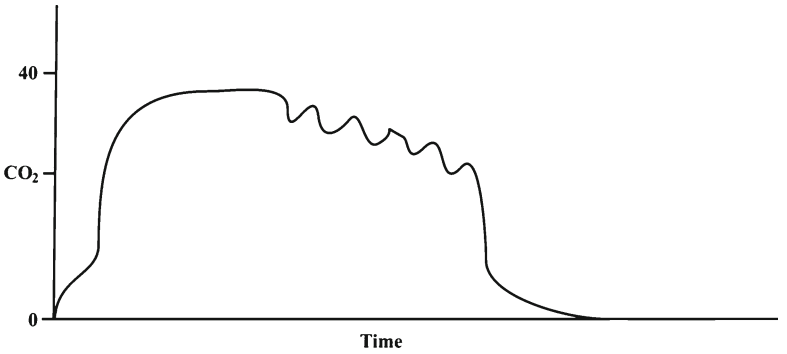

Fig. 15.10 Capnogram showing cardiac oscillations due to contraction and relaxation of the heart

- Sudden fall and rise of $EtCO_2$ is due to small air embolus (Fig. 15.9).
- Cardiac oscillations are due to contraction and relaxation of the heart (Fig. 15.10).
- This shows a sedated and inadequately paralyzed patient having spontaneous respiratory efforts (Fig. 15.11).
- This shows respiratory efforts wearing off after giving muscle relaxant, called as curare effect (Fig. 15.12).
- It is helpful in weaning as it shows the return of spontaneous respiration (Fig. 15.13).

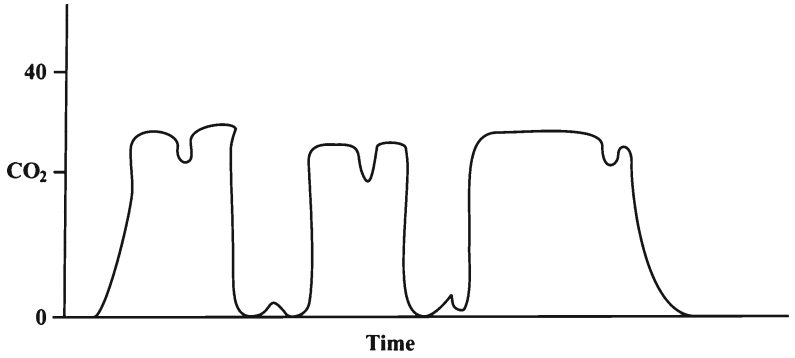

Fig. 15.11 Capnogram showing sedated and inadequately paralyzed patient having spontaneous respiratory efforts

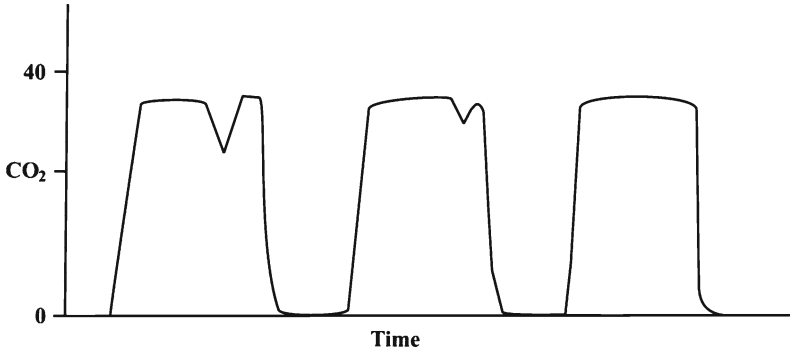

Fig. 15.12 Capnogram showing curare effect after neuromuscular blockade

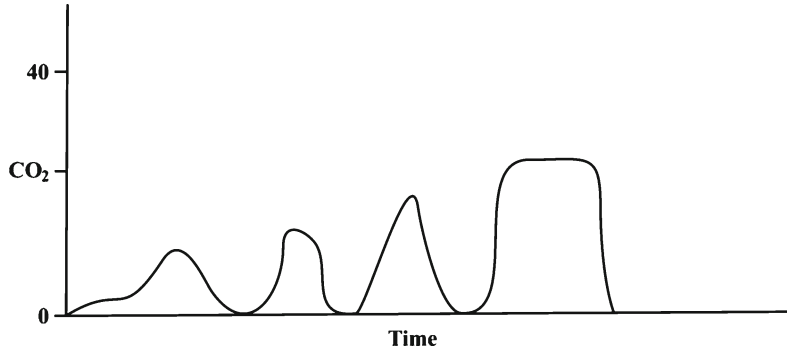

Fig. 15.13 Capnogram showing return of spontaneous respiration

Conclusion

Capnogram is a very useful tool for ventilated patients, and it gives us a real-time idea of various lung interactions that can have the implications on the outcome of the patient.

Suggested Reading

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   This updated clinical practice guideline is based on 234 clinical studies and systematic reviews, 19 review articles investigating the use of capnography/capnometry during mechanical ventilation.
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   Pulse oximetry overestimates ABG-determined SaO_2 by a mean of 2.75% in emergency department patients with severe sepsis and septic shock. This overestimation is exacerbated by the presence of hypoxemia. When SaO_2 needs to be determined with a high degree of accuracy, arterial blood gases are recommended.
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   Pulse oximeters overestimate arterial oxygen saturation during hypoxia in dark-skinned individuals.
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   Despite problems and limitations, pulse oximetry remains the standard of care in all clinical situations, and its use for all patients under anesthesia must be mandated.
7. Van de Louw A, Cracco C. Accuracy of pulse oximetry in the intensive care unit. Intensive Care Med. 2001;27(10):1606–13.
   Large SpO_2 to SaO_2 differences may occur in critically ill patients with poor reproducibility of SpO_2. A SpO_2 above 94% appears necessary to ensure an SaO_2 of 90%.
8. Hampson NB. Pulse oximetry in severe carbon monoxide poisoning. Chest. 1998;114(4): 1036–41.
   Presently available pulse oximeters overestimate arterial oxygenation in patients with severe CO poisoning. Accurate assessment of arterial oxygen content in patients with CO poisoning can currently be performed only by analysis of arterial blood with a laboratory CO-oximetry.

Websites

1. www.pulseox.info
   Basic information on pulse oximetry
2. www.pulseoximeteronline.com
   Industry website to review different types of pulse oximeters
3. www.capnography.com
   Website produced by Bhavani Shankar Kodali. An atlas of capnograms
4. www.linxdown.com
   Downloadable atlas of capnograms

Part II

Cardiovascular System

Jigeeshu V. Divatia, Farhad N. Kapadia,
Shyam Sunder Tipparaju and Sheila Nainan Myatra

Hemodynamic Monitoring

16

Sheila Nainan Myatra, Jigeeshu V. Divatia,
and Ramesh Venkatraman

A 55-year-old male patient presented with respiratory distress, heart rate of 140/min, BP of 70/40 mmHg, and respiratory rate of 34 breaths/min. Core temperature was 34.4°C. He was oliguric and the abdomen was tender, firm, and distended. He remained tachycardic and hypotensive.

Hemodynamic monitoring is an integral part of intensive care unit (ICU) management. These monitoring devices, if applied injudiciously, may also be harmful. Need for invasive monitoring should be assessed carefully, and its indication should be documented clearly. Attention to technical details, correct interpretation of the data, and its application in selecting an intervention should be individualized within the clinical context.

Step 1: Start basic hemodynamic monitoring

- Clinical examination—check for central and peripheral pulses, manual blood pressure: follow the trend and compare with patients' normal values, capillary refill, core temperature, and peripheral temperature at extremities.
- Noninvasive—noninvasive blood pressure, pulse oximetry, and plethysmographic signals.
- Hourly urine output.
- Screening echocardiography (See Chapter 17).
- Base deficit (arterial blood gas).

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- Central venous pressure (CVP).
- Intra-arterial blood pressure.
- Serum lactate level.
- Central venous oxygen saturation ($ScvO_2$).

Step 2: Start advanced hemodynamic monitoring in selected cases
- These should be initiated in patients with one or more of the following features:
  - On high vasopressors, high ventilatory support, compromised cardiac and renal function, and where empirical fluid challenge may be harmful
- Options of monitoring techniques include one or more of the following:
  - Cardiac output-minimally invasive (pulse contour analysis, esophageal Doppler monitoring)
  - Pulmonary arterial catheter monitoring
  - Pulse pressure/stroke volume variation
  - Continuous $ScvO_2$ monitoring

Step 3: Set up the pressure transducing system
- This consists of a pressure transducing assembly with a flushing system.
- The accuracy of invasive pressure measurement will depend on the proper setup and function of the pressure transducing system.
  - *The pressure transducing* assembly consists of a coupling system, pressure transducer, amplifier and signal conditioner, analog to digital converter, and microprocessor which converts the signal received from the vein or the artery into a waveform on a bedside monitor.
  - *The flushing system* is set up using a 500-mL sterile saline bag encased in a pressurized system to 300 mmHg. At this pressure, the catheter will be flushed with 3 mL saline per hour and help keep the catheter patent. The flushing device helps flush the assembly as required. Before connecting, flush the pressure transducing system with saline using the flushing device, remove all air bubbles, and keep it ready to connect to the catheter. Heparinized saline is no longer routinely used in view of concerns about heparin-induced thrombocytopenia also, continuous heparin flush solution has been shown to affect coagulation studies if the sample is drawn via the indwelling line.

Step 4: Zero the transducer (static calibration) (Fig. 16.1)
- To obtain accurate pressure measurements, the air fluid interface must be aligned with the chamber or the vessel being measured.
- The reference point is usually at the level of the heart. Use the phlebostatic axis (junction of the fourth intercostal space and the midpoint between the anterior and posterior chest walls).
- A spirit level should be used to level this point with the stopcock of the pressure transducing system which is used for zeroing.
- The stopcock is opened to air, and the recorded pressure (atmospheric pressure) is used by convention as the reference value of 0 mmHg.

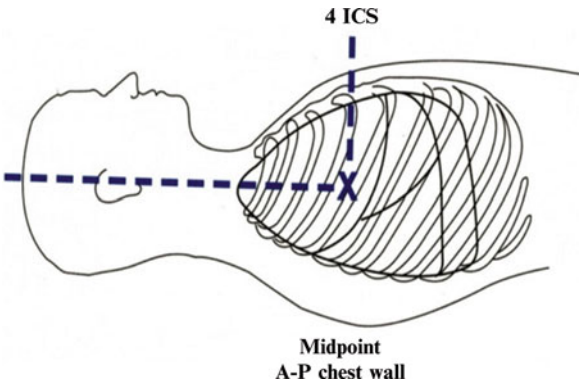

Fig. 16.1 Phlebostatic axis

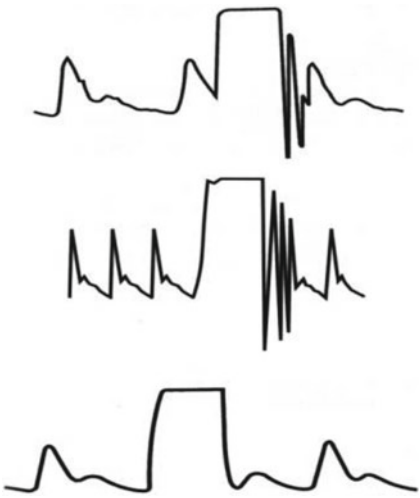

Fig. 16.2 Square wave test

Step 5: Check if the system is optimally damped (dynamic calibration) (Fig. 16.2)

- Damping indicates the tendency of an oscillating system to return to its resting state.
- *Underdamped waveform* is a narrow and peaked tracing (will record higher systolic and lower diastolic pressure) and seen when long tubing is used or with increased vascular resistance.
- *Overdamped waveform* (will record lower systolic and higher diastolic pressure) is commonly seen when there are air bubbles or blood clots, overly compliant tubing, catheter kinks, stopcocks not properly closed, no fluid in flush bag, or low flush bag pressure.
- In both the above situations, the mean arterial pressure (MAP) will not change. Hence, always rely on the MAP, especially when you are not sure whether the system is optimally damped.

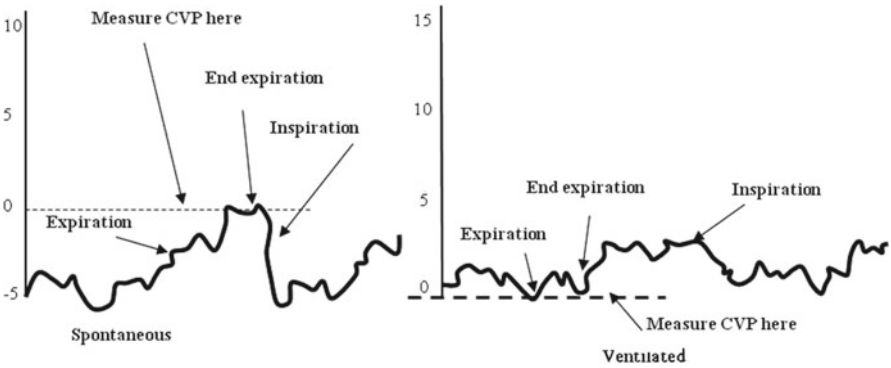

Fig. 16.3 CVP or PAOP measurement in the spontaneously breathing and ventilated patient

- Damping can be checked by performing a "square wave test"—activate the flush device, quickly release it, and observe the waveform on the monitor. The waveform sharply rises and "squares off" at the top when the flush is activated, and then, the tracing returns to baseline when it is released. Check the number of oscillations.
  1. Optimally damped—one or two oscillations before returning to tracing
  2. Underdamped—more than two oscillations before returning to tracing
  3. Overdamped—less than one oscillation before returning to tracing

Repeat the square wave test every 8–12 h whenever the waveform looks over- or underdamped, when the accuracy of the measurement is doubtful and particularly when implementing interventions based on intra-arterial pressure values.

Step 6: Interpret the CVP

- The CVP is used as an index of preload of the heart or as an index of intravascular volume status. However, the CVP is influenced not only by the volume status but also by myocardial contractility, afterload, and intrathoracic and intra-abdominal pressures. Hence, the CVP can be confusing at times and difficult to interpret.
- A single measurement of the CVP helps somewhat in defining the circulatory status but leaves considerable overlap in possible interpretations. Hence, single values of CVP should not be relied on. Instead, response of CVP to fluid challenge and the trend of values should be used in clinical decision making.
- In order to minimize the effects of respiration, the CVP measurement should be taken at end exhalation when the muscles of respiration are at rest and intrathoracic pressure is stable at its resting level (Fig. 16.3). For this, the CVP tracing should be studied on the monitor after freezing the screen or printed out and studied. In mechanically ventilated patients, inspiration is positive and expiration negative, and end-expiratory values should be read just before the beginning of the inspiration. In spontaneously breathing patients, it is the reverse.

- In some patients, "a" and "v" waves are identifiable in CVP tracing. To correctly identify these, a two-channel recorder with a CVP tracing and a concurrent electrocardiogram tracing should be taken. "a" wave is located corresponding to the PR interval and "v" wave to the QT interval. CVP should be measured at the end of "a" wave.
- When positive end-expiratory pressure (PEEP) is applied, pleural pressure is transmitted to the right atrium and the CVP increases. However, the transmural right atrial pressure [right atrial pressure (RAP)—intrapleural pressure], which is the true filling pressure, actually decreases, resulting in underfilling of the right side of the heart.
- It is best not to remove PEEP for measurements of vascular pressures. The beneficial effect of PEEP on gas exchange is lost very quickly when it is removed and may take a prolonged period to recover when PEEP is reapplied.
- Avoid subtracting half or any other proportion of PEEP value (external + auto PEEP) to the CVP measurement to get an approximate of "true" CVP.
- In a nonmechanically ventilated patient, the CVP of 8–10 mmHg is judged to be adequate.
- If the patient is clinically stable without evidence of hypoperfusion, refrain from giving fluids to attain a particular CVP value.
- A higher CVP value of 10–12 mmHg is recommended in some situations such as:
  - Mechanically ventilated patients
  - Diastolic dysfunction (e.g., previous hypertension)
  - Pulmonary hypertension (e.g., chronic obstructive pulmonary disease)
  - Increased intra-abdominal pressure (e.g., pancreatitis)
- A controlled fluid challenge and response of CVP may be used to interpret volume status (see Chap. 18):
  - Select the type of fluid: usually normal saline or a colloid.
  - Infuse rapidly. The rate of infusion: 500 mL of crystalloid or 200 mL of colloid over 20–30 min.
  - Target the desired therapeutic response: the parameters are set empirically by the physician. These could be MAP >70 mmHg, HR <100/min, and hourly urine output >0.5 mL/kg/h.
  - Set the danger/safety limits: again, they are set empirically by the physician, for example, CVP 16 mmHg or 4–5 mmHg more than the baseline value.
  - Assess the response to the initial bolus of fluid.
  - Repeat bolus infusion of fluid if:
    - Therapeutic target is not reached
    - Danger CVP value is not reached
  - Discontinue fluid infusion if:
    - Therapeutic target is achieved
    - Danger value of CVP is reached
  - Reassess at frequent intervals.
- Interpret appropriately the change in CVP in response to a fluid bolus. As a rule of thumb, if the increase in the CVP measured before and 5 min after a fluid bolus is 0–3 mmHg, more fluid should be given. If it is 3–5 mmHg, the patient is

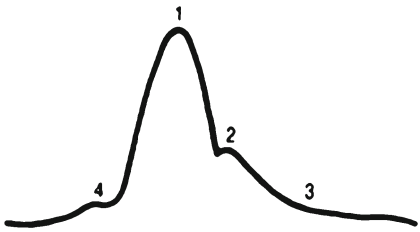

Fig. 16.4 Components of the arterial waveform. *1* Peak systolic pressure, *2* dicrotic notch, *3* diastolic pressure, and *4* anacrotic notch

probably adequately filled, and if the CVP increases more than 5 mmHg after the fluid bolus, fluid loading should be stopped.

Step 7: Interpret intra-arterial pressure waveform (Fig. 16.4)

- The arterial pressure waveform differs at different sites. As the arterial pressure is recorded more distally, the trace gets progressively more peaked and the dicrotic notch migrates away from the peak. The MAP, however, does not vary widely as one measures more distally. Besides more accurate and real-time recording of arterial pressure, other hemodynamic interpretations can be made from the arterial waveform:
  - Systolic blood pressure variations (swing in the waveform) can be seen during hypovolemia.
  - Steep slope of upstroke means good contractility and vice versa.
  - Area under the curve represents the stroke volume.
  - Position of the dicrotic notch—low (low systemic vascular resistance [SVR]) and high (high afterload).
  - Slope of the descent—steep (low SVR).

Step 8: Interpreting pulmonary artery occlusion pressure (PAOP)

The four most important measurements obtained from the pulmonary artery catheter (PAC) are the following:

1. PAOP (Pulmonary artery Occlusion pressure)
2. Pulmonary artery systolic (PASP) and diastolic pressure (PADP)
3. Thermodilution cardiac output
4. Mixed venous oxygen saturation
   - PAOP provides an accurate and indirect measurement of left atrial pressure (LAP) and the left ventricular end-diastolic pressure (LVEDP), which are related to the left ventricular preload: the left ventricular end-diastolic volume (LVEDV).
   - The PADP displayed on the monitor gives a continuous estimate of the LVEDP, subject to the assumptions in Table 16.1.
   - Pulmonary artery systolic pressure gives an estimate of pulmonary hypertension and is useful in calculating pulmonary vascular resistance (PVR).
   - West has described three physiological lung zones that are based on the gravitationally determined relations between pulmonary artery pressure (PAP), pulmonary venous pressure, and alveolar pressure.

Table 16.1 Assumptions inherent in using PAOP or CVP

Statement	Assumption	Fallacy
LVEDV = LVEDP (preload)	Left ventricular compliance is normal; pressure and volume are linearly related	Compliance may change with pathology, for example, left ventricular hypertrophy, myocardial ischemia, or infarction; P-V relationship is nonlinear
LAP = LVEDP RAP = RVEDP	Mitral and tricuspid valves are normal and fully open in diastole	It does not hold true if valves are stenotic or regurgitant or when A-V valves are closed in diastole (nodal rhythm, A-V dissociation)
RAP = LAP	Equivalent function of the right and left ventricles	Relationship between the right and left sides of the heart is affected by several factors

- In zones 1 and 2, alveolar pressure exceeds pulmonary vascular pressures. Thus, if the catheter is positioned in any of these zones, it will monitor alveolar or airway pressure instead of the vascular pressures. Fortunately, in most clinical settings where a PAC is inserted, the patient is in the supine position, which facilitates zone 3 formation where alveolar pressure is less than pulmonary venous and arterial pressure thereby reflecting true vascular pressure.
- Criteria for confirming the placement of the PAC are:
  - A tracing consistent with the arterial pressure waveform
  - A mean wedge pressure lower than mean PA diastolic pressure
  - Arterialized blood aspirated from the catheter tip with the balloon inflated
  - Free flow when the catheter is wedged (as determined by the absence of "overwedging" and by ability to aspirate blood through the catheter tip)
- The PAC has been regarded as the gold standard for hemodynamic measurements for many years. However, several physiological assumptions are made when stating that the PAOP is a measure of the preload (LVEDV) (Table 16.1).
- Lately, the use of PAC has decreased due to availability of other less invasive technique of measuring cardiac output, observational data showing poor outcome with PA catheters and poor training in interpreting PA catheter values, but in selected situation and in proper hands, this catheter is still a useful tool.
- Ventilation causes significant swings in pleural pressure. Pulmonary vascular pressure, when measured relative to atmospheric pressure, will reflect these respiratory changes. To minimize this, impact, variables are conventionally measured at the end of expiration. An index of transmission has been described to account for the effects of PEEP (subtract half of PEEP from the pressures). However, the fluid challenge as it is applied to CVP is a method of assessing PAOP during mechanical ventilation with PEEP.

Step 9: Understand the concept of preload responsiveness (Fig. 16.5)

- Fluid resuscitation is essential to treat hypovolemia and restore organ perfusion. However, excessive fluid administration will contribute to tissue and pulmonary edema, right ventricular dysfunction, and increased intra-abdominal pressure.
- Fluid resuscitation is commonly guided by static measures of preload (e.g., CVP and PAOP). However, cardiac preload is not preload responsiveness. Preload responsiveness is the increase in cardiac output in response to fluid loading. The

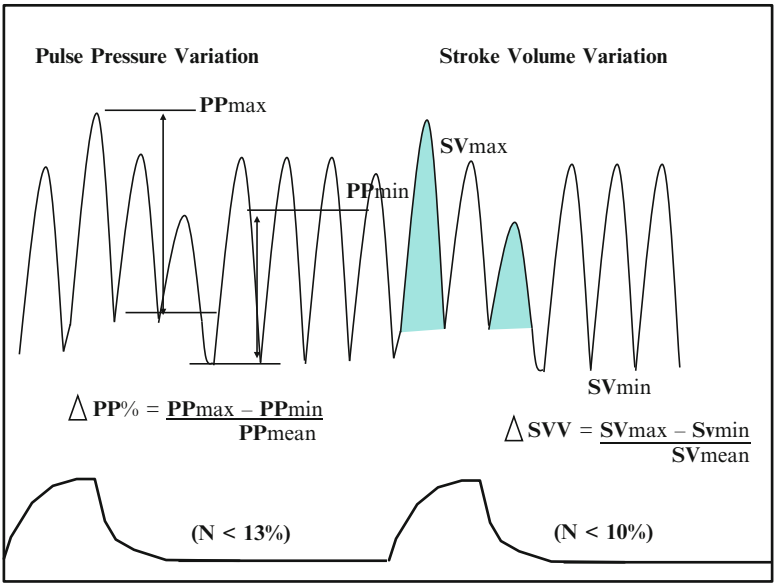

Fig. 16.5 Pulse pressure variation and stroke volume variation

static measures of preload fail to predict fluid responsiveness in half of fluid challenges, that is, they do not predict whether fluid loading will result in an increase in cardiac output. In addition, fluid has to be given before the response to fluid challenge can be evaluated. This is potentially hazardous in some patients.

- Dynamic parameters predict the response to fluid loading without having to give a fluid challenge. Hence, they may avoid the potential hazards of a fluid challenge. The principles of these parameters are outlined below.
- During inspiration in a fully controlled mechanically ventilated patient, afterload to the left ventricle decreases due to decrease in transmural pressure (pressure inside the aorta – pressure outside [pleural]) and preload to left ventricle increases due to squeezing of pulmonary capillary blood to the left side of the heart. This causes increase in the left ventricle output during inspiration, leading to increased systolic pressure, increased pulse pressure, and increased stroke volume.
- During inspiration, the right ventricle preload decreases due to less venous return (less preload) and afterload increases due to lung inflation resulting in decreased right ventricle output, leading to decrease in systolic pressure, pulse pressure, and stroke volume which is reflected during expiration due to transit time from the right- to the left-sided heart.
- During expiration, this phenomenon is reversed.
- These changes will result in stroke volume variation (SVV), systolic pressure variation (SPV), and pulse pressure variation (PPV) with the respiratory cycle with increase in these parameters during inspiration and decrease during expiration and are referred to as dynamic indicators of preload responsiveness.

- In hypovolemic patients, these changes are exaggerated. Values more than 13% are indicative of fluid responsiveness.
- Volume responsiveness or pressure variation with respiration is a physiological phenomenon related to a normal preload reserve because both ventricles of healthy subject operate on the steep portion of the preload–stroke volume relationship. Therefore, detecting the volume responsiveness must not systematically lead to the decision to infuse fluid. Such a decision must be based on the presence of signs of cardiovascular compromise and must be balanced with the potential risk of pulmonary edema formation and/or worsening gas exchange.
- SPV, PPV, SVV cannot be used in patients with spontaneous breathing activity and/or with arrhythmias. They are not reliable in patients ventilated with low tidal volume and in patients with increased intra-abdominal pressure.
- In these cases, passive leg raising is an alternative choice.
- Passive leg raising maneuver is an endogenous fluid challenge. A continuous monitor of stroke volume, SVV, PPV, or aortic blood flow by esophageal Doppler is required. Increase in stroke volume of more than 10%, aortic blood flow of more than 10%, or decrease in SVV/PPV after PLR predicts a good response to fluid loading.

Step 10: Interpret $ScvO_2/SvO_2$

- Shock is defined as the disruption of the balance between oxygen demand (VO_2) and supply (DO_2) to the tissues.
- A low DO_2 can be because of anemia, hypoxia, low cardiac output, or maldistribution of blood flow in the microcirculation.
- VO_2 can be increased in sepsis and systemic inflammation.
- We thus need to assess the balance between oxygen supply and demand.
- SvO_2 estimates all components of DO_2. It reflects cardiac output (CO) if VO_2 and Hb are constant, and most importantly, it reflects the balance between oxygen supply and demand.
- An SvO_2 below 65% implies low oxygen delivery, while a value below 60% indicates that there is a serious risk of tissue hypoxia if corrective measures are not taken.
- A low SvO_2 (<40%) implies critical oxygen supply–demand imbalance.
- If SvO_2 is high (>80%), then either the demand has declined, the O_2 supply has increased, or the cells are unable to utilize the oxygen.
- Thus, a falling or low SvO_2 is an important indicator that the oxygen delivery is compromised and is deficient relative to the needs of the tissues.
- The measurement of mixed venous oxygen saturation (SvO_2) from the pulmonary artery is an indirect index of tissue oxygenation.
- However, sampling of mixed venous blood requires insertion of a PAC, which is an invasive procedure with risks, and is not universally used. An alternative is to measure $ScvO_2$. Central venous catheterization is a simpler and safer procedure and is commonly used.
- In this case, a catheter is positioned in the superior vena cava or the upper right atrium.

- In circulatory shock, the $ScvO_2$ is generally greater than SvO_2 with a difference of 5–18%.
- The goal of early resuscitation, within 6 h of septic shock, is to keep SvO_2 more than 65% or $ScvO_2$ more than 70%.
- A fiberoptic central venous and a pulmonary artery (PA) catheter is available for continuous measurement of $ScVO_2$ and SvO_2, respectively, by reflection spectrophotometry for continuous monitoring.

Step 11: Interpret lactate levels

- Lactate levels often reflect anaerobic metabolism due to tissue hypoxia.
- High and rising levels (>2 mmol/L) has adverse prognosis, while falling lactate levels indicate an adequate response to resuscitation of the shocked patient.
- Lactate levels may increase due to increased production due to global or local tissue hypoxia but also due to stimulation of glycolysis and metabolic pathways that accelerate lactate formation in sepsis. Adrenaline infusions can increase lactate levels by accelerating glycolysis.
- High lactate levels may also represent decreased clearance due to reduced liver blood flow or hepatic dysfunction.
- Thus, interpretation of lactate levels may be complicated.
- Also, arterial lactate levels are a global measure, and regional hypoperfusion of some vascular beds may exist even in the presence of normal lactate levels.

Step 12: Integrate findings (see Appendix 2)

- The aim is to use hemodynamic monitoring to optimize preload using either CVP or fluid challenges, dynamic indices such as SVV or PPV, or passive leg raising.
- The cardiac output should be monitored, and oxygen delivery variables should be optimized.
- Determine improvement of oxygen delivery and demand ratio by noting increase in $ScvO_2$ and decrease in lactate levels.
- Clinical improvement in mentation, heart rate, blood pressure, and hourly urine output should be checked.
- Calculated hemodynamic and oxygenation parameters (see Appendix 2).

Suggested Reading

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One of the most important recommendations is that hypotension is not required to define shock, and as a result, importance is assigned to the presence of inadequate tissue perfusion on physical examination. Given the current evidence, the only biomarker recommended for diagnosis or staging of shock is blood lactate. It was also recommended against the routine use of (1) the pulmonary artery catheter in shock and (2) static preload measurements used alone to predict fluid responsiveness.

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Websites

1. Lane.stanford.edu
   Basic guideline on interpretation of vascular waveform
2. www.edward.com
   An industry website with nice illustrations
3. www.covidien
   An industry website with advanced monitoring technology
4. Clinicalcenter.nih.gov
   NIH guideline on basic hemodynamic monitoring

Echocardiography

17

Rahul Pandit and Jigeeshu V. Divatia

A 55-year-old male patient was admitted to the intensive care unit (ICU) with a history of shortness of breath for the past 1 day. His pulse rate was 104/min, blood pressure was 80/40 mmHg, and respiratory rate was 32/min. His peripheries were cool. What is the role of bedside echocardiogram in evaluating this patient's shock state?

Noninvasive, echocardiographic point-of-care monitoring has increasingly been used in ICUs. This has the advantage of easy and quick availability, repeatability, and avoids transportation of an unstable patient.

Intensivists should be familiar with basic echocardiography and use this as a basic screening tool for rapid assessment of the circulation in hemodynamically unstable patients as an extension of clinical examination. Detailed examination should be undertaken by intensivists who have had advanced training in echocardiography. Caution should however be exercised during interpretation of data provided, and patient management should be individualized within the clinical context.

Step 1: Urgent assessment and resuscitation

While resuscitation efforts are under way, a quick assessment with bedside echocardiogram can guide the clinician in rationalizing the use of volume resuscitation, inotropes, and vasopressors. This can be repeated to assess the response to therapy.

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R. Chawla and S. Todi (eds.), *ICU Protocols: A stepwise approach*,
DOI 10.1007/978-81-322-0535-7_17, © Springer India 2012

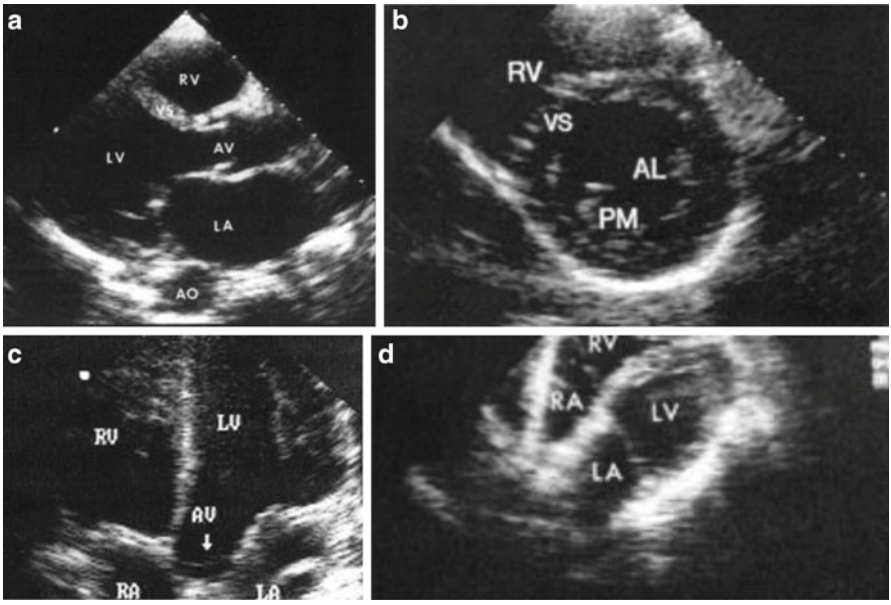

Fig. 17.1 Four basic views: (**a**) left parasternal long axis, (**b**) left parasternal short axis, (**c**) apical four chambers, and (**d**) subcostal

Using the bedside echocardiogram, one can assess the following:

- Left ventricular (LV) function
- Right ventricular (RV) function
- Presence of pericardial effusion and tamponade
- Preload assessment and fluid responsiveness
- Valve lesions

Step 2: Understand the limitation of bedside echo in the ICU

- ICU echos are often different.
  - Patients are often supine, ventilated, and unconscious, leading to limited echo window.
  - Other equipment can affect examination.
  - The situation may be dynamic with concurrent resuscitation under way.
  - Repeated studies may be required to determine the efficacy of treatment.

Step 3: Familiarize with practical aspects of bedside echo (Fig. 17.1a–d)

- Four basic views
  1. Parasternal long axis
  2. Parasternal short axis (papillary muscle level, mitral level, aortic level, and apex)
  3. Apical view—four-chamber, five-chamber, and two-chamber view
  4. Subcostal view

Table 17.1 Normal echo values

Size and wall thickness	
M-mode performed in the parasternal long axis measuring perpendicular to LV through the mitral valve leaflet will give a reasonable estimation of LV systolic and diastolic diameter and interventricular septum and LV posterior wall thickness.	
Dimensions	*Normal range*
End-diastolic LVID	40–56 mm
End-systolic LVID	20–38 mm
End-diastolic IVS and PW thickness	<11 mm
Left atrium and aortic root	
It can be measured by M-mode at the level of aortic valve and will give an estimation of LA size and aortic root.	
LA normal range: <40 mm	
Aortic root normal range: ≤25–30 mm	
Ejection fraction (EF)	
Normal contractility—EF > 50%	
Hyperdynamic—EF > 70%	
Low—EF < 50%	

Step 4: Assess left ventricle (Table 17.1)

- This is best viewed in Parasternal long axis, short axis, and apical views.
- Focused left-sided heart examination
  - Cavity size—small, normal, or dilated
  - Contractility—normal, decreased, hyperdynamic
  - Left ventricular wall thickness
  - Aortic valve appearance, mitral valve appearance
  - Segmental wall motion abnormality
- Size and wall thickness
  - M-mode performed in the parasternal long axis measuring perpendicular to LV through the mitral valve leaflet will give a reasonable estimation of LV systolic and diastolic diameter and interventricular septum and LV posterior wall thickness.
- Left atrium and aortic root
  - It is measured by M-mode at the level of the aortic valve. This will give an estimation of left atrium (LA) size and aortic root.
- Left ventricular wall thickness
  - Presence of significant left ventricular hypertrophy (LVH) points to likely diastolic dysfunction.
  - Systolic wall thickening is a guide to segmental wall motion defects.
- Contractility
  - On 2D echo, subjective assessment by "eyeballing" is often used specially in emergency situations. It is useful to look at multiple views to make a reliable conclusion. Formal estimation of ejection fraction by different formulae is time consuming and needs good echo window and some experience.

- Presence of spontaneous echo contrast (swirly smokelike movement in the ventricle) is an indication of the poor flow state

Step 5: Assess valves

- In the hemodynamically unstable patient, only the gross evaluation of appearance of valves is satisfactory.

Step 6: Assess the right ventricle

- This may be challenging due to the "U" shape of RV. A global assessment is sufficient.
  - RV size—small, normal, or dilated
  - RV contractility—decreased, normal, hyperdynamic
  - Elevated RV pressure
  - Tricuspid valve appearance
- RV size and contractility
  - Size
    - Subjective assessment: Apex of RV should be lower than the apex of LV in apical four-chamber view.
    - Objectively, the RV–LV area ratio is estimated in apical four-chamber view. Normal: <0.6; mild to moderate dilatation: 0.6–1.0; major dilatation: >1.0.
  - Contractility
    - Tricuspid annulus peak systolic excursion calculated in apical four chambers by M-mode at the tricuspid annulus is a good estimation of RV contractility (normal: >20 m).
    - Increased RV pressure.
  - Dilated right atrium (RA) and RV
  - Hyperdynamic RV contraction
  - Paradoxical septal motion (Bowing of septum toward left ventricle)
  - Pathognomic sign of markedly *elevated* RV pressures:
    - Systolic septal flattening—pressure overload
    - Diastolic septal flattening—volume overload
    - Fixed septal flattening (bowed to the left, D-shaped LV)—both pressure and volume overload
- Tricuspid valve
  - In an emergency situation, appearance with color Doppler for regurgitation is sufficient.
  - Pulmonary artery peak pressure can be estimated using continuous wave Doppler in the presence of tricuspid regurgitation.
  - $4\,V^2 + CVP$ (where V is the velocity of regurgitant flow) is equal to pulmonary artery systolic pressure.

Step 7: Assess intravascular volume (preload)

- Care must be taken while estimating the preload as various pathophysiological states, mechanical ventilation, and position of the patient may alter its estimation.
- To assess preload, examine the inferior vena cava, right atrium, right ventricle, and left ventricle.

- Inferior vena cava (IVC)
  - The IVC is best viewed by the subcostal approach. Measure using M-mode perpendicular to the IVC in subcostal view and look for diameter and collapsibility during inspiration and expiration in spontaneously breathing patients.

IVC diameter	Inspiration collapse (%)	Estimated right atrial pressure (RAP) (mmHg)
Small or normal (<2.1 cm)	>55	0–5
	30–50	0–10
	<35	Indeterminate
Large (>2.1 cm)	>55	0–10
	35–55	10–15
	<35	10–20

- This method does not apply to mechanically ventilated patients. In positive-pressure ventilation, IVC size and respiration response have poor correlations with RAP.
- However, an IVC size of more than 12 mm still predicts an RAP of approximately 10 mmHg.
- A large IVC may not necessarily imply elevated RAP. However, if there is IVC collapsibility of more than 35%, then small aliquots of fluid may be given until the collapse reduces.
- Right atrium
  - Enlarged RA with persistent leftward septal bowing suggests elevated RAP.
  - Enlarged LA with persistent rightward septal bowing suggests elevated left atrial pressure (LAP).
- Left ventricle
  - Reduced or obliterated LV diameter in systole is indicative of volume depletion.
  - Kissing LV septum and posterior wall is highly indicative of significant volume depletion.

Step 8: Assess pericardium

- Transthoracic echo is highly specific for diagnosing pericardial effusion and tamponade but has poor sensitivity for diagnosing pericardial thickening and constrictive pericarditis.
- The pericardial space is best viewed in the parasternal long axis and subcostal views.
- An echo-free space separating the epicardium and pericardium is suggestive of a pericardial effusion.
- The size of the effusion can be assessed by measuring the largest echo-free space in diastole.

Severity	Characteristics
Physiological	End-systolic separation of epi- and pericardium posteriorly
Small	Echo-free space of ≤10 mm
Moderate	Echo-free space of 10–20 mm surrounding the entire heart
Large	Echo-free space of >20 mm around the entire heart

- Signs of tamponade
  - Right atrium—early systolic collapse
  - Right ventricle—early diastolic collapse
  - IVC diameter and collapsibility—dilated and/or fixed.

Suggested Readings

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3. www.criticalecho.com/content/icu-echo-tutorials
   An excellent site from CMC Vellore, India
4. www.sonoguide.com/cardiac.html
   Excellent virtual illustration of bedside echo windows

Fluid Therapy, Vasopressors, and Inotropes

18

Jigeeshu V. Divatia and Parvez Ali Khan

A 55-year-old male patient presented with acute respiratory distress. His heart rate was 140/min, BP was 70/40 mmHg, and respiratory rate was 34 breaths/min. Core temperature was 34.4°C. He was oliguric, and the abdomen was tender, firm, and distended. He was intubated and mechanically ventilated. A central venous catheter was inserted, and the central venous pressure (CVP) was 18 mmHg. He remained tachycardic and hypotensive.

Fluids (crystalloid or colloid), vasopressors, and inotropes are common interventions in managing unstable patients in the ICU. These interventions should be used judiciously to maintain perfusion to vital organs while definitive therapy is being instituted. On the other hand, if they are used injudiciously, these interventions may be potentially harmful.

Step 1: Start fluids for resuscitation

- In patients with new-onset hypotension, tachycardia, unexplained oliguria, or other evidence of hypoperfusion such as increased lactate or base deficit, consider a fluid challenge, if this seems to be of low risk clinically, for example, patients with no evidence of overt heart failure.
- Administer 500–1,000 mL crystalloid or 250–500 mL colloid over 30 min. In patients with sepsis, crystalloids are the preferred initial resuscitation fluid.

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- Fluid challenge in the ICU should be protocolized with clear direction about the various components of fluid challenge—type of fluid, rate of administration, clinical and pressure end points, and safety limits (see Chap. 16).
- Target CVP should be 8–12 mmHg in spontaneously breathing patients and 12–15 mmHg in mechanical ventilated patients or those with preexisting decreased ventricular compliance, for example, in hypertensives.
- These parameters need to be individualized depending on patients' clinical status, comorbidity, and underlying pathology.
- Careful monitoring of patients clinically and hemodynamically is mandatory during fluid challenge to assess response as well as evidence of fluid overload.

Step 2: Select fluid for resuscitation

- There is no ideal fluid for resuscitation. Outcomes are similar using either 0.9% normal saline (crystalloid) or 4% albumin (colloid) for fluid resuscitation. However, hemodynamic goals tend to be achieved faster with colloid resuscitation.
- Crystalloids are cheaper but infusion of large volumes of normal saline can cause hyperchloremic acidosis, while colloids may cause coagulopathy, renal dysfunction and anaphylactoid reactions.
- The total volume of HES 130/0.4 should be restricted to 50 mL/Kg/day. The older generation of starches (HES 200/0.5) should be avoided, as they have been shown to be associated with higher incidence of renal failure and coagulopathy, and if at all used, the volume should be restricted to 33 mL/Kg/day. The new generation of starches (HES 130/0.4) appear to have a lower incidence of coagulopathy.
- All hyperoncotic colloids (including 10% HES and 20% albumin) can precipitate renal dysfunction. They should always be combined with crystalloids.
- Most synthetic colloids are prepared in solution with normal saline. Hence, large volumes of such colloids can also cause hyperchloremic acidosis with resultant coagulopathy.
- Crystalloids (lactated Ringer's solution) and colloids in balanced solution do not cause hyperchloremic acidosis and may be preferable to normal saline for large volume resuscitation.

Step 3: Assess response

- Response to a fluid challenge should be assessed clinically by features of increased perfusion like improved sensorium, increased sense of well-being, and increased urine output.
- This should also be assessed by improvement of hemodynamic parameters such as decreased tachycardia, improved blood pressure, and improved CVP or wedge pressure.
- Increasingly, it has been realized that static measures of preload such as CVP or pulmonary artery occlusion pressure (PAOP) do not adequately reflect need for fluid challenges. There are two principal reasons for this realization:
  - As per Frank–Starling law, preload (CVP or PAOP) is related to stroke volume or cardiac output in a curvilinear manner; that is, rise in preload will result in

increasing stroke volume in the steep part of the curve till the flat part is reached when increasing preload will not lead to further increase in stroke volume. In a given patient, it is difficult to predict the position of a preload measure on this curve by static values as it is dependent on ventricular compliance which is variable.
  - Left ventricular compliance varies among patients and may vary at different times in the same patient, so the pressure–volume curves are variable; thus, a stiff ventricle (hypertrophy) will lead to a decrease in ventricular compliance with shift of pressure–volume curves of the ventricle to the left. It means high pressure values (CVP or PAOP) for the same or low ventricular volume and a more compliant (dilated) ventricle will shift this curve to the right; thus, a low pressure (CVP or PAOP) reading may indicate a high ventricular volume. Thus, it is difficult to predict ventricular volume by a given pressure index (CVP or PAOP).
- Dynamic indices such as pulse pressure variation (PPV), systolic pressure variation (SPV) or stroke volume variation (SVV), echocardiographic vena cava diameter, or esophageal Doppler aortic blood flow changes during controlled positive-pressure ventilation or during passive leg raising in spontaneously breathing patients are more representative for predicting fluid responsiveness (see Chap. 16).
- When the risk of fluid challenge is not trivial, for example, in patients with compromised lung or cardiac function, consider using a dynamic predictor to guide fluid boluses.
- Since the hemodynamic state changes rapidly, reassessment of hemodynamics should be done frequently.

Step 4: Select inotrope or vasopressors
- Despite adequate volume replacement, if the patient is hypotensive and perfusion of vital organs is jeopardized, vasoactive agents may be administered to improve cardiac output and blood pressure.
- It is useful to understand the receptors through which adrenergic agents exert their effect.
- Three broad groups of agents may be identified:
  1. Predominant β-agonists (dobutamine, dopexamine, isoprenaline)
  2. Predominant α-agonists (phenylephrine)
  3. Those with mixed β- and α-effects (adrenaline and noradrenaline).
- In general, when the heart is failing, and the peripheral vascular resistance is normal, an agent with predominant inotropic effect (especially a β-1 selective agent) would be a good choice.
- If there is vasodilatation, a vasoconstrictor with predominant α-agonist activity is appropriate.
- Familiarize with doses and effects of commonly used inotropes and vasopressors.
- Consider practical aspects of vasopressor infusion:
  - Infuse through large veins preferably central veins.
  - Use multi-lumen catheters and use dedicated lumen for vasopressor infusion.
  - No other drug bolus or infusion should be given through the same lumen.

  - Use infusion or syringe pumps or other infusion controllers.
  - Invasive arterial pressure should be measured.
  - Dobutamine and other inodilators may be given through peripheral line.
- Volume deficit should always be corrected as much as possible before resorting to vasopressors which would lead to a false sense of security by increasing blood pressure while underlying hypovolemia and resultant low perfusion will lead to subsequent organ dysfunction.

Step 5: Titrate inotropes and vasopressors

- All inotropes and vasopressors should be titrated so that tissue perfusion is restored with the lowest dose of drug and to the desired end points with minimal or no side effects:
  - Titrate to clinical improvements in heart rate (HR) and mean arterial pressure (MAP).
  - Titrate inotropes to desired cardiac output.
- Do not aim for supranormal cardiac output:
  - Titrate vasopressors to MAP of 65–70 mmHg.
  - In patients with long-standing hypertension, renal failure, recent cerebral infarct, and increased intra-abdominal pressure, a higher MAP may be desirable.
  - In trauma with active bleeding, a lower MAP till bleeding source is controlled is advisable.
  - Aiming for higher MAP than desired may result in unnecessary vasoconstriction.
  - Titrate to achieve adequacy of organ perfusion
    - Urine output more than 0.5 mL/Kg/h
    - $ScvO_2$ more than 70%
    - Reduction in lactate levels over time (e.g., 20% over 2 h)
- Watch for side effects: tachycardia, arrhythmias, cardiac ischemia.

Step 6: Customize use of inotropes and vasopressors (Tables 18.1 and 18.2)

- Choice of inotropes and vasopressors may vary depending on clinical situation.
- *Levosimendan*

Table 18.1 Agents used in myocardial infarction and cardiogenic shock

Clinical picture	Low cardiac index (CI) but systolic blood pressure (SBP) > 100 mmHg, high left ventricular (LV) filling pressures	Low CI < 2.2 L/min/M^2, SBP < 90 mmHg, high LV filling pressures	Low CI < 2.2 L/min/M^2, SBP < 90 mmHg, high right atrium and right ventricular diastolic pressures
Choice of inotropic agents	Dobutamine/milrinone	Dopamine/ noradrenaline/ intra-aortic balloon pump (IABP)	Volume replacement/ dobutamine and noradrenaline/IABP

Table 18.2 Doses and effects of commonly used inotropes and vasopressors

Drug	Dose/range (μg/Kg/min)	Predominant receptor	Effects
Adrenaline	0.01–0.02	β-2	Lowered systemic vascular resistance (SVR), BP
	0.03–0.20	β-1	Increased contractility, HR, cardiac output (CO), lactic acidosis, hyperglycemia
	0.20–0.30	Alpha	Increased SVR, BP, impaired splanchnic perfusion
Noradrenaline	0.01–0.40	α-1, α-2, β-2	Raised SVR, BP, possible reflex fall in HR, possible fall in CO
			In fluid-resuscitated patients, improved renal and splanchnic blood flow
Dopamine	0.01–3.00	Dopaminergic	Renal and splanchnic
			Vasodilatation
	3.0–7.0	β-1	Increased contractility, HR, CO
	>7.0	Alpha 1	Increased SVR, BP, variable effects on splanchnic circulation and gastric mucosal flow
Dobutamine	3.0–20.0	β-1 (plus some β-2, α)	Increased contractility, decreased
			SVR, increased CO, increased HR
Dopexamine	0.5–6.0	β-2 (plus some β-1, α and dopaminergic)	Increased contractility, decreased
			SVR, increased CO, increased HR, increased renal and splanchnic blood flow at low dose
Isoprenaline	0.01–0.03	β-1, β-2	Decreased SVR, increased HR
Milrinone bolus	50 μg/Kg		Increased cAMP, increased contractility, coronary blood flow
	0.35–0.75		Decreased SVR, PVR, arrhythmias
Phenylephrine	0.1–3.0	Alpha 1	Prolonged action potential, Increased SVR, inotropy
Levosimendan	6–12 μg/Kg loading dose over 10 min followed by 0.05–0.2 μg/Kg/min as a continuous infusion	Calcium sensitizer	Increased sensitivity of actinomycin to calcium. Increased myocardial contractility.

- It is a myofilament calcium sensitizer. It increases myocardial contractility without increasing myocardial ATP consumption, thereby improving contraction at low energy cost.
- It causes normal or improved diastolic relaxation and vasodilatation.
- It has been studied in acute decompensated heart failure, during and after cardiac surgery, and postmyocardial infarction.

- *Digitalis glycosides*
  - The digitalis glycosides have long been used as inotropic agents.
  - However, today their role in the treatment of acute heart failure or cardiogenic shock is limited to control of the ventricular rate response in fast atrial fibrillation.
  - The onset of action of effects of digoxin takes 90 min after an intravenous loading dose, and peak effect occurs at 2–6 h.
  - The effects of digoxin are modest and unpredictable, and it has a narrow therapeutic index.
- *Agents used in septic shock*
  The Surviving Sepsis Campaign makes the following evidence-based recommendations in patients with sepsis:
  - *Vasopressors*
    - Recommend to maintain MAP ≥ 65 mmHg.
    - Recommend noradrenaline centrally administered as the initial vasopressors of choice.
    - Suggest that dopamine, adrenaline, phenylephrine, or vasopressin should not be administered as the initial vasopressor in septic shock.
    - Vasopressin at dose of 0.03 unit/min may be subsequently added to noradrenaline with anticipation of an effect equivalent to noradrenaline alone.
    - Use adrenaline as the first alternative agent in septic shock when blood pressure is poorly responsive to noradrenaline
    - Recommend not to use low-dose dopamine for renal protection.
    - Recommend to insert an arterial catheter in patients requiring vasopressors, as soon as practical.
  - *Inotropic therapy*
    - Recommend the use of dobutamine in patients with myocardial dysfunction as supported by elevated cardiac filling pressures and low cardiac output.
    - Do not increase cardiac index to predetermined supranormal levels.

Step 7: Understand limitations of vasopressor and inotrope therapy

- All inotropic and vasopressor drugs may increase myocardial oxygen demand.
- Increasing blood pressure by use of vasopressors does not lead to increased perfusion all the time; in certain circumstances like hypovolemia, it might lead to decreased flow to end organs.
- Tachycardia may occur, especially in volume-depleted patients.
- Arrhythmias.
- Catecholamines also have significant neurohumoral and metabolic effects, which might be deleterious, for example, hyperglycemia and hyperlactatemia induced by adrenaline and suppression of prolactin by dopamine.

Step 8: Wean inotropes and vasopressors

- All attempts should be made to treat underlying cause of low perfusion state whenever feasible and vasopressors should be weaned off at the earliest.
- If necessary, additional fluid challenges may be used judiciously in order to wean off vasopressors.

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   Powerpoint slide collection on the topic

Cardiorespiratory Arrest

19

Sheila Nainan Myatra, Amol T. Kothekar,
and Jigeeshu V. Divatia

A 60-year-old female diabetic patient with ischemic heart disease was operated for a cholecystectomy. On the first postoperative day in the ICU, she complained of sudden chest discomfort. While taking the history, the patient suddenly stopped speaking and fell back in the bed.

Step 1: Early recognition of sudden cardiac arrest—check responsiveness and breathing

- Check response—gently tap the patient on her shoulders and check for a response.
- Check breathing—no breathing or no normal breathing (i.e., only gasping). Remember that short period of seizure-like activity or agonal gasps may occur in victims of cardiac arrest and often confuse the rescuer.
- Suspect cardiac arrest if there is no response and absent or agonal respiration.

Step 2: Activate the emergency system

- Activate the emergency system if present in your hospital or just shout for help. Get the defibrillator or send someone to get it.

Step 3: Check the pulse

- There is a de-emphasis on pulse check. Check the pulse using a central pulse (carotid or femoral) for no more than 10 s. If pulse is not felt in 10 s or there is any doubt, start chest compression.

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Step 4: Start cardiopulmonary resuscitation (CPR)—initiate chest compressions before giving rescue breaths (airway, breathing, and circulation [ABC] is now circulation, airway, and breathing [CAB])

Positioning

- The victim should lie supine on a hard surface.
- The rescuer should kneel beside the victim's thorax (either side).
- Keep arms straight, elbows locked, and the shoulder directly above the hand.
- Hand placement: Place the heel of the hand on the lower half of the victim's sternum in the center (middle) of the chest, between the nipples, and then place the heel of the second hand on top of the first so that the hands are overlapped and parallel. Interlock fingers to avoid compression on the ribs.

Technique

During CPR, remember to "push hard and push fast" (all you need is two hands):

- Compressions rate—at least 100/min.
- Depth of sternal compression—at least 2 in., i.e., 5 cm (one-third anteroposterior diameter in children and infants).
- Compression ventilation ratio—the adult patient 30:2 (with one or more rescuers) and the child or infant 30:2 (with one rescuer) and 15:2 (with more than one rescuer).
- Compression relaxation ratio—1:1 (allow complete recoil of the chest).
- Perform five cycles (approximately 2 min) of compression and ventilation (ratio 30:2).
- Switch the compressor every 2 min.
- Give 2 min of uninterrupted CPR (limit interruptions to <10 s and interrupt only during intubation and just when you are ready to deliver a shock).

To easily achieve the above, one could use simple counting at the speed of approximately 100/min—"one and two and three and …." Every time you say a number, compress, and when you say "and," you relax.

Ventilation

- After every 30 compressions, give two slow rescue breaths using the face mask and the AMBU bag (using the reservoir bag) to deliver 100% oxygen.
- Before you start ventilation, open the airway using a jaw thrust or a head tilt/chin lift maneuver (avoid this in trauma victims with suspected cervical spine injury).
- Give one breath over 1 s (rapid ventilation could cause gastric insufflations and increase the risk of aspiration, should be avoided).
- Give sufficient tidal volume to ensure visible chest rise.
- Reposition mask if there is a leak and insert an oral or nasal airway if there is airway obstruction due to fall of the tongue.
- The use of cricoid pressure during ventilation is generally not recommended.

Complete five cycles of compression followed by ventilation (it will take approximately 2 min if you give it at the correct rate).

Step 5: Attach the defibrillator (automated external defibrillators [AED] or manual defibrillators) and shock if indicated

- As soon as an AED/manual defibrillator is available, attach it and shock if indicated, i.e., in ventricular fibrillation (VF) and pulseless ventricular tachycardia (VT).
- Prefer a biphasic defibrillator; if unavailable, use a monophasic defibrillator.
- Ensure that no one is touching the patient before you shock.
- Electrode placement should be in the anterior-lateral pad position (default). Alternative positions are anterior-posterior, anterior-left infrascapular, and anterior-right infrascapular.
- Shock energy—(a) Biphasic: Use the manufacturer's recommendation (120–200 J); if unknown, use maximum available. Second and subsequent doses should be equivalent, and higher doses may be considered if available. (b) Monophasic: 360 J (in children and infants, use 2–4 J/Kg first and 4 J/Kg for subsequent shocks; higher energy may be considered but not to exceed 10 J/Kg).
- No pulse check is recommended after defibrillation; resume CPR immediately.
- Reattach the defibrillator after every 2 min of CPR.
- Reduce time between the last compression and shock delivery and the time between shock delivery and resumption of compressions. CPR should be performed while the defibrillator is readied.
- There is no upper limit to the number of shocks you give. Remember that the shockable rhythms are the ones with the better prognosis, so never give up on a VF or pulseless VT.
- AEDs can now be used even in infants with a pediatric dose attenuator if the manual defibrillator is not available. If neither is available, the AED without the pediatric dose attenuator can be used. (All AEDs are biphasic.)
- The precordial thump may be considered in witnessed, monitored, and unstable ventricular tachyarrhythmias only when a defibrillator is not available.
- Electric pacing is not recommended for routine use in cardiac arrest.

Step 6: Drug therapy

- Use intravenous (IV) or intraosseous (IO) route for bolus delivery of drugs. For IV use, give the bolus drug followed by a 20-mL saline push and raise the extremity.
- If both IV and IO are unavailable, then tracheal route may be used. Epinephrine, vasopressin, and lidocaine may be administered through this route. (Use 2–2½ times the dose diluted in 5–10 mL of distilled water or saline.)
- Give a vasopressor soon after giving the shock. Epinephrine IV/IO dose should be 1 mg every 3–5 min (vasopressin IV/IO dose—40 units can replace the first or second dose of epinephrine and repeated again after 20 min).
- Amiodarone should be given when VF/VT is unresponsive to CPR, defibrillation, and vasopressor therapy. IV/IO first dose should be 300 mg bolus, and the second dose should be 150 mg (after 3–5 min if VF/VT recurs or persists). This may be followed by a 24-h infusion. (Use lidocaine only if amiodarone is unavailable.)
- Atropine should not be used during pulseless electrical activity or asystole as it is unlikely to have a therapeutic benefit.

- Other drugs are not routinely used and should be considered only in specific situations:
  - Magnesium sulfate (1–2 g) for torsades de pointes associated with a long QT interval.
  - Sodium bicarbonate (initial dose is 1 mEq/Kg) should be used only if there is hyperkalemia, bicarbonate-responsive acidosis, or tricyclic antidepressant overdose. It is harmful in hypercarbic acidosis.

Step 7: Advanced airway

- Weigh the need for minimally interrupted compressions against the need for insertion of an advanced airway, i.e., the endotracheal tube or the supraglottic airway (laryngeal mask airway, esophageal tracheal tube—Combitube, or laryngeal tube).
- Continue bag mask ventilation if advanced airway is not placed.
- Confirm the placement of advanced airway by the clinical method (chest expansion and breath sound), and in addition, use the capnography to confirm and monitor the correct placement. Record the depth and secure the tube.
- Once advanced airway is in place, give 8–10 breaths per minute and do uninterrupted chest compressions.

Step 8: Treat reversible causes

During each 2-min period of CPR, review the most frequent causes—five H's and five T's—to identify factors that may have caused the arrest or may be complicating the resuscitation:

Five H's	Five T's
Hypovolemia	Tension pneumothorax
Hypoxia	Tamponade, cardiac
Hydrogen ion (acidosis)	Toxins
Hypo-/hyperkalemia	Thrombosis, pulmonary
Hypothermia	Thrombosis, coronary

Step 9: Monitor the CPR quality throughout resuscitation

- Give emphasis on delivering high-quality CPR. This means giving compressions of adequate rate and depth, allowing complete chest recoil between compressions, minimizing interruptions in compressions, avoiding excessive ventilation, and rotating the compressor every 2 min.
- Use quantitative waveform capnography to monitor end tidal CO_2 if available (expressed as a partial pressure in mmHg—$PetCO_2$) in intubated patients. If $PetCO_2$ is less than 10 mmHg, attempt to improve CPR quality.
- If intra-arterial pressure monitoring is present and diastolic pressure is less than 20 mmHg, attempt to improve CPR quality.
- Return of spontaneous circulation (ROSC) can be confirmed by return of pulse or blood pressure or abrupt sustained increase in $PetCO_2$ (typically ≥40 mmHg) or spontaneous arterial pressure waves with intra-arterial monitoring.

Step 10: Postcardiac arrest care after ROSC

- The goal should be to optimize cardiopulmonary function and vital organ perfusion.
- Transfer the patient to an appropriate hospital or ICU with facility to deliver postcardiac arrest care.
- Optimize ventilation to minimize the lung injury. Do chest X-ray to confirm airway position and to diagnose pneumonia/pulmonary edema. Use lung-protective ventilation if there is pulmonary dysfunction; adjust settings using blood gas values. Avoid excessive ventilation and hyperoxia.
- Once ROSC is achieved, the fraction of inspired oxygen (FiO_2) should be adjusted to the minimum concentration needed to achieve arterial oxyhemoglobin saturation of ≥94%, with the goal of avoiding hyperoxia while ensuring adequate oxygen delivery.
- Treat hypotension (systolic blood pressure [SBP] < 90) with fluid and vasopressors and treat other reversible causes.
- Consider induced hypothermia. Adult patients with persistent coma after ROSC should be cooled to 32–34°C for 12–24 h provided SBP is more than 90 mmHg or mean arterial pressure (MAP) is more than 70 with or without vasopressors.
- Patients comatose before cardiac arrest or another reason to be comatose (e.g., drug overdose and status epilepticus) should be excluded. Avoid hypothermia in patients with coagulapathy/bleeding or refractory arrhythmias because hypothermia exaggerates these conditions. Cooling can be done using cold IV fluid bolus of 30 mL/Kg, surface cooling (ice packs, mattresses), endovascular cooling, etc. Sedation/muscle relaxants may be used to control shivering, agitation, or ventilator dyssynchrony as needed. After 24 h, start slow rewarming at 0.25°C/h. Prevent hyperpyrexia (>37.7°C).
- Maintain glucose control—moderate glycemic control (144–180 mg/dL).
- Use anticonvulsants if the patient is seizing (use EEG monitoring if available).
- Identify and treat acute coronary syndrome (ACS). Patients with suspected ACS should be sent to a facility with coronary angiography and interventional reperfusion facility (primary percutaneous coronary intervention).
- Reduce the risk of multiorgan injury and support organ function if required.

Step 11: Prognostication after cardiac arrest

In patients treated with therapeutic hypothermia:

- Clinical neurologic signs, electrophysiologic studies, biomarkers, and imaging should be performed where available 3 days after cardiac arrest.
- Presently, there is limited evidence to guide decisions regarding limitation/withdrawal of life support in these patients as favorable outcomes have been seen in those in whom studies predicted poor outcome. Use your best clinical judgment based on this testing to make a decision.

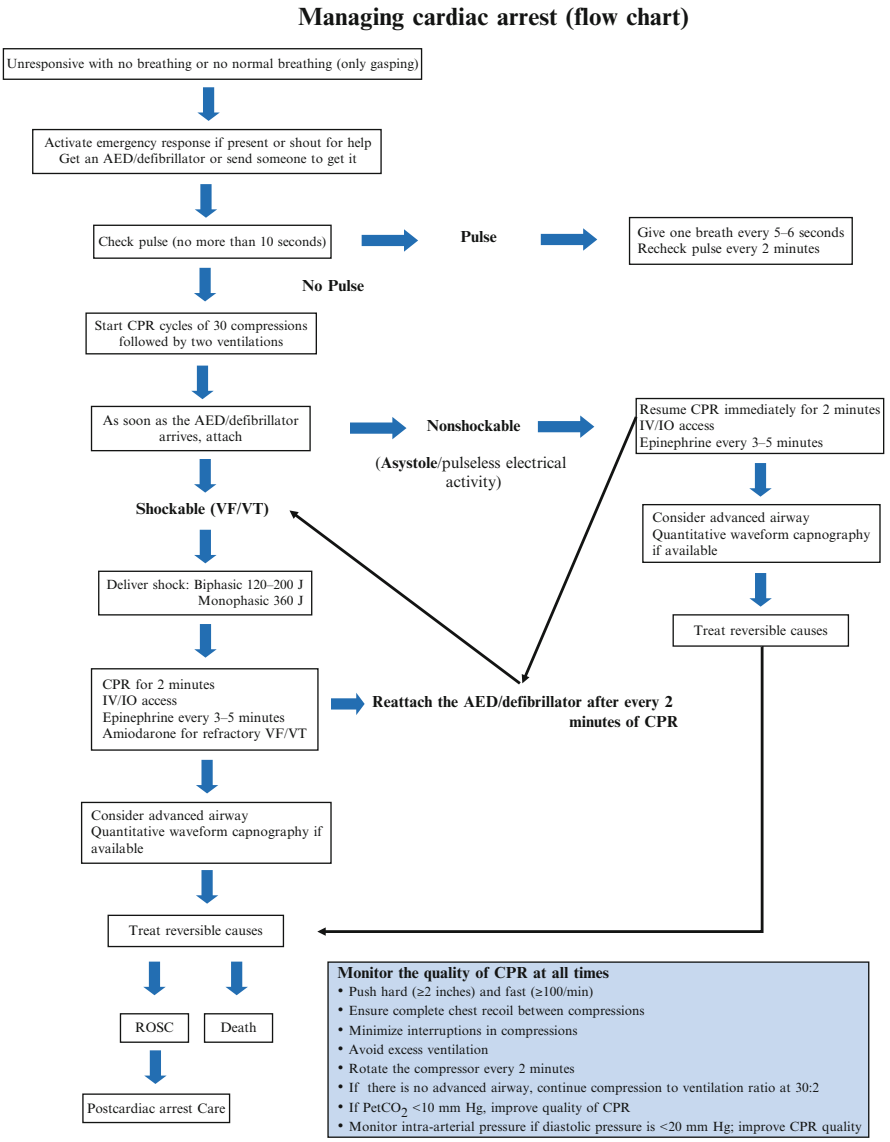
In patients who have not undergone therapeutic hypothermia, the following features are present:

- Absence of pupillary response to light on the day 3
- Absence of motor response to pain by the day 3

- Absence of bilateral cortical response to median nerve somatosensory evoked potentials in those comatose for at least 72 h after a hypoxic-ischemic insult

Limitation/withdrawal of life support in this situation can be considered.

Step 12: Assist survivors from cardiac arrest who require rehabilitation services



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Cardiogenic Shock

20

Ashit V. Hegde and Khusrav Bajan

A 55-year-old male patient was admitted to the hospital with history of chest pain for about 3 h. He was drowsy, extremities were cold, and his blood pressure was 84/60 mmHg. His electrocardiogram showed extensive anterior ST elevation myocardial infarction.

The management of acute coronary syndrome and its complications has increasingly been protocolized. Timely implementation of these protocols especially in patients with shock is the essence as "time is muscle." Cardiogenic shock carries a high 30-day mortality within the range of 30–40%.

Step 1: Urgently resuscitate

- The patient with prolonged cardiogenic shock needs to be ventilated in spite of normal oxygenation parameters to decrease oxygen consumption by the respiratory muscles and utilization of low cardiac output by vital organs.
- Use sedatives that are less likely to worsen hypotension during intubation, namely, etomidate, ketamine, and fentanyl.
- In patients who are not clinically in heart failure, cautious fluid resuscitation with proper hemodynamic monitoring should be initiated.

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Step 2: Take a focused history and quick physical examination to differentiate causes of chest pain with shock

- Acute myocardial infarction (AMI)
- Pulmonary embolism
- Pneumothorax
- Pericardial tamponade
- Acute dissection of the aorta
- Esophageal perforation
- Pneumonia

Step 3: Investigate urgently to confirm cardiogenic shock

- Cardiac enzymes (Trop T, Trop I, CPK MB)
- ECG—serially
- 2D echocardiogram

Step 4: Ascertain the cause of cardiogenic shock (Table 20.1)

- Complicated AMI is the most common cause of cardiogenic shock.

Table 20.1 Causes of cardiogenic shock

Acute myocardial infarction
Large infarction
Right ventricular infarction
Papillary muscle rupture
Free left vetricular wall rupture
Pericardial tamponade
Ventricular septal defect
Dilated cardiomyopathy
Myocarditis
Myocardial contusion
Acute mitral/aortic regurgitation
Left ventricular outflow tract obstruction
Pericardial tamponade

Step 5: Initiate medical management

- *Aspirin*: 160–325 mg of soluble or chewable aspirin should be administered, but the decision to administer clopidogrel should be made only after angiography (in case the patient needs urgent coronary artery bypass graft [CABG]).
- *Thrombolysis*: In the presence of hypotension, thrombolytic drugs may not reach the coronary vessel. Thrombolytic therapy is therefore not very effective in established cardiogenic shock. Consider thrombolysis only if primary percutaneous intervention (PCI) is not possible urgently. Thrombolytic drugs are more effective if administered after the BP has been raised (preferably after the use of an intra-aortic balloon pump [IABP]).

Step 6: Initiate hemodynamic management (see Chap. 18)

- A central venous line preferably under ultrasound guidance to avoid arterial punctures and an intra-arterial line (preferably radial) should be urgently inserted.
- The use of a pulmonary artery catheter is optional.
- Urine output should be monitored hourly.
- Urgent 2D echo is mandatory to rule out mechanical causes of shock (papillary muscle rupture, acute ventricular septal defect, free wall rupture, and pericardial tamponade). 2D echo also gives an idea of left ventricular ejection fraction (LVEF) and left ventricular (LV) filling pressures.
- Fluid boluses may be cautiously administered to most patients with cardiogenic shock. Even patients with pulmonary edema may have intravascular volume depletion because there is redistribution of fluid from the intravascular compartment into the alveolus. These fluid boluses should be guided carefully by frequent physical examination and intravascular pressure monitoring.
- Most patients will also need a vasopressor and an inotrope. The least dose of these medications required to maintain adequate perfusion to the tissues should be used. Dobutamine (2.5–10 mcg/Kg/min) is the inotrope of choice in patients with a BP of more than 80 mmHg. Levosimendan, a calcium sensitizer inotrope, has also been increasingly used in cardiogenic shock as it has a relatively less effect on increase in oxygen consumption by the myocardium. Dopamine (5–20 mcg/Kg/min) is used if the BP is less than 80 mmHg or if the patient's BP drops further with dobutamine. There is increasing evidence that many patients with cardiogenic shock are inappropriately vasodilated because of an inflammatory response. Noradrenaline (or vasopressin) may be tried in patients not responding to dopamine/dobutamine.

Step 7: Consider inserting an IABP (see Chap. 101)

- Early insertion of IABP helps to support the coronary and cerebral circulation.
- It acts as a bridge to cardiac revascularization procedures, insertion of other mechanical assist devices, or cardiac transplant.
- In cases of myocardial stunning, it buys time while other therapeutic measures take effect.

Step 8: Consider coronary revascularization

- Urgent left heart catheterization and revascularization, if coronary anatomy is suitable, should be undertaken.
- Timely primary PCI is the preferred mode of reperfusion in patients with cardiogenic shock complicating AMI.
- Proper hydration and *N*-acetylcysteine (600 mg b.i.d for 3 days) should be given to prevent contrast-induced nephropathy as these patients are at risk of acute kidney injury (AKI).
- Urgent CABG is indicated in patients with coronary anatomy not favorable for PCI.

- The shock study demonstrated a 13% decrease in mortality in patients with cardiogenic shock assigned to early revascularization (primary PCI or CABG).
- Although revascularization should be performed as early as possible, there is a survival benefit for up to 48 h after MI and within 18 h of the onset of shock.

Step 9: Manage specific situations

Mechanical complications	Mechanical complications of MI, including rupture of the ventricular septum, free wall, or papillary muscles, need urgent surgical correction (after temporary stabilization with an IABP).
Right ventricular (RV) infarction	Patients with RV dysfunction and shock need adequate right-sided filling pressures to maintain cardiac output. However, overzealous fluid therapy may do more harm by overdistending the RV and compromising LV filling. RV end-diastolic pressure of 10–15 mmHg is optimum. If the patient remains hypotensive in spite of reasonable fluid therapy, inotropes and IABP are indicated.
Pericardial tamponade	It is an uncommon but rapidly reversible cause of cardiogenic shock. Its existence should be actively sought in all cases of shock by a bedside echo looking for evidence of diastolic compression of the right side of the heart. Immediate pericardiocentesis is lifesaving. Fluid boluses and vasopressors may be used as a temporizing method.

Step 10: Consider rescue therapy in refractory shock

- The left ventricular assist device (LVAD) placed surgically or percutaneously should be considered in patients' refractory to medical therapy and IABP.
- It should be instituted early before irreversible organ damage occurs to work as a "bridge" before definitive therapy like cardiac transplantation is available.
- Extracorporeal assist devices have been increasingly used in the ICU as a bridge to definitive therapy (Fig. 20.1).

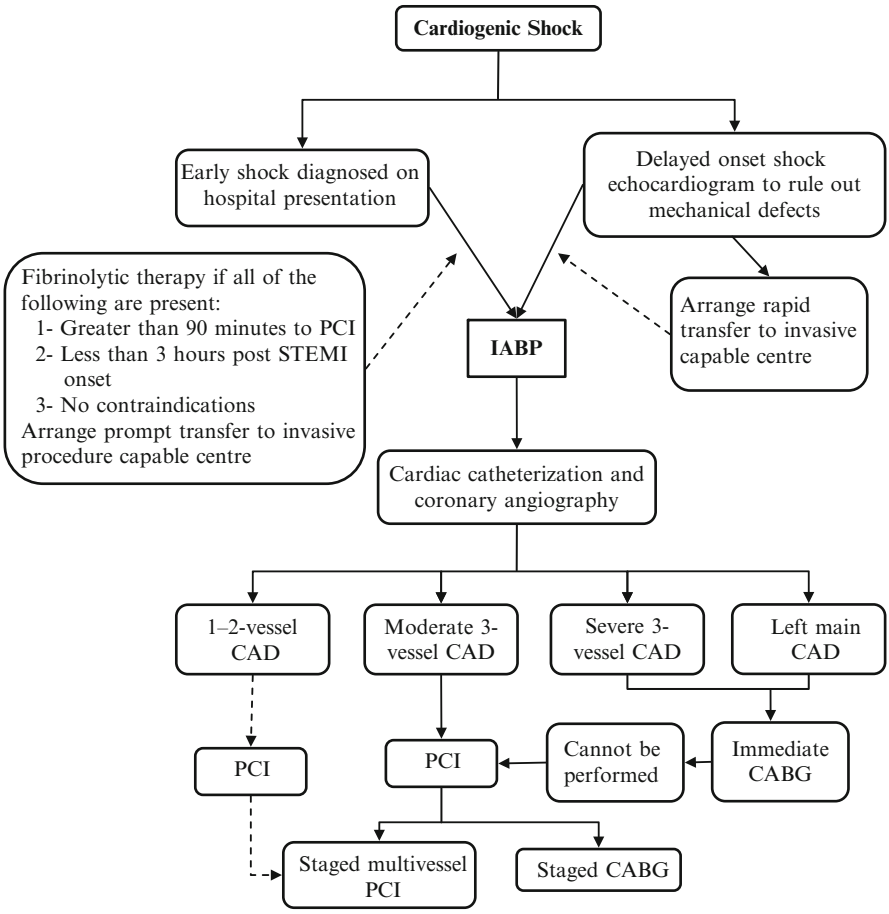

Fig. 20.1 Cardiogenic shock

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   A review article
2. Hollenberg SM. Cardiogenic shock. Crit Care Clin. 2001;17(2):391–410.
   A comprehensive review article on the subject
3. Hochman JS, Sleeper LA. Early revascularization in acute myocardial infarction complicated by cardiogenic shock. SHOCK investigators. N Engl J Med. 1999;341(9):625–34.
   In patients with cardiogenic shock, emergency revascularization did not significantly reduce overall mortality at 30 days. However, after 6 months, there was a significant survival benefit.

Acute Heart Failure

21

Rajesh Chawla and Rajeeve Kumar Rajput

A 60-year-old male patient, a known case of coronary artery disease (CAD) and type 2 diabetes, presented with history of acute onset of breathlessness and orthopnea for 2 days. On examination, he was found to have tachycardia, tachypnea, and bilateral basal crepitations, and SpO_2 was 87%.

Heart failure is defined as a pathophysiological state in which heart is unable to pump blood at a rate commensurate with the requirements of the metabolic demand.

New York Heart Association (NYHA) classification of heart failure comprises of four classes which has therapeutic and prognostic significance.

Class I—patients have no limitation of physical activity.
Class II—patients have slight limitation of physical activity.
Class III—patients have marked limitation of physical activity.
Class IV—patients have symptoms even at rest and are unable to carry on any physical activity without discomfort.

The management of heart failure comprises of stabilizing the clinical state of the patient, making a diagnosis, detect etiology and initiate definitive treatment.

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Step 1: Initial resuscitation (see Chap. 78)

- Administer oxygen in high concentration to maximize tissue oxygenation as hypoxia can depress myocardial function.
- Assess the response clinically, by SpO_2 and arterial blood gas assessment.
- Continuous positive airway pressure (CPAP) or noninvasive ventilation (NIV) is indicated if the patient does not respond to oxygen alone.
- With aggressive conservative management, intubation can be avoided in many patients of heart failure presenting with respiratory distress.
- If poor gas exchange is present despite conservative management, the patient should be intubated and initiated on invasive ventilation.
- Invasive ventilation helps in reducing oxygen demand and reverses respiratory muscle fatigue.
- Assess the circulatory status by pulse and blood pressure and the status of major organ perfusion.
- Assess the volume status, whether volume depleted or congested.
- Some patients with pulmonary edema are centrally fluid depleted. It may be very difficult to assess this in critically ill patients, so invasive monitoring may be required.
- Initiate inotropes or vasopressors or advanced cardiac support based on severity of the hemodynamic compromise.
- Therapy should be directed to treat the cause of heart failure to improve circulation and optimize BP and cardiac output.

Step 2: Take clinical history

- Clinical history should be obtained to find out the cause of acute heart failure.
- History of cardinal cardiac symptoms such as dyspnea, angina, palpitation syncope, fatigue, weakness, swelling of ankles or abdomen, and previous cardiac surgery.
- Make an attempt to detect whether acute heart failure is due to acute coronary syndrome, which requires urgent revascularization.
- Look for precipitating conditions such as severe anemia, sepsis, severe hypertension, arrhythmia, thyroid disorders, medical, and dietary noncompliance.

Step 3: Do quick physical examination

Look for signs of congestion/cardiac involvement:

- Raised jugular venous pressure, peripheral edema, ascites, hepatomegaly
- Displaced apical pulse due to cardiomegaly
- Gallop rhythm
- Cardiac murmur

Look for signs of low cardiac output:

- Hypotension
- Level of consciousness, confusion
- Cool peripheries and low volume carotid pulse

Table 21.1 Types of heart failure

Forward	Backward left	Backward right
Fatigue or weakness, confusion, drowsiness	Mild exertion dyspnea, orthopnea	Dyspnea not prominent
Pallor, peripheral cyanosis	Pulmonary edema	Acute tricuspid regurgitation
Cold, clammy skin		V wave on central venous pressure trace
Low BP, oliguria		Hemodynamic compromise, arrhythmia
Cardiogenic shock		Cardiogenic shock
Cause	Cause	Cause
Acute myocardial infarction (MI), acute valvular dysfunction	Acute valvular disease	Acute pulmonary embolism
Pulmonary embolism, cardiac tamponade	Acute MI	Right ventricular infarction
	Sudden rise in BP (flash pulmonary edema)	

- Tachycardia or bradycardia
- Decreased urine output
- Peripheral cyanosis

The signs may also depend on whether it is right- or left-sided heart failure, systolic or diastolic failure, or forward or backward failure (Table 21.1).

Step 4: Send investigations

- ECG may suggest acute MI, pulmonary embolism, and arrhythmia
- Chest radiograph:
  - Cardiac size, shape
  - Presence of pulmonary congestion—alveolar and interstitial edema
  - Rule out pneumothorax, pneumonitis
- Hemogram
- Urea, electrolytes
- Arterial blood gases with lactate levels
- Blood glucose
- Coagulation profile—prothrombin time/partial thromboplastin time
- Cardiac markers—CPK, CPK-MB, troponins T and I
- B-type natriuretic peptide of less than 100 pg/mL rules out heart failure
- Liver function tests
- Echocardiography most helpful—global and regional LV function, valvular abnormalities, diastolic function, diagnostic of cardiac tamponade and RV dysfunction due to pulmonary embolism
- Invasive hemodynamic monitoring—cardiogenic shock, unstable hemodynamics, poor response to therapy
- Holter monitoring, TEE (Trans esophageal echocardiography) in selected cases
- Cardiac catheterization, coronary angiography

Table 21.2 Vasodilators—doses

Vasodilator	Dosing
Nitroglycerine	Start 10–20 μg/min, increase up to 200 μg/min
Nitroprusside	Start with 0.1 μg/Kg/min and increase up to 5 μg/Kg/min
Nesiritide	Bolus 2 μg/Kg + infusion 0.01 mcg/Kg/min

Table 21.3 Diuretics—doses and clinical indications

Fluid retention	Diuretic	Daily dose (mg)
Moderate	Furosemide	20–40
	Bumetanide	0.5–1
	Torsemide	10–20
Severe	Furosemide	40–100
	Furosemide infusion	(5–40 mg/h)
	Bumetanide	1–10
	Torsemide	20–100
Refractory to loop diuretic	Add hydrochlorothiazide	50–100
	Metolazone	2.5–10
	Spironolactone	25–50
With alkalosis	Acetazolamide	250–375

Step 5: Specific treatment

1. *Reduce demand*
   - Control heart rate.
   - Relieve anxiety—provide reassurance and anxiolytics.
   - Prevent and treat pain—1.5–3 mg morphine or 50–100 mcg fentanyl IV can be given.
   - Use β-blockers cautiously in selective cases. Carvedilol (3.125–25 mg) or metoprolol (12.5–50 mg) can be used. Start with low dose and titrate gradually to higher dose to achieve the heart rate of less than 60/min.
   - The patient on chronic β-blocker should have their dose reduced during acute decompensated heart failure.
2. *Decrease preload*
   - Vasodilator—nitroglycerine, isosorbide nitrate (Table 21.2)
   - Diuretics (Table 21.3)
   - Fluid restriction
   - Mechanical ventilation
   - In refractory volume overload state along with renal compromise, continuous ultrafiltration (SCUF) should be considered
3. *Reduce afterload*
   - Control of blood pressure—nitroglycerine, nitroprusside
   - Inotropes—dobutamine
   - Intra-aortic balloon pump (IABP)—specially in acute coronary syndrome

Table 21.4 Inotropes—mode of administration and doses

	Bolus	Infusion rate
Dobutamine	No	2–20 μg/Kg/min
Dopamine	No	3–5 μg/Kg/min: inotropic
		>5 μg/Kg/min: vasopressor
Milrinone	25–75 μg/Kg over 10–20 min	0.375–0.75 μg/Kg/min
Enoximone	90 mcg/Kg/min over 10–30 mins	5–20 mcg/Kg/min
Levosimendan	12 μg/Kg over 10 min (optional)	0.1 μg/Kg/min which can be decreased to 0.05 or increased to 0.2 μg/Kg/min
Norepinephrine	No	0.2–1.0 μg/Kg/min
Epinephrine	Bolus: 1 mg can be given IV during resuscitation, repeated every 3–5 min	0.05–0.5 μg/Kg/min

4. *Increase contractility* (Table 21.4)
   - Dopaminergic agonists—dopamine, dobutamine
   - Sympathomimetic agents—adrenaline, norepinephrine
   - Phosphodiesterase inhibitors—amrinone, milrinone:
     - Mainly useful in patients with refractory acute severe heart failure
     - Postoperative decompensation
   - Levosimendan (calcium channel sensitizer)
   - Nesiritide
   - In patients with severe hypotension, use vasopressor judiciously to maintain adequate perfusion pressure and taper them off at the earliest.
5. *Optimize blood supply—early reperfusion therapy*
   - Thrombolytic agents, streptokinase, rTPA, tenecteplase
   - Percutaneous coronary intervention (PCI)
6. *Ensure adequate oxygen*
   - Face mask/noninvasive ventilation or CPAP
   - Intubation and ventilation in refractory heart failure:
     - Mechanical assist devices—IABP
     - Left or right ventricular assist devices in refractory cases
   - Early referral to appropriate centers should be considered

Step 6: General care
- Thromboprophylaxis
- Adequate nutrition
- Correct electrolyte imbalance
- Prevent and treat infection

Step 7: Treat the specific cause
- Pulmonary embolism—thrombolysis or surgical thrombectomy if indicated (see Chap. 5)
- Valvular defect—repair or replace
- Coronary artery disease—CABG or PTCA
- Cardiac tamponade—urgent pericardiocentesis

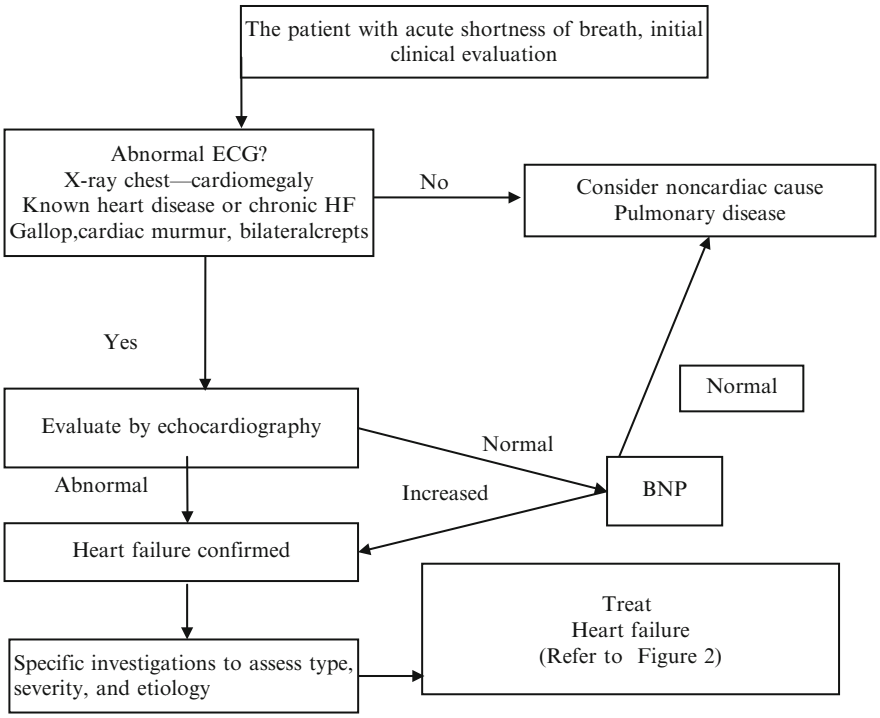

Fig. 21.1 Initial assessment of the patient presenting with acute dyspnea

Step 8: Long-term care

- Advise regarding diet, salt intake, rehabilitation.
- Essential medication known to improve survival like β-blockers, ACE inhibitors or ARBs, and mineralocorticoid inhibitors should be started.
- Statins should be prescribed specially for CAD patients.
- Regular follow-up is very critical.
- Patients who remain symptomatic (NYHA III, IV) despite optimal medical treatment and have LVEF less than 30% with wide QRS more than 120 ms are candidates for biventricular pacing.
- AICD implantation is recommended to prevent sudden cardiac death in the following conditions:
  - All patients with LVEF less than 30% in nonischemic cardiomyopathy.
  - LVEF less than 30% at least 6 weeks after myocardial infarction.
  - Secondary prevention: Episodes of Prior Ventricular fibrillation/ventricular tachycardia and resuscitated sudden cardiac arrest.
- Patients who are very symptomatic despite best medical treatment are candidate for cardiac transplantation or assist devices.

An approach to the management of heart failure is summarized in Figs. 21.1 and 21.2.

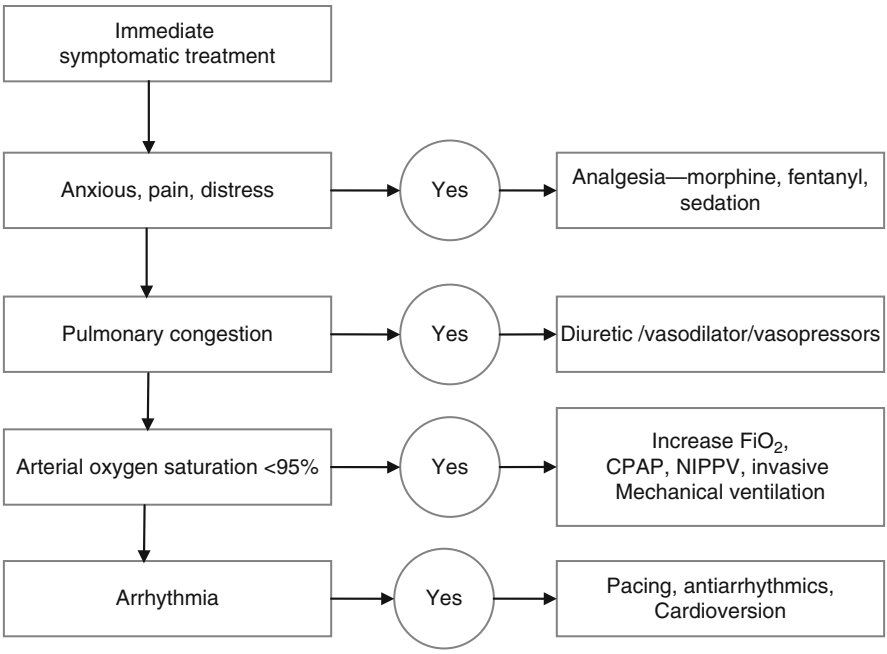

Fig. 21.2 Stepwise medical management of the patient presenting heart failure

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Cardiac Arrhythmias

22

Shyam Sunder Tipparaju and Gopinath Ramachandran

A 40-year-old hypertensive diabetic male patient was admitted with the history of dizziness and a sensation of passing out. He had no significant past medical history. On examination he was alert and oriented, with well-perfused extremities, pulse rate of 130/min irregular, BP of 120/70 mmHg (usual BP 150/90 mmHg), and soft systolic murmur on cardiac auscultation.

Cardiac arrhythmias are caused by disorders of impulse formation or disorders of impulse conduction, or both. Arrhythmias in the ICU pose a diagnostic and therapeutic challenge. A systematic approach to interpretation of electrocardiogram, identifying urgency of management, and proper consultation when required is needed for an optimum outcome.

Step 1: Start resuscitation

- Establish an intravenous (IV) access as these patients may deteriorate suddenly.
- In cardiac arrest situations, follow the advanced cardiac life support (ACLS) protocol (see Chap. 19).

Step 2: Urgently cardiovert the hemodynamically unstable patient if indicated (see Chap. 94)

- If the patient is in shock or in severe respiratory distress with atrial or ventricular tachyarrhythmia, immediate synchronized cardioversion is attempted.

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- In the conscious patient, IV midazolam should be judiciously used in aliquots of 1–2 mg prior to cardioversion.

Step 3: Urgently insert temporary transvenous pacemaker if indicated (see Chap. 95)
- In patients with symptomatic bradycardia not responding to atropine, transvenous pacemaker should be inserted.
- Temporizing measure with the transcutaneous pacemaker may be tried.

Step 4: Take focused history
- Cardiorespiratory symptoms
- Low-output state symptoms such as fatigue, dizziness, syncope, and oliguria
- Past history of cardiac disorders
- History of hypertension, diabetes, hyperlipidemia, or systemic diseases such as thyrotoxicosis
- Alcohol, nicotine, or other substance abuse
- Drug history—antiarrhythmic and antihypertensive

Step 5: Perform focused physical examination
- General physical examination to look for thyroid enlargement, tremor, anemia, pedal edema, and low perfusion state
- Cardiovascular system:
  - Listen for gallop rhythm or murmur
  - Palpate all peripheral and central pulses
  - Take blood pressure in both arms
- Other system examination

Step 6: Send basic investigation
- Complete blood count—anemia
- Trop T/I—raised in myocardial infarction
- Electrolytes (Na, K, Mg, Ca, PO4)
- Arterial blood gas (ABG)—acid–base disorders
- Renal and liver function test
- Echocardiogram—left ventricular function, left atrial size and clot, and valvular disorders
- Chest X-ray—cardiomegaly and the left atrial enlargement

Step 7: Analyze 12-lead electrocardiogram (ECG) (Fig. 22.1)
- Systematically analyze 12-lead ECG.
- Any previous ECG if available should be compared with the present.
- Check the name and the date.
- Check calibration (1 mV deflection for two large squares = 10 mm).
- Check the speed of tracing (25 mm/s).
- Check the correct limb lead placement—P wave inverted in aVR.

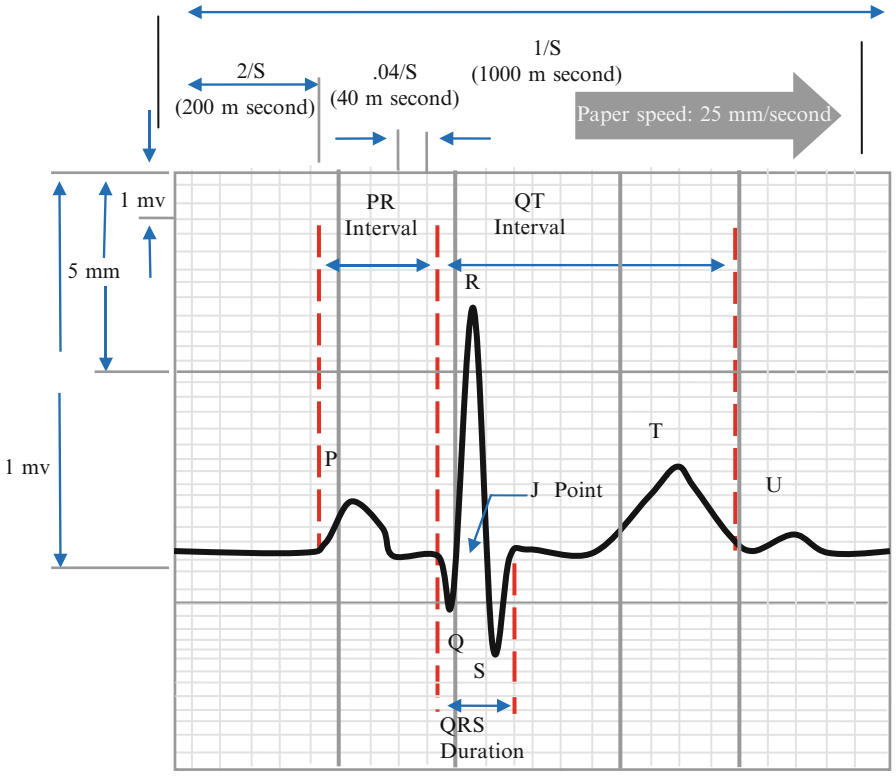


Fig. 22.1 Electrocardiogram

Step 8: Calculate the ventricular rate

- One small square = 0.04 s.
- One large square = 0.2 s.
- Measure R–R interval.
- Count the number of small squares in R–R interval and divide into 1,500.
- Or count the number of large squares in R–R interval and divide into 300.
- Or for each big square in R–R interval decremental heart rate of 300, 150, 100, 75, 60, 50 (e.g., for one big square in between R–R interval, heart rate is 300; for two big squares, it is 150; and so on).
- If irregular cardiac rhythm, count the number of beats in 6 s (two 3-s intervals) and multiply by 10.
- Bradycardia is less than 60/min.
- Tachycardia is more than 100/min.

Step 9: Analyze ventricular rhythm

- Check Lead II rhythm strip.
- Check RR interval for regularity.

- Mark two consecutive R waves and match the distance with subsequent RR intervals to check for regularity of cardiac rhythm.

Step 10: Identify P waves
- Absent P waves suggest atrial fibrillation, ventricular tachycardia, or rhythms originating from the AV node.
- Look for flutter waves.

Step 11: Examine QRS complex, normal or wide (normal less than 0.08 s)
- Normal—rhythm originates from the AV node or above.
- Wide—rhythm usually originates infranodal or supranodal with aberrant AV conduction.

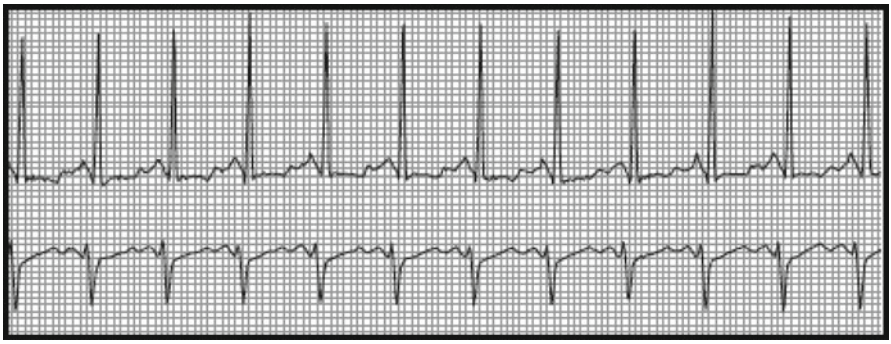
Step 12: Find out the relationship between the P waves and QRS complexes
- More P waves than QRS complexes
  - Second- or third-degree AV block
- More QRS complexes than P waves
  - Accelerated junctional rhythm
  - Ventricular tachycardia

Step 13: Describe arrhythmias based on
- Rate (bradycardia or tachycardia)
- Rhythm (regular or irregular)
- Origin of impulse (supraventricular, ventricular, or artificial pacemaker)
- Intraventricular conduction (narrow or wide-complex QRS)

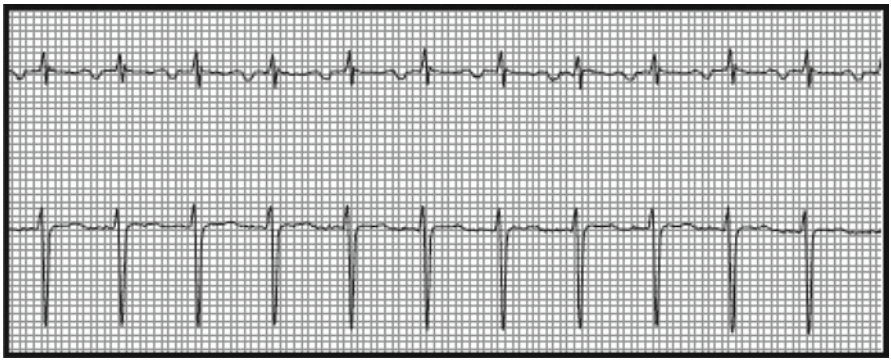
Step 14: Investigate and treat the underlying disease
- Clinically, significant tachy- or bradyarrhythmias are a reflection of the underlying cardiac disease—ischemic, hypertensive, valvular, or infective—which should be managed concurrently.
- Systemic diseases such as thyroid disorders, electrolyte imbalance, or drugs can also cause significant arrhythmias and should be managed.
- Look for preexcitation syndrome (Wolff–Parkinson–White [WPW] syndrome).

Step 15: Identify and manage precipitating cause
- Precipitating factors, such as fever, acidosis, drugs and alcohol intoxication, should be sought for and managed in all cases of clinically significant arrhythmias.

Step 16: Analyze and manage narrow complex, regular tachycardias
- *Sinus tachycardia*
  - Rate is usually less than 150/min. Maximum sinus heart rate is age-dependent (220 age in years).
  - P wave morphology is normal and precedes each QRS complex.
  - Treat the underlying cause such as pain, fever, anxiety, hypovolemia, and hypoxia.

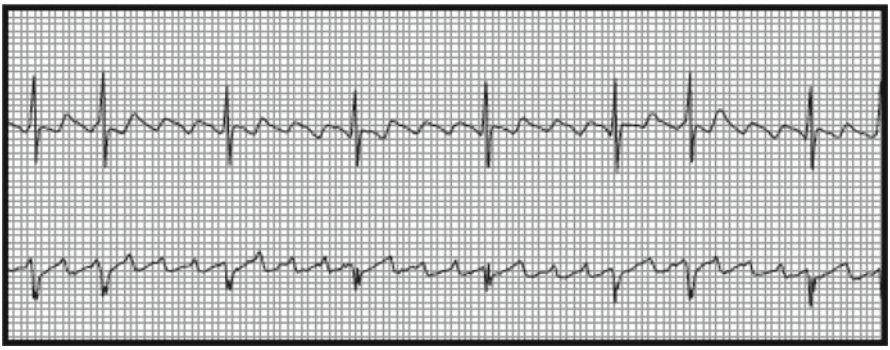


- *Paroxysmal supraventricular tachycardia*
  - Ventricular rate 150–250/min
  - P waves absent or after QRS.
  - Abrupt onset and offset.
  - Try vagal maneuvers such as carotid massage and Valsalva to terminate tachycardia.
  - Intravenous adenosine 6 mg IV bolus; if ineffective, 12 mg IV bolus twice.
  - AV nodal blocking agents like calcium channel blockers, beta-blockers, and digoxin may be tried.
  - In patients with WPW syndrome, avoid AV nodal blocker. Cardioversion or amiodarone is preferable.



- *Atrial flutter*
  - Atrial rate usually 300/min, sawtooth pattern.
  - Ventricular rate 150 (due to 2:1 conduction).
  - Cardiovert if unstable.
  - For rate control, AV nodal blocking agents (diltiazem, verapamil, metoprolol, digoxin), amiodarone, or procainamide.
  - In patients with ejection fraction of less than 40%, consider digoxin or amiodarone.

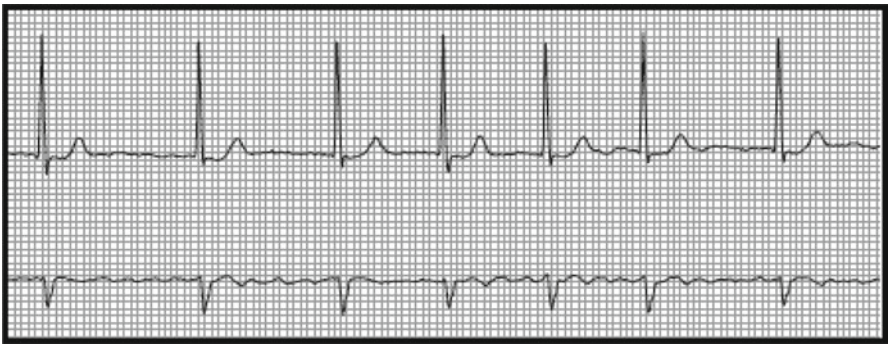
- For rhythm control, amiodarone, procainamide, ibutilide, flecainide, and propafenone.
- Avoid rhythm control if arrhythmia persists for more than 48 h as conversion to sinus rhythm may cause embolization.
- In WPW syndrome, avoid the AV nodal blocking agent. Consider amiodarone, sotalol, procainamide, flecainide, or propafenone.
- Anticoagulate if arrhythmia persists for more than 48 h or echo shows left atrial clot.



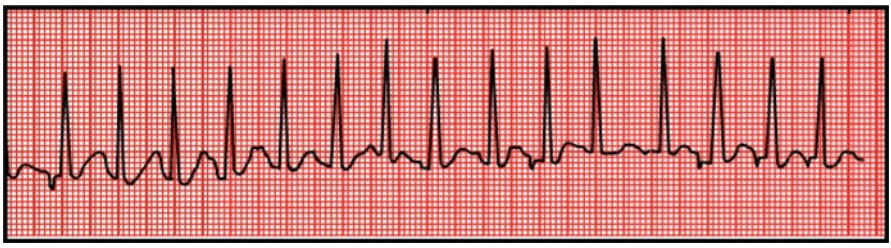
- *Ectopic atrial tachycardia*
  - Rate more than150/min.
  - Altered P wave axis.
  - P wave precedes each QRS.
  - Use AV nodal blocking agents.

Step 17: Analyze and manage narrow complex irregular tachycardia

- *Atrial fibrillation*
  - Absent P waves.
  - Ventricular rate variable.
  - Manage like atrial flutter (see above).
  - Special attention should be given for anticoagulation.

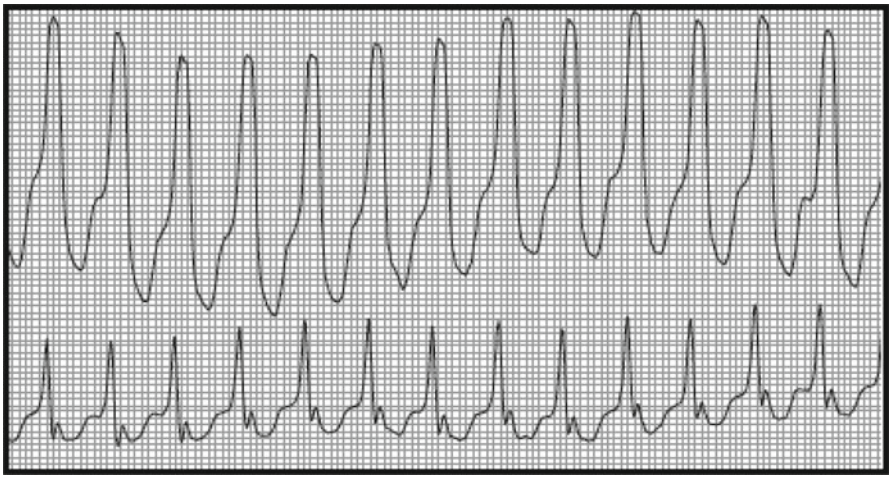


- *Multifocal atrial tachycardia (MAT)*
  - Varying P wave morphology of three or more in the same lead.
  - Seen with digitalis toxicity, theophylline toxicity, severe cardiopulmonary disease.
  - Treatment is to manage the underlying disease.

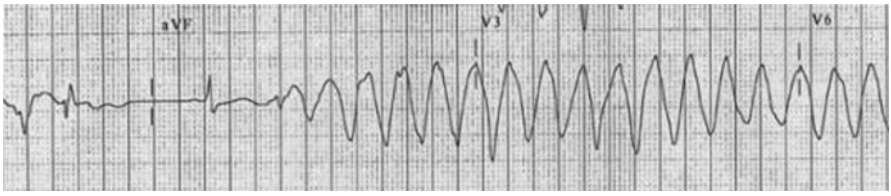


Step 18: Analyze and manage wide-complex regular tachycardia

- *Monomorphic ventricular tachycardia*
  - Ventricular rate 100–200/min
  - QRS wide (>0.12 s)
  - Nonsustained ventricular tachycardia (NSVT) lasts less than 30 s and carries a better prognosis and usually requires only observation without any intervention.
  - Sustained ventricular tachycardia (VT) lasts for more than 30 s and usually requires treatment.
  - Symptomatic VT with detectable pulse should be managed with urgent synchronized cardioversion.
  - In the hemodynamically stable patient, consider amiodarone, lidocaine, or procainamide.
  - For pulseless VT, follow the ACLS protocol (see Chap. 19).



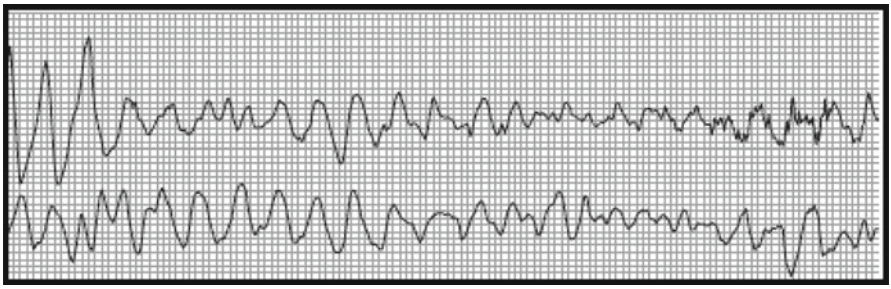
- *Polymorphic ventricular tachycardia*
  - Variable QRS morphology.
  - It usually occurs in the setting of acute ischemia or infarction.
  - It may be associated with prolonged QT interval (torsades de pointes) as may be seen with electrolyte disorders such as hypokalemia, hypomagnesemia, and drugs (tricyclic antidepressant, macrolide, fluoroquinolone), or it may be congenital.
  - Torsades de pointes show twisting of QRS around the baseline in ECG.
  - Polymorphic VT should be cardioverted asynchronously as they are usually unstable.
  - If stable, manage like monomorphic VT (see above).
  - For stable torsades de pointes, give 2 g IV magnesium sulfate.
  - Withdraw causative drugs; correct the electrolyte abnormality.
  - Torsades is sometimes bradycardia-dependent; isoproterenol infusion or temporary pacemaker may be tried to abort the rhythm.



- *Supraventricular tachycardias with aberrant conduction*
  - Wide-complex tachycardias should be assumed to be VT unless proven otherwise and treated accordingly.
  - As all unstable patients require immediate cardioversion, this distinction is academic in such situation.
  - Consider VT than aberrant conduction in following ECG findings:
    - Change in axis or morphology of QRS from the baseline ECG in sinus rhythm
    - AV dissociation (P waves not associated with QRS)
    - Beginning of R to the nadir of S wave greater than 0.1 s
    - Lack of RS complex V1 till V6
    - Fusion beats
    - Capture beats
  - Look for short PR with delta wave in sinus rhythm favoring WPW syndrome.

Step 19: Analyze and manage wide-complex irregular tachycardia

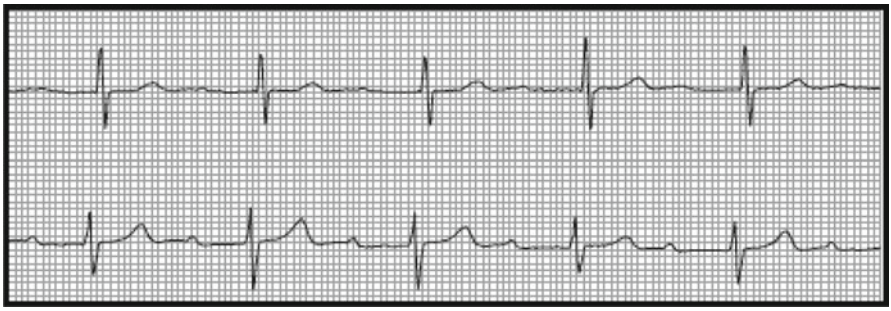
- *Ventricular fibrillation*
  - Chaotic rhythm without any discernible QRS complex.
  - Requires immediate defibrillation—follow ACLS protocol (see Chap. 19).



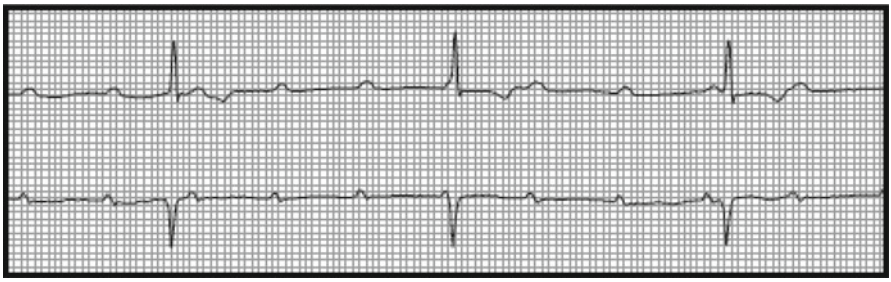
- *Atrial fibrillation with aberrant conduction*
  - Approach is similar to regular tachycardias with aberrant conduction.

Step 20: Analyze narrow complex regular bradycardia

- *Sinus bradycardia*
  - Rate less than 60/min
  - May be secondary to a variety of underlying diseases like hypothyroidism, obstructive jaundice, increased intracranial pressure
  - Usually asymptomatic and requires treatment of the underlying condition only
  - May be associated with brady–tachy syndrome
- *First-degree heart block*
  - Prolonged PR interval (>200 ms)
  - Usually asymptomatic and do not require any specific treatment
  - May progress to higher degrees of block in some cases, so should be monitored closely

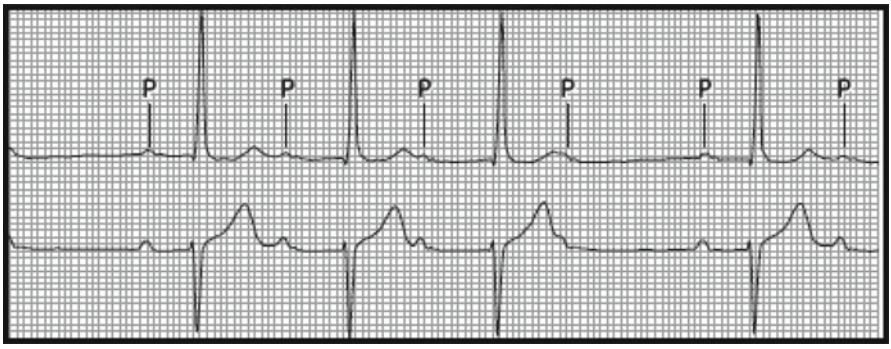


- *Third-degree heart block–AV nodal block*
  - Heart rate varies from 40 to 60 depending on the site of block.
  - When the block occurs in the AV node, rate is 40–60 beats/min.
  - The patient is usually stable.

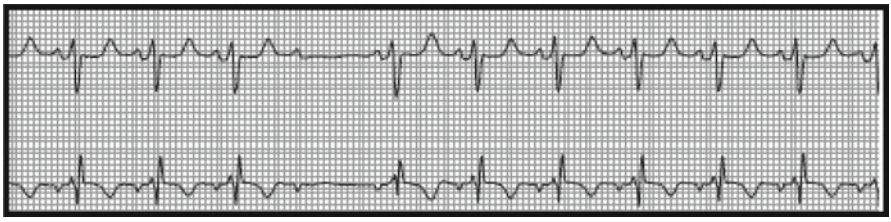


Step 21: Analyze narrow complex irregular bradycardia

- *Second-degree AV block (Mobitz type 1—Wenckebach)*
  - Progressively prolonged PR followed by a nonconducted atrial beat.
  - Escape ventricular rhythm is 40–60/min.
  - Usually a hemodynamically stable rhythm.
  - Commonly seen with inferior wall infarction and AV nodal blocking agents.



- *Second-degree AV block (Mobitz type II)*
  - Fixed PR interval with one or more nonconducting beats.
  - More likely to progress to complete heart block.
  - Escape ventricular rate is 25–40/min.
  - Unstable rhythm; usually requires treatment.



- *Atrial fibrillation, MAT with high-degree AV block*
  - Usually due to toxicity of AV nodal blocking drugs which are used for rate control.

Step 22: Analyze broad complex regular bradycardia

- *Third-degree AV block (distal to AV node)*
  - Ventricular escape rate is usually 25–45/min.
  - Usually symptomatic requiring treatment with transvenous pacemaker.
  - AV dissociation, with atrial rate (P wave) greater than QRS, with no relation between these two.

Step 23: Analyze broad complex irregular bradycardia

- Atrial fibrillation, MAT with aberrant conduction, and high-degree AV block

Step 24: General management of bradycardia

- All symptomatic bradycardia should be managed urgently.
- Atropine 0.5 mg IV may be repeated to a total dose of 3 mg.
- Atropine is more successful in sinus bradycardia or block within the AV node.
- If the patient remains symptomatic, temporary transvenous pacing should be started.
- Transcutaneous pacing may be started as a temporary measure.
- Consider epinephrine infusion (2–10 mcg/min) or dopamine infusion (2–10 mcg/Kg/min) as an interim measure.
- Treat the underlying cause and the precipitating factor.
- Withdraw any offending drug.
- Consider permanent pacing in selected cases (advanced, prolonged AV block) in consultation with the cardiologist.

Suggested Reading

1. Field JM, Hazinski MF, Sayre MR, et al. Part 1: executive summary: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation. 2010; 2;122(18 Suppl 3):S640–56.
   The publication marks the 50th anniversary of modern CPR and highlights detailed management of brady- and tachyarrhythmias.
2. Annane D, Sébille V. Incidence and prognosis of sustained arrhythmias in critically ill patients. AJRCCM. 2008;178:20–5.
   *This study estimates a 12% prevalence of sustained arrhythmias in general ICU patients. Ventricular arrhythmias increase the risk of death and the risk of neurological sequelae***.**
3. Trappe HJ, Brandts B. Arrhythmias in the intensive care patient. Curr Opin Crit Care. 2003;9(5):345–55.
   A comprehensive review of the article

Website

1. circ.ahajournals.org
   American Heart Association website with downloadable guidelines

Acute Coronary Syndromes

23

Rajesh Rajani and Farhad N. Kapadia

A previously healthy smoker presented with severe chest pain to the emergency department. On arrival he was clinically stable. The ECG showed ST-segment elevation in the anterior leads and blood test showed elevated troponin T and CK-MB. The echocardiograph showed hypokinesia in the anteroseptal region. In the emergency department, his symptoms progressively worsened with ongoing intense chest pain, and he became increasingly restless and breathless.

Acute coronary syndrome (ACS) is a common diagnosis in patients presenting to the emergency department with acute onset chest pain. Timely and appropriate management in a protocolized manner is mandatory to salvage patients from this life-threatening syndrome.

Step 1: Initiate resuscitation

- Patients with acute chest pain should have immediate intravenous access as they may deteriorate suddenly.
- A continuous ECG monitor and pulse oximeter should be placed. Give oxygen and assist breathing if needed.
- In the case of cardiac arrest, follow ACLS (advanced cardiac life support) protocol (see Chap. 19).
- Cardiovert immediately if ventricular or atrial tachyarrhythmia is detected and patient is hemodynamically unstable (shock or pulmonary edema).

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Urgent transcutaneous or temporary intravenous pacing is required if severe symptomatic bradycardia is not responding to intravenous atropine.

Step 2: Take focused history and perform physical examination

- Elaborate the symptom of chest pain—site, type, severity, relation to exertion
- Sweating
- Cardiorespiratory symptoms
- Symptoms of low output state such as fatigue, dizziness, and syncope
- Risk factors for ischemic heart disease—hypertension, diabetes, hyperlipidemia, smoking, positive family history
- History of bleeding diathesis or recent blood loss
- BP in both arms
- Palpate all peripheral and central pulses
- Auscultate the heart for gallop or murmurs
- Auscultate the chest for basal crepitations

Step 3: Perform basic investigation

- 12-lead ECG
  - Look for features of new ST elevation acute myocardial infarction (STEMI)
    - New ST elevation in two or more contiguous leads (inferior or anterior) Threshold values for new ST-segment elevation consistent with STEMI are:
      - J-point elevation 0.2 mV (2 mm) in leads V2 and V3 and 0.1 mV (1 mm) in all other leads (men more than 40 years old)
      - J-point elevation 0.25 mV (2.5 mm) in leads V2 and V3 and 0.1 mV(1 mm) in all other leads (men less than 40 years old)
      - J-point elevation 0.15 mV (1.5 mm) in leads V2 and V3 and 0.1 mV (1 mm) in all other leads (women)
    - New LBBB (left bundle branch block)
    - ST elevation in right precordial leads $V4_r$ for right ventricular myocardial infarction (MI)
    - ST depression in precordial leads (V1–V3) for posterior MI
    - Pathological "Q" waves
  - Echocardiogram
    - Regional wall motion abnormality
    - Poor ejection fraction
    - Mechanical complication–papillary muscle rupture, VSD
  - Chest X-ray
    - Cardiomegaly
    - Pulmonary congestion
  - Cardiac enzymes
    - Raised troponins, CPK-MB
  - A complete blood count
    - Leukocytosis in MI
  - Platelet count, prothrombin time, activated partial thromboplastin time (APTT)
  - Liver and renal function test
  - Electrolytes
    - Look for hypokalemia, hypomagnesemia

Table 23.1 Causes of acute chest pain

Life-threatening causes
ACS (unstable angina, NSTEMI, STEMI)
Pulmonary embolus (may be associated with ↑ troponin)
Aortic dissection (may be overlooked due to associated MI)
"Benign" causes
Pericarditis (both ↑ troponin and ST elevation may occur)
Gastrointestinal (esophageal reflux, spasm)
Musculoskeletal (e.g., costochondritis)
Neurologic (cervical radiculopathy, herpes zoster)

Table 23.2 Causes of raised troponin

ACS (unstable angina, NSTEMI, STEMI)
Pulmonary embolism
Chronic renal insufficiency
Intracranial hemorrhage
Ingestion of sympathomimetic agents
Cardiac contusion
DC cardioversion
Cardiac infiltrative disorder
Chemotherapy
Myocarditis/pericarditis
Cardiac transplantation

Step 4: Confirm diagnosis of ACS

- Typical chest pain in patients at risk of myocardial ischemia with classical ECG changes and raised cardiac enzymes establishes diagnosis in many cases.
- Consider other causes of chest pain (Table 23.1).
- Consider other causes of raised troponin (Table 23.2).
- Occasional patients have typical chest pain without ECG abnormalities or atypical chest pain (diabetics, female, elderly) and nonspecific changes on ECG. In these situations, perform serial monitoring of ECG and cardiac enzymes. An early echo is useful to look for regional wall motion abnormalities.

Step 5: Give pain relief

- Sublingual nitroglycerine (0.3–0.6 mg) may be repeated twice or thrice or as an intravenous infusion (5–200 mcg/min) or as a transdermal patch.
- Avoid nitrates in the following situations:
  - Hypotension (systolic <90 mmHg) or fall of more than 30 mmHg from baseline
  - Bradycardia (<50/min)
  - Intake of phosphodiesterase inhibitors like sildenafil for erectile dysfunction in the previous 24–48 h
  - In patients with inferior wall MI and suspected right ventricular (RV) involvement because these patients require adequate RV preload

- Morphine sulfate (2–4 mg IV) with increments of 2 mg IV should be repeated at 5–15 min for persistent chest pain unresponsive to nitroglycerine.
- Avoid nonsteroidal anti-inflammatory drugs (except aspirin) due to increased risk of mortality, reinfarction, hypertension, and heart failure, and myocardial rupture has been associated with their use.

Step 6: Give antiplatelets

- A combination of uncoated aspirin (160–325 mg orally or chewed) and clopidogrel (300–600 mg orally) should be given as a loading dose.
- This should be followed by aspirin (150 mg/day) indefinitely and clopidogrel (150 mg/day) for 7 days, then 75 mg/day for at least 1 year.
- Prasugrel (60 mg) can be used as an alternative to clopidogrel.
- Due precautions should be taken regarding complications such as known allergies and gastric intolerance.
- Proton pump inhibitors are often used concurrently to prevent gastric complications. These should be spaced out (mainly omeprazole) for 12 h after clopidogrel to prevent potential drug interaction.
- Clopidogrel may need to be withheld if the need for early surgery is anticipated in the following:
  - Elderly
  - Diabetics
  - Known multivessel disease
  - Cardiogenic shock
  - Mechanical complications

Step 7: Stratify and document risk category

- The categorization of the type and extent of the myocardial infarction is primarily determined by the presence or absence of ST elevation and cardiac biomarkers of tissue injury.
- Based on this, the management should proceed for a STEMI (with or without Q waves) or non-ST elevation myocardial infarction (NSTEMI) (positive troponin) or unstable angina (negative troponins).
- Patients with unstable angina or NSTEMI should be risk stratified to conservative or invasive strategies (Table 23.3).
- Proper documentation of findings, ECG interpretation, medications given, and plan of action should be made in patient's case notes (Table 23.4).
- Proper coordination among all disciplines concerned with patient care should be organized in a timely fashion.

Step 8: Consider reperfusion therapy (Table 23.5)

- This can be accomplished by pharmacological (fibrinolysis) or catheter-based (primary percutaneous coronary intervention [PCI]) approaches or by emergency coronary artery bypass grafting (CABG).

Table 23.3 Selection of initial treatment strategy for patients with non-ST elevation ACS: invasive versus conservative strategy

Preferred strategy	Patient characteristics
Invasive	Recurrent angina or ischemia at rest or with low-level activities despite intensive medical therapy
	Elevated cardiac biomarkers (TnT or TnI)
	New or presumably new ST-segment depression
	Signs or symptoms of heart failure or new or worsening mitral regurgitation
	High-risk findings from noninvasive testing
	Hemodynamic instability
	Sustained ventricular tachycardia
	PCI within 6 months
	Prior CABG
	High-risk score (e.g., TIMI [thrombolysis in myocardial infarction])
	Reduced LV function (left ventricular ejection fraction [LVEF] < 40%)
Conservative	Low-risk score (e.g., TIMI)
	The patient or physician preference in absence of high-risk features

Table 23.4 ACS: drug orders (for the initial 24 h)

Time of the onset of chest pain: ECG taken at:					
ECG diagnosis: ACS-ST elevation/non-ST elevation					
Is the patient a candidate for primary angioplasty (PAMI)? Y/N					
Drug class	Drug	Prescribed? (Y/N)	Dose	Time given	Given by
Antiplatelets	Aspirin				
	Clopidogrel				
Thrombolytic therapy					
Contraindications to thrombolytic therapy? (Y/N)					
Hemorrhagic stroke at any time, ischemic stroke within 1 year, intracranial neoplasm, active internal bleeding, suspected aortic dissection, major surgery (<3 weeks), major trauma (2–4 weeks), uncontrolled hypertension >180/110 mmHg					
Heparin/low-molecular-weight heparin					
Nitrates					
β-blocker					
ACEI					
Analgesia					
Statin					
Laxative					
Sedation					

- Implementation of these strategies varies on the basis of capabilities at the treating facility and transport time to advanced facility.

Table 23.5 Initial documentation, choice of reperfusion strategy, and medication: assessment of reperfusion options for STEMI patients

Step 1: Assess time and risk
Time since the onset of symptoms
Risk of STEMI
Risk of fibrinolysis
Time required for transport to a skilled PCI laboratory
Step 2: Determine if fibrinolysis or invasive strategy is preferred
If presentation is <3 h and there is no delay to an invasive strategy, there is no preference for either strategy
Step 3: Fibrinolysis is generally preferred if
Early present (≤3 h from symptom onset and delay to invasive strategy)
Invasive strategy is not an option
Catheterization laboratory occupied or not available:
Vascular access difficulties
Lack of access to a skilled PCI laboratory
Delay to invasive strategy
Prolonged transport
Door-to-balloon time more than 1 h
Medical contact-to-balloon or door-to-balloon more than 90 min
Step 4: An invasive strategy is generally preferred if
Skilled cardiac catheterization laboratory is available with surgical backup
Medical contact-to-balloon or door-to-balloon less than 90 min
High-risk score (TIMI)
Cardiogenic shock
Killip class ≥3
Contraindications to fibrinolysis including increased risk of bleeding and intracranial hypertension
Late presentation
Symptom onset was more than 3 h ago
Diagnosis of STEMI is in doubt

Step 9: Consider primary angioplasty as the preferred mode of treatment for all suitable STEMI patients

- Coronary angioplasty with or without stent placement is the treatment of choice for the management of STEMI when it is performed effectively with a door-to-balloon time (<90 min) by a skilled provider, at a skilled PCI facility.
- Documented outcome benefits of PAMI (primary angioplasty in myocardial infarction) included a trend for a reduction of in-hospital mortality, reduction in combined end point of death or reinfarction, and intracranial hemorrhage.
- Treatment with primary angioplasty appears to reduce infarct rupture and has been associated with a significant reduction in acute mitral regurgitation, ventricular septal rupture, and a lower risk of free wall rupture.
- PAMI was also beneficial when comparing surrogate markers such as ST-segment resolution and the tissue myocardial perfusion.

Table 23.6 Comparison of approved fibrinolytic agents

	Streptokinase	Alteplase	Reteplase	TNK-t-PA (tenecteplase)
Dose	1.5 MU in 30–60 min	Up to 100 mg in 90 min (based on weight)	10 U×2 (30 min apart) each over 2 min	30–50 mg based on weight
Bolus administration	No	No	Yes	Yes
Antigenic	Yes	No	No	No
Allergic reactions (hypotension most common)	Yes	No	No	No
Systemic fibrinogen depletion	Marked	Mild	Moderate	Minimal

- The degree of benefit depends on the severity of the disease, age, and delay in instituting therapy. "Door-to-balloon" time should be kept as short as possible and should be regularly audited.
- The contraindications to primary angioplasty are limited to patients who cannot receive heparin, aspirin, or thienopyridines (clopidogrel), documented life-threatening contrast allergy, or lack of vascular access.
- High-risk patients who receive fibrinolysis in a non-PCI center should be transferred to a PCI center within 6 h of presentation to receive early PCI if indicated.

Step 10: Consider fibrinolysis in selected patients (Table 23.6)

- Fibrinolysis is restricted to patients with STEMI.
- This modality of reperfusion is best suited for patients presenting early (<3 h) and at low risk of bleeding.
- At centers without PCI facility, fibrinolysis can be given as a definitive treatment or as a bridging therapy prior to triaging to the higher center for PCI.
- STEMI patients best suited for are those presenting early after symptom onset with low bleeding risk.
- The benefit of fibrinolytic therapy appears to be greatest when agents are administered as early as possible, with best results when the drug is given less than 2 h after symptoms begin. "Door-to-needle" time should be kept as short as possible and should be regularly audited.
- Mortality reduction may still be observed in patients treated with thrombolytic agents between 6 and 12 h from the onset of ischemic symptoms, especially if there is an ongoing chest pain.
- Tenecteplase (TNK-t-PA) given as a 30–50-mg bolus is associated with the least bleeding complications and is generally seen as the preferred agent.
- The accelerated dose regimen of t-PA over 90 min produces more rapid thrombolysis than the standard 3-h infusion of t-PA.

- The recommended dosage regimen for t-PA is a 15-mg intravenous bolus followed by an infusion of 0.75 mg/Kg (maximum 50 mg) over 30 min, followed by an infusion of 0.5 mg/Kg (maximum 35 mg) over 60 min.
- It is associated with lower mortality and slight increase in incidence of intracranial hemorrhage but with a better overall composite outcome of death and disabling stroke.
- Contraindications for thrombolysis should be considered prior to using lytic agents (see Chap. 9).
- Intracranial hemorrhage may be fatal in half to two-thirds of patients and remains a devastating peril of thrombolytic therapy.
- In a comparative analysis, the risk of intracranial hemorrhage was found to be 1% with thrombolysis and 0.05% with PCI.
- Bleeding can also occur in sites like the gut or other sites including those of recent trauma or surgery.
- Other complications are reperfusion arrhythmias and allergic reactions.

Step 11: Consider adjunctive therapies

- *Nitroglycerine*
  - Nitrates have a limited role in ACS.
  - The indication in the setting of an ACS is limited to ongoing chest pain or ischemia, hypertension, or as a vasodilator in the management of pulmonary edema secondary to left ventricular (LV) failure.
  - Route and dose of nitrate should be individualized.
  - Due precaution should be taken while using nitrates (see Step 5).
- *β-Blockers*
  - Oral β-blockers should be used within the first 24 h in those without evidence of heart failure, low cardiac output, shock, bradyarrhythmias, or conduction blocks and other conventional contraindication like asthma.
  - Cardioselective agents without intrinsic sympathomimetic activity are preferred. Metoprolol (50–200 mg/day) is the most commonly used agent.
  - Intravenous β-blocker is used (metoprolol 5 mg IV thrice a day) titrated to patient response, heart rate (avoid if <50/min), and blood pressure (avoid if less than 100 mmHg systolic).
  - Its use is best limited to situations with ongoing chest pain or uncontrolled tachycardia or hypertension.
  - Calcium channel blocking agents (diltiazem) may be used as alternative therapy in patients with contraindication to β-blockers but should be avoided in patients with poor left ventricular function and pulmonary congestion.
- *Anticoagulants: Indications*
  - Low-molecular-weight heparins (enoxaparin 1 mg/Kg 12-hourly SC or dalteparin 120 U/Kg 12-hourly SC), or fondaparinux 2.5 mg SC once daily, are commonly used agents.
  - Bivalirudin (0.1 mg/Kg bolus followed by 0.25 mg/Kg/h infusion) may be considered as an alternative agent.
  - Appropriate dosing adjustments need to be done for renal dysfunction.

  - As with antiplatelets, active bleeding and other contraindications need to be excluded, and the regime should be timed in consultation with cardiologist for patients requiring intervention.
  - Conventional unfractionated heparin is preferable if rapid reversal prior to surgery (CABG) is anticipated.
  - It should be given as a bolus of 60 U/Kg (maximum 4,000 units), then 14 U/Kg/h (maximum 1,000 U/h)—titrate to APTT 2.5 times control (see in Chap. 9).
  - A weight-based nomogram may be followed for heparin titration.
  - If intervention is not done, the duration for continuing anticoagulation is usually 5–10 days.
- *GP IIb/IIIa inhibitors*
  - Abciximab 0.25 mg/Kg IV bolus and then 0.125 mcg/Kg/min (maximum 10 mcg/ min) may be given "upstream" prior to primary PCI in the catheterization laboratory.
  - Eptifibatide 180 mcg/Kg bolus, then 2 mcg/Kg/min infusion or tirofiban 0.4 mcg/Kg/min for 30 min, and then 0.1 mcg/Kg/min infusion should be started as a part of early intervention strategy in high-risk patients with non-STEMI.
- *Angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers*
  - These drugs should be used within the first 24 h of ACS in patients without hypotension.
  - They are most beneficial in patients with pulmonary congestion and depressed LV systolic function.
- *Statins*
  - The primary role of these agents is in long-term secondary prevention by lipid control.
  - They may have some additional advantage in the early phase of ACS. An agent like atorvastatin is initially used in a relatively high dose (40–80 mg), and the dose can later be decreased to achieve the target lipids (LDL < 70–100 mg/dL).
  - Patients who are already on statin should be continued on it.

Step 12: Manage arrhythmic complication

- Primary ventricular fibrillation (VF) accounts for the majority of early deaths during AMI. The incidence of primary VF is highest during the first 4 h after the onset of symptoms but remains an important contributor to mortality during the first 24 h.
- Secondary VF occurring in the setting of congestive heart failure or cardiogenic shock can also contribute to death from AMI.
- Prompt defibrillation and appropriate pharmacotherapy should be instituted (see Chap. 19).
- Maintain serum potassium more than 4 mEq/L and magnesium more than 2 mEq/L.
- Prophylactic antiarrhythmics are not recommended.

Step 13: Manage mechanical complications

- Cardiogenic shock, LV failure, and congestive heart failure should be managed with appropriate pharmacological therapy and rarely with mechanical devices (see Chaps. 20 and 21).
- Ventricular, septal, or papillary muscle rupture.
- RV infarction or ischemia may occur in up to 50% of patients with inferior wall MI.
- Suspect RV infarction in patients with inferior wall infarction, hypotension, and clear lung fields.
- In patients with inferior wall infarction, obtain an ECG with right-sided leads. Look for ST-segment elevation (>1 mm) in lead V4r.
- Nitrates, diuretics, and other vasodilators (ACE inhibitors) should be avoided because severe hypotension may result.
- Hypotension is initially treated with an IV fluid bolus.

Step 14: Consider other supportive therapy

- Sedatives and laxatives are useful in the initial stage.
- Hyperglycemia, either stress-induced or due to preexisting diabetes, should be controlled preferably at near-normal levels.
- Routine medication taken by the patient prior to the ACS should be reintroduced as appropriate.

Suggested Reading

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   The 7 TIMI risk score predictor variables were 65 years or older, at least three risk factors for coronary artery disease, prior coronary stenosis of 50% or more, ST-segment deviation on electrocardiogram at presentation, at least two anginal events in prior 24 h, use of aspirin in prior 7 days, and elevated serum cardiac marker.

Website

1. www.acc.org
   A comprehensive website of American College of Cardiology

Hypertensive Urgencies and Emergencies

24

Simran Singh and Chandrashekhar K. Ponde

A 55-year-old male patient was admitted to the emergency department with severe headache and giddiness. His blood pressure was 240/130 mmHg, pulse was 100/min regular, and sensorium was intact. He had also a left ventricular gallop, and room air oxygen saturation was 90%. Peripheral pulses were well felt. He was a known diabetic and hypertensive but was on irregular treatment.

Severe hypertensive crisis is occasionally seen in the ICU. Proper triaging, monitoring, and a balanced approach to lowering blood pressure are mandatory in these situations as overjealous reduction in pressure may lead to organ underperfusion, and undertreatment will lead to vital organ damage.

Step 1: Assess severity of hypertension and urgency of treatment

- Severe hypertension is defined when blood pressure exceeds 180/110 mmHg in the absence of symptoms beyond mild or moderate headache and without evidence of acute target organ damage.
- Hypertensive urgency is defined when blood pressure exceeds 180/110 mmHg in the presence of significant symptoms, such as severe headache or dyspnea, but has nil or only minimal acute target organ damage.
- Hypertensive emergency is defined when very high blood pressure (often >220/140 mmHg) is accompanied by evidence of life-threatening organ dysfunction such as cardiac, renal, retinal, or neurological.

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Table 24.1 Target organ damage

Cardiovascular	Myocardial infarction
	Unstable angina
	Aortic dissection
	Left ventricular failure
Central nervous system	Cerebral edema
	Altered mental status (hypertensive encephalopathy)
	Intracerebral or subarachnoid bleeding
	Cerebral infarct or transient ischemic attack
Renal	Microhematuria
	Proteinuria
	Acute renal failure
Ophthalmologic	Retinal hemorrhages or exudates
	Papilledema

Step 2: Assess target organ involvement

- Perform focused history and physical examination
- History—duration and severity of hypertension and previous BP records
- Relevant symptoms:
  - Headache and chest pain
  - Dyspnea, edema, and acute fatigue
  - Epistaxis
  - Seizure
  - Change in the level of consciousness
  - Palpitation, diaphoresis, and tremors suggestive of pheochromocytoma
  - Weight gain and thinning of skin suggestive of Cushing's syndrome
- History of comorbid conditions—diabetes, smoking, hyperlipidemia, and chronic kidney disease:
  - History of adherence to any prescribed antihypertensive medication is necessary
  - Recent use of OCP (oral contraceptive pill), MAOI (monoamine oxidase inhibitors), nonsteroidal anti-inflammatory drug, cyclosporine, steroids, over-the-counter medicines, and herbal remedies
  - Use of alcohol, cocaine, amphetamine, and phencyclidine
- Physical examination:
  - Feel all peripheral pulses
  - Measure the blood pressure using appropriate technique
  - Measure the blood pressure in both arms and at least one leg if pedal pulses are diminished
  - Carry out fundoscopy to look for papilledema and hypertension retinopathy
  - Other systems examination—look for pedal edema, assess jugular venous pressure, and auscultate for abdominal bruits, crepitations and gallop, and basal crepitations
  - Check the mental status
- Look for target organ damage (Table 24.1).

Step 3: Send relevant investigations

- Initial evaluation
  - Electrocardiogram—ST, T wave changes, evidence of left ventricular hypertrophy
  - Hematocrit, white blood cell count, and peripheral blood smear—anemia, evidence of hemolysis
  - Urea and creatinine
  - Urinalysis with microscopic examination—hematuria and proteinuria
  - Chest radiograph—cardiomegaly and pulmonary congestion
  - Thyroid function tests
  - Noncontrast computed tomography of the head (if neurologic findings are abnormal)
  - Echocardiogram (left ventricular dysfunction, valve abnormalities, wall motion abnormalities)
  - Lipid profile
- Tests to be done once the patient stabilizes
  - Renal artery imaging (if renal stenosis is suspected)
  - Other evaluations as guided by clinical presentation, namely, urinary VMA/metanephrines/5-HIAA-phochromocytoma
  - Plasma cortisol and dexamethasone suppression test—Cushing's syndrome

Step 4: Understand treatment goals

- Hypertensive urgency
  - Immediate goal—lower blood pressure within 24–72 h
  - Treatment setting—clinical discretion is required
  - Medications—oral medications with rapid onset of action; occasionally intravenously
- Hypertensive emergency
  - Immediate goal—lower BP by 15–25% within 2 h, 25% within 12 h, 30% within 48 h
  - Treatment setting—intensive care unit and intra-arterial monitoring
  - Medications—intravenous

Step 5: Get familiar with drugs used in hypertensive urgencies and emergencies (Tables 24.2 and 24.3)

Table 24.2 Drugs for hypertensive urgencies

Agent	Dose	Onset of action	Comment
Captopril	12.5–25 mg PO	15–60 min	Can precipitate acute renal failure in patients with bilateral renal artery stenosis
Nifedipine (extended release)	10–20 mg PO	20 min	Avoid short-acting or sublingual nifedipine due to risk of sudden hypotension, stroke, cardiac event
Labetalol	200–400 mg PO	20–120 min	Heart failure, bradycardia, bronchospasm

(continued)

Table 24.2 (continued)

Agent	Dose	Onset of action	Comment
Clonidine	0.1–0.2 mg PO	30–60 min	Rebound hypertension due to abrupt withdrawal
Prazosin	1–2 mg PO	2–4 h	First-dose hypotension, syncope, tachycardia
Amlodipine	5–10 mg	30–50 min	Headache, tachycardia, flushing

Table 24.3 Drugs for hypertensive emergencies

Sodium nitroprusside
Dose: 0.25–10 mcg/Kg/min IV infusion
Onset/duration of action after discontinuation: seconds/2–3 min
Comments
Arterial and venodilator with rapid onset and offset of action
Preferred agents for most hypertensive emergencies
Titrate to goal BP
Infusion bag and delivery set must be light resistant or covered
Nausea, vomiting, muscle twitching on prolonged use (>24–48 h)
Thiocyanate/cyanide intoxication, metabolic acidosis in patients with renal impairment
Thiocyanate level >10 mg/dL should be avoided
Nitroglycerine
Dose: 5–100 mcg/min IV infusion
Onset/duration of action after discontinuation: 2–5 min/5–15 min
Comments
Mostly venodilator with modest arterial dilation
Headache, tachycardia, flushing, vomiting
Develops tolerance with prolonged use
Methemoglobinemia
Useful in emergencies with cardiac failure or ischemia
Labetalol
Dose: 10–80 mg IV bolus every 10 min to a maximum dose of 300 mg
Infusion: 0.5–2 mg/min
Onset/duration of action after discontinuation: 5–10 min/3–6 h
Comments
Combined α- and β-blockade
Bradycardia, bronchospasm
Avoid in congestive heart failure (CHF), bronchial asthma
Commonly used in pregnancy-induced hypertension
Enalapril
Dose: 1.25 mg every 6 h
Onset/duration of action after discontinuation: 15–30 min/6–12 h
Comments
Mainly afterload reduction
Contraindicated in pregnancy, renal artery stenosis
Useful in patients with CHF

(continued)

Table 24.3 (continued)

Esmolol
Dose: 500 mcg/Kg IV bolus can be repeated after 5 min
Infusion: 50–200 mcg/Kg/min
Onset/duration of action after discontinuation: 1–5 min/15–30 min
Comments
Avoid in patients with heart block, CHF, asthma
Short-acting cardioselective β-blocker
Bradycardia, CHF, heart block, may precipitate bronchospasm
Hydralazine
Dose: 10–20 mg IV bolus may be repeated every 30 min till goal BP is reached or unacceptable tachycardia develops
Onset/duration of action after discontinuation: 10–30 min/2–4 h
Comments
Direct arteriolar vasodilator
Reflex tachycardia, flushing
Avoid in patients with increased ICP, ischemic heart disease, and aortic dissection (without β-blockade)
Phentolamine
Dose: 5–15 mg IV bolus, repeat every 5–15 min
Infusion: 0.2–5 mg/min
Onset/duration of action after discontinuation: 1–2 min/10–30 min
Comments
Pure α-blockade
Reflex tachycardia, orthostatic hypotension
Used in syndromes with excess catecholamine (pheochromocytoma)
Nicardipine
Dose: 5 mg/h IV infusion; titrate up by 2.5 mg/h every 20 min up to maximum dose of 15 mg/h
Onset/duration of action after discontinuation: 15–30 min/1–4 h
Comments
Dihydropyridine calcium channel blocker
Reflex tachycardia
Avoid in acute heart failure
Useful in subarachnoid hemorrhage
Fenoldopam
0.1 mcg/Kg/min IV infusion, titrate up every 15 min to a maximum of 0.8 mcg/Kg/min
Onset/duration of action after discontinuation: 3–5 min/30 min
Comments
Selective peripheral dopamine-1 receptor agonist
Arterial vasodilator
Improves renal perfusion, useful in patients with hypertensive emergencies with renal failure
Contraindicated in glaucoma

Step 6: Select appropriate drugs for specific situation

- *Pregnancy-induced hypertension*
  - Preeclampsia, eclampsia, HELLP (hemolysis, elevated liver enzyme, low platelet) syndrome.
  - Posterior reversible encephalopathy syndrome (PRES) is a specific hypertensive emergency during pregnancy.
  - It is characterized by headache, confusion, seizures, and visual loss.
  - It occurs predominantly due to accelerated hypertension and eclampsia.
  - For pregnancy-associated hypertensive crises, labetalol, methyldopa, hydralazine, and magnesium sulfate are the drugs of choice.
- *Neurologic Hypertensive Emergencies*
  - Use of a continuous nitroglycerin infusion and nitroprusside should be avoided in the acute management of hypertensive emergencies complicated by cerebral ischemia because these drugs may worsen cerebral perfusion.
  - Labetalol or calcium channel blockers are preferred in such a patient population.
- *Acute aortic dissection*
  - Aortic dissection is a life-threatening condition. Upon diagnosis, blood pressure should be reduced to less than 120 mmHg within 20 min. β-Blockers such as labetalol and esmolol as well as sodium nitroprusside along with a beta-blocker can be used.
- *Acute coronary syndrome*
  - The drugs of choice are intravenous nitroglycerin, β-blockers, and angiotensin-converting enzyme (ACE) inhibitors.
- *Acute pulmonary edema*
  - Treatment of severe hypertension with pulmonary edema requires NTG, diuretics, and ACE inhibitors like captopril.
- *Renal emergencies*
  - Sodium nitroprusside and labetalol are useful.
  - Short-term dialysis is sometimes necessary.
  - ACE inhibitors may worsen renal function in the setting of bilateral renal artery stenosis, dehydration, or acute renal failure.
- *Adrenergic crises*
  - Examples of adrenergic crises include a pheochromocytoma crisis, cocaine or amphetamine intoxication, and patients on MAO inhibitors ingesting tyramine-containing food.
  - Pure α-blocker like phentolamine is generally prescribed.
  - A β-blocker can be added if an additional antihypertensive is required.

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Aortic Dissection

25

Shyam Sunder Tipparaju, Gopinath Ramachandran, Ravinuthala Venkat Kumar, and Muppiri Vijay Kumar

A 57-year-old male patient with long-term, poorly controlled hypertension developed severe precordial chest pain, radiating to the back while gardening. The physical examination showed temperature 99°F, pulse 110/min, respiration 20/min, BP 200/100 mmHg (right arm) and 180/90 mmHg (left arm), decreased left brachial and radial pulses, and diastolic murmur along the left sternal border.

Aortic dissection is a relatively uncommon disorder as compared to other cardiac emergencies such as acute myocardial infarction (AMI) or congestive heart failure (CHF). It carries a high mortality of 1% every hour for initial 48 h, if not properly recognized and managed.

Step 1: Resuscitate urgently

- Emergent control of hypertension and maintaining organ perfusion is the priority in initial resuscitation (see Chap. 24).

Step 2: Assess urgently

- Time is of essence in managing aortic dissection, and a focused history and focused physical examination should be quickly performed to differentiate causes of acute chest pain (Tables 25.1 and 25.2).

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Table 25.1 Causes of acute chest pain

Acute coronary syndrome with and without ST elevation
Acute aortic regurgitation without dissection
Aortic aneurysms without dissection
Musculoskeletal pain
Pericarditis
Mediastinal tumors
Pleuritis
Pulmonary embolism
Cholecystitis

Table 25.2 Clinical features of aortic dissection

Sudden severe chest pain radiating to back	96%
Syncope (cardiac tamponade or new stroke)	13%
Congestive cardiac failure (severe AR or tamponade)	7%
Cerebrovascular accident	6%
Ischemic peripheral neuropathy/paraplegia/ cardiac arrest/sudden death	
Hypertension	70% of cases with type B dissections and 36% with type A dissection
Hypotension	25% of cases with proximal dissections and 4% with distal dissection
Acute severe aortic regurgitation	33%
Pulse deficit	30% of proximal dissection and 15% of distal dissection
Neurological manifestations	6–19%
Acute MI	1–2%
Renal ischemia	5–8%
Mesenteric ischemia	3–5%
Diminished femoral pulses	12%

- An urgent 12-lead ECG should be performed to look for features of AMI.
- If aortic dissection is a possibility, antiplatelet, anticoagulant, and thrombolysis should be avoided.
- Chest X-ray—a routine chest radiograph is abnormal in 60% of cases with suspected aortic dissection; the commonest finding are widening of mediastinum and left-sided pleural effusion.
- D-dimer may be falsely elevated in some cases.

Step 3: Initiate treatment for suspected aortic dissection (Table 25.3)

- All patients suspected of having acute aortic syndrome should be admitted to the ICU for invasive monitoring and hemodynamic stabilization.
- Pain control with morphine should be started.

Table 25.3 Antihypertensive and heart rate control therapy

Drug	Dosing	Remarks
Labetalol	20 mg IV over 2 min, then 40–80 mg every 15 min until adequate response or excessive bradycardia, then continuous. IV infusion at 2–10 mg/min, (maximum daily IV dose is 300 mg) titrated to effect (maximum daily IV dose is 300 mg), may be switched to oral once stabilized	Alpha- and beta-blocker
Esmolol	500 mcg/Kg IV bolus, then continuous infusion at 50–200 mcg/Kg/min	Short half-life
	Titrated to effect	
Sodium nitroprusside	No bolus, continuous infusion titrated to effect, 0.3–0.5 mcg/Kg/min titrated to a maximum of 10 mcg/Kg/min	Use only in presence of rate-controlling agent
Enalapril	0.625–1.25 mg IV, then increase every 6 h to a maximum of 5 mg every 6 h	Ideal for renal artery dissection
Diltiazem	0.25 mg/Kg IV over 2 min, then continuous IV infusion at 5–15 mg/h	Use when beta-blocker is contraindicated

- An arterial line in the well-perfused hand should be inserted.
- Reduction of systolic blood pressure, decreasing heart rate, and diminution of the rate of rise of the left ventricular ejection time (dP/dT) are the goals of the primary medical treatment.
- Beta-blockers (labetalol and esmolol) as a group of drugs that have the most desirable effect in reducing the force of the left ventricular ejection (dP/dT). However, if beta-blockers alone do not control hypertension, vasodilators are ideal additional agents to control blood pressure. Because vasodilators alone can increase the left ventricular ejection, they should always be combined with beta-blockers.
- The goal of therapy is to manage the heart rate less than 70 beats/min and to keep blood pressure as low as possible without compromising organ perfusion.
- In patients with hypotension at presentation, possible volume depletion, which may be the result of blood sequestration in the false lumen, pleura, or pericardial space, has to be ruled out.
- Pericardiocentesis is usually avoided for cardiac tamponade secondary to dissection, as bleeding is recurrent. A definitive surgery is indicated in these cases.

Step 4: Perform confirmatory investigation for acute aortic dissection (Table 25.4)

- The diagnostic goal of imaging is to achieve the following:
  - Confirm diagnosis.
  - Classify the dissection/delineate the extent.
  - Differentiate true and false lumen, localize intimal tears, and distinguish between communicating and noncommunicating dissection.
  - Assess side branch involvement (including coronary arteries).
  - Detect and grade aortic regurgitation.
  - Detect extravasation (periaortic or mediastinal hematoma, pleural or pericardial effusion).

Table 25.4 Diagnostic imaging

Modality	Sensitivity (%)	Specificity (%)	Comments
CT scan	90–100	90–100	Quick, readily available, familiarity
			Shows pleural/pericardial spaces
			Shows head and neck vessels
			IV contrast may cause renal failure
MRI	98–100	98–100	Gold standard
			Detailed dynamic images
			Flow in true and false lumen
			Branched vessels
			Limitation is availability
			Time taken in emergency situation
Echo			
Transthoracic	60–80	86–90	Readily available and can be used in emergency situations
Transesophageal	90–99	85–98	Shows coronary ostia, AR, and pericardium
			LV function
			Contraindicated in esophageal and cervical pathology
Aortography	80–90	88–94	Shows true and false lumen perfusion
			Flap, coronaries, AR
			Invasive, can precipitate rupture
			Facilities and expertise not widely available
Intravascular ultrasound	94–100	97–100	Used to complement information of aortography
			Clearly differentiates dissection Intramural hematoma, and penetrating ulcer

- Assess clinical stability (for transport), availability, and experience with the investigation before deciding on the confirmatory imaging modality.
- Because of good sensitivity and specificity, CT angiography and MRI angiography are considered current standards of evaluation.
- If the patient is hemodynamically unstable and cannot be shifted for imaging, transesophageal echocardiography can be done to confirm the diagnosis.
- Transthoracic echo has a low sensitivity and specificity especially for type B dissection.
- Coronary angiography—because the recent generation CT/MRI imaging modalities can demonstrate proximal third of coronary arteries, routine use of conventional coronary angiogram is not recommended.

Step 5: Understand types of aortic dissection and their outcome (Fig. 25.1)

- Aortic dissection refers to formation of a tear in aortic intima, directly exposing the blood to the diseased medial layer and splitting the aortic wall, producing true lumen and false lumen with driving force (pulse pressure).

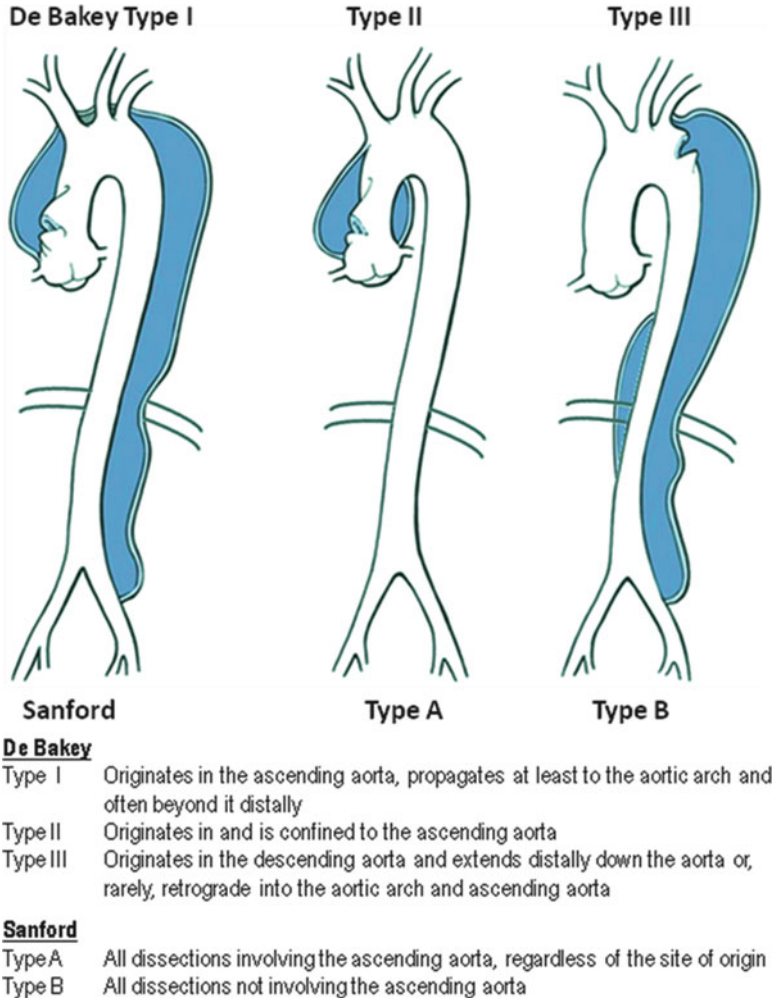

Fig. 25.1 Classification of aortic dissection

- The dissecting process extends antegradely but sometimes retrogradely from the site of intimal tear.
- For prognostic and therapeutic reasons, aortic dissections are classified into three major types, which share the basic principle whether the ascending aorta is involved (Fig. 25.1).
- Proximal dissection (involves ascending aorta) includes De Bakey type I and type II or Stanford type A.
- Distal dissection (spares ascending aorta) includes De Bakey type III or Stanford type B.

- For prognostic reasons, dissection has also been classified as acute or chronic depending on duration (less or more than 2 weeks).
- Recent years have brought recognition of two important variants of aortic dissection.
  - Intramural hematoma (IMH)
    - Aortic IMH is considered as a precursor of dissection originating from ruptured vasa vasorum in the aortic medial wall layer and resulting in an aortic wall infarct that may provoke a secondary tear, causing a classic aortic dissection. Although clinical manifestations of IMH are similar to acute aortic dissection, IMH is an imaging diagnosis in an appropriate clinical setting. Treatment is similar to classic aortic dissection.
  - Penetrating aortic ulcer
    - Deep ulceration of atherosclerotic plaque can lead to IMH, aortic dissection, or perforation. In association with IMH, these ulcers are seen almost exclusively with type B dissection.
- At present, these three lesions—aortic dissection, IMH, and penetrating aortic ulcers—are called acute aortic syndromes.
- Acute aortic dissection of ascending aorta (De Bakey type I and type II, Stanford type A) is highly lethal, with a mortality rate of 1–2% every hour after the onset of symptoms. Without surgery, the mortality rate exceeds 50% after 1 month.
- Uncomplicated type B (De Bakey type III) aortic dissection has a 30-day mortality of 10% and may be managed medically.
- Intramural hematoma of ascending aorta has a prognosis similar to type A dissection.

Step 6: Definitive surgery

- Type I and II (A) dissections are managed primarily by surgery.
- Type III (B) is managed conservatively, and surgery is only indicated if complications such as organ hypoperfusion, refractory hypotension, refractory pain, or aortic rupture occur.
- There is increasingly use of percutaneous endovascular stent grafting in selected cases of distal dissection.

Step 7: Identify underlying risk factors for aortic dissection

- These include hypertension, hyperlipidemia, trauma, hereditary connective tissue disorders like Marfan's syndrome, arteritis, and cocaine use.

Step 8: Long-term follow-up and treatment

- The cornerstone of medical therapy is with beta-blockers. Excellent blood pressure control, less than 120/80 mmHg, is paramount to prevent long-term complications. Close follow-up by a specialized team includes the assessment of signs of aortic expansion, aneurysm formation, signs of leakages at anastomoses/stent sites, and malperfusion.

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Part III

Nervous System

Shiva Iyer and Nagarajan Ramakrishnan

Cerebrovascular Accident

26

V. Dedeepiya Devaprasad and Nagarajan Ramakrishnan

A 60-year-old male with diabetes presented with weakness of the left arm and leg. He was conscious, alert, oriented and denied any headache or vomiting. Clinical examination suggested a left-sided hemiparesis.

Acute stroke (cerebral infarct or intracerebral hemorrhage) is the most frequent cause of admission in neurocritical care units. Time is brain in these situations, and prompt attention and intervention may salvage some patients from this catastrophic problem.

Step 1: Initiate resuscitation and exclude common stroke mimics such as hypoglycemia

- Initiate resuscitation as mentioned in Chap. 78.
- Intubation is done routinely when the Glasgow coma scale (GCS) is less than or equal to 8, when there is insufficient ventilation ($PO_2 < 60$ mmHg or $PCO_2 > 50$ mmHg), obvious signs of pupillary asymmetry, and depressed consciousness that threatens the airway.
- The patient should be intubated after maximal preoxygenation and administration of drugs to avoid reflex arrhythmias, blood pressure derangements, and fluctuations in ICP (intracranial pressure).

Step 2: Perform urgent noncontrast CT scan of the brain

- CT scan can reveal either a normal study, a hyperdense lesion (white) suggestive of hemorrhage, or a hypodense lesion (black) suggestive of ischemia.

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- Normal CT scan excludes intracerebral hemorrhage (ICH), but it is possible that the patient may have an ischemic stroke.
- MRI of the brain, especially with diffusion-weighted image/perfusion-weighted image (DWI/PWI) (bright lesion), may be a superior tool in identifying early ischemic stroke when a CT scan is reported as normal. In these patients, a diffusion–perfusion mismatch will help in identifying early ischemia.
- However, for all practical considerations including cost, easy availability, and time taken to perform the test, a non-contrast CT scan of the brain is preferable as the initial investigation in the management of stroke.

Step 3: Ascertain the duration of stroke

- It is sometimes difficult to determine the time when stroke occurred. Time of stroke onset is not the time when deficit was first noticed, but the time when the patient was last seen normal.

Management of Ischemic Stroke

Step 4: Urgently thrombolyze if indicated in ischemic stroke

- Restoration of perfusion is one of the most important measures to achieve in an ischemic stroke. This is usually accomplished by using thrombolytic agents.
- The National Institute of Neurological Disorders and Stroke (NINDS) study group trial showed that thrombolysis was safe and effective if performed within 3 h of stroke onset.
- There is increasing evidence that this time window may be extended to 4.5 h in selected patients (age less than 80 years, nondiabetics, no previous stroke).
- The only approved agent is recombinant tissue plasminogen activator (tPA) given at a dose of 0.9 mg/Kg up to a maximum of 90 mg (10% of dose given as a bolus over 1 min and the remainder infused over 1 h).
- Appropriate informed consent should be taken from the patient or surrogate.
- The most important considerations in the use of thrombolytic therapy are:
  - Appropriate inclusion and exclusion criteria (Table 26.1).
  - To get the exact time window of 3–4.5 hours from stroke onset
- Anticoagulant and antithrombotic agents, such as warfarin, heparin, or antiplatelet drugs, should not be administered for at least 24 h after the tPA infusion is completed.
- Invasive procedures, such as vascular puncture, urinary catheter placement, and nasogastric tube insertion, should be avoided for at least 24 h.
- Hemodynamic and close neurologic monitoring with half hourly GCS scoring should be charted.
- A follow-up noncontrast head CT scan should be obtained at 24 h particularly if treatment with antithrombotic agents, such as aspirin or heparin, is planned.
- Although thrombolysis has been shown to result in good functional outcome, it is still not widely used because of late presentation, fear of complications, and cost factors.

Table 26.1 Eligibility criteria for thrombolysis of acute stroke

Inclusion criteria
Clinical diagnosis of ischemic stroke
With measurable neurological deficit consistent with ischemic stroke
Within 3–4.5 h of onset of symptoms (if exact time of stroke onset is unclear, it is defined as the time when the patient was last noted to be normal)
Exclusion criteria
History
Stroke or head trauma within the prior 3 months
Any prior history of intracranial hemorrhage
Major surgery in the previous 14 days
Gastrointestinal or genitourinary bleeding within the previous 21 days
Myocardial infarction (MI) within the prior 3 months
Arterial puncture at a noncompressible site within 7 days
Lumbar puncture within 7 days
Clinical
Rapidly improving stroke symptoms
Only minor and isolated neurological signs
Seizure at the onset of stroke with postictal residual neurological impairments
Symptoms suggestive of subarachnoid hemorrhage, even if the CT scan is normal
Clinical presentation consistent with acute MI or post-MI pericarditis
Persistent SBP > 185 mmHg, DBP > 110 mmHg, or requiring aggressive therapy to control BP
Pregnancy or lactation
Active bleeding or acute trauma (fracture)
Laboratory
Platelets <100,000/mm^3
Serum glucose <50 mg/dL (2.8 mmol/L) or >400 mg/dL (22.2 mmol/L)
International normalized ratio >1.7 if the patient is on warfarin and increased activated partial thromboplastin time if on heparin
Head CT scan
Evidence of hemorrhage
Evidence of early major infarct such as diffuse swelling of the affected hemisphere, parenchymal hypodensity, and/or effacement of >33% of the middle cerebral artery territory

- Consider intracerebral hemorrhage (ICH) to be the likely cause of neurological worsening after the use of a thrombolytic drug until a brain scan confirms or refutes hemorrhage.
- Immediately discontinue ongoing infusion of the thrombolytic drug if intracerebral bleed is suspected.
- Obtain emergent head CT scan.
- Obtain blood samples for type and crossmatch, prothrombin time, activated partial thromboplastin time (APTT), platelet count, and fibrinogen assay.
- If ICH is confirmed by imaging:
  - Give 10 units of cryoprecipitate to increase the levels of fibrinogen and factor VIII.
  - Give 6–8 units of random donor or equivalent single donor platelets.

  - In patients receiving unfractionated heparin (UFH), consider giving 1 mg of protamine for every 100 units of UFH received in the preceding 4 h.
  - Obtain neurosurgical consultation, and consider evacuation of the hematoma if feasible.

Step 5: Maintain hemodynamics

- In ischemic stroke, it is recommended that if the patient is to undergo thrombolysis, the patient's blood pressure (BP) should be kept below 185/110 mmHg prior to thrombolysis and for 24 h after.
- If the patient is not eligible for thrombolysis, BP need not be treated unless it is more than 220/120 mmHg or the patient has heart failure, acute coronary syndrome, aortic dissection, or worsening renal function.
- The BP can be lowered by 15% during the first 24 h, ensuring that the patient is neurologically stable. A slower reduction to baseline may then be attempted over the next 7–10 days after stroke.
- Intravenous (IV) labetalol is the drug of choice, preferably by IV infusion.
- Initial bolus dose of 10 mg IV should be followed by infusion of 2–8 mg/min, or intermittent boluses of 10 mg every half an hour. Maximum daily dose of IV labetalol is 300 mg/day. Switch to oral labetalol once patient is stable.
- Monitor the heart rate and hold infusion if it is less than 60/min.
- Other agents that are recommended for treating hypertension in ischemic stroke are sodium nitroprusside, nicardipine, angiotensin-converting enzyme inhibitor, and hydralazine. Nitrates should be avoided because they tend to increase intracranial pressure (ICP) (refer to Chap. 24).

Step 6: Start antiplatelet therapy

- Because ICH is an anticipated side effect of thrombolysis, antiplatelets should not be initiated for 24 h until a repeat CT scan is performed to rule out significant bleed.
- If for any reason thrombolysis is not given, it is imperative to start antiplatelet therapy (aspirin, clopidogrel, aspirin in combination with extended release dipyridamole) without delay.
- In contrast to the patients with coronary artery disease where dual antiplatelet therapy is the rule, only a single antiplatelet therapy is recommended in patients with ischemic stroke.
- Aspirin is the preferred drug and is recommended to be initiated at a loading dose of 325 mg then 150–325 mg/day within 48 h of stroke onset. If the patient has documented aspirin allergy or has peptic ulcer disease, then clopidogrel 75 mg is recommended.

Step 7: Consider other adjunctive measures

- Anticoagulants are recommended in prophylactic doses in an attempt to prevent deep vein thrombosis after 24 h of stroke.
- Full-dose anticoagulation is not recommended even in patients with atrial fibrillation until about 3 weeks after a stroke because of the low risk of recurrent re-embolization.

- However, if the risk of re-embolization is high (e.g., mechanical valve prosthesis), full-dose anticoagulation may be initiated within a week.
- Other adjunctive treatment would include statins, for example, atorvastatin 40 mg/day or equivalent.
- There should be appropriate glycemic control, hypoglycemia should be avoided, and serum glucose level should be kept below 150 mg/dL.
- Treat fever aggressively.
- Maintain proper hydration and normovolemia particularly in patients on mannitol therapy.

Step 8: Anticipate complications in the first week of stroke

- If the patient has worsening sensorium, perform an urgent CT brain scan.
- Three common complications to watch for include infarct expansion, infarct-related edema, and hemorrhagic transformation.
- *Infarct expansion*
  - Infarct expansion can be suspected if there is worsening of sensorium or appearance of new neurological deficits.
  - In such patients, hypertension should not be aggressively corrected; if necessary, antihypertensive drugs should be withheld.
  - A cautious trial of induced hypertension may be tried. With an increase in mean arterial pressure (MAP), if the neurological deficits improve, it is reasonable to assume that it was due to infarct expansion, and in such patients an elevated MAP needs to be maintained.
- *Infarct-related edema*
  - Infarct-related edema usually starts at day 2 of stroke and lasts until day 7, but may rarely persist until day 14.
  - Pupillary asymmetry and deepening coma are clinical pointers to edema occurrence and worsening.
  - It may lead to secondary infarction and loss of more brain tissue due to ischemia. It also leads to subfalcine herniation and tentorial herniation that can result in brain death.
  - It is treated with bolus therapy of 10–20% mannitol (1 g/Kg IV) given over 10–20 min repeated as frequently as needed, or hypertonic saline, and head of bed elevation to 30°.
  - Infarct-related edema can be prevented by avoiding hypoxemia, hypoventilation, hypovolemia, hypotonic solution, dehydration, seizures, and fluctuations in serum glucose levels.
  - Fever should be suppressed by physical (surface cooling) or chemical methods (antipyretic drugs) because it can also lead to infarct-related edema.
- *Hemorrhagic transformation*
  - Hemorrhagic transformation is suspected clinically by a decrease in sensorium and confirmed by a CT scan.
  - It should be managed by withholding antiplatelets and anticoagulants.

Step 9: Consider investigating the risk factor for stroke
- Lipid profile.
- Echocardiogram—for cardioembolic source.
- Carotid Doppler study—for critical carotid stenosis.
- HbA1c—for glycemic control.
- Holter monitoring to detect paroxysmal atrial fibrillation.
- In a young stroke patient, vasculitis profile and thrombophilia profile should be performed.

A 60-year-old hypertensive male was admitted with sudden-onset slurring of speech, vomiting, headache, and rapidly progressive drowsiness. His blood pressure was measured as 190/100 mmHg. An urgent noncontrast CT brain scan suggested the occurrence of a hemorrhagic stroke.

Step 1: Maintain airway
As mentioned above in Step 1.

Step 2: Reduce BP judiciously
- *Current guidelines for managing BP in spontaneous ICH*
  - If systolic blood pressure (SBP) is 200 mmHg or MAP (SBP + 2 × DBP)/3 is 150 mmHg, then consider aggressive reduction of BP with continuous IV infusion and frequent BP monitoring.
  - If SBP is 180 mmHg or MAP is 130 mmHg and there is a possibility of elevated ICP, then consider reducing BP using intermittent or continuous IV medications.
  - If SBP is 180 mmHg or MAP is 130 mmHg and there is no evidence of elevated ICP, then consider a modest reduction of BP (e.g., MAP of 110 mmHg or target BP of 160/90 mmHg) using intermittent or continuous IV medications to control BP and examine the patient frequently.
  - IV labetalol is the drug of choice, preferably by IV infusion.
  - Initial bolus dose of 10 mg IV followed by infusion of 2–8 mg/min, or intermittent boluses of 10 mg every half an hour. Maximum daily dose of IV labetalol is 300 mg/day.
  - Monitor heart rate, and hold infusion if it is less than 60/min.
  - Other agents that are recommended for treating hypertension in hemorrhagic stroke are nicardipine, angiotensin-converting enzyme inhibitor, and hydralazine. Nitrates should be avoided because they tend to increase ICP (refer to Chap. 24).
- Addressing pain may also help to reduce hypertension.

Step 3: Consider management of raised ICP

- Raised ICP is expected to follow ICH and is defined as ICP ≥20 mmHg for >3 min, with the therapeutic goal being decrease of ICP to <20 mmHg or maintaining the cerebral perfusion pressure between 50 and 70 mmHg.
- Generally, it is recommended that a patient with GCS ≤8 or with rapidly deteriorating GCS that is attributable to raised ICP or features of transtentorial herniation may benefit from an ICP monitor.
- Patients with intraventricular hemorrhage and hydrocephalus may also benefit from ICP measurement.
- This is not usually done in many centers for fear of infection risk and lack of outcome studies showing reduction in mortality (see Chap. 31).
- Raised ICP is treated with bolus therapy of 20% mannitol (1mg/kg) IV given over 10–20 minutes repeated as frequently as needed or hypertonic saline and head of bed elevation to 30°.

Step 4: Cautious use of fresh frozen plasma (FFP), platelet transfusion, or aFVII (activated factor VII)

- Current recommendations are against the use of aFVII in unselected patients.
- This can be considered for patients who are coagulopathic and require urgent surgical evacuation and at risk for volume overload with FFP infusion and do not have the potential for thrombogenic complication such as active coronary artery disease.
- The usefulness of platelet transfusion in patients who have received antiplatelets earlier is investigational and unclear.
- However, if the patient has severe thrombocytopenia, they should receive platelet transfusion.
- Routine use of FFP is not recommended.
- However, if the patient has severe coagulation abnormalities or has been on oral anticoagulants, FFP should be administered.
- In addition to FFP, patients on oral anticoagulation should also receive vitamin K and have further doses of oral anticoagulation withheld.
- In patients with urgent need for anticoagulation (such as mechanical valve prosthesis), continuous infusion of UFH with APTT monitoring with lower than the usual therapeutic goal may be instituted.
- It is preferable to use unfractionated heparin because it can be easily reversed.

Step 5: Selected use of antiepileptics

- There is no role for prophylactic anticonvulsants, and hence they should not be used.
- In selected cases of lobar hemorrhage, they can be used for 1 month.
- However, if the patient has clinical seizures, they should receive antiepileptics.
- If the patient has deterioration in mental status, that is, out of proportion to the degree of brain injury, a continuous electroencephalogram (EEG) monitor is indicated to exclude non-convulsive seizures, and should these patients have any evidence of seizures on EEG, they should receive anticonvulsants.
- In the absence of continuous EEG monitoring, introduction of antiepileptics in the presence of disproportionate mental status changes may be considered with closed neurological monitoring.

Step 6: Consider cerebral angiography

- Angiography is not recommended in elderly patients with hypertension and who have hemorrhage in typical territories such as basal ganglia, thalamus, cerebellum, or brain stem and in whom CT scan shows no suggestion of a structural lesion.
- However, if the patient is young, normotensive with no definite cause of hemorrhage, an angiogram would be recommended especially if he/she is a candidate for surgical intervention.

Step 7: Consider surgical management

- In most patients, benefits of surgery are debatable unless:
  - They have cerebellar hemorrhage and are deteriorating.
  - They have brain stem compression and/or hydrocephalus.
  - There is intraventricular bleed or hydrocephalus requiring external ventricular drain.
  - There is lobar clot of more than 30 mL located within 1 cm of the cortical surface.
  - Decompressive craniectomy may be considered in some patients who are young with involvement of nondominant hemisphere.

Step 8: General care

- Deep vein thrombosis prophylaxis with mechanical compression device should be started at the earliest in ICH and low molecular weight heparin or UFH in cerebral infarct.
- Antiulcer prophylaxis should be started with H_2 blocker.
- Proper skin and eye care should be provided.
- Aspiration precaution should be taken.
- Proper nutrition should be provided.
- Bowel and bladder functions should be taken care of.
- Contractures should be prevented by supervised physiotherapy.
- Fever and glycemic control should be properly managed.

Suggested Reading

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   As compared with placebo, intravenous alteplase administered between 3 and 4.5 h after the onset of symptoms significantly improved clinical outcomes in patients with acute ischemic stroke; alteplase was more frequently associated with symptomatic intracranial hemorrhage.
   Early intensive BP-lowering treatment is clinically feasible, well tolerated, and seems to reduce hematoma growth in ICH.
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Websites

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   Neurological teaching site for ICU residents
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   A comprehensive site for neurological examination
4. med.harvard.edu
   A comprehensive atlas of brain imaging

Subarachnoid Hemorrhage

27

Charu Gauba and Pushpendra Nath Renjen

A 25-year-old woman had a sudden severe headache on waking up one morning. She described this as the worst headache she had ever experienced in her life. A few minutes later, she vomited and then fell unconscious. There was no witnessed seizure. She was arousable when she was brought to the emergency department and was talking coherently and obeying commands. There was no localizing sign, but she had neck stiffness.

Subarachnoid hemorrhage (SAH) should be suspected in patients presenting with severe headache of acute onset with an altered mental state. The most important cause of SAH is a ruptured aneurysm. Other causes include trauma, vascular malformations, hemorrhagic infarctions and hypertensive hemorrhages. The high morbidity and mortality associated with aneurysmal SAH mandates a high degree of suspicion to allow timely and appropriate treatment.

Step 1: Start resuscitation

- Urgent airway protection is necessary in obtunded patients to avoid hypercarbia and rise in intracranial pressure.
- In patients with suspicion of SAH, volume loading and vasopressors should be avoided during initial resuscitation to prevent aneurysmal rebleeding.

Step 2: Take focused history and perform clinical examination

- The classic features of an SAH include a sudden explosive headache (often called a thunderclap headache). This may be accompanied by decreased consciousness, photophobia, neck pain, nausea and vomiting.

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Table 27.1 The Hunt and Hess scale

1.	Asymtomatic or, mild headache, slight neck rigidity
2.	Moderate-to-severe headache, neck rigidity, no neurological deficit other than cranial nerve palsy
3.	Drowsiness/confusion, mild focal neurological deficit
4.	Stupor, moderate-to-severe hemiparesis
5.	Coma, decerebrate posturing

- In SAH patients, history of trauma, hypertension, bleeding diathesis, use of antiplatelet agents or anticoagulants and drug abuse like cocaine should be taken.
- Sentinel headaches occur in about half of patients before rupture.
- Lateralizing signs may occur if there is an intracerebral hematoma.
- Neck stiffness is a useful sign when present.
- Close neurological monitoring and serial neuroexamination are essential as these patients might deteriorate suddenly.
- Fundus examination may be carried out to rule out subhyaloid hemorrhage.

Step 3: Assess severity of SAH

- The Hunt and Hess scale is one of the grading systems used to classify the severity of SAH based on the patient's clinical condition. It is used as a predictor of the patient's prognosis, with a higher grade correlating with lower survival rate (Table 27.1).
- The Hunt and Hess scale is now used less frequently and has largely been replaced by the World Federation of Neurosurgical Societies classification, mentioned as follows:
  1. Glasgow coma score (GCS) 15, motor deficit absent
  2. GCS 13 or 14, motor deficit absent
  3. GCS 13 or 14, motor deficit present
  4. GCS 7–12, motor deficit absent or present
  5. GCS 3–6, motor deficit absent or present

Step 4: Perform an urgent noncontrast CT scan of the head

- CT is the imaging method of choice to diagnose an acute SAH. MRI is less effective in detecting blood early.
- The sensitivity of CT for detecting SAH is 90–95% at 24 h and 80% at 72 h. A negative CT scan in a patient with a typical history of SAH should be followed by a lumbar puncture, which will show xanthochromia and crenated RBCs.

Step 5: Start initial treatment

- Strict bed rest is advisable to prevent rebleeding of the aneurysm. Stool softeners, cough suppressants and a quiet environment are useful adjuncts.
- Pain control should be achieved with titrated doses of opioids. Nonsteroidal anti-inflammatory drugs should be avoided.

- Rebleeding may be related to changes in blood pressure rather than absolute blood pressure. Rebleeding has been found to be more common in those with a systolic pressure of more than 160 mmHg. Blood pressure should be controlled (see Chap. 24) to balance the risk of hypertension-related rebleeding and to maintain cerebral perfusion pressure. Short-acting, continuous infusion intravenous agents with a reliable dose–response relationship and a good safety profile are desirable. Labetalol, nicardipine, and esmolol seem to meet these criteria the best. Intravenous nitroprusside is best avoided due to its tendency to raise intracranial pressure and cause toxicity with prolonged administration.
- Mannitol is best avoided as it has been reported to precipitate rebleeding presumably by affecting transmural gradients across the aneurysm.

Step 6: Perform cerebral angiography

- If CT or lumbar puncture test report is positive, imaging of the cerebral vessels is required to delineate the aneurysm.
- The gold standard imaging modality is four-vessel cerebral digital subtraction angiography (DSA). All the vessels need to be included as multiple aneurysms occur in 20% patients.
- Approximately 80–85% aneurysms arise from the anterior circulation and the remaining from the posterior circulation.
- If DSA cannot be performed immediately, CT or MR angiography of the brain may be done initially. This needs to be followed up with DSA, however, to decide the ideal treatment modality for securing the aneurysm.
- Measures to prevent contrast-induced nephropathy should be instituted for patients at risk.

Step 7: Take measures to prevent rebleeding

- Early definitive treatment of the aneurysm improves outcome by decreasing rebleeding and enabling effective treatment of vasospasm once the aneurysm is secured.
- Two forms of treatment may be used to secure the aneurysm—microsurgical clipping and endovascular coiling. Complete obliteration of the aneurysm is recommended whenever possible.
- An experienced interventional radiologist and a neurosurgeon should be involved early in the management.
- In the large prospective randomized international subarachnoid aneurysm trial (ISAT) trial, it was found that in patients equally suited for both treatment options, endovascular coil treatment produced substantially better patient outcomes than surgery in terms of disability-free survival at 1 year. The relative risk of death or significant disability at 1 year in patients treated with coils was 22.6% lower than in surgically treated patients, an absolute risk reduction of 6.9%.
- However, the choice between coiling and clipping should be made after studying the characteristics of the aneurysm. Surgical intervention may be required with wide necked aneurysms or if there is an associated large intracerebral hematoma that requires evacuation.

Step 8: Prevent, identify and manage vasospasm

- Close neurological examination needs to be emphasized even after securing the aneurysm as vasospasm is a common and dreaded complication. This usually presents as a delayed focal neurological deficit but sometimes as an encephalopathy.
- In patients with SAH, 32% of deaths occur due to delayed ischemia from vasospasm, 25% due to the direct effects of aneurysmal rupture and 18% due to rebleeding.
- Onset of vasospasm typically occurs on days 3–5, peaks on days 5–14, and resolves over 2–4 weeks.
- The Fisher scale (CT scan appearance) has been used to predict the likelihood of symptomatic cerebral vasospasm:
  1. Grade 1: No bleeding is detected.
  2. Grade 2: Diffuse deposition of subarachnoid blood, no clots, and no layers of blood greater than 1 mm.
  3. Grade 3: Localized clots and/or vertical layers of blood 1 mm or greater in thickness.
  4. Grade 4: Diffuse or no subarachnoid blood, but intracerebral or intraventricular clots are present.
- Diagnosis of vasospasm is made by clinical examination, presence of fresh infarct on CT or by angiography. Transcranial Doppler studies permit bedside diagnosis of vasospasm by detecting high blood flow velocities in intracranial vessels.
- Oral nimodipine—an oral calcium channel antagonist, 60 mg 4-hourly for 21 days—is indicated to reduce poor outcome due to vasospasm. Side effects are infrequent and include peripheral edema, hypotension, tachycardia, abdominal discomfort, headache, and rash. The value of other oral or intravenous calcium antagonists remains uncertain. Benefit of nimodipine may be due to its neuroprotective property rather than to its vasodilatory property.
- Early treatment of the aneurysm enables maintenance of normal circulating blood volume, which is essential for management of vasospasm.
- Symptomatic cerebral vasospasm can be managed with "triple-H therapy," that is, hypervolemia, induction of hypertension and hemodilution. This may be performed by infusing normal saline or colloids to increase the CVP to 10–12 cm of saline. If hypervolemia alone does not improve the patient's condition, the systemic blood pressure is raised by withdrawing antihypertensives, if any, and giving dopamine infusion at 5 μg/Kg/min titrated to obtain a systolic BP of 160–180 mmHg. Hematocrit should be maintained at 30% ± 3%.
- Hypervolemic and hypertensive therapy puts patients at increased risk of arrhythmias and pulmonary edema, which needs to be closely monitored.
- Cerebral angioplasty and/or intra-arterial vasodilator therapy may be required, together with or in place of triple-H therapy in documented cases of vasospasm with deteriorating neurological status.

Step 9: Manage hydrocephalus

- Acute hydrocephalus occurs in 20% patients and appears within 3 days of the SAH. Delayed ventricular dilatation usually occurs after the tenth day and is seen in 23% patients.
- Ventriculostomy can be beneficial in patients with ventriculomegaly and decreased level of consciousness after an acute SAH. However, it has been reported that abrupt lowering of the intracranial pressure could lead to rebleeding due to decreased transmural pressure or removal of the clot, sealing the previously ruptured aneurysm.
- Temporary or permanent cerebrospinal fluid diversion is required in symptomatic patients with chronic hydrocephalus after SAH.

Step 10: Prevent and treat seizures

- Because of the potential risk of rebleeding with a seizure, the administration of prophylactic anticonvulsants is recommended in the immediate (up to 3 days) posthemorrhage period. The long-term use of anticonvulsants is not routinely recommended for patients with no seizure episodes and should be considered only for patients with risk factors such as thick cisternal clot, prior seizure, hematoma, infarct or middle cerebral artery aneurysms. Phenytoin or fosphenytoin has been the most common agent that has been used for prophylaxis.
- About 3–5% patients with SAH have seizures during their hospitalization. If seizures occur, they need to be treated like any other seizure (see Chap. 28).
- Epilepsy develops in approximately 15% patients with SAH, and it develops within 18 months in more than 90% patients.
- Risk factors for development of late epilepsy are poor neurological grades on admission, rupture of a middle cerebral artery aneurysm, cerebral infarction secondary to vasospasm and shunt-dependent hydrocephalus.

Step 11: Manage hyponatremia

- The reported incidence of hyponatremia after SAH ranges from 10% to 30% and may be an independent risk factor for poor outcome.
- Fluid restriction is required in patients with hyponatremia due to the syndrome of inappropriate antidiuretic hormone secretion. This can precipitate delayed ischemic deficits, and therefore, a careful balance has to be maintained.
- Hyponatremia in many cases with SAH is due to the "cerebral salt-wasting syndrome." This state is associated with features of volume depletion differentiating it from syndrome of inappropriate antidiuretic hormone (SIADH). Correction of hypovolemia with isotonic fluids is indicated in such cases.

Step 12: Manage neurogenic pulmonary edema

- This is characterized by rapid onset of respiratory failure in the setting of raised intracranial pressure. It is thought to be due to pulmonary capillary endothelial damage.
- Most of these patients are comatose.
- Treatment includes reduction of intracranial pressure, mechanical ventilation with positive-end expiratory pressure and attaining the lowest central venous or pulmonary wedge pressure that maintains an effective cardiac output by cautious diuresis.

Step 13: Look for ECG changes

- Alterations of the electrocardiogram are the most frequent cardiac abnormality in patients with SAH due to sympathetic activation causing reversible cardiac injury.
- These include prolongation of the QT interval, ST segment elevation or depression, and increased amplitude or deep inversion of the T waves ("cerebral" T waves).
- These are believed to be caused by a derangement of autonomic control of the heart and usually do not require treatment.
- Occasionally, arrhythmias may be precipitated, which need to be managed accordingly (see Chap. 22).

Step 14: Prognostication

- Unfavorable outcome was associated with increasing age, worsening neurological grade, ruptured posterior circulation aneurysm, larger aneurysm size, more SAH on admission computed tomography, intracerebral hematoma or intraventricular hemorrhage, elevated systolic blood pressure on admission, fever 8 days after SAH, use of anticonvulsants, symptomatic vasospasm and cerebral infarction.
- The use of prophylactic or therapeutic hypervolemia or induced hypertension was associated with a lower risk of unfavorable outcome.

Suggested Reading

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Websites

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   Updated Guidelines on SAH

Status Epilepticus

28

Jagarlapudi M. K. Murthy

A 31-year-old female patient, with a known case of epilepsy for 10 years on irregular treatment (phenytoin 300 mg/day and clobazam 10 mg/day), was brought to the emergency department with recurrent generalized tonic–clonic seizures and not regaining consciousness for half an hour.

Status epilepticus or recurrent seizures carry a mortality as high as 30% in adults and should be managed in a systematic way.

Step 1: Initiate resuscitation

- Initial priority in an ongoing seizure patient is airway protection.
- This can be achieved by proper positioning, oral suctioning, and oral/nasopharyngeal airway devices.
- If necessary, the patient should be intubated.
- Urgent peripheral intravenous (IV) access should be established.
- Blood glucose should be checked and corrected.

Step 2: Terminate seizures

- Immediate measures should be taken to end ongoing seizure activity (Table 28.1).
- Operational definition for convulsive status epilepticus (CSE) for adults and older children (>5 years old) is "a continuous, generalized, convulsive seizure lasting more than 5 min, or two or more seizures during which the patient does not return to baseline consciousness."

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Table 28.1 Treatment algorithm for convulsive status epilepticus

I.	*Premonitory stage—prolonged seizures (out-of-hospital) (5 min)*
	• Children and young adults: Rectal diazepam 0.5 mg/kg; buccal midazolam 0.2 mg/kg
	• Adults: Intravenous lorazepam 2 mg × 1 or diazepam 5 mg × 1, buccal midazolam 10 mg
II.	*First stage/out-of-hospital or in-hospital (5–20 min)*
	• Children and adults: Lorazepam 0.1 mg/kg IV (maximum, 4 mg) over 1 min or diazepam 0.2 mg/kg/ IV (maximum 10 mg) over 1 min. Allow 5 min to determine whether seizures terminate; if no response, repeat once
III.	*Second stage or established GCSE (20–60 min)*
	• Children and adults: Phenytoin 15–20 mg/kg IV at maximum rate of 50 mg/min or fosphenytoin 15–20 mg phenytoin equivalent (PE) IV mg/kg at maximum rate of 150 mg PE/min
	If seizure continues after 10 min of phenytoin/fosphenytoin
	• Repeat phenytoin 5 mg/kg IV at a maximum rate of 50 mg/min or fosphenytoin 5 mg PE/kg IV at a maximum rate of 150 mg/min or valproic acid 40–60 mg/kg IV at a maximum rate of 6 mg/kg/h or phenobarbital 20 mg/kg IV at 60 mg/min
IV.	*Refractory status epilepticus (>60 min)*
	• Adults and children: Midazolam 0.2 mg/kg IV (maximum 10 mg) bolus over 2 min followed by 0.05–0.5 mg/kg/h cIV or propofol 2–5 mg/kg IV bolus followed by 5–10 mg/kg/h cIV or thiopental 10–20 mg/kg IV bolus followed by 0.5–1 mg/kg/h cIV or pentobarbital bolus 10 mg/kg at <25 mg/min followed by cIV 0.5–2 mg/kg/h
	If seizures continue, consider the following emerging therapies
	• Topiramate 150–800 mg bid via NGT or levetiracetam 20–30 mg/kg IV at 5 mg/kg/min (maximum 3 g)
	• Inhalational anesthetic agents: Isoflurane at 0.8–2 vol.%, titrated to obtain the EEG burst suppression pattern
	• Ketamine: 1.5 mg/kg bolus, cIV 0.01–0.05 mg/kg/h

IV intravenous, *cIV* continuous intravenous infusion, *NGT* nasogastric tube, *GCSE* generalized convulsive status epilepticus

- This definition is based on the observations that spontaneous cessation of generalized convulsive seizures is unlikely after 5 min.
- For the purpose of standardization, initial pharmacotherapy of seizure has been divided into four stages (Table 28.1):
  1. Premonitory stage—epileptic seizure (out-of-hospital) (5 min)
  2. First stage—out-of-hospital or in-hospital (5–20 min)
  3. Second stage—established status epilepticus (20–60 min)
  4. Third stage—refractory status epilepticus (RSE) (>60 min)
- Benzodiazepines (lorazepam, midazolam, and diazepam) are effective in terminating seizures in 59–78% of patients. A clear benefit of IV lorazepam over diazepam has been shown in terminating CSE.

Step 3: Prevent further seizures (Table 28.1)

- When benzodiazepines fail to terminate CSE and to control further seizures once the initial seizure is controlled, a second-line drug like phenytoin or fosphenytoin is considered.

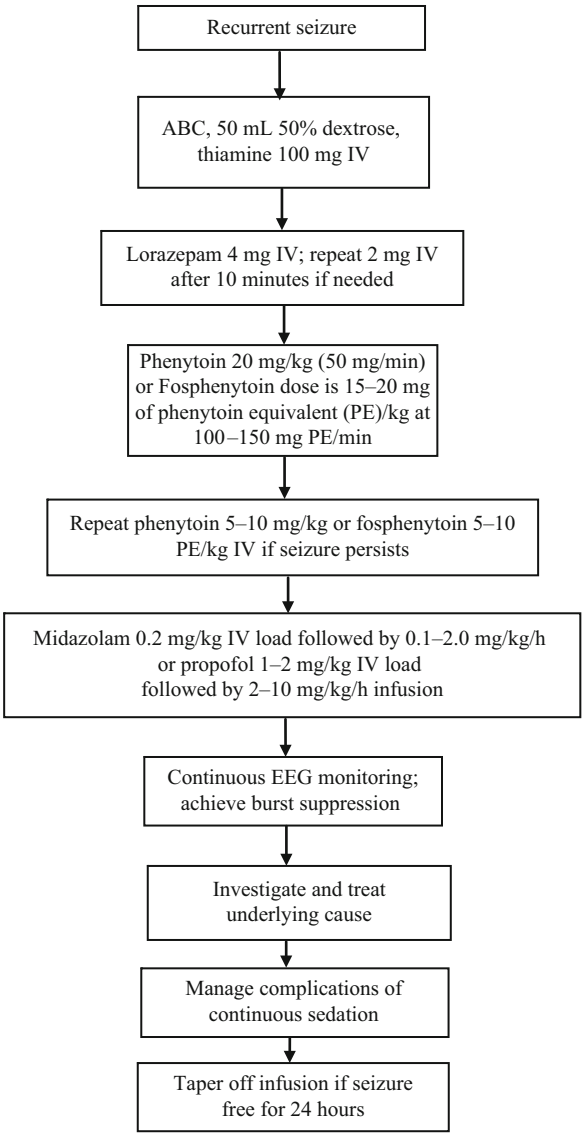

Fig. 28.1 Recurrent seizure management

- Fosphenytoin is preferred to phenytoin because of its water solubility and neutral pH, thereby allowing more rapid intravenous administration with less adverse effects and its compatibility with all IV fluids.
- Phenytoin or fosphenytoin is incompatible with dextrose-containing solution.
- Phenytoin should be given through a larger vein and caution should be taken to prevent extravasation as it is highly irritant.
- Experience with IV valproic acid suggests that it is as effective as phenytoin/fosphenytoin in terminating SE in patients who have previously failed benzodiazepines and also as first-line treatment to prevent recurrent seizures (Fig. 28.1).

Table 28.2 Status epilepticus—general measures

I.	*Premonitory stage (5 min)*
	• Secure airway, breathing, and circulation, physical safety; check random blood glucose (glucometer)
II.	*First stage (5–20 min)*
	• Oxygen supplement; obtain IV access; stabilize airway, respiration, and hemodynamics as needed; monitor ECG and SpO_2
	• Thiamine 100 mg IV, 50 mL of 50% dextrose if low glucose (less than 60 mg/dL). In children younger than 2 years, pyridoxine should be added.
	• Investigations: Random blood glucose, LFT, RFT, electrolytes, toxicology screening, magnesium, phosphorous, CSF if CNS infection a possibility, and CT/MRI of brain
III.	*Second stage or established GCSE (20–60 min)*
	• Cardiorespiratory function monitoring: ECG, blood pressure, SpO_2; identify and treat medical complications, treat acidosis
	• Investigations: EEG monitoring if the facilities are available
IV.	*Refractory status epilepticus (>60 min)*
	• Shift to the ICU with facility for hemodynamic monitoring and cEEG monitoring, identification and treatment of medical complications including hyperthermia
	• Consider treating acidosis if pH 7.2 or if hemodynamically unstable

CNS central nervous system, *CSF* cerebrospinal fluid, *CT* computer tomography, *ECG* electrocardiogram, *EEG* electroencephalogram, *cEEG* continuous electroencephalography, *LFT* liver function tests, *RFT* renal function tests, *BUN* blood urea nitrogen, *MRI* magnetic resonance imaging

Step 4: Initiate general measures of support and further investigation (Table 28.2)

- General supportive measures should be started concurrently with seizure treatment.
- Appropriate investigations to ascertain cause of seizures and any associated complication should also be undertaken.

Step 5: Manage refractory status epilepticus (RSE) (Table 28.1)

- Patients with refractory seizures should have their airway protected, ventilated, and hemodynamically monitored.
- Most experience is with continuous infusion (cIV) of anesthetic agents such as midazolam, propofol, and pentobarbital.
- No difference is found in mortality among the groups treated with these agents.
- Pentobarbital is associated with a lower frequency of acute treatment failures and breakthrough seizures.
- Superior pharmacokinetics and favorable adverse effect profile makes propofol a useful drug in RSE in both adults and children and successfully terminates RSE in about two-thirds of patients.
- Midazolam is an effective, short-acting benzodiazepine, which is given as an infusion, and has an efficacy in RSE.
- Studies using IV levetiracetam also suggest the efficacy and safety of the drug.

- If available, continuous EEG monitoring should be performed.
- Pharmacologic coma should be maintained for 12 h after the last seizure, with EEG goal of attaining burst suppression, after which gradually taper off infusion of the anesthetic agent every 3 h with EEG monitoring, and if there are no clinical or electrographic seizures, then discontinue the infusion.
- Continue EEG monitoring for at least 24 h after end of infusion.
- If clinical or electrographic seizures recur, reinstitute coma therapy with the same anesthetic agent to which the seizures were responsive.
- Make another attempt after 24 h of seizure freedom.
- Look for complications and manage hypotension, bradycardia, pulmonary edema, nosocomial sepsis, ileus, venous thromboemboli, skin breakdown, and exposure keratitis.

Step 6: Initiate maintenance treatment (Table 28.2)

- In parallel with emergency treatment, attention must be given to maintain antiepileptic drug (AED) therapy to prevent recurrence of seizures in close consultation with the neurologist.
- In patients known to have epilepsy, their usual AEDs should be maintained and dose adjustments should be made depending on AED levels.
- In patients presenting de novo, the AEDs, phenytoin/fosphenytoin, or valproic acid used to control the status can in principle be continued as oral maintenance therapy.
- In others, unless relatively short-lived treatment is anticipated, the preference is to initiate oral maintenance therapy with valproic acid or carbamazepine or any of the newer AEDs, topiramate or levetiracetam.
- Duration of antiepileptic is variable, depending on reversibility of underlying etiology, and should be decided with neurology consultation.

Step 7: Identify and manage the nonconvulsive status

- The nonconvulsive status may present as unexplained coma and fluctuating level of consciousness and is diagnosed by seizure activities in EEG monitoring.
- No concurrent motor activity is usually noticed.
- IV benzodiazepines—lorazepam or diazepam—are the drugs of choice.
- Allow 5 min to determine whether seizures terminate; if there is no response, repeat benzodiazepines once.
- If EEG monitoring still shows continuous electrographic seizures, consider valproic acid in case of absence type of nonconvulsive status epilepticus and consider phenytoin/fosphenytoin or valproic acid in case of other types of nonconvulsive status epilepticus the alternative option, particularly in the elderly will be intravenous levetiracetam.

Suggested Reading

1. Millikan D, Rice B, Silbergleit R. Emergency treatment of status epilepticus: current thinking. Emerg Med Clin North Am. 2009;27(1):101–13.

Current thinking about the acute treatment of status epilepticus (SE) emphasizes a more aggressive clinical approach to this common life-threatening neurologic emergency. In this review, the authors consider four concepts that can accelerate effective treatment of SE. These include (1) updating the definition of SE to make it more clinically relevant, (2) consideration of faster ways to initiate first-line benzodiazepine therapy in the prehospital environment, (3) moving to second-line agents more quickly in refractory status in the emergency department, and (4) increasing detection and treatment of unrecognized nonconvulsive SE in comatose neurologic emergency patients.

2. Meierkord H, Holtkamp M. Non-convulsive status epilepticus in adults: clinical forms and treatment. Lancet Neurol. 2007;6:329–39.
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3. Bassin S, Smith TL, Bleck TP. Clinical review: status epilepticus. Crit Care. 2002;6(2): 137–42.
   This review discusses current definitions of SE, as well as its clinical presentation and classification. The recent literature on epidemiology is reviewed, including morbidity and mortality data. An overview of the systemic pathophysiologic effects of SE is presented. Finally, significant studies on the treatment of acute SE and refractory SE are reviewed, including the use of anticonvulsants, such as benzodiazepines and other drugs.
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   Treatment with pentobarbitone, or any cIV-AED infusion to attain EEG background suppression, may be more effective than other strategies for treating RSE. However, these interventions were also associated with an increased frequency of hypotension, and no effect on mortality was seen.
5. Treiman DM, Meyers PF, Walton NY. A comparison of four treatments for generalized convulsive status epilepticus: Veterans Affairs Status Epilepticus Cooperative Study Group. N Engl J Med. 1998;339:792–8.
   As initial intravenous treatment for overt generalized convulsive status epilepticus, lorazepam is more effective than phenytoin. Although lorazepam is no more efficacious than phenobarbital or diazepam plus phenytoin, it is easier to use.

Acute Flaccid Paralysis

29

Charu Gauba, Mukul Verma, Vinit Suri, and Pooja Chopra

A 50-year-old male patient was admitted to hospital with a history of rapidly ascending paraparesis for the past 6 days followed by difficulty in breathing. He had an episode of acute gastroenteritis 2 weeks prior to the onset of the illness. His deep tendon reflexes were absent. Cerebrospinal fluid (CSF) examination showed raised protein with normal sugars and normal cell count.

Patients with rapid onset of flaccid paralysis pose a diagnostic and therapeutic challenge to the treating clinician. Systematic assessment, constructing a differential diagnosis, and rational approach to this problem will help in preventing intercurrent complication of this condition.

Step 1: Assess the patient

- Initiate resuscitation (see Chap. 78).
- Acute weakness may directly lead to admission to the ICU (Table 29.1) or may occur during an episode of critical illness.
- Immediate assessment of the patient's clinical condition and the duration of symptoms are the most important factors for determining the need for ICU care.
- Airway and breathing should be assessed for the need for airway protection and ventilatory support (Tables 29.2 and 29.3).
- Assess circulation by pulse rate, pulse volume, and blood pressure. If tachycardia is present or BP is low, IV fluid bolus should be given.

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Table 29.1 Causes of admission to the ICU

Inability to cough out secretions
Inability to swallow and at risk of aspirating orogastric secretions
Impaired respiratory muscle function leading to respiratory failure
Secondary complications of primary disease—sepsis

Table 29.2 Clinical criteria that point toward respiratory failure

Tachypnea, variable respiratory pattern, paradoxical abdominal breathing, with alveolar hypoventilation and carbon dioxide retention
Dyspnea might not be a predominant symptom in patients with respiratory failure due to neuromuscular weakness
Impaired forced expiration results in ineffective cough causing accumulation of secretions
Retention of secretions results in segmental collapse and ventilation perfusion mismatch

Table 29.3 Bedside procedures that indicate requirement of intubation

Inability to count till 20 in a single breath
Forced vital capacity of less than 15 mL/kg
Negative inspiratory pressure of less than 25–30 cm H_2O
Arterial PO_2 of less than 70 mmHg on room air
Dysphagia with bulbar muscle involvement

Step 2: Neurologic assessment

- Detailed history about presenting complaints, preceding illness, immunization, or other comorbidities should be taken from the patient and the family.
- Detailed examination helps in pointing toward a diagnosis. Specific therapy may then be given.
- The first step is to decide whether it is an upper motor neuron or lower motor neuron lesion. Further anatomic localization along the neuraxis can then be done depending on the specific features.
  - Upper motor neuron diseases may be caused by lesions in the brain or spinal cord.
  - Upper motor neuron weakness has a pyramidal distribution with greater involvement of extensors in upper limbs and flexors in lower limbs. Spasticity, brisk reflexes, clonus, and extensor plantars with usually no muscle wasting are seen.
  - In the acute stage of a cerebral or spinal insult, patients may present with flaccid weakness and areflexia. This is called cerebral or spinal shock; typical upper motor neuron signs develop later in the illness. Differentiation from lower motor neuron causes of weakness may be done by noting the associated features.
    - Altered sensorium, seizures, hemiparesis unless bilateral involvement—cerebral lesions
    - Craniopathies with crossed hemiparesis—brainstem lesions

Table 29.4 Neuromuscular diseases causing respiratory failure

Anterior horn cells and nerves	Neuromuscular junction	Myopathies
Amyotrophic lateral sclerosis	Myasthenia gravis (MG)	Poly-/dermatomyositis
GBS	Lambert–Eaton syndrome	Periodic paralysis
Toxic neuropathies	Botulism	Critical illness myopathy
Critical illness polyneuropathy	Drugs	Mitochondrial diseases
Phrenic neuropathy		Metabolic myopathies

    - Root pains, girdle sensation, sensory level over the trunk, bladder involvement—spinal cord lesions
  - *Lower motor neuron* diseases may be caused by lesions in the anterior horn cells, roots, plexus, nerves, neuromuscular junction, or muscles (Table 29.4).
  - Wasting, fasciculations, hypotonia, and diminished or absent reflexes may be seen in lower motor neuron diseases.
  - In anterior horn cell disease, weakness and wasting may be patchy, muscle fasciculations are present, and there is no sensory involvement.
  - Root or plexus lesions are painful and asymmetrical, involving the corresponding myotomes or dermatomes.
  - In lesions of peripheral nerves, there is symmetrical, usually distal, weakness with glove and stocking sensory loss and distal reflexes are absent. In Guillain–Barré syndrome (GBS), however, proximal weakness is often found and sensory symptoms may be present though without any sensory signs.
  - In diseases of the neuromuscular junction, there is history of true fatigability. Ptosis, eye movement abnormalities, faciobulbar weakness, proximal limb weakness, and absence of sensory involvement are the characteristic abnormalities.
  - In myopathies, there is symmetrical, usually proximal, muscle weakness and deep tendon reflexes are present unless there is severe muscle wasting and there is no sensory loss.
- Neuromuscular pathology in the critically ill patient develops in two settings: primary neurological diseases that require admission to the ICU for close monitoring or mechanical ventilation, and peripheral nervous system manifestations secondary to critical systemic diseases.
- The most frequent conditions in the first group are GBS, myasthenia gravis, and anterior horn cell disease, and in the second group, critical illness polyneuropathy and myopathy.
- The presenting picture is different since the former group includes acute pathologies that motivate ICU admission, whereas the latter group comprises polyneuropathy or myopathy acquired during hospitalization.
- Of the above illnesses, GBS and critical illness neuropathy/myopathy may be difficult to differentiate from each other. Involvement of the facial and bulbar muscles and autonomic nervous system along with CSF albuminocytologic dissociation is common in GBS, which does not occur in critical illness polyneuropathy.

- GBS is typically an acute demyelinating neuropathy though axonal variants also occur. Critical illness neuropathy, on the other hand, is of the axonal type.
- The functional prognosis of primary muscle impairment tends to be quite good, but both critical illness polyneuropathy and myopathy resolve very slowly over weeks or months with the possibility of a significant residual deficit after 2 years in the most severe cases.

Step 3: Send investigations

- Blood tests
  1. Serum potassium, calcium, and creatine phosphokinase are required when muscle pathology is suspected.
  2. Blood sugar levels, renal and liver function tests, vitamin B_{12} levels, and serum protein electrophoresis should be tested in diseases of the peripheral nerves.
  3. Thyroid function tests and vasculitic markers are useful in the case of both neuropathies and myopathies.
  4. Anti-acetylcholine receptor antibodies are a sensitive test for diagnosis of myasthenia gravis.
- Imaging: It is required in suspected CNS disease.
- Electromyogram (EMG) and nerve conduction velocity (NCV) studies are required to diagnose nerve and muscle disease.
  1. In demyelinating neuropathy, distal latencies are prolonged with dispersed compound muscle action potentials (CMAP). There may be conduction block, and nerve conduction velocity may be decreased on nerve conduction studies.
  2. In axonal neuropathy, there is decrease in amplitude of action potential on nerve conduction studies. EMG shows spontaneous activity in the form of fibrillation potentials and positive sharp waves with decreased recruitment.
  3. In myopathies, small-amplitude, short-duration, polyphasic action potentials are seen on EMG with rapid recruitment.
- CSF examination: Albuminocytologic dissociation (increased protein with normal cell count) is seen in GBS. On the other hand, high protein levels with pleocytosis and normal or low sugars are seen in infectious diseases.
- Spirometry: It is required for the measurement of vital capacity and peak flow.
- Muscle/nerve biopsy: It is required in selected cases of myopathy or neuropathy.

Step 4: Management

1. Airway protection—indications
   - Bulbar palsy leading to dysarthria, dysphonia, dysphagia, and poor gag reflex
   - Acute aspiration leading to respiratory arrest

   Insidious aspiration leading to pneumonia and gradual respiratory decompensation
2. Respiratory support

   Bedside tests and clinical assessment determine the need for respiratory support.
   - ICU admission is needed if vital capacity is less than 1 L or less than 50% predicted value, respiratory rate more than 30, or if the patient is unable to maintain patent airway.
   - Arterial blood gas analysis should be performed regularly. Hypoxia and hypercarbia with respiratory acidosis are late features. The patient may need

assisted ventilation even with normal blood gas in neuromuscular respiratory failure.
- Early tracheotomy should be considered in patients who require prolonged ventilatory support.
- Physiotherapy should be encouraged.

3. Nutritional support
   - Enteral nutrition should be initiated as soon as the patient becomes hemodynamically stable.
   - Nasogastric route should be preferred. Proper precaution should be taken to prevent regurgitation and aspiration. Head end should be elevated. Give prokinetics. Give continuous feed through enteral pump and check residual volume. Start nasojejunal feed in selected cases.
   - Oral feed can be considered in some tracheotomized patients after proper swallowing assessment.
   - Percutaneous endoscopic gastrostomy may be required for long-term use.
4. Venous thromboembolism prevention
   - Due to immobilization, the risk of deep venous thrombosis and pulmonary embolism (PE) is high.
   - Low-molecular-weight heparin or unfractionated heparin and gradient compression stockings are useful.
   - Passive leg exercises should be initiated.
5. Pain control
   - Both acute and chronic pain should be treated.
   - Opioid analgesics, anticonvulsants, or antidepressants may be used for neuropathic pains.
6. Autonomic disturbance
   - Common in small fibre neuropathies.
   - Depending on the symptoms—treat excessive secretions with anticholinergics.
   - β-Blocker for disproportionate tachycardia—cardiac pacing can be done for severe symptomatic bradycardia.
7. Pressure sores
   - Frequent turning should be done and pressure-relieving mattresses should be used.
8. Physiotherapy
   - It is important in the early course of the disease and in rehabilitation.
   - Passive exercises, cough assist devices, and splints are useful.
9. Specific treatment
   - Depending on the etiology

29.1 Specific Illnesses

1. *Critical illness neuropathy*
   - History will be suggestive of some critical illness, for example, sepsis, severe trauma, or burns.

- Clinical signs include generalized flaccid weakness with distal predominance and absent or decreased deep tendon reflexes. Facial and bulbar muscles are usually spared. Pain or paresthesia is not seen.
- Sensorium is intact.
- It often presents as failure to wean from the ventilator.
- Investigations: NCV studies will reveal decreased amplitude of motor and sensory action potentials with preserved conduction velocity, suggestive of an axonal neuropathy. EMG will reveal fibrillations and decreased motor unit potentials. CSF is almost always normal.
- It is diagnosed after excluding other neuropathies or neuromuscular junction abnormalities.
- Treatment is supportive care, intense glucose control, and early treatment of sepsis.
- Recovery is spontaneous in 3–6 months and is often partial.
- Prognosis depends on the underlying illness.

2. *Critical illness myopathy*
   - It is difficult to distinguish clinically from its neuropathic counterpart, and both may occur concurrently.
   - It usually occurs in patients with acute respiratory distress syndrome or severe asthma, who have been treated with intravenous corticosteroids, aminoglycosides and nondepolarizing neuromuscular blocking agents, or both.
   - Plasma creatine kinase levels are transiently and marginally elevated.
   - EMG shows small-amplitude, short-duration, polyphasic motor unit potentials, and sensory nerve conduction studies are normal.
   - Repetitive nerve stimulation studies should be performed to exclude a defect of neuromuscular transmission caused by defective clearance of neuromuscular blocking agents.
   - Treatment is supportive care, intense glucose control, and early treatment of sepsis.
   - Recovery is spontaneous in 3–6 months and is often partial.
   - Prognosis depends on the underlying illness.
3. *GBS syndrome*
   - History of acute gastrointestinal or respiratory tract infection 1–3 weeks before the onset of neurological symptoms is present in 70% cases. Predisposing factors such as HIV infection, Hodgkin's disease, history of recent immunization, recent surgery, and organ transplant should be sought.
   - It begins with paresthesia in the legs followed by rapidly ascending weakness which can progress up to a month.
   - Usually there is symmetric weakness in both proximal and distal muscle groups with loss or attenuation of deep tendon jerks. Objective sensory loss is mild. Bifacial and bulbar muscle involvement is frequently present. Autonomic dysfunction and respiratory involvement may occur in the acute stage and may be fatal.
   - Investigations are usually normal in the first week of illness. CSF examination later reveals albuminocytologic dissociation with normal CSF glucose.

Table 29.5 Drugs exacerbating myasthenia

α-Interferon	Quinolones
D-Penicillamine	Macrolides
Botulinum toxin	β-Blockers
Neuromuscular blockers	Calcium channel blockers
Quinine, quinidine, procainamide	Magnesium salts
Aminoglycosides	Iodinated contrast agents

Note: In severe infection, the above-mentioned antibiotics may still be used if no other alternative exists

Electrodiagnostic studies may reveal only abnormalities of F waves in the beginning. This is followed by other features of demyelination such as prolonged distal latencies and decreased conduction velocities. MRI of spinal cord shows enhancement of lumbar nerve roots in some cases.

- Treatment
  - Intravenous Immunoglobulin (IV IG) 400 mg/kg/day for 5 days
  - Plasmapheresis 40–50 mL/kg/exchange(total 200–250 mL/kg) in three to five exchanges over 7–14 days

4. *Myasthenia gravis* (autoimmune disorder characterized by muscle weakness and exaggerated muscle fatigue)
   - The patient requires admission to the ICU when there is impending/full-blown myasthenic crisis. This is characterized by dramatic worsening particularly of respiratory symptoms and bulbar weakness.
   - Predisposing factors for crisis are systemic infections, drugs (Table 29.5), exacerbating weakness, surgery, and anesthesia.
   - It commonly begins with fluctuating and asymmetric ptosis and weakness of extraocular muscles. This may be followed by weakness of bulbar and proximal limb muscles. Respiratory muscle involvement indicates myasthenic crisis. Muscle bulk, tone, reflexes, and sensory examination are normal.
   - Investigations: Serum anti-acetylcholine receptor antibodies are positive in more than 90% cases of generalized myasthenia. Some seronegative patients have anti-muscle-specific tyrosine kinase antibodies. Edrophonium test: Pretreat with 0.5 mg atropine, give 2 mg edrophonium intravenously, and then give 3 mg and then 5 mg edrophonium intravenously; observe at each dose for 1–3 min for increase in muscle strength. Electrodiagnostic tests reveal decremental (15% or more reduction in amplitude) response in compound muscle action potential on repetitive nerve stimulation (RNS). Chest imaging should be done to rule out thymoma.
   - Treatment
     - Plasmapheresis 50 mL/kg/exchange)(total 200–250 mL/kg) in five to six exchanges over 7–14 days.
     - IV IG 400 mg/kg/day for 5 days (preferred if severe infection coexists).
     - Corticosteroids 1.5–2 mg/kg/day. In about one-third of patients, myasthenic weakness worsens 7–10 days after starting steroids.
     - Steroid sparing—azathioprine, cyclosporine, mycophenolate mofetil.

  - Pyridostigmine 60 mg oral; neostigmine 15 mg oral, 0.5 mg IV. (These should be discontinued if the patient is ventilated and reintroduced on weaning.)
  - Thymectomy may be useful especially in young (<50 years) females, but response is delayed. Its role is still being studied. It is mandatory in thymomas.
  - Supportive treatment.

5. *Anterior horn cell disease*

- The commonest of these is amyotrophic lateral sclerosis.
- It is usually sporadic and slightly more common in males.
- Peak incidence is in 65- to 74-year-old people.
- Mean disease duration from the onset to death is about 3 years.
- Wasting and weakness are usually patchy. Fasciculations are prominent. Both upper and lower motor neuron signs are seen and there is no sensory loss.
- Bulbar and respiratory muscles are involved in later stages, and respiratory failure is the usual mode of death.
- So far, there is no known drug which significantly prolongs survival.

Suggested Readings

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Coma

30

Kayanoosh Kadapatti and Shivakumar Iyer

A 30-year-old male patient, who was found unconscious in his room, was brought to the emergency department. On examination, he was found to be tachypneic and febrile with normal blood pressure. He was not opening his eyes and was withdrawing arms on pain.

The comatose patient in the ICU poses a diagnostic and therapeutic challenge to the physician. A broad range of differential diagnoses necessitate a systematic approach and judicious use of investigation in these patients.

Step 1: Assess and stabilize the patient

- In any unexplained, unresponsive patient, caution should be taken to avoid cervical spine movement while managing airway.
- If there is hypoglycemia (<60 mg/dL), it should be urgently corrected with 50 mL of 25% dextrose intravenously.
- Thiamine should be given prior to glucose to avoid Wernicke's encephalopathy, especially in patients with malnutrition and alcoholism.
- Control seizure, if present, with intravenous lorazepam.
- In patients who show features of increased intracranial pressure (ICP), 100 mL of 10% intravenous mannitol should be given (see Chap. 31).
- Give prompt antibiotics in patients with signs suggestive of meningitis.
- Check core temperature, and if hypothermic warm the patient.

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Step 2: Review history

Detailed history should be taken from the accompanying person:

- Rapidity of onset of the coma
- Rate of progression of coma
- The patient's circumstances at the time of onset of coma
- Any precipitating injury or seizure
- Any history of headache or neurological symptoms
- Any recent fever or illness
- Any history of depression or suicide ideation
- Any evidence of empty pill bottles, prescription, or suicide notes
- Any known chronic medical problems
- Any previous neurosurgery, for example, intracranial shunts
- Any history of alcohol or other drug abuse
- Any known exposure to toxins, gas fumes, or possible carbon monoxide/cyanide exposure
- Recent travel

Step 3: Perform focused physical examination

- *The level of consciousness may be assessed by AVPU and the Glasgow Coma Scale*
  A Alert
  V Responds to verbal stimuli
  P Responds to painful stimuli
  U Unresponsive
- *Glasgow Coma Scale* (GCS) (Table 30.1)

Table 30.1 Glasgow Coma Scale

Best eye opening (E)	
Nil	1
Pain	2
Verbal	3
Spontaneous	4
Best verbal response (V)	
Nil	1
Incomprehensible sounds	2
Inappropriate but recognizable words	3
Confused conversation	4
Oriented	5
Best motor response (M)	
Nil	1
Abnormal extension (decerebrate response)	2
Abnormal flexion (decorticate response)	3
Withdraws to pain	4
Localizes to pain	5
Obeys commands	6

  - The GCS measures the best eye, verbal, and motor response. The worst is 3 points and the best is 15 points, recorded as E4M6V5 = 15. A tracheostomy tube/ETT (endotracheal tube)/facial injury invalidates V.
- A GCS of less than 8 (e.g., E2M4V2) indicates severe traumatic brain injury. One must assess the airway carefully and decide for intubation for airway protection in this group of patients.
- Focused physical examination should be performed to assess the evidence of lateralizing signs like hemiplegia, features of increased ICP like pupillary changes, features of meningoencephalitis, or any systemic problem requiring immediate attention by imaging or neurosurgical consultation.
- Physical examination is useful in assessing the severity of coma and anatomical localization of neurological insult. These examinations need to be repeated frequently to elicit any deterioration of the patient's status.
- Posture—look for any seizure activity, tremors, myoclonus, or spontaneous decerebration. Myoclonic jerks point toward an anoxic cause of coma and portend a bad prognosis. Subtle rhythmic movements may suggest ongoing seizures.
- Skin—look for pallor, icterus, cyanosis of methemoglobinemia, petechiae, scars, burns, pigmentation, and needle marks.
- Facial muscles—look for asymmetry of the face.
- Oral cavity—look for tongue bite, smell of alcohol or ammonia (liver disease), gingival hyperplasia (phenytoin-induced), oral thrush (immunodeficient state).
- HEENT—head, eye, ear, neck, and throat should be examined for the evidence of injury, hematoma, bleeding (Battle's sign, Raccoon eyes) or any purulent discharge, skull fractures, cerebrospinal fluid (CSF) rhinorrhea, or otorrhea. Neck stiffness examination should be avoided in patients with suspected cervical spine injury. Check pupils for symmetry and light reflex.
- Blood pressure—elevation of blood pressure can indicate long-standing hypertension, which predisposes to intracranial hypertension or hypertensive encephalopathy due to increased ICP.
- Temperature
  - *Hypothermia* can occur in ethanol or sedative drug intoxication, Wernicke's encephalopathy, hepatic encephalopathy, and myxedema.
  - *Hyperthermia* can occur in status epilepticus, pontine hemorrhage, heat stroke, malignant hyperthermia, and anticholinergic intoxication.
- Optic fundi—look for papilledema and vitreous hemorrhage.
- Specific neurological examination of a comatose patient should include mental status, level of consciousness, awareness of self and environment, cranial nerve, motor response, and brainstem reflexes.
- *Assess the brainstem reflexes*
  - Check pupillary size and response to light.
  - Pupils that are equal in size, and react briskly to light, usually imply normal brainstem function and suggest metabolic coma or cortical injury.
  - Poorly reactive (but equal) pupils offer no clinical clues to the etiology or severity of the coma.

  - Small (1–2.5 mm) reactive pupils—diencephalon (thalamic hemorrhage), metabolic encephalopathy.
  - Pinpoint pupils (<1 mm) with reaction—pontine pathology, narcotic or barbiturate overdose.
  - Midposition/large (5–7 mm), fixed pupils—midbrain lesion
  - Bilateral widely dilated, fixed pupils—severe midbrain damage, brain death, rarely drugs, for example, barbiturates, atropine
  - Unilateral, dilated, fixed pupils—third nerve compression
- *Ocular movements*
  - Abducted eyes—third nerve dysfunction.
  - Adducted eyes—sixth nerve dysfunction; increased ICP.
  - Spontaneous horizontal eye movement, whether conjugate or disconjugate, implies normal brainstem function and suggests a metabolic coma.
  - Induced conjugate eye movement, oculocephalic reflex (doll's eye maneuver) or the oculovestibular reflex (cold caloric test)—in patients with suspected cervical spine injury, cold caloric test is preferable.
  - Resting position of the eyes on opening the eyelids—persistent conjugate deviation of the eyes toward one side suggests a stroke or seizure. Tonic conjugate downward deviation of the eyes often implies thalamic upper brainstem compression.
  - Corneal reflex should be tested by putting a few drops of sterile saline in the eyes rather than cotton wool to avoid corneal injury.
- *Motor response*
  - Motor responses can be characterized as appropriate, posturing, or flaccid.
  - Posturing refers to stereotyped arm and leg movement occurring spontaneously or elicited by sensory stimulation. Abnormal posturing can occur in early brainstem compression due to increased ICP and transtentorial herniation and manifest first with decorticate (arm flexion, leg extension) posturing due to diencephalon compression. The patient can then manifest decerebrate (arm extension, leg extension) posturing due to midbrain and upper pons compression, and further as the lower brainstem (medulla) is compressed, the extremities become flaccid. Posturing cannot be precisely used for anatomical location.
- *Respiratory patterns*
  - Various respiratory patterns such as Cheyne–Stokes breathing and central neurogenic hyperventilation may be observed depending on the location of the lesion.

Step 4: Perform relevant diagnostic tests

- A methodical way of appropriate investigation should be adopted to elicit the cause of coma and need for any immediate surgical intervention.
- Time is of the essence as these patients may deteriorate suddenly.
- Transportation of comatose patients for imaging should be carefully monitored and airway protection should be evaluated.

- A team of the intensivist, radiologist, neurophysician, neurosurgeon, and other paramedical staff is essential in coordinating the care of comatose patients.
- Complete blood count, complete metabolic profile—blood glucose, serum electrolytes (Na, K, Ca, Mg), liver function tests, ammonia, serum osmolality, blood urea nitrogen, creatinine, thyroid function test, ABG—toxicologic analysis of blood and urine.
- Chest skiagram, ultrasound, ECG.
- Cranial CT/MRI.
- CSF analysis.
- EEG.

Step 5: Ascertain the cause of coma and treat if possible (Table 30.2)

- Structural lesions can cause coma in one of two ways: directly by injuring the reticular activating system itself (e.g., brainstem stroke or hemorrhage) or indirectly by compression on the RAS (reticular activating system).
- This process is due to herniation whereby a mass lesion or swelling causes displacement of cerebral structures, ultimately compressing the brainstem, often in a rostrocaudal pattern.
- Look for common causes of structural coma (Table 30.2).
- Toxins and drugs account for an important cause of coma, which affects the brain diffusely and must be thought of in every patient of coma with normal brain imaging.

Table 30.2 Causes of coma

Supratentorial lesions
Subdural or extradural hematomas
Intracerebral hemorrhage
Infarction, tumor, abscess, and hydrocephalus
Infratentorial lesions
Brainstem infarct or hemorrhage
Cerebellar infarct
Hemorrhage, tumors, or abscesses
Diffuse cerebral or metabolic
Hypoxia
Concussion
Meningitis, encephalitis, sepsis
Seizures (postictal states or status epilepticus)
Subarachnoid hemorrhage
Endocrine disturbances (hypoglycemia, diabetic ketoacidosis hyperosmolar state, myxedema, hyperthyroidism)
Electrolyte abnormalities (hyponatremia, hypernatremia)
Endogenous toxins or deficiencies (uremia, hepatic failure)
Exogenous toxins or drugs (benzodiazepines, barbiturates, anticonvulsants, opiate analgesics, tricyclic antidepressants, antihistamines, organophosphorus compounds, anesthetic drugs, narcotic overdose in ICU, cyanide, carbon monoxide poisoning)

Table 30.3 Coma mimics

Persistent vegetative state
Locked in syndrome
Akinetic mutism
Hypersomnia
Brain death
Generalized muscle weakness (snake bite, organophosphorus poisoning, Guillain–Barré syndrome, myasthenia gravis, severe hypokalemia, neuromuscular blockade)
Pseudocoma (malingering catatonia, conversion reaction, hysteria)

Step 6: Rule out coma mimics (Table 30.3)

- Some clinical entities may be confused with coma and need to be differentiated.

Step 7: Assess prognosis and communicate to the family

- This is dependent on the underlying cause. Reversible causes such as metabolic, toxic, and surgically amenable lesions have a better prognosis.
- Anoxic brain injury, diffuse cortical, or brainstem lesions carry a bad prognosis.
- Prognostication should be guarded initially in all cases of coma; frequent examination and time course of comatose state will ultimately dictate the prognosis.

Suggested Reading

1. Karanjia N, Geocadin RG. Post-cardiac arrest syndrome: update on brain injury management and prognostication. Curr Treat Options Neurol. 2011;13(2):191–203.
This article focuses on the neurological care of patients after they have been resuscitated from cardiac arrest. Maximizing neurological outcome after cardiac arrest requires attention to prevention of primary and secondary brain injury.
2. Geocadin RG, Eleff SM. Cardiac arrest resuscitation: neurologic prognostication and brain death. Curr Opin Crit Care. 2008;14(3):261–8.
Evidence-based tests of prognostication for neurological outcome after cardiac arrest are presented. A review of the practice of withdrawal of life-sustaining therapies and the diagnosis of brain death is also provided. The reader is cautioned that most prognostic studies do not include possible amelioration with the use of therapeutic hypothermia.
3. Wijdicks EF, Hijdra A, Young GB. Practice parameter: prediction of outcome in comatose survivors after cardiopulmonary resuscitation (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2006; 67(2):203–10.
Pupillary light response, corneal reflexes, motor responses to pain, myoclonus status epilepticus, serum neuron-specific enolase, and somatosensory evoked potential studies can reliably assist in accurately predicting poor outcome in comatose patients after cardiopulmonary resuscitation for cardiac arrest.

Intracranial Pressure Monitoring and Management

31

Rajagopal Senthilkumar and Nagarajan Ramakrishnan

A 30-year-old male with head injury was on a ventilator. He was withdrawing from painful stimulus. His pupillary responses were equal and brain CT scan showed bilateral frontal contusion and subarachnoid hemorrhage. His blood pressure (BP) was 100/60 mmHg, and SpO_2 was 93% on 0.6 FiO_2. His temperature was 100°F and blood sugar was 70 mg/dL. He had been nursed with the head elevated at 45°.

Increased intracranial pressure (ICP) should be suspected in all patients with altered mental state, especially due to an intracranial pathology. Prompt assessment and management of this problem prevents secondary brain injury.

Step 1: Initiate resuscitation

- If elevated ICP is suspected, care should be taken to minimize its rise during intubation through careful positioning and adequate sedation.
- Avoid hypercapnia as it raises ICP by causing vasodilation.
- Avoid succinylcholine during intubation as it may increase ICP.
- Pretreat with mannitol if pupils are unequal.
- Large shifts in blood pressure should be minimized, with particular care taken to avoid hypotension. Hypotension, especially in conjunction with hypoxemia, can induce reactive vasodilation and elevations in ICP.
- Vasopressors have been shown to be safe in most patients with intracranial hypertension and may be required to maintain cerebral perfusion pressure (CPP) of more than 50 mmHg.

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Step 2: Recognize features of increased ICP

- Raised ICP may present with symptoms of headache, altered level of consciousness, weakness of extremities, or as respiratory arrest. Careful clinical examination would reveal one or more of the following nonspecific signs. Frequent neurological examination is essential as these patients may deteriorate suddenly.
  - Dilatation of ipsilateral or contralateral pupil
  - Ptosis
  - Hemiparesis
  - Alteration of respiration
  - Decerebrate posturing
  - Bradycardia
  - Hypertension

Step 3: Urgently manage increased ICP

- Urgent measures may need to be instituted prior to a more detailed workup (e.g., imaging or ICP monitoring) in a patient who presents acutely with history or examination findings suggestive of elevated ICP.
- Many of these situations will rely on clinical judgment, but the following combination of findings suggests the need for urgent intervention:
  - A Glasgow Coma Scale (GCS) ≤8 in the absence of other systemic problems such as severe hypoxia, hypercapnia, hypotension, hypoglycemia, hypothermia, or intoxication to explain the mental state.
  - In such patients
    - Osmotic diuretics should be used urgently, 10–20% intravenous mannitol (1–1.5 g/kg)
    - Head elevation to 30–45°
    - Hyperventilation to a PCO_2 of 26–30 mmHg
- In addition, standard resuscitation techniques should be instituted as soon as possible.
- Prolonged hyperventilation is contraindicated in the setting of traumatic brain injury and acute stroke as hypocapnia and respiratory alkalosis will cause cerebral vasoconstriction and worsen perfusion.
- Ventriculostomy is a rapid means of simultaneously diagnosing and treating elevated ICP (Fig. 31.3).

Step 4: Identify causes of raised ICP (Table 31.1)

- Brain is enclosed in a closed compartment formed of bony skull. It consists of three essential elements: brain matter (noncompressible), CSF, and blood (arteries and veins). Increase in any one of the elements will displace the others to keep ICP constant till a point when there will be an exponential rise of ICP. Displacement of brain will cause herniation syndromes.

Step 5: Initiate ICP monitoring

- An important early goal in management of the patient with presumed elevated ICP is placement of an ICP monitoring device.

Table 31.1 Common reasons for raised intracranial lesions

1. Localized mass lesions • Traumatic hematomas (extradural, subdural, and intracerebral) • Abscess • Neoplasms • ICH and massive cerebral infarction
2. Impaired CSF circulation • Obstructive and communicating hydrocephalus
3. Obstruction to venous outflow • Cerebral venous thrombosis • Depressed fractures overlying major venous sinuses
4. Diffuse brain edema • Infections and inflammations (encephalitis, meningitis) • Diffuse head injury • Hepatic encephalopathy • Water intoxication • Near-drowning

- The only way to reliably determine cerebral perfusion pressure (CPP defined as the difference between mean arterial pressure [MAP] and ICP) is to continuously monitor both ICP and BP.
- Normal ICP is below 20 mmHg.
- CPP should be kept between 50 and 70 mmHg in patients with elevated ICP in an attempt to avoid hypoperfusion and ischemic injury.
- Cerebral autoregulation maintains cerebral blood flow (CBF) by altering cerebral arteriolar diameter in response to changing CPP. Increase in CPP constricts the blood vessel, and decrease in CPP dilates the arterioles. Thus, CPP is a useful surrogate for CBF. In the injured brain, this autoregulation is lost, so CPP should be closely monitored and kept in a safe zone by monitoring ICP.
- Indications of ICP monitoring in severe head injury:
  - Comatose patients with Glasgow coma score (GCS) of 3–8, and with abnormal cranial findings on computed tomographic (CT) scan
  - Comatose patients with normal CT scans and more than 40 years of age
  - Unilateral or bilateral motor posturing and systolic blood pressure (SBP) of less than 90 mmHg
- ICP monitoring is not widely practiced for fear of risk of infection and absence of definite outcome data on reduction of mortality.
- There are four main anatomical sites used in the clinical measurement of ICP: intraventricular, intraparenchymal, subarachnoid, and epidural.
- Intraventricular monitors are considered the gold standard of ICP monitoring catheters. They are surgically placed into the ventricular system and affixed to a drainage bag and pressure transducer with a three-way stopcock.
- Intraventricular monitoring has the advantage of accuracy, simplicity of measurement, and the unique characteristic of allowing for treatment of some causes

of elevated ICP via drainage of cerebrospinal fluid (CSF). The primary disadvantage is infection, which may occur in up to 20% of patients. This risk increases the longer a device is in place. A further disadvantage of intraventricular systems includes a small (~2%) risk of hemorrhage during placement, which is increased in coagulopathic patients. In addition, it may be technically difficult to place an intraventricular drain into a small ventricle, particularly in the setting of trauma and cerebral edema complicated by ventricular compression.

Step 6: Analyze ICP waveform (Figs. 31.1 and 31.2)

- ICP is not a static value; it exhibits cyclic variation based on the superimposed effects of cardiac contraction, respiration, and intracranial compliance.
- Under normal physiological conditions, the amplitude of the waveform is often small, with B waves related to respiration and smaller C waves related to the cardiac cycle.
- Pathological A waves (also called plateau waves) are abrupt, marked elevations in ICP of 50–100 mmHg, which usually last for minutes to hours.
- The presence of A waves signifies a loss of intracranial compliance and heralds imminent decompensation of autoregulatory mechanisms and needs urgent intervention to lower ICP.

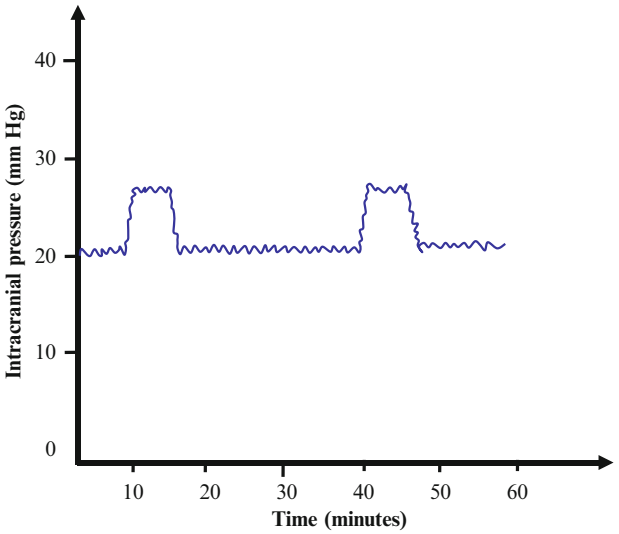

Fig. 31.1 A waves

Step 7: Start specific management of increased ICP (Fig. 31.3)

Intracranial hypertension (ICH) is a medical emergency. The best therapy for ICH is resolution of the proximate cause of elevated ICP. Examples include the evacuation of a blood clot, resection of a tumor, CSF diversion in the setting of hydrocephalus, or treatment of an underlying metabolic disorder. Measures to lower ICP

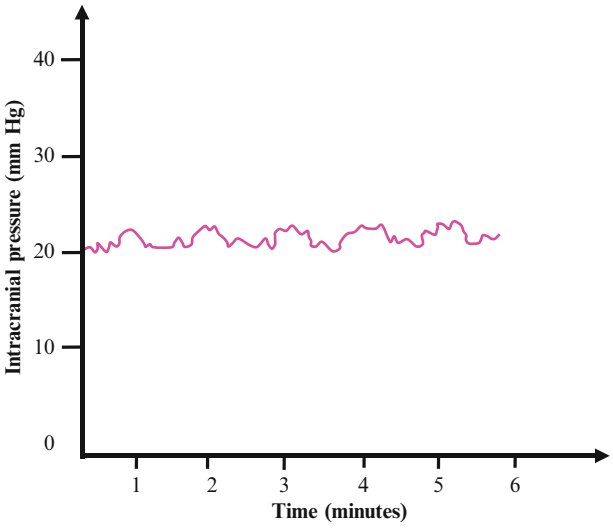

Fig. 31.2 B waves

are generally applicable to all patients with suspected ICH. Some measures (particularly glucocorticoids) are reserved for specific causes of ICH.

- *Mannitol*
  - Osmotic diuretics reduce the brain volume by drawing free water out of the tissue and into the circulation, where it is excreted by the kidneys, thus dehydrating brain parenchyma.
  - The most commonly used agent is 20% solution of mannitol given as a bolus of 1 g/kg.
  - Repeated dosing can be given at 0.25–0.5 g/kg as needed, generally every 6–8 h.
  - Use of any osmotic agent should be carefully evaluated in patients with renal and cardiac insufficiency.
  - Useful parameters to monitor in the setting of mannitol therapy include serum sodium, serum osmolality, and renal function.
  - Concerned findings associated with the use of mannitol include serum sodium of more than 150 mEq, serum osmolality of more than 320 mOsm, or rising blood, urea, and creatinine suggestive of evolving acute tubular necrosis (ATN).
  - Mannitol can lower systemic BP, necessitating careful use if associated with a fall in CPP.
  - It can cause massive diuresis and loss of potassium, magnesium, and phosphorus.
  - In patients on mannitol therapy, euvolemia should be maintained by replacing volume loss with normal saline and additive electrolytes.
  - Measuring osmolar gap (measured—calculated serum osmolality) may be useful in titrating mannitol therapy and should be kept below 18.

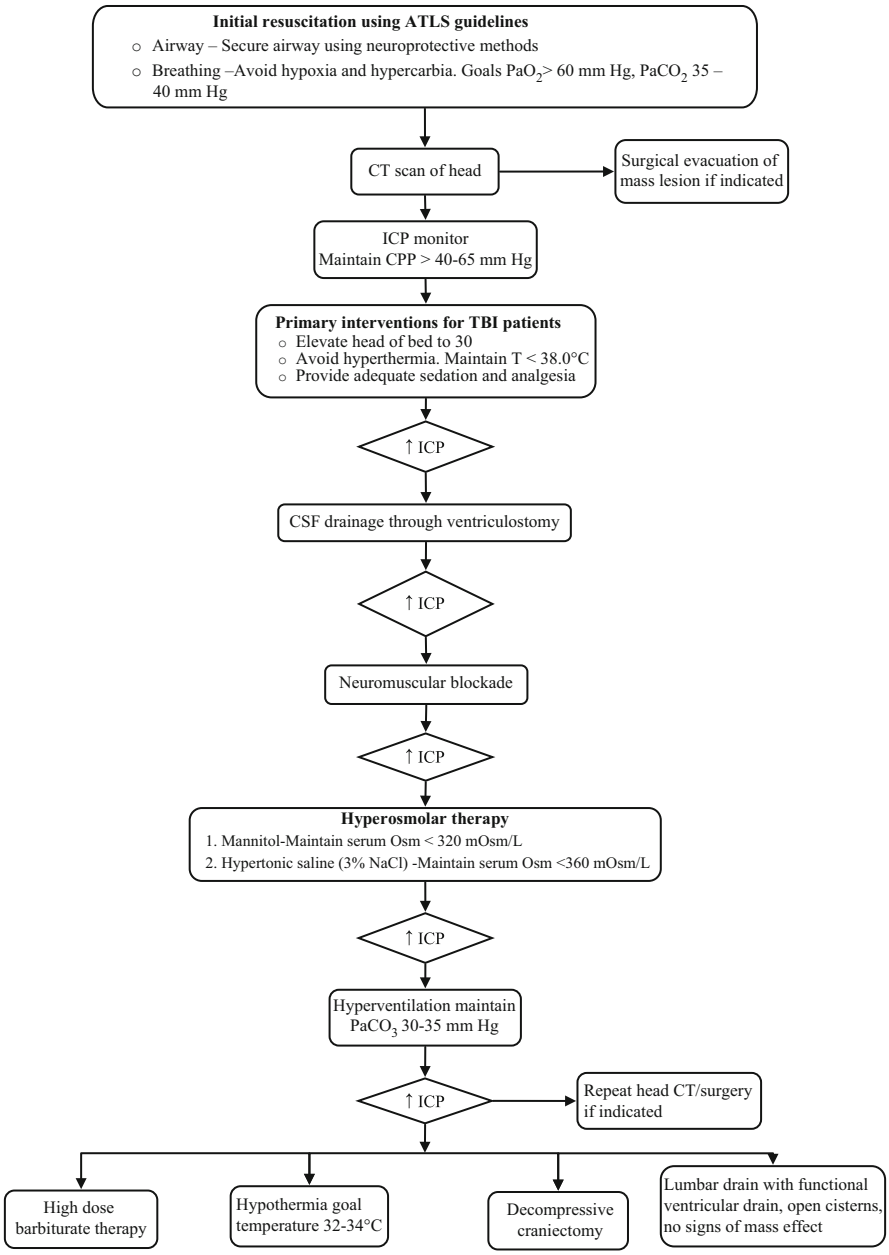

Fig. 31.3 Raised ICP Management

- *Loop diuretics*
  - Furosemide, 0.5–1.0 mg/kg intravenously, may be given with mannitol to potentiate its effect. However, this effect can also exacerbate dehydration and hypokalemia.
- *Hypertonic saline*
  - Hypertonic saline in bolus doses may acutely lower ICP.
  - Advantages of hypertonic saline are its use in hypotensive patients, reduced potential to cause renal damage, and less hyponatremia.
  - The volume and tonicity of saline (3–23.4%) used in these reports have varied widely.
  - Use of the central line is recommended for 23% saline to prevent venous thrombosis.
  - In patients without central venous access, continuous infusion of hypertonic saline (1.25–3%) may help to keep serum osmolality elevated.
  - Target the serum sodium level of 150–160 mEq/L.
  - Weaning from osmotherapy should be gentle as sharp decrease in serum sodium may cause cerebral edema. Every day, 5–8 mEq decrease in serum sodium is generally recommended.
- *Glucocorticoids*
  - In general, glucocorticoids are not considered to be useful in the management of increased ICP due to cerebral infarction or intracranial hemorrhage.
  - In contrast, glucocorticoids may have a role in the setting of intracranial hypertension caused by brain tumors and CNS infections.
- *Hyperventilation*
  - The use of mechanical ventilation to lower $PaCO_2$ to 26–30 mmHg has been shown to rapidly reduce ICP through vasoconstriction and a decrease in the volume of intracranial blood.
  - The effect of hyperventilation on ICP is short-lived (1–24 h).
  - Therapeutic hyperventilation may be considered as an urgent intervention when elevated ICP complicates cerebral edema, intracranial hemorrhage, and tumor.
  - Hyperventilation should not be used on a chronic basis, regardless of the cause of ICH.
  - Hyperventilation should be minimized in patients with traumatic brain injury or acute stroke. In these settings, vasoconstriction may cause a critical decrease in local cerebral perfusion and worsen neurological injury, particularly in the first 24–48 h.
  - This might be used as a temporizing measure for patients awaiting a definitive therapy like surgical evacuation of a cerebral clot or tumor.
- *Barbiturates*
  - The use of barbiturates is predicated on their ability to reduce brain metabolism and cerebral blood flow, thus lowering ICP and exerting a neuroprotective effect. However, the therapeutic value of this remains unclear.
  - Pentobarbital is generally used, with a loading dose of 5–20 mg/kg as a bolus, followed by 1–4 mg/kg/h.

  - Treatment should be assessed based on ICP, CPP, and the presence of unacceptable side effects.
  - Continuous electroencephalogram (EEG) monitoring is generally recommended with EEG burst suppression as an indication of maximal dosing.
- *Glycerol and urea*
  - These were used historically to control ICP via osmoregulation.
  - The use of these agents has decreased because equilibration between brain and plasma levels occurs more quickly than with mannitol.
  - Furthermore, glycerol has been shown to have a significant rebound effect and to be less effective in ICP control.
- *Therapeutic hypothermia*
  - It is not currently recommended as a standard treatment for increased intracranial pressure.
- *Neuromuscular paralysis*
  - This should generally be avoided unless the patient has refractory rise of ICP and is being closely monitored.
- *Removal of CSF*
  - When hydrocephalus is identified, a ventriculostomy should be inserted.
  - Rapid aspiration of CSF should be avoided because it may lead to obstruction of the catheter opening by brain tissue.
  - In patients with aneurysmal subarachnoid hemorrhage, abrupt lowering of the pressure differential across the aneurysm dome can precipitate recurrent hemorrhage.
  - CSF should be removed at a rate of approximately 1–2 mL/min, for 2–3 min at a time, with intervals of 2–3 min in between until a satisfactory ICP has been achieved (ICP < 20 mmHg) or until CSF is no longer easily obtained.
  - Slow removal can also be accomplished by passive gravitational drainage through the ventriculostomy, with positioning of the bag raised at the desired level of intracranial pressure.
  - A lumbar drain is generally contraindicated in the setting of high ICP due to the risk of transtentorial herniation.
- *Decompressive craniectomy*
  - Decompressive craniectomy removes the rigid confines of the bony skull, increasing the potential volume of the intracranial contents.
  - It has been demonstrated that in patients with elevated ICP, craniectomy alone lowers ICP up to 15%.
  - Opening the dura in addition to the bony skull results in an average decrease in ICP of 70%.
  - A recent study (DECRA) has shown the worse 6-month outcome with this procedure in the severe traumatic brain injury patient.

Step 8: Start general measures of management

- *Fluid management*
  - In general, patients with elevated ICP do not need to be severely fluid restricted.

  - Patients should be kept euvolemic and normo- to hyperosmolar.
  - This can be achieved by avoiding free water and employing only isotonic fluids (such as 0.9% saline).
  - Serum osmolality should be kept to more than 280 mOsm/L and often is kept in the 295–305 mOsm/L range.
- *Sedation and pain management*
  - Keeping patients appropriately sedated and pain-free can decrease ICP by reducing metabolic demand, ventilator asynchrony, venous congestion, and the sympathetic responses of hypertension and tachycardia.
  - Propofol has been utilized to good effect in this setting, as it is easily titrated and has a short half-life, thus permitting frequent neurological reassessment. Newer agents like dexmedetomidine may also be used for this purpose.
  - Fentanyl should be used cautiously as it may raise ICP.
  - Agitated patients may be sedated with short-acting benzodiazepines.
  - The use of end-tidal CO_2 should be performed frequently in sedated patients with increased ICP to maintain normocarbia. Trending upward of end-tidal CO_2 should warrant urgent attention.
- *Blood pressure control*
  - In general, BP should be sufficient to maintain CPP of more than 50 mmHg.
  - Vasopressors can be used safely without further increasing ICP. This is particularly relevant in the setting of sedation, when drug-induced hypotension can occur.
  - Hypertension should generally only be treated when CPP is more than 120 mmHg and ICP is more than 20 mmHg.
  - Labetalol and nicardipine are the ideal choice.
  - Nitrates should be avoided as they increase CBF.
- *Position*
  - Patients with elevated ICP should be positioned to maximize venous outflow from the head and are traditionally managed with the head elevated above the heart (usually 30°).
  - Important maneuvers include reducing excessive flexion or rotation of the neck, avoiding restrictive neck taping, and minimizing stimuli that could induce Valsalva responses, such as endotracheal suctioning.
- *Temperature control*
  - Fever increases brain metabolism and has been demonstrated to increase brain injury.
  - Aggressive treatment of fever, including acetaminophen and mechanical cooling, is recommended in patients with increased ICP.
- *Anticonvulsant therapy*
  - Seizures can complicate and contribute to elevated ICP.
  - Anticonvulsant therapy should be instituted if seizures are suspected.
  - Prophylactic treatment may be warranted in some cases.
  - There are no clear guidelines for prophylactic antiepileptic, but examples include high-risk mass lesions, such as those within supratentorial cortical locations, or lesions adjacent to the cortex, such as subdural hematomas or subarachnoid hemorrhage.

Suggested Reading

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7. Albanese J, Leone M, Alliez JR, et al. Decompressive craniectomy for severe traumatic brain injury: evaluation of the effects at 1 year. Crit Care Med. 2003;31(10):2535–8.
In 40 patients with intractable intracranial hypertension and at very high risk of brain death, decompressive craniectomy allowed 25% of patients to attain social rehabilitation at 1 year. In adults with severe diffuse traumatic brain injury and refractory intracranial hypertension, early bifrontotemporoparietal decompressive craniectomy decreased intracranial pressure and the length of stay in the ICU but was associated with more unfavorable outcomes.

Websites

1. www.avon.nhs.uk/bristolitutrainees
Use of barbiturates in managing increased ICP
2. www.yorkshire-cancer-net.org.uk
Managing raised ICP in pediatrics
3. www.ihrfoundation.org
Homepage for intracranial hypertension research foundation

Acute Febrile Encephalopathy

32

Jignesh Shah and Shivakumar Iyer

A 40-year-old male patient was admitted to hospital with a 2-day history of fever, headache, and increasing confusional state. On examination, he was disoriented to time and place, was opening eyes on verbal command, had an incomprehensible speech, and was moving all limbs appropriately. His neck was stiff and fundi were normal.

A high index of suspicion should be maintained for a diagnosis of an infection involving the nervous system in any patient with fever and altered mental state. Time is essence in managing these patients as any delay could lead to irreversible brain damage (Fig. 32.1).

Step 1: Initiate resuscitation and assess neurological status

- In neurological problems, assessment of airway and need for intubation is of paramount importance as these patients are at high risk of aspiration.
- Glasgow coma scale (GCS) below 8 usually requires airway protection (see Chap. 78).

Step 2: Take history and perform focused examination

- Patients presenting with fever and altered mental status can be broadly divided into three categories.
  1. Primary central nervous system infection such as meningitis, encephalitis, and brain abscess

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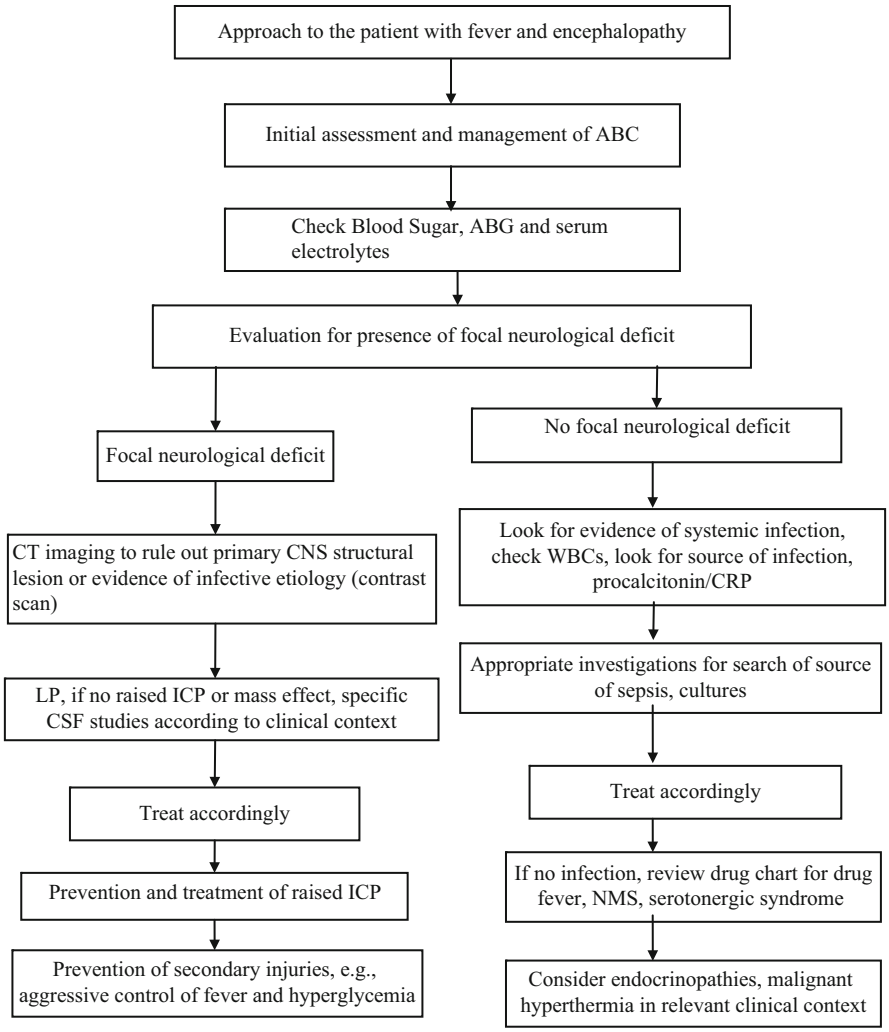

Fig. 32.1 Acute febrile encephalopathy management

2. Systemic infection with confusional state
3. Noninfectious causes of fever and encephalopathy

- History and physical examination should be carried out systematically to identify the category in which the patients belong.
  - Travel history (malaria, dengue, typhus, arbovirus infection)
  - Drug history (steroids, other immunosuppressive)
  - Trauma (splenectomy)
  - Symptoms of ENT infection
  - Neurosurgery

  - Medical history of immunosuppressive disease, tuberculosis
  - History of tuberculosis in close family members
- Neurological examination should be performed.
  - Look for papilledema, airway reflexes, focal or lateralizing neurological signs, and neck stiffness.
- Perform systemic examination to look for a source of sepsis.
- Perform general examination for skin rash, eschar, injection marks (intravenous drug abuse).

Step 3: Initiate empirical treatment (Table 32.1)

- In neurological infection, time is of essence, so empirical therapy should be started, pending investigation especially in cases of suspected meningoencephalitis.
- Correct any obvious metabolic causes.

Table 32.1 Therapy for meningoencephalitis

Herpes encephalitis	Acyclovir 10 mg/kg IV 8 hourly (adjust for renal impairment) for 2 weeks
Bacterial meningitis	
Empirical (duration of therapy 14 days)	Ceftriaxone 2 g IV twice daily plus
	Vancomycin 10–15 mg/kg IV thrice daily
	Dexamethasone 0.15 mg/kg IV thrice daily for 4 days (prior to or concurrently with antibiotics) useful mainly in pneumococcal infection
Streptococcus pneumoniae (duration of therapy 14 days)	Ceftriaxone 2 g IV twice daily or
	Ceftriaxone 2 g IV twice daily plus
	Vancomycin 10–15 mg/kg IV thrice daily (if MIC of ceftriaxone >1 mcg/mL)
Neisseria meningitidis (duration of therapy 7 days)	Ampicillin 2 g IV 4 hourly or
	Ceftriaxone 2 g IV twice daily (if MIC to penicillin >0.1 mcg/mL)
Listeria monocytogenes (duration of therapy 21 days)	Ampicillin 2 g IV 4 hourly or
	Trimeth/sulpha 5 mg/kg 8 hourly (if allergic to penicillin)
Postneurosurgery (*Gram-negative bacilli and Staphylococcus aureus*)	Carbapenem + vancomycin
Tubercular meningitis	INH 5 mg/kg (300 mg in adults)
	Rifampicin (RIF) 10 mg/kg (600 mg in adults)
	Pyrazinamide (PZA) 15–20 mg/kg (maximum 2 g)
	Ethambutol (EMB) (15–25 mg/kg)
	Streptomycin (STM) (in selected cases) 15 mg/kg/day IM (maximum 1 g)
Duration	A four-drug regimen that includes INH, RIF, PZA, and either EMB or STM for 2 months followed by INH and RIF alone if the isolate is fully susceptible, for an additional 10 months

Step 4: Send basic investigations

- General investigation workup, such as Complete blood count (CBC), blood culture, liver and renal profile, coagulation parameters, electrolyte (e.g., calcium) panel, chest X-ray, echocardiogram (to exclude vegetation), should be performed in all patients.
- Exclude systemic infection.
  - In endemic areas, look for malaria (peripheral smear and antigen), leptospira (antibody), enteric fever (blood culture, antibody), dengue (antibody), typhus (antibody), and Japanese B encephalitis (antibody in serum and CSF). These will depend on geographic location of the patient.

Step 5: Send specific investigations

- It should be done expeditiously as time is of essence in these conditions.
- Empirical treatment should be started pending the investigation to prevent further brain damage.
- Neuroimaging
  - CT scan/MRI of the brain (with contrast if not contraindicated).
  - Care should be taken to transport these patients for neuroimaging, and judicious use of sedation should be done to avoid oversedation while facilitating proper image acquisition.
  - If necessary, the patient should be intubated prior to imaging.
  - Brain abscess is characterized by ring-enhancing lesion either single (frontal sinus infection), temporal (middle ear infection), or multiple (systemic infection). Herpes encephalitis will show bitemporal involvement.
  - Decision for imaging should not delay starting the empirical therapy.
- Cerebrospinal fluid (CSF) study (see Table 32.2) (see Chap. 100)
  - CSF examination is essential to diagnose meningoencephalitis.
  - Coagulopathic state and thrombocytopenia need to be corrected prior to lumbar puncture (keep international normalized ratio [INR] <1.4 and platelet count >50,000).
  - Prior brain imaging is required in patients with papilledema, seizures, or focal neurological signs.
  - CSF should be examined immediately.
    - Cell count and type
    - Protein
    - Glucose (simultaneous blood glucose estimation is important; CSF glucose value is normally 60–70% of blood glucose)

Table 32.2 CSF analysis in untreated meningitis

CSF parameters	Bacterial	Tubercular	Viral	Fungal
White cell count	1,000–10,000	100–1,000	<300	50–200
Neutrophil (%)	>80	<10	<20	<50
Protein (mg/dL)	100–500	>250	Normal	Mild rise
Glucose (mg/dL)	<40	<10	>40	<40

- Adenosine deaminase (ADA) (if tuberculosis is suspected)
- Gram stain, culture, and sensitivity
- Acid-fast bacilli (AFB) stain
- India ink for cryptococcal infection
- DNA PCR for herpes virus
- Cryptococcal antigen
- TB PCR and BACTEC TB culture
- Pneumococcal antigen

– A sample of CSF should be preserved by the laboratory for further testing.
– Classical CSF findings may change in partially treated meningoencephalitis.

Step 6: Take isolation precaution

- Proper respiratory isolation precaution should be taken in patients with suspected bacterial meningitis (see Chap. 48).
- The patient should wear mask during transportation.

Step 7: Look for noninfectious causes of fever and neurological features

- *Structural brain lesions*
  – Intracerebral hemorrhage, pontine bleeding, and subarachnoid hemorrhage
- *Drugs and toxins*
  – Organophosphorus, atropine, tricyclic antidepressants, phenothiazines, cocaine, and amphetamines
- *Heat stroke*
  – Take history of exposure to extreme heat and exertion. Look for evidence of rhabdomyolysis.
- *Neuroleptic malignant syndrome*
  – It is caused by central dopamine antagonism.
  – Clinical features include hyperpyrexia with "lead-pipe" rigidity, extrapyramidal effects, and seizures.
  – Other effects include rhabdomyolysis, renal failure, hepatic failure, and disseminated intravascular coagulation. Metabolic acidosis and elevated transaminases are common.
  – Typical agents involved are haloperidol, chlorpromazine, promethazine, and prochlorperazine.
  – A few atypical agents such as risperidone, olanzapine, and quetiapine are also responsible.
  – Onset of symptoms is usually days to weeks after the inciting agent is started.
  – Management includes withdrawal of inciting agents, cooling, dantrolene, and bromocriptine.
- *Serotonergic syndrome*
  – It occurs within minutes to hours of initiating an offending agent.
  – Symptoms are hyperreflexia, myoclonus, and hyperthermia.
  – Inciting agents are selective serotonin receptor uptake inhibitors (SSRIs), tricyclic antidepressants, and trazodone.

- *Malignant hyperthermia (MH)*
  - MH is a specific inherited muscle membrane disorder.
  - It causes a dangerous hypermetabolic state after anesthesia with suxamethonium and/or volatile halogenated anesthetic agents.
  - Dantrolene sodium is a specific antidote and induces flaccidity of muscle due to inhibition of excitation–contraction coupling in skeletal muscle.
- *Endocrine abnormalities*
  - Thyrotoxic crisis

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   A practical review of managing CNS infections.
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3. Ziai WC, Lewin JJ III. Update in the diagnosis and management of central nervous system infections. Neurol Clin. 2008;26(2):427–68.
   This review focuses on early aggressive management of common infections of the central nervous system that require monitoring in an ICU setting.
4. Zunt JR, Marra CM. Cerebrospinal fluid testing for the diagnosis of central nervous system infection. Neurol Clin. 1999;17(4):675–89.
   This article discusses how these CSF tests are performed and addresses the sensitivity and specificity of such tests for the diagnosis of selected CNS infections.

Sedation and Analgesia

33

Ashwin Kumar Mani, Nagarajan Ramakrishnan, and Sheila Nainan Myatra

A 48-year-old male patient was admitted to the ICU with acute respiratory distress syndrome secondary to H1N1 influenza. He was noted to be markedly hypoxemic requiring high FiO_2. He was intubated and put on a ventilator. He was tachypneic, tachycardic, and restless and was breathing at the rate of 40 per min and struggling with the ventilator.

Critically ill patients on mechanical ventilation are frequently managed with sedative and analgesics. Pain is a very common experience in the ICU. Failure to recognize pain leads to agitation and increase use of sedatives. Majority of patients find even routine ICU procedures uncomfortable and painful. Inability to communicate about pain due to presence of an endotracheal tube may lead to high levels of anxiety and may precipitate development of posttraumatic stress disorder. Now it is recommended to aggressively manage pain.

Step 1: Identify the need for sedation and analgesia (Table 33.1)

- Appropriate analgesia might obviate the need for sedation or decrease the sedation needs.
- In certain groups of patients, sedation is very important to prevent them from self-harm (removing lines) or to decrease the work of breathing and oxygen demand.
- Common indications of analgesia and sedation (Table 33.1).

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Table 33.1 Indications of sedation and analgesia

Facilitation of endotracheal intubation and mechanical ventilation (for amnesia, anxiolysis, reduction of agitation, toleration of endotracheal tube (ETT) and to reduce cough, to alleviate dyspnea, to minimize pain, and to prevent self-extubation)
While performing invasive procedures
To facilitate nursing care
Postoperative/trauma pain
To tolerate ICU environmental influences (stressful environment, monitoring devices, noise, fear of illness, separation from family)
During severe hypoxemia (low tidal volume ventilation, high-frequency oscillation (HFO), and prone positioning)
To bear underlying or hospital-acquired medical illnesses

Step 2: Consider the use of commonly used sedatives and analgesics (Table 33.2)

Step 3: Choose an appropriate agent

- There is no ideal agent for ICU sedation.
- An ideal sedative and analgesic regimen should provide adequate sedation and pain control, rapid onset of action, and allow rapid recovery after discontinuation, minimal adverse effects, minimal systemic accumulation, and minimal delirium without increasing overall health-care costs.
- In different clinical scenarios, some agents have been shown to be better than others. Consider the following before choosing an agent:
  - All patients need analgesia with or without sedation. Recent studies have shown that minimal use of continuous sedation is feasible without apparent adverse effects.
  - Have a patient-focused approach. Select analgesic and sedative drugs based on patients' needs.
- Remember that the degree of sedation/anxiolysis and analgesia required varies between patients and in the same patient over time (physiotherapy, weaning).
- Identify predisposing and precipitating factors—underlying medical conditions such as chronic pain or arthritis, history of alcohol, or substance abuse. Psychiatric illness can influence medication. For example, patients who appear delirious or severely agitated in the ICU may become overmedicated with sedative drugs because their medications have been omitted.
- Adequate analgesia should be ensured prior to sedating the patient.
- In a nonintubated patient agitated due to pain, when opioid analgesics such as morphine or fentanyl are used, remember that they can cause respiratory depression. In patients with obstructive sleep apnea, even small doses should be used with caution.
- For postoperative pain/trauma, epidural analgesia, if available, is a suitable option.
- Gamma-aminobutyric acid agonists (benzodiazepines, propofol) are prone to cause acute cognitive dysfunction.

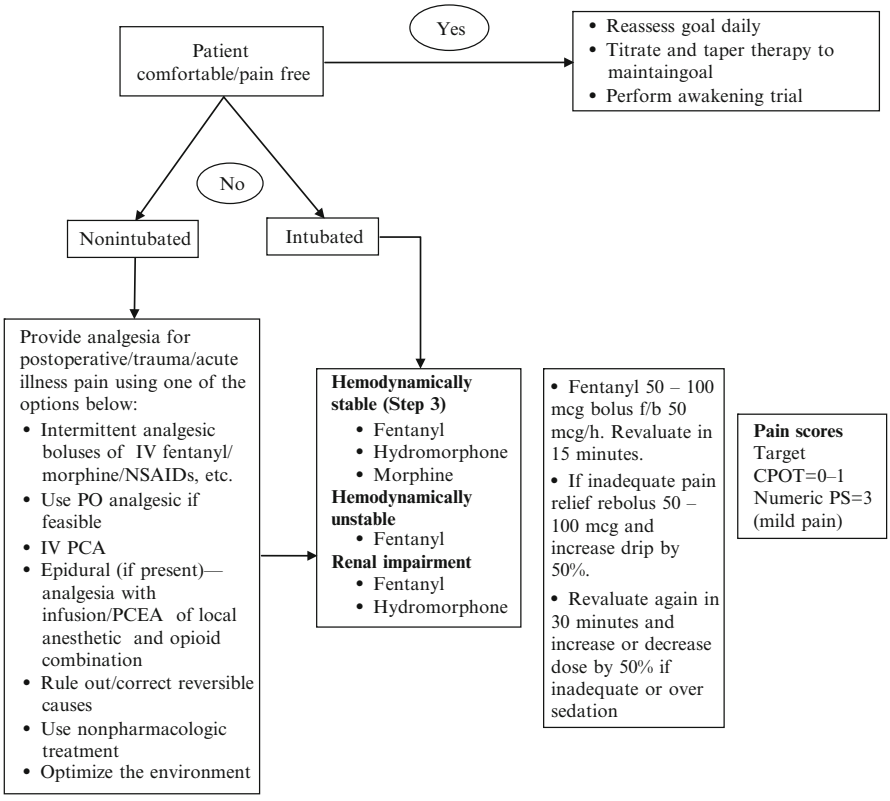
Table 33.2 Drug details for sedation and analgesia

Drug	Time to onset (min)	Duration of effect of one dose (h)	Presence of active metabolites	Accumulation in renal failure	Dose (IV)	Comments
Fentanyl	1–2	2–4	No	No	B+ = 50–100 mcg	Reduces tachypnea
						Respiratory depression
					I+ = 0.7–10 mcg/kg/hr	Accumulation in hepatic/renal failure
Morphine	5–10	2–4	Yes	Yes	B = 1–10 mg	Same as other opioids
					I = 2–10 mg/h	
Remifentanil	1–2	10–20 mt	No	No	B = 1 mcg/kg	Decreased heart rate and blood pressure
					I = 0.25–1.0 mcg/kg/min	Increased intracranial pressure
Hydromorphone	5–10	2–4	Yes	Yes	B = 0.2–0.6 mg	May work in patients tolerant to morphine and fentanyl, respiratory depression
					I = 0.5–3 mg/h	Highly addictive
Lorazepam	5–20	6–8	No	Yes	B = 2–4 mg	Propylene glycol toxicity (anion gap metabolic acidosis, renal insufficiency)
					2–6 mg q4 to q6 (duration too long for effective infusions)	Independent risk factor for delirium
Midazolam	2–10	1–4	Yes	Yes	B = 2–5 mg	Many drug interactions
					I = 1–20 mg/h	May increase midazolam levels
Propofol	30–50 s	3–10 (dose dependent)	No	Insignificant	B = 0.2–2	Hypotension
					mg/kg (maximum 20 mg)	Increased serum triglyceride
					I = 10–150 mcg/kg/min	Propofol infusion syndrome (>5 mg/kg/h for more than 48 h)
Dexmedetomidine	30	4	No	No	B = 1 μg/kg (should be given over 15–20 min)	Sedative, anxiolysis, with analgesic property (reduces opioid requirement by >50%)
					I = 0.2–0.7 μg/kg/h	Notable adverse event is bradycardia

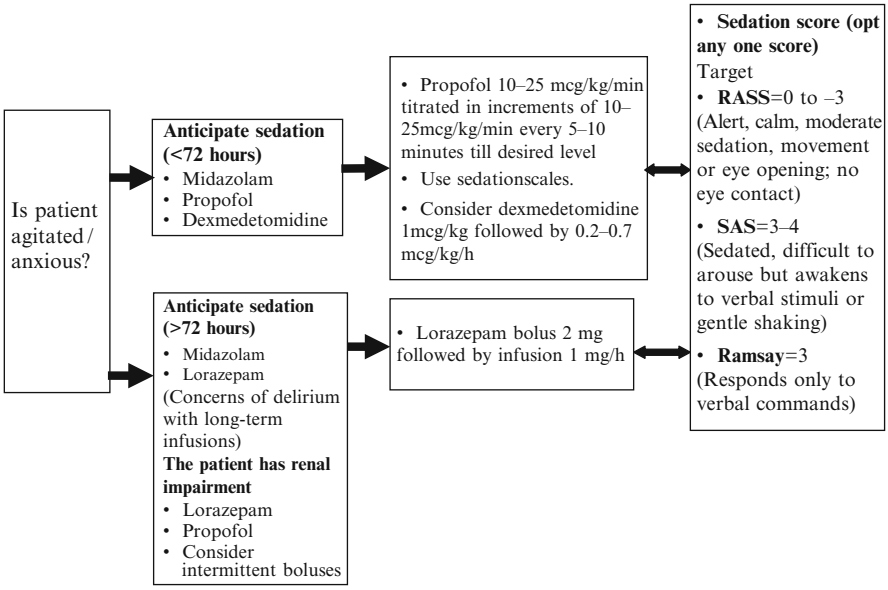
B+ bolus dose, I+ infusion dose

- Lorazepam is an independent risk factor for transitioning to delirium.
- Sedation with dexmedetomidine causes less delirium than with midazolam or propofol.
- Analgosedation or co-sedation—often analgesic medications are added to a sedative infusion (e.g., midazolam and fentanyl) with reduced doses of both agents and in some cases more effective therapy.

Pain (Refer Table 33.3)



Sedation (Refer Table 33.4, 33.5, 33.6)



Delirium

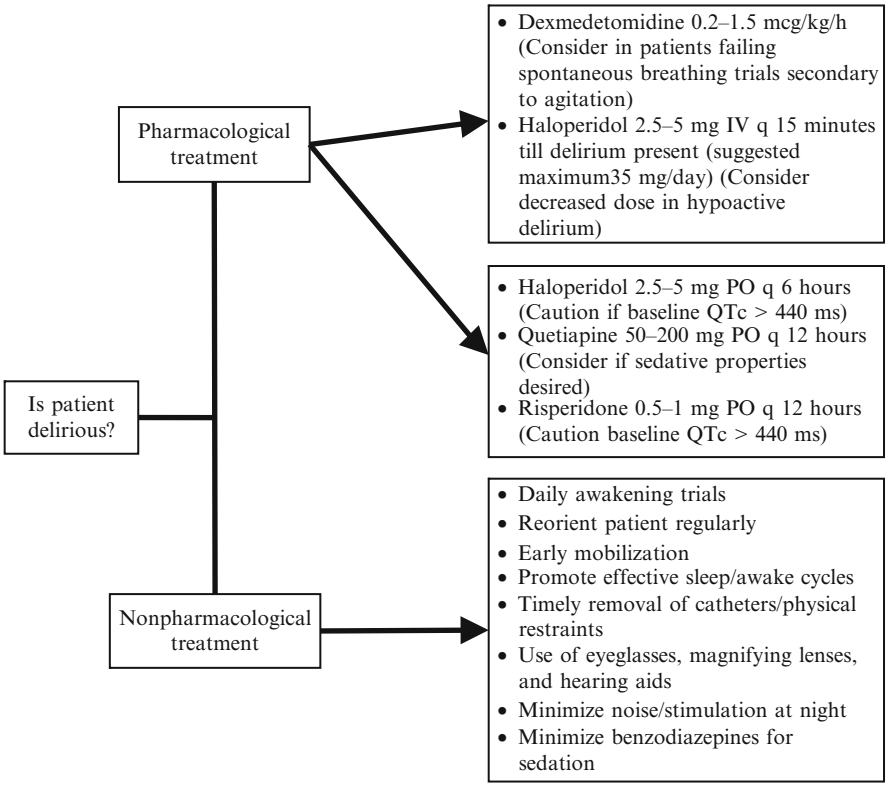


Table 33.3 The critical care pain observation tool (CPOT) (target 0 to 1)

Facial expression	Tense	1
	Grimacing	2
Body movements	Absence of movement or normal position	0
	Protection	1
	Restlessness	2
Compliance with ventilator (intubated patients)	Tolerating the ventilator or movement	0
	Coughing but tolerating	1
	Fighting the ventilator	2
Vocalization (extubated patients)	Talking in normal tone or no sound	0
	Sighing or moaning	1
	Crying out, sobbing	2
Muscle tension	Relaxed	0
	Tense, rigid	1
	Very tense or rigid	2

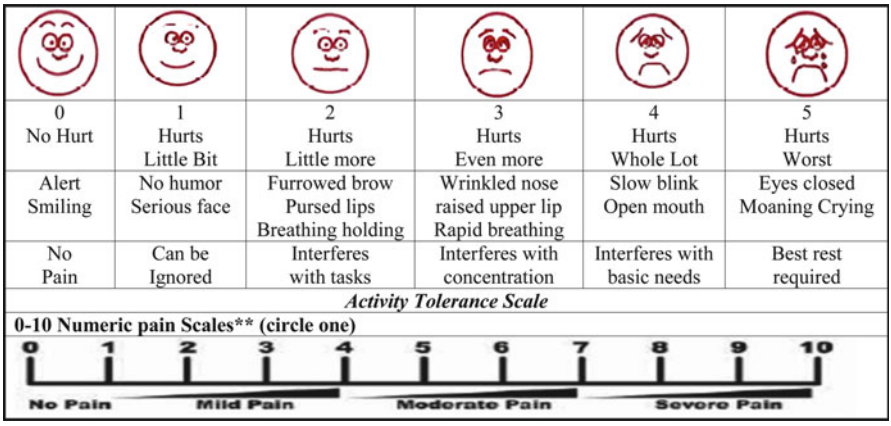


Fig. 33.1 Wong-Baker FACES pain rating scale

Step 4: Assessment of pain, sedation, and delirium

- Use of sedation and pain scales is recommended to titrate the appropriate level of analgesia and sedation.
- There are many scores, but one score should be followed for uniformity in the ICU.
- The following scales/scores may be used:
  A. *Pain*
    - A critical care pain observation tool (Table 33.3)
    - Self-reporting of pain
    - Wong-Baker FACES pain rating scale (Fig. 33.1)
    - 0–10 numeric pain scales

Table 33.4 Richmond agitation-sedation scale (RASS) (target 0 to −3)

Combative, violent, danger to staff	+4
Pulls or removes tubes or catheters, aggressive	+3
Frequent nonpurposeful movement, fights the ventilator	+2
Anxious, apprehensive, but not aggressive	+1
Alert and calm	0
Awakens to voice (eye opening/contact) >10 s	−1
Light sedation, briefly awakens to voice (eye opening/contact) <10 s	−2
Moderate sedation, movement or eye opening (no eye contact)	−3
Deep sedation, no response to voice, but movement or eye opening to physical stimulation	−4
Unarousable, no response to voice or physical stimulation	−5

Table 33.5 Riker sedation-agitation scale (SAS) (target sedation 3 to 4)

Dangerous agitation, pulling the ETT, trying to remove catheters, climbing over bedrail, striking at staff, thrashing side to side	7
Very agitated, requiring restraint and frequent verbal reminding of limits, biting the ETT	6
Agitated, anxious or physically agitated, calms to verbal instructions	5
Calm and cooperative easily arousable, follows commands	4
Sedated, difficult to arouse but awakens to verbal stimuli or gentle shaking, follows simple commands but drifts off again	3
Very sedated, arouses to physical stimuli but does not communicate or follow commands, may move spontaneously	2
Unarousable, minimal or no response to noxious stimuli, does not communicate or follow commands	1

Table 33.6 Ramsay sedation score (target sedation 3)

Level/score	Clinical description
1	Anxious and agitated
2	Cooperative, oriented, tranquil
3	Responds only to verbal commands
4	Asleep with brisk response to light stimulation
5	Asleep with sluggish response to stimulation
6	Asleep without response to stimulation

B. *Sedation*
- Richmond agitation-sedation scale (RASS) (Table 33.4)
- Riker sedation-agitation scale (SAS) (Table 33.5)
- Ramsay sedation score (Table 33.6)

C. *Delirium*
- Confusion assessment method for the ICU
- The intensive care delirium screening checklist

Step 5: Titrate sedation and analgesia

The titration of the sedative/analgesic dose to a defined endpoint is recommended.

Titrating infusions

Analgesia

The potential for opioid withdrawal should be considered for patients receiving high doses or 7 days of continuous therapy. Doses should be tapered systematically (i.e., 10–30% per day) to prevent withdrawal symptoms.

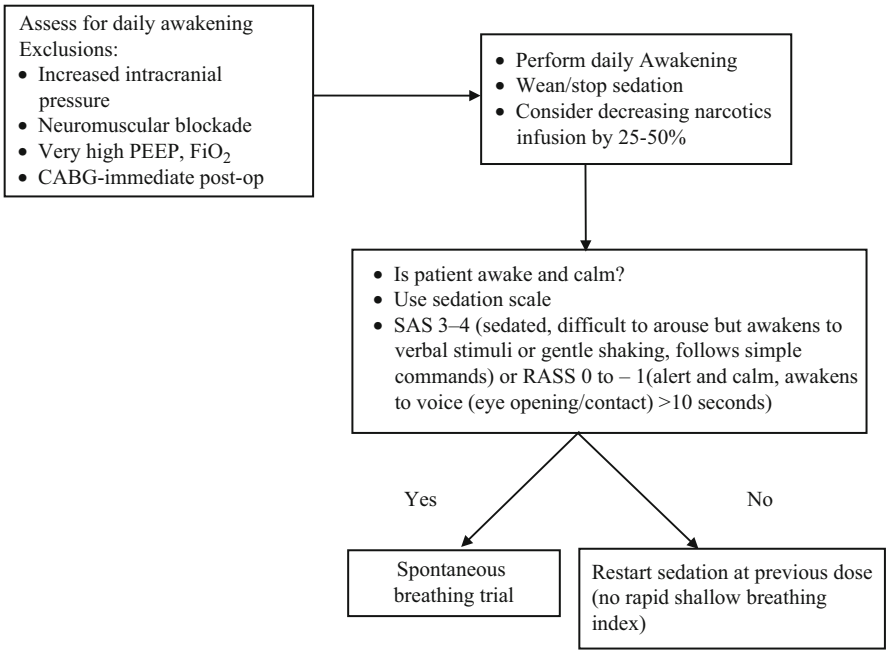
Sedation

Use RASS/SAS/Ramsay scores to evaluate. Titrate according to the target table.

- Lorazepam/midazolam continuous infusion: Hold infusion until the patient reaches RASS goal, and then resume at one-half the previous rate. Titrate as per written orders.
- Propofol continuous infusion: Decrease at the rate of 5–10 mcg/kg/min every 10 min until the patient reaches RASS goal. Titrate as per written orders.
- Morphine/fentanyl continuous infusion: Hold until the patient reaches RASS goal, and then resume at one-half the previous rate. Titrate as per written orders.

Step 6: Daily awakening trial

- Daily awakening trial is required to assess sedation and minimum effective dose for sedation.
- It is recommended to couple spontaneous breathing trial (SBT) protocols with sedation protocols. Findings show that combined approach of spontaneous breathing trial and daily awakening results in less time on mechanical ventilation and less intensive care and the hospital stay.
- Early exercise and mobilization (physical and occupational therapy) during periods of daily interruption of sedation has been shown to be safe and well tolerated and results in better functional outcomes at hospital discharge, a shorter duration of delirium, and more ventilator-free days compared with standard care.



Step 7: Weaning from sedation and analgesia
Once the patient passes the SBT successfully, then converting the continuous infusion of the sedatives and analgesics into intermittent boluses is an effective option for early weaning.

Step 8: Reversal of oversedation
Excessive sedation involving benzodiazepines

Flumazenil
Dose—0.2 mg (2 mL) IV over 30 s. Wait 30 s and reassess. You may give additional 0.3 mg over 30 s, if needed, and reassess. Additional doses of 0.5 mg can be administered over 30 s at 1-min intervals as needed. Maximum cumulative dose is 3 mg.

Opioid reversal
Naloxone
Dose—0.1–2 mg IM/IV/SC. Titrate to patients' response. It may be repeated at the interval of 2–3 min. Maximum dose is 10 mg.

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The use of propofol sedation allowed more rapid tracheal extubation than when midazolam sedation was employed. This did not result in earlier ICU discharge.

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   Sedation scales
3. www.consensus-conference.org/data/Upload/Consensus/1/pdf/1641.pdf
   A full text article on analgesia and sedation in mechanically ventilated patients
4. www.icudelirium.org
   A website of Vanderbilt University for update and practice parameters on ICU sedation

Brain Death

34

Babu K. Abraham and Nagarajan Ramakrishnan

A 25-year-old male motorbike rider was brought to the intensive care unit (ICU) following a head-on collision with a car while traveling on a motorway. On arrival, he was found to have blood oozing out of his external auditory meatus and nostrils. Neurological assessment revealed Glasgow coma scale (GCS) of 2T, pupils equal, 3 mm bilaterally, and not reacting to light. Family and colleagues questioned whether he was "brain dead."

The role of the ICU physician in these situations is to proceed systematically and according to the institutional protocol to diagnose and confirm brain death, counsel family, and support the patient for potential organ donation if indicated.

Step 1: Establish the underlying cause

- The potential cause may be obvious in some cases.
- This may not be clear in every situation, and if there is any doubt about the cause, be cautious in diagnosing brain death.
- Investigations such as brain imaging (CT scan and MRI) and cerebrospinal fluid (CSF) analysis may be useful in evaluation of etiology but is not confirmative of brain death.
- A search for confounders (see below) should be made systematically.

Step 2: Look for confounders before proceeding for brain death verification

- Complicating medical conditions that may mimic brainstem dysfunction (severe electrolyte abnormalities, hypoglycemia, and acid–base abnormalities).
- Severe hypothermia (core temperature of ≤32°C).

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- Severe hypotension (systolic blood pressure <100 mmHg).
- Any evidence of drug intoxication including alcohol, poisoning, or recent use of sedation or neuromuscular blocking agents.
- If any of the confounders are present, they need to be corrected, and in case of suspected poisoning, an extended observation period is needed before proceeding to further test.
- In circumstances, where these cannot be done, confirmatory test (see below) for brain death is needed.

Step 3: Identify brain death by complete neurological examination

This consists of three essential documentations:

1. *Documentation of coma*
   - Absence of motor response to a standardized painful stimulus (pressing on supraorbital nerve, temporomandibular joints, or nail bed of a finger).
   - Beware of local spinal reflexes causing spontaneous or stimulus-related motor movements.
2. *Documentation of the absence of brainstem reflexes*
   - As brain death occurs, reflexes are lost in a rostral-to-caudal direction with the reflexes in medulla oblongata being the last to cease.
   - Absent pupillary reflex—the pupils will be round or oval, with midposition dilatation (4–9 mm) and no reaction to bright light.
   - Oculocephalic movements (doll's eye reflex) will be absent. Ensure integrity of the cervical spine. This test should be done by rapid turning of the head horizontally and vertically and looking for eye movements. There should be no movement of the eyes to the opposite side in brainstem dysfunction. This test may be difficult to interpret at times.
   - Oculovestibular reflex—cold calorie test will show the absence of provoked tonic eye movement toward the side of cold stimulus. This test is performed by irrigating the tympanum with 50 mL ice-cold water with the head tilted to 30°. Presence of clotted blood or cerumen in the external auditory canal can diminish this response even in the absence of brain death.
   - Corneal reflex will be absent. This is checked by instilling a few drops of sterile saline over cornea.
   - Cough reflex will be absent. This is best tested by passing a suction catheter through the endotracheal tube.
3. *Documentation of apnea (apnea test)*
   - This test is carried out only after documenting the absence of brainstem reflexes and is performed to stimulate the respiratory center, which is in the medulla oblongata.
   - The patient is first preoxygenated with 100% oxygen for 15 min, and an arterial blood gas analysis (ABG) is obtained.
   - The patient is then disconnected from mechanical ventilation and continued to oxygenate through a catheter placed in the trachea with oxygen flow at 6–10 L/min. Alternatives include using a T-piece system with oxygen flow at

12 L/min or using continuous positive airway pressure (CPAP) at 10 cm H_2O with FiO_2 titrated to keep oxygen saturation above 95%.
- $PaCO_2$ is allowed to climb (usually at a rate of 3 mmHg/min). The threshold for maximal stimulation of the respiratory center is thought to be $PaCO_2$ of 60 mmHg or a $PaCO_2$ of 20 mmHg above the normal baseline value.
- ABG is repeated within about 8–10 min of disconnection from the mechanical ventilation, and the increase in the $PaCO_2$ is documented.
- Visual observation is the standard method for detecting respiratory movement. About 8–10 min with no observable respiratory effort is a standard observation period. During this period of observation, if the subject does not have spontaneous respiration and arterial PCO_2 is 60 mmHg (or 20 mmHg increase over the baseline arterial PCO_2), the apnea test result is positive (i.e., supports the clinical diagnosis of brain death).
- This test should not be performed or should be terminated if the patient becomes hemodynamically unstable or hypoxemic.
- If the test is inconclusive but the patient is hemodynamically stable during the procedure, it may be repeated for a longer period (10–15 min) after the patient is again adequately preoxygenated.

Step 4: Perform confirmatory tests

These tests are optional in adults but recommended in children younger than 1 year. In certain countries, these tests are required by law to confirm brain death:
- *Cerebral angiography (conventional or CT)*
  - Angiography of both the anterior and posterior circulations has to be carried out. The absence of contrast flow into the intracerebral portions of the carotid and vertebral arteries at the level of their entry into the skull is taken as a sign of brain death.
  - External carotid circulation should be patent.
  - Delayed filling of the superior longitudinal sinus may be seen.
  - Limitation of the test is the need for transporting the patient.
- *Electroencephalography (EEG)*
  - A complete absence of electroencephalographic activity to intense somatosensory and audiovisual stimulation is taken as a sign of brain death.
  - It is important to ensure that EEG recordings are done in a standardized manner.
  - Limitations are presence of artifacts leading to an EEG pattern for false-negative brain death diagnosis.
- *Transcranial Doppler (TCD) ultrasound*
  - The TCD abnormalities that indicate brain death are a lack of diastolic or reverberating flow and the documentation of small systolic peaks in early systole.
  - Complete absence of flow in the TCD may not be reliable owing to inadequate transtemporal windows.
  - Limitation is the need for expertise and appropriate interpretation of the flow pattern.

- *Cerebral scintigraphy*
  - Demonstration of absent cerebral blood flow using radiolabeled (99mTc-labeled) hexamethylpropyleneamine oxime (HMPAO), followed by single photon emission computerized tomography (SPECT) scanning, provides a confirmatory test in the diagnosis of brain death.
  - The absence of isotope uptake ("hollow skull phenomenon") indicates no brain perfusion and supports the diagnosis of brain death.
  - Limitation is lack of availability and need for transportation.

Step 5: Follow institutional protocol for certifying brain death (Fig. 34.1)

- Institutes should have a predefined protocol as regards to certifying authority and frequency of examination.
- Most places would mandate two sets of brain death examinations, the second typically done a minimum of 6 h after the first, to declare brain death in adults.
- In neonates and pediatrics, this period of observation is usually longer varying from 12 to 48 h.
- There is no consensus about how long a patient needs to be observed before being certain that the brain functions have ceased irreversibly.

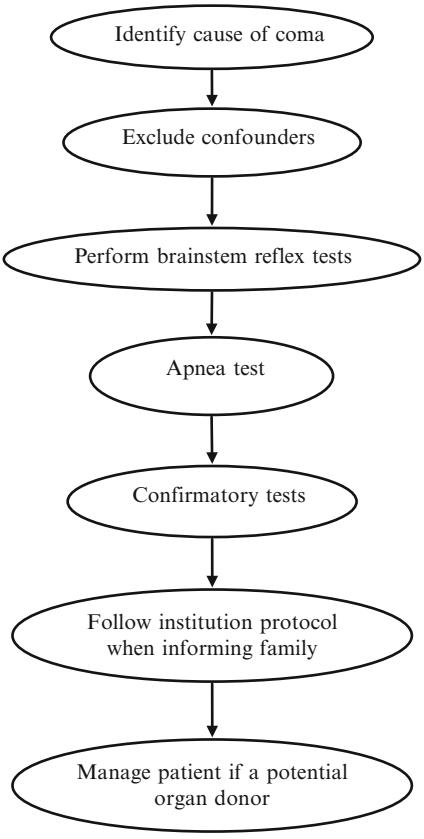

Fig. 34.1 Brain death management

Step 6: Inform the family

- As soon as it is suspected that the patient is nearing brain death, the clinician should keep family members informed of the clinical status of the patient and maintain the patient in a hemodynamically stable state if he/she is a potential organ donor.
- As declaring brain death is a sensitive issue, the senior member of the team, ideally the primary consultant, should inform the next of kin after the clinical criteria for brain death have been confirmed.
- He or she then can be approached for organ donation as per the regulations of the state law.
- If the next of kin declines to donate organs, then it is good medical judgment to discontinue the mechanical ventilation (Fig. 34.1).

Steps in Managing a Brain-Dead Patient

Step 1: Monitor and manage hemodynamics

- Adequate monitoring is essential for managing a potential organ donor.
- If not already placed, an arterial line, a central venous line, and a urinary catheter will be useful.
- These will help in assessing resuscitation and monitoring the hemodynamic status closely.
- Adequate volume status should be maintained.

Step 2: Replace hormones

- Brain death is associated with a panhypopituitary state that can lead to refractory hypotension. Hormone replacement therapy not only helps in correcting this but also decreases cardiovascular instability and improves organ protection and graft function.
- The common hormones replaced are the following:
- Levothyroxine
  - Thyroxine (T4) is initially given at 20 mcg IV bolus. T4 has been shown to be more beneficial than using T3.
  - Bolus administration of T4 can cause hyperkalemia, and it is advisable to administer 10 units of regular insulin and 50 mL of 50% dextrose prior to bolus administration of T4, unless the serum glucose is greater than 300 mg/dL.
  - If intravenous preparation is not available, thyroxine needs to be replaced enterally.
- Methylprednisolone
  - Methylprednisolone is given as 15 mg/kg IV bolus and repeated on a daily basis.
  - This has been shown to improve the potential for lung donation.
- Insulin
  - The aim should be to maintain the blood glucose level below 140 mg/dL. Insulin is initiated at the rate of 1 unit/h IV infusion, and the infusion rate is adjusted appropriately to achieve this target.
  - Frequent blood glucose analysis (hourly) may be required to maintain the target.

- Vasopressin
  - Diabetes insipidus (DI) should be suspected in a brain-dead patient when urine output is greater than 5 mL/kg/h for two consecutive hours, and this can be associated with hemodynamic instability.
  - If urine-specific gravity is less than 1.005, urine osmolality is less than 200 mOsm/kg, serum osmolality is more than 300 mOsm/kg, and serum sodium is more than 145 mEq/L, a diagnosis of DI can be confirmed.
  - Once the diagnosis of DI is confirmed, vasopressin needs to be started.
  - Therapy is usually initiated with an infusion of vasopressin at 0.5 unit/h and titrated to a maximum of 6 units/h with an aim of bringing urine output down to 0.5–3 mL/kg/h and serum sodium to 135–145 mEq/L.
  - Caution—serum sodium values should be checked every 6 h to assist with titration. Side effects of vasopressin include hyponatremia, digital vasoconstriction, and thrombosis.
  - Desmopressin (DDAVP) can be an alternative choice. It is usually given at a dose of 1–4 mcg IV followed by 1–2 mcg IV every 6 h until the above-mentioned targets are met. However, its drawbacks are that it is more difficult to titrate and does not provide significant hemodynamic support.
- There is still no clear consensus about when to initiate hormonal replacement therapy. Some prefer to initiate methylprednisolone and insulin components of hormonal replacement therapy soon after the first brain death declaration, while levothyroxine and/or vasopressin are initiated only if the patient becomes hypotensive or has diabetes insipidus. Others start all hormones simultaneously as soon as brain death is declared, even if they are hemodynamically stable.

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Websites

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2. www.thamburaj.com/brain_death.htm
   Neurosurgeons insight into brain death criteria.
3. www.neurologyindia.com
   An archive of leading articles on brain death.

Part IV

Gastrointestinal System

Ajay Kumar and Pravin Amin

Upper Gastrointestinal Bleeding

35

Rupa Banerjee and Duvvur Nageshwar Reddy

A 46-year-old male patient was brought to hospital having several episodes of vomiting of bright red blood. He had no medical history, but he had a decade-long history of excess alcohol intake, consuming 60–70 units a week.

He was pale, sweaty, and restless with a marked tremor. His pulse was 110 beats/min and blood pressure was 90/50 mmHg. He was not jaundiced, but his abdomen was distended with shifting dullness in the flanks. The liver could not be palpated, but the spleen was palpable 5 cm below the costal margin. His hemoglobin was 8.5 g/L, with platelets 45×10^9/L, bilirubin 2.5 mg/L, and creatinine 1.2.

Upper gastrointestinal (UGI) bleeding originates proximal to the ligament of Treitz, from the esophagus, stomach, and duodenum. Acute UGI bleeding is a common medical emergency, which carries a significant mortality risk. Initial triage, assessment, and prompt action can save lives.

Step 1: Initiate resusc itation and assessment of hemodynamic stability

- The first step in the management of such a patient is initial clinical assessment of the hemodynamic instability and the requirement for immediate resuscitation. Initial resuscitation is done as mentioned in Chap. 78.
- Patients who present with hemodynamic instability and significant hematemesis will have resting tachycardia (pulse ≥100 per min), hypotension (systolic blood

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Table 35.1 Clinical features of significant upper GI bleeding

• Shock
• Orthostatic hypotension
• Profuse active bleeding
• Decrease in HCT ≥10%
• Anticipated transfusion >2 units of RBCs

pressure <100 mmHg), or postural changes (increase in the pulse of ≥20 beats/min or a drop in systolic blood pressure of ≥20 mmHg on standing) (Table 35.1).

- In patients with exsanguinating bleeding or the patient who is delirious, airway should be protected by elective intubation. In conscious patients, give oxygen by nasal cannula.
- Two large-bore intravenous channels should be placed at the earliest.
- Fluid resuscitation should be started with Ringer's lactate or normal saline. Crystalloid or colloid solutions may be used for treating hypotension aiming a systolic blood pressure of more than 100 mmHg.
- Do typing and crossmatching of blood. Target hemoglobin usually around 7–8 g% for otherwise healthy individuals without active bleeding. A target hemoglobin concentration of about 9 g% would be appropriate in patients older than 65 years or those with cardiovascular disease.
- The patient should be kept nil orally. This is necessary because an urgent endoscopy or even intubation may be needed in the event of a repeat bleeding.
- Stop factors that enhance bleeding—anticoagulants (warfarin, heparin) and antiplatelet agents (aspirin, clopidogrel).

Step 2: Find etiology and stratify risk

- The severity of presenting symptoms, current medications, and history are instrumental in establishing the etiology of UGI bleeding.
- The history of use of aspirin and nonsteroidal anti-inflammatory drugs (NSAIDs) suggests a bleeding ulcer. The history of prolonged alcohol intake and the stigmata of chronic liver disease including jaundice and ascites would indicate a possible variceal hemorrhage.
- Hematemesis that follows prolonged vomiting or retching may be suggestive of a Mallory–Weiss tear. Bright red blood vomit in large amounts is usually suggestive of severe hemorrhage from an arterial or variceal source.
- The presence of the characteristic coffee-ground vomitus implies that bleeding has ceased or has been relatively modest.
- The common causes of UGI bleeding are shown in Table 35.2. Patients are usually stratified into variceal or nonvariceal hemorrhage as the treatment algorithms and prognosis differ accordingly.
- Majority (~80%) of acute episodes of UGI bleeding have been attributed to peptic ulcer disease.
- Peptic ulcer bleeding is predominant in the elderly, with 70% of patients older than 60 years.
- Majority of episodes are related to the use of aspirin and nonsteroidal anti-inflammatory drugs.

Table 35.2 Common causes of UGI hemorrhage

• Peptic ulcer disease
• Gastric erosions and ulcers (drug induced)
• Esophageal or gastric varices (variceal bleeding)
• Esophageal ulcers/esophagitis
• Mallory–Weiss tear
• Malignancy
• Angiodysplasia and vascular malformations

Table 35.3 Factors associated with a poor outcome in UGI bleeding

1.	Age	Mortality increases with age among all age groups
2.	Comorbidity	No comorbidity: low mortality; any comorbidity doubles risk
3.	Liver disease	Cirrhosis increases mortality rate; mortality due to variceal bleeding up to 14%
4.	Initial shock	Increased mortality and need for intervention
5.	Continued bleeding	Postadmission continued bleeding: ↑ intervention, almost 5 times ↑ mortality
6.	Hematemesis	Presence of initial hematemesis doubles mortality
7.	High urea	Poor outcome; increased need for intervention

NSAIDs and anticoagulants do not adversely affect clinical outcome of UGI bleeding

- The annual incidence of bleeding from peptic ulcer has shown a decline, but the mortality rate remains high at approximately 6–8%.
- Variceal bleeding is related directly to portal hypertension, and cirrhosis is the commonest etiology. The mortality rate for variceal bleeding is high at 30–40%, with a 70% risk of rebleeding in a year.

Risk stratification

- Patients with hematemesis need to be stratified according to the risk of poor outcome including uncontrolled bleeding, rebleeding, need for intervention, and mortality.
- These factors should be taken into account when determining the need for ICU admission or suitability for discharge.

  The factors associated with a poor outcome are shown in Table 35.3.

Simple and widely validated scoring systems are needed to identify patients at high risk of rebleeding, death, and active intervention for optimum management. Modified Glasgow–Blatchford bleeding score and the Rockall score are the two common scores used for risk stratification. Modified Glasgow–Blatchford bleeding score is a good tool, and it helps to decide the need for endoscopy.

- The Rockall score is the sum of each component, calculated before and after endoscopy (Table 35.4). This predicts rates of rebleeding and mortality and can be used in management algorithms.
- The full Rockall score comprises the initial score as well as additional points for endoscopic diagnosis (0–2 points), and endoscopic stigmata of recent hemorrhage (0–2 points) giving a maximum score of 11 points.

Table 35.4 The Rockall score for prognostication of UGI bleeding

	Score			
	0	1	2	3
Preendoscopy				
Age (years)	<60	60–79	>80	
Shock				
Blood pressure (mmHg)	>100	>100	<100	
Heart rate (per minute)	<100	>100	>100	
Comorbidity	None		Heart failure, ischemic heart disease, and any major comorbidity	Renal/liver failure, disseminated malignancy
Postendoscopy				
Diagnoses	Mallory–Weiss/ no lesion found	All other malignancy	Gastrointestinal malignancy	
Major stigmata of bleeding	None/dark spot only		Bleeding in UGI tract, nonbleeding visible vessels, spurting vessels, adherent clot	

- Postendoscopy risk scores of more than 2 are associated with a 4% risk of rebleeding and 0.1% mortality. Overall, patients with a score of 0, 1, and 2 have a lower risk of hemorrhage, whereas approximately 80% of patients with a postendoscopy score of 8 or more will rebleed. Accordingly, significant health savings could be achieved by early endoscopy and discharge of patients with low scores.

Step 3: Send investigations

- Hemoglobin levels are required in all patients. It must however be noted that initial levels may be falsely high and underestimate true blood loss due to hemoconcentration.
- Blood should be sent urgently for crossmatching and availability.
- Send blood parameters including prothrombin time, partial thromboplastin time, and platelet count.
- Blood urea, creatinine, and liver function tests may assist in diagnosing the cause and severity of bleeding.
- Baseline ECG.

Step 4: Further treatment

- Any coagulopathy found needs to be corrected by appropriate blood products. If prothrombin time/international normalized ratio is prolonged, give fresh frozen plasma or vitamin K injection.
- Proton-pump inhibitors: 80 mg IV bolus should be administered followed by intravenous infusion of 8 mg/h or 40 mg 12 hourly.

- If there is known or suspected variceal bleeding (or known or suspected chronic liver disease), empiric treatment with terlipressin 2 mg IV stat followed by 2 mg IV QDS and a dose of broad-spectrum antibiotics should be given.
- If there is history of active alcohol abuse, thiamine replacement should be started.

Step 5: Insert the nasogastric tube

- The nasogastric tube insertion is helpful in many ways. The type of aspirate such as fresh blood, bilious, or altered blood helps in determining whether bleeding is ongoing or has stopped.
- Gastric lavage before endoscopy also helps in giving a clear view for endoscopy.
- It may be avoided in uncooperative and delirious patients or in the patient who is retching as it may precipitate further bleeding.

Step 6: Carry out endoscopy

- Endoscopy is a mainstay for all cases of UGI bleeding. It enables:
  - Identification of the source of bleeding
  - Therapeutic intervention to achieve hemostasis if required
- UGI barium studies are contraindicated as they interfere with subsequent endoscopy or surgery. Also, the yield is very poor.
- Timing of endoscopy: After resuscitation, an endoscopy is arranged. Patients with profuse hemorrhage may need emergency endoscopy; the endoscopy should take place within 24 h of presentation, both to guide management and to facilitate the early discharge of patients with a low risk of recurrent bleeding.
- In nonvariceal bleeding, the endoscopic risk factors for rebleeding are to be identified, as they help in deciding when to offer endoscopic therapy.

Step 7: Specific treatment

- Cases of 80% of UGI bleeding stop spontaneously. Mortality is approximately 10%.
- The endoscopic therapy for bleeding is summarized in Fig. 35.1.

  A. For nonvariceal bleeding
    - Intravenous proton-pump inhibitor bolus is followed by infusion for 72 h after endoscopic hemostasis; oral proton-pump inhibitors can be started after completion of intravenous therapy.
    - Stop NSAIDs and substitute with less toxic drugs.
    - There is no role for H2 blocker, somatostatin, or octreotide.
    - Oral intake of clear liquids can be initiated 6 h after endoscopy in patients with hemodynamic stability.
    - Helicobacter pylorus testing is required, and appropriate treatment should be started if the result is positive.
    - Surgical or interventional radiologic consultation should be taken for angiography for selected patients with failure of endoscopic hemostasis or massive rebleeding.

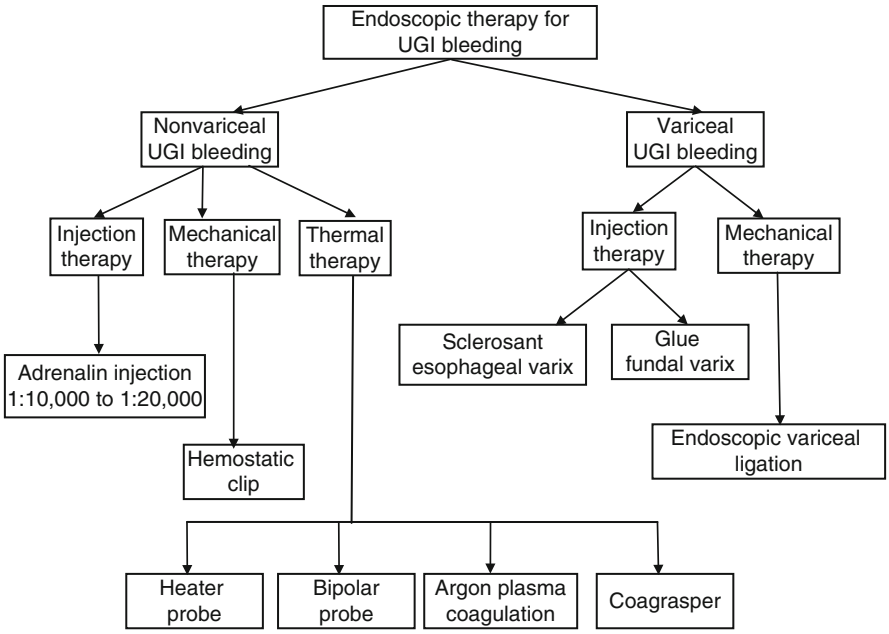

Fig. 35.1 Endoscopic therapy for UGI bleeding

B. For variceal bleeding

- Vasoactive drug treatment should be continued (terlipressin for 48 h, octreotide, or somatostatin each for 3 days).
- Antibiotic therapy should be commenced/continued.
- Balloon tamponade should be considered as a temporary salvage treatment for uncontrolled bleeding.
- Transjugular intrahepatic portosystemic stent shunting is recommended as the treatment of choice for uncontrolled variceal hemorrhage.
- An opinion of a hepatologist must be taken for further management of chronic liver disease.

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Lower Gastrointestinal Bleeding

36

Surinder S. Rana and Deepak Kumar Bhasin

A 70-year-old male patient presented to the emergency department with the massive acute painless passage of bright red blood per rectum with postural symptoms. He had no history of fever, weight loss, anorexia, or recent change in bowel habits. There was no significant history of drug ingestion. The patient was a chronic alcoholic and nonsmoker. There was no significant history of any medical or surgical illness.

Majority of patients with hematochezia bleed from the large bowel, but in 10–25% of patients, the small bowel is the source of bleeding, and it poses difficult diagnostic dilemma. Also, some patients with massive upper GI bleeding can present with hematochezia. Lower GI bleeding represents a diverse range of bleeding sources and severities, ranging from mild hemorrhoidal bleeding to massive blood loss from vascular small bowel tumors.

Step 1: Initiate evaluation and resuscitation

The evaluation of the hemodynamic status and resuscitation is the most important step in the initial treatment of patients with lower gastrointestinal (GI) bleeding:

- Initiate resuscitation as mentioned in Chap. 78.
- Massive lower GI bleeding is defined as any bleeding requiring more than 3–5 units of blood during 24 h to maintain hemodynamic stability.
- Effort should be made to identify patients with hemodynamic compromise. Postural changes, pallor, dyspnea, tachycardia, and hypotension suggest hemodynamic compromise.

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- Two large-caliber peripheral venous lines or a central venous line should be placed in patients with hemodynamic compromise.
- Blood should be transfused if indicated.

Step 2: Make a diagnosis

- An initial history and clinical evaluation should be done to arrive at a list of possible differential diagnosis and plan further investigations.
- The use of anticoagulants or nonsteroidal anti-inflammatory drugs (NSAIDs), the presence of liver disease, and serious comorbid medical conditions like cardiac conditions should be assessed.
- The character and frequency of stool output should be noted, as it allows critical assessment of the severity of bleeding as well as likely source of bleeding.
- Hematochezia must be differentiated from melena, as melena is suggestive of an upper GI bleeding source (although bleeding from the cecum and right-sided colon occasionally presents with melena).
- Patients with brown or infrequent stools are unlikely to have brisk bleeding; those with frequent passage of red or maroon stool, however, may have ongoing bleeding.
- Careful digital rectal examination should be done to exclude anorectal pathology as well as confirm patient's description of stool color. Hematochezia should also be differentiated from bloody diarrhea, by proper history.
- The most common etiologies of lower GI bleeding vary according to the age groups of the patients.
- In young adults and adolescents, the most common causes of bleeding are inflammatory bowel disease, Meckel's diverticulum, and polyps.
- In adults younger than 60 years, the most frequent source of lower GI bleeding includes colonic diverticula, inflammatory bowel disease, and neoplasms, whereas angiodysplasia, diverticula, neoplasms, and ischemia are the most common cause of lower GI bleeding in the elderly.
- With history of 2–3 weeks of fever in the patient with lower GIT bleeding, rule out enteric fever in countries with high incidence.

Step 3: Send investigations

- Initial laboratory studies should include a complete blood count, coagulation profile, blood grouping, renal function tests, and serum electrolytes.
- Coagulopathy (international normalized ratio >1.5) or thrombocytopenia (<50,000 platelets/μL) should be treated using fresh frozen plasma or platelets, respectively.

Step 4: Risk stratification

- Risk stratification is important because diagnostic and therapeutic interventions are time- and resource-consuming and often involve risk and discomfort (i.e., bowel preparation) to the patient.
- In contrast to the upper GI bleeding, predictors of poor outcome in the lower GI bleeding are not well defined.

- Hemodynamic instability, ongoing hematochezia, and presence of comorbid illness have been associated with poor outcome.
- About 75% of patients stop bleeding spontaneously without any treatment and are unlikely to benefit from aggressive interventions.

Step 5: Rule out the upper GI tract as the source of bleeding

- About 10–15% of patients presenting with severe hematochezia have the bleeding source localized in the upper GI tract.
- Patients with hemodynamic compromise and bleeding per rectum should at least have a nasogastric (NG) tube, and if the NG aspirate is bilious, an upper GI source of bleeding is unlikely.
- If the aspirate is nondiagnostic (no blood or bile), or if there is a strong suspicion of an upper bleeding source (i.e., history of previous peptic ulcer disease or frequent NSAID use), or an abdominal aortic surgery, then an upper GI endoscopy should be done.
- Nasogastric tube also helps in further preparation of the colon.
- High blood urea nitrogen to creatinine ratio has also been shown to be helpful in predicting an upper GI source of bleeding.

Step 6: Colonoscopy

- Colonoscopy is the preferred next diagnostic step after stabilization in most of the patients with lower GI bleeding as it can provide both a diagnosis and hemostasis. The diagnostic yield of colonoscopy is more than radiographic tests like tagged RBC scan or angiography, which requires active bleeding at the time of the radiological examination. Colonoscopy is also better than the flexible sigmoidoscopy, which visualizes only the left side of the colon.
- The diagnostic yield of urgent colonoscopy in acute lower GI bleeding has been reported to be between 75% and 97%, depending on the definition of the bleeding source, patient selection criteria, and timing of colonoscopy.
- Thoroughly clean the colon with bowel preparation in acute lower GI bleeding, as this procedure facilitates endoscopic visualization, improves diagnostic yield, and improves the safety of the procedure by decreasing the risk of perforation. Bowel preparation is not believed to dislodge clots or precipitate bleeding.
- The cecum should be reached, if at all possible, because a substantial proportion of bleeding sites are located in the right hemicolon.
- An attempt should be made to intubate the terminal ileum, especially in nondiagnostic colonoscopy, as substantial number of causes of lower GI bleeding can be found in the terminal ileum.
- Unlike early endoscopy in upper GI bleeding, colonoscopy should be performed after bleeding has stopped owing to fear of increased complications, need for colon preparation, and lack of proven benefit. However, recent studies have suggested that performing colonoscopy shortly after presentation within 24 h is advantageous, but studies comparing this approach with traditional delayed colonoscopy are limited.
- Early colonoscopy also helps in identifying low-risk patients and thus reduces the need for prolonged hospitalization and costs of care.

- The following criteria have been suggested for identifying the site of bleeding from colonoscopy:
  - Active colonic bleeding
  - Nonbleeding visible vessels
  - Adherent clot
  - Fresh blood localized to a colonic segment
  - Ulceration of diverticulum with fresh blood in adjoining area
  - Absence of fresh bleeding in the terminal ileum with fresh blood in the colon

Step 7: Achieve hemostasis

- Endoscopic treatment modalities for lower GI bleeding include injection, contact and noncontact thermal coagulation, and mechanical devices such as metallic clips and band ligation.
- Endoscopic clipping is considered as a safer alternative to thermal contact methods. Hemoclips can be applied directly to the stigmata, visible vessels, or used to oppose the sides of small diverticula or postpolypectomy defects.
- Thermal coagulation in the colon should be performed using moderately low power settings in 1- to 3-s bursts with light to moderate pressure. Thermal coagulation should be used carefully in the right colon, in the dome of diverticula, and in the presence of mucosal defects.
- Epinephrine (dilution, 1:10,000 or 1:20,000) can be injected in 1–2-mL aliquots in four quadrants around the lesion in cases of active bleeding.
- Argon plasma coagulation (APC) is useful for diffuse lesions such as radiation proctitis and large or multiple angiodysplasia.
- Ligation with bands is used for bleeding hemorrhoids and bleeding rectal varices, and, in certain circumstances, for treatment of focal lesions that are less than 2 cm in diameter on nonfibrotic tissue.
- The amount of tissue suctioned into the cap before the application of the rubber band must be carefully monitored to avoid perforation.

Step 8: Investigate further if colonoscopy is unhelpful or not possible

- The following radiological investigations are used in the management of severe lower GI bleeding who cannot be stabilized for colonoscopy or for ongoing bleeding of obscure etiology:
  - Angiography
  - Radionuclide scintigraphy
  - Computed tomography (CT) angiography
  - Magnetic resonance (MR) angiography
- They are useful in brisk bleeding as there is no need for bowel preparation. However, in contrast to colonoscopy, these investigations require active bleeding at the time of examination for diagnosis and treatment. Barium studies are not required in patients with lower GI bleeding.
- Computed tomography (CT) angiography and MR angiography are evolving as the modality of choice before digital subtraction angiography (DSA) and surgery if upper GI endoscopy and colonoscopy are normal.

Angiography

- Angiography is the only radiographic modality that is both diagnostic and therapeutic but requires a bleeding rate of at least 0.5–1.0 mL/min to be positive.
- Systolic blood pressure of less than 90 mmHg and a requirement of at least 5 units of packed red blood cells within a 24-h period have been shown to predict positive mesenteric angiography.
- This should be reserved for patients who have massive bleeding with hemodynamic compromise that precludes colonoscopy or in patients where colonoscopy is nonconclusive and the patient continues to bleed.
- Vasopressin is the first therapeutic modality employed during angiography, and it controls bleeding in up to 91% of cases, but major complications occur in 10–20% of patients and include arrhythmias, pulmonary edema, hypertension, and ischemia.
- Rebleeding occurs in up to 50% of patients after cessation of the infusion, and, therefore, it is often used to stabilize a patient before surgery rather than as a definitive intervention.
- Early attempts at embolization occasionally cause bowel infarction, but technologic advances in coaxial microcatheters and embolic materials have enabled the embolization of specific distal arterial branches with increased success and fewer complications.

Radionuclide scintigraphy

- Nuclear scintigraphy is a more sensitive method than angiography for detecting GI bleeding as it detects bleeding as low as 0.1 mL/min.
- The major disadvantage of nuclear imaging technique is that it localizes bleeding only to an area of the abdomen and also has high false localization rates because the intraluminal blood is moved away by intestinal motility.
- Currently, it is recommended that scintigraphy should be used as a screening test for patients before the angiography or colonoscopy.

CT angiography/MR angiography

- Multidetector row CT (MDCT), where scan time is considerably reduced, has brought CT also into the diagnostic armamentarium for patients with lower GI bleeding.
- Reduction of scan time thus enables the accurate acquisition of arterial images, which can show contrast extravasation into any portion of the GI tract.
- Bleeding rates as low as 0.3–0.5 cc per minute have been detected using MDCT.
- The yield of MDCT is highest among patients with severe ongoing lower GI bleeding.
- The average yield of MDCT for lower GI bleeding is 60%, with yields ranging from 25% to 95%.
- Lack of therapeutic capability is a major limitation of MDCT. However, MDCT can guide further angioembolization.
- Recently, advances in MR have shown good results with MR angiography.

Step 9: Surgery

- Surgery is usually reserved for patients who are having life-threatening bleeding, and other hemostatic techniques have failed to control the bleeding.
- An emergency operation for lower GI hemorrhage is ultimately required in 10–25% of patients.
- The usual indications for an operation are hemodynamic instability, clinical deterioration, transfusion requirements of more than 6 units, and persistent or recurrent hemorrhage.
- In real-life situations, it is usually difficult to make decisions based solely on criteria, and, therefore, surgical consultation should be obtained early in the course of severe bleeding.
- Surgery is also used in patients with recurrent diverticular hemorrhage.
- Surgery in lower GI bleeding is associated with high morbidity and mortality, and localization of the bleeding source before surgery is important for better outcomes. For this, per operative panendoscopy or laparoscopic assisted endoscopy may be done.

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Acute Diarrhea

37

Mahesh Kumar Goenka and Nisha D. Kapoor

A 40-year-old male patient with no significant previous medical history was admitted to the ICU with 1-day history of passing watery diarrhea, about 20–25 episodes with crampy pain in the abdomen. On examination, he was afebrile with signs of dehydration in the form of dry skin, loss of skin turgor, pulse of 100/min, and BP of 90/60 mmHg. He was drowsy and had the reduced urinary output. His central venous pressure (CVP) was 3, and arterial blood gas (ABG) analysis revealed metabolic acidosis.

Acute severe diarrhea in the ICU may be seen in two situations: a patient with acute severe diarrhea gets admitted to the ICU or a patient admitted to the ICU for any other illness develops a new-onset diarrhea.

Step 1: Initiate resuscitation

- After taking care of airway and breathing, fluid and electrolyte resuscitation is the mainstay of therapy. It is important to assess the severity of dehydration and treat it.
- Check vital signs such as tachycardia, hypotension, orthostatic hypotension, skin turgor, sunken eyes, sensorium, and dry mucous membranes.
- Abdomen—bowel sounds, distension, and tenderness.
- Place the central line and check CVP. Give fluids to maintain CVP between 8 and 12 cm H_2O.

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Table 37.1 Various causes of diarrhea

1. Infectious causes:
   a. Bacteria—Vibrio cholerae, *Shigella*, *Salmonella*, *Campylobacter*, *E. coli*
   b. Virus—Rotavirus, Adenovirus, Norovirus
   c. Parasites—Giardia, amoeba, Microsporidium, Cryptosporidium, Cyclospora, Strongyloides
2. Inflammatory causes: Inflammatory bowel disease, Ischemic colitis, Diverticulitis
3. Food poisoning/allergy
4. First presentation of any chronic diarrhea
5. Medications:
   a. Acid-reducing agents (e.g., histamine H2-receptor antagonists and proton pump inhibitors) and antacids (e.g., those that contain magnesium)
   b. Antiarrhythmics (e.g., quinidine)
   c. Antibiotics (most)
   d. Anti-inflammatory agents (e.g., nonsteroidal anti-inflammatory drugs [NSAIDs], gold salts, and 5-aminosalicylates)
   e. Antihypertensives (e.g., β-adrenergic receptor blocking drugs)
   f. Antineoplastic agents (many)
   g. Antiretroviral agents
   h. Colchicine
   i. Herbal products, heavy metals
   j. Theophylline
   k. Vitamin and mineral supplements (e.g., vitamin C and magnesium)
   l. Recent antibiotic use or hospitalization
   m. Prostaglandin (e.g., misoprostol)
   n. Hyperosmolar feeds
   o. Laxatives, Sorbital

- Fluids to be used:
  - Ringer's lactate
  - Normal saline with potassium chloride 20 mEq/L
- Additional potassium and magnesium are required as suggested by the biochemistry results.
- Place Foley's catheter and measure hourly urinary output.

Step 2: Take detail history from the patient/family

Take a detail history of the following:

- Duration of symptoms, frequency, characteristics of stool, amount, and weight loss
- Medications (see Table 37.1)—very common causes of diarrhea in the ICU
- Abdominal symptoms or constitutional symptoms
- Travel, food habits, and sexual activity
- Water source
- Sick contacts

- Comorbidities (e.g., diabetes and pancreatitis)
- Family history or past history of bowel disease (e.g., inflammatory bowel disease)

Step 3: Identify the cause of diarrhea
Severe diarrhea is usually of infective origin. However, other etiologies should be kept in mind (Table 37.1).

Step 4: Send investigations
Detailed investigations should be done if the patient has any one of the following:
- Profuse diarrhea with dehydration
- Grossly bloody stools
- Fever of more than 38°C
- Duration of more than 48 h without improvement
- Recent antibiotic use
- New community outbreak
- Associated severe abdominal pain in the patient older than 50 years
- Elderly (>70 years)
- Immunocompromised patients

Investigations
- Hematology
  - Hemoglobin and hematocrit, total leukocyte count, and differential count
  - Biochemistry—arterial blood gases, renal functions, liver functions and electrolytes, and blood glucose
- Stool tests
  - Fecal WBCs—suggest mucosal invasion, especially in Shigella, Campylobacter, EHEC (Entero Hemorrhagic Escherichia coli), and EIEC (Entero Invasive Escherichia coli)
  - Absent fecal WBCs in viruses, ETEC (Enterotoxic Escherichia coli), amebiasis, Giardiasis.
  - *C. difficile* toxin
  - Aerobic culture—for bacteria
  - Ova/parasites
  - The hanging drop for cholera
- Serology—amebic serology
- Imaging—plain abdominal radiograph can detect partial obstruction, perforation, colonic dilatation, contrast-enhanced computed tomography (CECT) of the abdomen is advised in protracted cases

Optional investigations
- Antigen—Giardia, rotavirus
- ELISA and PCR for viruses
- Dark field/phase contrast microscopy for Campylobacter

- Stool osmolal gap = stool osmolality–2 × (Na^++K^+); gap of more than 40–60 suggests osmotic diarrhea
- Endoscopy

Step 5: Specific pharmacotherapy
- May be given empirically in all severe diarrheas
- Usually Quinolones, Trimethoprim/sulfamethoxazole, Erythromycin, or Doxycycline are used
- If Giardiasis or Amebiasis suspected—Metronidazole
- If *C. difficile* suspected—Metronidazole or oral Vancomycin
- Antivirals (Acyclovir, Ganciclovir)—herpes simplex virus, cytomegalovirus
- Antihelminthics—Strongyloidiasis
- Empirical antibiotics are usually recommended especially in:
  a. Elderly
  b. Immunocompromised
  c. Mechanical heart valves
  d. Vascular grafts

Step 6: Symptom-relief agents
- If the cause of diarrhea is not known, palliative treatment can be started to decrease fluid loss and the patient's discomfort.
- Reduced stool frequency and stool weight may even relieve cramps, but close monitoring is required for complications.
  – Opiate derivatives—loperamide 2–4 mg four times a day
  – Anticholinergics—diphenoxylate 2.5–5 mg four times a day
  – Racecadotril (enkephalinase inhibitor), antisecretory activity without affecting intestinal transit—1.5 mg/kg thrice a day
  – Somatostatin analogs—octreotide 50–250 mcg thrice a day subcutaneously in GVHD and immunodeficiency syndrome and other causes of secretory diarrhea

Step 7: Probiotics

Various studies have shown that probiotics, especially *Lactobacillus*, *Bifidobacterium*, *Saccharomyces boulardii*, and combination of various pre- and probiotics, are helpful in avoiding recurrence of diarrhea and even *C. difficile*. However, they should be avoided in immunosuppressed patients (Fig. 37.1).

Case Scenario B

A 60-year-old diabetic man, known diabetic and hypertensive, was admitted to the ICU with cerebrovascular accident. After 1 week of stay, he had developed watery diarrhea.

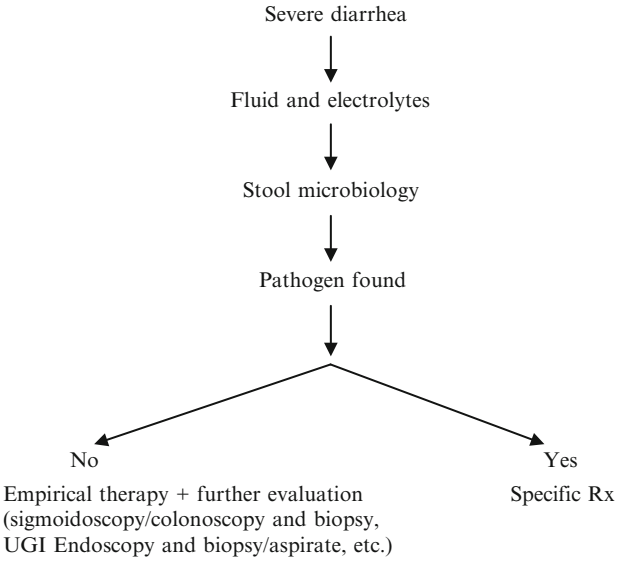

Fig. 37.1 Management of acute severe diarrhea

Step 1: Know the causes of acute-onset diarrhea in the ICU

- Tube feeding—most likely to occur with calorie-dense formulas infused directly into the small bowel, a variant of dumping syndrome
- Antibiotic-associated diarrhea, other medications as listed before (Table 37.1)
- Pseudomembranous enterocolitis—*Clostridium difficile*
- Underlying disease related—diabetic autonomic neuropathy
- Laxatives, lactose intolerance
- Fecal impaction with overflow diarrhea
- Ischemic colitis
- Diverticulitis
- First-time presentation of a disease such as malignancy, radiation colitis, inflammatory bowel disease, and Addison's disease

Step 2: Management is same as mentioned above with a few changes

- There should be a lower threshold for performing sigmoidoscopy/colonoscopy in these patients.
- For tube-feed-related diarrhea:
  - Slow the rate of infusion.
  - Dilute the feeds.
  - Modify the formula to increase fiber.
  - Give an antidiarrheal agent such as loperamide or diphenoxylate.
- For antibiotic/laxative/other medication-related diarrhea, stop the offender.

- For *C. difficile*, initiate oral vancomycin (125–500 mg QID) or metronidazole (250–500 mg TDS, QID) for 10–14 days. Probiotics (Lactobacillus GG, *S. boulardii*) and prolonged course of vancomycin are required for relapsers. In most cases, treatment is started empirically as it takes time for the *C. difficile* toxin in stool report to come in positive. Consider oral rifaximin and fidaxomicin in recurrent C. difficile.

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Acute Abdominal Distension

38

Mohd. Talha Noor and Rakesh Kochhar

A 75-year-old male patient presented with respiratory distress after a road traffic accident. On examination, he was dyspneic. Computed tomography (CT) revealed features suggestive of massive hemothorax. He underwent urgent open thoracotomy following which his condition improved. On the third day of hospitalization, he developed acute onset abdominal distension. The percussion note over the abdomen was tympanic, and bowel sounds were sluggish. Abdominal X-ray revealed dilated bowel loops with multiple air-fluid levels. The serum sodium level was 139 mEq/L, and the serum potassium level was 2.6 mEq/L.

Abdominal distension in the ICU patients occurs due to many reasons. Acute colonic pseudo-obstruction is not an uncommon cause of acute abdominal distension in this setting. This is characterized by clinical features of large bowel obstruction but without any mechanical cause. Early recognition and appropriate management are critical in minimizing the morbidity and mortality from complications.

Step 1: Initial resuscitation and assessment

- After initial resuscitation (Chap. 78), a detailed history should be obtained, and the patient should be carefully examined.
- The bowel frequency, stool character, bowel sounds, abdominal distension and abdominal girth, and intra-abdominal pressure should be monitored (see the chapter 39).

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- Crampy abdominal pain and exaggerated bowel sound suggest the presence of mechanical obstruction.
- Ileus presents with abdominal distention and abdominal pain that is typically mild and poorly localized. Other features include hypoactive or absent bowel sounds, lack of passage of flatus and stool, intolerance of oral intake, and nausea and emesis. Physical examination reveals a distended, tympanitic abdomen; hypoactive bowel sounds; and mild, diffuse abdominal tenderness. The patient may exhibit signs of dehydration, such as tachycardia, orthostatic hypotension, poor skin turgor, and dry mucous membranes.
- In critically ill patients, the possibility of a fecolith causing fecal impaction and obstruction should be kept in mind. Rectal examination should be performed with digital disimpaction if hard fecal matter is present.
- Send for the following investigations immediately:
  - Erect and supine abdominal X-ray
- Abdominal X-ray shows a cutoff point in mechanical obstruction. Free air under the diaphragm must be looked for perforation. Gas seen till the rectum rules out distal bowel obstruction.
- Stool for occult blood and *C. difficile* toxin.
- Serum electrolytes.

Step 2: Make a diagnosis

The following conditions commonly present with acute abdominal distension in the *ICU*:

- Acute colonic pseudo-obstruction (ACPO)
- Mechanical obstruction
- Intestinal perforation
- Ischemic bowel
- Toxic megacolon
  - Inflammatory bowel disease
  - *C. difficile* colitis

ACPO can be associated with a number of medical conditions (Table 38.1), which should be looked for and corrected if present.

- Correct important conditions:
  - Medications such as calcium channel blockers and narcotics can lead to paralytic ileus. These medications should be stopped or their dose should be reduced.
  - The presence of sepsis should be investigated, and samples for culture should be sent.
  - In elderly patients with risk factors such as hyperlipidemia, atrial fibrillation, and the presence of coronary artery disease, mesenteric ischemia should be excluded.
  - Rarely, endocrine disorders such as adrenal insufficiency, hypothyroidism and hypoparathyroidism can also lead to paralytic ileus.

Table 38.1 Common conditions associated with ACPO

Cardiovascular	*Metabolic*	*Neoplastic*	*Posttraumatic*
Heart failure	Alcohol	Disseminated	Femur fracture
Myocardial infarction	Electrolyte imbalance	Leukemia	Pelvic trauma
	Liver/kidney failure	Retroperitoneal	Spinal cord injury
Drugs	*Inflammation*	*Neurologic*	*Postsurgical*
Antidepressants	Acute cholecystitis	Alzheimer's	Cesarean
Antiparkinsonian	Acute pancreatitis	Multiple sclerosis (MS)	Hip surgery
Opiates	Pelvic abscess	Parkinsonian	Knee replacement
Phenothiazines	Sepsis	Spinal cord disease	Spinal cord injury
Respiratory problems			
Mechanical vent			
Pneumonia			

Step 3: Do appropriate imaging with proper interpretation

- Postoperative ileus must be differentiated from small bowel obstruction. Plain abdominal roentgenogram in ileus reveals pronounced small bowel dilatation but may reveal less pronounced large bowel dilatation.
- Additional imaging, such as abdominal CT, may be necessary to exclude mechanical obstruction. Abdominal CT is up to 90% specific and sensitive in excluding bowel obstruction.

Step 4: Initial treatment (Fig. 38.1)

- Continuous nasogastric decompression.
- Correction of fluid and electrolyte disturbance.
- Underlying conditions should be identified and aggressively treated.
- Discontinuation of drugs that promote an ileus.
- Metabolic disorders like diabetic ketoacidosis, if present, should be treated properly.

Step 5: Pharmacotherapy (Fig. 38.1)

The role of pharmacotherapy in the management of paralytic ileus is limited. However, the following drugs have shown some benefit:

- Metoclopramide—cholinergic agonist and dopamine antagonist—induces phase 3 of interdigestive migrating motor complex. Dose should be 0.5 mg/kg/24 h intravenously or intramuscularly.
- Alvimopan—selective mu-receptor opiate antagonist—antagonizes the gastrointestinal effects of nonselective opiates without affecting its central analgesic properties and enhances recovery of bowel function. Dose should be 6 mg orally.
- Neostigmine—reversible acetylcholine esterase inhibitor—enhances the activity of the neurotransmitter acetylcholine at the muscarinic receptors. It is the first-line treatment for colonic ileus. It is used in dosages of 2.0 mg infused over

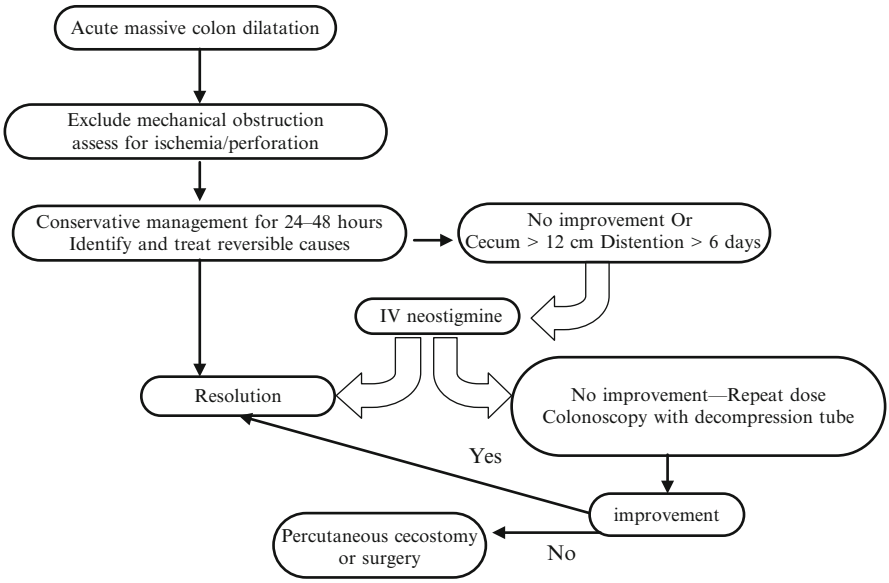

Fig. 38.1 Algorithmic approach to ACPO

3–5 min. Atropine should be kept ready when it is done. EKG should be constantly monitored during infusion. Vital signs should be monitored for about 30 min after infusion. The patient should be kept in supine or semisupine position, and a bedpan should be provided. Randomized controlled trials (RCTs) have shown benefit.

Step 6: Colonoscopic decompression

- Colonoscopy is required in some patients to rule out distal obstructive lesions, but its role for colonic decompression is controversial.
- Its use has decreased after neostigmine has been accepted for treatment. Now it is resorted to if neostigmine fails.
- This is done without any preparation, and attempt has to be made to use minimum insufflation and reach cecum.
- Some centers use a decompression tube, which is kept inside to constantly decompress.
- This is initially successful in 70–90% of patients, but 10–20% may recur. In such patients, the second decompression can be tried.

Step 7: Surgery

- Surgery is rarely required in patients with persistent colonic dilatation in spite of colonoscopic decompression and in patients with peritonitis.
- Surgery recommended in such cases is cecostomy or loop colostomy. If there is any nonviable bowel, it is resected. In patients who are unfit for surgery, percutaneous cecostomy just like percutaneous endoscopic gastrostomy is performed.

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Intra-abdominal Hypertension

39

Rajesh Chawla and Sananta K. Dash

A 53-year-old female patient was admitted to the ICU postoperatively after cholecystectomy for a failed endoscopic retrograde cholangiopancreatography for retrieval of common bile duct stones. She had recent history of gallstone-induced pancreatitis. On the fifth postoperative day, she suddenly became tachypneic and complained of abdominal tightness. She continued to have respiratory distress and later on was intubated in view of severe respiratory distress and hypoxemia. While on the ventilator, her peak airway pressure and the plateau pressure were very high.

Raised intra-abdominal pressure and abdominal compartment syndrome are commonly noticed in critically ill patients. In the recent past, their presence in a variety of medical and surgical conditions other than trauma has been emphasized. Early detection, prevention, and treatment reduce the morbidity and mortality in these critically ill patients.

Understand definitions

- *IAP* (intra-abdominal pressure): It is the pressure concealed within the abdominal cavity. Normal IAP is approximately 5–7 mmHg in critically ill adults. Physiological changes occur when the IAP rises up to 15 mmHg.
- APP (abdominal perfusion pressure) (MAP-IAP): It is a better reflection of gut perfusion.

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- IAH (intra-abdominal hypertension): A sustained or repeated pathologic elevation of IAP more than or equal to 12 mmHg and is divided into four grades:
  - Grade I, IAP 12–15 mmHg
  - Grade II, IAP 16–20 mmHg
  - Grade III, IAP 21–25 mmHg
  - Grade IV, IAP >25 mmHg
- ACS (abdominal compartment syndrome): A sustained IAP of more than 20 mmHg (with or without an APP <60 mmHg) that is associated with new organ dysfunction/failure.
- Primary goal is an APP more than or equal to 60 mmHg.
- Primary *ACS*: A condition associated with injury or disease in the abdominopelvic region that frequently requires early surgical or radiological intervention.
- Secondary *ACS*: ACS due to conditions that do not originate from the abdominopelvic region.
- Recurrent ACS: The condition in which ACS redevelops following previous surgical or medical treatment of the primary or secondary ACS.
  Approach to a patient with IAH

Step 1: Initial resuscitation
- Initiate resuscitation as mentioned in Chap. 78.
- The elevated IAP has a direct effect on pulmonary and cardiac functions.
- Pulmonary compliance suffers with resultant progressive reduction in total lung capacity, functional residual capacity, and residual volume and is manifested by hypoxia, hypercapnia, and increasing ventilatory pressure.
- Elevated IAP above 20 mmHg consistently correlates with reduction in cardiac output.
- IAP above 20 mmHg produces elevations in measured hemodynamic parameters including central venous pressure and pulmonary artery wedge pressure. Half of IAP should be subtracted from these measures of vascular pressures to arrive at an approximately true pressure.

Step 2: Assess the possible risk factors for IAH/ACS
- IAH or ACS can be the result of abnormality in any of the four constituents that determine the IAP (Fig. 39.1):
  I. Abdominal wall compliance
  II. Intraluminal contents
  III. Abdominal contents
  IV. Capillary leak/fluid resuscitation

Step 3: Take focused clinical history and do physical examination
The mode of presentation and associated conditions many a times gives a clue to the possible cause of IAH and ACS in a patient. History should be taken on the basis of the background condition. Do detailed general and abdominal examination (Fig. 39.2).

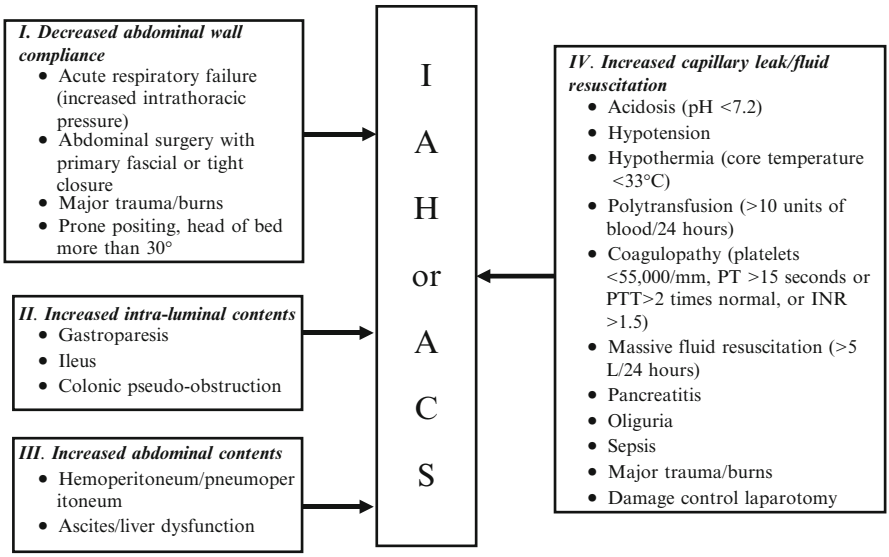


Fig. 39.1 Risk factors for IAH/ACS

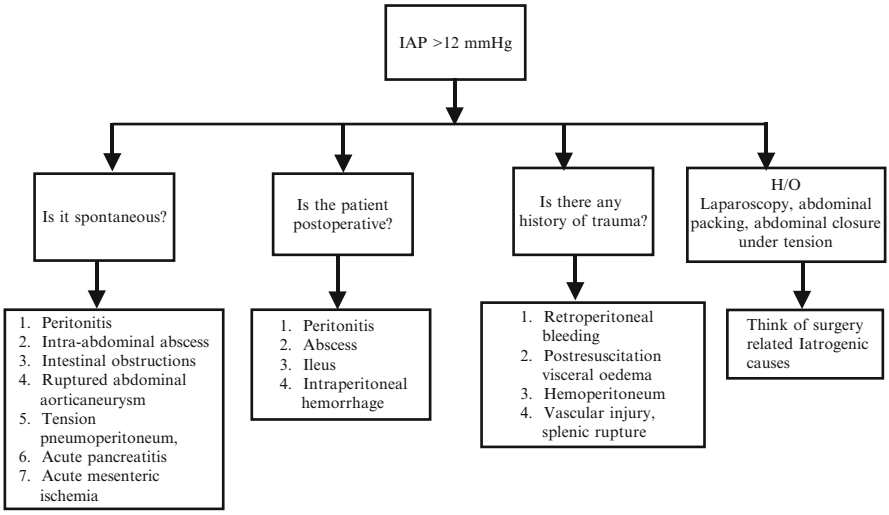


Fig. 39.2 General and abdominal examination

Step 4: Measure IAP

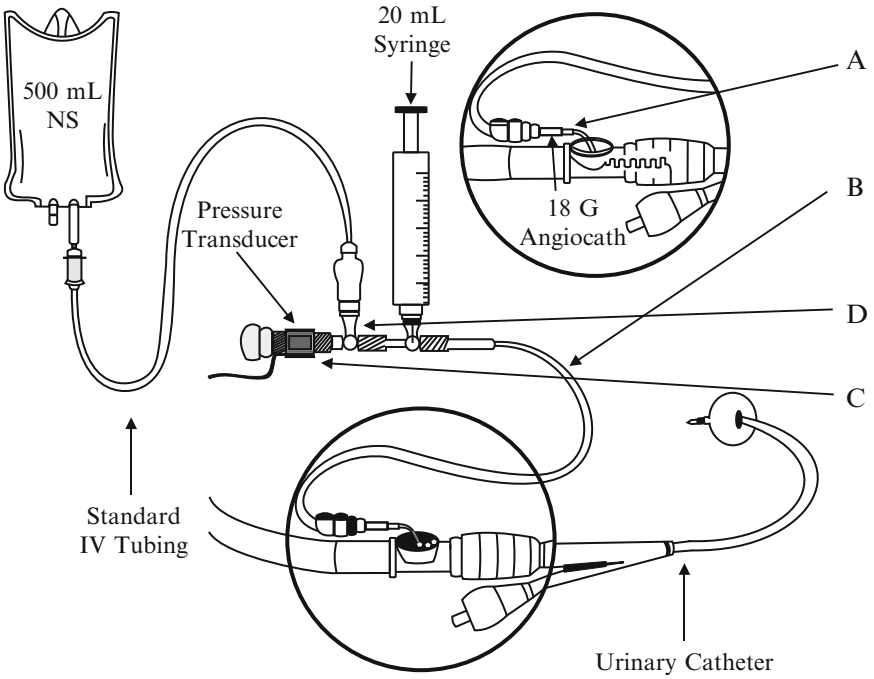
- IAP can be measured either directly (through needle puncture of the abdomen during laparoscopy or peritoneal dialysis treatment) or indirectly (using intravesicular pressure or gastric pressure through a balloon catheter as a surrogate of IAP). The transvesicular IAP measurement techniques are based on the same principle; namely, that a fluid column in the bladder catheter and tubing to the collecting bag serve as a pressure-transducing medium.

Method 1

– An assembly is made, as shown in Fig. 39.3.
– An 18-gauge needle or an angiocath (A) with tubing is inserted into the urinary catheter port, as shown in the figure.
– Clamp the urinary catheter distal to angiocath insertion site.
– The tubing (B) is then attached to a pressure transducer (C).
– Fill the syringe with saline and infuse 20–30 ml of saline in to the bladder.
– Keep the second stop cork (D) opened to air and closed to patient. Calibrate the transducer to zero at the level of iliac crest.
– IAP is measured 30–60 s after instillation to allow for bladder detrusor muscle relaxation (for bladder technique), and it is ensured that there are no active abdominal muscle contractions.
– The pressure is measured at end-expiration in the supine position, with iliac crest in the midaxillary line taken as the zero level.
– If available, Foley's catheter with a third sample collection port is preferable in place of needle or angiocath for IAP measurement as it avoids puncturing of the Foley's tube with needle.

Method 2

– The drainage tubing is first marked with a silk tape/permanent marker along its length.
– The drainage tube is marked as "0" which serves as the zero reference point when it is at the level of symphysis pubis.
– The drainage tubing is marked at an increment of 1 cm (up to 30–40 cm).
– A three way (E) is placed in the drainage tube past the marking. One hundred milliliters of sterile saline is introduced into the bladder.
– The drainage tubing is raised vertically keeping the zero point at the pubic symphysis and the three way open to patient's bladder side and atmosphere.
– The sterile saline is allowed to rise vertically. The distance of saline meniscus above the zero reference point is the IAP in cm of H_2O. 1 mm of Hg = 1.36 cm of H_2O.
– This is an effective and easy monitoring method of IAP and can be done hourly.
– This method is not advisable in ICU setting as it leads to risk of retrograde urinary infection.



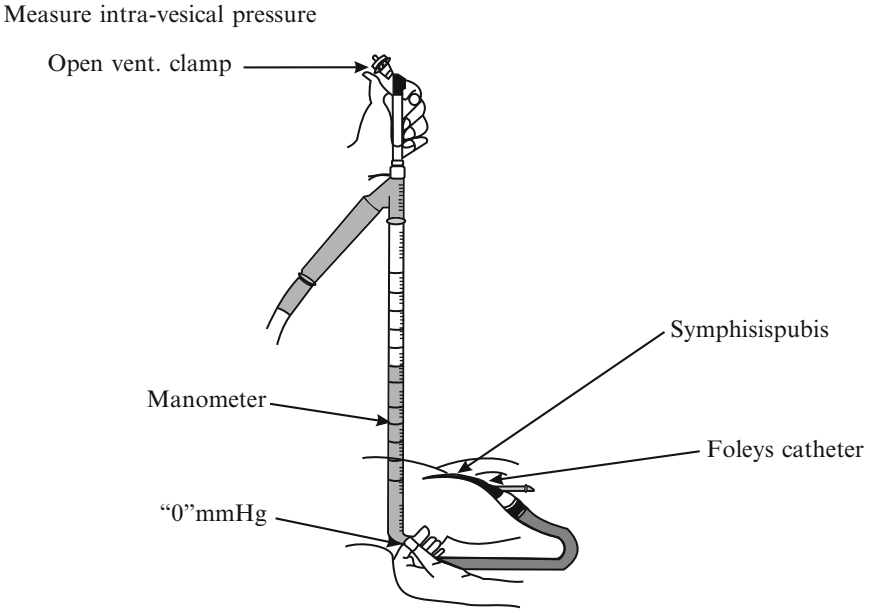


Fig. 39.3 (**a**) Intra-abdominal pressure monitoring (Method - 1) (**b**) Intrabdominal pressure monitoring (Method - 2)

Step 5: Start management

IAH/ACS evaluation and medical management is summarized in flow diagrams 4 and 5.

- Once a patient is detected to be having a raised IAP and possible ACS, the approach to treat the underlying condition should be aggressive.
- A prompt response by a physician at the impending ACS can be lifesaving for his patient.
- Many a times early detection and management prevents need for any surgical means of decompression, and a satisfactory result can be achieved by medical treatment only.
- Keys to success are the high level of suspicion and anticipation when managing patients who are prone to IAH and subsequent ACS.
- Medical interventions are aimed at decreasing IAP, targeting the four important contributors to IAH (as described in Step 2). Figure 39.4 and 39.5 analyzes each step of approach and specific medical management for each of the four contributing factors.
- When using medical management options to decrease IAP, it is important to always consider individualized pathophysiologic mechanisms leading to IAH because these may differ considerably from one patient to another, and the management depends on this (Fig. 39.4).
- Critically, in patients with IAH, small changes in intra-abdominal volume may have a pronounced effect on IAP.

Step 6: Surgical management

- In spite of early detection and adequate medical therapy, few patients may progress from a raised IAP state to ACS, and the ACS may be unresponsive to medical therapy.
- This state of no response to adequate medical therapy needs to be picked up early, and ACS refractory to medical therapy should be treated with timely surgical approach.
- IAH/ACS surgical management.
- While doing surgical management of IAH/ACS, certain precautions should be taken:
  - Prevent heat loss from the viscera (by plastic sheet).
  - Protect the swollen viscera.
  - Allow free drainage of fluid that may accumulate within the cavity with continued resuscitation.
  - Do not damage the fascia and skin so that closure will be easier at a later period.

Method

- Midline laparotomy.
- Abdomen is left open and fascia is not closed.

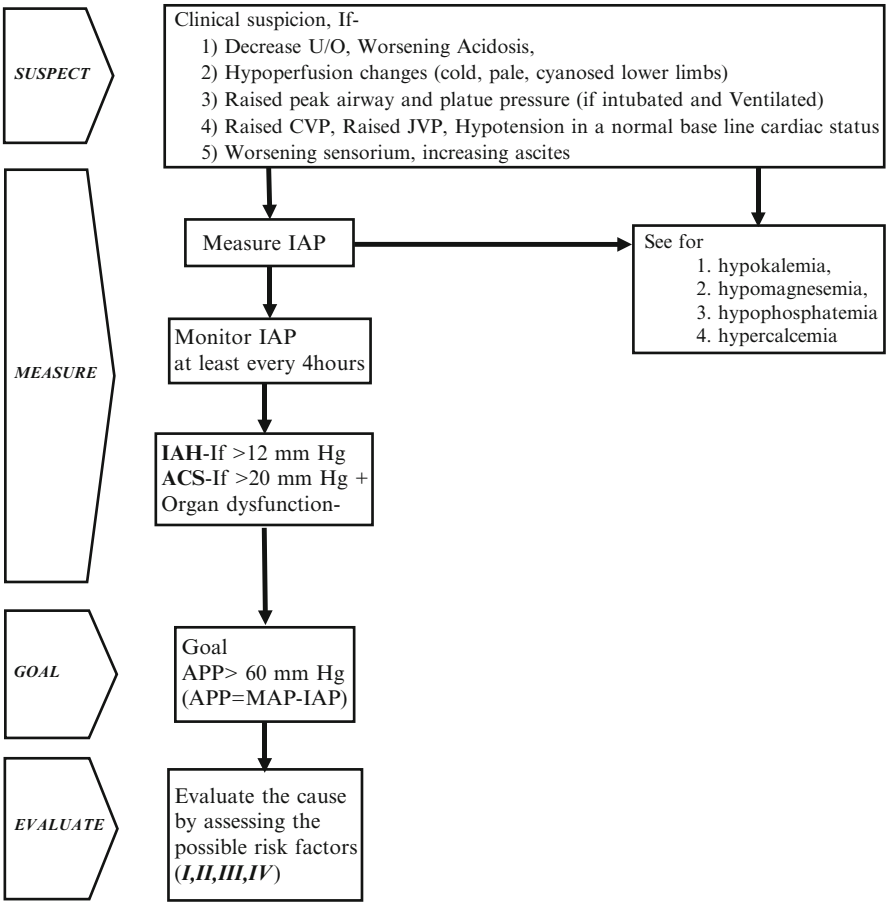


Fig. 39.4 IAH/ACS evaluation

- A large plastic sheet is laid over the bowel and tucked deep in the paracolic gutters in both sides, over the stomach/spleen and liver superiorly, and deep into the pelvis inferiorly. It protects viscera, prevents heat loss, and prevents adhesion formation between the bowel surface and the abdominal wall.
- Small perforations are made in this sheet to allow fluid drainage.
- Moistened gauze bandage is placed on top of this plastic sheet, and drains made up of red rubber with multiple holes are placed within the bandage and are connected, through collecting buckets, to wall suction at about 100 mmHg.
- A Steri-Drape large enough to cover the bandage and adhere to the surrounding skin is placed over the bandage.

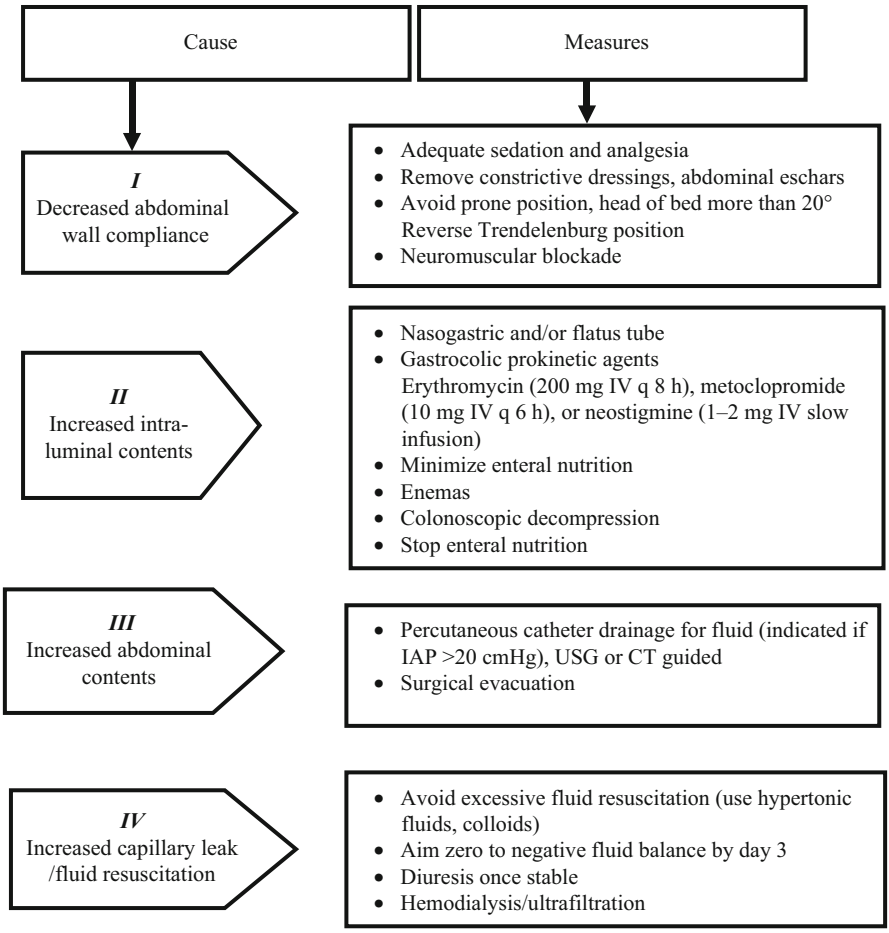


Fig. 39.5 IAH/ACS management

Suggested Reading

1. Cheatham ML. Nonoperative management of intraabdominal hypertension and abdominal compartment syndrome. World J Surg. 2009;33(6):1116–22.
This comprehensive review discusses the risk factors that predict the development of IAH/ACS, the appropriate measurement of IAP, and the current resuscitation options.
2. Irwin RS, Rippe JM. Irwin and Rippe's intensive care medicine. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2008. pp. 1795–1803.
The chapter discusses the practical application of IAP monitoring in detail, with pictorial depiction of pathophysiology of raised IAP.

Website

1. www.wsacs.org
The all-in-one website for intra-abdominal hypertension and abdominal compartment syndrome

Acute Pancreatitis

40

Ajay Kumar and Akshat Kumar

A 45-year-old nonalcoholic male patient presented with severe continuous upper abdominal pain for 1 day, associated with vomiting and mild abdominal distension. He had history of right hypochondrium pain 6 months back. His vital signs were stable. Abdomen examination showed mild tenderness and distension. Bowel sounds were sluggish. Investigations showed leukocytosis (13,000), serum bilirubin of 2.5 mg/dl, and fourfold increase in transaminases. Serum amylase was 1,420 IU and serum lipase was 1,200 IU. Ultrasonography of the abdomen showed 7-mm gallstones, normal common bile duct (CBD), and bulky pancreas with peripancreatic fluid collection. He was diagnosed to have biliary pancreatitis.

Acute pancreatitis (AP) can have significant morbidity and mortality. Outcome of AP is determined by its severity, which is, to a large extent, determined by the amount of pancreatic necrosis. Organ failure or infected necrosis is associated with adverse outcome.

Step 1: Initiate resuscitation and take focused history

- Initiate resuscitation, as mentioned in Chap. 78.
- Take detailed history.
- Most of the patients (95%) present with acute epigastric abdominal pain. About 50% of these patients will have this pain referred to the back. This can be accompanied by nausea, vomiting, and abdominal distension or fever. Give attention to

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Table 40.1 Etiology of AP

Biliary tract stone disease	Traumatic
Viral infections (mumps)	Idiopathic pancreatitis
Postoperative—duct exploration	Drugs
Iatrogenic—post-endoscopic retrograde cholangiopancreatography (ERCP)	Parasites—ascaris and clonorchis
Pancreatic neoplasm	Hypertriglyceridemia
Ethanol abuse	

history of alcohol intake, previous gallstone disease, drug intake, and hypertriglyceridemia or known malignancy.
- History should be directed toward the known causes of pancreatitis (Table 40.1) in a suspected case.

Step 2: Perform focused detailed examination
- The patient may have signs of shock or may be hemodynamically stable depending on the severity of disease.
- The patient may have low-grade fever, mild jaundice, abdominal distension, tenderness, ileus, ascites, and pleural effusion.

Step 3: Send investigations
- Complete hemogram.
- Serum amylase—initially elevated but may decrease after 2–3 days if the necrosis is widespread. False positive occurs in gastrointestinal perforation, renal failure, severe burns, and diabetic ketoacidosis.
- Serum lipase—it persists longer than amylase. If the necrosis is widespread, it may be normal.
- Serum calcium is usually low.
- Arterial blood gas (ABG) and electrolytes, blood glucose, and serum triglyceride test.
- Renal functions test.
- Altered liver function tests suggest biliary etiology.
- C-reactive protein.
- Blood culture.
- Chest and abdominal skiagram helps to rule out perforation and ileus.
- Ultrasound of the whole abdomen.

Step 4: Assessment of severity
- The outcome depends on severity.
- According to the Atlanta classification, severity is defined by the presence of organ failure and/or local complications. The Mayo group defines an additional group of moderate severity, which is characterized by local complications without organ failure.
- Various scoring systems (Table 40.2), such as Ranson's and Acute Physiology and Chronic Health Examination (APACHE) II, have been used in evaluating the severity of AP for many years. They have their own limitations.

Table 40.2 Method to predict the severity of AP

(1) Ranson's criteria	
	0 h
Age	>55 years
White blood cell count	>16,000/mm^3
Blood glucose	>200 mg/dL (11.1 mmol/L)
Lactate dehydrogenase	>350 U/L
Aspartate aminotransferase	>250 U/L
	48 h
Hematocrit	Fall by ≥10%
Blood urea nitrogen	Increased by >5 mg/dL (1.8 mmol/L) despite fluids
Serum calcium	<8 mg/dL (2 mmol/L)
PO_2	<60 mmHg
Base deficit	>4 mEq/L
Fluid sequestration	>6,000 mL
The presence of one to three Ranson's criteria represents mild pancreatitis; the mortality rate rises significantly with four or more criteria	
The presence of three or more Ranson's criteria within the first 48 h is indicative of severe pancreatitis	
(2) The BISAP score for early mortality prediction (within the first 24 h)	
Five parameters	
Blood urea nitrogen (BUN) >25 mg/dL	
Impaired mental status	
SIRS 2 or more	
Age >60 years	
Pleural effusion	
Predictive accuracy of BISAP is similar to APACHE II	
The BISAP score of more than 3 predicts persistent organ failure ($p<0.0001$) and necrosis ($p<0.0004$)	
Mortality increases from BISAP score of 1–5	
Patients with predicted severe disease should be shifted to the specialist center or ICU, and aggressive management should be rapidly instituted	

- A new prognostic scoring system, the bedside index for severity in acute pancreatitis (BISAP), has been found to be an accurate means for risk stratification in patients with AP (Table 40.2). Its components are clinically relevant and easy to obtain. This score is simple, easy, and inexpensive. The prognostic accuracy of BISAP is similar to those of the other scoring systems.
- The simple score like SIRS alone has also been used for predicting mortality. SIRS is defined by the presence of two or more of the following criteria: pulse of more than 90 beats/min, respirations of more than 20/min, or $PaCO_2$ of less than 32 mmHg, temperature of more than 100.4°F or less than 96.8°F, and white blood cell count of more than 12,000 or less than 4,000 cells/mm^3, or more than 10% immature neutrophils. It is very simple and inexpensive and can be done multiple times. SIRS of two or more for over 48 h predicts mortality of 25%.

Table 40.3 CT grading of AP

(A) Balthazar–Ranson's grading system (can be done without contrast)	
A Normal appearing pancreas	
B Focal or diffuse enlargement of pancreas	
C Pancreatic gland abnormalities associated with mild peripancreatic inflammatory changes (stranding)	
D Fluid collection in a single location, usually within anterior pararenal space	
E Two or more fluid collections near the pancreas and/or presence of gas in or adjacent to the pancreas	
(B) Severity of AP	
CT grade	Score
A	0
B	1
C	2
D	3
E	4
Necrosis (needs IV contrast)	Score
None	0
<33%	2
33%–50%	4
≥50%	6
–	
CT severity index (0–10)	
CT grade (0–4) + necrosis (0–6) = total score	
• MRI of the abdomen should be done if CECT is contraindicated	

Step 5: Do imaging

- Ultrasound is noninvasive and the best tool available for the initial evaluation of pancreatitis. This may reveal gallstones or edema of the pancreas.
- CT scan should be postponed till 72 h or more.
- A contrast-enhanced CT (CECT) of the abdomen is one of the finest modalities available to morphologically diagnose and quantify the necrosis, which predicts prognosis (Table 40.3). These changes may not appear in the first few days.
- The only indication for early CT scan is when one is not certain about the diagnosis.
- The follow-up CT scan is required if one suspects the development of a complication.
- CT should be done with a proper pancreatic protocol. Dynamic CECT is must for this (100–150 mL of contrast at 3 mL/s). Necrosis is diagnosed by less than 50 HU enhancement (normal pancreas 100–150 HU).

Step 6: Start treatment

- All patients with AP who have severe pain, vomiting, dehydration, and raised amylase should be hospitalized.

- The patient who is hemodynamically unstable and has tachypnea, hypoxia, and decreased urine output indicates severe course and should be admitted to the ICU.
- There are a number of drugs which have been specifically used to inhibit the process of pancreatitis but have not been shown to have any therapeutic benefit in controlled trials.
- General supportive care is the mainstay of the treatment in AP.
  (A) Fluids
    - Patients with severe pancreatitis should be resuscitated with aggressive fluid resuscitation.
    - These patients have a huge fluid loss in the third space, which leads on to hemoconcentration, and relative pancreatic bed ischemia, which can further increase the pancreatic necrosis. So rapid restoration of intravascular fluid volume is the priority.
    - Their fluid requirement in 24 h may vary from 5 to 7 L, generally in the form of crystalloids.
    - Use vasopressors after ensuring adequate intravascular volume.
    - Invasive hemodynamic monitoring should be done especially in cases of poor cardiac functions and in patients who are hemodynamically unstable with the aim of keeping the urine output above 0.5 mL/kg/h, hematocrit below 30%, and central venous pressure of 6–8 cmH_2O.

  (B) Relief of pain
    - Try conventional analgesics by the IV route.
    - Opioids are not contraindicated. Transdermal fentanyl patch of 25–50 mcg may be used to relieve pain.
    - Avoid nonsteroidal anti-inflammatory drugs (NSAIDs).

  (C) Antibiotics
    - The use of antibiotics in AP has been quite controversial and still remains so. In the initial phase, clinical features are primarily of inflammation (SIRS) and do not require antibiotics.
    - Only definite indication of therapeutic antibiotics is cholangitis due to CBD stones. Gram-negative pathogens such as *Escherichia coli* and anaerobes are the typical pathogens. The third-generation cephalosporins, fluoroquinolone are good initial choices.
    - The other rationale of antibiotics has been for prophylactic use to prevent infection of the pancreatic necrosis. For this purpose, multiple studies have been performed over the past 15 years, on the basis of which guidelines have been changing every few years. Current guidelines do not recommend the use of prophylactic antibiotics.
    - In practice, lot of these patients of severe pancreatitis will be in the ICU with the central line and urinary catheters, and some of them may be on ventilator support or dialysis. Thus, they are prone to hospital-acquired sepsis. Antibiotic choice for these patients depends on the local epidemiology of infections in the ICU and the sensitivities of these organisms. To treat the hospital-acquired sepsis, antibiotics may be used as per the hospital guidelines.

(D) Nutrition

- AP is a hypercatabolic state and can lead to severe nutritional deficiencies.
- While mild pancreatitis patients can start oral intake in 5–7 days, most of the severe AP patients cannot be fed orally for a significant period and thus require nutritional support.
- Moreover, traditionally the only way of treating pancreatitis was to give rest to the pancreas by not feeding and by nasogastric tube aspiration. Now, nasogastric tube aspiration is advisable only in patients of gastric ileus who are repeatedly vomiting.
- In such patients, enteral nutrition with the nasojejunal (NJ) tube should be started as early as within 48 h. The NJ tube is placed 30 cm distal to the ligament of Treitz under endoscopic/fluoroscopic guidance or at the bedside by gastric insufflations technique. It helps in nutrition as well as in prevention of sepsis.
- Recently, there has been some evidence which shows that nasogastric feeding in patients who cannot tolerate oral feed is as good as NJ feed, but this remains controversial.
- Administer enteral solutions as a continuous 24-h pump-driven infusion. Start with 500 mL/day and increase the diet gradually (250–500 mL/day) until the patient's targeted calorie needs are tolerated.
- If the nutritional target cannot be met exclusively by the enteral route after a 5- to 7-day trial, consider combined enteral and parenteral nutritional support (TPN plus EN).
- Earlier, total parenteral nutrition was used for nutritional support. It is expensive and increases the risk of line sepsis. Fasting promotes gut atrophy with decreased mucosal lymphocytes and immunoglobulin A (IgA), which predisposes to bacterial translocation and infection of the pancreatic necrosis. So TPN is recommended only when enteral nutrition is not possible or to supplement inadequate enteral nutrition.
- Monitor serum glucose and give IV insulin infusion if indicated.
- Avoid overfeeding and improve glucose tolerance by supplying some calories as lipids and maintain the triglyceride level below 400 mg.
- When patients can resume orally, they should initially be fed low-calorie and low-fat diet, which should be gradually increased. This can be continued till the patient starts taking adequately orally, which may be after 2–3 weeks.

Step 7: Early ERCP in acute biliary pancreatitis

Early ERCP (48–72 h) is indicated only in patients of acute biliary pancreatitis with evidence of cholangitis. If in doubt, endoscopic ultrasound/magnetic resonance cholangiopancreatography (EUS/MRCP) can be done to decide if the stone is still retained in CBD. It should be undertaken only by experts as it has high failure and complication rate.

Step 8: Manage complications and surgery

(A) Pseudocyst
- A pseudocyst is a collection of pancreatic juice, which is enclosed by a wall of granulation tissue. This takes at least 4 weeks to form.
- Drainage—percutaneous ultrasound-guided endoscopic or surgical—is required in those with large and/or symptomatic pseudocysts.
- The common complication of the pseudocyst includes compression of adjacent structures, rupture, infection, and bleeding in 5% of cases.

(B) CT-guided drainage of infected collection
- Multiple drains may be required.

(C) Surgery
- This is indicated in the following conditions:
  - Pancreatic necrosectomy is advised in patients of infected pancreatic necrosis not doing well or when percutaneous/other techniques are not possible. Effort should be made to delay intervention to the fourth week as the results before that are not good.
  - Pancreatic necrosis with pseudoaneurysms and massive intra-abdominal hemorrhage is best managed by angiographic embolization.
  - Abdominal compartment syndrome in which percutaneous/other drainage techniques are not successful.
  - Local complications of the pseudocyst.
- Bowel infarction.

(D) Controversial indications of surgery
- Extensive (>50%) sterile pancreatic necrosis with persisting multiple-organ failure despite intensive care therapy.
- Most surgeons avoid surgery for this indication as this is associated with increased mortality.

Step 9: Removal of the gallbladder
- Removal of the gallbladder should be scheduled early to avoid recurrence of biliary pancreatitis (30%).
- In severe attacks, it is recommended to wait 4–6 weeks to allow inflammation to subside.
- The laparoscopic approach has proved to be feasible and safe, even in cases where surgical debridement is required.

Suggested Reading

1. Talukdar R, Vega Santhi S. Early management of severe acute pancreatitis. Curr Gastroentrol Rep. 2011;13:123–30.
   A recent article on the early management of acute severe pancreatitis
2. Gardner TB, Vege SS, Chari ST, Petersen BT, Topazian MD, Clain JE, et al. Faster rate of initial fluid resuscitation in severe acute pancreatitis diminishes in-hospital mortality. Pancreatology. 2009;9:770–6.

Patients with severe acute pancreatitis who do not receive at least one-third of their initial 72-h cumulative intravenous fluid volume during the first 24 h are at risk of greater mortality than those who are initially resuscitated more aggressively.

3. Jafri NS, Mahid SS, Idstein SR, Hornung CA, Galandiuk S. Antibiotic prophylaxis is not protective in severe acute pancreatitis: a systematic review and meta-analysis. Am J Surg. 2009;197:806–13.
   Antibiotic prophylaxis of SAP does not reduce mortality or protect against infected necrosis, or frequency of surgical intervention.
4. Petrov MS, Pylypchuk RD, Emelyanov NV. Systematic review: nutritional support in acute pancreatitis. Aliment Pharmacol Ther. 2008;28:704–12.
   The use of either enteral or parenteral nutrition, in comparison with no supplementary nutrition, is associated with a lower risk of death in acute pancreatitis. Enteral nutrition is associated with a lower risk of infectious complications compared with parenteral nutrition.
5. Forsmark CE, Baillie J. AGA Institute technical review on acute pancreatitis. Gastroenterology. 2007;132:2022–44.
6. Balthazar EJ, Robinson DL, Megibow AJ, Ranson JH. Acute pancreatitis: value of CT in establishing prognosis. Radiology. 1990;174:331–6.
   A CT severity index, based on a combination of peripancreatic inflammation, phlegmon, and the degree of pancreatic necrosis as seen at initial CT study, was developed. Patients with a high CT severity index had 92% morbidity and 17% mortality; patients with a low CT severity index had 2% morbidity, and none died.

Website

1. http://gut.bmjjournals.com/cgi/content/full/54/suppl_3/iii1

Acute Liver Failure

41

Shalimar and Subrat Kumar Acharya

A 25-year-old male patient presented with recent-onset fever and jaundice, followed by altered sensorium. He had bradycardia, HR 50/min, icterus, and bilateral equal pupils reacting to light. Liver span was one intercostal space without splenomegaly. He was unconscious, responding only to painful stimuli. Liver function tests showed total bilirubin of 15 mg/dL, with conjugated fraction of 10 mg/dL, and aspartate transaminase, alanine transaminase, and alkaline phosphatase were 2,500, 3,000, and 450 IU, respectively. Prothrombin time was more than 1 min over the control. Platelet counts were normal. IgM hepatitis E virus (HEV) antibodies were positive.

The life of an individual is endangered in acute liver failure (ALF) as a consequence of multiple metabolic and hemodynamic disturbances resulting from severe acute liver injury. This disease carries high morbidity and mortality in the absence of hepatic transplantation.

Step 1: Initiate resuscitation

- Ensure the maintenance of airway, breathing, and circulation as in any critical illness, as described in Chap. 78.
- Extra precaution needs to be taken while intubating these patients to avoid sudden increase of intracranial pressure (ICP) and herniation.
- Proper sedation, anti-edema measures, and experienced personnel are prerequisites for intubation.

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Table 41.1 Causes of FHF

Broad categories
Infections
Metabolic diseases
Drugs
Toxins
ALF of pregnancy
Autoimmune hepatitis
Acute Budd–Chiari syndrome
Shock liver
Individual etiological agents
Hepatotropic viruses (A to E)
Cytomegalovirus, herpes simplex virus
Wilson's disease, galactosemia
Paracetamol, isoniazid, rifampicin, sodium valproate
Amanita phalloides

Step 2: Identify ALF and its causes

- In a clinical setting, hepatic injury is usually recognized by appearance of jaundice, and liver failure is recognized by occurrence of encephalopathy, ascites, and coagulopathy.
- Proper history should be taken regarding medications, rash, needlestick injury, blood transfusion, previous surgery, and history of jaundice in family members, to identify the cause of fulminant hepatic failure (FHF) (Table 41.1).
- Other causes of fever with encephalopathy such as bacterial sepsis and tropical infections in endemic areas such as malaria, enteric fever, leptospira, dengue, meningitis, encephalitis, cholangitis, and underlying chronic liver disease should be ruled out.

While initial supportive therapy is being given, diagnostic workup should be sent. These include the following:

- Complete blood count, blood glucose, blood urea nitrogen, creatinine, electrolytes, liver function tests, and prothrombin time
- Arterial blood gases, arterial ammonia and lactate
- Chest X-ray, ECG
- Endotracheal aspirate for aerobic culture in intubated patients, blood culture and urine culture
- Serology including HBsAg, IgM anti-HBc, IgM anti-HEV, IgM anti-HAV, anti-HCV, anti-HDV, and anti-HIV
- Copper studies, autoimmune markers
- Bedside ultrasound

Step 3: Assess prognosis

The assessment of the grade of encephalopathy and prognostic indicators should be done, as described in Tables 41.2 and 41.3. Patients who develop ALF within 7–10 days of the onset of icterus have significantly higher survival rates than those who develop encephalopathy later. However, this is not a universal finding.

Table 41.2 Clinical stages of hepatic encephalopathy

Stage	Mental status	Neuromuscular function
1	Impaired attention, irritability, depression	Tremor, incoordination, apraxia
2	Drowsiness, behavioral changes, memory impairment, sleep disturbances	Asterixis, slowed or slurred speech, ataxia
3	Confusion, disorientation, somnolence, amnesia	Hypoactive reflexes, nystagmus, clonus, muscular rigidity
4	Stupor and coma	Dilated pupils and decerebrate posturing, oculocephalic reflex

Table 41.3 Prognostic criteria in ALF predicting high mortality: King's College and other criteria

Nonparacetamol	Paracetamol
Prothrombin time (PT) >100 s or	Plasma pH < 7.30 or
Any three of the following:	Arterial lactate level >3.5 mmol/L at 4 h or
(a) Age <10 or >40 years	Arterial lactate level >3.0 mmol/L at 12 h
(b) Etiology—non-A, non-B hepatitis	Or
(c) Drug-induced hepatitis	PT > 100 s (INR >6.5) and serum creatinine >3.4 mg/dL in patients with grade 3–4 encephalopathy
(d) Icterus–encephalopathy interval >7 days	
(e) PT > 50 s (INR > 3.5)	
(f) Serum bilirubin > 17.5 mg/dL	
Clichy criteria (France):	
(a) Factor V levels <20% of normal in patients <30 years of age	
(b) Factor V levels <30% of normal in patients >30 years of age	
Prognostic markers in Indian patients with ALF:	
1. Age ≥40 years	Presence of ≥3 of these factors—90% mortality
2. Cerebral edema at admission	
3. Serum bilirubin ≥15 mg/dL	
4. PT ≥ 25 s than normal	

Step 4: Early referral for liver transplant

- If orthotopic liver transplant (OLT) is available, early referral of such patients who have adverse prognostic factors to the transplant center is recommended.
- If the patient is in the transplant center, he or she should be on the transplant list and workup for that should start before the development of advanced encephalopathy or other complications of liver failure develop, which are usually fatal (Table 41.4).
- A balanced view regarding chances of spontaneous recovery with supportive measures, contraindications for transplantation, resources available, and cost consideration needs to be taken judiciously by a multidisciplinary team in each case.
- Prognostic models such as King's College criteria and Acute Physiology and Chronic Health Examination (APACHE) II are helpful in this regard. An APACHE II of more than 15 is associated with increased need for transplantation.

Table 41.4 Causes of death

Cerebral edema
Sepsis
Renal failure
Gastrointestinal bleeding

Step 5: General supportive measures

- Correct fluid status and avoid hypo- or hypervolemia.
- Strict aseptic precautions should be practiced while handling catheter and tubes.
- Administer supplemental oxygen in case of hypoxemia and avoid hypercapnia.
- Avoid hypertension/hypotension.
- Manage fever with surface cooling.
- Neck should be kept in neutral position.
- Minimize external stimuli.
- Monitor blood glucose 2 hourly and maintain between 140 and 180 mg%.
- Monitor serum electrolytes and correct it.
- Nutrition—nasogastric feeding should be started early with gradual increase in protein supplementation.
- Strict aseptic precautions should be followed while handling the lines and catheters.

Step 6: Manage specific problems

(a) Cerebral edema and increased ICP
  - Raise head end 30–45°.
  - Avoid unnecessary stimulation and movement of the patient—it may induce overt features of cerebral edema.
  - Identification of elevated ICP and its management is important because cerebral edema resulting in brainstem herniation is the commonest cause of death among patients with ALF (Table 41.5). Usual recommendation is to keep the ICP below 15 mmHg; however, it is probably more important to maintain the cerebral perfusion pressure (mean arterial pressure minus intracranial pressure) above 50 mmHg.
  - The placement of intracranial transducers is usually avoided in patients with ALF as it may be associated with life-threatening bleeding and sepsis. Further, such interventions do not improve survival, so it is not practiced widely.

(b) Sepsis is the second major cause of death among ALF.
  - Gram-negative bacteria are the major cause of sepsis in these patients.
  - Prophylactic parenteral antibiotics using third-generation cephalosporins may reduce the incidence of sepsis.
  - Fungal infection is also common in this population. Prophylactic fluconazole, in selected cases with multiple-site colonization with yeast, may be used.
  - Surveillance cultures should be sent, and high index of suspicion and low threshold for starting broad-spectrum antibiotics should be practiced.

(c) Renal failure: Both intermittent hemodialysis and continuous renal replacement therapy (CRRT) are equally effective, with later more suitable for unstable patients as it avoids fluctuation in ICP.

Table 41.5 Cerebral edema and raised ICP

Symptoms/signs	Management
Hyperventilation	Elevate the head and the trunk 35–40°
	Avoid vigorous endotracheal suction
	Avoid hyperthermia
	Remove constricting tapes
	Sedate the patient
Bradycardia	100 mL mannitol (20%) stat followed by 1 g/kg q8 hourly
	Hypertonic saline
Focal seizures	Elective intubation in grades 3–4 encephalopathy
	Hyperventilation (target $PaCO_2$ 30–32 mmHg) and hypothermia in selected cases
Decerebrate postures	
Absent pupillary reflexes	

(d) Coagulopathy: Prophylactic use of fresh frozen plasma (FFP) is not helpful unless a planned procedure is followed. Once bleeding occurs, only then FFP and platelet transfusion should be given. FFP can precipitate volume overload in these patients, and in selected cases, off-label use of recombinant factor VII may be considered.
(e) Seizures: Prophylactic therapy with phenytoin is not useful. Levetiracetam may be used for the treatment as it does not have hepatotoxicity.

Step 7: Manage specific situation

(a) Paracetamol overdose—*N*-acetyl cysteine (NAC): 150 mg/kg over 1 h, followed by 12.5 mg/kg/h for 4 h and then 6.25 mg/kg/h for 67 h. NAC has been found to be useful in both acetaminophen and non-acetaminophen-induced ALF.
(b) Special situation—pregnancy
  – Pregnant women who develop acute viral hepatitis are more likely to develop ALF than nonpregnant women.

Step 8: Remember that many therapies have doubtful role in the management of ALF and should not be used (Table 41.6)

Table 41.6 Therapies not useful in ALF

Lactulose
L-Ornithine L-aspartate
Branched-chain amino acids
FFP transfusion in absence of bleeding
Prophylactic phenytoin
Enteral decontamination
Prophylactic hyperventilation for raised intracranial hypertension

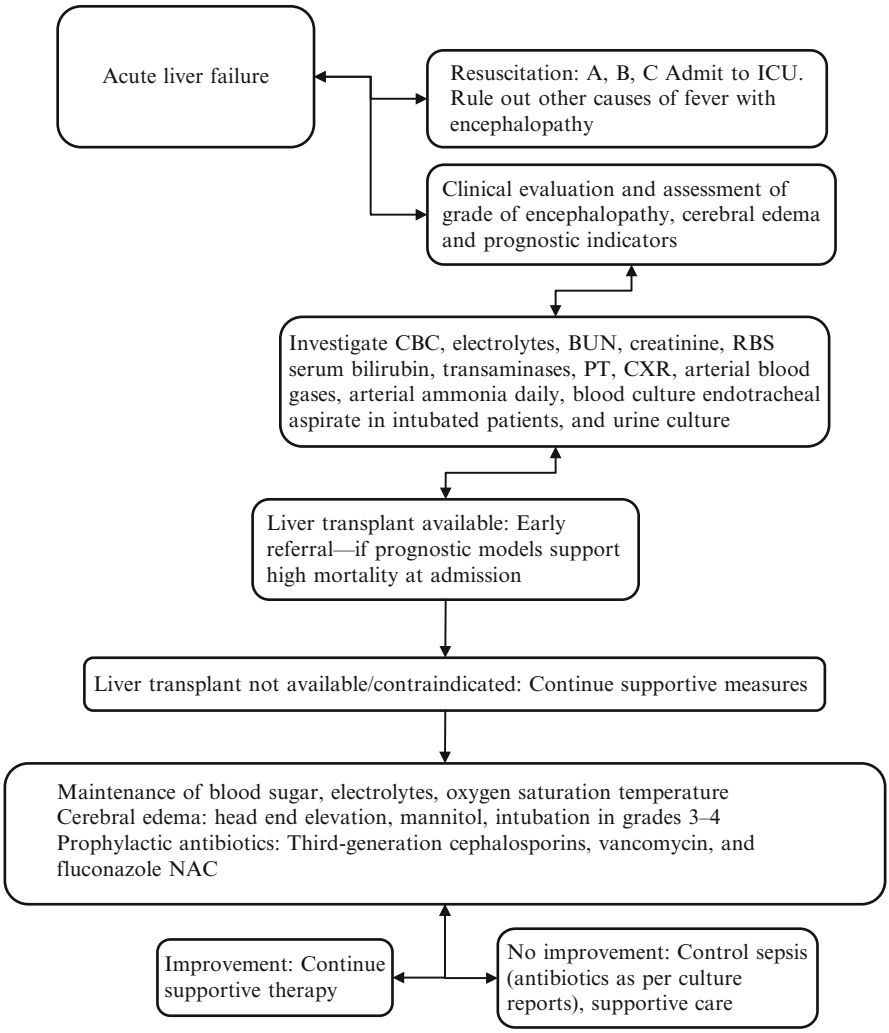

Fig. 41.1 A summary of approach to FHF

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Acute Decompensation in Chronic Liver Failure

42

Deepak Amarapurkar

A 54-year-old male patient, diagnosed to have cryptogenic cirrhosis 3 years back, was brought to the hospital, with abnormal behavior, inability to walk, edema over the feet, and distention of the abdomen for 3 days. On examination, the patient was found conscious but disoriented, having flapping tremors, icteric with edematous feet, and moderate ascites.

Hepatic encephalopathy of any form is seen in 50–70% patients of cirrhosis. Mortality in patients of cirrhosis with encephalopathy ranges from 30% to 50% at the end of 1 year and 70% at the end of 3 years.

Step 1: Initiate resuscitation

- All patients who have altered sensorium and cannot maintain their airway require immediate attention to airway. This assessment is done mainly by clinical means.
- They should be put on high-flow oxygen to increase SpO_2 to above 90%. Patients who are unable to maintain their oxygenation are put on assisted ventilation.
- Circulation needs to be maintained by fluid infusion. If clinically there is evidence of cardiac impairment, fluids should be given cautiously.

Step 2: Take history to identify precipitating factors

In a patient of cirrhosis with acute worsening, take history to identify the precipitating factors. Usual precipitating factors in acute encephalopathy are shown in Table 42.1.

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Table 42.1 Precipitating factors in portosystemic encephalopathy

Gastrointestinal bleeding
Constipation
Large protein meal
Psychoactive drugs
Electrolyte imbalance—hypokalemia and hyponatremia
Infections
Superimposed acute hepatic injury
Alkalosis
Sedation

Step 3: Send investigations

The following investigations should be sent:

- Complete blood count
- Liver function tests including prothrombin time
- Blood glucose, urea, serum creatinine, serum electrolytes
- Blood culture
- Arterial ammonia level
- Urine examination including culture
- Chest X-ray posteroanterior view
- Ultrasound examination of the whole abdomen including liver, spleen, portal vein, kidneys, ureter, and bladder (KUB) and ascites
- Ascitic fluid examination including culture of the fluid, inoculated in the blood culture bottle at bedside

Step 4: Stage encephalopathy

Once hepatic encephalopathy is diagnosed, it should be staged as shown in Table 42.2.

Table 42.2 Clinical stages of hepatic encephalopathy

Stage	Mental status	Neuromuscular function
1	Impaired attention, irritability, depression	Tremor, incoordination, apraxia
2	Drowsiness, behavioral changes, memory impairment, sleep disturbances	Asterixis, slowed or slurred speech, ataxia
3	Confusion, disorientation, somnolence, amnesia	Hypoactive reflexes, nystagmus, clonus, muscular rigidity
4	Stupor and coma	Dilated pupils and decerebrate posturing, oculocephalic reflex

Step 5: Manage hepatic encephalopathy

(A) *Standard Therapeutic Measure in Hepatic Encephalopathy*

- Nutritional management:
  - Normal protein diet for episodic hepatic encephalopathy
  - 1–2 g of protein per kg/day
  - Zinc replacement

- Reduction in nitrogenous load arising from the gut.
- Bowel cleansing.
- Nonabsorbable disaccharides—lactulose is a first-line pharmacological treatment for hepatic encephalopathy. Lactulose should be given to have two to three loose stools per day.
- Antibiotics—a therapeutic alternative to nonabsorbable disaccharides for treatment in acute and chronic encephalopathy and cirrhosis. Rifaximin is equally effective as lactulose. Rifaximin is used up to 1,200 mg/day in divided doses.
- Ornithine aspartate in oral or intravenous form is only useful for a short duration. It should be avoided in renal dysfunction.
- Drugs that affect the neurotransmission—flumazenil and bromocriptine administration may have a therapeutic role in selected patients.
- Manipulation of the splanchnic circulation—closure of large portosystemic shunts.

(B) *Renal Failure in Cirrhosis*

Step 1: Assess the renal function

- Measuring renal function in cirrhosis:
  - Creatinine of more than 1.5 mg/dL is considered renal failure.
- Fallacies of measuring creatinine:
  - Underestimation of severity of renal dysfunction due to poor muscle mass. Creatinine may be falsely low.
  - Small changes in creatinine (0.4–0.8) may signal significant declines in glomerular filtration rate.

Step 2: Assess the cause of renal dysfunction

- Important causes of renal failure are given in Table 42.3.

Table 42.3 Causes of renal dysfunction in cirrhosis

Acute	Chronic
Hypovolemia	Glomerulonephritis
Diuretics	Hepatitis B
Gastrointestinal bleed	Hepatitis C
Diarrhea (lactulose-induced)	IgA nephropathy (alcoholic)
Nephrotoxic drugs	Diabetic nephropathy
Aminoglycosides	
Nonsteroidal anti-inflammatory drugs	
Contrast agents	
Sepsis	
Acute kidney injury	

Step 3: Workup of renal dysfunction in patients with cirrhosis

- Evaluate to find the cause and severity of renal dysfunction in cirrhosis.
- One of the very important investigations of such a patient is urine examination (Table 42.4).

Table 42.4 Typical urinalysis in renal dysfunction in cirrhosis

Cause	Osmolality (mOsm/kg)	Urine sodium (mmol/L)	Sediment	Protein (mg/day)
Prerenal hypovolemia	500	<20	Normal	<500
Hepatorenal syndrome (HRS)	500	<20	Nil	<500
Intrinsic				
ATN	<350	>40	Granular casts	<500
Acute interstitial nephritis (AIN)	<350	>40	RBC and eosinophils	500–2,000
Acute glomerulonephritis (AG)	Variable	Variable	WBCs, red cell casts	

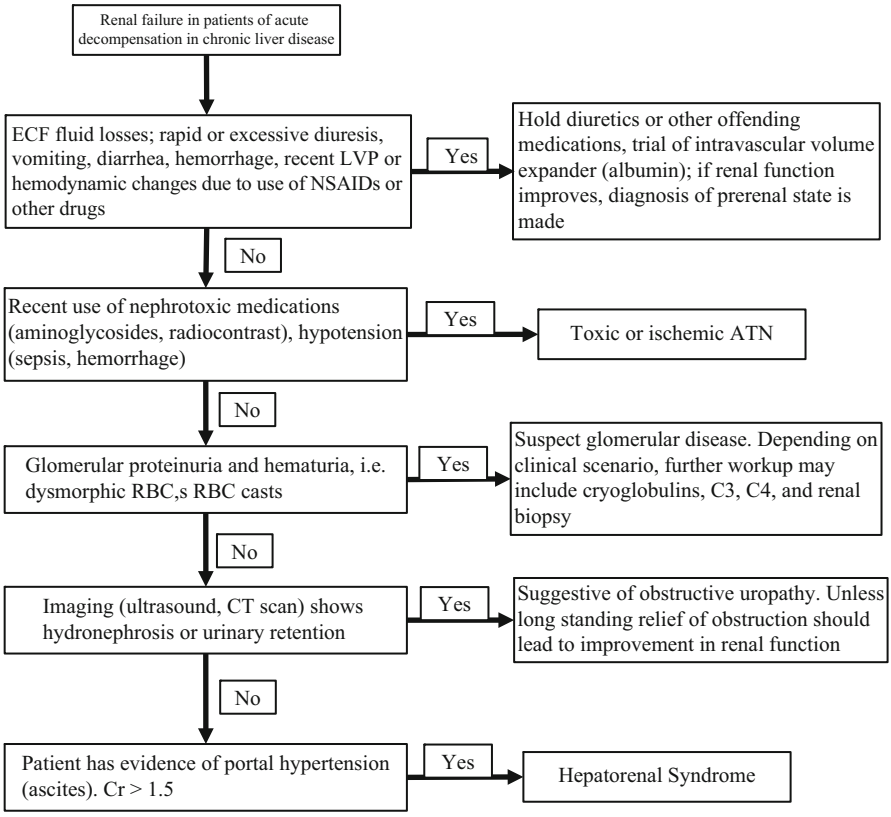

Fig. 42.1 Evaluation and management of renal failure

Step 4: Diagnose and manage renal failure

- Management depends on the type of injury. If there is an obvious precipitating factor like volume depletion, it should be corrected. Nephrotoxic drugs should be stopped, and diuretics should be withheld. If there is sepsis, appropriate antibiotics should be used (Fig. 42.1).

Step 5: Identify Hepatorenal syndrome

- (HRS) HRS is a reversible functional renal impairment that occurs in patients with advanced liver cirrhosis or those with fulminant hepatic failure. It requires quick recognition of type of hepatorenal syndrome (Table 42.5) and aggressive management; otherwise outcomes are bad.

Table 42.5 Hepatorenal syndrome

Type 1	Type 2
Rapid reduction in renal function in less than 2 weeks	Renal function slowly deteriorates over weeks to months
Doubling of initial serum creatinine to >2.5 mg/dL or 50% Reduction of the initial 24-h creatinine clearance to <20 mL/min	Increase in serum creatinine to more than 1.5 mg/dl or creatinine clearance less than 40 ml/mt
	Occurs in cirrhotic patients with refractory ascites
Severely ill patients	Mild jaundice
Jaundice	Some degrees of coagulopathy
Coagulopathy	

Step 6: Treat hepatorenal syndrome

- Measure creatinine clearance in the patient with tense ascites.
- Use diuretics judiciously if creatinine clearance is low.
- Avoid nonsteroidal anti-inflammatory drugs.
- Avoid aminoglycosides.
- Treat volume depletion aggressively.
- Treat infection and sepsis aggressively.
- Restrict Na+ intake to 1 g/day.
- If serum Na+ is less than 125 mEq/L, restrict fluid intake.
- Treat gastrointestinal bleeding.
- Use intravenous plasma expanders and vasoconstrictors.
- Consider liver transplant if the patient has refractory ascites or refractory hypotension.
- Recommendations for the use of vasoconstrictors in patients with type 2 hepatorenal syndrome:
  - The goal of treatment is to reduce serum creatinine concentrations to ≤1.5 mg/dL (130 μmol/L).
  - Terlipressin at a dose of 0.5 mg should be given intravenously every 4 h; the dose can be increased in a stepwise fashion (i.e., every 2 days) to 1 mg every 4 h and then up to 2 mg every 4 h in cases of where there is no reduction in the serum creatinine concentration.
  - Alternatively a continuous infusion of terlipressin at a dose of 2 mg/day can be given. When the serum creatinine concentration does not reduce by at least 30%, the dose can be increased every 2 days up to 12 mg/day.

- Alternative drugs are midodrine, octreotide, and norepinephrine; the doses are as follows:
  - 2.5–7 mg midodrine should be given orally three times daily, increasing to 12.5 mg three times daily if needed.
  - 100 μg octreotide should be given subcutaneously or intravenously three times daily, increasing to 200 μg three times daily if required.
  - Norepinephrine titrated to 0.5–3 mcg/kg/min should be given as a continuous intravenous infusion.
  - Contraindications include coronary artery disease, peripheral vascular disease, and/or cerebrovascular disease because of the potential risk of ischemic events.
- Concomitant intravenous albumin infusion (1 g/kg body weight on the first day, followed by 20–40 g per day) is recommended.
- The duration of therapy should be approximately 7–14 days.

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Nutrition Support

43

Pravin Amin

A 25-year-old male patient (175 cm in height and 80 kg in weight), involved in a motorcycle accident, was admitted to the ICU. He had several high rib fractures and a flail segment on his left chest wall with associated major lung contusion and hemopneumothorax on the left side. He had blunt injury to abdomen with large bruises in the epigastrium. He had fractured both tibia and femur in the right lower limb. His blood pressure on arrival was 70/40 mmHg, heart rate was 145/min, and respiratory rate was 42/min. He was fully conscious but in distress. You had been asked to formulate a nutritional plan for him.

Nutritional support is an integral part of organ support in the ICU. A systematic and protocolized approach to nutrition support by a dedicated nutrition support team is ideal to minimize complications of the ICU stay.

Step 1: Initial resuscitation

- Achieving hemodynamic stability is of paramount importance before considering nutritional support. Nutrition should be started as soon as the patient is resuscitated.

Step 2: Assess nutritional status

- Initial assessment of nutritional status is important as many patients are malnourished on admission and require early nutritional support.
- Traditional methods of nutritional assessment like calculation of body mass index = weight (kg)/height (m^2). Anthropometry—triceps skinfold, mid-arm

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Table 43.1 Subjective global assessment of nutritional status

(A) History
1. Weight change
2. Dietary intake change relative to normal
3. Gastrointestinal symptoms (persisting for more than 2 weeks)
4. Functional capacity
5. Disease and its relationship to nutritional requirements
(B) Physical examination (for each specify: 0 = normal, 1 + = mild, 2 + = moderate, 3 + = severe)
Loss of subcutaneous fat (triceps, chest)
Muscle wasting (quadriceps, deltoids)
Ankle edema/sacral edema/ascites
(C) Subjective global assessment rating
Well nourished
Moderately malnourished
Severely malnourished

muscle circumference, and creatinine-height index. Laboratory assessment—albumin, prealbumin, transferrin, serum cholesterol, and C-reactive protein are not very reliable in critically ill patients.

- Bedside clinical assessment by "eye balling" and subjective global assessment by history and simple physical examination are more reliable (Table 43.1).

Step 3: Calculate ideal (predicted) body weight

- In most critically ill patients, body weight cannot be measured, and ideal (predicted) body weight (IBW) needs to be calculated by height. Most of the nutritional formulae are based on ideal body weight:
  - Male IBW (kg) = 50 + (0.91 × (height in centimeters − 152.4)) or 50 kg for 5 ft, add 2.3 kg for every 1 in. above 5 ft.
  - Female IBW (kg) = 45.5 + (0.91 × (height in centimeters − 152.4)) or 45.5 kg for 5 ft, add 2.3 kg for every 1 in. above 5 ft.

Step 4: Estimate energy (calories) requirement

- Rule of the "thumb": 25–30 kcal/kg IBW meets most patients' needs.
- In undernourished patients, initial calorie should be 25% less than IBW to prevent refeeding, and in overweight patients, initial calorie should be 25% more than IBW to meet requirement.
- In a malnourished patient, a large glucose and calorie load can cause a massive shift of potassium, phosphate, and magnesium to intracellular compartment, leading to a precipitous fall of these electrolytes in the plasma, resulting in cardiorespiratory failure. This phenomenon is called refeeding syndrome. Phosphate, magnesium, and potassium should be checked and adequately replaced, and calories and glucose load should be gradually increased in such patients.
- Formulas like Harris–Benedict may be used to calculate calorie requirement, but are time-consuming and not validated in critically ill patients (Table 43.2).

Table 43.2 Harris–Benedict equation with Long's modification

Harris–Benedict formula for women	Basal metabolic rate (BMR) = 655 + (9.6 × weight in kg) + (1.8 × height in cm) − (4.7 × age in years)		
Harris–Benedict formula for men	BMR = 66 + (13.7 × weight in kg) + (5 × height in cm) − (6.8 × age in years)		
Actual energy needs = BMR × AF × IF			
Activity factor (AF)	*Use*	*Injury factor (IF)*	*Use*
Confined to bed	1.2	Minor surgery	1.2
Out of bed	1.3	Skeletal trauma	1.3
		Major sepsis	1.6

Table 43.3 Protein requirements

No stress	0.7–0.8 g/kg/day
Mild stress	0.8–1.0 g/kg/day
Moderate stress	1.0–1.5 g/kg/day
Severe stress	1.5–2.0 g/kg/day

- Carbohydrates usually form 70–75% of calories. Fats usually form 25–30% of calories, not more than 40–50%.
- Protein intake should not be calculated as a calorie source.
- Indirect calorimetry may be used for calorie calculation and measuring respiratory quotient. A high respiratory quotient of more than 1 indicates carbohydrate as a predominant source of energy. It cannot be used in patients requiring high inspired oxygen, air leaks, or chest tubes.

Step 5: Estimate protein (nitrogen) requirement

- Rule of the "thumb": 1.5–2 g of protein/kg IBW meets most patients' needs (Table 43.3):
  - 6.25 g of protein is equal to 1 g of nitrogen.
  - Non Protein Calorie (NPC)–nitrogen ratio = 150 cal (NPC): 1 g nitrogen.
- Nitrogen requirement may also be assessed by calculating nitrogen balance:
  - Nitrogen balance = nitrogen intake − nitrogen output.
  - Nitrogen intake = protein intake/6.25.
  - Nitrogen output = 24-h urinary urea nitrogen + 4 (nonurinary nitrogen).
  - This should be done once weekly in all severely ill patients with a normal renal function. Try to achieve at least equal nitrogen balance.

Step 6: Supplement micronutrients

- Vitamins and the trace of elements should be added as per recommended daily allowance, which are present in formula feed.

Step 7: Estimate fluid and electrolyte requirement

- Rule of the "thumb": 1 ml/cal is the minimum requirement of fluid to deliver isocaloric feed.
- Electrolyte should be tailored to individual patients' requirement.

Step 8: Select route of delivering nutrition

- Whenever the gut is working, use it. Advantages of enteral feed are as follows:
  - Preservation of the integrity and function of the gastrointestinal tract
  - Maintenance of splanchnic blood flow
  - Provision of nutrition to the enterocytes
  - Fewer infectious and metabolic complications
  - Ease of administration, lower costs, and avoiding the disadvantages of total parenteral nutrition (TPN)
- Enteral feeding may be given through nasogastric, nasojejunal, gastrostomy, or jejunostomy tubes. There is no significant difference in the efficacy of jejunal versus gastric feeding in critically ill patients.
- Intragastric feeding should be the first choice because it is easy and relatively safe, and the majority of patients tolerate it:
  - The head of the bed should be elevated to 30–45°.
  - Give continuous rather than bolus feedings; start with 25 cc intragastrically every hour to a target rate of 50–75 cc/h, in most adults preferably through a feeding pump.
  - Check residual 2 h after initiating feeding and every 8 h thereafter.
  - IV administration of metoclopramide should be considered in patients with intolerance to enteral feeding, for example, with high gastric residuals (>300 in 4 h or more than one-third of enteral feed being aspirated).
- Jejunal feed can be tried if the patient has high gastric residue despite prokinetic and correction of electrolytes.

Step 9: Select the type of enteral feed

- Blenderized diets: It may not be complete and balanced. Nutritive value is difficult to estimate, and highly viscous solution needs a large-bore nasogastric tube. Large particles may block the feeding tubes, and nutrients are not predigested. Bacterial overgrowth is a distinct possibility.
- Polymeric diets: These contain nitrogen as whole protein and are balanced and compete. The carbohydrate source is partially hydrolyzed starch, and the fat contains long-chain triglycerides. Their fiber content is very variable.
- Predigested diets: These feeds contain nitrogen either as short peptides or, in the case of elemental diets, as free amino acids. Carbohydrate provides much of the energy. The rest of the calorie proportion is provided as long-chain triglycerides and medium-chain triglycerides. The aim of "predigested diets" is to improve nutrient absorption in the presence of significant malabsorption.
- Disease-specific diets: Patients with respiratory failure are often given feeds with a low carbohydrate-to-fat ratio to minimize carbon dioxide production. Renal patients often require modified protein, electrolyte, and volume feeds. Liver patients may need low sodium, low volume feeds. There is no good evidence that patients with hepatic encephalopathy should have low protein intakes, and the evidence for the benefit of feeds rich in branched-chain amino acids is weak.
- Immunonutrition: Glutamine should be added to a standard enteral formula in burned patients and trauma patients. The immune-modulating formula enriched with arginine, nucleotides, and ω-3 fatty acids may be given to selective upper

gastrointestinal surgical patients, but can be harmful to patients with severe sepsis and septic shock. As per current guidelines, patients with acute respiratory distress syndrome should receive enteral nutrition (EN) enriched with omega-3 fatty acids and antioxidants.

Step 10: Look for tolerance to enteral feed

- Signs of intolerance include bloating, nausea, cramps, abdominal distention, or diarrhea, but these signs are nonspecific.
- Intragastric feeds should not be stopped for residuals of less than 200 ml.
- Significant distention or complaints of cramping by the patient should warrant slowing or discontinuing the feeds.
- In case of diarrhea, follow a standard protocol (see Fig. 43.1).

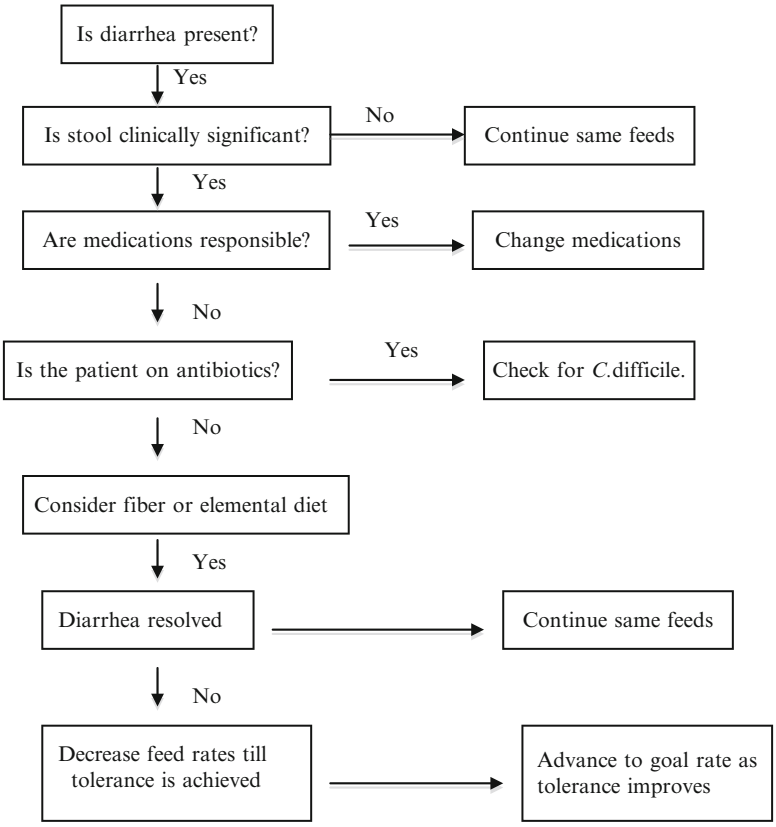

Fig. 43.1 Resolving tube feeding-associated diarrhea

Step 11: Select candidates for parenteral nutrition

- Parenteral nutrition is indicated for some critically ill patients in the following situations:

  - Signs of abnormal gut function (complete intestinal obstruction, mesenteric ischemia, bowel fistula).
  - Patients cannot consume adequate amounts of nutrients by enteral feeding.
  - They are not expected to be able to eat orally by 3–7 days and are malnourished.

Step 12: Select the route of total parenteral nutrition (TPN)
TPN can be provided by peripheral or central route:
- Peripheral (partial or supplemental) parenteral nutrition:
  - Minimizes cost and complications of the central catheter
  - Can provide supplemental calories and protein not met by enteral route
  - Phlebitis, requires frequent site rotations and fluid overload
- TPN by central route:
  - Preferably a multilumen catheter with a single lumen dedicated to TPN.
  - TPN being delivered as an "all-in-one" solution as a commercially available standard solution, or made-to-order solution from a pharmacist-based mixing center.
  - Supplementing parenteral glutamine to the TPN formula is known to reduce infectious complication, length of ICU stay, and mortality in burn and trauma patients.

Step 13: Monitor patients on parenteral nutrition
- This consists of clinical examination, fluid balance, catheter care, and blood glucose monitoring.
- Renal, liver, and lipid profiles should be measured weekly.

Step 14: Look for complications of TPN
- Mechanical complications:
  - Related to vascular access technique
  - Venous thrombosis
  - Catheter occlusion
- Metabolic complications:
  - Hyper-/hypoglycemia
  - Electrolyte abnormalities
  - Acid–base disorders
  - Hyperlipidemia
  - Steatosis
- Infectious complications

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Part V

Renal System

Raj Kumar Mani and Arghya Majumdar

Acute Renal Failure

44

Raj Kumar Mani and Arghya Majumdar

A 30-year-old male victim of a road traffic accident was admitted with pelvic fracture. An external fixator was applied the same day. The following day he suffered a massive pulmonary embolism requiring thrombolysis. He started becoming oliguric. On the fourth day, he developed retroperitoneal hemorrhage with an intra-abdominal pressure of 22 mmHg, as a complication of anticoagulation. He required surgical drainage. He went on to develop progressive renal failure requiring dialysis support.

A systematic approach to oliguria in the ICU patient is mandatory due to the multifactorial etiology of this problem, potential to deteriorate to anuria, and need for renal replacement therapy. Timely diagnosis and prompt intervention will decrease morbidity and mortality from this potentially preventable problem. Mortality rate in patients with acute kidney injury in the ICU is in excess of 50%.

Step 1: Resuscitate

- Optimizing oxygenation and hemodynamics is of prime importance in preventing kidney injury (refer to Chap. 78).

Step 2: Differentiate urinary retention from oliguria

- By definition, oliguria is less than 0.5 mL/kg urine output for at least 2 h.
- Perform suprapubic percussion for bladder fullness in all cases of low urine output to exclude retention of urine.

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- Sudden drop of urine output, no urine or fluctuating levels of urine output in a catheterized patient who is otherwise stable, may indicate a partial or complete catheter block with clot or debris or pericatheter leak. Ascertain this by physical examination, bladder wash, or replacing the catheter.
- Bedside ultrasonography differentiates retention from oliguria and at the same time confirms the catheter position.

Step 3: Ascertain the cause of oliguria (Table 44.1)

- First consider whether it is a prerenal, renal, or postrenal cause.
- Proper history should be taken including fluid loss, drug history (nonsteroidal anti-inflammatory drugs [NSAIDs]), exposure to contrast, urinary symptoms, and fever; perform physical examination for evidence of hypovolemia, abdominal distension, and skin rash.
- Prerenal factors are by far the most frequent. Volume deficit is the commonest cause.
- For renal factors, pay attention to the nephrotoxic potential of antibiotics, analgesic, or radiocontrast agent.
- Postrenal factors like urethral injury and bladder outflow tract obstruction are common causes.

Step 4: Send biochemical investigations to ascertain severity and cause of acute kidney injury (AKI)

- Serum chemistry including sodium; potassium; creatinine; blood urea nitrogen (BUN); calcium; magnesium; phosphate; uric acid; creatine phosphokinase (if rhabdomyolysis is suspected); total protein, albumin, globulin, and unconjugated bilirubin (to exclude hemolysis); and lactate dehydrogenase (LDH) should be checked.
- If clinically indicated, antinuclear factor (ANA), antiglomerular basement membrane antibody, antineutrophil cytoplasmic antibodies (ANCA), complement levels (C_3, C_4), cryoglobulin, and hepatitis B and C serology test may be performed.
- Serum and urine protein electrophoresis should be performed in patients with bone pain, hypercalcemia, and hyperglobulinemia where paraproteinemia is suspected.

Step 5: Examine the urine (Table 44.2)

- This can yield vital clues with regard to the type of renal failure. Microscopic examination of the urinary sediment should not be neglected.
- In prerenal failure, urine examination is usually bland, and no casts or cells will be obvious. Hyaline casts may be the only finding.
- In intrinsic renal disease, one may find RBC casts and dysmorphic RBCs indicating glomerular hematuria, eosinophil casts in allergic interstitial nephritis, muddy brown epithelial casts in acute tubular damage, or coarse granular or broad casts, which might indicate background chronic kidney disease (CKD).

Table 44.1 Causes of AKI

Prerenal	Renal	Postrenal
Hypovolemia	Acute tubular necrosis	Ureteric
Gastrointestinal fluid loss—vomiting and diarrhea	Ischemic	Obstruction
Renal fluid loss—diuretics, osmotic diuresis (diabetes), hypoadrenalism	Toxins	External compression (retroperitoneal fibrosis)
Burns	(a) Exogenous: IV contrast, antibiotics (e.g., aminoglycosides), CyA, chemotherapy (e.g., cisplatin), ethylene glycol	Calculi
Hemorrhage	(b) Endogenous: Hb, myoglobin, uric acid, oxalate, myeloma	Sloughed papilla
Sequestration in extravascular space—pancreatitis, trauma, and low albumin		Cancer
		Blood clot
	Acute interstitial nephritis	
	Idiopathic	
	Infection: viral (CMV), fungal, bacterial (pyelonephritis)	
Low cardiac output states	Infiltration: lymphoma, leukemia, sarcoid	
Disease of myocardium, valves, pericardium, tamponade	Allergic drugs: antibiotics, NSAIDs, diuretics	*Bladder neck obstruction*
Arrhythmias	*Disease of the glomeruli*	Neurogenic
Massive pulmonary embolus	Acute glomerulonephritis	Calculi
	Vasculitis	Cancer
Low renal perfusion pressure	Hemolytic uremic syndrome, thrombotic thrombocytopenic purpura, disseminated intravascular coagulation, preeclamptic toxemia, systemic lupus erythematosus, scleroderma, radiation	Prostatic hypertrophy
Shock (e.g., sepsis)		Blood clot
Abdominal compartment syndrome		
Altered renal—systemic vascular resistance ratio		
Systemic vasodilatation—sepsis, antihypertensives, anesthesia		

(continued)

Table 44.1 (continued)

Prerenal	Renal	Postrenal
Hypovolemia	Acute tubular necrosis	Ureteric
	Renovascular	
	Renal vein—thrombosis	*Urethral obstruction*
	Renal artery—stenosis, plaque, embolism, thrombus, aneurysm	Stricture
	Intratubular deposition and obstruction	Congenital valves
Renal vasoconstriction	Myeloma proteins	Phimosis
Hypercalcemia	Uric acid	
Norepinephrine, vasopressor agents	Oxalate	
CyA, tacrolimus	Acyclovir crystals	
Cirrhosis with hepatorenal syndrome	Methotrexate	
Hyperviscosity	Sulfonamides	
Multiple myeloma	Renal allograft rejection	
Macroglobulinemia		

Table 44.2 Urinary biochemistry

	Prerenal	Renal
Urine osmolality	>500 mosmols/kg	<350 mosmols/kg
Urine sodium	<10 mEq/L	>20 mEq/L
Urine/plasma osmolality ratio	>1.5	<1.2
Urine/plasma urea nitrogen ratio	>8	<3
Urine/plasma creatinine ratio	>40	<20
Plasma BUN/creatinine ratio	>20	<10
Urine specific gravity	>1.020	~1.010
Fractional excretion of sodium (FeNa)%	<1	>1
Urine/plasma Na divided by urine/plasma creatinine × 100		

- Uric acid or calcium oxalate crystals may highlight a background metabolic problem.
- RBC and WBC casts are fragile, and their absence does not exclude underlying parenchymal disease.
- Dipstick test is vital. It might reveal proteinuria, hematuria, glycosuria, ketonuria, bilirubin, or urobilinogen. A positive dipstick for hemoglobin in the absence of RBCs in the urine sediment may suggest hemolysis or myoglobinuria (which can be confirmed by specific assays).
- A positive nitrite test may indicate infection. High specific gravity and ascorbic acid may interfere with the test.
- Urine biochemistry test should be performed to differentiate prerenal from renal failure (Table 44.2).

Step 6: Monitor the patient carefully

- Ensure continuous monitoring of urine output, by placing an indwelling urinary catheter.
- Continuous monitoring of hemodynamic parameters is also mandatory.
- Intra-abdominal pressure (IAP) monitoring is very important, especially when large volumes of fluids or blood products are infused, as they may third space into the peritoneal cavity if there is capillary leak due to systemic inflammatory response syndrome (SIRS) after trauma, sepsis, or abdominal surgery.
- IAP of less than 12 mmHg indicates normal condition, 12–20 mmHg indicates intra-abdominal hypertension, and more than 20 mmHg with organ dysfunction indicates abdominal compartment syndrome.

Step 7: Perform renal imaging

- Abdominal ultrasound or noncontrast CT scan would be useful to diagnose renal and postrenal oliguria.
- An ultrasonography may reveal echogenic or small kidneys with loss of corticomedullary differentiation, which might indicate a background of chronic kidney disease. However, in some conditions such as diabetes, amyloidosis, and multiple myeloma, kidney size may be normal even with chronic disease. A

discrepancy in kidney size (>2 cm) may suggest unilateral renal artery stenosis. Color Doppler flow can be used to assess renal perfusion and rule out thrombosis. Multiple bilateral cortical cysts may indicate polycystic kidney disease.
- The presence of hydronephrosis and/or hydroureter is suggestive of a postrenal cause. However, a dehydrated patient may not exhibit significant hydronephrosis. Postvoidal residual urine of more than 100 mL is suggestive of bladder outlet obstruction.
- Volume status can be assessed by checking the diameter and collapsibility of the inferior vena cava.
- Radiologic examination is useful for detecting renal stones and pelvic fractures. However, fecoliths may masquerade as stones, and without proper bowel preparation, it is difficult to delineate stones.
- Occasionally an intravenous urogram, contrast CT (if renal function is normal), MRI, or retrograde/antegrade (percutaneous) contrast studies may be necessary to delineate the site or nature of obstruction or injury.
- Nuclear scans may be used to assess renal function, perfusion, or obstruction.

Step 8: Be wary of sepsis
- Always suspect sepsis, whether as the primary cause or as an intercurrent complication. In such instances, the promptness and appropriateness of antibiotics can save lives.
- In case of postrenal oliguria and urosepsis, urgent urological intervention such as urinary drainage using ureteric catheterization, DJ stents, or percutaneous nephrostomy may be required, as source control is vital. Perinephric collections of pus or blood may need drainage too (Fig. 44.1).

Step 9: Maintain renal perfusion pressure
- Maintain mean arterial pressure (MAP) of more than 65 mmHg by adequate volume loading and with vasopressors if necessary. MAP may have to be kept higher if the patient is hypertensive or has a high IAP.
- Individual titration is necessary in this regard. In cases of high IAP, renal perfusion pressure is equal to MAP–2 × IAP, and a higher MAP is desirable. Dose of vasopressors should be kept to minimum, which is necessary for maintaining an adequate MAP, and every attempt should be made to reduce dose of vasopressors.
- Invasive hemodynamic monitoring (arterial line and central line) is usually needed in these cases.
- There is no role of renal dose of dopamine to increase renal perfusion.
- Dobutamine should be used to optimize cardiac output, provided there is no tachycardia or arrhythmia (refer to Chap. 18).
- Occasionally one may have to take recourse to an intra-aortic balloon pump (IABP) for hemodynamic optimization in cardiogenic shock.
- Medical (e.g., diuresis, drainage of ascites) and surgical measures (e.g., opening up of abdominal sutures) should be taken up, where possible, to reduce intra-abdominal hypertension.

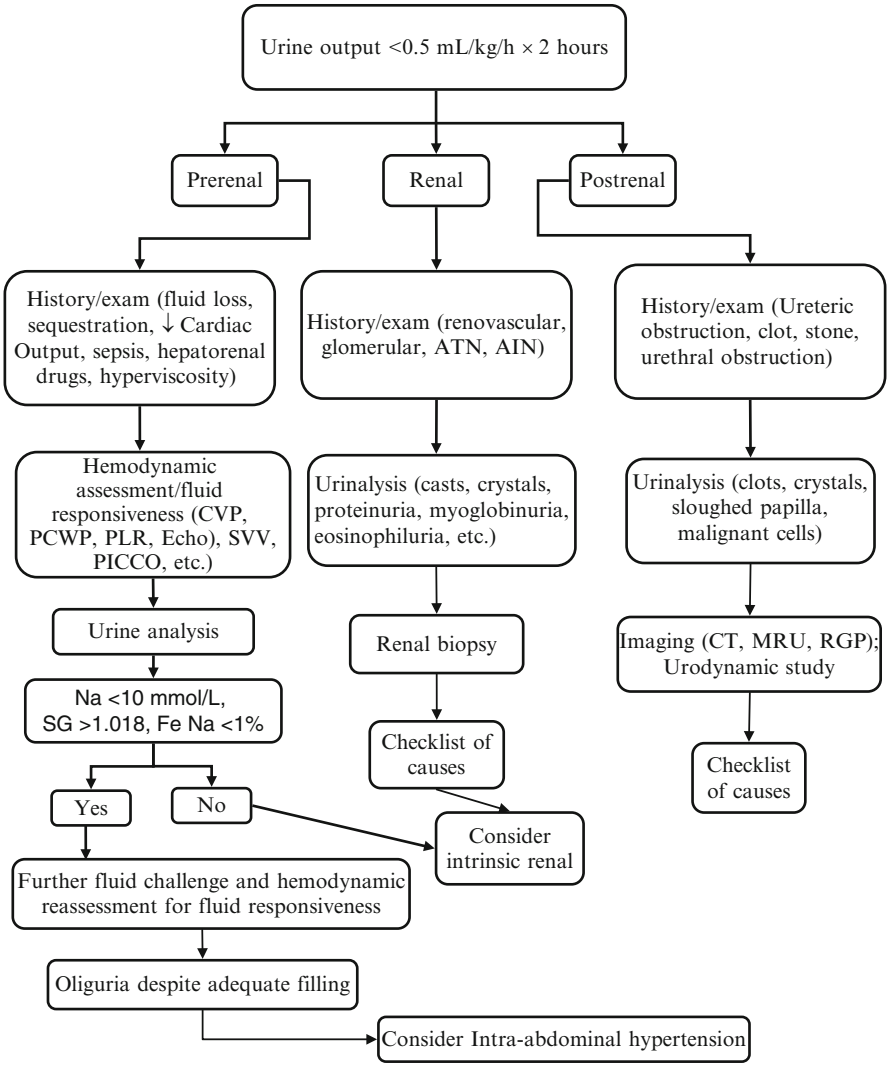

Fig. 44.1 Approach to oliguria

Step 10: Use diuretics judiciously

- Weigh the potential benefits versus risks of a trial of intravenous diuretics. The role of diuretic therapy has been questioned as it does not affect renal outcome. However, in nonoliguric renal failure, management of the patient becomes easier. It creates some intravascular space for administering nutrition, intravenous antibiotics, blood, and blood products, where necessary.

However, diuretics have been shown to be detrimental too. They create an acidic urine milieu, which might predispose to myoglobin precipitation and oxalate crystallization. The potential toxicities of diuretics include worsening of hypovolemia,

metabolic alkalosis, and interstitial nephritis. Further, a diuretic response may delay a search for correctable causes of oliguria.

Step 11: Correct metabolic abnormalities

- Look for and manage metabolic abnormalities, which may be a result of renal impairment such as hyperkalemia, hyper/hyponatremia, and hypocalcemia.
- Look for causative factors such as hypercalcemia or hyperuricemia.
- Frequent monitoring of electrolytes may be necessary.
- The usual urea–creatinine ratio is 10:1. An unusually high urea–creatinine ratio is suggestive of volume depletion, gastrointestinal bleeding, catabolic state, or high protein feed.
- A high creatinine–urea ratio is associated with rhabdomyolysis or may indicate chronic kidney disease (CKD).
- If rhabdomyolysis is suspected, the maintenance of urinary pH to more than 7 by systemic alkalinization is indicated.

Step 12: Avoid any potentially nephrotoxic agent

- In high-risk cases, along with hydration with 0.9% saline, *N*-acetyl cysteine at a dose of 600 mg twice per day may be administered for 3 days from a day prior to elective radiocontrast imaging study.
- Low osmolality or preferably iso-osmolar contrast should be used.
- Avoid nephrotoxic antibiotics. Aminoglycosides, if used, should be dosed once daily.
- Lipid formulations of amphotericin are preferable.
- Intravenous use of voriconazole may cause nephrotoxicity due to β-cyclodextrin.
- Intravenous acyclovir may cause crystal nephropathy.
- High-dose mannitol may lead to osmotic nephropathy.
- NSAIDs should be avoided.

Step 13: Strive to detect acute kidney injury (AKI) as early as possible (Table 44.3)

- The Acute Dialysis Quality Initiative (ADQI) group, composed of nephrologists and intensivists, has laid down definitive criteria for diagnosing AKI, which has been universally accepted and validated.
- This is the RIFLE criteria (risk, injury, failure, loss, end-stage kidney disease), which should now be followed in all ICUs to stratify AKI.

Table 44.3 RIFLE criteria

Category	Glomerular filtration rate (GFR) criteria	Urine output (UO) criteria
Risk	Increased creatinine × 1.5 or GFR decrease >25%	UO <0.5 mL/kg/h × 6 h
Injury	Increased creatinine × 2 or GFR decrease >50%	UO <0.5 mL/kg/h × 12 h
Failure	Increased creatinine × 3 or GFR decrease >75%	UO <0.3 mL/kg/h × 24 h or anuria × 12 h
Loss	Persistent acute renal failure = complete loss of kidney function in >4 weeks	
ESKD	End-stage kidney disease (>3 months)	

- Once a patient is considered to be in failure according to this criterion, the issue of renal replacement therapy arises, and early nephrology consultation is useful.
- Serum and urinary biomarkers like NGAL (neutrophil gelatin-associated lipocalin) have been found to be useful in early detection of AKI.

Limitations of using these parameters for differentiating prerenal from renal injury: use of diuretics, postcontrast i.v. contrast, CKD, elderly, acute glomerulonephritis, acute interstitial nephritis, hyperglycemia, and hepatorenal syndrome.

Suggested Reading

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Websites

1. www.renalandurologynews.com
   A comprehensive site for clinical trial summary on AKI
2. www.ADQI.net
   Homepage for RIFLE criteria network
3. www.kidneycare.nhs.uk
   A site for information on preventive aspects of AKI

Renal Replacement Therapy

45

Sunil Prakash and Arghya Majumdar

A 50-year-old diabetic and hypertensive male patient was admitted with acute pancreatitis requiring ventilatory support. Despite aggressive volume resuscitation, he had a mean arterial pressure (MAP) of 60 mmHg on multiple vasopressors. An echo showed global hypokinesia. His intra-abdominal pressure was 20 mmHg. He was catheterized but had 100 mL of urine output in the past 12 h. Serum urea was 150 mg/dL, creatinine was 3.5 mg/dL, and potassium was 6.5 mEq/L.

Acute kidney injury is a common occurrence in the ICU and often requires renal replacement therapy (RRT). ICU physicians should be aware of the different modalities of renal replacement therapy (RRT) with their advantages and disadvantages.

Step 1: Initiate resuscitation and decide on RRT

- Along with resuscitation measures with ventilatory and hemodynamic support, early RRT should be considered in patients with acute kidney injury.
- Optimal timing of starting RRT remains controversial, and a joint decision between the nephrologist and the intensivist should be taken.
- The usual indications of commencing RRT are the following:
  - Volume overload/pulmonary edema
  - Refractory hyperkalemia (>6.5 mEq/L)
  - Severe metabolic acidosis (pH <7.1)
  - Anuria

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- Uremic encephalopathy
- Uremic pericarditis

Step 2: Decide on appropriate modality of RRT (Table 45.1)

- Continuous RRT (CRRT)—this modality of RRT may be preferable in the following situations:
  - Hemodynamically instability patients on multiple vasopressor therapy
  - Unable to maintain MAP of more than 70 mmHg
  - Need of large volume infusions (e.g., total parenteral nutrition [TPN])
  - Raised intracranial pressure (ICP)
- Sustained low efficiency dialysis (SLED) may be preferable in some situations:
  - If the patient is able to maintain MAP of more than 70 mmHg on low-dose vasopressors, this may be a reasonable option.
- Intermittent hemodialysis (IHD):
  - If the patient is hemodynamically stable
  - No significant volume overload

Table 45.1 Different modalities of RRT

Modality	Mechanism	Methodology
Hemodialysis (HD)	Diffusion	Here, the solute passively diffuses down its concentration gradient from one fluid compartment (either blood or dialysate) into the other. The dialysate is made to flow in a direction which is opposite to blood flow (countercurrent flow) through the hollow fiber dialyzer, to maintain a continuous concentration gradient between the two compartments and therefore maximize solute removal. Diffusion-based dialysis mostly removes small molecular weight solutes of less than 1 kD (kilodalton)
Hemofiltration (HF)	Convection	Hydrostatic pressure gradient is used to induce the filtration (or convection) of plasma water across the membrane of the hemofilter. The frictional forces between water and solutes (called "solvent drag") result in the convective transport of small and middle molecular weight solutes (less than 5,000 D) in the same direction as water
Hemodiafiltration (HDF)	Diffusion and convection	This modality offers the maximum solute removal as it combines convection with diffusion for achieving this
Ultrafiltration (SCUF)	Hydrostatic pressure	Slow continuous removal of fluid alone, by steady hydrostatic pressure
Peritoneal dialysis (PD)	Diffusion, convection, and osmosis	Solute removal is accomplished by diffusion, and most of the ultrafiltration is by osmosis

The extracorporeal blood purification procedures are usually performed by a veno-venous circuit, and the modalities are accordingly referred to as CVVHD, CVVH, or CVVHDF

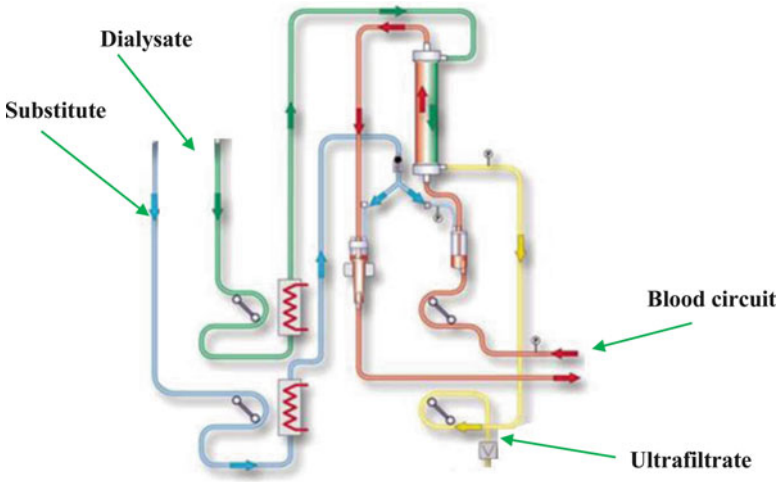

Fig. 45.1 Algorithm for choosing modalities of RRT

- Besides the medical indications, the selection of a particular modality of RRT is based on infrastructure, available resources, affordability, availability of appropriate fluids, hemofilters, and preference of the physician.

Step 3: Understand different modalities of RRT (Table 45.1)

1. *CRRT* (Figs. 45.1, 45.2, and 45.3 and Tables 45.2 and 45.3)
   - CRRT more closely mimics normal kidney function, by gradually processing the blood and slowly removing excess fluid, uremic toxins, and electrolytes, 24 h a day and thereby improving hemodynamic stability.
   - CRRT can provide up to 24–30 L of fluid exchange each day compared to 3–6 L per dialysis session for IHD. This greater fluid elimination can prevent fluid overload.
   - CRRT improves the nutritional status of critically ill patients by allowing infusion of necessary volume of parenteral nutrition (2–3 L).
   - It is the preferred therapy in septic shock.
   - CRRT is gentler than IHD as electrolyte concentrations are slowly and continuously corrected, thereby preventing osmotic shift and variations in intracranial pressure.
   - However, CRRT has failed to show unequivocal survival advantage though it may portend a better renal recovery.
   - Maintain adequate anticoagulation during CRRT:
     – Normally, 1,000–2,000 units of heparin are given as a bolus followed by a continuous infusion of 300–500 units per hour. Therapy is monitored every 6 h with the aim of maintaining the APTT 1.5–2 times control.
     – Saline infusions sometimes suffice if the patient has already a bleeding diathesis.

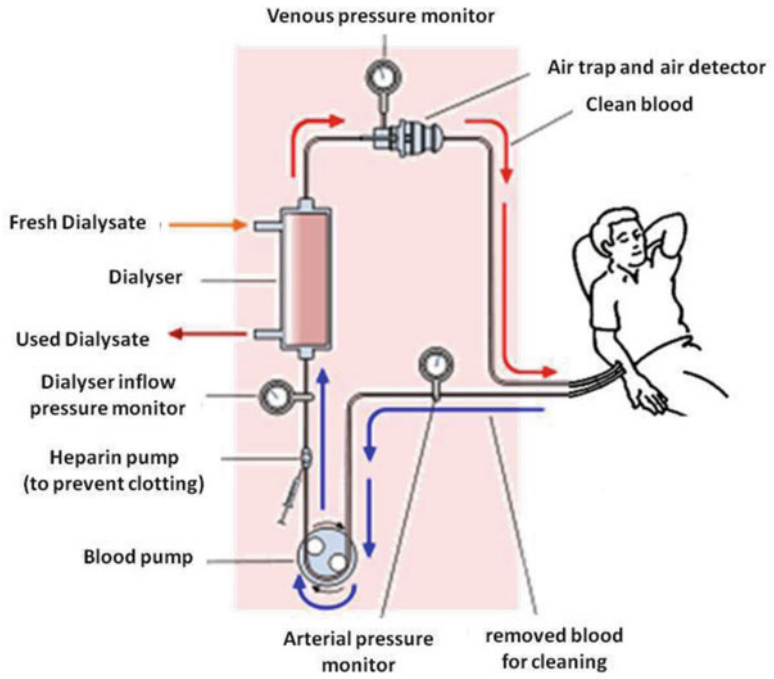

Fig. 45.2 CVVHDF

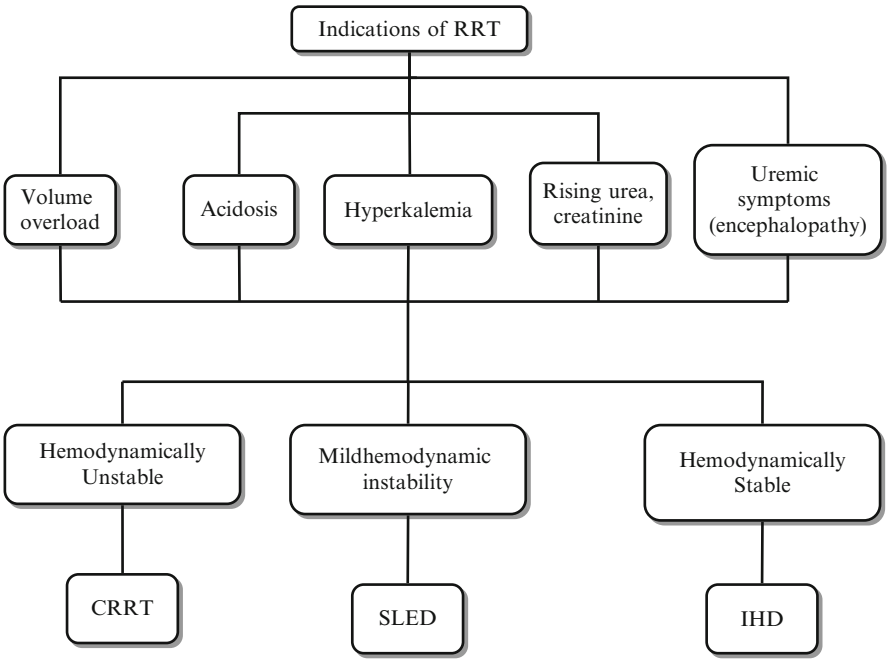

Fig. 45.3 The dialysis circuit

Table 45.2 CRRT advantages

Advantage	Methodology
Hemodynamic stability	Avoids hypotension, which is seen in ultrafiltration
	Avoids major swings in intravascular volume
	Allows slow and continuous tissue refilling
	Maintains steady cardiac filling pressures
	Avoids swings in intracranial pressures (beneficial in patients with raised ICP)
Easy to replenish and regulate fluid volume	Ultrafiltration is continuous and gentle
	Can adjust ultrafiltration rate according to hourly MAP status
	Can vary ultrafiltrate according to hourly variation in rate of infusates
	Can accurately adjust it to the intravascular blood volume or stroke volume variation when such monitors are being used
Customize replacement solutions	According to the metabolic parameters, replacement fluid composition may be altered like high lactate, calcium, high/low potassium, high/low sodium

CVVHD will probably be more effective than CVVH in the highly catabolic patient with a large solute load. CVVHDF with its convective removal of larger solutes is preferred in the patient with septic shock in whom the removal of inflammatory mediators is desirable. CVVHDF combines the convective solute removal of CVVH with the diffusive solute removal of CVVHD

Table 45.3 CRRT disadvantages

Lack of rapid solute and fluid removal
Glomerular filtration rate equivalent of 15–20 mL/min
Limited role in drug overdose setting
During filter clotting, entire system shuts down and the patient loses a lot of blood
Necessitates continuous anticoagulation
Limits mobility for various investigations
Requirement of ultrapure fluids and high-flux dialyzers

  - Citrate anticoagulation may be used with custom-made, calcium-free dialysate. Frequent calcium monitoring and calcium infusion may be required.
  - Bivalirudin and argatroban may be considered as an anticoagulant in cases of heparin-induced thrombocytopenia requiring RRT.
  - Regional anticoagulation can be achieved with heparin and protamine.
  - Prostacyclin infusions are an option, but may cause hypotension.
- Continuous RRT must be provided with an effluent flow rate (the sum of hemofiltration rate and dialysate flow rate) of at least 20 mL/kg/h.
- There is improved survival at effluent flow rates of 35 mL/kg/h but not much with 45 mL/kg/h (57% and 58%, respectively) as compared to an effluent flow rate of 20 mL/kg/h (41%) in patients with septic shock.

2. *SLED*
   - SLED is not a continuous therapy and achieves lower solute clearances that are maintained for longer period.

- Treatments are deliberately intermittent rather than attempting to be continuous, with session longer in duration than conventional hemodialysis (HD).
- Solute and fluid removal is slower than conventional HD, but faster than CRRT. This allows for down timing of dialysis duration compared to CRRT without compromise in dialysis dose.
- They are easy to perform with modification of the standard dialysis machine, allow flexibility for procedure and diagnostic tests, allow a break in anticoagulation exposure, and are less staff intensive.
- SLED and other hybrid therapies such as SLED-F have a lot of potential to be of use when CRRT is not available.

3. *Intermittent hemodialysis*
   - This is the conventional hemodialysis modality.
4. *Slow continuous ultrafiltration (SCUF)*
   - This modality does not require dialysate or any replacement fluids.
   - Here, therapeutic goal is to safely remove large volumes of fluid by hydrostatic pressure, with no intent to substantially remove solute.
   - Ultrafiltration (UF) can be adjusted to cause dramatic fluid shifts; however, average UF rate ranges up to 2 L/h.
   - As SCUF is a longer duration therapy, blood flow rates are less than intermittent HD, about 100–180 mL/min.
   - SCUF is primarily used when the fluid removal goals are gradual and modest.
5. *Peritoneal dialysis*
   - This modality of RRT utilizes the peritoneum as the dialyzer membrane.
   - The dialysate fluid is instilled periodically in the peritoneum and drained out to achieve solute removal across a diffusion gradient.
   - Fluid removal is achieved by osmosis by changing the glucose content of the dialysate fluid as necessary.
   - This modality is effective when the patient is not too catabolic or hypotensive, or on vasopressor support.
   - It is advantageous as it is gentle and continuous and it does not need anticoagulation, suitable for patients who have had a bleed, especially intracranial.
   - Due to infection risk, this is not practiced commonly.

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Website

1. www.renalandurologynews.com

Managing a Patient on Dialysis

46

Arghya Majumdar and Raj Kumar Mani

A 60-year-old diabetic and hypertensive male patient, with a history of coronary artery bypass grafting a year ago, was admitted to the ITU, with pneumonia and septic shock. He was started on vasopressors. He remained oliguric (urine output <30 mL/h) for more than 12 h, with creatinine 2 mg/dL, potassium 6.5 mEq/L, and pH 7.1. He was commenced on continuous renal replacement therapy (CRRT).

Patients on dialysis need close supervision due to their underlying unstable clinical state, hemodynamic effects of extracorporeal circulation, and technical problems commonly encountered during renal replacement therapy (RRT).

Step 1: Ensure all possible steps to prevent acute kidney injury (AKI) (Table 46.1)

- AKI is a preventable condition, and all attempts should be made to avoid the kidney damage as the mortality doubles once renal failure sets in.

Step 2: Recognize the need to start RRT

- Volume overload/pulmonary edema which is refractory to combination of high-dose loop diuretics (e.g., frusemide + metolazone).
- Refractory hyperkalemia (>6.5 mEq/L) persisting after failure of medical measures (e.g., calcium chloride i.v. 10% of 10 mL, i.v. insulin with dextrose, potassium exchange with enteral calcium resonium, i.v. sodium bicarbonate, and nebulized beta-agonist).

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Table 46.1 Preventive measures for AKI

1. Resuscitate with adequate fluid and administer antibiotics promptly
2. Avoid nephrotoxic antibiotics, nonsteroidal anti-inflammatory drugs, or radiocontrast agents
3. Improve cardiac output (e.g., dobutamine) to increase renal perfusion
4. Use minimum vasopressor to keep mean arterial pressure of more than 60 mmHg
5. Avoid "renal-dose" dopamine
6. Measure and manage raised intra-abdominal pressure

- Severe metabolic acidosis (pH < 7.1).
- Anuria. RRT becomes necessary to create space for intravenous fluid, drugs, and nutrition.
- Uremic encephalopathy.
- Uremic pericarditis.
- Ideal time to start RRT is controversial, and a joint decision between the nephrologist and the intensivist should be made.

Step 3: Establish vascular access for dialysis

- Urgent vascular access may be achieved by inserting a double-lumen hemodialysis catheter, preferably under (USG) ultrasonographic guidance.
- Coagulation profile and platelet count should be checked.
- A tunneled line may be preferable if the access is expected to be kept in for a long time, if there are multiple malfunctioning temporary catheters, or if the patient is going to receive immunosuppressive treatment.
- Site
  - Central vein—internal jugular (IJ), subclavian (SC), or femoral (F).
  - IJ is the preferred route.
  - SC route may be opted for, if the patient has a tracheostomy, but it should be avoided to prevent subclavian vein stenosis, which may restrict future vascular access for dialysis like fistula in the arm.
  - Femoral route is accompanied by increased risk of infection and/or thrombosis, but it is preferred as a short-term measure in severely coagulopathic patient.
- Size: 11.5 Fr and length of catheter: 13.5 cm for (R) IJ or SC, 16.5 cm for (L) IJ or SC, and 19.5 cm for F.
- Meticulous sterile handling of dialysis line by health-care workers is mandatory.
- The hemodialysis line should not be used for any other purpose.
- After each dialysis session, heparin lock should be used. In spite of heparin lock, if there is a clot formation inside the catheter, attempt at clot lysis may be made by instilling thrombolytic agent like 2 mg of alteplase into each catheter lumen.
- Platelet counts should be followed periodically.

Step 4: Start CRRT (see Chap. 45)

- Patients in shock with high dose of vasopressor should ideally be started on CRRT.
  - Use central venous double-lumen hemodialysis catheter, which will ensure a blood flow of at least 200 mL/min.

- Before starting, check electrolytes, arterial blood gas, and lactate.
- If custom-made fluid is not available, one has to improvise on substitution fluids, maintaining the balance of essential electrolytes. Custom-made fluids often have lactate. If liver function is impaired, it may not be converted to bicarbonate and lead to worsening of hyperlactatemia.
- Electrolytes like Na, K, Ca, and Mg should be monitored frequently.
- If the patient is very catabolic and higher solute clearance is required, substitution fluid should be added postdilution (i.e., after the filter) to maintain a higher diffusion gradient of solutes. On the other hand, in situations where one needs to avoid anticoagulation, it may be added prefilter (i.e., predilution). Heparin is the safest anticoagulant. Target an APTT of 1.5–2 times the control. If the patient has coagulopathy, regional anticoagulation may be tried with heparin/protamine or one may try prostacyclin. If citrate is used, ensure that all fluids are free of calcium. Calcium has to be added separately as an infusion, with regular monitoring.
- Convection at 20 mL/kg/h has been shown to be as effective as 35 mL/kg/h. Some studies have found a benefit of high volume ultrafiltration in sepsis.
- Adjust the dose of drugs especially antibiotics. Roughly one may use the dosing for the glomerular filtration rate at 10–15 mL/min.
- Hourly ultrafiltrate rate depends on central volume status (guided by invasive hemodynamic monitoring, if needed) and hourly fluid intake and output.
- Change the circuit, at least once in 72 h.
- Protein intake should be planned, taking into account the daily loss on CRRT
- (40 g/day, over and above 1.5 g/kg/day).
- Water-soluble vitamins should be replaced daily.

Step 5: Use slow extended dialysis (SLED), as a step-down dialytic support or initial support in less hemodynamically unstable patients

- This can be done when the patient is recovering from shock.
- A modified hemodialysis machine will suffice for SLED.
- The dialysate flow rate can be adjusted to 100–200 mL/min.
- SLED can be done for 8–10 h at one stretch, during the daytime, enabling better utilization of skilled dialysis staff and resources.
- The patient can be mobilized for investigations and procedures.
- Drug dosing should be adjusted accordingly. Supplemental doses of most antibiotics are needed after a session.
- Partial TPN may be given in between sessions when required.

Step 6: Manage the patient with conventional intermittent hemodialysis (HD) once hemodynamically stable

- Ensure a vascular access blood flow of 250–400 mL/min.
- Dialysate flow may be varied from 300 to 800 mL/min.
- Pre-HD potassium should be checked. Dialysate fluids have a potassium level of 2.2 mmol/L. So if serum potassium is less than 3.5 mmol/L, potassium should be replaced accordingly.

- In cases of severe hyperkalemia or hypercalcemia, dialysate fluids without potassium or low calcium may be used.
- A bolus of heparin, usually 1,000–2,000 U, is followed by an infusion. Adjust according to APTT. In the patient with bleeding diathesis, dialysis without added heparin may be done.
- Check glucose preferably hourly. Normal dialysate fluids do not contain glucose. Dialysate fluids containing glucose should be used, or it should be added when hypoglycemia is anticipated (e.g., in patients with liver dysfunction and sepsis).

Step 7: Assess adequacy of a dialysis session

- Urea reduction ratio: predialysis urea—postdialysis urea/predialysis urea. The target is 65%.
- Kt/V: a dimensionless ratio representing volume of plasma cleared (Kt) divided by the urea distribution volume (V). The latest generation of hemodialysis machines is equipped with this measurement capability. The target is 1.2.
- In clinical practice, postdialysis urea and creatinine are compared with subsequent predialysis levels. A steady state reflects recovering of renal function, and dialysis sessions may be spaced out accordingly.

Step 8: Optimize adequacy of dialysis

- Blood flow rate depends to a large extent on the position and patency of the central venous access catheter used for dialysis.
- Dialysate flow rate can be varied from 300 to 800 mL/min.
- Dialyzer efficiency: a high-efficiency (high mass transfer area coefficient) dialyzer with a thin, large-surface-area membrane, wide pores, and a design, which increases contact between blood and dialysate, will remove more waste products. However, the water used for dialysis in such situations needs to be ultrapure.
- Molecular weight (MW) of solute. Urea (MW 60) will be removed from blood more efficiently than creatinine (MW 113). Larger molecules like β_2-microglobulin (MW 11,800) can only be removed by high-flux dialyzers.
- Access recirculation, which depends on the proximity of the "arterial" inflow and venous outflow of the dialysis catheter. Separate tunneled lines cause less recirculation.
- Hypercatabolic patients: high urea nitrogen generation rate from endogenous protein breakdown may give a false impression of "inadequate solute clearance."
- Residual renal function when present may give an impression of "higher solute clearance."
- Protein-bound molecules are not well removed by dialysis. Charcoal hemoperfusion is a better alternative.

Step 9: Assess hypotension during dialysis

- Hypotension is the commonest complication during dialysis. It occurs most commonly in intermittent hemodialysis.
- Commonest cause is reduction of intravascular volume due to mismatch of rate of ultrafiltration and tissue refilling.
- Assess central volume status (CVP).

- Look for features of sepsis.
- Look for underlying cardiac dysfunction, anemia, prior intake of antihypertensive medications, arrhythmia (commonly atrial fibrillation), and autonomic neuropathy.
- Acute coronary syndrome, pericardial tamponade, or air embolism may also present as hypotension.
- Dialyzer reaction is rare now, with the use of biocompatible polysulfone membranes.

Step 10: Manage hypotension promptly

- Put the patient in the Trendelenburg position (with airway precaution), stop ultrafiltrate, and connect to a cardiac monitor.
- Do a 12-lead ECG and troponin I if clinical features are suggestive of ischemic heart disease. Do not treat supraventricular tachycardia or atrial fibrillation unless the patient is in shock or arrhythmia persists post-HD.
- A cautious bolus of 100 mL NS or more may be needed, or 25% dextrose if blood glucose is low.
- Check Hb and transfuse if it is less than 8 g/dL.
- Ensure that the dialysate fluid contains bicarbonate and not acetate, as the latter causes more hypotension.
- Dialysate temperature may be lowered to 36.5°C to promote vasoconstriction.
- Reassess the dry weight and restart ultrafiltrate at a slower rate when stable.
- Avoid antihypertensives pre-HD.
- If the patient gets chills or fever, screen for an underlying infection.

Step 11: Monitor for other potential complications (Table 46.2)

- Apart from hypotension, various other local and systemic complications may be seen in a patient on dialysis, which should be assessed and managed promptly.

Table 46.2 Complications of dialysis

1. Hypotension
2. Muscle cramps
3. Nausea and vomiting
4. Headache
5. Chest pain or back pain
6. Itching
7. Disequilibrium syndrome
8. Dialyzer reactions
9. Bleedings—gastrointestinal, epistaxis, intracranial
10. Seizures
11. Hemolysis
12. Air embolism
13. Visual or hearing loss
14. Hypertension
15. Hypoglycemia, hypothermia

Step 12: Assess recovery of renal function and try to wean from RRT

- Urine output: increasing urine output especially after an oliguric phase and when the patient has not been on diuretics is considered the best sign of recovery.
- Change of urea or creatinine levels from postdialysis levels, when they remain steady or decline in between dialysis session, might be particularly helpful in nonoliguric patients.
- Trend of biomarkers like NGAL (neutrophil-gelatinase-associated lipocalin) may be helpful in indicating renal recovery. NGAL is not removed by dialysis.

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Websites

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   Homepage for ADQI network on acute kidney injury
2. www.crrtonline.com
   Practical aspects of managing CRRT, including nursing perspective
3. www.asn-online.org
   American Society of Nephrology webpage with information on various aspects of AKI

Drug Dosing

47

Pratik Das and Arghya Majumdar

A 55-year-old diabetic and hypertensive male was admitted with acute kidney injury secondary to urosepsis. He was anuric and hemodynamically unstable and had been put on slow extended dialysis. He was a known epileptic on phenobarbitone and levetiracetam. He underwent coronary artery bypass grafting 2 years ago and had congestive cardiac failure. He was on isosorbide mononitrate, digoxin, aspirin, atenolol, hydralazine, pantoprazole, atorvastatin, fenofibrate, and insulin. He had been commenced on meropenem and needed noradrenaline infusion.

Polypharmacy is very common in the ICU due to multiple comorbidities of the patient. Adverse side effects and drug interaction, especially in the patient with renal impairment and renal replacement therapy (RRT), should be carefully looked for, and drug dose may need to be adjusted; drugs may need to be withdrawn or substituted.

Step 1: Assess need for dose adjustment in renal failure

- The pharmacokinetics and pharmacodynamics of most drugs are altered in patients with renal failure, especially those with a predominant renal clearance (e.g., meropenem with 70% renal clearance).
- The volume of distribution of several drugs and their metabolites is altered in renal failure (e.g., digoxin).
- The risk of side effects is much higher for some drugs, in patients with renal failure (e.g., phenobarbitone).

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- For drugs with only minor or no dose-related side effects, very precise modification of the dosage regimen is not essential (e.g., pantoprazole). However, for more toxic drugs, with a small safety margin (e.g., digoxin), dose regimens based on glomerular filtration rate (GFR) is mandatory.

Step 2: Calculate GFR

- Cockroft–Gault formula:
  - It is commonly used to calculate the creatinine clearance (Clcr) and has traditionally been used to approximate the GFR.
  - It is fairly accurate for chronic kidney disease with a stable serum creatinine, but in acute kidney injury (AKI) with unstable serum creatinine, this formula may not be accurate and may overestimate the GFR.

$$\text{Clcr} = \frac{(140 - \text{age in years}) \times \text{lean body weight}}{72 \times \text{serum creatinine in mg / dL}} \times (0.85 \text{ for female})$$

- In ICU, actual body weight is difficult to measure in most situations, and ideal body weight is taken instead for calculation of GFR.
- Ideal body weight (IBW) may be calculated in the ICU by the following formulas:
  - Males (IBW in kg): 50 + 2.3 (height in inches −60)
  - Females (IBW in kg): 45.5 + 2.3 (height in inches −60)
- Modification of diet in renal disease (MDRD) formula for estimation of GFR and eGFR and radioisotope methods are other ways of calculating GFR but not commonly used in the ICU.
- Anuric AKI patients have a GFR less than 10 mL/min, as a rule, irrespective of serum creatinine value and need no calculation.
- For the patient on dialysis, GFR is taken as less than 15 mL/min.

Step 3: Calculate loading dose of a drug

- The patient with renal failure of any severity should receive the same loading dose as the patient with normal renal function to achieve a rapid therapeutic level.

Step 4: Calculate maintenance dose

- Before adjusting the maintenance dose, the route of excretion should be ascertained. The maintenance dose should be adjusted only for drugs with the following properties:
  - Greater than 50% renal excretion
  - Low rate of protein binding
  - Small volume of distribution
- The maintenance dosage in patients with renal insufficiency can be adjusted in three ways:
  - Dosing interval prolongation, dosage reduction, or both (Table 47.1)

Table 47.1 Meropenem (>70%) renal excretion

Creatinine clearance	Dose (based on unit dose of 500 mg, 1 g, and 2 g)	Frequency
>50	One unit dose	Every 8 h
26–50	One unit dose	Every 12 h
10–25	One-half unit dose	Every 12 h
<10	One-half unit dose	Every 24 h

- Increasing the dosage interval to correspond to the degree of renal dysfunction can be calculated from the following formula:

$$\text{Dosing interval} = \frac{\text{Normal Clcr} \times \text{normal interval}}{\text{Patient Clcr}}$$

- Dosage reduction without changing the dosing interval can be calculated from the following formula:

$$\text{Maintenance dose} = \frac{\text{Patient Clcr} \times \text{normal dose}}{\text{Normal Clcr}}$$

  - Dosage interval extension allows for adequate peak concentration but may risk subtherapeutic trough levels.
  - Dosage reduction may provide for more constant drug levels but increases the risk of toxicity from higher plasma trough concentrations.

Step 5: Utilization of the drug dosing chart (See Appendix A.2)

- Every critical care unit should use a detailed drug dosing chart in renal failure and should consult this prior to prescription.
- Package insert of a medicine is a "ready reckoner" for drug dose modification.
- The dosage modifications are an approximation and guided by features of drug toxicity and, if feasible, drug levels.
- Remember to supplement some medications postdialysis like carbapenems.
- These are approximations and drug dosing need to be individualized in critically ill patient depending on various factors as described in previous steps.

Step 6: Dosing on continuous renal replacement therapy (CRRT)

- CRRT is most often used for the management of critically ill patients who are too hemodynamically unstable to tolerate intermittent hemodialysis.
- There is very limited information about how CRRT affects the clearance of individual pharmacologic agents.
- During CRRT, most drugs can be approximately dosed for a GFR of 10–30 mL/min.
- However, for some drugs, the diffusion process significantly increases drug clearance during CRRT due to high-flux dialysis.

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Part VI

Infectious Diseases

Subhash Todi

General Measures of Infection Control

48

Sheila Nainan Myatra and Raghu S. Thota

A 72-year-old male patient with non-Hodgkin's lymphoma was neutropenic after chemotherapy and presented to the ICU with breathlessness and hypotension. He was intubated and kept on a ventilator and received broad-spectrum antibiotics. He had a peripheral, central, and arterial line in place. A Foley's catheter and a nasogastric tube were also placed.

Health-care-associated infections are a common cause of increased morbidity, mortality, and cost of care in ICUs. Infection control and judicious antibiotic use are the mainstay of management of these patients. A systematic and multidisciplinary approach to infection control practice goes a long way in minimizing this problem.

Step 1: Assess the need for isolation

- *Screen all ICU patients for the following:*
  - Neutropenia and immunological disorder
  - Diarrhea
  - Skin rashes
  - Known communicable disease
  - Known carriers of an epidemic strain of bacterium

Step 2: Identify the type of isolation needed

- There are two types of isolation in the ICU:
  - Protective isolation for neutropenic or other immunocompromised patients to reduce the chances of acquiring opportunistic infections.

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  - Source isolation of colonized or infected patients to minimize potential transmission to other patients or staff.
- Isolation rooms should have tight-fitting doors, glass partitions for observation, and both negative-pressure (for source isolation) and positive-pressure (for protective isolation) ventilations.

Step 3: Identify the patient at risk of nosocomial infections

- There are patient-, therapy-, and environment-related risk factors for the development of nosocomial infection:
  - Age more than 70 years
  - Shock
  - Major trauma
  - Acute renal failure
  - Coma
  - Prior antibiotics
  - Mechanical ventilation
  - Drugs affecting the immune system (steroids, chemotherapy)
  - Indwelling catheters
  - Prolonged ICU stay (>3 days)

Step 4: Observe hand hygiene

- Hands are the most common vehicle for transmission of organisms, and "hand hygiene" is the single most effective means of preventing the horizontal transmission of infections among hospital patients and health-care personnel.
- When and why—follow WHO's five moments for hand hygiene (Fig. 48.1):
  1. Before touching a patient—to protect the patient from harmful germs carried on your hands
  2. Before aseptic procedures—to protect the patient against harmful germs, including the patient's own germs
  3. After body fluid exposure/risk—to protect yourself and the health-care environment from the harmful patient's germs
  4. After touching the patient—to protect yourself and the health-care environment from the harmful patient's germs
  5. After touching the patient's surrounding—to protect yourself and the health-care environment from the harmful patient's germs

     (Remember, there are two moments before and three moments after touching the patient)
- How
  - Wash hands with soap and water when they are soiled or visibly dirty with blood or other body fluids. Wet your hands, apply soap and then scrub them vigorously for at least 15 s. Cover all surfaces of the hands and fingers, wash with water, and then dry thoroughly using a disposable towel.
  - Use an alcohol-based hand rub (e.g., 0.5% chlorhexidine with 70% w/v ethanol) if hands are not visibly dirty. A combination of chlorhexidine and alcohol is ideal as they cover Gram-positive and Gram-negative organisms, viruses, mycobacteria, and fungi. Chlorhexidine also has residual activity.

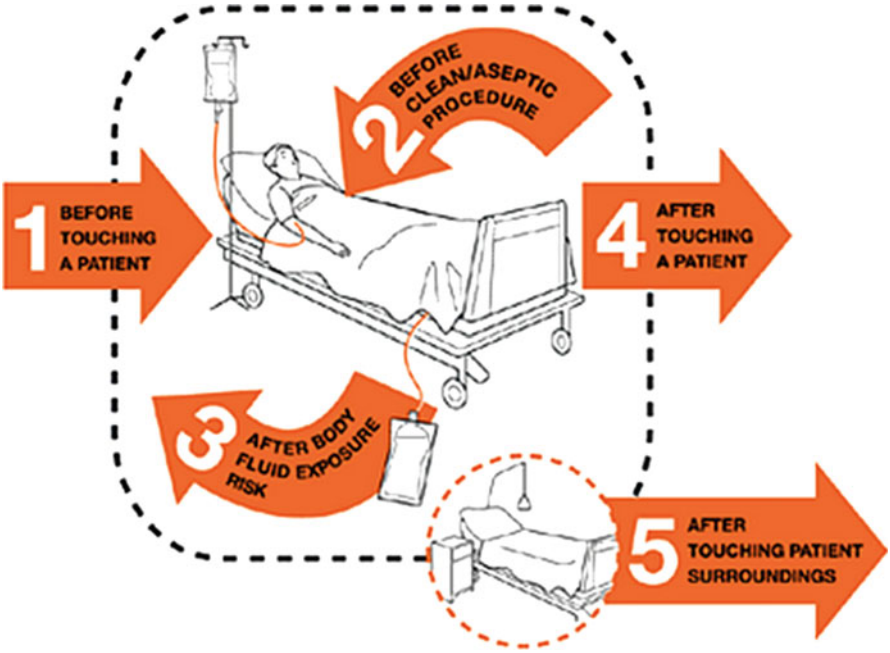

Fig. 48.1 WHO's five moments for hand hygiene (Adapted from WHO)

- During surgical hand preparation, all hand jewelries (e.g., rings, watches, bracelets) must be removed.
- Finger nails should be trimmed with no nail polish or artificial nails.
- Avoid wearing long sleeves, ties should be tucked in, house coats are discouraged, and wearing scrubs is encouraged.

Step 5: Follow standard precautions

- Standard precautions include prudent preventive measures to be used at all times, regardless of a patient's infection status.
- *Gloves*
  - Sterile gloves should be worn after hand hygiene procedure while touching mucous membrane and nonintact skin and performing sterile procedures (e.g., arterial, central line, and Foley catheter insertion).
  - Clean, nonsterile gloves are safe for touching blood, other body fluids, contaminated items, and any other potentially infectious materials.
  - Change gloves between tasks and procedures in the same patient especially when moving from a contaminated body area to a clean body area.
  - Never wear the same pair of gloves for the care of more than one patient.
  - Remove gloves after caring for a patient.
  - Practice hand hygiene whenever gloves are removed.
- *Gown*
  - Wear a gown to prevent soiling of clothing and skin during procedures that are likely to generate splashes of blood, body fluids, secretions, or excretions.

  - The sterile gown is required only for aseptic procedures, and for the rest, a clean, nonsterile gown is sufficient.
  - Remove the soiled gown as soon as possible, with care to avoid contamination.
- *Mask, eye protection/face shield*
  - Wear a mask and adequate eye protection (eyeglasses are not enough) or a face shield to protect mucous membranes of the eyes, nose, and mouth during procedures and patient-care activities that are likely to generate splashes/sprays of blood, body fluids, etc.
  - Patients, relatives, and health-care workers presenting with respiratory symptoms should also use masks (e.g., cough).
- *Shoe and head coverings*
  - They are not required for routine care.
- *Patient-care equipment*
  - Used patient-care equipment soiled with blood, body fluids, secretions, or excretions should be handled carefully to prevent skin and mucous membrane exposures, contamination of clothing, and transfer of microorganisms to health-care workers, other patients, or the environment.
  - Ensure that reusable equipment is not used for the care of another patient until it has been cleaned and sterilized appropriately.
  - Ensure that single-use items and sharps are discarded properly.

Step 6: Follow transmission-based precautions

- In addition to standard precautions, the following should be observed in those patients known or suspected to have airborne, contact, or droplet infections:
- *Airborne precautions*
  - Disease-causing microorganisms may be suspended in the air as small particles, aerosols, or dust and remain infective over time and distance, for example, *Mycobacterium tuberculosis* (pulmonary/laryngeal), varicella zoster virus (chickenpox), herpes zoster (shingles), and rubeola virus (measles).
  - Isolate with negative-pressure ventilation.
  - Respiratory protection must be employed when entering the isolation room.
  - Use the disposable N95 respirator mask, which fits tightly around the nose and mouth to protect against both large and small droplets. This should be worn by all persons entering the room, including visitors.
- *Contact precautions*
- Infections can be spread by usual direct or indirect contact with an infected person, the surfaces or patient-care items in the room, for example, parainfluenza virus infection, respiratory syncytial virus infection, varicella (chickenpox), herpes zoster, hepatitis A, and rotavirus infections.
  - Isolation is required.
  - Noncritical patient-care equipment should preferably be of single use. If unavoidable, then clean and disinfect them adequately before using to another patient.
  - Limit transport of the patient.

- *Droplet precautions*
  - Microorganisms are also transmitted by droplets (large particles >5 μm in size) generated during coughing, sneezing, talking, or a short-distance traveling, for example, influenza virus, *Bordetella pertussis*, *Hemophilus influenzae* (meningitis, pneumonia), *Neisseria meningitidis* (meningitis, pneumonia, bacteremia), *Mycoplasma pneumoniae*, SARS-associated coronavirus (SARS-CoV), group A *Streptococcus*, adenovirus, and rhinovirus.
  - Isolation is required.
  - Respiratory protection must be employed when entering the isolation room or within 6–10 ft of the patient. Use the disposable N95 respirator mask, which fits tightly around the nose and mouth to protect against both large and small droplets. This should be worn by all persons entering the room, including visitors.
  - Limit transport of the patient.

Step 7: Use specific strategies focused on prevention of specific nosocomial infections

In addition to the standard and transmission-based precautions, there are several strategies focused on prevention of specific nosocomial infections in critically ill patients. Of these, ventilator-associated pneumonia (VAP), catheter-related bloodstream infection (CRBSI), and urinary tract infection (UTI) are the most important.

- *Strategies to reduce VAP*
  - Avoid intubation whenever possible.
  - Consider noninvasive ventilation whenever possible.
  - Prefer oral intubations to nasal unless contraindicated.
  - Keep head elevated at 30–45° in the semi-recumbent body position.
  - Daily Oral Care with Chlorhexidine solution of strength 0.12%.
  - Daily sedation vacation if feasible and assessment of readiness to extubate.
  - Consider early extubation.
  - Avoid reintubation whenever possible.
  - Routine change of ventilator circuits is not required.
  - Monitor endotracheal tube cuff pressure (keep it >20 cmH_2O) to avoid air leaks around the cuff, which can allow entry of bacterial pathogens into the lower respiratory tract.
  - Prefer endotracheal tubes with a subglottic suction port to prevent pooling of secretions around the cuff leading to microaspiration.
  - The heat moisture exchanger may be better than the heated humidifier.
  - Closed endotracheal suction systems may be better than the open suction.
  - Periodically drain and discard any condensate that collects in the tubing of a mechanical ventilator.
- *Strategies to reduce CRBSI*
  - Prefer the upper extremity for catheter insertion. Avoid femoral route for central venous cannulation (CVC).
  - If the catheter is inserted in a lower extremity site, replace to an upper extremity site as soon as possible.

- Use maximal sterile barrier precautions (cap, mask, sterile gown, sterile gloves) and a sterile full-body drape while inserting CVCs, peripherally inserted central catheters (PICC), or guidewire exchange.
- Clean skin with more than 0.5% chlorhexidine preparation with alcohol (usually 2% chlorhexidine with 70% w/v ethanol) before CVC, arterial catheter insertion, etc.
- Use chlorhexidine/silver sulfadiazine or minocycline/rifampin-impregnated CVCs when the catheter is expected to remain in place for more than 5 days and only if the bloodstream infection rates are high in the unit.
- Use ultrasound-guided insertion if technology and expertise are available.
- Use either sterile gauze or sterile, transparent, semipermeable dressing to cover the catheter site. Replace the catheter site dressing only when the dressing becomes damp, loosened, or visibly soiled.
- Evaluate the catheter insertion site daily and check if a transparent dressing is present and palpate through the dressing for any tenderness.
- Insertion date should be put on all vascular access devices.
- Use 2% chlorhexidine wash daily for skin cleansing to reduce CRBSI.
- Use needleless intravascular catheter access systems and avoid stopcocks. Closed catheter access systems should be preferred to open systems.
- Clean injection ports with an appropriate antiseptic (chlorhexidine, povidone-iodine, an iodophor, or 70% alcohol), accessing the port only with sterile devices. Cap stopcocks when not in use.
- Assess the need for the intravascular catheter daily and remove when not required.
- Peripheral lines should not be replaced more frequently than 72–96 h. Routine replacement of CVCs is not required.
- Replace administration sets, including secondary sets and add-on devices, every day in patients receiving blood, blood products, or fat emulsions.
- If other intravenous fluids are used, change no less than 96-h intervals and at least every 7 days.
- Needleless connectors should be changed frequently (every 72 h).
- Replace disposable or reusable transducers at 96-h intervals.

- *Strategies to reduce UTI*
  - Insert catheters only for appropriate indications.
  - Follow aseptic insertion of the urinary catheter.
  - Maintain a closed drainage system.
  - Maintain unobstructed urine flow. At all times, the urinary catheter should be placed and taped above the thigh and the urinary bag should hang below the level of the bladder.
  - The urinary bag should never have floor contact.
  - Changing indwelling catheters or drainage bags at fixed intervals is not recommended. Change only if there are clinical indications such as infection or obstruction or when the closed system is compromised.
  - Remove the catheter when it is no longer needed.

Step 8: Consider environmental factors

- *Cleaning and disinfection*
  - High-quality cleaning and disinfection of all patient-care areas is important, especially surfaces close to the patient (e.g., bedrails, bedside tables, doorknobs, and equipment).
    - Some pathogens can survive for long periods in the environment, particularly methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant Enterococcus (VRE), *Acinetobacter* species, *Clostridium difficile*, and norovirus.
  - EPA-registered disinfectants or detergents that best meet the overall needs of the ICU should be used for routine cleaning and disinfection.
  - Frequency of cleaning should be as follows: surface cleaning (walls) twice weekly, floor cleaning two to three times per day, and terminal cleaning (patient bed area) after discharge or death.
- *Architecture and layout, especially while designing a new ICU*
  - The unit may be situated close to the operating theater or emergency department for easy accessibility but should be away from the main ward areas.
  - Central air-conditioning systems are designed in such a way that recirculated air must pass through appropriate filters.
  - It is recommended that all air should be filtered to 99% efficiency down to 5 μm.
  - Suitable and safe air quality must be maintained at all times. Air movement should always be from clean to dirty areas.
  - It is recommended to have a minimum of six total air changes per room per hour, with two air changes per hour composed of outside air.
  - Isolation facility should be with both negative- and positive-pressure ventilations.
  - Clearly demarcated routes of traffic flow through the ICU are required.
  - Adequate space around beds is ideally 2.5–3 m.
  - Electricity, air, vacuum outlets/connections should not hamper access around the bed.
  - Adequate number of washbasins should be installed.
  - Alcohol gel dispensers are required at the ICU entry, exits, every bed space, and every workstation.
  - There should be separate medication preparation area.
  - There should be separate areas for clean storage and soiled and waste storage and disposal.
  - Adequate toilet facilities should be provided.

Step 9: Organizational and administrative measures

- Work with hospital administration for better patient-to-nurse ratio in the ICU.
- Policies for controlling traffic flow to and from the unit to reduce sources of contamination from visitors, staff, and equipment.
- Waste and sharp disposal policy.
- Education and training for ICU staff about prevention of nosocomial infections.
- ICU protocols for prevention of nosocomial infections.

- Audit and surveillance of infections and infection control practices.
- Infection control team (multidisciplinary approach).
- Antibiotic stewardship.
- Vaccination of health-care personnel.

Suggested Reading

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   VAP remains a significant problem in the hospital setting, with very high morbidity, mortality, and cost. This evidence-based review focuses clinically on relevant pharmacological and nonpharmacological interventions to prevent VAP.
2. Coffin SE, Klompas M, Classen D, Arias KM, Podgorny K, Anderson DJ, Burstin H, Calfee DP, et al. Strategies to prevent ventilator-associated pneumonia in acute care hospitals. Infect Control Hosp Epidemiol. 2008;29(Suppl 1):S31–40.
   This document gives practical recommendations in a concise format designed to assist acute care hospitals in implementing and prioritizing their VAP prevention efforts.
3. Lorente L, Blot S, Rello J. Evidence on measures for the prevention of ventilator-associated pneumonia. Eur Respir J. 2007;30:1193–207.
   Evidence-based guidelines have been issued by the European Task Force on ventilator-associated pneumonia, the Centers for Disease Control and Prevention, the Canadian Critical Care Society, and also by the American Thoracic Society and Infectious Diseases Society of America, which have produced a joint set of recommendations. This review article is based on a comparison of these guidelines, together with an update of further publications in the literature.

Websites

1. http://whqlibdoc.who.int/hq/2009/WHO_IER_PSP_2009.07_eng.pdf
   WHO guidelines on hand hygiene in health care: a summary
2. http://www.cdc.gov/hicpac/pdf/guidelines/bsi-guidelines-2011.pdf
   Guidelines for the prevention of intravascular catheter-related infections
3. http://www.cdc.gov/hicpac/pdf/CAUTI/CAUTIguideline2009final.pdf
   Guidelines for prevention of catheter-associated urinary tract infections
4. http://www.cdc.gov/hicpac/pdf/isolation/Isolation2007.pdf
   Guideline for isolation precautions: preventing transmission of infectious agents in healthcare settings

Antibiotic Stewardship

49

Subhash Todi and Rajesh Chawla

A 70-year-old male patient had been admitted to the ICU with left-sided hemiparesis for 4 days. He was catheterized on admission and intubated for airway protection. He had spiked a fever of 102°F with chills and became drowsy. A broad-spectrum antibiotic was started empirically after sending blood cultures.

Judicious antibiotic prescription along with infection control is the cornerstone for preventing emergence of drug-resistant organisms in the ICU. Appropriate (right choice) and adequate (right time, right dose) antibiotic coverage improves outcome in infected patients.

Step 1: Formulate a plan for antibiotic selection

- Antibiotics in the ICU are given either empirically for presumed infection with culture report pending, or prophylactically mainly perioperative or definitively when infection is documented with positive culture results.
- Reason for antibiotic selection should be clearly documented in the antibiotic order form, which should be audited periodically for correctness.
- Appropriate antibiotics should be chosen depending on local epidemiology and resistance pattern.

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Step 2: Send appropriate cultures
- This should ideally be done prior to starting antibiotics.
- Blood, urine, sputum, and endotracheal secretion should be promptly transported to the microbiology laboratory and expeditiously processed.

Step 3: Start antibiotics early
- Every hour delay in starting effective antibiotics from the onset of septic shock increases the risk of death from sepsis by 6–10%.
- Antibiotics should be started within 1 h of recognition of septic shock as "Time is tissue."

Step 4: Choose empirical antibiotics appropriately
- Empirical antibiotics should be chosen carefully as initial wrong choice increases mortality, even if the antibiotic is changed appropriately after culture results are obtained.
- Initial antibiotic choice should be based on the patient's history, underlying disease or clinical syndrome, susceptibility pattern of the pathogen in the community and hospital, and previous colonization pattern.
- Recently used antibiotic class should generally be avoided.
- Choose broad-spectrum antibiotics that have activity against most likely bacterial pathogens.

Step 5: Stratify the risk of infection with drug-resistant organisms (Table 49.1)
- The patient should be assessed for risk of infection with multidrug-resistant bacteria.
- If one or more risk factors are present, antibiotic choice should be broadened to cover these organisms.

Table 49.1 Risk factors for drug-resistant bacteria

Antimicrobial therapy in preceding 90 days
Current hospitalization of 5 days or more
High frequency of antibiotic resistance in the community or in the specific hospital unit
Immunosuppressive disease and/or therapy
Hospitalization for 2 days or more in preceding 90 days
Residence in the nursing home or extended care facility
Chronic dialysis within 30 days
Home infusion therapy (including antibiotic)
Home wound care
Having a family member with a recent history of infection with multidrug-resistant pathogens

Step 6: Follow pharmacokinetic and pharmacodynamic principles while prescribing antibiotics (Fig. 49.1)
- Give adequate intravenous dose (Table 49.2).
- Give antibiotics that penetrate in adequate concentrations into the presumed source of sepsis.

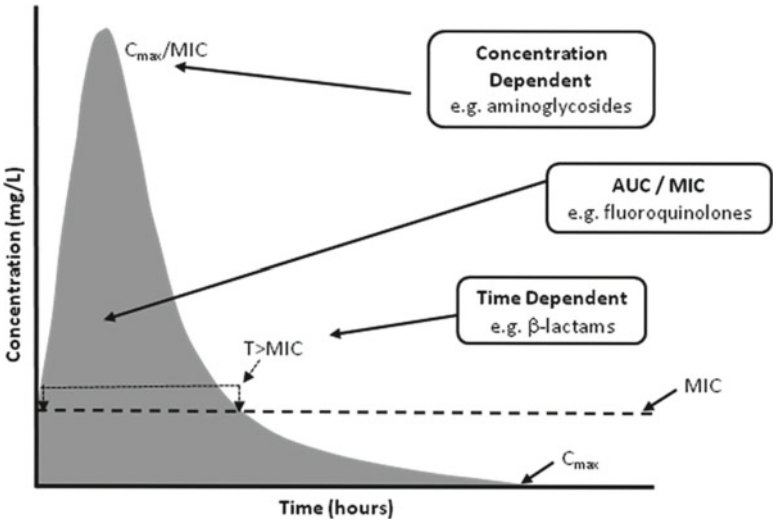

Fig. 49.1 Pharmacokinetic and pharmacodynamic principles

Table 49.2 Appropriate doses of common antibiotics (Refer to Appendix 1)

Antipseudomonal cephalosporin
Cefepime, 1–2 g every 8–12 h
Ceftazidime, 2 g every 8 h
Carbapenems
Imipenem, 500 mg every 6 h or 1 g every 8 h
Meropenem, 1 g every 8 h
Doripenem, 500 mg every 8 h
Ertapenem, 1 g once daily
β-Lactam/β-lactamase inhibitor
Piperacillin–tazobactam, 4.5 g every 6 h
Aminoglycosides
Gentamicin, 7 mg/kg/day
Tobramycin, 7 mg/kg/day
Amikacin, 20 mg/kg/day
Antipseudomonal quinolones
Levofloxacin, 750 mg/day
Ciprofloxacin, 400 mg every 8 h
Vancomycin, 15 mg/kg every 12 h
Linezolid, 600 mg every 12 h
Colistin: 1–2 million units every 8 h

Dosages are based on normal renal and hepatic function
Peak drug levels for gentamicin and tobramycin should be 8–10 mcg/mL and trough levels less than 2 mcg/mL
Peak drug levels for amikacin should be 25–30 mcg/mL and trough levels should be less than 4–8 mcg/mL
Trough levels for vancomycin should be 15–20 mcg/mL

- Time-dependent antibiotics like β-lactams (maximum bacterial inhibition depends on time above minimum inhibitory concentration) should be given as a continuous infusion.
- Dose-dependent antibiotics like aminoglycoside (maximum bacterial inhibition depends on peak antibiotic concentration) should be given as a once-daily bolus dose.
- Adjust the dose of antibiotics depending on renal and hepatic dysfunction.

Step 7: Assess the patient daily and de-escalate antibiotics once culture results are obtained

- Clinical response should be assessed frequently, and if the patient is responding favorably, antibiotics should be de-escalated to a narrower spectrum, and unnecessary antibiotics should be stopped if culture results permit.
- Decisions to continue, narrow, or stop antimicrobial therapy must be made on the basis of clinician judgment and laboratory information like decrease in leukocytosis, decreasing C reactive protein, and a low procalcitonin level.

Step 8: Consider the combination of antibiotics in specific situations

- The combination of antibiotics (two appropriate antibiotics against the same organism) is indicated in difficult to treat multidrug-resistant pathogens like *Acinetobacter* and *Pseudomonas* sp. Combination therapy is also indicated for neutropenic patient with severe sepsis and selected patients with severe *Pseudomonas* infection with respiratory failure and shock. Similarly, a combination of beta-lactam and macrolide is recommended for pneumococcal bacteremia.

Step 9: Decide on duration of antibiotic therapy

- Duration of therapy should typically be 7–10 days.
- Longer courses may be appropriate in patients who have a slow clinical response, undrainable foci of infection, or immunologic deficiencies including neutropenia.
- If culture result is negative and there is a favorable clinical response, most antibiotics can be stopped in 5 days.
- In *Pseudomonas* and *Acinetobacter* infection, severe sepsis should be treated for 2 weeks.

Step 10: Implement antibiotic stewardship program

- Constitute an antibiotic stewardship team along with the microbiologist, infection control nurse, infectious disease consultant, and clinical pharmacist.
- Educating ICU staff the principles of antibiotic stewardship is of prime importance.
- Proper utilization of local antibiogram should be done.
- Utilize optimally the information obtained from the microbiology laboratory.
- Work in close collaboration with microbiologists and other physicians involved in antibiotic prescribing.

Suggested Reading

1. Dellinger RP, Levy MM, et al. Surviving sepsis campaign: International guidelines for management of severe sepsis and septic shock: 2008. Crit Care Med. 2008;36:1394–6.
2. Kumar A, Roberts D, Wood KE, et al. Duration of hypotension prior to initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. Crit Care Med. 2008;34:1589–96.
Administration of an antimicrobial effective for isolated or suspected pathogens within the first hour of documented hypotension was associated with a survival rate of 79.9%. Each hour of delay in antimicrobial administration over the ensuing 6 h was associated with an average decrease in survival of 7.6%. Median time to effective antimicrobial therapy was 6 h.
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Multiple logistic regression analysis identified the administration of inadequate antimicrobial treatment as an independent determinant of hospital mortality.

Website

1. www.survivingsepsis.org

Septic Shock

50

Mohit Kharbanda and Suresh Ramasubban

A 60-year-old diabetic male patient presented with a history of dysuria and fever. His vital signs on admission were as follows: pulse 120/min, BP 80/50 mmHg, and respiratory rate 28/min. He was disoriented and agitated.

Sepsis, which is a host response to an infection, can have a varied presentation and carries a poor prognosis. Early identification and appropriate risk stratification will help in early resuscitation with a decrease in morbidity and mortality.

Step 1: Take care of airway and breathing

- Proper airway care and, if needed, assisted ventilation should be promptly initiated in all patients with severe sepsis and shock (see Chap. 78).

Step 2: Assess severity of sepsis

- After initial resuscitation, it is important to identify and assess severity of sepsis.
- Categorizing patients into sepsis, severe sepsis, and septic shock helps in triaging, prognostication, and choosing appropriate therapy (Table 50.1).

Step 3: Maintain circulation

- Fluid resuscitation is of utmost importance in initial management of severe sepsis and septic shock patients.

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Table 50.1 Definitions

SIRS—two or more of the following:
Temperature >38°C or <36°C
Heart rate >90/min
Respiratory rate >20/min or $PaCO_2$ < 32 mmHg
WBC > 12,000 or < 4,000 (>10% bands)
Sepsis—SIRS plus infection
Severe sepsis
Sepsis with sepsis-induced organ dysfunction or evidence of tissue hypoperfusion like elevated lactate
Sepsis-induced hypotension
Systolic blood pressure (SBP) < 90 mmHg or MAP < 70 mmHg or SBP decrease >40 mmHg or <2 SD below normal for age in the absence of other causes of hypotension
Septic shock
Sepsis with hypotension (systolic <90 mmHg) despite fluid resuscitation

- Insert a wide-bore peripheral line and give initial fluid challenge of 1,000 mL of crystalloids (normal saline or Ringer lactate) to achieve a minimum of 30 ml/kg of crystalloids over 30–60 min with careful monitoring of vital signs.
- Albumin may be added to the initial resuscitation fluid in patients having or anticipated to have a low albumin value.
- Hydroxyethyl starches with a molecular weight >200 and degree of substitution >0.4 should be avoided as these may cause nephrotoxicity.
- Fluid resuscitation should be continued as long as the hemodynamics, based on either dynamic (delta pulse pressure or stroke volume variation) or static variable (CVP, urine output), continues to improve and serum lactate continues to decrease.
- Recent trial conducted in Africa on a pediatric population with severe sepsis have shown fluid loading may be detrimental in this population.

Step 4: Send initial investigations

- As the patient is being resuscitated, send blood for complete hemogram, blood cultures (two sets), and other appropriate cultures depending on the clinical situation, urea, creatinine, electrolytes, liver function test, ECG, and chest X-ray.
- Blood lactate—send arterial blood for arterial blood gas and lactate analysis. Increased lactate is a feature of global hypoperfusion and needs urgent attention.
- Serial lactate measurement is useful in monitoring response to resuscitation.
- If lactate is not available, base deficit (metabolic acidosis) can be taken as a surrogate marker of lactic acidosis.
- Appropriate viral cultures and real-time PCR (more sensitive and specific) should be obtained but should not delay prompt administration of antiviral therapy.

Step 5: Start antimicrobial agent

- Appropriate broad-spectrum antibiotics as per hospital protocol should be started immediately, preferably within 1 h of presentation.

- Appropriate cultures should be sent before starting antibiotics, but if these are delayed for logistic reasons beyond 45 min, antibiotics should be started.
- One or more agents active against likely bacterial/fungal or viral pathogens and with good penetration into presumed source should be selected (see Chap. 49).
- Combination therapy with an extended-spectrum beta-lactam and an aminoglycoside or a fluoroquinolone is recommended for *Pseudomonas aeruginosa* bacteremia. Combination therapy may also be used for patients at high risk for multidrug-resistant bacteria like *Acinetobacter* and in neutropenic and immunocompromised patients.
- A combination of beta-lactam and a macrolide should be used in patients with pneumococcal bacteremia with septic shock.
- The duration of therapy is typically 7–10 days; longer courses may be appropriate in patients who have a slow clinical response, undrainable foci of infection, some fungal or viral infection, or immunologic deficiencies including neutropenia.
- Antiviral therapy should be initiated as early as possible in patients with severe sepsis or septic shock of viral origin, when available, such as for severe influenza infection.
- In patients at high risk like those with neutropenia and severe immunosuppression, empirical antifungal therapy should be started (refer to Chap. 53).

Step 6: Initiate hemodynamic monitoring

- For patients who do not maintain mean arterial pressure (MAP) of more than 65 mmHg in spite of initial fluid administration, central and arterial lines should be inserted under aseptic technique.
- Further fluid resuscitation should be done according to the principles of early goal-directed therapy.
- This has been proved to be useful for patients presenting within 6 h of septic shock.
- Keep central venous pressure (CVP) 8–10 cm H_2O and 12–15 cm H_2O in patients on the ventilator.
- Maintain urine output of more than 0.5 mL/Kg of body weight by fluid resuscitation.
- Keep MAP of more than 65 mmHg by fluids and vasopressors.
- Maintain $ScvO_2$ more than 70% by fluids, by keeping hemoglobin more than 10 g% (blood transfusion), and if necessary by adding dobutamine (Table 50.2).

Step 7: Optimize vasopressor use

- If the patient remains hypotensive in spite of fluid resuscitation of more than 20 mL/Kg of crystalloid or its equivalent, the vasopressor (preferably norepinephrine) needs to be started to keep MAP more than 65 mmHg (see Chap. 16).
- Intra-arterial line should be placed in all these patients.
- Epinephrine should be the first chosen alternative agent in septic shock that is poorly responsive to norepinephrine.

Table 50.2 Severe sepsis resuscitation bundle (6-h bundle): complete tasks within 6 h of identifying severe sepsis

Measure serum lactate
Obtain blood cultures prior to antibiotic administration
Administer broad-spectrum antibiotics within 3 h of emergency department (ED) admission and within 1 h of non-ED admission
In the event of hypotension and/or serum lactate >4 mmol/L:
Deliver an initial minimum of 20 mL/Kg of crystalloid
Begin vasopressors for hypotension not responding to initial fluid resuscitation to maintain MAP >65 mmHg
In the event of persistent hypotension despite fluid resuscitation (septic shock) and/or lactate >4 mmol/L:
Achieve a central venous pressure (CVP) of >8 mmHg
Achieve a central venous oxygen saturation ($ScvO_2$) ≥70% or mixed venous oxygen saturation (SvO_2) ≥ 65%

- Add low-dose vasopressin (0.03 unit/min) if the patient remains hypotensive on catecholamine.
- Vasopressin should not be used as a first-line agent for hypotension.
- Dopamine may be used as an alternative vasopressor agent to norepinephrine in highly selected patients at very low risk of arrythmias and with low cardiac output and/or low heart rate.
- High-dose vasopressors should always be given through the central line.
- All attempts should be made to taper off vasopressors once blood pressure stabilizes.
- Low-dose renal dopamine should not be used in managing these patients.
- Dobutamine infusion should be administered or added to vasopressor (if in use) in the presence of myocardial dysfunction as suggested by elevated cardiac filling pressures and low cardiac output.

Step 8: Optimize hemodynamics

- If the patient becomes hemodynamically unstable during monitoring, give further fluid challenge: 1,000 mL of crystalloids or 300–500 mL of colloids over 30 min.
- This fluid is given in addition to the maintenance fluid.
- Rate of fluid administration should be reduced if cardiac filling pressures increase without concurrent hemodynamic improvement or the patient develops signs of fluid overload and decreasing oxygen saturation.

Step 9: Identify source and assess severity of organ dysfunction

- Further investigation should be performed depending on the specific disease state.
- A specific anatomic site of infection (Table 50.3) should be established as rapidly as possible with the help of early imaging such as ultrasonography and CT scan.
- The patient should be transported for diagnostic imaging only when stable and with appropriate monitoring.

Table 50.3 Primary source of sepsis

Pulmonary: 50%
Abdomen/pelvis: ~25%
Primary bacteremia: ~15%
Urosepsis: 10%
Skin: 5%
Vascular: 5%
Other: ~15%

- Close liaison with the radiologist and concerned specialist is needed.
- SOFA (Sequential Organ Function Assessment) should be done to stratify severity of organ dysfunction (see Chap. 84, Table 1).

Step 10: A2chieve initial resuscitation sepsis bundle within 6 h of hospital admission (Table 50.2)

- "Time is tissue" so far as sepsis is concerned, and all attempts should be made for rapid assessment and attainment of early resuscitation goals in a protocolized manner.

Step 11: Control source of infection (Table 50.3)

- Source control measures should be undertaken as soon as possible following successful initial resuscitation (exception is infected pancreatic necrosis, where surgical intervention is best delayed).
- A specific anatomic diagnosis of infection requiring consideration for emergent source control, for example, necrotizing fasciitis, diffuse peritonitis, cholangitis, and intestinal infarction, should be sought and diagnosed or excluded as rapidly as possible and within the first 12 h after the diagnosis is made, if feasible.
- Remove intravascular access devices if potentially infected.

Step 12: Maintain glycemic control

- Frequent monitoring of blood glucose needs to be done.
- A protocolized approach to blood glucose management in ICU is recommended in patients with severe sepsis, commencing insulin infusion when two consecutive blood glucose levels are equal to or more than 180 mg/dL. This protocolized approach should target an upper blood glucose less than or equal to 180 mg/dL rather than an upper target blood glucose greater than or equal to 110 mg/dL.
- Keep blood sugar between 110 and 180 mg/dL, preferably with intravenous insulin infusion.
- Take care to avoid hypoglycemia.
- Avoid variability of blood sugar levels.

Step 13: Consider corticosteroids in specific situations

- If the patient remains vasopressor dependent after fluid resuscitation (especially if vasopressor requirement is high), hydrocortisone, 50 mg 6-hourly or 100 mg 8-hourly IV, should be started ideally within 24 hours.

- This can also be given by continuous infusion for better glycemic control.
- Close monitoring of glucose control needs to be maintained during steroid therapy.
- Steroid therapy may be continued till the patient is on vasopressor and gradually tapered off over a week.
- Replacement dose of steroid should be continued in patients on chronic steroid therapy.
- ACTH (adrenocorticotropic hormone) stimulation test is not routinely recommended.

Step 14: Following therapies are no more recommended in the management of severe sepsis

- Activated protein C
- Immunoglobulins
- Intravenous selenium

Step 15: Achieve sepsis management bundle goals within 24 h of hospital admission (Table 50.4)

- After initial resuscitation, the focus should be on further stabilization and starting adjunctive therapy for sepsis, which can be achieved by attaining the management bundle goals.

Table 50.4 Severe sepsis management bundle (24-h bundle): complete tasks within 24 h of identifying severe sepsis

Administer low-dose steroids for septic shock in accordance with a standardized hospital policy
Maintain glucose control (110–180 mg/dL)
Maintain inspiratory plateau pressure (IPP) ≤30 cm H_2O for mechanically ventilated patients

Step 16: Organ support

- Organ support such as ventilator and renal support should be instituted as and when necessary as per the ICU protocol (see Chap. 70).

Step 17: General support

- General ICU support such as nutrition, stress ulcer prophylaxis, and deep vein thrombosis prophylaxis should be instituted (see Chap. 70).

Suggested Reading

1. Dellinger RP, Levy MM, Carlet JM, et al. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock. Crit Care Med. 2008;36(1):296–327. *Evidenced-based recommendations regarding the acute management of sepsis and septic shock, consensus conference of 55 international experts.*

2. Kortgen A, Niederprum P, Bauer M, Implementation of an evidence-based "standard operating procedure" and outcome in septic shock. Crit Care Med. 2006;34:943–9.
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Effective antimicrobial administration within the first hour of documented hypotension was associated with increased survival to hospital discharge in adult patients with septic shock. Despite a progressive increase in mortality rate with increasing delays, only 50% of septic shock patients received effective antimicrobial therapy within 6 h of documented hypotension.
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Severe Tropical Infections

51

Hemant Tewari and Vivek Nangia

A 32-year-old male patient was admitted with high-grade fever for 7 days, fatigue and tiredness for around 6 days, jaundice for 2 days, and confusion for 1 day. He had history of travel to a seaside resort 10 days ago. He was drowsy, confused, disoriented, and icteric; hepatomegaly was present. There was an erythematosus rash on both the shins.

Severe infection with multiorgan involvement is one of the most common cause of ICU admission in tropical countries. Close monitoring and supportive therapy is the mainstay of treatment in most of these infections, but some of them have specific therapies. Rapid identification of treatable infection is imperative for a better outcome.

Step 1: Initial assessment and resuscitation

- Fluid resuscitation is the mainstay of initial management in most of the tropical infections as they present late, have predominant diarrheal component, and are usually dehydrated.
- Close monitoring for volume overload and pulmonary edema should be done.
- Recent trial conducted in Africa on a pediatric population with severe sepsis have shown fluid loading may be detrimental in this population.
- Patients presenting with encephalopathic syndromes need airway assessment and assisted ventilation.
- While resuscitation is going on, send investigations:
  - Complete blood count—neutropenia is a common feature in many tropical infections. Leptospirosis typically has leukocytosis.

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Table 51.1 Tropical infections presenting as fever

Malaria
Typhoid
Dengue fever
Leptospirosis
Chikungunya
Viral hepatitis A and E
Typhus
Tuberculosis
Brucellosis
Hepatic amebiasis
Visceral leishmaniasis
Parasitic hyperinfection (*Strongyloides*)
Relapsing fever
Viral hemorrhagic fever
Yersiniosis
Plague
Tularemia
Trypanosomiasis

  - C-reactive protein (CRP).
  - Malarial parasite (MP), dual malarial antigen.
  - Dengue antigen and serology (IgM).
  - Blood, urine, and sputum cultures as appropriate.
  - Leptospira antibody (IgM).
  - Widal test, blood culture.
  - Liver and renal profile.
- Depending on local epidemiology, further specific investigations for appropriate organisms should be done.

Step 2: Take focused history

- Tropical infections can have a variety of nonspecific presentations and generalized constitutional symptoms.
- Specific symptoms characteristic of some organisms should be carefully looked for.
- Fever:
  - Many tropical infections have febrile episodes, which are nonspecific (Table 51.1). Rarely, fever pattern can be diagnostic, such as alternate-day fever in tertian malaria (vivax or falciparum) and saddle back biphasic fever (dengue). Biphasic fever with the first phase lasting 5–7 days is followed by a second febrile phase for 1–2 days.
- Anorexia and weight loss:
  - History of severe weight loss is present in some tropical infections such as tuberculosis, visceral leishmaniasis, brucellosis, giardiasis, and schistosomiasis.

- Diarrhea and vomiting:
  - Acute watery diarrhea is a presenting feature of cholera, *Giardia*, rotavirus, *Cryptosporidium*, *Isospora*, and *Bacillus cereus* (toxin).
  - Bloody diarrhea occurs in amebic dysentery, enteroinvasive and enterohemorrhagic *Escherichia coli*, *Shigella*, *Salmonella*, *Yersinia*, *Clostridium perfringens*, and *Campylobacter.*
  - Chronic diarrhea (>2 weeks) is characteristic of giardiasis, amebiasis, ileocecal tuberculosis, strongyloidiasis, schistosomiasis, and Trichuris infestation.
- Abdominal pain:
  - Acute abdomen with features of peritonitis may be present in typhoid perforation and ruptured amebic liver abscess.
  - Other tropical infections presenting as acute abdomen are amebic liver abscess, splenic rupture (malaria, typhoid), biliary colic (*Ascaris*), intestinal obstruction or volvulus (*Ascaris*), acute salpingitis (*Chlamydia*), and severe gastroenteritis.
- Jaundice:
  - Jaundice with fever may be a presenting feature of certain tropical infections such as viral hepatitis, leptospirosis, typhus, typhoid, yellow fever, brucellosis, amebic liver abscess, miliary tuberculosis, malaria (hemolysis—G6PD deficiency), ascending cholangitis (*Ascaris*), and hemolytic uremic syndrome (*Shigella*, *E. coli*).
- Cough and dyspnea:
  - These may be prominent in infections such as extensive pulmonary tuberculosis, amebic lung abscess, acute respiratory distress syndrome (leptospirosis, malaria), diffuse intra-alveolar hemorrhage (dengue, leptospirosis, hemorrhagic fever), pulmonary hydatid disease, paragonimiasis, and pneumonic plague.
- Headache:
  - Most febrile illnesses—especially malaria, typhoid, and dengue fever—are accompanied by headache.
- Sore throat:
  - Severe sore throat with painful swallowing is characteristic of *Corynebacterium diphtheriae* infection, though rare due to vaccination programs.
- Hematuria, dysuria, and renal colic:
  - Some tropical infections such as schistosomiasis, renal tuberculosis, and chlamydial urethritis can present with hematuria.
- History of skin rash (*see Step 3*).
- Travel history: A list of places visited in recent past in chronological order should be elicited. Endemic infections in different geographical areas should be considered in differential diagnosis.
- Occupational history: Exposure to contaminated water source may be a clue to leptospirosis.
- Seasonal variation: Many tropical infections have propensity to occur during the monsoon season.
- Rash: Presence and distribution of rash can point toward different infections.
- Animal exposure: pet dogs (ticks—rickettsial infection).

Step 3: Perform focused physical examination

- General examination: Examine for anemia, lymphadenopathy, jaundice, and edema.
- Skin: Many tropical infections present with skin manifestations, and these should be searched meticulously:
  - Maculopapular rash—dengue, typhus, measles, and rubella
  - Urticaria—strongyloidiasis and schistosomiasis
  - Petechial rash—typhus, meningococcemia, and viral hemorrhagic fever
  - Vesicles—chicken pox, herpes simplex, and herpes zoster
  - Eschar—typhus
- Abdomen: Examine for hepatosplenomegaly and abdominal distension:
  - Predominant hepatomegaly—viral hepatitis, amebic liver abscess, leptospirosis, yellow fever, and brucellosis.
  - Predominant splenomegaly—malaria, typhoid, typhus, visceral leishmaniasis, and hydatid disease.
  - Abdominal distension could be due to ascites (tuberculosis) or dilated bowel loops (*Shigella* dysentery).
- Cardiorespiratory system:
  - Relative bradycardia is a feature of typhoid and typhus fever.
  - Pleural effusion (tuberculosis).
  - Appearance of new murmurs—especially regurgitant—and infective endocarditis.
- Central nervous system:
  - Confusion and decreased conscious level: cerebral malaria, typhoid, dengue fever, leptospirosis, typhus, rabies, and viral hemorrhagic fever
  - Predominant encephalitic features: arbovirus, herpes simplex, measles, chickenpox, yellow fever, and rabies
  - Predominant meningitic feature: enterovirus, tuberculosis, amebiasis, and strongyloidiasis, bacterial
  - Seizures: cerebral malaria, schistosomiasis, neurocysticercosis, tuberculoma, and cerebral hydatid
- Eyes: conjunctival infection, petechiae (leptospirosis and typhus), viral infection.

Step 4: Send investigations

These should be sent on the basis of initial presentation and suspected infection.

- Presenting syndrome
  - *Fever with a rash:* dengue serology, platelet count, chikungunya serology, meningococcal serology, rickettsial serology, Widal test (typhoid), Epstein–Barr virus serology
  - *Fever with hepatorenal dysfunction:* malaria parasite thick and thin blood film and antigen, *Leptospira* antibody, hepatitis E and A (hepatitis serology), sputum for acid-fast bacilli (disseminated tuberculosis), Widal test, blood cultures
  - *Fever with severe sepsis and multiorgan failure:* malaria antigen, MP smears, *Leptospira* serology, dengue serology, *Legionella* serology, varicella and influenza serology

  - *Fever with decreased level of consciousness—specific investigation:* MP smear and antigen; lumber puncture; CT scan for tubercular meningitis, pyogenic meningitis, and viral encephalitis; herpesvirus serology and PCR
- Specific tests
  - *Dengue*
    - ELISA test for IgM antibodies (positive day 6)—IgG antibodies appear after 7–10 days and last for months to years. In the secondary dengue, IgG antibodies are present in high titer early in illness.
    - The gold standard test is the detection of antibodies by hemagglutination inhibition assay showing at least fourfold rise in titer of neutralizing antibodies in paired samples.
    - Dengue NS 1 antigen which becomes positive in 4–5 days.
  - *Leptospirosis*
    - Serology with the microscopic agglutination test is the gold standard with either a fourfold rise in titers between acute and convalescent serum or a single titer of more than 1:800 being diagnostic.
    - Other serological tests are IgM antibody by an enzyme-based dot immunoassay with a sensitivity of 30% at 3 days and of 100% at 10 days into the illness.
    - Polymerase chain reaction (PCR) test for *Leptospira* antigen shows considerable promise.
  - *Malaria*
    - Three thick and thin smears 12–24 h apart should be obtained. The highest yield of peripheral parasites occurs during or soon after a fever spike; however, smears should not be delayed while awaiting fever spikes.
    - Thick smears are 20 times more sensitive than thin smears, but speciation may be more difficult. The parasitemia can be calculated based on the number of infected RBCs.
    - Thin smears are less sensitive than thick smears but facilitate speciation. This should be considered a qualitative test.
    - The quantitative buffy coat is a technique that is as sensitive as thick smears.
    - Malarial antigen—immunochromatographic tests based on antibodies to malarial antigen like histidine-rich protein-2 (PfHRP2), parasite LDH (pLDH), or plasmodium aldolase appear to be very sensitive and specific.
  - Rickettsial infection
    - Look for eschar
    - Serology for typhus fever
  - Special investigations
    - Procalcitonin, ESR, CRP.
    - Aspirates, scrapings, and pustular fluid may be obtained for Gram staining and culture. When a herpes simplex virus infection is suspected, a Tzanck test may be performed by unroofing a lesion and taking a scraping of the lesion base.

- Biopsy samples from nonhealing or persistent purpuric lesions: Biopsy of inflammatory dermal nodules, ulcers, and muscles (tropical pyomyositis) should be done.
- HIV serology.
- Imaging: chest x-ray, echo, ultrasound of abdomen, and CT scan (when indicated).

Step 5: Start general supportive care and specific organ support (see Chap. 79)

- Many tropical infections are self-limiting. Close monitoring and general organ support in the initial days or weeks of viremia or parasitemia will salvage many patients.

Step 6: Initiate empirical therapy based on initial presentation

- Specific therapy is available only for a few tropical infections.
- Depending on the clinical presentation and endemicity of a particular infection in the geographical region, an educated guess for initial therapy has to be decided till definitive investigations are available.
- Usually, intravenous ceftriaxone, 2 g IV twice daily, to cover typhoid fever and leptospirosis is started if MP and dual antigen is negative.
- In patients with shock and MODS, broad-spectrum antibiotics should be started immediately. De-escalate antibiotics once specific infection is identified.

Step 7: Start specific treatment once the diagnosis is confirmed

- Dengue
  - A protocol for intravenous fluid therapy has been developed by the World Health Organization (WHO).
  - An initial bolus of 5% dextrose in normal saline or Ringer lactate (20 mL/kg of body weight) is infused over 15 min, followed by continuous infusion (10–20 mL/kg/h, depending on the clinical response) until vital signs and urine output normalize.
  - Crystalloids are equally effective as colloids in fluid resuscitation.
  - Normalization of the hematocrit is an important goal of early fluid repletion.
  - However, a normal or low hematocrit may be misleading in patients with overt bleeding and severe hypovolemia.
  - Close clinical observation is essential, even after normal blood volume is restored, because patients can develop shock for 1–2 days after initial fluid resuscitation, which represents the period of increased vascular permeability in dengue hemorrhagic fever.
  - Management of fever:
    - Control fever with paracetamol, cold sponging, and cold IV fluids.
    - Avoid aspirin and nonsteroidal anti-inflammatory drugs due to bleeding risk and risk of developing Reye syndrome (encephalopathy).
  - Manage shock and multiorgan failure.
  - Manage secondary infections.

  - Manage complications.
  - Platelet transfusions need to be given for symptomatic thrombocytopenia.
  - Platelet transfusions have not been shown to be effective in preventing or controlling hemorrhage but may be warranted in patients with severe thrombocytopenia (<10,000/mm^3) and active bleeding. Prophylactic platelet transfusions in patients with severe thrombocytopenia but without active bleeding are generally not recommended.
  - Manage complications of fluid therapy in dengue fever.
  - A decrease in hematocrit together with stable hemodynamic status and adequate urine output indicates hemodilution and/or reabsorption of extravasated fluids.
  - Judicious use of intravenous fluids with proper monitoring is recommended.
  - Fluid therapy may have to be discontinued if required, immediately, to avoid pulmonary edema, electrolyte imbalance, hypo- or hypernatremia, and hyperchloremic metabolic acidosis.
- Leptospirosis
  - Treatment involves the use of crystalline penicillin at a dose of six million units daily or ceftriaxone 1 g every 12 h.
  - In penicillin-allergic patients, intravenous or oral doxycycline, 100 mg every 12 h, can be used.
  - Manage shock, disseminated intravascular coagulation, and multiorgan failure.
- Falciparum malaria
  - For *Plasmodium falciparum* infections acquired in areas without chloroquine-resistant strains, patients should be treated with oral chloroquine. A chloroquine dose of 600 mg base (=1,000 mg salt) should be given initially, followed by 300 mg base (=500 mg salt) at 6, 24, and 48 h after the initial dose for a total chloroquine dose of 1,500 mg base (=2,500 mg salt).
  - For chloroquine-resistant strains, treatment options are as follows:
    - Quinine sulfate: Quinine has a rapid onset of action and, in combination with tetracycline, doxycycline, or clindamycin, it has been shown to be a very efficacious treatment option for *P. falciparum* infections acquired in regions with chloroquine-resistant strains.
    - Artemisinin derivatives clear parasites very rapidly, are now a key component of malaria treatment worldwide, and have been shown to reduce mortality in severe malaria compared with parenteral quinine. Artemisinin-based combination therapies, including artesunate–mefloquine, artemether–lumefantrine, artesunate–amodiaquine, and dihydroartemisinin–piperaquine, are highly efficacious.
    - Under the CDC protocol, intravenous artesunate is administered in four equal doses of 2.4 mg/kg of body weight over a period of 3 days. The dosing schedule recommended by the WHO entails doses every 12 h on day 1 and then once daily.
    - Up to 7 days of therapy may occasionally be indicated in very ill patients.

Suggested Reading

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   Fluid boluses significantly increased 48-h mortality in critically ill children with impaired perfusion in the resource-limited settings in Africa.
2. Hess KM, Goad JA. Intravenous artesunate for the treatment of severe malaria. Ann Pharmacother. 2010;44(7–8):1250–8.
   Three major studies regarding the use of intravenous artesunate are reviewed. Several international studies comparing intravenous quinine and artesunate conclude that artesunate has the highest treatment success, with lower incidence of adverse events.
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   Leptospirosis is an important infection with high mortality when associated with organ dysfunction. The poor prognostic factors are preponderance of male sex, alcohol dependence, age group more than 50 years, MODS, acute respiratory distress syndrome (ARDS), presence of acidosis, and need for mechanical ventilation.

Websites

1. www.thehtd.org
   The Hospital for Tropical Diseases is dedicated to the prevention, diagnosis, and treatment of tropical diseases and travel-related infections.
2. www.who.int/topics/tropical_diseases
   An extensive repository on guidelines for many tropical infections

New-Onset Fever

52

Subhash Todi and Rajesh Chawla

A 70-year-old male patient was admitted to the ICU with hemorrhagic stroke. On the fifth day of admission, he spiked a fever of 100°F orally. He was not intubated and had an indwelling urinary catheter, peripheral intravenous cannula, and a nasogastric tube. His sensorium remained unchanged, and he was hemodynamically stable.

New onset of fever is an everyday problem encountered in the ICU. The reason could be manifold such as noninfectious cause, mild infection, or an initial presentation of severe infection. This should trigger a careful clinical assessment and a systematic approach to differentiate these possibilities.

Step 1: Record temperature

- All patients in the ICU should have, as a minimum, hourly temperature recorded and charted in the nursing record as per the ICU protocol.
- The site of recorded temperature should be marked in the nursing chart (O = oral, R = rectal, A = axillary, T = tympanic).
- All ICUs should have access to a core temperature measurement device (tympanic, rectal), properly calibrated and sterilized.
- Temperature may be recorded as centigrade or Fahrenheit.
- Uniformity of the scale should be maintained.

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- In immunocompetent patients who are stable, temperature below 101°F in which clinical examination does not reveal any definite source of fever may be observed for a few hours before initiating investigation.
- As a general rule, temperature of more than 38.3°C (101°F) warrants special attention in all patients.
- In immunocompromised patients, temperature of any degree should be investigated.

Step 2: Take a detailed history

- Take proper history from the bedside nurse and do a thorough chart review.
- Inquire about medications, blood transfusion, diarrhea, rash, new procedure, dressing changes, and line manipulation.
- Duration of indwelling urinary catheter and central line placement.

Step 3: Perform focused clinical examination

- Examine for any source of infection or noninfectious causes of fever (Tables 52.1 and 52.2).
- Perform systematic head-to-toe examination:
  - Purulent nasal discharge, sinus tenderness
  - Parotid swelling, oral hygiene
  - Chest auscultation (including bases)
  - New murmur
  - Abdominal examination, suprapubic tenderness
  - Vascular device sites for purulence and erythema, note insertion date
  - Urinary catheter site

Table 52.1 Noninfectious causes of fever in the ICU

Drug fever
β-Lactam, antiepileptics, sulfonamides
Antipsychotics (neuroleptic malignant syndrome, serotonin syndrome)
Blood products, IV contrast, immunoglobulins, albumin
CNS causes: blood in cerebrospinal fluid, pontine bleed
Pulmonary/cardiac causes: acute respiratory distress syndrome, pulmonary emboli, fat emboli, pericarditis
Abdominal causes: ischemic gut, pancreatitis, acalculous cholecystitis
Metabolic: adrenal insufficiency, thyroid storm, gout
Postoperative fever (48 h), postprocedure (bronchoscopy)
Thrombophlebitis, decubitus ulcer, hematoma, deep venous thrombosis (DVT)

Table 52.2 Infectious causes of new-onset fever in the ICU

Ventilator-associated pneumonia
Sinusitis
Catheter-related sepsis
Urinary tract infection
Clostridium difficile diarrhea
Complicated wound infections

- Surgical wounds, drain sites (take off dressings)
- Skin rash
- Gynecological examination
- Painful leg swelling
- Decubitus ulcer

Step 4: Send investigations

- If clinical examination does not strongly suggest a noninfectious source, a pair of blood cultures should be sent in the following:
  - In patients with temperature above 101°F
  - In patients who are hemodynamically unstable or develop new organ dysfunction or immunosuppressed, with new onset of fever of any degree
- All ICUs should have a blood culture drawing protocol in consultation with microbiology department:
  - Skin disinfection: 2% chlorhexidine or 2% iodine, give 30 s for drying.
  - Site: two peripheral venepunctures, or one from distal lumen of the central line and another from periphery.
  - Minimum two sets—20 mL in each—to be inoculated directly into the culture bottle.
  - Labeling should be done carefully for site, date, and time.
- If infection is suspected clinically and there is a focus on infection, the following investigations should be sent:
  - Total and differential white blood cell count, C-reactive protein (CRP), procalcitonin when presence of infection is in doubt.
  - Focused imaging such as chest X-ray, abdominal ultrasonography, CT scan of the abdomen/chest.
  - If there is a history of diarrhea, send stool for occult blood, pus cells, *Clostridium difficile* toxin.
  - Urinalysis and culture sensitivity.
  - Transthoracic/transesophageal echocardiogram—look for vegetations.
  - Sputum, endotracheal suction, bronchoscopy with bronchoalveolar lavage sent for Gram stain and quantitative bacterial culture and sensitivity.
- Trend of white blood cell count or CRP is valuable to ascertain any new infection.

Step 5: Remove lines if there is a suspicion of line sepsis

- All patients with a vascular access of some duration and persistent fever without any other obvious source of infection should have the line removed at the earliest if any of the following criteria are met:
  - Inflammation or purulence present at the insertion site or along the tunnel
  - No other identifiable source of infection
  - An abrupt onset, associated with fulminant shock
  - Nonfunctioning lumen
  - Fever on starting infusion/dialysis
  - Persistent bacteremia or fungemia

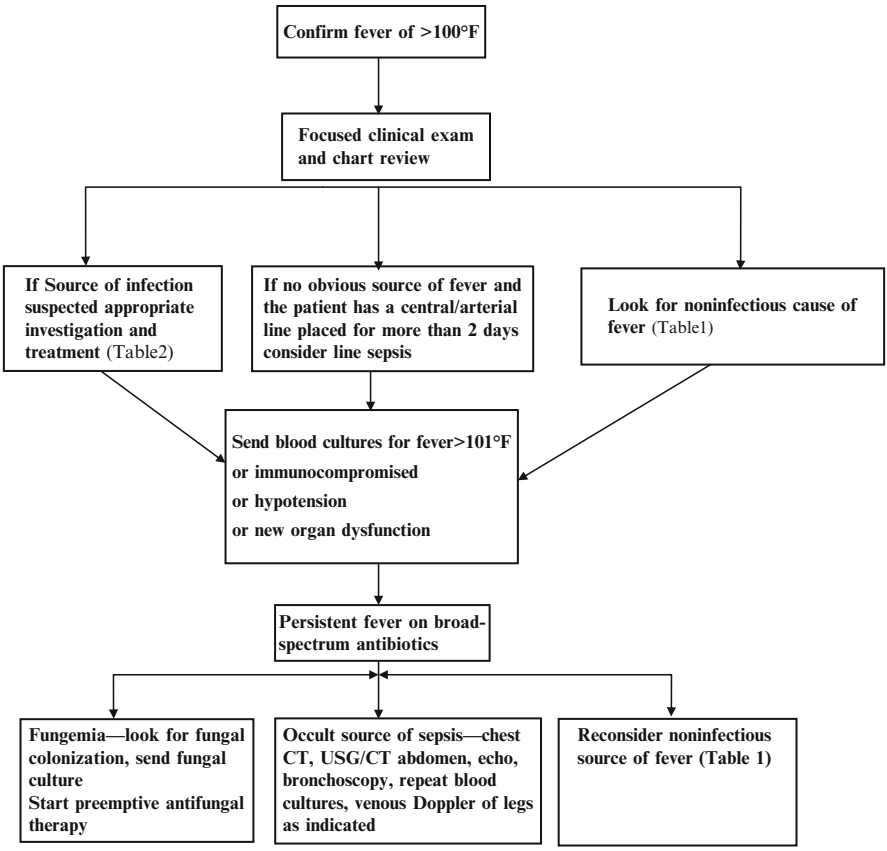

Fig. 52.1 An approach to new onset of fever in the ICU

- The intracutaneous and tip of the central line should be sent for semiquantitative culture.
- Central line infection is considered significant for the following situations:
  - Culture of the same organism from both the catheter tips and at least one percutaneous blood culture
  - Multiple blood cultures containing organisms that might otherwise be disregarded as contaminants such as *Staphylococci* (especially coagulase-negative *Staphylococci*) and *Candida*
  - Positive semiquantitative culture of the catheter tip (>15 cfu)
  - Differential time to positivity—growth detected from the catheter sample at least 2 h before growth detected from the peripheral vein sample (Fig. 52.1)

Step 6: Make a diagnosis

- In patients on the ventilator, pneumonia should be considered by clinical examination, purulence of endotracheal secretions, raised white blood cell count, and new infiltrate on chest skiagram.

- Consider urosepsis in patients with an indwelling bladder catheter and increased pus cells in urine.
- Consider sinusitis in patients with the nasogastric tube and purulent nasal discharge.
- Consider inflammatory diarrhea (stool positive for occult blood) with abdominal distension, and in patients on antibiotics, investigate for *C. difficile* colitis.
- Consider gynecological infection if vaginal discharge is present.

Step 7: Start treatment

- If infectious cause for fever is suspected, empirical antibiotic therapy should be started.
- The choice of antibiotics should be guided by the hospital antibiotic policy and suspected source of infection (see Chap. 49).
- In patients with persistent fever despite broad-spectrum antibiotics, look for occult source of sepsis.
- Consider fungemia in patients colonized by fungus.
- Never forget noninfectious causes of fever.

Suggested Reading

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Fungal Infections

53

Subhash Todi and Rajesh Chawla

A 50-year-old diabetic male patient was admitted to hospital with pancreatitis. He had received imipenem for 2 weeks. He had spiking fever and abdominal CT showed peripancreatic collection. Growth of *Candida* species was found in his urine.

With increasing incidence of elderly patient population, comorbidities, prolonged ICU stay, invasive therapies, and use of broad-spectrum antibiotics, there is a rising incidence of fungal infection and use of antifungal drugs. Candidemia is the most common invasive fungal infection encountered in the ICU and is the fourth most common cause of bloodstream infection. *Candida albicans* is the most common identified species, but there is an increasing shift to non-*albicans Candida* species. Attributable mortality with candidemia could be as high as 47%. Other fungal infections seen in the ICU are invasive aspergillosis and zygomycosis. With increasing threat of developing resistance, antifungal drugs should be used judiciously, either prophylactic, empiric, or as a definitive therapy.

Step 1: Take focused history and perform physical examination to identify the patient at risk of candidemia

- Classical risk factors described for candidemia are as follows:
  - Prolonged ICU stay
  - Use of broad-spectrum antibiotics

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  - Central venous catheters
  - Parenteral nutrition
  - Neutropenia
  - Candida colonization
  - Diabetes
  - Renal replacement therapy
  - Pancreatitis
  - Implantable prosthetic devices
  - Immunosuppressive agents (glucocorticoid, chemotherapeutic agents, immunomodulating agents)
  - Abdominal surgery
- All patients with suspected candidemia should have an ophthalmological examination to rule out endophthalmitis.
- Cardiac examination should be performed to look for features suggestive of endocarditis.
- Abdominal examination is required for hepatosplenomegaly suggestive of visceral candidiasis.
- Neurological examination is performed to look for features of meningoencephalitis in patients with intraventricular catheters.
- Cutaneous examination to look for skin changes of disseminated candidiasis.

Step 2: Send blood for fungal cultures for persistent fever
- Presence of *Candida* in blood culture is usually pathological.
- Fungal cultures can be obtained in the aerobic culture bottles used for aerobic bacterial cultures.
- Blood cultures are positive in only 50–70% of patients with invasive candidiasis.
- In patients with documented candidemia, repeat blood cultures should be obtained frequently, preferably daily or alternate days, till they become negative.

Step 3: Differentiate colonization from infection with *Candida*
- Growth of *Candida* from respiratory secretions usually represents colonization, and therefore, it should not be treated.
- In the absence of systemic features, growth of *Candida* in the urine often represents colonization.

Step 4: Identify patients in whom empiric antifungal therapy should be considered
- Early empirical therapy in patients with candidemia has been proved to reduce mortality.
- Empirical antifungal therapy should be considered in patients with one or more risk factors for invasive candidiasis and if they show one or more of the following features:
  - Persistent fever without a definite source
  - Fever not responding to antibiotics

- Positive serological markers for systemic fungal infection (β-D-glucan)
- *Candida* colonization of one or more sites (e.g., urine, sputum, and skin)

Step 5: Get familiar with antifungal agents used in patients with suspected or proven candidemia

- Choice of antifungal agents in candidemia is guided by many factors:
  - History of recent azole exposure—avoid azoles.
  - Local epidemiological data from the ICU regarding predominant *Candida* species and susceptibility pattern—choose most effective antifungal agents initially pending culture results.
  - Severity of illness—use fungicidal drugs in severely ill patients.
  - Comorbidity—check renal and hepatic function and avoid amphotericin deoxycholate and voriconazole respectively.
  - Involvement of CNS, cardiac valves, and eyes—choose antifungal agents for penetration at the infected site.
  - History of intolerance to any antifungal agent or drug interactions.
- Antifungal agents used for candidemia are triazoles, echinocandins, and amphotericin B.

Triazoles

- Triazoles include fluconazole, itraconazole, voriconazole, and posaconazole. In the ICU, fluconazole and voriconazole are used most often.
- They all have similar activity against most *Candida* species and are fungistatic. They have less activity against *Candida glabrata* and *Candida krusei*.
- They inhibit cytochrome P450 and are prone to drug–drug interaction.
- Fluconazole is available both as an oral and as intravenous formulations. It is readily absorbed orally. It has the greatest penetration into the cerebrospinal fluid and vitreous body.
- In patients with invasive candidiasis, fluconazole should be administered with a loading dose of 800 mg (12 mg/kg), followed by a daily dose of 400 mg (6 mg/kg); a lower dosage is required in patients with creatinine clearance of less than 50 mL/min.
- Voriconazole is available in both oral and intravenous forms. It is used mainly for infection with *Aspergillus*. Its clinical use in candidiasis has been primarily for step-down oral therapy for patients with infection due to *C. krusei* and fluconazole-resistant, voriconazole-susceptible *C. glabrata*.
- In adults, the recommended oral dosing regimen includes a loading dosage of 400 mg twice daily for 1 day, followed by 200 mg twice daily.
- Intravenous voriconazole is complexed to a cyclodextrin molecule; after two loading dosages of 6 mg/kg every12 h, a maintenance dosage of 3–4 mg/kg every 12 h is recommended. Because of the potential for cyclodextrin accumulation among patients with significant renal dysfunction, intravenous voriconazole is not recommended in patients with a creatinine clearance less than 50 mL/min.

- Oral voriconazole does not require dosage adjustment for renal insufficiency, but it is the only triazole that requires dosage reduction for patients with mild-to-moderate hepatic impairment.
- Common polymorphisms in the gene encoding the primary metabolic enzyme for voriconazole result in wide variability of serum levels. Therapeutic drug level monitoring is advisable when using voriconazole.
- Drug–drug interactions are common with voriconazole and should be considered when initiating and discontinuing treatment with this compound.

Echinocandins
- Echinocandins are caspofungin, anidulafungin, and micafungin and are available only as parenteral preparations.
- These are fungicidal drugs and have equal efficacy.
- All echinocandins have a few adverse effects and minimal drug–drug interaction.
- The pharmacological properties in adults are also very similar, and echinocandins are administered intravenously once daily.
- None of the echinocandins require dosage adjustment for renal insufficiency or dialysis.
- Caspofungin is the only echinocandin for which dosage reduction is recommended for patients with moderate-to-severe hepatic dysfunction.
- Intravenous dosing regimens for invasive candidiasis with the three compounds are as follows: caspofungin, loading dose of 70 and 50 mg daily thereafter; anidulafungin, loading dose of 200 and 100 mg daily thereafter; and micafungin, 100 mg daily.
- All echinocandins have a broad-spectrum activity against most of the *Candida* species.

Amphotericin B (Amph B)
- This is available in non-lipid formulation (Amph B deoxycholate AmB-d) or lipid formulation (ABLC, ABCD, and L-AmB).
- These are fungicidal drugs.
- The three lipid formulations have different pharmacological properties and rates of treatment-related adverse events and should not be interchanged.
- All amphotericin preparations have a very broad-spectrum activity against most *Candida* species.
- For most forms of invasive candidiasis, the typical intravenous dosage for AmB-d is 0.5–0.7 mg/kg daily, but dosages as high as 1 mg/kg daily should be considered for invasive *Candida* infections caused by less susceptible species, such as *C. glabrata* and *C. krusei*.
- The typical dosage for liposomal preparations of AmB is 3–5 mg/kg daily when used for invasive candidiasis.
- Nephrotoxicity is the most common serious adverse effect associated with AmB-d therapy, resulting in acute renal failure in up to 50% of recipients. This can be minimized by avoiding concomitant use of other nephrotoxic agents,

proper hydration, and saline loading prior to use of AmB-d. Its use is associated with hypokalemia and hypomagnesemia due to renal wasting, and levels of these electrolytes should be monitored and replaced.
– Liposomal preparations of AmB are considerably more expensive than AmB-d, but all have considerably less nephrotoxicity.
– AmB-d and other liposomal preparations have infusion-related toxicity with fever and rigor and require pretreatment with antipyretics.

Step 6: Choose appropriate antifungal regimen for patients with suspected or proven candidemia
- Fluconazole is recommended in patients who are less critically ill and who have no recent azole exposure and no known resistance to fluconazole.
- Echinocandins are recommended in patients with moderately severe to severe illness or patients who have had recent azole exposure and in neutropenic patients.
- Amphotericin B, preferably lipid formulation, may replace echinocandins in patients with normal renal function, cost consideration, and nonavailability of echinocandins.
- Amphotericin B, preferably liposomal preparations, may be considered in neutropenic patients where invasive *Aspergillus* or mucormycosis is a possibility.
- Transition from an echinocandin to fluconazole is recommended for patients who have isolates that are likely to be susceptible to fluconazole (e.g., *C. albicans*) and who are clinically stable.
- Combination antifungal therapy is sometimes used in the following situations:
  – Invasive aspergillosis refractory to amphotericin B—voriconazole with caspofungin.
  – Central nervous system infection (cryptococcal meningitis)—amphotericin B with flucytosine.
- Voriconazole is recommended as step-down oral therapy for selected cases of candidiasis due to *C. krusei* or voriconazole-susceptible *C. glabrata*.
- Recommended duration of therapy for candidemia without obvious metastatic complications is 2 weeks after documented clearance of *Candida* species from the bloodstream (last negative blood culture) and resolution of symptoms attributable to candidemia.
- Intravenous catheter removal is strongly recommended for nonneutropenic patients with candidemia.
- In patients with endophthalmitis, consider amphotericin B deoxycholate along with flucytosine for 4–6 weeks. Consider early partial vitrectomy in severe cases.

Step 7: Manage persistent candiduria in a catheterized patient
- Avoid treating with antifungal drugs in an asymptomatic, afebrile, stable patient.
- Remove the catheter if possible.
- In high-risk patients such as neutropenic, urological surgery, consider fluconazole therapy if the species is susceptible.

Step 8: Consider central nervous system candidiasis in patients with an intraventricular device

- Consider liposomal amphotericin B at a dosage of 3–5 mg/kg/day with or without flucytosine at a dosage of 25 mg/kg/dose four times daily.
- After initial response, deescalate to fluconazole 400–800 mg daily.
- Remove the infected ventricular device.

Step 9: Consider azole prophylaxis in the selected group of patients

- Prophylactic antifungal therapy has not been proven to decrease mortality from invasive candidiasis in medical/surgical ICU patients and should be avoided.
- For high-risk patients such as neutropenic, solid organ transplant, or stem cell transplant, fluconazole 400 mg (6 mg/kg) daily, posaconazole 200 mg three times a day, or an echinocandin is recommended during the period of neutropenia.

Step 10: Consider possibility of invasive aspergillosis in some situations

- Invasive aspergillosis should be suspected in the following group of patients:
  - Prolonged neutropenia more than 10 days
  - Hematopoietic stem cell transplantation
  - Solid organ transplantation
  - Corticosteroid therapy
- Look for involvement of lungs and paranasal sinuses by CT scan, which may show a "halo sign," a haziness surrounding nodular pulmonary infiltrate.
- Serum galactomannan assay has a moderate sensitivity and specificity for diagnosing invasive aspergillosis. It will be falsely positive in patients treated with piperacillin–tazobactam.
- Isolation of *Aspergillus* hyphae from nonsterile sites like respiratory secretions may represent colonization. Demonstration of the organism in tissue biopsy is considered a gold standard, but it is difficult to perform in ICU patients.
- Voriconazole is considered a first-line agent for treatment of invasive aspergillosis. Echinocandins have in vitro sensitivity against *Aspergillus* and may be considered in selected cases.
- In nonresponder combination, antifungal therapy may be tried.

Step 11: Consider zygomycosis (mucormycosis) in some specific situations

- Consider this mould infection in patients with uncontrolled diabetes presenting with rhinocerebral disease.
- This mould also infects immunosuppressed patients and mainly involves the lung.
- Diagnosis is based mainly on tissue biopsy.
- High-dose amphotericin B is considered standard first-line therapy (amphotericin B deoxycholate 1–1.5 mg/kg body wt/day or lipid amphotericin preparation at 5 mg/kg body wt/day).
- Echinocandins and azoles are ineffective against zygomycosis.
- Surgical intervention is usually required in this angioinvasive disease.

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The use of early antifungal therapy should be reserved for patients with a high risk (10–15%) of developing invasive candidiasis (IC). There is no single predictive rule that can adequately forecast IC in critically ill patients. Clinicians should assess patients on a case-by-case basis and determine the need for early antifungal treatment strategies based on frequent evaluations of risk factors and clinical status.

Infections in the Immunocompromised Host

54

Subhash Todi and Om Srivastav

A 29-year-old female patient, 2 years after kidney transplant, on mycophenolate, sirolimus, and prednisolone, presented with semiconsciousness, ulcerating lesions around right elbow, and oliguria for the past 6 h.

Managing infection in an immunocompromised patient is a challenge to any ICU physician, as the presentation is varied and subtle and needs high index of suspicion for diagnosis and multiple possible etiologies. A methodological approach to investigation and choice of empirical therapy is warranted in these patients. Complexity of the problem necessitates close liaison between the microbiologist, infectious disease consultant, and hemato-oncologist.

Step 1: Resuscitate

- If assisted respiration is required, initially noninvasive ventilation should be tried.
- The patient should be closely monitored, and if no improvement or deterioration occurs in 2 h, invasive ventilation should be initiated.
- Invasive catheters and lines should be avoided as these patients are coagulopathic and neutropenic and have a high risk of line sepsis.
- Careful maintenance of the peripheral channel is extremely vital in these patients.

Step 2: Take a focused history (Table 54.1)

- This should be done to determine the type and duration of the immunocompromised state.

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Table 54.1 Syndromic approach to infection in immunocompromised patients

Pneumonia
Focal/nodular infiltrate
Bacteria, *Aspergillus*, mycobacteria, *Nocardia*, *Histoplasma*
Diffuse Infiltrate
Virus (cytomegalo, herpes), *Pneumocystis*, *Strongyloides*
Meningoencephalitis
Bacteria: *Neisseria, Hemophilus, Pneumococcus, Listeria*
Mycobacteria: typical and atypical
Fungus: *Cryptococcus*
Focal CNS lesions
Toxoplasma
Tuberculoma
Nocardia
Severe sepsis or septic shock
Gram-positive and Gram-negative bacteria
Candidemia
Gastroenteritis
Strongyloides
Cryptococcosis
Amebiasis

- Disease states such as hematological malignancy (leukemia and lymphoma), solid organ tumor, and conditions associated with neutropenic state should be looked for.
- History of any organ transplant and duration since transplant should be taken.
- HIV status should be determined, with proper consent.
- History of chemotherapy or radiotherapy should be taken.
- Detailed drug history should be elicited.
- Neurological, respiratory, gastrointestinal symptoms need to be elicited to narrow down differential diagnosis of opportunistic infection.

Step 3: Perform focused physical examination (Table 54.1)

- Any breach of skin or mucosal abrasion, skin ulcer, oral ulcer, oral thrush, and perianal lesion should be searched for.
- Look for skin rash.
- All insertion sites of invasive lines should be inspected for tenderness or discharge.
- All suture lines and drain sites should be inspected in postoperative patients after removing the dressing.
- Look at the back for decubitus ulcer.
- Do neurological, respiratory, and gastrointestinal system examination to determine organ system involvement.

Step 4: Send basic investigations

- There is a broad differential diagnosis of opportunistic infection—bacterial, viral, or fungal—in immunocompromised patients.

Table 54.2 Immunodeficiency states

T-lymphocyte deficiency
Causes
HIV/AIDS
Lymphoma
Corticosteroids
Drugs (methotrexate)
Organisms
Intracellular bacteria (mycobacteria, *Legionella*)
Virus (herpes, cytomegalovirus)
Fungi (*Pneumocystis*, *Cryptococcus*, *Histoplasma*)
Parasites (*Strongyloides*, *Toxoplasma*)
Nocardia
B-lymphocyte deficiency
Causes
Multiple myeloma
Acute leukemia
Drugs (corticosteroid, azathioprine, mycophenolate)
Plasmapheresis
Burn
Organisms
Encapsulated bacteria (*Neisseria, Pneumococcus, Hemophilus*)
Salmonella
Campylobacter
Giardia

Neutropenia
Causes
Chemotherapy
Hematological malignancy
Myelodysplasia
Severe viral infection
Hypersplenism
Organisms
Gram-negative bacilli (enteric and nonenteric)
Staphylococcus aureus
Coagulase-negative *Staphylococcus*
Streptococci, enterococci
Fungi (*Aspergillus* spp., *Candida* spp.)
Neutrophil dysfunction
Causes
Diabetes
Uremia
Alcoholism
Cirrhosis
Burn
Organisms
Staphylococcus aureus
Streptococci
Mucor (Zygomycoses)
Gram negative bacilli (enteric and non-enteric)
Coagulase negative staphylococcus
Fungi (Aspergillus spp., Candida spp.)

- These patients are also prone to infections which are common in nonimmunocompromised patients.
- In these patients, infection mimics drug reaction, transfusion reaction, radiation-induced complications, and disease-associated problems, which all need to be properly investigated.
- Focused investigation, initially noninvasive and then invasive, should be performed to confirm the causative organism in order to narrow down anti-infective agents.

Step 5: Identify underlying immune deficiency states and suspected pathogens (Table 54.2)

- Based on history, physical examination, and basic investigation, an approximation of underlying immunodeficiency states needs to be recognized.

Table 54.3 Diagnostic test and treatment of opportunistic pathogens

Organism	Test	Treatment
Bacteria		
Gram-positive/negative	Gram Stain: BAL, Fluid, Urine Cultures (aerobic and anaerobic): Blood, BAL, Fluids, Urine	Vancomycin/teicoplanin/ daptomycin (Gm+) Carbapenem, piperacillin–tazobactam (Gm−)
Mycobacterium tuberculosis	Induced sputum/BAL/AFB stain	Four-drug therapy
Nontuberculosis mycobacteria	Induced sputum/BAL/AFB stain	Variable
Nocardia spp.	Sputum/biopsy/modified AFB stain	Trimethoprim-Sulphamethoxazole (TMP-SMX)
Legionella	Sputum/BAL culture/urine antigen	Macrolide / Respiratory fluoroquinolone
Fungi		
Candida	Blood culture/biopsy	Echinocandin, amphotericin B, azoles
Aspergillus	BAL/TBB/sputum Fungal stain, galactomannan, H & P	Amphotericin B/voriconazole
Pneumocystis jiroveci	Induced sputum/BAL/DFA	TMP-SMX/corticosteroid (pao2 < 70)
Cryptococcus	Serum/CSF antigen/blood culture	Ampho B/flucytosine
Histoplasma	Urine antigen/histology/fungal culture	Ampho B/itraconazole
Parasites		
Toxoplasma	CSF/blood PCR	Pyrimethamine/sulfadiazine
Virus		
Cytomegalovirus	Blood CMVPCR/PP65 antigen/ BAL Biopsy—H & P, culture	Ganciclovir/foscarnet
Varicella zoster	BAL/CSF PCR, histology	Acyclovir
Herpes simplex	CSF/blood PCR	Acyclovir
Influenza	Nasopharyngeal swab BAL DFA/ culture	Oseltamivir/zanamivir
Epstein–Barr	CSF PCR	Lymphoma chemo
RSV	Nasopharyngeal swab/BAL DFA	Palivizumab

For doses, see Appendix 1

- Specific immunodeficiency states are associated with alteration of natural defense system (neutrophils, T cell, B cells).
- Patients with specific defense system alteration have propensity to be infected with certain groups of organisms, which need to be recognized.

Step 6: Initiate empirical anti-infective agents (Table 54.3)

- Guided by the type and duration of immunosuppression and primary organ system involvement, broad-spectrum anti-infective agents should be initiated against suspected organisms.

- These agents need to be deescalated once an organism is confirmed.
- The dose of these agents needs to be modified depending on renal and liver function tests.
- The duration of therapy with these agents depends on clinical response of the patient.

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Website

1. cid.oxfordjournals.org
   Free text available on many references on the subject

Part VII

Endocrine and Metabolic System

Sandhya Talekar and Rajesh Chawla

Hyponatremia

55

Rajesh Chawla, Subhash Todi,
and Devendra Kumar Agarwal

A 67-year-old chronic male smoker, a known case of small cell carcinoma, was admitted to hospital with altered sensorium, nausea, and dizziness. His vital signs were stable. Liver function tests, urea, and creatinine were normal. Serum sodium was 118 mEq/L and serum potassium was 3.0 mEq/L.

Hyponatremia is a very common condition encountered in the ICU in isolation or as a complication of underlying medical illness. Hyponatremia is defined as serum sodium less than 135 mEq/L. It is considered severe if serum sodium is less than 125 mEq/L. Too rapid correction can result in neurological complications.

Step 1: Initiate resuscitation (refer to Chap. 78)

- Assess and secure the airway in a patient with severe hyponatremia who cannot maintain airway.
- The patient may require assisted ventilatory support.
- Put a peripheral line and resuscitate with suitable fluids as deemed necessary.
- In the hyponatremia patient, initial fluid resuscitation should be done cautiously.

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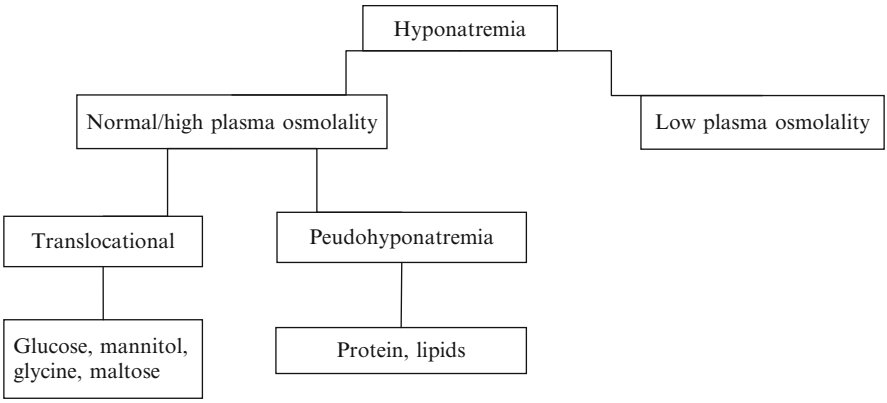

Fig. 55.1 Diagnostic approach to hyponatremia

Step 2: Take focused history and perform physical examination

- This should be done to assess severity of hyponatremia and urgency of correction.
- Pay immediate attention to neurological symptoms such as disorientation, drowsiness, impaired consciousness, or seizures irrespective of duration of hyponatremia.
- Other symptoms of hyponatremia are anorexia, nausea, dizziness, and lack of balance.
- Examine previous records of serum sodium to assess chronicity.
- Take drug history, especially for thiazide diuretics.
- Ask for history suggestive of fluid loss such as vomiting, diarrhea, or excessive water intake.
- Look for features of fluid overload such as pedal edema, ascites, and pleural effusion.

Step 3: Identify etiology

- Assess volume status, measure serum and urine osmolality, and measure spot urine sodium (see Table 55.1 and Fig. 55.2).
- Calculate serum osmolality:
  - $2 \times [Na] + [\text{glucose mg/dL}]/18 + [\text{BUN mg/dL}]/2.8$.
- Normal: 275–290 mOsm/kg.
- Serum osmolarity should always be measured rather than calculated to differentiate hypo-, hyper-, and iso-osmolar types of hyponatremia (Fig. 55.1).
- A patient with true hyponatremia will have low serum osmolality.
- Urine osmolality of less than 100 mOsm/kg: with low serum osmolarity: suggests excess water intake.
- Urine osmolality of more than 100 mOsm/kg: impaired renal excretion of water (eg. CCF, cirrhosis of liver, prerenal renal failure) or salt (eg. salt loosing nephropathy).
- Urine osmolality may be calculated by the last two digits of urine specific gravity $\times 30$.

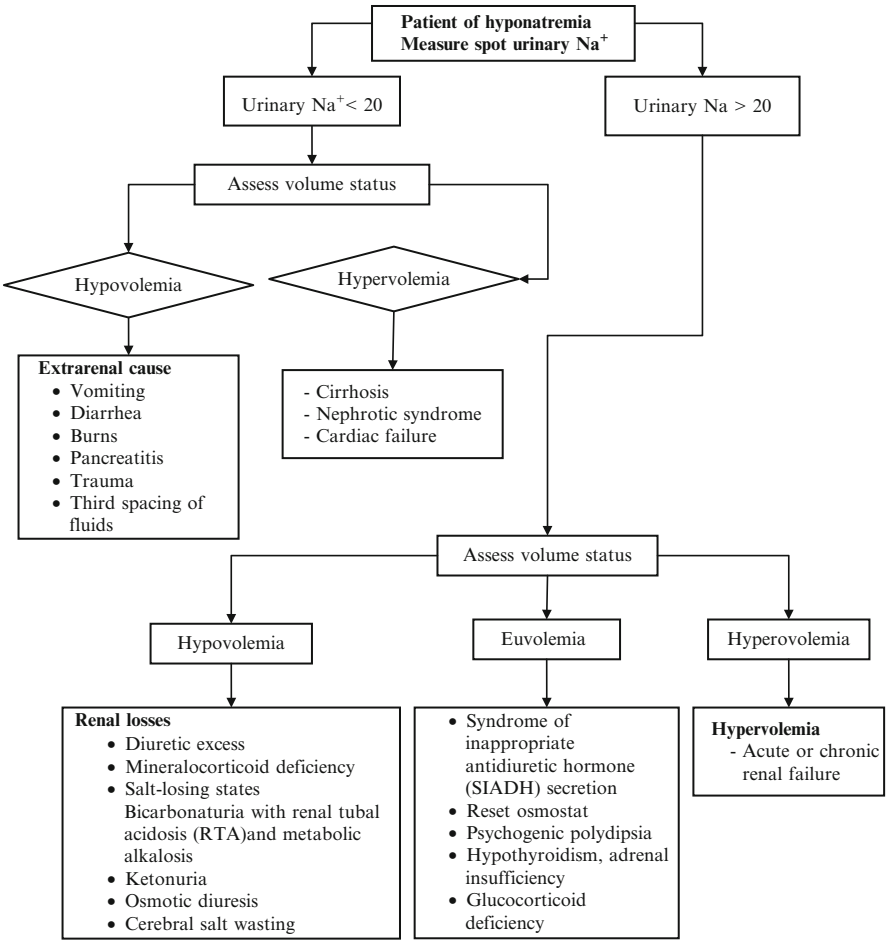

Fig. 55.2 Diagnostic approach to hyponatremia—measure urinary sodium and assess volume status

- Measure spot urine sodium: less than 20 mEq/L or more than 20 mEq/L.
- Measurement of spot urinary sodium and assessment of the volume status can help to know the etiology (Fig. 55.2).

Step 4: Assess severity of hyponatremia

- Mild hyponatremia—130–135 mmol/L
- Moderate hyponatremia—125–130 mmol/L
- Severe hyponatremia—less than 125 mmol/L

Step 5: Send further investigations

In addition to serum osmolality, urine osmolality, and urinary sodium, send further investigations to ascertain the cause and severity of hyponatremia.

- Serum K, Cl, bicarbonate
- Serum glucose, urea, creatinine, total proteins, triglycerides, uric acid
- Arterial blood gases
- Serum TSH, cortisol
- Urine—creatinine, uric acid
- Fractionated excretion of sodium (FE Na) = (U Na × P Cr)/(P Na × U Cr) × 100

Step 6: Correct serum sodium

- Treatment of hyponatremia must be individualized.
- Factors to be considered are as follows:
  - Severity
  - Duration
  - Symptoms
- Risks of treatment (osmotic demyelination) should be balanced against benefit (see Table 55.1). Too rapid correction of sodium is the most important risk factor for the development of osmotic demyelination syndrome.

Table 55.1 Risk factors of neurological complications in hyponatremia

Acute cerebral edema	Osmotic demyelination syndrome
Postoperative patients and young females	Too rapid correction of sodium
Children	Malnourished patients
Psychiatric polydipsic patients	Alcoholics
	Burn patients
	Elderly women taking thiazides

Step 7: Determine the rate of correction of sodium

- In asymptomatic patients, the rate of correction should not be more than 0.5–1.00 meq/L/h and less than 12 meq over the first 24 h.
- Avoid overcorrection of serum sodium concentration.
- In symptomatic patients, sodium may be corrected at the rate of 1–2 mEq/L for an initial few hours or till seizure subsides.

Step 8: Calculate sodium deficit and rate of rise of sodium

- Sodium deficit = total body water (TBW) × (desired serum Na − measured serum Na)
- TBW = body weight (kg) × Y.

Y =	Children	Adult men	Adult women	Elderly men	Elderly women
	0.6	0.6	0.5	0.5	0.45

- The main use of this formula is in the volume depletion state and in SIADH to estimate initial rate of fluid administration.

For example, in a 60-kg woman with a serum sodium of 115 mEq/L with a goal of increasing sodium by 8 mEq/L in first 24 h,

$$\text{Sodium deficit} = (60 \times 0.5) \times (123 - 115) = 240 \text{ mEq.}$$

- Three percent hypertonic saline contains approximately 500 mEq of sodium per liter or 1 mEq per 2 mL. So, 480 mL (240 meq of sodium) of hypertonic saline given over 24 h or 20 mL/h will raise serum sodium by 8 mEq (from 115 meq/L to 123 meq/L in 24 h or 0.25 mEq/h.
- This should be confirmed by serial measurements of serum sodium.
- Increase in serum sodium by any fluid = (infusate sodium − serum sodium)/TBW + 1.
- In cases when potassium is added to intravenous fluid, increase in serum sodium = [(infusate sodium + potassium) − (serum sodium)]/TBW + 1.

For example, in a 60-kg woman with a serum sodium of 110 mEq/L, if 1 L of isotonic saline (containing 154 mEq/L of sodium) is administered, the estimated rise of serum sodium will be

$$(154 - 110)/(30 + 1) = 1.4 \text{ mEq/L.}$$

That is, serum sodium will be 111.4 mEq/L after giving 1 L of normal saline.

- *Rule of thumb*
  - For hypertonic (3%) saline
  - Infusion rate = weight (kg) × desired rate of correction

  For example, to correct at 1 mEq/L/h in a 50-kg person,
  - Infusion rate = 50 × 1 = 50 mL/h.

  To correct at 0.5 mEq/L/h in a 70-kg person,
  - Infusion rate = 70 × 0.5 = 35 mL/h.
- For isotonic (0.9%) saline,
  - 0.9 NaCl corrects at 1–2 mEq/L for every 1 L of NaCl.
- Remember that these formulas are just an approximation as they do not take into account translocation of water, correction of underlying cause, or ongoing water loss.
- Rise of sodium should always be verified by repeated sodium measurement.

Step 9: Euvolemic, hypoosmolar, hyponatremia

Consider SIADH

- Clinical euvolumia
- Urine osmolality more than 300 mOsm/kg H_2O
- Urinary sodium concentration more than 40 mmol/L
- Normal renal, hepatic, adrenal, and thyroid function
- Serum osmolality less than 275 mOsm/kg H_2O
- Serum sodium less than 134 mEq/L
- In severely symptomatic patients:
  - Give 3% hypertonic saline
  - Check serum sodium frequently
- In asymptomatic and mildly symptomatic patients:
  - Restrict total water intake approximately to 600–1,000 mL/day (intake = 50% of output).

  - Addition of salt to diet.
  - Loop diuretics may be added if urine output very low.
  - Consider vasopressin antagonist (vaptans), if available.
  - Demeclocycline 600–1,200 mg/day.
  - In all cases of SIADH, correct the underlying cause and withdraw any offending drug.
- Other causes of euvolemic, hypo-osmolar hyponatremia such as hypothyroid, adrenal insufficiency, renal disease, and psychogenic polydipsia should be managed by water restriction, hormone replacement, and treatment of the underlying disease

Step 10: Hypervolemic, hypoosmolar, hyponatremia
- Consider edematous states such as cirrhosis, nephrotic syndrome, cardiac failure, and renal failure.
- These should be managed by the following:
  - Fluid restriction
  - Loop diuretics
  - Treating the underlying disease
  - Avoiding extra sodium

Step 11: Hypovolemic, hypoosmolar, hyponatremia
- Consider the volume-depleted state (renal or extrarenal).
- These should be managed by the following:
  - Volume replacement
  - Treating the underlying disease

Diuretic-Induced Hyponatremia
- This may mimic SIADH, as it may be clinically euvolemic.
- Occurs predominantly with thiazide diuretics.
- May occur within a few days of starting diuretics.
- Elderly patients with low body mass are more vulnerable.
- May be associated with increased water intake.
- Managed by stopping diuretics, isotonic or hypertonic saline, in symptomatic patients.
- At high risk of rapid correction after stopping diuretics.
- Careful monitoring is required to avoid osmotic demyelination.

Cerebral Salt Wasting (CSW)
- This may mimic SIADH as laboratory findings are similar.
- Hyponatremia with a low plasma osmolality.
- An inappropriately elevated urine osmolality (>100 mOsm/kg and usually >300 mOsm/kg).
- A urine sodium concentration above 40 mEq/L.
- Much less common than SIADH.
- Occurs with acute CNS disease, mainly subarachnoid hemorrhage.
- Clinically hypovolemic.

Table 55.2 Differentiating SIADH from CSW

	CSW	SIADH
Plasma volume	Decreased	Normal or increased
Salt balance	Negative	Normal
H_2O balance	Negative	Increased or no change
Signs of dehydration	Present	Absent
Weight	Decreased	Increased or no change
PCWP and CVP	Decreased	Increased or normal
Hematocrit	Increased	Increased or normal
BUN/creatinine ratio	Increased	Normal
Serum protein concentration	Increased	Normal
Serum K concentration	Increased or no change	Decreased or no change
Serum uric acid concentration	Normal	Decreased

PCWP pulmonary capillary wedge pressure, *CVP* central venous pressure, *BUN* blood urea nitrogen

- Normal serum uric acid.
- Increased fractional excretion of urate.
- This can be differentiated from SIADH as mentioned in Table 55.2.

Management
- Treat the underlying causes of CSW like subarachnoid hemorrhage.
- Put the central line to assess volume status.
- Volume replacement—match urine loss.
- Amount of sodium required = sodium deficit × total body water (See step 8).
- Blood product if anemia is present.

Step 12: Hyperosmolar hyponatremia
Consider hypertonic mannitol or other osmotic agents and hyperglycemia.
- Stop infusion.
- Hyperglycemia—stop or decrease glucose administration.
- Give insulin and fluids.
- Target a drop in glucose concentration of 75–100 mg/dL/h.

Step 13: Iso-osmolar hyponatremia
Consider pseudohyponatremia (drip arm sample, hyperlipidemia, paraproteinemia); usually asymptomatic and no treatment is required.

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Hypernatremia

56

Rajesh Chawla, Sudha Kansal, and Sanjiv Jasuja

A 75-year-old male patient, a case of chronic obstructive pulmonary disease (COPD), was transferred from another hospital with complaints of fever, increased breathlessness for 5 days, and altered sensorium since one day. He also had an episode of seizure one day. He was being managed on the lines of acute exacerbation of COPD with cor pulmonale with pneumonia. He received antibiotics and diuretic therapy in the previous hospital. On evaluation, his laboratory values showed hemoglobin 13 g/dL, packed cell volume of 38.5%, serum sodium 160 mEq/L, serum potassium 3.0 mEq/L, serum urea 146 mg/dL, and serum creatinine of 1 mg/dL.

Hypernatremia is a common problem characterized by a rise in serum sodium above 145 mEq/lt. This is a hyperosmolar condition caused by a decrease in total body water relative to the sodium content. Hypernatremia is caused by impaired thirst and restricted water intake which is often exacerbated by conditions leading to increased fluid loss. The goal of management involves identification of hypernatremia and correction of volume disturbances and hypertonicity.

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Table 56.1 Clinical features suggestive of hypernatremia

Central nervous system			
Anorexia	Restlessness	Confusion	Weakness
Lethargy	Seizure	Respiratory failure	Coma
Musculoskeletal symptoms			
Twitching	Hyperreflexia	Ataxia	Tremor

Step 1: Initiate resuscitation (refer to Chap. 78)
- Assess and secure the airway and provide ventilatory support when required.
- Infuse isotonic sodium chloride in hypovolemic patients.

Step 2: Take history and do physical examination

This should be done to assess the etiology of hypernatremia and severity of the problem.
- Look for symptoms suggestive of hypernatremia (Table 56.1). These are nonspecific and may even mimic rapid fall of serum sodium.
- History should be taken focusing on of the following problems:
  - Extrarenal fluid losses (e.g., burns, vomiting, diarrhea, fever, high minute ventilation in mechanically ventilated patients)
  - Decreased fluid intake
  - Polyuria (i.e., signs of diabetes insipidus [DI] or osmotic diuresis)
  - Review drug chart (drugs causing DI, osmotic diuretics, osmotic laxatives)
  - Review previous sodium levels to assess chronicity
  - Hypertonic solution infusion (sodium bicarbonate, hypertonic saline, total parenteral nutrition)
  - Hypertonic feed (high-protein formula, concentrated formula)

Step 3: Assess volume status
- This is important to understand the underlying pathophysiology of hypernatremia (Table 56.2) and plan the treatment strategy.
- Volume status can be assessed by clinical means, hemodynamic monitoring, and urine biochemistry (Table 56.3).

Step 4: Send investigations
- Arterial blood gases and serum electrolytes
- Blood glucose, blood urea, and serum creatinine
- Serum uric acid
- Hematocrit
- Serum osmolality and urine osmolality
- Urinary sodium and chloride
- If indicated do imaging studies: Head CT scan or MRI

Table 56.2 Pathophysiology of hypernatremia

Hypovolemic (i.e., water deficit > sodium deficit)
Extrarenal losses—diarrhea, vomiting, fistulas, significant burns
Renal losses
Osmotic diuretics
Diuretics
Postobstructive diuresis
Intrinsic renal disease(renal tubular disease)
Adipsic hypernatremia is secondary to decreased thirst
Damaged hypothalamic thirst centers
Hypervolemic (i.e., sodium gain > water gain)
Hypertonic saline
Sodium bicarbonate administration
Accidental salt ingestion (e.g., error in preparation of infant formula)
Mineralocorticoid excess (Cushing's syndrome)
Euvolemic
Extrarenal losses—increased insensible loss (e.g., hyperventilation)
Renal losses—central DI, nephrogenic DI
Mostly free water loss is from intracellular and interstitial spaces

Table 56.3 Assessment of low volume status

A. Clinical
Increasing thirst
Dry tongue, sunken eyes, reduced skin turgor on forehead and sternal skin
Orthostatic tachycardia (>20/min rise of pulse rate)
Orthostatic hypotension (>20 mmHg fall in systolic BP or >10 mmHg fall in diastolic BP)
Resting tachycardia and hypotension
Low urine output, concentrated urine (extrarenal loss)
B. Hemodynamic
Low central venous pressure
Arterial pressure variation (in ventilated patients)
Rising arterial pressure on passive leg raising (spontaneously breathing patients)
C. Biochemistry
Rising hematocrit
Rising albumin
Raised urea in proportion to serum creatinine
High serum uric acid
High urine osmolarity
Low urine sodium (extrarenal loss)
Low urine chloride (metabolic alkalosis)

Step 5: Make a diagnosis

- Serum osmolality is always increased in patients with hypernatremia.
- Urine osmolality of less than 300 mOsmols/Kg with high serum osmolality or, <100 mOsmols/Kg with normal serum osmolality may be due to DI (central or nephrogenic), which can be distinguished by response to vasopressin.
- Urine osmolality of more than 600 mOsmols/Kg could be due to unreplaced gastrointestinal or insensible loss (urine sodium <20 mEq/L) or excess sodium administration by enteral or parenteral route (urine sodium >40 mEq/L).
- Urine osmolality of 300–600 mOsmols/Kg may be due to osmotic diuresis (check for glycosuria), partial central or nephrogenic DI.
- Calculate total solute excretion (urine osmolality × urine volume); if more than 1,000 mosmols per day—osmotic diuresis.

Step 6: Treatment

- Aim for symptom resolution, 10–15% improvement in sodium levels in first 24 h.
- Correction in chronic (>48 hours) settings:
  - Less than 1.5 mEq/h
  - Total less than 12 meq/24 h
- Rapid correction will cause rapid shift of water inside the brain causing cerebral edema and seizures.

Step 7: Calculate water deficit

$$\text{Water deficit } (\text{L}) = \text{total body water}(\text{TBW}) \times [(\text{measured Na}/140) - 1]$$

$$\text{TBW} = \text{body weight } (\text{Kg}) \times \text{ “Y”}$$

Y = children	Adult men	Adult women	Elderly men	Elderly women
0.6	0.6	0.5	0.5	0.45

(This is percentage of water in total body weight.)

For example:

- 60 kg adult woman with serum sodium of 160 mEq/L.
- Free water deficit = $[(0.5 \times 60)] \times [(160/140) - 1] = 4.2$ L.
- This can be given as 5% dextrose or free water by the nasogastric tube or orally.
- Free water deficit = 4.2 L (see above).
- Thus, 4.2-L positive water balance must be achieved to get serum sodium down from 160 to 140 mEq/L or by 20 mEq.
- Rate of correction = 0.5 mEq/h.
- 4.2 L of free water to be given over 40 h at a rate of approx.100 mL/h.
- Insensible water loss (30 mL/h) should be added.
- Thus, 130 mL/h of free water needs to be replaced for 40 h.

- This can be done with IV 5% dextrose, 0.45% saline or plain water by the tube or orally.
- Large volume of 5% dextrose will lead to hyperglycemia, and if needed, insulin should be given to prevent glycosuria, otherwise osmolar diuresis can worsen hypernatremia.
- Sodium and/or potassium can be added to the intravenous fluid as necessary to treat concurrent volume depletion and/or hypokalemia (e.g., due to diarrhea).
- The addition of solutes decreases the amount of free water that is given.
- If potassium is also added, then even less free water is present and a further adjustment to the rate must be made.
- Repeat sodium level and entire calculation every 12 h and replan infusion rate. (This is because the urinary free water loss is not taken into account and it keeps on changing.)

Step 8: Manage specific hypernatremic states

Hypovolemic hypernatremia	Volume deficit always takes precedence over correcting water deficit
	Correct volume deficit initially by isotonic saline until improvement of orthostasis, tachycardia, and urine output
	Calculate and correct water deficit
	Treat the etiology of volume loss
	After correction of volume deficit, administer 0.45% saline, 5% dextrose, or oral water, replacing deficit and ongoing losses
Euvolemic hypernatremia	Correct water deficit
	Administer 0.45% saline, 5% dextrose, or oral water, replacing deficit and ongoing losses
	Follow serum [Na] carefully to avoid water intoxication
	Central DI—treat underlying disease, long-term nasal pitressin
	Nephrogenic DI—correct calcium, potassium; remove offending drugs; low-sodium diet
Hypervolemic hypernatremia	Remove the source of extra sodium
	Correct the cause
	Loop diuretics alone can worsen hypernatremia. Thus combining with metolazone or thiazide diuretics will be a better choice
	Hemodialysis may be performed in renal failure

Suggested Reading

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Hypokalemia and Hyperkalemia

57

Subhash Todi and Rajesh Chawla

A 50-year-old male patient was admitted with generalized weakness and abdominal distension. On examination, he was found to be alert and hemodynamically stable. Neurological examination revealed quadriparesis. Abdominal examination revealed distension with sluggish bowel sounds. His serum potassium level was 2 mEq/L.

Disorder of potassium balance—both hypo- and hyperkalemia—is a common finding in the ICU. These abnormalities might be subtle requiring minimal intervention or life-threatening requiring urgent measures. A methodological approach is warranted to manage this problem.

Step 1: Initial resuscitation

- Patients should be resuscitated, as mentioned in Chap. 78.
- Patients with quadriparesis need to be assessed for airway protection and if needed should be intubated or ventilated.
- Circulatory status needs to be maintained with intravenous fluids as hypokalemic patients are usually volume depleted.

Step 2: Assess severity of hypokalemia

- After initial resuscitation, the patient should be assessed for urgency of correction of hypokalemia.

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Table 57.1 ECG changes in hypokalemia

ST segment depression
Decrease in amplitude of T waves
Increase in amplitude of U wave (occurring at the end of T)
Premature atrial or ventricular ectopics
Sinus bradycardia
Paroxysmal atrial or junctional tachycardia
Atrioventricular block
Ventricular tachycardia (torsade de pointes)
Ventricular fibrillation

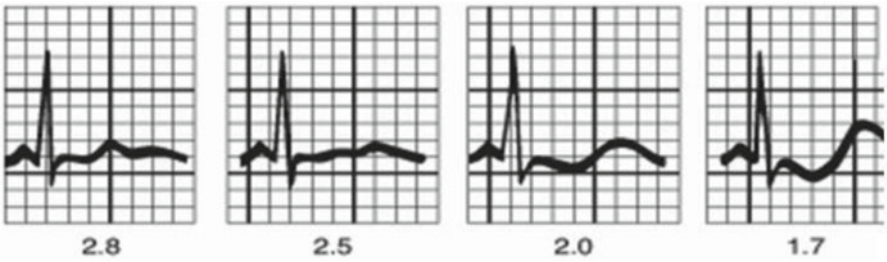

Fig. 57.1 Hypokalemia

- Urgent intravenous correction is needed in the following conditions:
  - ECG changes in hypokalemia (see Table 57.1 and Fig. 57.1)
  - Cardiac arrhythmia
  - Severely impaired neuromuscular function
  - Diaphragmatic weakness and respiratory failure
  - Patients on digoxin or antiarrhythmic therapy
  - Old age
  - Organic heart disease
  - Serum potassium of less than 3.0 mEq/L
  - Diabetic ketoacidosis
  - Hyperosmolar nonketotic diabetes

Step 3: Estimate potassium deficit

- Approximately 200 mEq potassium deficit is required to decrease serum potassium by 1 mEq/L in the chronic hypokalemic state.
- In acute situations, the serum potassium concentration falls by approximately 0.27 mEq/L for every 100 mEq reduction in total body potassium stores.
- These are only an approximation, and careful monitoring of serum potassium is required.

Step 4: Replace intravenous potassium chloride

Peripheral route
It is safe
It is used in mild-to-moderate hypokalemia (3–3.5 mEq/L)
20–40 mEq/L of KCl is added to each liter of fluid given over 4–6 h
A saline rather than dextrose solution should be used. Half-strength saline with 20 mEq of KCl makes the solution isotonic and suitable for peripheral use
Do not use high concentrations over 60 mEq/l; it can lead to pain and sclerosis of peripheral vein
Volume overload is a potential risk in susceptible subjects
Central route
Prepare 20 mEq KCl in 100 mL normal or half-strength saline
5–20 mEq/h (through syringe pump) can be safely given by central route (preferably femoral vein)
Life-threatening arrhythmias
Up to 40 mEq/h of KCl can be given for few hours
No other infusion should be going through the same catheter
Avoid blood sampling and flushing the catheter
Frequently monitor potassium till 3–3.5 mEq/L
Continuous ECG monitoring is required

Step 5: Replace intravenous magnesium

- Hypomagnesemia is usually concurrently present with hypokalemia and needs to be corrected.

Step 6: Ascertain the cause of hypokalemia and manage specifically (Table 57.2)

- Detailed history and physical examination should be performed to look for systemic causes of hypokalemia.
- History of increased urinary or gastrointestinal loss of fluid (vomiting, diarrhea, polyuria) should be taken.
- Detailed drug history to rule out drug-induced hypokalemia should also be taken.
- Urinary potassium level of more than 30 mEq/day is a feature of loss of potassium in the urine.

Step 7: Send investigation

- Complete blood count
- Na, K, Ca, Mg, PO_4, HCO_3
- Urea, creatinine
- Creatine phosphokinase (CPK)
- Arterial blood gas analysis
- ECG

Table 57.2 Causes of hypokalemia

Increased entry into cells
Metabolic alkalosis
Initial phase of DKA
Elevated β-adrenergic activity—stress or administration of β-agonists
Hypokalemic periodic paralysis
Hypothermia
Chloroquine intoxication
Others
Vomiting
Diarrhea
Tube drainage
Laxative abuse
Increased urinary losses
Diuretics
Primary mineralocorticoid excess
Hypomagnesemia
Amphotericin B
Salt-wasting nephropathies—including Bartter's or Gitelman's syndrome
Renal Tubular Acidosis, Polyuria
Increased sweat losses
Dialysis
Plasmapheresis
Decreased potassium intake (rare)

- Urine for K
- Urinalysis

Step 8: Replace potassium orally

- Once serum potassium has been raised to a safe limit of above 3 mEq/L, the rest of the replacement may be done slowly by oral route. This could be achieved by adding potassium-rich diet, potassium salt, or potassium chloride suspension.
- Treatment is usually started with 10–20 mEq of potassium chloride given two to four times per day (20–80 mEq/day).

Step 9: Reduce the loss of potassium

- In patients with hypokalemia due to increased urinary losses, potassium-sparing diuretics such as spironolactone, amiloride, or eplerenone may be tried.
- Oral/IV potassium should be used with caution in these situations specially in patients with impaired renal function.

57.1 Hyperkalemia

A 60-year-old diabetic male patient, hypertensive and on angiotensin-converting enzyme (ACE) inhibitors, was admitted with dizzy spells. On admission, his pulse was 60/min, BP was 110/70 mmHg, and sensorium was normal. His blood biochemistry showed urea 90 mg/dL, creatinine 2.0 mg/dL, Na 130 mEq/L, and K 6.5 mEq/L.

Table 57.3 ECG changes in hyperkalemia

Tall, peaked T waves with a shortened QT interval
Progressive lengthening of the PR interval and QRS duration
Disappearance of P waves
QRS widening and a sine wave pattern
Asystole and a flat ECG

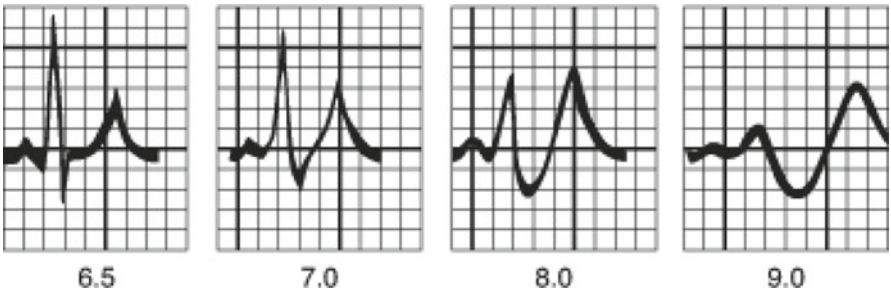

Fig. 57.2 Hyperkalemia

Step 1: Initiate resuscitation

- Patients with severe hyperkalemia need an urgent intravenous access and continuous ECG monitoring.
- They can have sudden bradycardic arrest. ACLS protocol should be followed in these situations (See Chap. 19).

Step 2: Assess severity of hyperkalemia and urgency of correction

- Hyperkalemia should be urgently managed in the following circumstances:
  - ECG changes (see Table 57.3 and Fig. 57.2)
  - Muscle weakness or paralysis
  - Rhabdomyolysis
  - Crush injury
  - Tumor lysis syndrome
  - Serum potassium of more than 7.0 mEq/L
  - Rapidly rising potassium above 5 mEq/L

Step 3: Rapidly correct severe hyperkalemia

- *Intravenous calcium*
  - Give calcium gluconate or calcium chloride—10 mL of 10% solution over 2 min under continuous ECG monitoring.
  - Intravenous calcium works within minutes, but effect is short-lasting (30–60 min).
  - Calcium acts by directly antagonizing the membrane action of hyperkalemia and does not cause lowering of serum potassium.
  - Calcium chloride contains three times elemental calcium compared to calcium gluconate (13.6 vs. 4.6 mEq in 10 mL of 10% solution) and is the preferred drug.
  - Intravenous calcium can be repeated after 5 min, if ECG abnormalities persist.
  - Concentrated calcium solution is tissue-irritant and should be given in a large peripheral vein or central vein.
  - Calcium should not be given in a bicarbonate-containing solution to avoid precipitation of calcium carbonate.
  - Calcium should be given cautiously as a slow infusion in patients on digitalis.
- *Insulin with glucose*
  - Give 10 units of regular bolus insulin intravenously along with 50 mL of 50% dextrose.
  - Monitor blood glucose every 30 min.
  - In patients with baseline hyperglycemia above 250 mg/dL, only insulin can be given.
  - The effect of insulin begins within 10 min and lasts for 4–6 h.
  - Insulin and glucose lowers serum potassium by driving potassium inside the cells.
  - It decreases serum potassium by 0.5–1.2 mEq/L.
  - Beware of hypoglycemia in renal failure.
- *Salbutamol (albuterol) nebulizer*
  - 10 mg in 4 mL of saline to be nebulized over 10 min (four times the usual bronchodilator dose) is given.
  - Its effect is seen within 90 min of nebulization.
  - Serum potassium usually decreases by 0.5–1.2 mEq/L.
  - It works by driving potassium inside the cell.
- *Sodium bicarbonate*
  - It should be given cautiously in selected cases of hyperkalemia associated with severe metabolic acidosis.
  - Usual dose is 25 mEq (25 ml of 8.4%) infused over 5 min.

Step 4: Assess the cause of hyperkalemia

- Detailed history and physical examination should be performed to look for features of diseases associated with hyperkalemia such as renal failure and adrenal disease.

- History of renal disease or potassium levels should be looked for to assess sudden deterioration of renal function.
- Drug history should be taken to exclude drugs such as angiotensin-receptor blockers, ACE inhibitors, nonsteroidal anti-inflammatory drugs, aldosterone antagonist, and potassium-containing syrup that can cause hyperkalemia specially in renally impaired patients.

Step 5: Send investigations
- Serum potassium should be monitored frequently.
- Blood urea, creatinine.
- Sodium, calcium, magnesium, phosphate.
- Arterial blood gases.
- Complete hemogram.
- Blood glucose.
- CPK.
- Lactate dehydrogenase.

Step 6: Stop the intake of potassium
- Start potassium-free diet.
- Avoid the use of drugs containing potassium.
- Avoid drugs that can cause hyperkalemia.

Step 7: Remove potassium
- *Diuretics*: A trial of loop diuretics in patients with preserved renal function and volume overload state may be made.
- *Cation exchange resin*: Sodium polystyrene sulfonate.
  - In the gut, sodium polystyrene sulfonate takes up potassium (and calcium and magnesium to lesser degrees) and releases sodium (1 gm binds to 1 meq of potassium).
  - It is usually given orally three times daily but may be given rectally.
  - Oral dose is usually 20 g given with 100 mL of a 20% sorbitol solution to prevent constipation.
  - A major concern with sodium polystyrene sulfonate in sorbitol is the development of intestinal necrosis, usually involving the colon and the ileum.
  - The serum potassium falls by at least 0.4 mEq/L in the first 24 h.
- *Dialysis*
  - It is indicated if hyperkalemia persists in spite of above measures or patients have any other indication of dialysis. Hemodialysis can remove 25–50 mEq of potassium per hour, with variability based on the initial serum potassium concentration, the type and surface area of the dialyzer used, the blood flow rate, the dialysate flow rate, the duration of dialysis, and the potassium concentration of the dialysate.
  - Beware of rebound hyperkalemia after dialysis.

Step 8: Ascertain the cause of hyperkalemia and manage specifically (see Table 57.4)

Table 57.4 Causes of hyperkalemia

Increased potassium release from cells
Pseudohyperkalemia (hemolytic sample, marked leukocytosis, thrombocytosis, vigorous fist clenching during phlebotomy)
Metabolic acidosis
Insulin deficiency, hyperglycemia, and hyperosmolality (diabetic ketoacidosis (DKA), Hyperglycemic Hyperosmolar State (HHS), octreotide infusion)
Increased tissue catabolism
β-adrenergic blockade
Rhabdomyolysis
Digitalis overdose
Hyperkalemic periodic paralysis
Succinylcholine
Tumor lysis syndrome
Severe exercise
Reduced urinary potassium excretion
Renal failure
Hypoaldosteronism (drugs, diabetes, adrenal insufficiency)
Hyperkalemic type 4 renal tubular acidosis
Ureterojejunostomy

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Arterial Blood Gases

58

Rahul Pandit

A 45-year-old alcoholic male patient was admitted to the hospital for 2 weeks. He was being treated for pyogenic lung abscess. He seemed to be improving but became unwell again. A blood gas analysis showed pH 7.31, $PaCO_2$ 30 mmHg, PaO_2 106 mmHg (0.3 FiO_2), HCO_3^- 14 mmol/L, standard base excess (SBE) 15 mmol/L, Na^+ 131 mmol/L, K^+ 5 mmol/L, Cl^- 96 mmol/L, osmolar gap 8 mmol/Kg, lactate 2 mmol/L, and albumin 3 g/dL.

Arterial blood gas analysis is an essential component of diagnosing and managing critically ill patients in the ICU. The proper understanding and application of the concepts of acid–base balance will help the clinician to follow the progress of the patient and also to evaluate the effectiveness of the treatment provided to them.

Step 1: Take an arterial blood sample

- If possible, take an arterial blood gas (ABG) sample at room air and start oxygen supplementation immediately.
- The radial artery is preferred for collecting the sample.
- Prefer to use 22-gauge needle.
- Avoid air bubbles.
- Cool the sample immediately.

  A. Potential sampling error.
    - Air contamination—spurious increase in PO_2.
    - Duration of exposure is more important than volume of air bubbles.
    - Expel air immediately.
    - Discard the sample if froth is present.

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B. Venous sample—absence of flash of blood on entry into the vessel and pulsations during syringe filling and absence of autofilling of the syringe.
   - Venous admixture.
   - Cross-check with pulse oximetry and clinical status.
   Anticoagulant effects: Dilution error—drop in PCO_2 and PO_2. pH usually remains unchanged.

D. Metabolism: Blood cells consume O_2, produce CO_2, and lower pH. Magnitude of changes depends on the initial level.

Step 2: Take detailed history and do proper clinical examination

- Very often, it is the presenting symptom or signs which are a clue to the interpretation of the acid–base status.
- For example in a patient with vomiting, the primary acid–base problem could be metabolic alkalosis (due to loss of hydrochloric acid) as opposed to someone with diarrhea, whose primary problem could be metabolic acidosis (due to loss of bicarbonate ions).
- The important aspect to remember is that it is the underlying disorder of the patient which determines the acid–base status and not just the pH of the blood.
- A stepwise approach helps to interpret ABG correctly.
- Interpretation of serum electrolytes is also important for an accurate estimation of mixed acid–base disorders.

Step 3: Know the normal values

	Normal range	For calculation
pH	7.34–7.45	7.4
PCO_2	35–45	40
HCO_3	22–26	24
PO_2	>80	>95

Step 4: Assess oxygenation (Ref Appendix 2)

- Look at oxygenation (PaO_2 and SaO_2).
- Look at the PaO_2/FiO_2 ratio.
  - Normally, the ratio is around 1:400–1:500 given the fact that at 0.21 FiO_2, the PaO_2 is approximately 100 mmHg.
  - Less than 1:400—suggestive of V–Q mismatch or diffusion defect or intracardiac shunt.
  - Less than 300 with bilateral lung infiltrate in chest skiagram—ARDS.
- A-a gradient
  - A-a gradient = $PAO_2 - PaO_2$

Here, PAO_2 is alveolar PO_2 (calculated from the alveolar gas equation) and PaO_2 is arterial PO_2 (measured in arterial blood A-a gradient).

  - In general, the A-a gradient can be calculated by:
  - $\text{A} - \text{a gradient} = \left[FiO_2 \times (\text{Patm} - PH_2O) - (PaCO_2 / 0.8) \right] - PaO_2$

On room air and at sea level, the FiO_2 is 0.21, the Patm is 760 mmHg, and P_{H2O} is 47 mmHg.

– On room air, PAO_2 can be calculated by:

$$150 - PaCO_2 / 0.8$$

- Normal A-a gradient in a 20-year-old person is 5 mmHg, which increases to 10 mmHg in a 35-year-old person. If A-a gradient is 20 mmHg at any age, it is abnormal. If FiO_2 is above 0.21, it is unreliable.

Step 5: Assess acid–base disorder (Ref Appendix 2)

I. Look at the pH—is there acidemia or alkalemia?
   A normal pH would suggest a mixed disorder or a normal acid–base status.
II. Check CO_2 and HCO_3^- to determine whether the primary problem is metabolic or respiratory in origin.
III. If the primary disorder is respiratory, determine whether it is an acute disorder or a chronic disorder.
IV. Apply the rules of compensation to know if it is a simple or a mixed disorder.
V. Mind the gaps—anion gap, delta gap, and osmolar gap.

I. *Look at the pH*
   The pH is actually the −log $[H^+]$. By altering either the PCO_2 or the HCO_3^-, $[H^+]$ will change, and so will pH.
   - An acidemia (low pH) can result from either a low HCO_3 or a high CO_2.
   - An alkalemia (high pH) can result from either a high HCO_3 or a low CO_2.

II. *Look at the CO_2 and HCO_3^- to determine if the primary problem is metabolic or respiratory in origin*
   The primary acid–base disturbances include the following:
   - Low HCO_3—metabolic acidosis
   - High HCO_3—metabolic alkalosis
   - High PCO_2—respiratory acidosis
   - Low PCO_2—respiratory alkalosis

   A. *Metabolic acidosis*
      - Metabolic acidosis results from a primary decrease in plasma $[HCO_3-]$.
      - It is due to either an excretion of bicarbonate-containing fluids or by utilization of bicarbonate.
      - It is very important to calculate the anion gap (AG) if the primary disorder is metabolic acidosis.
      - AG = Na+ − (Cl− + HCO_3−); the normal AG is 12 ±2 mEq/L.
      - A higher gap usually denotes the presence of unmeasured anions in the body (Table 58.1).
      - In non-AG metabolic acidosis, the bicarbonate losses are accompanied by cation loss, hence no change in AG (Table 58.2).

Table 58.1 Causes of a raised AG metabolic acidosis (MUDPILERS)

M	⇒ Methanol
U	⇒ Uremia (chronic)
D	⇒ Diabetic ketoacidosis
P	⇒ Paraldehyde
I	⇒ Isoniazid, iron
L	⇒ Lactate
E	⇒ Ethanol, ethylene glycol
R	⇒ Rhabdomyolysis/renal failure
S	⇒ Salicylate

Table 58.2 Causes of a non-AG metabolic acidosis (HARDUP)

H	⇒ Hyperalimentation
A	⇒ Acetazolamide
R	⇒ Renal tubular acidosis
D	⇒ Diarrhea
U	⇒ Uremia (acute)
P	⇒ Post ventilation hypocapnia

- Remember to correct AG for hypoalbuminemia, which is very common in ICU patients. For this, for every 1 g% drop in albumin below 4 g%, add 2–3 to the calculated gap.
- Check urinary AG in non-AG metabolic acidosis (U Na^+ + U K − U Cl)
  - Normal—negative
  - Nonrenal loss of bicarbonate (diarrhea)—negative
  - Renal loss of bicarbonate or decrease H+ excretion (renal tubular acidosis)—positive

B. *Metabolic alkalosis (high HCO_3)*
- Metabolic alkalosis reflects an increase in plasma [HCO_3^-].
- It is due to either gain of HCO_3^- or extracellular volume contraction.
- It can be classified into saline responsive or nonresponsive. For this, spot urinary chloride can be checked.
- More than 20 mEq/L urinary chloride is saline unresponsive (Table 58.3), and less than 20 mEq/L urinary chloride is saline responsive (Table 58.4).

C. *Respiratory acidosis (high PCO_2)*
- Respiratory acidosis is due to a primary rise in CO_2.
- Hypercapnia almost always results from alveolar hypoventilation due to one of the following causes:
  1. Respiratory center depression
  2. Neuromuscular disorders
  3. Upper airway obstruction
  4. Pulmonary disease

Table 58.3 Urine Cl^- more than 20 mEq/L (usually saline unresponsive)

Primary hyperaldosteronism
Cushing's syndrome, ectopic ACTH
Exogenous steroids, licorice ingestion, tobacco chewing
Adrenal 11 or 17 OH defects
Liddle's syndrome
Bartter's syndrome
K+ and Mg2+ deficiency
Milk-alkali syndrome
Hypercalcemia with secondary hypoparathyroidism

Table 58.4 Urine Cl^- less than 20 mEq/L (usually saline responsive)

Vomiting, nasogastric suctioning
Chloride-wasting diarrhea
Villous adenoma of colon
Posthypercapnia
Poorly reabsorbed anions like carbenicillin
Diuretic therapy

D. *Respiratory alkalosis (low PCO_2)*
- A respiratory alkalosis is due to decrease in PCO_2.
- It results from hyperventilation leading to decrease in CO_2.

Causes of respiratory alkalosis
- Hypoxemia from any cause
- Respiratory center stimulation
- Mechanical hyperventilation
- Sepsis, pain

III. *If the primary disorder is respiratory, determine whether it is an acute disorder or a chronic disorder*

You must also take into consideration the patient's history while interpreting ABG. However, the following formulae help in this:
- Normal pH is 7.4
- Calculate the change in pH (from 7.4)

A. In acute respiratory disorder (acidosis or alkalosis)

$$\text{Change in pH} = 0.008 \times (PaCO_2 - 40)$$

$$\text{Expected pH} = 7.4 \pm \text{change in pH}$$

B. In chronic respiratory disorder (acidosis or alkalosis)

$$\text{Change in pH} = 0.003 \times (PaCO_2 - 40)$$

$$\text{Expected pH} = 7.4 \pm \text{change in pH}$$

- *Compare the pH on ABG*
  - If pH on ABG is close to **A**, it is an acute disorder
  - If pH on ABG is close to **B**, it is a chronic disorder

IV. *CO_2 and HCO_3^- compensatory mechanism*

Primary disorder	Initial chemical change	Compensatory response	Compensatory mechanism	Expected level of compensation
Metabolic acidosis	↓ HCO_3^-	↓ PCO_2	Hyperventilation	$PCO_2 = (1.5 \times [HCO_3^-]) + 8 \pm 2$
				PCO_2 = last two digits of pH
Metabolic alkalosis	↑ HCO_3^-	↑ PCO_2	Hypoventilation	$PCO_2 = (0.7 \times [HCO_3^-]) + 21 \pm 2$
				PCO_2 = last two digits of PH
Respiratory acidosis	↑ PCO_2	↑ HCO_3^-		
Acute			Buffering—rule of 1	↑ $[HCO_3^-])] = 1$ mEq/L for every 10 mmHg delta PCO_2
Chronic			Generation of new HCO_3^-—rule of 3	↑ $[HCO_3^-]) = 3$ mEq/L for every 10 mmHg delta PCO_2
Respiratory alkalosis	↓ PCO_2	↓ HCO_3		
Acute			Buffering—rule of 2	↓ $[HCO_3^-]) = 2$ mEq/L for every 10 mmHg delta PCO_2
Chronic			Decreased reabsorption of HCO_3^-—rule of 4	↓ $[HCO_3^-]) = 4$ mEq/L for every 10 mmHg delta PCO_2

V. *Mind the gaps*

A1. Calculate AG in case of metabolic acidosis.
High denotes raised AG metabolic acidosis, and normal or narrow denotes non-AG acidosis.
A2. Calculate adjusted AG.
Adjusted AG = calculated AG + 2.5 × (4 − serum albumin in gm%)
B. In less obvious cases, the coexistence of two metabolic acid–base disorders may be apparent by calculating the difference between the change in AG (delta AG) and the change in serum HCO_3^- (delta HCO_3^-). This calculation is called the bicarbonate gap or the delta gap:
- Delta gap = delta AG − delta HCO_3 −
- Where delta AG = patient's AG − 12 mEq/L{normal AG}
- Delta HCO_3^- = 24 mEq/L{normal HCO_3^-} − patient's HCO_3^-

- Normally, the delta gap is zero if there is only AG acidosis. A positive raised delta gap or a decreased delta gap denotes presence of mixed lesion.
- A positive delta gap of more than 6 mEq/L is suggestive of presence of metabolic alkalosis and/or HCO_3^- retention.
- The delta gap of less than 6 mEq/L is suggestive of presence of hyperchloremic acidosis and/or HCO_3^- excretion.

C. *Osmolar gap*
The difference between calculated plasma osmolality and the measured osmolality is called the osmolar gap. Normally, the gap is less than 20 mosmo/kg H_2O. If it is raised, then it denotes presence of unaccounted ions.

Causes of increased osmolar gap
- Ethanol
- Isopropyl alcohol
- Methanol, glycine, glycerol
- Ethylene glycol

Step 6: Look for alerts to mixed acid–base disturbances
- Absence of compensation
- Longstanding pulmonary or renal disease
- Excessive compensation
- Respiratory assistance
- Settings conducive to mixed disturbances

Step 7: If there is some discrepancy between ABG values and clinical condition of the patient, do validity check to authenticate the report
A. $H^+ = 24 \times PCO_2/HCO_3$.
Place the value of PCO_2 and HCO_3 and calculate H^+.
B. Calculate H^+ from pH as seen on ABG.
At pH of 7.4, H^+ concentration is 40.
For every 0.1 ↓ in pH, multiply H^+ concentration sequentially by 1.25.
For every 0.1 ↑ in pH, multiply H+ concentration sequentially by 0.8.
Last two digits of $pH = H^+$.
C. Match the H^+ concentration by two methods: A and B.
If it is matching, ABG is valid.
If it is not matching, recheck the ABG.

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4. www.merck.com

Diabetic Emergencies

59

Sandhya Talekar and Jayant Shelgaonkar

A 63-year-old male patient with insulin-dependent type 2 diabetes mellitus was brought to the emergency department with altered sensorium and breathlessness since 24 h. On examination, he was found to be febrile with a temperature of 101°F. His pulse rate was 130/min regular, and blood pressure was 110/70 mmHg. He had a Glasgow coma score of 9. His random plasma glucose on arrival was 963 mg/100 mL.

Diabetic emergencies consist of hyperglycemic conditions such as diabetic ketoacidosis (DKA), hyperglycemic hyperosmolar state (HHS) HHS diabetic state, and hypoglycemic emergencies.

All these emergencies may be life-threatening, but if they are properly identified and treated, a gratifying result can be obtained. DKA usually occurs in young patients with type 1 diabetes who are insulin dependent, and HHS usually occurs in the elderly with type 2 diabetes on either oral hypoglycemic agents or on insulin. The basic pathophysiological difference is absence of circulating insulin in DKA and some residual insulin present in HHS, which prevents lipolysis, and ketosis, coupled with impaired renal function leads to severe hyperglycemia and a hyperosmolar state.

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59.1 Hyperglycemic Emergencies

59.1.1 DKA and HHS

Step 1: Start initial resuscitation (refer to Chap. 78)
- Urgently insert two wide-bore intravenous peripheral catheters for volume infusion.
- A central line is needed in presence of hypotension, lack of peripheral access, multiple infusions, severe acidosis, and impaired cardiorespiratory or renal parameters.
- Airway should be maintained as HHS patients could be obtunded on presentation.
- Hyperventilation is prominent with acidosis and may require assisted breathing.

Step 2: Take focused history and perform physical examination
- History of insulin omission in a diabetic patient is common and often points toward a diagnosis of DKA.
- A thorough physical examination helps in finding a cause/possible focus of infection which is often a cause for the hyperglycemic crisis.

Step 3: Send essential investigations
- Serum glucose
- Serum electrolytes, Na, K, chloride, Mg, phosphate (with calculation of the anion gap)
- Blood urea nitrogen and plasma creatinine (may be spuriously high due to chemical analysis interference with ketones)
- Serum bicarbonate
- Complete blood count with differential count
- Urinalysis and urine ketones by dipstick
- Plasma osmolality
- Serum ketones
- Arterial blood gas
- Electrocardiogram
- Serum amylase, lipase
- Chest X-ray
- Infection screening

Step 4: Infuse fluid
- Patients with DKA and HHS usually have severe hypovolemia due to absolute or relative deficiency of insulin leading to osmotic diuresis.
- Average fluid loss in DKA and HHS is 3–6 and 8–10 L, respectively. Approximately half of total fluid deficit is replaced in first 12 h and remaining over next 12–24 h depending on the initial response.
- Restore intravascular volume rapidly with either colloids or isotonic saline. Aim is to restore the circulating volume rapidly and then correct interstitial and intracellular fluid deficits.

- In hypotensive patients, use colloids or crystalloids to restore circulating volume. More important than the type of fluid used is the rapidity with which the circulating volume is restored.
- Initially, give a bolus of 1 L of isotonic saline or 500 mL of colloid to correct shock. This is given over 30 min. Subsequently, fluid may be given at rates of 50–200 mL/h till hypovolemia is corrected.
- Irrespective of initial serum sodium, which may be high in HHS, initial crystalloid fluid resuscitation should be with 0.9% saline as hypovolemia correction should be given precedence over osmolality correction with hypotonic fluid.
- Clinical signs such as heart rate, blood pressure, and skin perfusion may be used as guides to fluid resuscitation. In patients with HHS, comorbidities like renal and cardiac dysfunctions warrant more close monitoring of hemodynamics.
- Hypotonic (0.45%) saline resuscitation may be appropriate in the nonshocked and hypernatremic patients (after correcting for high blood glucose) patient as hypotonic saline does not correct hypovolemia rapidly. This might also be appropriate in patients with concomitant potassium infusion to maintain isotonicity of infusion fluid. Calculate free water deficit to assist fluid replacement in patients with hypernatremia (see Chap. 56) and replace with dextrose or enteral water.
- Replace total body water losses slowly with 5% glucose solution (50–200 mL/h) once circulating volume and serum sodium are restored (usually when the blood glucose falls to <200 mg/dL). This is in order to avoid sudden osmolarity changes, which may lead to cerebral edema and convulsions, seen more frequently in the pediatric age group.

Step 5: Correct electrolyte abnormalities

- The average sodium loss is 400–700 mmol, and average potassium loss is 250–400 mmol in DKA.
- Serum sodium is usually high in HHS and variable in DKA. The measured sodium value should be corrected to a true sodium value. For each 100 mg/dL increase in blood glucose above 200 mg/dL, serum sodium decreases by 2.4 mEq/L.
- Replacement of serum potassium should begin early in the management of DKA as serum potassium concentration does not reflect total body potassium accurately. Potassium replacement should begin as soon as serum potassium concentration is less than 5.5 mEq/L. Target potassium concentration is 4–5 mEq/L.
- Ensure adequate urine output before replacing intravenous potassium.
- Guideline for replacing potassium is as follows:
  - If K is less than 3.5 mEq/L, give K at 40 mEq/h (given diluted in a liter).
  - If K is 3.5–5.0 mEq/L, give K at 20 mEq/h.
  - If K is more than 5.0 or anuric, no supplements are required.
- Potassium concentration falls precipitously after starting treatment with insulin and correction of acidosis, which leads to intracellular shift of potassium.
- Potassium should be added to 0.45% saline instead of 0.9% saline to avoid hypertonicity of infused fluid.
- If potassium is less than 3 mEq/L, avoid insulin initially and replace potassium first.

- Hypomagnesemia occurs early in the course of DKA and requires correction. Monitor serum magnesium levels.
- Phosphorous depletion is common in DKA. Replacement is advised when it is severely depressed (<1 mg/dL).
- Sodium bicarbonate infusion: metabolic acidosis improves with restoration of intravascular volume and tissue perfusion. There is a limited role of bicarbonate therapy as it has not been shown to improve outcome in DKA. Moreover, bicarbonate therapy is associated with adverse effects such as increased paradoxical intracellular and cerebrospinal fluid acidosis, increased CO_2 production, adverse effect on tissue oxygenation, and post resuscitation metabolic alkalosis.
- Bicarbonate therapy may be considered in the following situations:
  - When pH is persistently less than 7.0 after 2–3 h of treatment
  - When hypotensive shock is unresponsive to rapid fluid replacement and persistent severe metabolic acidosis
  - In severe hyperkalemia
- Even in these circumstances, bicarbonate can only "buy time" until other treatment corrects acidosis.
- Bicarbonate may be given as an infusion of 100 mEq over 4 h with frequent arterial pH monitoring.

Step 6: Start intravenous insulin infusion

- Insulin therapy should be started only after fluid and electrolyte resuscitation is underway. Specially ensure that the potassium level is more than 3.5 mEq/L.
- Restoration of intravascular volume brings down the blood glucose levels even prior to insulin therapy.
- Prepare a regular insulin infusion of 1 unit/mL and infuse by the infusion pump.
- Use regular (rapid acting) insulin as 0.1 U/Kg body weight as a bolus dose and then 0.1 U/Kg/h as a continuous infusion or 0.14 U/Kg body weight as a continuous infusion without a bolus dose.
- Initially, measure the blood glucose level 1-hourly. If the blood glucose level does not decrease by 50–75 mg/dL/h, the rate of insulin infusion should be doubled.
- Titrate the insulin infusion rate to blood glucose levels.
- Once the blood glucose level reaches 250 mg/dL, decrease insulin infusion to 0.5 IU/Kg/h.
- Remember that intravenous insulin has a half-life of 2.5 min. It is important that the insulin infusion is not interrupted.
- Rate of reduction of blood glucose should be less than 50–75 mg/dL/h.
- Rapid correction of blood glucose levels could lead to cellular edema seen mainly in pediatric population, which can lead to convulsion and electrolyte disturbances (hypokalemia, hypomagnesemia, and hypophosphatemia).

Step 7: Monitor effectiveness of therapy clinically and biochemically

- The following features indicate clinical improvement:
  - Increased sense of well-being

  - Decreased tachycardia
  - Decreased tachypnea
  - Improved mental status
  - Able to take oral food
- The following biochemical parameters should be followed:
  - Serum glucose below 200 mg/dL in DKA and below 250–300 mg/dL in HHS.
  - Serum bicarbonate more than 18 mEq/L.
  - Venous pH more than 7.30.
  - Serum anion gap less than 12 mEq/L or delta anion gap/delta bicarbonate improving—due to sodium chloride resuscitation, these patients develop nonanion gap metabolic acidosis, so anion gap may still be falsely high in the patient who is improving.
  - Decreasing glycosuria.
  - Urine or serum ketones by nitroprusside test are not reliable parameters to follow as this test predominantly measures acetoacetate and acetone, whereas β-hydroxybutyrate is the predominant ketone in severe DKA, which is not measured usually in the laboratory. There may be a paradoxical rise of serum or urinary ketones as patients improve due to conversion of beta-hydroxybutyrate to acetone and acetoacetic acid.
  - Stabilizing urea, creatinine.
  - Plasma effective osmolality (exclude urea in osmolality calculation) below 315 mosmol/Kg.

Step 8: Switch to subcutaneous insulin when stable

- Maintain IV insulin until biochemically stable and the patient has taken at least two meals.
- Switch to subcutaneous regular insulin with half dose of total intravenous insulin requirement either as a fixed dose or sliding scale insulin as per protocol (see Chap. 60).
- IV infusion should be stopped 2 h after the first dose of subcutaneous insulin.

Step 9: Identify precipitating factors

- They should be sought and treated. Common precipitants include the following:
  - Missed insulin therapy
  - Infections—pneumonia, sepsis, urinary tract infection
  - Trauma
  - Pancreatitis
  - Myocardial infarction
  - Pregnancy
  - Stroke
  - Steroid use

Step 10: Continue supportive care

- The urinary catheter: Consider in persistent hypotension, renal failure, anuria, and impaired consciousness. Maintain strict asepsis during catheterization.
- The CVP line: A must have for all patients who present with shock. Also consider in the elderly with concomitant illness, cardiac failure, or renal failure even in the absence of hypotension.
- Thromboembolic complications are common, and DVT prophylaxis should be initiated (see Chap. 79).
- The nasogastric tube: If consciousness is impaired, use it to avoid aspiration of gastric contents.
- Antibiotics: Keep low threshold for use.

59.2 Hypoglycemia

A 42-year-old male patient, with type 1 diabetes mellitus, was brought to the emergency department with history of feeling unwell, nausea, vomiting for 2 days, sudden onset of giddiness, sweating, palpitations, and altered sensorium. Blood glucose on a glucomete r was 42 mg/dL.

Impaired consciousness in diabetic patients is most commonly due to hypoglycemia that is most often drug-induced. Symptoms of hypoglycemia are nonspecific, and this can masquerade as cardiorespiratory, neurological, and even psychiatric problems. A low threshold for checking blood sugar in all diabetic patients to exclude hypoglycemia is warranted as it is an imminently treatable condition and if left unattended leads to mortality and severe morbidity.

Step 1: Promptly identify clinical features of hypoglycemia

- Features of hypoglycemia could be neurogenic such as diaphoresis, tremor, anxiety, palpitation, hunger, paraesthesia, and tachycardia caused by sympathetic stimulation.
- These may be absent in patients with autonomic neuropathy or on β-blockers.
- In some patients, neuroglycopenic features such as drowsiness, behavioral abnormalities, coma, and seizures predominate.

Step 2: Check blood glucose immediately

- Urgent capillary sugar should be checked with the bedside glucometer. If possible, a simultaneous venous sample should be sent to the laboratory for glucose analysis. Point of care glucometers generally overestimate glucose values in the lower range. Whenever hypoglycemia is suspected, always send blood for glucose estimation by glucose analyzer.
- Administration of dextrose should not be delayed if blood glucose checking cannot be done immediately.

Table 59.1 Causes of hypoglycemia in the ICU

Insulin
Oral hypoglycemic agents
Sepsis (including malaria)
Hepatic failure
Alcohol
Adrenal crisis (including steroid withdrawal)
Drugs

- If the blood glucose level is less than 70 mg/dL and symptoms improve with glucose administration, then patient symptomatology may be attributed to hypoglycemia.

Step 3: Give intravenous dextrose
- Reverse hypoglycemia rapidly with 50 mL of 25–50% glucose given intravenously.
- Check blood glucose after dextrose infusion and repeat the injection till the glucose is above 70 mg/dL for at least two consecutive readings and the patient is asymptomatic.
- Start intravenous dextrose infusion 6-hourly with frequent blood glucose monitoring in patients on long-acting insulin, oral hypoglycemic drugs, or renal impairment as they are prone to recurrent hypoglycemia.

Step 4: Consider alternative agents in specific circumstances
- Injection glucagon may be given in a dose of 1 mg intramuscularly or subcutaneously if venous access is not possible.
- Injection octreotide 25–50 mcg may be given subcutaneously or as an intravenous infusion in patients with resistant hypoglycemia, sulfonylurea-induced hypoglycemia, or hypoglycemia induced by drugs like quinine or quinidine.

Step 5: Consider precipitating factors of hypoglycemia in diabetic patients
- Missed meals/inadequate food intake
- Insulin overdose
- Change of therapy/dosage of hypoglycemic drugs or insulin
- Concomitant ingestion of drugs causing hypoglycemia
- Presence of hepatic or renal failure

Step 6: Consider disorders and drugs associated with hypoglycemia (see Tables 59.1 and 59.2)
- In an intensive care unit, certain disorders are associated with hypoglycemia, and frequent blood glucose monitoring should be done in these patients.
- Hypoglycemia is more common if there is intolerance to enteral feeding and the patient is not started on parenteral nutrition.
- Many patients in the ICU have altered mental state and/or are under sedation, and hypoglycemic episode may remain unnoticed in these patients, and so, frequent blood glucose monitoring is essential in these groups of patients.

Table 59.2 Drugs associated with hypoglycemia

Insulin
Oral hypoglycemic agents
Gatifloxacin
Quinine
Artesunate derivatives
Pentamidine
Lithium
Propoxyphene

- Many patients in ICUs are on intravenous insulin infusion. Discontinuation or intolerance to enteral feeding and stopping parenteral nutrition without simultaneously stopping insulin lead to hypoglycemia.
- At lower glucose range and in low perfusion states, bed side glucometer lose their accuracy.

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Glycemic Control in the ICU

60

Rajesh Chawla and Subhash Todi

A 45-year-old male patient was admitted to hospital with cough, breathlessness, dizziness, and fever for the past 5 days. He was hypoxemic (SpO^2 88% on a nonrebreathing mask) and hypotensive (blood pressure 82/34 mmHg after 2 L of IV fluid). He was intubated and started on mechanical ventilation. His blood glucose was 350 mg/dL on the glucometer.

Hyperglycemia is commonly seen in both diabetic and nondiabetic patients in ICUs. Hyperglycemia is also an independent risk factor for mortality and morbidity in medical and surgical ICU patients. Various factors contribute to hyperglycemia in the ICU. These include increased counterregulatory hormones (glucagon and cortisol), hepatic insulin resistance, glucocorticoid therapy, dextrose-containing solutions, and high-calorie enteral and parenteral nutrition. It is also believed to be a marker of more severe disease.

Step 1: Initiate resuscitation and check blood glucose

- Initiate resuscitation as mentioned in Chap. 78.
- Check venous or arterial glucose (in patients with the arterial line) in glucose analyzer. As an alternative, capillary glucose may be checked in correctly calibrated glucometer.

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- Treatment for the underlying disease should not be withheld while one is waiting for a laboratory glucose value.

Step 2: Assess glycemic risk
- Patients should be asked about history of diabetes and current and past treatment and check for HbA1c to assess control of blood glucose.
- Check comorbidities such as hypertension, renal disease, liver disease, pancreatitis, chronic obstructive airway disease (COAD), obesity, and coronary artery disease.
- Look for medication history causing hyperglycemia—corticosteroids, octreotide, β-blockers, epinephrine, thiazide diuretics, niacin, pentamidine, protease inhibitors, and antipsychotic agents.

Step 3: Decide on frequency of blood glucose measurement
- All hemodynamically unstable patients, especially those on intravenous insulin infusion, should have blood glucose checked every hour.
- As the condition stabilizes or in less sick patients, this interval may be prolonged.
- With any change in patients' condition or nutrition delivery regimen, initiate more frequent glucose monitoring.

Step 4: Decide on the target blood glucose level
- The present recommendation in mixed medical/surgical ICU patients is to keep blood glucose between 140 and 180 mg/dL.
- This is mainly applicable to patients staying in the ICU for 3 days or more as they benefit from long-term control of hyperglycemia.
- In short-stay patients (staying less than 3 days), specially those who are eating, one may have a more liberal approach.

Step 5: Decide on insulin delivery route
- All oral hypoglycemic agents and long-acting insulin should be discontinued during initial days of instability.
- Intravenous infusion of regular insulin is the treatment of choice in critically ill patients.
- The following groups of patients may be candidates for periodic subcutaneous insulin:
  - Step-down therapy from intravenous insulin
  - Less sick patients on oral diet

Step 6: Decide on insulin delivery protocol (Tables 60.1 and 60.2)
- Insulin protocol should be institution specific and nurse driven.
- All efforts should be made to educate nurses and residents and ensure compliance by periodic audits.
- Dynamic insulin protocols, ideally computerized, which can monitor trend of rise or fall of blood glucose and adjust insulin doses, tend to keep blood glucose at a more desirable range.

Table 60.1 An example of algorithm of IV insulin therapy in a critically ill patient

	Initiation		Maintenance	
Random blood sugar (RBS) (mg/dL)	Bolus (U)	Infusion (U/h)	At 1–5 U/h	At >5 U/h
151–199	0	2	Increase 1 U/h	Incr 2 U/h
200–249	3	2	Bolus 3 U + incr 1 U/h	Bolus 3 U + incr 2 U/h
250–299	5	3	Bolus 5 U + incr 1 U/h	Bolus 5 U + incr 2 U/h
300–349	8	3	Bolus 8 U + incr 1U/h	Bolus 8 U + incr 2U/h
350–399	10	4	Bolus 10 U + incr 2U/h	Bolus 10 U + incr 3U/h
400–449	10	5	Bolus 10 U + incr 3U/h	Bolus 10 U + incr 4U/h
>450	10	6	Bolus 10 U + incr 4U/h	Bolus10 U + incr 4U/h

Target RBS: 140–180 mg/dL

Table 60.2 Another example of algorithm of IV insulin therapy in a critically ill patient

RBS (mg/dL)	Scale 1 (IV—U/h)	Scale 2 (IV—U/h)	Scale 3 (IV—U/h)	Scale 4 (IV—U/h)
<60	Treat as hypoglycemia	Do	Do	Do
60–140	Nil	Nil	Nil	Nil
141–200	1	2	3	4
201–250	2	4	6	8
251–300	3	6	9	12
301–350	4	8	12	16
351–400	5	10	15	20
>400	10	15	20	25

The patient should be started on a particular scale depending on initial sugar and clinical scenario. In this scale, in order to arrive at a target glucose level of 140–180 mg/dL, insulin infusion rate should be shifted horizontally to the next or previous scale in the same row if sugar remains within the range for that row. If sugar increases or decreases to the other range, the infusion rate should be shifted vertically for that range in the same scale

Step 7: Avoid hypoglycemia (blood glucose <70 mg/dL)

- Rigorous blood glucose control (80–110 mg/dL) leads to hypoglycemic episodes in a mixed medical/surgical ICU, which may be detrimental to their outcome.
- The following groups of patients are more prone to hypoglycemia:
  - Renal failure
  - Dialysis
  - Liver failure
  - Malnourished
  - Adrenal insufficiency
- Stop insulin infusion immediately and give 50 mL of 25% dextrose intravenously and repeat this till blood glucose is more than 90 mg/dL and the patient is asymptomatic.
- Check blood glucose every 15 min and then decrease frequency depending on clinical response.

- Ensure adequacy of carbohydrate calorie intake either enterally or parenterally and avoid abrupt discontinuation.

Step 8: Avoid large variations in glucose concentrations in ICUs

- Glycemic variability is expressed as the standard deviation of each patient's blood glucose levels.
- Glycemic variability is an independent predictor of mortality in a heterogeneous population of ICU patients.
- The efficacy of continuous or near-continuous glucose monitoring and/or new algorithms targeted more specifically to reduce glycemic variability as well as mean blood glucose requires further clinical studies in ICU patients before the final recommendation is made.

Step 9: Avoid under or overtreatment and safety issues

- Overtreatment and undertreatment of hyperglycemia represent major safety concerns.
- Education to hospital personnel is essential in engaging the support of those involved in the care of inpatients with hyperglycemia.
- Caution is required in interpreting results of point-of-care glucose meters in patients with anemia, polycythemia, hypoperfusion, or use of medications.
- Buy-in from hospital administration are required for promoting a rational system approach to inpatient glycemic management.

Step 10: Change to intermittent treatment before discharge

- Switch over to subcutaneous insulin.
- Use a sliding scale with short-acting insulin along with long-acting insulin (NPH or glargine), which will lead to better glycemic control.
- Long-acting insulin should overlap discontinuation of insulin infusion to prevent hyperglycemia.
- Calculate the dosage taking into account the history of diabetes, type of diabetes, stress level, steroid use, and general clinical status.

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Within 24 h after admission to an ICU, adults who were expected to require treatment in the ICU on three or more consecutive days were randomly assigned to undergo either intensive glucose control, with a target blood glucose range of 81–108 mg/dL (4.5–6.0 mmol/L), or conventional glucose control, with a target of 180 mg/dL or less (≤10.0 mmol/L). Intensive glucose control increased mortality in adults in the ICU: a blood glucose target of 180 mg/dL or less resulted in lower mortality than did a target of 81–108 mg/dL.
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Intensive insulin therapy to maintain blood glucose at or below 110 mg/dL reduces morbidity and mortality in critically ill patients in the surgical intensive care unit.

Part VIII

Oncology

Atul Kulkarni and Vijaya Patil

Transfusion Practices and Complications

61

Nayana Amin and Vijaya Patil

A 54-year-old male patient with carcinoma of the rectum was admitted to the ICU with profuse bleeding per rectum for the previous 12 h. He was hypotensive and tachycardic. His hemoglobin (Hb) was 6.0 g/dL, platelet count was 150×10^3/mm^3, international normalized ratio (INR) was 1.8, and activated partial thromboplastin time (APTT) was 30 s. He was transfused with three units of packed red blood cell.

Blood transfusion is a common practice in the ICU with an estimate of 40% patients having transfusion. It is generally safe but occasionally may lead to minor or life-threatening consequences if attention to details and protocols is not met during transfusion.

Step 1: Resuscitate

- Secure two large-bore (14G/16G) IV cannulae.
- Send blood for grouping, cross-matching, complete blood count (CBC), coagulation profile, and other appropriate investigations.
- Proper coordination with blood bank is mandatory in these situations for early and proper acquisition of blood products.

Step 2: Transfuse packed RBCs or blood components (Tables 61.1 and 61.2)

- If the patient is bleeding profusely and hemodynamically unstable, use group-specific uncross-matched blood or O Rh-negative packed cells while waiting for cross-matched blood.

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Table 61.1 Alternative red blood cell products

Technique	Purpose	Indications	Comments
Leukoreduction	Minimize the risk of cytomegalovirus transmission	High-risk immunocompromised patients, patients needing multiple transfusions, patients who have had FNHTR	Does not prevent TA-GVHD (transfusion-associated graft vs. host disease)
Separate type of filters to allow for RBC and platelet passage only, ideally should be used during collection but may be used during transfusion	Febrile nonhemolytic transfusion reactions (FNHTR) and alloimmunization		
Washed RBCs	Prevent allergic reaction	Recurrent severe allergic reactions in spite of premedication, IgA-deficient patients, patients at risk of hyperkalemia	Not equivalent to leukoreduction, 15–20% loss of RBCs
RBCs washed with saline to remove >98% of plasma proteins, antibodies, leukocytes, and electrolytes	Reduce risk of hyperkalemia		
Gamma irradiation to inactivate leukocytes	Prevents TA-GVHD	Premature infants, patients with malignancy, recipients of allogenic hemopoietic transplants, transfusion to blood relatives	Does not reduce infectious risks or FNHTR

Table 61.2 Blood components and antifibrinolytics

Product	Content	Indications	Dose	Caution	Expected correction
FFP (fresh frozen plasma)	All coagulation factors in normal concentration and plasma proteins	Deficiencies and consumption of coagulation factors	15 mL/kg	Should be group specific	15 mL/kg of FFP will increase coagulation factor concentration by 25–30%, which is enough for adequate clotting
	Thawed plasma may be stored (1–6°C) up to 5 days	Reversal of factor VI and factor V anticoagulants effect (warfarin)		Thawed plasma should be transfused within 24 h if kept at room temperature	
		Massive blood transfusion (>1 blood volume within several hours)		Use blood filters	
		Replacement in plasmapheresis			
		Raised INR and planned invasive procedure			
		Treatment of thrombotic thrombocytopenic purpura			

(continued)

Table 61.2 (continued)

Product	Content	Indications	Dose	Caution	Expected correction
Cryoprecipitate	Fibrinogen, factor VIII/vWF (von Willebrand's factor), factor XIII, and fibronectin	Decreased fibrinogen, liver disease, post-thrombolysis bleeding	1 unit/7–10 kg body weight	Should be transfused within 6 h of thawing	1 unit cryoprecipitate/10 kg body weight
				Use blood filters	Raises plasma fibrinogen concentration by ~50 mg/dL
Platelet	Random donor platelets—approximately 8.0×10^{10} platelets with 50 mL plasma	Bleeding due to critically decreased circulating platelet counts or functionally abnormal platelets	Infused over 30–60 min	Should be group specific	Expect an adult platelet count increment of ~7,000–10,000/mm^3 for each RDP (random donor platelet) given or 30,000–60,000/mm^3 for each SDP (single donor platelet)given
	Single donor platelets—$3.5–4.0 \times 10^{11}$ platelets with 250 mL plasma	Maintain platelet count >10,000/mm^3 in stable nonbleeding patients, >30,000/mm^3 in unstable nonbleeding patients, and >50,000/mm^3 in patients undergoing invasive procedures or actively bleeding >100,000/mm^3 or for CNS trauma		Do not refrigerate	In pediatrics, a dose of 5–10 mL/kg of platelets (RDP or SDP) should result in 50–100,000/mm^3 increment

Desmopressin	Stimulate the endothelial release of factor VIII and vWF into the plasma (V2 receptor-mediated effect), where they form a complex with platelets and enhance their ability to aggregate	Hemophilia A, von Willebrand's disease, uremic thrombocytopathy	0.3mcg/kg repeated as clinically necessary at intervals of 12–24 h		Tachyphylaxis may occur after three or four doses
Antifibrinolytic drugs					
Epsilon-aminocaproic acid	Competitive inhibitor of plasminogen activation	Situations associated with hyperfibrinolysis such as operations requiring cardiopulmonary bypass, liver transplantation, and some urological and orthopedic operations	100 mg/kg as an IV bolus followed by an infusion of 15 mg/kg/h (max 24 gm/day)		
Tranexamic acid	Competitive inhibitor of plasminogen activation		Bolus dose of 10–15 mg/kg IV followed by 1 mg/kg/h for 5–8 h		
Aprotinin	Powerful inhibitor of plasmin, trypsin, chymotrypsin, kallikrein, thrombin, and activated protein C	Cardiac surgery, major orthopedic surgeries, liver transplant	Loading dose of 2 million international unit followed by continuous infusion of 500,000 KIU/h		
Activated factor VIIa		Factor VIIa deficiency, retropubic prostatectomy, bleeding in trauma, orthotopic liver transplantation	30 up to 90 mcg/kg Repeat every 2–3 h till satisfactory hemostasis is achieved		Target trough activity of at least 10–15 IU% (10–15%) is needed

- In the presence of active bleeding, transfuse blood rapidly over 30 min (if available, use the rapid infusion pump, which can give fluids at a faster rate).
- 4 mL/Kg of packed RBCs (usually one unit) increases the hemoglobin by 1 g/dL and hematocrit by 3% in absence of active bleeding.
- Blood should be transfused within 4 h except in emergency. Rate of transfusion can be adjusted as per need, that is, rapidly in hypovolemic patients and slowly in stable patients; however, once issued from blood bank, blood transfusion should get over within 4 h to prevent growth of organisms. If blood cannot be transfused fully within this time, it is advisable to discard it.
- Transfuse blood and blood products through the filter adequate to prevent passage of small clots that may form in stored blood.
- The filter with a pore size of 170–200 μm is recommended for routine transfusions of RBCs, platelets, fresh frozen plasma (FFP), and cryoprecipitate.
- Filters with smaller pore size are more efficient, but they would increase resistance and filter out platelet aggregates, reducing efficiency of transfused platelets.
- Microaggregate filters with 20–40 μm size are recommended during cardiopulmonary bypass only.
- Filters can slow down the rate of blood transfusion. So the standard recommendation is to use a new set for every transfusion. In case of rapid transfusion if filter does not look clogged, change the set every two transfusions.
- Use fluid warmer to transfuse blood in massive blood loss. This helps to prevent hypothermia, which can contribute to the coagulopathy by causing reversible platelet dysfunction, altering coagulation kinetics, and enhancing fibrinolysis.
- Hypothermia also causes ventricular dysrhythmias and citrate toxicity due to reduced citrate metabolism.
- Do not use unconventional and uncontrolled methods such as keeping near heat source or immersing the bag in hot water bath.

Step 3: Correct coagulopathy (see Chap. 62)

- Correct high INR with FFP or low platelets with platelet transfusions only in an actively bleeding patient.
- Do not correct raised INR prophylactically in a nonbleeding patient unless a surgical intervention is contemplated.
- Other coagulopathic abnormalities need to be corrected.
- Antifibrinolytic agents may be used to minimize bleeding in situation like trauma.
- Correct hypothermia.
- Normalize calcium.
- Consider activated factor VII in some specific situations.

Step 4: Control the source of bleeding

- Investigate to find out the source of bleeding and consider options available for controlling the bleeding (interventional radiology or surgery).
- Urgent consultation is required if needed with these specialities.

Step 5: Assess the severity of bleeding

- Massive blood loss may be defined as:
  - Loss of one blood volume within a 24-h period
  - Loss of blood equivalent to 7% of in lean body weight in an adult (5 L) and 8–9% in a child
  - Loss of 50% of blood volume within 3 h
  - Loss of blood at a rate in excess of 150 mL/min

Step 6: Manage massive blood loss

- Institute continuous invasive pressure monitoring for fluid management if the patient continues to remain hypotensive due to ongoing bleeding.
- Serial CBC (Hb and platelets) and coagulation tests (prothrombin time, APTT, and fibrinogen), blood gas analysis, serum electrolytes (Na, K, Mg, ionized calcium), and serum lactate should be done.
- These should be repeated frequently in ongoing bleeding and after every component therapy.
- Transfusion of platelets, FFPs, and cryoprecipitate should be guided by laboratory results.
- FFP administration should begin after loss of one blood volume and platelets after loss of 1.5 times the blood volume.
- 1:1:2 ratio should be maintained for packed RBCs, FFP, and random donor platelets to prevent dilutional coagulopathy and dilutional thrombocytopenia due to massive blood transfusion, which results in a vicious cycle of bleeding diathesis.
- Administer cryoprecipitate if fibrinogen is less than 100 mg/dL or there is a fear of volume overload by use of FFP.
- If patients with A or B blood group have received multiple units of O Rh-positive whole blood, then they can be switched back to their inherent group-specific blood only after subsequent testing by the blood bank indicates it is safe to do so.

Step 7: Identify and manage transfusion-induced complications (Table 61.3)

- Stop blood transfusion immediately if any acute hemolytic transfusion reaction is suspected.
- Hypotension may be due to acute ongoing hemorrhage, acute severe transfusion reaction, allergic reaction/anaphylaxis, or rarely due to septic shock (due to transfusion of blood with bacterial contamination).
- Check the identity of the recipient with the details on the bag and the cross-match form.
- Transfusion-associated circulatory overload (TACO) is circulatory overload following transfusion of blood or blood product.
- Transfusion-associated acute lung injury (TRALI) is defined as new acute lung injury (with hypoxemia and bilateral infiltrates on chest radiograph but no evidence of left atrial hypertension) occurring during or within 6 h after a transfusion, with a clear temporal relationship to the transfusion, and not explained by another acute lung injury (ALI) risk factor.

Table 61.3 Transfusion-related complications

Reaction	Cause	Clinical signs	Treatment
Febrile nonhemolytic transfusion reaction (FNHTR)	Reaction between the recipient's antibodies and transfused leukocytes	Fever, temperature rise	Give paracetamol and resume transfusion at a slow rate
	Pyrogenic cytokines released from the leukocytes in stored blood		
Allergic reaction	Reaction to soluble allergens in the donor's plasma	Urticaria, flushing, pruritus	Give 10 mg IV chlorpheniramine maleate and resume transfusion
Anaphylaxis	IgA-deficient individuals react to IgA in transfused units	Flushing, pruritus, laryngospasm, bronchospasm	Stop transfusion
			Supplement O_2
			SC/IV epinephrine, 100 mg IV hydrocortisone, 10 mg IV chlorpheniramine maleate
			Salbutamol nebulization
			IV fluids
			Send the blood back to the blood bank along with a sample of the patient's blood
			Use washed RBCs in future
Sepsis	Bacterial contamination of blood and blood products, Yersinia, bacteria, malaria	Fever, chills, hypotension	Stop transfusion
			Contact the blood bank and send the remaining blood to the blood bank
Acute hemolytic transfusion reaction (<24 h)	Immune-mediated—due to cytokines in transfused blood	Fever, chills, flushing, chest pain, back pain, vomiting, tachycardia, hypotension	Send blood for CBC, coagulation profile, direct Coombs' test, lactate dehydrogenase, haptoglobin, liver function tests for indirect bilirubinemia, peripheral smear for evidence of hemolysis
Delayed hemolytic transfusion reaction (24 h to 28 days)	Nonimmune-mediated—transfusion of damaged red cells		
			Gram staining and blood culture if bacterial contamination is suspected

			Send urine for hemoglobinuria O_2 supplementation, fluid resuscitation, and vasopressors to maintain mean arterial pressure >65 mmHg
			Broad-spectrum antibiotics if sepsis is suspected
ABO (major blood group) incompatibility	Mismatched transfusion, IgM antibody against major RBC antigen, leading to intravascular hemolysis, renal failure, disseminated intravascular coagulation (DIC)	Fever, chills, flushing, chest pain or low back pain, hypotension, and dyspnea	Stop transfusion
			Reconfirm the patient's identity and blood group
			Inform the blood bank and return blood to the blood bank
			Infuse saline to maintain urine output of 100 mL/h
			Give diuretics if urine output falls
			Treat DIC with appropriate blood components
Transfusion-associated graft-versus-host disease (TA-GVHD) 2–30 days after transfusion	Donor lymphocytes initiate an immune attack against recipient's cells	Fever, skin rash, liver dysfunction, diarrhea, severe pancytopenia	No treatment
			Prevention by using gamma-irradiated blood products in high-risk patients
	Cause	*Presentation*	*Treatment*
TACO	Volume overload	Dyspnea, rales, hypertension, and desaturation, raised central venous pressure (CVP)	O_2 supplementation, diuretics, ventilatory support
TRALI	Antibodies in the donor's blood react with neutrophil antigen in the recipient	Dyspnea, rales, hypotension, and desaturation, normal or low CVP	Supportive management
			Ventilate according to acute respiratory distress syndrome network protocol
			Steroids not indicated

Step 8: Use less allergenic blood products

- In patients with multiple blood transfusion and transfusion-related complications, alternatively processed blood products should be considered (Table 61.1).

Step 9: Consider threshold for blood transfusion

- If the bleeding has stopped and serum lactate is normal, do not transfuse any more blood or blood products.
- In the absence of active bleeding, keep a transfusion threshold of less than 7.0 g% and keep 7–9 g/dL Hb in critically ill patients who are hemodynamically stable.
- RBC transfusion may be beneficial in anemic patients with acute coronary syndrome (keep Hb >10 g/dL).

Step 10: Use blood products judiciously

- In the absence of bleeding, do not correct high INR with FFP.
- Patients having inadequate intake or on anticoagulants and broad-spectrum antibiotics are likely to have vitamin K deficiency, which can cause deranged INR.
- They will benefit from intravenous vitamin K supplementation.

Suggested Reading

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Disseminated Intravascular Coagulation and Thrombocytopenia

62

Vijaya Patil, Nayana Amin, Reshma Ambulkar, and Atul Kulkarni

A 40-year-old male patient was admitted with acute pancreatitis. He developed fever, tachycardia, hypotension, and respiratory distress on the third day of admission. His abdomen was severely tender and distended. Next morning the nurse noticed excessive oozing from arterial and central line insertion site, and his abdomen was further distended.

Bleeding manifestation due to disseminated intravascular coagulation (DIC) occurs in 1% of hospital admission. Assessing and managing these patients require a systematic approach as DIC is a reflection of underlying systemic disease affecting the coagulation system, resulting in procoagulant activation, fibrinolytic activation, consumption coagulopathy, and end organ damage, which needs to be recognized and treated.

Step 1: Initial resuscitation

- Special emphasis should be placed on stabilizing hemodynamics, and if needed, blood and blood product transfusion should be started.
- Care should be taken in establishing venous access in actively bleeding patients who may be coagulopathic.
- Peripheral access is preferable to central.
- Use ultrasound-guided venous cannulation if possible and preferably choose compressible sites like internal jugular or femoral vein.
- Avoid arterial punctures.

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Table 62.1 Conditions associated with DIC

Infections	Bacterial—Gram-negative and Gram-positive sepsis
	Viral—cytomegalovirus, HIV, hepatitis, dengue
	Fungal
	Parasitic—malaria, leptospirosis
Malignancy	Solid tumors
	Hematological—acute promyelocytic leukemia is commonly associated with DIC
Obstetric	Amniotic fluid embolism
	Placenta abruption
	Preeclampsia
	Intrauterine fetal death/retained products of conception
Toxic and immunological insults	Viper snake bites
	Massive transfusion
	ABO transfusion incompatibility
	Transplant rejection
Massive inflammation	Severe trauma
	Crush injuries
	Massive burns
	Fulminant liver failure
	Severe hypo-/hyperthermia
	Severe pancreatitis
Vascular disorders	Aortic aneurysms
	Giant hemangiomas

Step 2: Take relevant history and perform focused physical examination

- Take history of known systemic conditions associated with DIC and coagulation disorders (Table 62.1).
- Review the drug history, particularly the use of heparin and warfarin, and consumption of antiplatelet agents including nonsteroidal anti-inflammatory drugs.
- Look for bleeding manifestation, superficial like skin and mucosal (petechiae, purpura) or visceral and deep seated (gastrointestinal bleeding).
- Look for thrombotic manifestations like deep vein thrombosis (DVT) of lower limbs or venous or arterial thrombosis at any other site (e.g., cerebral).

Step 3: Investigate to ascertain the type and cause of bleeding (Table 62.2)

- Complete blood count, including platelet count and peripheral smear, for the presence of fragmented RBCs.
- Prothrombin time (PT), activated partial thromboplastin time (APTT), thrombin time (TT).
- Fibrinogen level, fibrin degradation product (FDP), D-dimer.
- Renal and liver function tests.
- The commonest laboratory abnormality is thrombocytopenia followed by elevated FDPs, prolonged PT, prolonged APTT, and a low fibrinogen.

Table 62.2 Coagulation profile

Test	What does it monitor	Normal value	Inference
Prothrombin time	Factors that are in the extrinsic pathway and common pathway: factors VII, X, V, and II	11–13 s	Prolongation of the PT is most often a result of deficiencies in factor VII but can also be caused by any of the extrinsic and common pathway factors. Decreased fibrinogen, levels less than 100 mg/dL, will also prolong the PT
			Cholestatic jaundice
			Acute or chronic liver failure
			DIC
			Malabsorption
			Vitamin K deficiency
			Coumadin (warfarin) therapy
			Factors I, II,V, VII, X deficiency
Activated partial thromboplastin time	Factors that are designated in the intrinsic pathway: factors XII, XI, IX, VIII, X, V, II, and fibrinogen	28–34 s	Heparin therapy
			Factor deficiency
			Presence of an inhibitor like lupus anticoagulants
Platelet count	Quantifies platelet number	130–400 × 10^9/L	Decreased production (bone marrow disorder), increased destruction, idiopathic thrombocytopenic purpura (ITP), thrombotic thrombocytopenic purpura, sequestration (hypersplenism)
Thrombin time	Evaluates the last step of coagulation (conversion of fibrinogen to fibrin)	13–15 s	Heparin therapy
			DIC
			Qualitative fibrinogen abnormalities or hypofibrinogenemia
			Elevated FDPs (fibrin degradation products)
Fibrinogen level		200–500 mg/dL	Congenital and acquired hypofibrinogenemia
			DIC
D-dimer	Cross-linked D fragments of the protein fibrinogen	500 ng/mL	Deep venous thrombosis, DIC, pulmonary embolism, thrombolytic treatment, postoperative

Table 62.3 ISTH diagnostic scoring system for DIC

Platelet count		
	>100 × 10^9/L	0
	<100 × 10^9/L	1
	<50 × 10^9/L	2
Fibrin marker (e.g., D-dimer, FDP)		
	No increase	0
	Moderate increase	2
	Strong increase	3
Prolonged PT		
	<3 s	0
	>3 but <6 s	1
	>6 s	2
Fibrinogen level		
	>1 g/dL	0
	<1 g/dL	1

- D-dimer, FDP, and antithrombin levels can be used for rapid and specific diagnosis of DIC, with antithrombin providing an indicator for severity and prognosis.
- Diagnosis of DIC is essentially confirmed by demonstrating increased thrombin generation (decreased fibrinogen) and increased fibrinolysis (elevated D-dimer or FDP).

Step 4: Ascertain severity and prognosticate outcome

- Calculate the DIC score (Table 62.3) with the ISTH (International Society of Thrombosis and Haemostasis) scoring system which provides objective measurement of DIC and correlates with outcome.

Step 5: Continue resuscitation

- Continue resuscitation and maintain hemodynamic stability using crystalloids and/or colloids.
- In colloids, preferably use gelatins as they do not interfere with clotting.
- If you are using starches, use tetrastarch preferably, as they have less effect on the coagulation profile, but do not exceed maximum dose (50 mL/kg/day).

Step 6: Correct coagulopathy (see Table 61.2 in Chap. 61)

- Repeat the coagulation profile and complete blood count frequently and replace blood and blood products.
- In the presence of ongoing blood loss, try to normalize prothrombin time and APTT and aim to maintain platelet count of more than 50,000.
- Do not use antifibrinolytic agents as they may aggravate thrombosis.
- Patients who have DIC with a primary hyperfibrinolytic state and who have severe bleeding can be treated with lysine analogues, such as tranexamic acid (e.g., 1 g every 8 h).
- There is no role of heparin in actively bleeding patients.

- It should be considered only where thrombosis predominates such as arterial or venous thromboembolism or severe purpura fulminans associated with vascular skin infarction.

Step 7: Treat the underlying disorder
- Repeat the tests to monitor the dynamically changing scenario and continue treatment based on clinical observation and laboratory results.
- Once patient stops bleeding, do not try to correct laboratory abnormalities as transfusion of blood and blood products should be based on clinical condition and bleeding rather than laboratory values only.

Calculate score
- More than 5 overt DIC: repeat score daily.
- Less than 5 suggestive for nonovert DIC: repeat for the next 1–2 days.

Thrombocytopenia

A 50-year-old male patient was admitted with acute pancreatitis. His blood investigations showed Hb 10.7 g%, WBC 12,000/mm^3, and platelets 110,000/mm^3. On the third day, he worsened clinically. His WBC count was 20,000/mm^3 and platelets were 70,000/mm^3. However, the next day, he further deteriorated requiring inotropes and ventilatory support. His Hb dropped to 6.4 g%, WBC count rose to 28,000 mm^3, and platelets further dropped to 40,000/mm^3.

Step 1: Resuscitate
- Resuscitate, monitor, and stabilize in the ICU (refer to Chap. 78). In patients with low platelets and coagulopathy, ultrasound-guided jugular venous catheter insertion for fluid resuscitation should be performed.
- Send blood for peripheral blood smear, grouping, cross-matching, coagulation profile, and biochemistry.

Step 2: Assess severity of thrombocytopenia
- Thrombocytopenia is defined as a platelet count less than 150×10^9/L.
- In critically ill patients, a threshold of less than100×10^9/L may be taken.
- The ability to form a hemostatic plug is retained until the platelet count drops to less than 100×10^9/L

Step 3: Assess cause of thrombocytopenia (Table 62.4)
- Careful history, physical examination, previous medical records, and current chart review usually reveal the cause of low platelet count.
- Ask about bleeding from other sites in past, for example, frequent nosebleeds, gum bleeds, melena, hemoptysis, and blood in stool or urine.

Table 62.4 Causes of thrombocytopenia

Pseudothrombocytopenia seen in asymptomatic patients	EDTA causes in vitro clumping of platelets. Presence of platelet clumps in the peripheral smear and a normal repeat platelet count in citrated blood confirm pseudothrombocytopenia. In some patients, automated blood reports show thrombocytopenia due to presence of giant platelets that are counted as RBCs in automated machines; however, manual platelet count is normal
Dilutional thrombocytopenia	Massive blood transfusion
Ambulatory patients	ITP
	Drug-induced—chemotherapy, miscellaneous drugs
	Infections—Epstein–Barr virus (EBV), HIV, others
	Connective tissue disorders—rheumatoid arthritis, systemic lupus erythematosus (SLE), antiphospholipid antibody syndrome
	Hypersplenism
	Primary marrow disorder
Acutely ill patients	Infection/sepsis
	DIC
	TTP-HUS
	Posttransfusion purpura
Pregnant patient	Gestational (platelet count >70 resolves after pregnancy)
	ITP
	HELLP—hemolysis, elevated liver enzymes, low platelets
Cardiac patients	HIT
	Cardiac bypass
	Dilutional
	Gp IIb/IIIa inhibitor-related
	TTP related to clopidogrel or ticlopidine
Patient with thrombosis	HIT
	Antiphospholipid antibody syndrome
	Paroxysmal nocturnal hemoglobinuria

- History of previous platelet counts.
- History of previous blood or platelet transfusion.
- Medication history and review medication chart—particularly, use of heparin, warfarin, and antiplatelet agents including nonsteroidal anti-inflammatory drugs (Table 62.5).
- Heparin-induced thrombocytopenia (HIT) should be considered if the platelet count decreases by 50% and/or thrombosis occurs 5–14 days after starting heparin.
- History of known systemic conditions associated with defects in platelets like alcoholism, cirrhosis, HIV infection, systemic lupus erythematosus (SLE), and uremia.
- Family history of excessive bleeding.

Table 62.5 Drugs associated with thrombocytopenia

Mechanism	Drugs	
Drug-specific antibody	H_2 receptor blockers	Ranitidine, cimetidine
	Gp IIb/IIIa inhibitors	Abciximab
Drug-dependent antibody	Antibiotics	Vancomycin, rifampicin, chloroquine, amphotericin B, sulfonamides
	Salicylates/NSAIDs	Aspirin, diclofenac, ibuprofen
	Antiepileptics	Valproate, carbamazepine, phenytoin
	Antiarrhythmics	Amiodarone
	Miscellaneous	Quinine, furosemide, thiazide, morphine
Hapten-dependent antibody	Antibiotic	Penicillin, some cephalosporins
Induction of autoantibodies	Antiarrhythmics	Procainamide
	Miscellaneous	Gold salts
Myelosuppression	Antibiotics	Linezolid
	Chemotherapeutic agents	
Unknown	Antibiotics	Fluconazole, daptomycin, ganciclovir, nitrofurantoin, piperacillin
	Miscellaneous	Digoxin, haloperidol
	Gp IIb/IIIa inhibitors	Eptifibatide
Immune complex with PF4	Heparins	Unfractionated and low-molecular-weight heparin
Interference with folate metabolism	Antibiotic	Meropenem
Thrombotic microangiopathy		Clopidogrel, ticlopidine
Preexisting antibodies		Abciximab

Table 62.6 Factors associated with platelet refractoriness

Nonimmune factors	Clinical factors	Splenomegaly, fever, infection, bleeding, disseminated intravascular coagulation
	Drugs	Amphotericin B, vancomycin, ciprofloxacin, heparin
	Patient factors	previous pregnancies, previous transfusions
Immune factors	Antibodies	HLA, platelet specific, erythrocyte
	Others	Length of time the platelets are stored

- Perform physical examination to look for:
  - Evidence of bleeding in skin, mucous membrane, joints, soft tissue
  - Lymphadenopathy
  - Splenomegaly

Step 4: Transfuse platelets (Table 62.6)

- Three types of platelet products are commonly used in clinical practice:
  - Random-donor platelets (RDP)

Table 62.7 Approach for management of thrombocytopenia

Etiology	Mechanism	Presentation	Treatment
ITP, after viral illness, may be associated with antiphospho lipid antibody syndrome, may be initial presentation of connective tissue disease, lymphoploriferative malignancy	IgG antibodies against platelet antigens, platelet clearance by spleen, inadequate platelet production response	All ages, common in young adult females	Steroids, prednisolone 1 mg/kg/day for 1–2 weeks, taper
		Severe thrombocytopenia with normal RBC and WBC morphology and number	IVIG infusion 1g/kg/day for 2 days
		Diagnosis by exclusion	Anti RhD antibodies 50–75 μ/kg IV (Rh + Ve patients with intact spleen)
TTP-HUS	-Inherited or acquired deficiency of von Willebrand factor cleaving protease (ADAMTS13)	Microangiopathic hemolytic anemia, thrombocytopenia, renal insufficiency, fever, and mental status changes	FFP transfusions until the patient is ready for plasma exchanges
	Idiopathic or secondary to *Escherichia coli* diarrhea, HIV infection, certain drugs (ticlopidine, clopidogrel, quinine, cyclosporine A, mitomycin A, cisplatin, etc.), pregnancy, bone marrow transplant, and metastatic carcinomas	Schistiocytes in peripheral smear, raised LDH, normal coagulation profile	Plasma exchanges
			Platelet transfusions only in life-threatening bleeding
Drug-induced thrombocytopenia	Antiplatelet agents' and other drugs' immune mechanism	History—no other blood or coagulation abnormalities	Stop the offending drug
			Supportive care
	Chemotherapy and alcohol—directly inhibit megakaryocytes	Most chemotherapeutic drugs—nadir of blood counts in 7–10 days, recovers over 2–3 weeks Nitrosureas and mitomycin cause prolonged myelosuppression	Supportive care
	Heparin—antibodies against heparin–platelet factor 4 complex	Type I—modest transient thrombocytopenia in 2–3 days after heparin therapy	Spontaneous recovery
		Type II—less common, occurs 4–14 days after heparin therapy	Stop heparin
		ELISA assay for anti-PF 4 antibody, serotonin release assay, platelet aggregation studies	Doppler to rule out thrombosis
			Use direct thrombin inhibitors (argatroban, lepirudin) Fondaparinux should be used with caution
			LMWH and UFH should not be used

  - Single-donor platelets (SDP)
  - HLA-matched platelets
- Platelet transfusions are contraindicated in thrombotic thrombocytopenic purpura (TTP), idiopathic thrombocytopenic purpura (ITP), and HIT unless the patient is bleeding.

Step 5: Assess rise in platelet count after platelet transfusion
- Platelet counts should be measured 10–60 min after transfusion. Posttransfusion counts at 10–60 min are sensitive to immune platelet destruction. Posttransfusion counts at 24 h assess platelet survival, which is sensitive to nonimmune factors.
- The patient is considered refractory to platelet transfusions if two or three consecutive transfusions are ineffective.
- Alloimmunization is confirmed by demonstrating antibodies to specific human leukocyte antigen (HLA) or human platelet antigen (HPA).

Step 6: Understand strategies to improve response to platelet transfusions (Table 62.7)
- Treat underlying condition.
- Transfuse ABO identical platelets.
- Transfuse platelets less than 48 h in storage.
- Increase number of platelets transfused.
- Select compatible donor: HLA-matched, ABO compatible.

Step 7: Treat underlying cause
- Review and stop all offending medication.
- Evaluate the patient for evidence of secondary infection or DIC.

Suggested Reading

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Website

1. http://www.bcshguidelines

Onco-emergencies

63

Atul Kulkarni and Vandana Agarwal

A 58-year-old male patient with metastatic renal cell carcinoma presented with lethargy, confusion, anorexia, nausea, and constipation. He was polyuric and polydipsic over the past few days.

63.1 Hypercalcemia

Oncological emergencies such as hypercalcemia, tumor lysis syndrome, superior vena cava syndrome, and spinal cord compression are occasionally seen as an intercurrent problem or presenting manifestation in certain cancers.

Step 1: Resuscitate

- Hydration is of utmost importance in these patients, and intravenous saline should be given rapidly once hypercalcemia is confirmed (refer to Chap. 78).

Step 2: Send investigations

- Measure ionized serum calcium (arterial or venous).
- If total serum calcium is measured, correct for the albumin level. Corrected calcium = measured total calcium + [0.8 × (4.0−albumin)].
- Also, check serum creatinine, electrolytes, and alkaline phosphatase.
- A low serum chloride level (<100 mEq/L) suggests hypercalcemia of malignancy.
- ECG abnormalities reflect altered transmembrane potentials, affecting conduction such as QT interval shortening (common) and QRS interval lengthening (high levels). T waves may flatten or invert, and a variable degree of heart block may develop.

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R. Chawla and S. Todi (eds.), *ICU Protocols: A stepwise approach*,
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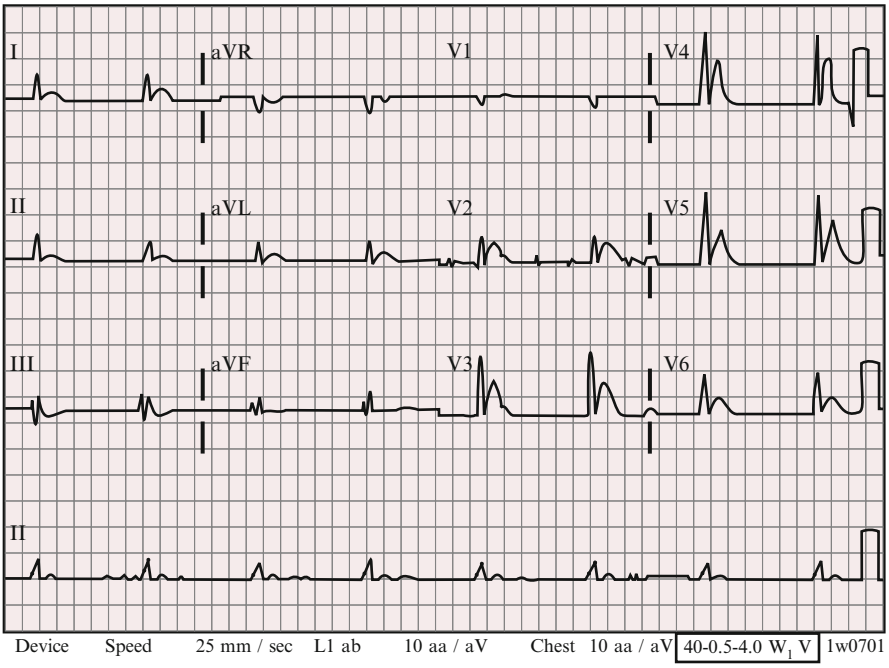
63.2 ECG Changes in Hypercalcemia



The above ECG shows a short QT interval with hardly any ST segment, characteristic of hypercalcemia. In this tracing, the QRS complexes are wide, indicative of an intraventricular conduction defect. No P waves are evident, and this is most likely a junctional escape rhythm.

Step 3: Infuse fluid

- Severe hypercalcemia is usually associated with marked hypovolemia.
- Give 500–1,000 mL of normal saline in the first hour and continue at a lower rate until volume repletion is achieved and urine output is established.
- In patients with impaired cardiorespiratory and renal function, aggressive fluid resuscitation should be done with close hemodynamic monitoring.

Step 4: Start diuretics after fluid repletion

- Consider loop diuretics only when euvolemia is achieved, as hypovolemia causes renal hypoperfusion hampering calcium excretion.
- Diuretics are specifically useful if features of hypervolemia, secondary to aggressive fluid resuscitation, develop.

Table 63.1 Treatment for hypercalcemia

Intervention	Dosage	Comment
Normal saline	250–500 mL/h until euvolemic, thereafter 100–150 mL/h IV, may require 3–4 L	Caution in patients with congestive heart failure
	Keep urine output 100–150 mL/h	
Furosemide	20–40 mg IV	After volume correction
Bisphosphonates	Pamidronate: 60–90 mg IV over 2–24 hours	Caution in renal impairment
	Zoledronic acid: 4 mg IV over 15 min	
Glucocorticoids	Prednisolone: 60 mg/day PO	Hyperglycemia, immunosuppression
	Hydrocortisone: 100 mg IV every 6 h	
Calcitonin	4–8 IU/kg SC or IM every 12 h	Rapid onset but short lived

Step 5: Start specific therapy

- Bisphosphonates block osteoclastic bone resorption.
- Use zoledronic acid with caution in patients with renal impairment, and adjust the dose according to creatinine clearance (Table 63.1).
- Subcutaneous or intramuscular calcitonin lowers calcium levels quickly, but the effect is short lived.
- In some patients with lymphomas, particularly Hodgkin's disease, hypercalcemia is caused by elevated levels of vitamin D ($1,25(OH)_2D$); glucocorticoids are particularly effective.

Step 6: Decrease intake

- Eliminate dietary sources of calcium.
- Discontinue medications such as thiazide diuretics (increase the reabsorption of calcium) and vitamin D that increase the calcium level.

Step 7: Consider dialysis

- Dialysis should be considered for patients with renal failure and/or congestive heart failure when aggressive hydration and bisphosphonates cannot be used safely.

Step 8: Treat the cause

- Treat the malignancy with chemotherapy and radiation to control the hypercalcemia if possible.

Step 9: Evaluate prognosis

- In patients with advanced malignancy, hypercalcemia may commonly occur.
- In such circumstances, it may be appropriate, ethical, and humane to institute only comfort measures if no effective treatment for malignancy exists (Fig. 63.1).

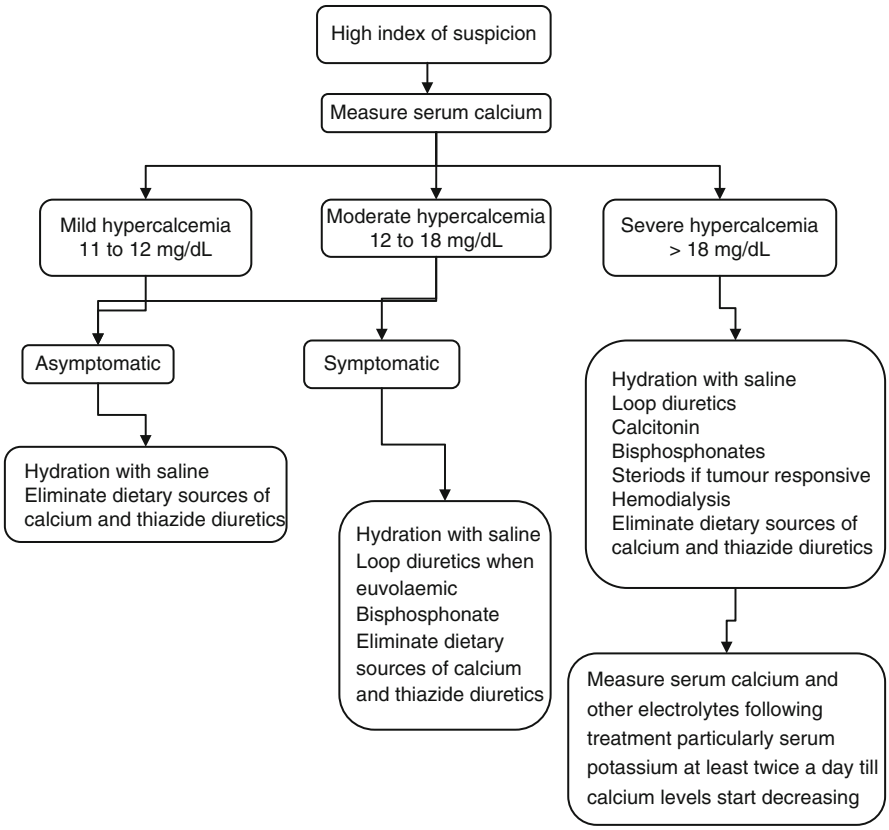


Fig. 63.1 Management of hypercalcemia

Tumor Lysis Syndrome

A 26-year-old patient with Burkitt's lymphoma recently started on chemotherapy presented with anorexia, lethargy, disorientation, vomiting, muscle cramps, tachypnea, and decreased urine output.

Step 1: Resuscitate

- These patients are usually dehydrated and will benefit with intravenous fluids (refer to Chap. 78).

Step 2: Make a diagnosis

- Investigations may show hyperuricemia, hyperkalemia, hyperphosphatemia, hypocalcemia, uremia, and raised lactate dehydrogenase levels.

- Obtain electrocardiogram to rule out serious arrhythmias and conduction abnormalities.
- Tumor lysis is associated with malignancies like acute lymphoblastic leukemia or Burkitt's lymphoma with high tumor burden and responds rapidly to chemotherapy.
- It usually follows chemotherapy, but may occur after radiation, corticosteroid therapy, or chemoembolization and rarely spontaneously.
- Check urine output and renal function.

Step 3: Start hydration
- A high infusion rate of fluids is appropriate.
- Patients with high risk of tumor lysis syndrome should have aggressive volume replacement as a preventive measure prior to chemotherapy.
- Infuse isotonic fluid at a rate of 200–300 mL/h.
- Volume should be adapted for the patient's age, cardiac function, and urine output.
- Increasing the urinary flow rate is the most effective strategy for preventing urate-induced obstructive uropathy.
- Urine output should be maintained within a range of 80–100 mL/m^2/h (4–6 mL/kg/h if <10 kg).
- Urine-specific gravity should be maintained at ≤1.010.

Step 4: Use diuretics cautiously
- Maintain adequate urine output.
- It is contraindicated if hypovolemia or obstructive uropathy exists.

Step 5: Alkalinization of the urine
- This was recommended earlier but is controversial as it can lead to the formation of urinary xanthine crystals.
- This may cause obstruction of renal tubules if allopurinol is used concurrently.
- It is not recommended with recombinant urate oxidase (rasburicase).

Step 6: Start allopurinol
- Purine catabolism results in the production of hypoxanthine and xanthine, which are metabolized to uric acid via the enzymatic action of xanthine oxidase.
- This pathway can be blocked by the use of allopurinol, a hypoxanthine analog that competitively inhibits xanthine oxidase.
- Start allopurinol PO at 600 mg/day if uric acid is less than 8 mg/dL.
- Allopurinol should be started prior to chemotherapy.
- After about 2–3 days, allopurinol therapy results in increased excretion of both hypoxanthine, which is more soluble than uric acid, and xanthine, which is less soluble than uric acid.
- A marked increase in xanthine excretion can occur when allopurinol is given for prevention of tumor lysis syndrome and may lead to acute renal failure or xanthine stones.

- It should be used cautiously in patients with renal impairment. It has many drug interactions and may cause skin hypersensitivity reactions.
- Febuxostat may be used if the patient is hypersensitive to allopurinol.

Step 7: Consider rasburicase (recombinant urate oxidase)
- Urate oxidase—present in most mammals, but not in humans—oxidizes preformed uric acid to allantoin, which is 5 to 10 times more soluble than uric acid in acid urine.
- When exogenous urate oxidase (uricase, rasburicase) is administered, serum and urinary uric acid levels decrease markedly within approximately 4 h.
- This should be used especially if the uric acid level is above 8 mg/dL.
- Uric acid levels should be monitored regularly to adjust dosing.
- Rasburicase degrades uric acid within the blood samples at room temperature, thus interfering with accurate measurement.
- Therefore, samples should immediately be placed on ice until the completion of assay.

Step 8: Treat associated electrolyte disorders
- Hyperkalemia—hemodialysis may be needed if renal insufficiency or volume overload is present.
- Hypocalcemia—if asymptomatic, no therapy is required.
- Hyperphosphatemia—restrict phosphate intake and increase loss with phosphate binders such as aluminum hydroxide or calcium carbonate, sevelamer hydroxide, and lanthanum carbonate.

Step 9: Consider hemodialysis
- This modality should be considered in specific situation such as:
  - Volume overload
  - Uric acid of more than 10 mg/dL despite rasburicase
  - Uncontrolled hyperkalemia and hyperphosphatemia
  - Renal failure (Table 63.2)

63.3 Superior Vena Cava Syndrome

A 19-year-old patient with lymphoma presented with dyspnea, swelling of the head and the neck, and upper limbs, and distended veins on the neck and the upper chest.

Step 1: Resuscitate
- Compression of the tracheobronchial tree causing airway compromise is an airway emergency, needing intubation (with a small endotracheal tube) and ventilation till definitive treatment (refer to Chap. 78)

Table 63.2 Treatment for tumor lysis syndrome

Intervention	Dosage	Comment
Fluids	3 L/m²/day (200 mL/kg/day if ≤10 kg)	Exercise caution if congestive heart failure
Allopurinol	Oral dose: 50–100 mg/m² every 8 h orally (maximum 300 mg/m²/day) or 10 mg/kg/day divided every 8 h (maximum 800 mg/day)	6-Mercaptopurine, azathioprine, cyclophosphamide, and methotrexate require dose reduction
	IV: 200–400 mg/m²/day in 1–3 divided doses (maximum 600 mg/day)	Renal impairment—50% dose reduction
		Drug interaction with thiazide diuretics, ampicillin/amoxicillin
Rasburicase	IV infusion 0.1–0.2 mg/kg/day in 50 mL normal saline over 30 min, for 5 days	Contraindicated in glucose-6-phosphate dehydrogenase deficiency
		Adverse reactions—anaphylaxis, rash, hemolysis, and methemoglobinemia
Hyperkalemia	Calcium gluconate: 10 ml of 10% solution or calcium chloride (5–10 ml of 10% solution) by slow IV infusion for life-threatening arrhythmias	ECG monitoring
	Albuterol nebulizer	Avoid PR route in neutropenics
	Regular insulin: 0.1 U/kg IV + 25% D (2 mL/kg) IV	Sodium bicarbonate and calcium not to be administered through the same line
	Sodium bicarbonate: 1–2 mEq/kg IV, push only if pH <7.2	
	Sodium polystyrene sulfonate: 1 gm/kg/day in 1–4 doses with 50% sorbitol PO/PR	
	Dialysis: if severe	
Hypocalcemia	Calcium gluconate: 10 ml of 10% solution IV administered slowly or calcium chloride	ECG monitoring
Hyperphosphatemia	Hydration	Limit aluminum hydroxide use to 1–2 days to avoid cumulative aluminum toxicity
	Aluminum hydroxide: 50–150 mg/kg/day in divided doses PO or nasogastrically every 6 h	
	Dialysis: if severe	

Step 2: Do imaging
- Computed tomography (CT) scan of chest with or without venography is diagnostic
- These patients may not be able to lie supine for CT chest
- They have to be intubated prior to CT or empirical therapy needs to be started
- Upper extremity venogram or duplex ultrasound for patients with a central venous catheter in upper extremity to exclude venous thrombus.

Step 3: Confirm diagnosis
- Obtain biopsies before instituting therapy if diagnosis is uncertain

Proper hemostatic measures should be taken while performing invasive procedures

Step 4: Chemotherapy and corticosteroids
- These can be used, especially in tumors that are chemosensitive

Step 5: Radiotherapy
- This is a standard treatment modality for sensitive tumors but may take a few weeks to show effect

Step 6: Stenting of the superior vena cava
- It has been shown to be effective and feasible in relieving the symptoms of superior vena cava syndrome

63.4 Malignant Spinal Cord Compression

A 68-year-old patient with carcinoma of prostrate developed worsening back pain progressively with radiating pain down the right leg associated with weakness and difficulty in walking and loss of bladder and bowel function.

Step 1: Resuscitate (see Chap. 78)
(a) Pain relief with adequate analgesics is a priority in these patients.
(b) Urgent neurosurgical, radiotherapy, oncology consultation for limb salvage is necessary.
(c) Special precaution needs to be taken while transporting these patients.

Step 2: Do imaging
- In patient with high index of suspicion and symptoms suggestive of metastatic bone disease, magnetic resonance imaging is gold standard for diagnosis.
- Alternative is CT scan of spine.
- It is important to image the entire spine as more than one area of compression may be present.

Step 3: Start glucocorticoids

(a) Dexamethasone is indicated in patients with motor deficits or radiologic evidence of neural compression.
(b) It is given as an initial intravenous dose of 10–16 mg followed by 4 mg every 4 h.
(c) This is later administered orally and tapered over 10–12 days.
(d) Use proton pump inhibitors or H_2 blockers along with high dose of corticosteroids.

Step 4: Consider radiation therapy

- This has been the mainstay of the treatment in patients with and without motor deficit.
- This is usually combined with surgery for spine stabilization.

Step 5: Consider surgery

- It is indicated in most cases, especially in patients with a good performance status. Indications are the following:
  - Gross instability of the spine
  - Rapidly progressive symptoms
  - Progressive symptoms during radiation therapy
  - When tissue for diagnosis is needed
  - Radioresistant tumors

Step 6: Consider chemohormonal therapy

- Hormonal chemotherapy and zoledronic acid should be considered in sensitive tumors such as prostate cancer, testicular tumor, or lymphoma.

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Part IX

Trauma and Burn

M.C. Mishra and Prasad Rajhans

General Management of Trauma

64

Vinay Gulati, Sanjeev Bhoi, and Rajesh Chawla

A 50-year-old male patient hit by a bus about 6 h ago presented to the emergency department. He had a labored breathing; his respiratory rate was 35/min with O_2 saturation of 94%. His heart rate was 130/min, blood pressure was 100/80 mmHg, and Glasgow coma score (GCS) was 9/15. After initial stabilization, the secondary survey revealed multiple rib fractures on the right side of the chest and fracture of the right femur.

Trauma is a major cause of death and disability in the first four decades of life. Improvement and organization of trauma care services are a cost-effective way of improving patient outcome. Proper organization of these systems reduces the time between injury and the definitive care, thereby reducing the morbidity and mortality.

Step 1: Preparation

- Alert the trauma team about the arrival of the injured patient.
- Trauma team includes the general/trauma surgeon, the emergency physician, the orthopedic surgeon and/or the ICU/anesthesia specialist on call, and at least two trained nurses and two paramedics.
- Besides the general surgeon, the team leader of the trauma team can be an emergency medicine or ICU/anesthesia specialist who is skilled in airway management.

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- Airway cart, crash cart, suction, monitors and IV cannula, warm IV fluids, and other equipment should be rechecked.
- The trauma team members should be ready with universal precautions by putting on mask, splash-resistant and lead gowns, eye protection, and gloves.
- The operating theater personnel should be informed.

Step 2: Triage

- Triage is a process of determining the priority of treatment based on the patient's airway (A), breathing (B), and circulation (C) as well as availability of resources.
- Triage separates the injured patients into five categories:
  1. The injured patient with compromised ABC who needs immediate treatment (red)
  2. The injured patient with stable ABC whose treatment can wait (yellow)
  3. Those with minor injuries (walking wounded), who need help less urgently (green)
  4. The unsalvageable patients who are beyond help (blue or gray)
  5. The injured patients who are already dead (black)
- A simple tool, which can be used for triage, is START (simple triage and rapid treatment) (Figure 1).

Emergency Department Management Protocol

Triage Protocol

Step 3: Primary survey and resuscitation

- The "ABCDE" of primary survey is, in essence, to identify the life-threatening conditions and institution of life-preserving therapies by priority based on their injuries, vital signs, and injury mechanisms.
- Take history from the accompanying person about the following:
  - Mechanism of injury
  - Injuries suspected
  - Vital signs
  - Treatment en route to hospital
- The management is concurrent with the assessment, resuscitation, and stabilization.

ABCDE
Airway maintenance with cervical spine control
Breathing and ventilation
Circulation/hemorrhage control
Disability/neurological status
Exposure/environmental control

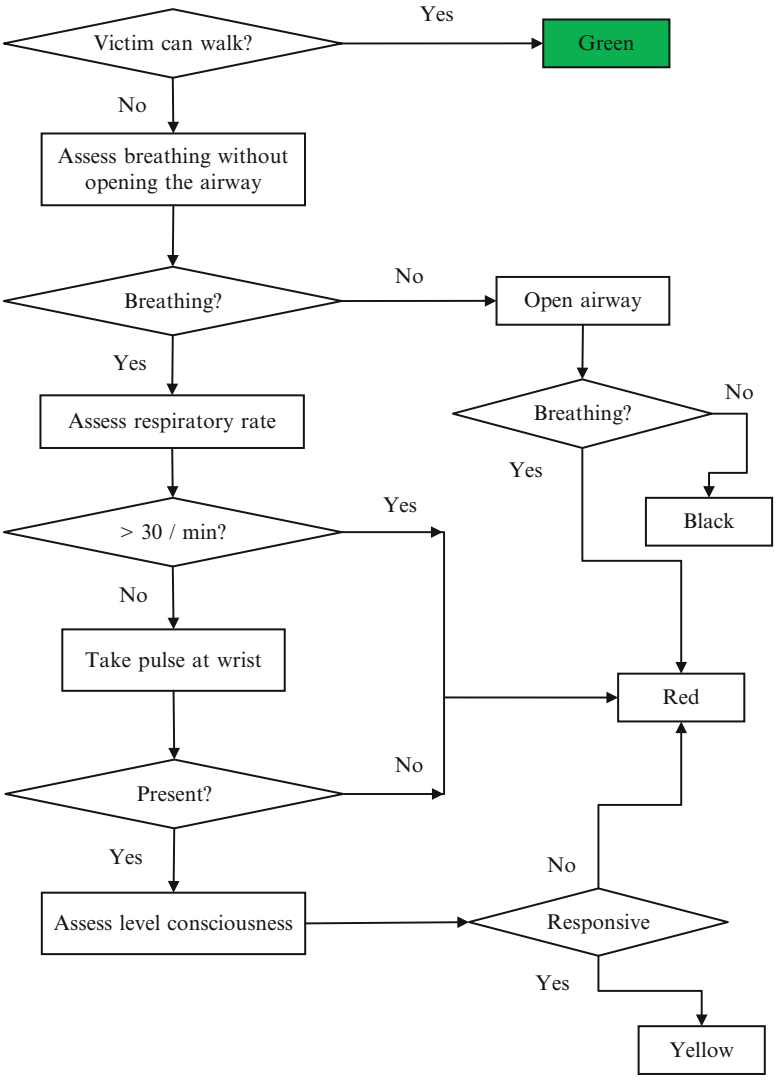

Fig. 64.1 START (simple triage and rapid treatment) algorithm

A-Airway with cervical spine control

- Airway is assessed immediately for patency, protective reflexes, foreign body, secretions, and injury.
- The patency of the airway should be assessed with special attention to foreign body or maxillofacial fractures that may result in airway obstruction.
- Absence of response, stridor, confusion, or a hoarse reply may indicate airway compromise.

- Chin-lift or jaw-thrust maneuver may be used to achieve airway patency, simultaneously protecting the cervical spine by inline cervical stabilization.
- Head tilt maneuver is avoided in an injured patient while managing airway.
- A definitive airway is required in the following conditions:
  - Inadequate ventilation and oxygenation
  - Impending or actual airway obstruction secondary to injury
  - Brain injury with a GCS of less than 8
  - Inability to adequately protect the airway from aspiration
  - Severe multisystem injury or hemodynamic instability
  - Facial burns or inhalation injury
  - Inability to closely monitor during ongoing resuscitation and investigation (e.g., angiography and CT scanning)
  - Uncooperative or combative behavior
  - An infant or a child unable to cooperate with investigations
- Cervical spine protection (by application of cervical collar) during airway maneuvers should be done in all trauma patients unless specifically cleared.
- Rapid-sequence intubation protocol should be followed for securing airway.

Unstable adult patient
1–2 mg/kg ketamine with 1–2 mg/kg IV succinylcholine
Adult head injury with normal pulse/BP
GCS of 3—intubate without drugs
GCS more than 4—0.3 mg/kg—etomidate with 1–2 mg/kg IV succinylcholine
Pediatric rapid-sequence intubation
With hypovolemia—0.1 mg/kg IV midazolam
With normovolemia—0.3 mg/kg IV midazolam

- Difficult or failed intubations
  - Call anesthesiologist or a more experienced person.
  - Anticipate airway problems with the following:
  - The decreased level of consciousness
  - Head trauma
  - Facial trauma
  - Neck trauma
  - Upper thorax trauma
  - Severe burns to any of these areas

Airway – management options with cervical spine control treatment include:
O_2 administration
Basic airway maneuvers: chin lift and jaw thrust
Oropharyngeal or nasopharyngeal airway, but caution in bleeding patient
Endotracheal intubation
Surgical airway, that is, cricothyroidotomy/tracheostomy

B-Breathing and ventilation

- Chest wall mechanics are altered due to rib fracture and pulmonary contusions.
- Breathing is assessed by determining the patient's respiratory rate and by subjectively quantifying the depth and effort of inspiration.
- The patient's chest should be exposed to adequately assess chest wall excursion.
- Visual inspection and palpation to detect chest wall injuries, percussion for hyperresonance or dullness to exclude air or blood respectively in the chest, and auscultation to detect adequate air entry in lungs should be carried out.
- Rapid respiratory effort, use of accessory muscles of respiration, hypoxia, hypercapnia, asymmetric chest wall excursions, and diminished or absent breath sounds will require treatment before proceeding further.
- Specific life-threatening problems that should be identified immediately and addressed during the primary survey are the following:
  - Tension pneumothorax
  - Open pneumothorax
  - Massive hemothorax
  - Flail chest
  - Cardiac tamponade

Breathing – treatment options include:
Endotracheal intubation and ventilation
Needle decompression
Intercostal tube drain
Pericardial drainage
Thoracotomy
Adequate analgesia

C-Circulation with hemorrhage control

- Hypotension in a trauma patient is always assumed to result from significant hemorrhage (>30% blood loss) unless proved otherwise.
- Hemorrhage is the primary cause of shock in trauma patients.
- Rapid and accurate assessment of the patient's hemodynamic status and identification of the site of hemorrhage is therefore essential.
- It is critical to establish two large-bore short-length intravenous cannulas (16G or bigger) in a trauma patient, preferably in the upper extremities, and resuscitation should be started with warm crystalloids (Ringer's lactate). The blood transfusion should be done in patients with ongoing hemodynamic instability after initial fluid boluses. The three body regions, which hide significant amounts of blood in cases of blunt injury, include the chest, abdomen, and pelvis.
- Chest and pelvic radiographs and a focused assessment by sonography in trauma (FAST) or a diagnostic peritoneal lavage (DPL) are mandatory screening studies for patients in shock.

- Hemorrhage control by direct application of external pressure and/or careful application of tourniquet may be done in all patients.
- Pelvic ring should be closed using pelvic binders if the bleeding is suspected from an unstable pelvis.
- Fractured long bones are reduced, and traction splint is applied if they are possible source of bleeding to decrease ongoing blood loss and pain as well as to prevent further local injury.

Circulation and hemorrhage control – treatment options include:
Warm fluids (crystalloid—Ringer's lactate)
Warm blood and blood products (e.g., fresh frozen plasma)
Arrest bleeding by direct local pressure
Arrest bleeding by splinting pelvis
Central line if inotropes/vasopressors are needed
Urinary catheter
Surgery—laparotomy, thoracotomy, and/or pelvic fracture fixation (damage control or definitive) may be undertaken to control bleeding

D-Disability/neurological status

- A rapid neurological evaluation is carried out at the end of primary survey only after the resuscitation and stabilization have been achieved as mentioned above.
- This assesses the patient's level of consciousness, pupillary size and reaction, and focal neurological deficit.
- The level of consciousness may be described in terms of the GCS.
- The GCS is used as a baseline determination of neurological function, and frequent reassessment is required to detect an early or previously missed injury.
- A complete neurological examination is not appropriate at this time and should be performed during secondary survey.

Disability – treatment options include:
O_2 administration
Intubation (to ensure normal PO_2 and PCO_2)
Avoid hypotension and hypoxia to prevent secondary brain damage
Inotropes/vasopressors (to ensure adequate cerebral perfusion)
Head up, ensure venous drainage
Emergency imaging of the brain or spine
Early neurosurgical consultation

E-Exposure/environmental control

- The patient should be completely undressed to facilitate thorough examination and assessment in front and back.
- At the same time, care should be taken to prevent hypothermia.
  - Remove wet or blood-soaked clothes, and warm IV fluids (39°C).

– Use blood warmers for transfusing and external warming (warmed blankets to all patients and forced, heated air, or radiant warmers as needed) to prevent hypothermia.

Step 4: Adjuncts to primary survey and resuscitation

(a) *ECG monitoring*
- The appearance of dysrhythmias may indicate blunt cardiac injury.
- Pulseless electrical activity, the presence of cardiac rhythm without peripheral pulse, may indicate cardiac tamponade, tension pneumothorax, or profound hypovolemia.

(b) *Urinary catheter*
- Urine output is a sensitive indicator of the volume status of the patient and reflects renal perfusion.
- All trauma victims should be catheterized to enable monitoring of the urine output and to plan intravenous fluid therapy.
- Transurethral catheterization is contraindicated in patients whom urethral transaction is suspected.

(c) *Gastric catheter*
- A naso/orogastric (in skull base fracture) tube is indicated to reduce stomach distension and decrease the risk of aspiration.

(d) *X-rays and diagnostic studies*
- The chest and pelvis X-rays help in the assessment of a trauma patient.
- The blood should be sent for crossmatching and arranging for packed cells, and important diagnostic parameters such as hemoglobin, coagulation profile, renal parameters, electrolytes, random blood sugar, and arterial blood gas (ABG) should be checked.
- Pulse oximetry is a valuable adjunct for monitoring oxygenation and adequacy of peripheral circulation in injured patients.

(e) *FAST(focused assessment with sonography for trauma)*

The FAST is a rapid, bedside, ultrasound examination performed to identify intraperitoneal hemorrhage or pericardial tamponade. FAST examines four areas for free fluid: perihepatic and hepatorenal space, perisplenic, pelvis, and pericardium

Step 5: Consideration for interhospital transfer
- Identify the early, potential need for transfer of the polytrauma patient to an institution where definitive care can be undertaken.
- Transfer decision should be on the basis of known injuries and patterns of injury.
- An effective communication including the condition of the patient, treatment given, and anticipated requirements during transfer should be made to the receiving hospital.
- The transfer to another center should not be delayed for the want of investigations.

Step 6: Admit in ICU

- Airway protection and mechanical ventilation
- Cardiovascular resuscitation
- Severe head injury
- Organ support
- Correct coagulopathy
- Invasive monitoring
- Active rewarming of hypothermic patients

Step 7: Secondary survey

- Once the primary survey is accomplished—life-threatening conditions are managed and resuscitative efforts are underway—secondary survey is carried out.
- This is a head-to-toe evaluation of the trauma patient, which includes a complete history and physical examination and reassessment of all the vital signs.
- History includes the following:
  - A—Allergies
  - M—Medications currently taken
  - P—Past illness/pregnancy
  - L—Last meal
  - E—Events/environment related to the injury
- Each region of the body is completely examined.
- The care should be continued with regular reevaluation of the patient for any deterioration and new findings so that appropriate measures can be taken.

Reevaluation

- After the completion of the secondary survey, the patient should be reevaluated beginning with the ABCs and thorough physical examination and examined for any missed injury (tertiary survey) such as fractures.
- Constant monitoring of the severely injured patient is required and may necessitate rapid transfer to the surgical intensive care unit, operating room, or to another center having better specialized facilities.
- Appropriate referral for specialists should be sent.
- Adequate pain relief, tetanus prophylaxis, and antibiotic should be given.
- Specific care should be taken to examine the possible missed injuries on the following:

Back of the head and the scalp
The neck, beneath semirigid collar
Back, buttocks, and flanks
Groin creases, perineum, and genitalia

Step 8: Sending investigations

Hemoglobin	ABG
Hematocrit	Renal function tests
Total leukocyte count	Electrolytes
Platelet count	Liver function tests
Prothrombin time	Blood grouping and crossmatching
Urine pregnancy test (14–45 years)	ECG (>40 years)
Breath/blood alcohol	
Radiological	
Plain radiographs	
CT scanning	
Contrast studies	
Angiography	
Ultrasound (including plain sonography echocardiography and color-flow Doppler)	
Endoscopy	

Step 9: Tertiary survey

- Tertiary survey consists of a repeat of the primary and secondary survey examinations, reassessment of the functions of all tubes and catheters, and review of all X-rays.
- It is routinely performed in the morning after the patient's admission to detect any injuries not picked up earlier to minimize the missed injuries.

Suggested Reading

1. American College of Surgeons Committee on Trauma. Initial assessment and management. Advanced trauma life support program for doctors. 8th ed. Chicago: American College of Surgeons Committee on Trauma; 2008. pp. 1–18.
   Comprehensive text in context with advanced trauma life support (ATLS) program.
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   This article explains the basis of triage of trauma victims.

Severe Head and Spinal Cord Injury

65

Deepak Agrawal

A 25-year-old adult traveling by a car suffered multiple injuries in a high-speed collision. On arrival to the emergency department, he was found unconscious, with bleeding from the right ear and obvious bleeding from the scalp. His pulse was 56/min and blood pressure (BP) was 180/96 mmHg. The right pupil was dilated and not reacting, and his breathing was labored. Smell of alcohol was also observed.

Head and spinal cord injuries are typically associated with major trauma from motor vehicle accidents, falls, sports injuries, and violence. These injuries are associated with high morbidity and mortality. Prompt and appropriate treatment can change the outcome of these patients.

Step 1: Initialasses sment

Airway, breathing, and circulation (ABC) approach takes precedence in spite of obvious head injury.

Airway and breathing

- Apply the cervical collar and check airway.
- Hypoxia (PaO_2 <60 mmHg or O_2 saturation <90%) should be avoided. Intubate and ventilate with 100% oxygen in case of threatened airway with manual in-line cervical immobilization.
- Mild hyperventilation ($PaCO_2$ ≥32 mmHg and ≤36 mmHg) is recommended as a temporizing measure for the reduction of raised intracranial pressure (ICP).
- Prophylactic hyperventilation ($PaCO_2$ ≤25 mmHg) is not recommended.

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Circulation

- Maintain systolic BP >100 mmHg.
- Avoid antihypertensives in suspected head injuries as arterial hypertension is a part of protective Cushing's reflex to maintain cerebral perfusion.
- Labetalol is the drug of choice for control of hypertensive emergency in the head injury patient (refer to Chap. 24 on hypertension).

Step 2: Secondary assessment

- Assess Glasgow coma score (GCS) and pupillary reaction, and check localizing signs (weakness in limbs).
- All patients with GCS of 8 or less should be intubated and electively ventilated (if not done at Step 1).

Step 3: Assess severity of head injury

On GCS grading	
	GCS of 14 or 15: mild head injury
	GCS of 9–13: moderate head injury
	GCS of 8 or less: severe head injury
Mild head injury	
Step A	Shift to observational area.
Step B	Maintain ABC.
Step C	Send for a noncontrast CT (NCCT) of the head and cervical spine (if any neck pain/tenderness) in the following conditions: Loss of consciousness for more than 5 min Amnesia Severe headache GCS of less than 15 Focal neurological deficit attributable to the brain
Step D	Inform the neurosurgeon.
Moderate head injury	
Step A	Shift to observational area.
Step B	Maintain ABC.
Step C	Inform the neurosurgeon.
Step D	Send for the plain CT scan of the head cervical spine. (All patients to have the CT scan of cervical spine including C7 vertebrae.)
Severe head injury	
Step A	Shift to the resuscitation room.
	Simultaneously inform the neurosurgeon.
Step B	Repeat ABC.
	Maintain temperature.
Step C	Send for baseline blood investigation (hemoglobin, hematocrit, platelets, coagulation profile, random blood sugar, serum sodium and potassium, urea, creatinine).
	Coagulation profile including prothrombin time, APTT, and platelet count should be done in all patients. Special tests like thromboelastography may be done, if available, to assess platelet function.

	Arrange packed RBC or fresh frozen plasma.
	Arterial blood gas (to be repeated after 1 h).
	Foley's catheterization.
	IV fluid maintenance—avoid dextrose-containing fluids as they may increase cerebral edema.
	Proton pump inhibitor.
	Phenytoin sodium IV loading dose of 20 mg/kg can be dissolved in normal saline and infused at a rate no faster than 50 mg/min. Fosphenytoin can also be used at a dose of 25 mg/kg and can be infused at a rate of up to 150 mg/min.
	Infuse 20% mannitol (1 g/kg IV stat) in 5 min (after BP correction).
	Give furosemide (0.3–0.5 mg/kg IV stat) (after BP correction).
Step D	A focused assessment by sonography in trauma (FAST) is required to assess any other site of free blood in case of persistent/recurrent hypotension.
Step E	Send for the non contrast CT scan of the head cervical spine on portable ventilator with the resident and the nurse, with prior information to the radiographer and radiology resident. All patients to have the CT scan of cervical spine up to C7.

The head injury patient should be monitored closely when he/she is kept for observation or waiting for admission.

In case neurosurgical facilities are not available in the hospital, the patient should not be denied initial assessment and management (Step 1) as these are critical to final outcome. The patient can be transferred to the nearest neurosurgical facility after initial management.

Step 4: Shift to the intensive care unit (ICU)

All patients with nonoperable lesions and requiring intubation should be shifted to the ICU for further management.

Step 5: Start analgesia and sedation

- Sedatives and analgesics can affect outcomes in head-injured patients.
- Adequate pain control and sedation can be used as initial measures to control raised ICP. Short-acting agents such as fentanyl, midazolam, or propofol are preferred for frequent neurological assessments.
- Propofol infusion and high-dose barbiturate administration are recommended to control elevated ICP refractory to maximum standard medical and/or surgical treatment.
- Hemodynamic stability is essential before and during barbiturate therapy.

Commonly used sedatives	
Fentanyl	2 mcg/kg test dose, 2–5 mcg/kg/h continuous infusion
Midazolam	2 mg test dose, 2–4 mg/h continuous infusion
Sufentanil	10–30 mcg test bolus, 0.05–2 mcg/kg continuous infusion
Propofol	0.5 mg/kg test bolus, 20–75 mcg/kg/min continuous infusion (not to exceed 5 mg/kg/h)

- Continuous use may increase the risk of ventilator-associated pneumonia; hence, daily interruption of sedation along with other VAP prevention measures should be used.

Step 6: ICP monitoring

Indications of ICP monitoring
ICP should be monitored in patients with GCS of 8 or less and an abnormal computed tomography (CT) scan.
An abnormal CT scan of the head is one that reveals hematomas, contusions, swelling, herniation, or compressed basal cisterns.
ICP should be monitored in patients with severe traumatic brain injury (TBI) with a normal CT scan if two or more of the following features are noted at admission: age over 40 years, unilateral or bilateral motor posturing, or systolic BP less than 90 mmHg.
All children (<12 years) should have ICP monitoring irrespective of CT findings if GCS is 8 or less.
Monitoring method
The ventricular catheter connected to an external strain gauge is the most accurate, low-cost, and reliable method of monitoring ICP with the additional benefit of having a therapeutic role by cerebrospinal fluid drainage. However, they carry a higher risk of infection and may be difficult to insert in brain swelling with effaced ventricles.
ICP transduction via fiber-optic or microstrain gauge devices placed in parenchyma is easy to insert, equally accurate, but much more expensive.
Treatment target
Treatment should be initiated with ICP thresholds above 20 mmHg.
A combination of ICP values, and clinical and brain CT findings, should be used to determine the need for treatment. Decompressive craniectomy may be considered for persistently high ICP (>20 mmHg) despite maximal medical therapy but its role is debatable.

Step 7: Start mannitol (refer to Chap. 31)

- In absence of hypotension, mannitol is effective for the control of raised ICP at doses of 0.25–1 g/kg body weight.
- Mannitol is contraindicated in extradural hematoma and should be given only after reviewing the CT scan of the head and under neurosurgical supervision.

Step 8: Tracheostomy

- Plan an early tracheostomy (within 72 h) for all patients whose motor response is 4 or less.

Step 9: Deep venous thrombosis (DVT) prophylaxis

- Intermittent pneumatic compression stockings or graduated compression stockings should be used (except in lower limb injuries) and continued till the patient is ambulatory.
- Low-molecular-weight heparin or low-dose unfractionated heparin should be used in combination with mechanical prophylaxis when it is safe, preferably after 72 h of intracranial hemorrhage/craniotomy with close monitoring and repeat NCCT head to detect expansion of hematoma.

Step 10: Seizure prophylaxis

- Phenytoin (5 mg/kg/day) or valproate (15 mg/kg/day) should be given for at least a week in all patients.
- Prophylactic use of phenytoin or valproate is not recommended for preventing late posttraumatic seizures. However, their use in the first week following injury decreases the incidence of early posttraumatic seizures.

Step 11: Maintain nutrition

- Good caloric intake (30–50 kcal/kg/day) and protein intake of 2 g/kg/day should be maintained. To achieve full caloric replacement in 7 days, nutritional replacement should begin no later than 72 h after injury.

Step 12: Other drugs/interventions

- Avoid steroids. Use of steroids is not recommended for improving outcome or reducing ICP.
- Use of high-dose methylprednisolone increases mortality, and therefore, it is contraindicated.
- Prophylactic mild hypothermia (33–35°C) remains experimental and is not recommended for routine clinical use presently.

Step 13: Surgical intervention

- *Head injuries: Decompressive craniectomy*
- If the patient continues to have persistently raised ICP (>20 mmHg) in spite of maximal medical management, decompressive craniectomy is the only available option to decrease ICP.
- Recent evidence has shown poor neurological outcome in patient undergoing decompressive craniectomy.

Management of High Cervical Spinal Cord Injuries

A 50-year-old male fell from a 20-ft height. On arrival to the emergency department, he was found to be conscious, with labored breathing and no limb movement. His pulse was 52/min and his BP was 70/40 mmHg.

Steps 1 and 2	*Remain the same as for severe head injuries*
Step 3	*ICU care*
	Management of patients with acute spinal cord injury (SCI), particularly patients with severe cervical level injuries, is recommended in an ICU or similar monitored setting.
Step 4	*BP management*
	Maintain mean arterial BP at 85–90 mmHg for the first 7 days following acute SCI as it improves spinal cord perfusion.
	If central venous pressure exceeds 10 cm of water, dopamine and/or noradrenaline infusion may be given to maintain BP at this level.

Step 5	*Avoid steroids*
	Routine use of steroids is not recommended in SCI.
Step 6	*DVT prophylaxis*
	Low-dose heparin in combination with pneumatic compression stockings for a minimum period of 3 months is recommended.
	Vena cava filters are recommended for patients who fail anticoagulation or who are not candidates for anticoagulation and/or mechanical devices.
Step 7	*Closed reduction/traction*
	Early closed reduction of cervical spinal fracture-dislocation injuries with craniocervical traction is recommended for the restoration of anatomic alignment of the cervical spine in awake patients.
Step 8	*Maintain nutrition*
	Nitrogen requirements are the same as in severe head-injured patients.
	Caloric requirements may be lower due to muscle paralysis and flaccidity.
	Indirect calorimetry may be more accurate in assessing the caloric requirements in these patients.
Step 9	*Operative intervention—decompression and fusion*
	All cervical SCIs with radiological evidence of cord compression should undergo spinal cord decompression and fusion as early as possible.

Suggested Reading

1. Brain Trauma Foundation, American Association of Neurological Surgeons. Guidelines for management of severe traumatic brain injury. J Neurotrauma. 2007;24(Suppl 1):S24–30.
This gives an excellent overview of evidence-based head injury management as well as gaps in our knowledge on this subject. A "must" reading for all those who manage severe head-injured patients.

Websites

1. www.aans.org
The American Association of Neurological Surgeons website has guidelines for both head and spinal injured patients which is freely downloadable.
2. https://www.braintrauma.org/coma-guidelines/
This website has useful information on the latest research in head injuries and the outcome of various trials.

Torso Trauma

66

Subodh Kumar, Amit Gupta, and Umashankkar Kannan

A 30-year-old male was hit by a motor vehicle about 3 h ago. At presentation, he had a threatened airway with labored breathing; his respiratory rate was 32/min with O_2 saturation of 85%. He had paradoxical chest movements and decreased air entry on the left side. His heart rate was 120/min, blood pressure was 100/80 mmHg, and Glasgow coma scale (GCS) score was 15/15. After initial stabilization and left-sided intercostal drainage (ICD), secondary survey revealed abdominal distention with tenderness over the left upper quadrant of the abdomen. A computed tomography (CT) scan of the chest and abdomen showed multiple rib fractures on the left side of the chest with underlying lung contusion and ICD in situ. It also revealed a shattered spleen and 3-cm laceration in segment 6 of the liver along with 1-cm laceration in the upper pole of the left-sided kidney. Exploratory laparotomy was performed. The liver and kidney were preserved, while the spleen was removed. The patient gradually recovered in intensive care unit (ICU).

Multiple life-threatening conditions can result from thoracic and abdominal trauma. Multiple factors including mechanism of injury, injured body region, hemodynamic status, and associated injuries determine the diagnostic approaches.

Step 1: Perform primary and secondary survey

Primary survey (A–E)

A. *Airway with cervical spine protection*: Evaluation of airways is the first priority during primary survey. All patients presenting with threatened airways and respiratory distress should have the airway secured.

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- Cervical immobilization is maintained till the injury is excluded by radiological and/or clinical means.

B. *Breathing and ventilation*: Expose the chest to observe chest wall movement, breathing pattern, and neck veins; to auscultate breath sounds; and to monitor SpO_2.
   - Injuries that should be identified and treated during the primary survey are the following:
     - Tension pneumothorax—with immediate needle thoracostomy and then with an intercostal tube
     - Massive hemothorax—with insertion of a large-bore (36F) chest tube and volume replacement
     - Open pneumothorax—with flutter valve dressing, taped on three sides, till ICD is placed; thereafter, closed dressing
     - Cardiac tamponade—with pericardiocentesis as a temporary manouever followed by definitive surgery
     - Flail chest with pulmonary contusion—with analgesia and elective intubation and positive pressure ventilation
C. *Circulation with hemorrhage control*: The pulse rate, blood pressure, and level of consciousness determine the grade of shock. Circulation volume has to be maintained with isotonic fluids and blood transfusions. Identify the source of bleeding and control it.
D. *Disability (neurologic evaluation)*: Assess GCS and evaluate the pupillary size and reaction to light. Low GCS score may be due to decreased cerebral oxygenation or perfusion (shock) or direct cerebral injury.
E. *Exposure/environment control*: Completely undress the patient for thorough examination and assessment. Do not forget to examine the back. A warm environment should be maintained to avoid hypothermia.

Secondary survey

This involves detailed pertinent history, complete in-depth physical examination, relevant radiological, and laboratory investigations with reassessment of vital signs to identify all the injuries.

Step 2: Triage for surgery

- Once the primary survey is concluded, the next step is to triage the nonresponders to emergency surgery—exploratory laparotomy or thoracotomy for damage control or definitive surgery as the clinical situation demands.
- The rest of the patients should undergo further necessary radiological investigations to identify and assess the exact anatomical injuries and their severity.

Chest injuries

Majority of the patients (85% of the patients) with thoracic injuries require intervention in the form of tube thoracostomy, observation, and pain control. Only 10–15% patients require a formal thoracotomy.

Abdominal injuries
Indications for urgent laparotomy include the following:
- Penetrating abdominal injury
- Hollow viscus injury
- Blunt trauma with ongoing intraperitoneal bleeding

Step 3: Triage the patients to the ICU
Triaging the patients to the ICU or to the floor (wards) is decided on the basis of the severity of the injury and the extent of surgery, requirement of the mechanical ventilator and inotropic support, age and comorbidities of the patient.

Step 4: Continue to observe and treat
While the need for complete and serial clinical examination in the ICU cannot be overemphasized, the following features will have to be focused during the daily examination of the patients:

A. *Ventilation and circulation assessment*
   - Monitor respiratory rate, oxygen saturation, and arterial blood gas analysis, and adjust ventilatory settings accordingly. In case of prolonged requirement of ventilation (usually more than 7 days), tracheostomy should be considered.
   - Pulse rate, blood pressure, central venous pressure, urine output, hematocrit, and lactate levels indicate the degree of perfusion and the grade of volume deficit. Unstable or critically ill patients might warrant other invasive monitoring techniques such as intra-arterial pressure and $ScVO_2$ measurements. Circulation is maintained with fluid and blood transfusion with or without inotropic support.

B. *Management of the ICD tube*
   Monitor volume and nature of the output daily, column movement, presence of air leak, and lung expansion clinically and radiologically.
   1. Volume
      - Common causes for persistent high output:
        – Hemorrhage
        – Thoracic duct injury
        – Hypoproteinemia
      - Sudden decrease in the volume of the output: Check for tube blockage or malpositioning. The tube should then be declotted or repositioned or changed to maintain the patency of the tube.
   2. Nature of the output
      - Sanguineous output—ongoing hemorrhage: Output of more than 200 mL/h of sanguineous fluid continuously for 2–4 h is an indication for thoracotomy.
      - Turbid output with pyrexia indicates an infective focus. Fluid should be sent for further microbiological analysis, and treatment should be started accordingly.

- Milky white, high-volume output points to thoracic duct injury (chylothorax). Presence of chyle may be confirmed at the bedside by dissolving the drained fluid in equal amount of ether. If it gets dissolved, then it is chyle; otherwise, it is pus. Check the triglyceride level. Low output (<1,000 mL/24 h) can be managed conservatively. High output usually requires surgical management.

3. Wide swinging of column movement (>5 cm) is suspicious of poor lung expansion or lung collapse and should be investigated further with the chest X-ray and bronchoscopy if needed.
4. Air leaks indicate the presence of tracheobronchial/parenchymal communication with the pleural cavity.
   - Chest tube insertion sites should be checked for peritubal air entry due to loose sutures.
   - Treatment of air leak: Minor air leaks usually heal with deep breathing exercises. Persistent air leaks, not settling down with chest physiotherapy alone, require application of negative pressure suction (usually 10 cm H_2O) to the underwater seal bottle. Massive air leaks causing oxygen desaturation will require insertion of a second ICD tube and usually thoracotomy.
   - After stoppage of air leak, check the chest X-ray after clamping the tube for 24 h to look for lung collapse, and the ICD tube can be removed if the chest X-ray is normal.
   - In case of subcutaneous emphysema, the extent should be marked and monitored daily for change in extent after insertion of the ICD tube. There is no role for skin incisions.
5. In cases of clotted hemothorax, declotting is done with streptokinase.
   - 1–1.5 million units of streptokinase is diluted in 100 mL and infused through the ICD tube under aseptic precautions. The tube is then clamped for 3–4 h; chest physiotherapy is done and then the tube is opened. This may be repeated once a day for 3–4 days till clots are evacuated. This procedure is not indicated in patients with coagulopathy or patients on systemic anticoagulation therapy like warfarin.
6. Fever, productive cough, and infiltrates in the chest X-ray indicate pulmonary infections. Broad-spectrum antibiotics should be started empirically and changed to specific antibiotics depending on the sensitivity pattern.
7. Radiological investigations
   - Chest X-rays should be done to monitor the lung expansion and after the removal of the ICD tube to look for pneumothorax.
   - Ultrasonogram and CT scans should be done for suspected loculated effusions and pneumothorax and to guide its drainage percutaneously.
   - The following conditions should be fulfilled before the removal of the ICD tube:
     – Less than 50–100 mL output and serous in nature
     – Less than 5 cm swinging of air column with normal breathing

  - Absence of fever and air leak
  - Full lung expansion
- Chest tube insertion sites must be inspected every day for infections and air or fluid leakage with regular care of the wound site.

C. *Tracheostomy site and surgical wound sites*
Inspect for surgical site infection.

D. *Regular active and passive chest physiotherapy*
This is required to prevent atelectasis and pneumonia.

E. *Pain control*
Control pain through nonsteroidal anti-inflammatory drugs, opioids, epidural analgesia, and patient-controlled analgesia devices.

F. *Nutrition*
Nutrition is maintained with enteral nutrition in most of the cases.

Abdominal injuries
Solid organ injuries are managed either nonoperatively or operatively depending on the severity of the injury and the hemodynamic stability of the patient. Hollow viscous injuries are usually managed operatively.

Step 5: Nonoperative management of solid organs (spleen, liver, and kidney)
- Nonoperative management should be practiced only in highly specialized trauma centers that have 24-h availability of trauma surgeons. Initial clinical examination and hemodynamic status dictate the decision rather than the grade of solid organ injury or the degree of hemoperitoneum.
- Daily clinical examination of the abdomen with hemodynamic status assessment is based on pulse rate, blood pressure, urine output, abdominal girth, intra-abdominal pressure, and fall in hemoglobin and hematocrit levels.
- Complete bed rest should be advised for the first 48 h and then gradual mobilization is done.
- No antibiotic coverage is needed in cases of nonoperative management of solid organ injury alone.
- Ultrasound examination of the abdomen is done, if clinical situation demands, to look for significant increase in the intra-abdominal collection.
- Abdominal distention, development of peritoneal signs, and decrease in urine output indicate ongoing hemorrhage and need for operative management. Progressive drop in hematocrit with hemodynamic instability should also indicate the consideration for operative management.
- In case of liver injuries, billary peritonitis may present the clinical picture of intestinal perforations. Clinical and radiological examinations should be performed to rule out missed intestinal injuries, and in their absence, percutaneous drainage of the bile collection can be done, avoiding laparotomy.

Step 6: ICU care after operative management of abdominal injuries
- Repeated complete physical examinations should be performed every day.

- In case the abdominal closure seems to be difficult during the primary surgery (due to bowel edema/retroperitoneal collection, etc.), it is prudent to leave it open as forceful closure would lead to increase in intra-abdominal pressure resulting in the abdominal compartment syndrome.
- Oral diet is started at the earliest and gradually advanced to regular diet as tolerated. Immediate enteral feeding is beneficial (in comparison to parenteral) in a critically ill patient regardless of the patient's premorbid nutritional status.
- Care of the feeding jejunostomy tube should be taken properly. Postoperatively, tube feed at the rate of 30 mL/h for 3–6 h should be given. If the patient tolerates, gradually increase feed as tolerated to meet calories and protein requirement over 24–48 h.
- Conditions suggesting the need for parenteral nutrition are as follows:
  - Oral intake less than 50% of the energy needs
  - Unable to tolerate nasogastric or nasojejunal feed for more than 7 days in previously well-nourished patient.
  - Nonfunctioning gastrointestinal tract
- Inspection of the surgical sites is done for signs of inflammation and infection.
- Monitoring of the drain output and nature of fluid should be done.
- In case the drains show persistent and or purulent output, it can be indicative of deep surgical site infections or intestinal fistulae. If such is the case, rapid clinical/radiological examination followed by opening of laparotomy incision site and thorough lavage is indicated. If intestinal fistulae are present, it should be treated either surgically or nonoperatively depending on its location and output.
- Persistent high drain output in cases of pancreatic and splenic injury should raise suspicion of the pancreatic fistula.
- Drain amylase should be requested on or after the third postoperative day in cases of suspected pancreatic fistula in cases of pancreatic and splenic injury. Drain amylase three times that of serum amylase confirms pancreatic fistula. Continuing the drains, antibiotic coverage (if signs of infections present), serial radiological examinations, and drainage of collections is recommended for the treatment of pancreatic fistulae. Use of somatostatin or its analogue may be useful in such situations.

Suggested Reading

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exercised with caution if blood transfusion is needed, fluid is identified on the screening ultrasonogram, or a significant quantity of blood is discovered on CT.
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Burn Management

67

Sushma Sagar, Kamal Kataria, and Maneesh Singhal

A 50-year-old male patient with history of alcohol abuse was admitted to the emergency department with burns while sleeping in a closed room. On arrival, he was conscious and oriented with cold, clammy extremities and feeble pulse. Blood pressure was 80/50 mmHg. He had 60% burns involving face, torso, and extremities. Over the right lower limb, there were circumferential burns and swelling with absent pulsations. There was hoarseness of voice with production of sooty sputum. Chest radiograph was normal.

The quality of life and outcome of the burn patient has improved due to improvement in the care over the past few decades. The removal of deep wounds and biological closure helps to attenuate the development of wound sepsis. The care of the burn patient requires very advanced critical care, preferably in the burn unit.

First Day

Step 1: Initial assessment and resuscitation

All burn patients should be approached as a polytrauma patient. Ideally, these patients should be managed in a dedicated burn unit.

Airway

- The airway is assessed first by asking the name of the patient and listening to hoarseness, which signifies upper airway burn.
- One hundred percent oxygen is administered, and oxygen saturation is monitored using pulse oximetry. Beware of falsely high saturation due to high

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carboxyhemoglobin levels in cases of carbon monoxide intoxication due to inhalation injury. Confirm oxygenation by blood gas analysis in a CO-oximeter.
- Wheezing, tachypnea, stridor, and hoarseness indicate impending airway obstruction due to an inhalation injury or edema, and immediate treatment is required.
- If the patient is not breathing or has labored respiration or signs of obstruction, clear the airway by oral/nasal suction followed by orotracheal intubation with in-line stabilization of the neck if an injury to the cervical spine is a consideration.
- Risk of upper airway obstruction increases with the following:
  - Inhalation burns—carbonaceous sputum, singed nasal hairs
  - All patients with deep burns of more than 35–40% TBSA (total burn surface area)
  - Burns involving face, neck, and upper torso
- Intubate early if progressive airway edema is suspected in cases of extensive burns or if the patient has signs of airway obstruction.
- Early intubation is also performed if the patient requires prolonged transport. Properly securing airway is of utmost importance in the patient.
- Awake fiberoptic intubation should be performed in difficult cases.

Breathing
- Breathing problem may be due to smoke inhalation injury, deep circumferential chest burn, or associated chest injury.
- Carbon monoxide (CO) is a by-product of incomplete combustion. Its intoxication is diagnosed by carboxyhemoglobin levels:
  - Less than 10% is normal.
  - More than 40% is severe.
- Treatment for carbon monoxide intoxication is to remove source and give 100% oxygen. Hyperbaric oxygen is also used to treat this condition. Patients with smoke inhalation injury often present with hoarseness, wheezing, carbonaceous sputum, facial burns, and singed nasal vibrissae.
- Diagnosis is often established by the use of bronchoscopy, which reveals early inflammatory changes such as erythema, edema, ulceration, sloughing of mucosa, and prominent vasculature in addition to infraglottic soot. Management of inhalation injury is directed at maintaining open airways and maximizing gas exchange.
- A patient who is able to cough with a patent airway can clear secretions very effectively, and efforts should be made to treat the patient without mechanical ventilation.
- If respiratory failure is imminent, intubation is instituted early, and frequent chest physiotherapy and suctioning are performed to maintain pulmonary hygiene.
- Frequent bronchoscopies may be needed to clear inspissated secretions.
- In addition to the preceding measures, adequate humidification and appropriate treatment for bronchospasm is indicated.
- These patients should be ventilated as per ARDSnet protocol with low tidal volume (6 mL/kg ideal body weight). Try to keep the plateau pressure below 30 cm H_2O. Deep circumferential chest burn may limit chest wall motility, so a higher plateau pressure up to 40 cm H_2O may be tolerated.
- Frequent escharotomies may improve breathing and airway pressures.

Table 67.1 Resuscitation formulas

Formula	Crystalloid volume	Colloid volume	5% dextrose or plain water by the nasogastric tube
Parkland	4 mL/kg/percent TBSA burn	None	None
Brooke	1.5 mL/kg/percent TBSA burn	0.5 mL/kg/percent TBSA burn	2.0 L
Galveston (pediatric)	5,000 mL/m^2 burned + 1,500 mL/m^2 total	None	None

TBSA total body surface area

Circulation

- Obtain IV access anywhere possible and start giving fluids:
  - Unburned areas are preferred.
  - Burned areas are acceptable.
  - Central access is obtained if expertise available.
  - Cutdowns.
- Perform resuscitation in burn shock (first 24 h):
  - Massive capillary leak occurs after major burns.
  - Fluids shift from intravascular space to interstitial space.
  - Fluid requirement increases with greater severity of burn (larger percent total body surface area(TBSA), increased depth, inhalation injury, associated injuries)
- IV fluid rate depends on physiologic response and goals:
  - Sensorium—comfortable, arousable.
  - Base deficit—less than 2.
  - Goal for adults—urine output of 0.5 mL/kg/h.
  - Goal for children—urine output of 1 mL/kg/h; if urine output is below these levels, increase fluid rate.
  - Preferred fluid—lactated Ringer's solution as it is isotonic, cheap, and easily stored.
  - Resuscitation formulas—resuscitation formulas are just a guide for initiating resuscitation (Table 67.1).

Parkland formula is most commonly used for fluid calculation:

- Give half of the calculated volume in the first 8 h (from the time of injury).
- Give the other half in the next 16 h.
- Warning: Despite the formula suggesting decrease the fluid rate to half at 8 h, the fluid rate should be gradually reduced throughout the resuscitation to maintain the targeted urine output.

Resuscitation endpoint

When maintenance rate is reached (approximately 24 h), change fluids to D5/NS with 20 mEq KCl at the maintenance level:

- Maintenance fluid rate = basal requirements + evaporative losses

Table 67.2 Rule of nines for establishing extent of burned body surface

Anatomic surface	Total body surface (%)
Head and neck	9
Anterior trunk	18
Posterior trunk	18
Arms, including hands	9% each
Legs, including feet	18% each
Genitalia	1

- Basal fluid rate
  - Adult basal fluid rate = 1,500 mL × body surface area (BSA) (for 24 h)
  - Pediatric basal fluid rate (<20 kg) = 2,000 mL × BSA (for 24 h)
- Evaporative fluid loss
  - Adult evaporative fluid loss (mL/h) = (25 + percent TBSA burn) × BSA
  - Pediatric evaporative fluid loss (<20 kg) (mL/h) = (35 + percent TBSA burn) × BSA

Role of albumin

- There is generally a profound hypoproteinemia following the initial resuscitation, and addition of intravenous albumin generally favors recruitment of interstitial fluid. Overall, no improvement in mortality has been noticed with albumin administration although complications are lowered by albumin compared with crystalloid in burn patients.

Step 2: Take detailed history

- Allergy
- Medication
- Pregnancy/past illness
- Last meal taken
- Environment (associated injuries)

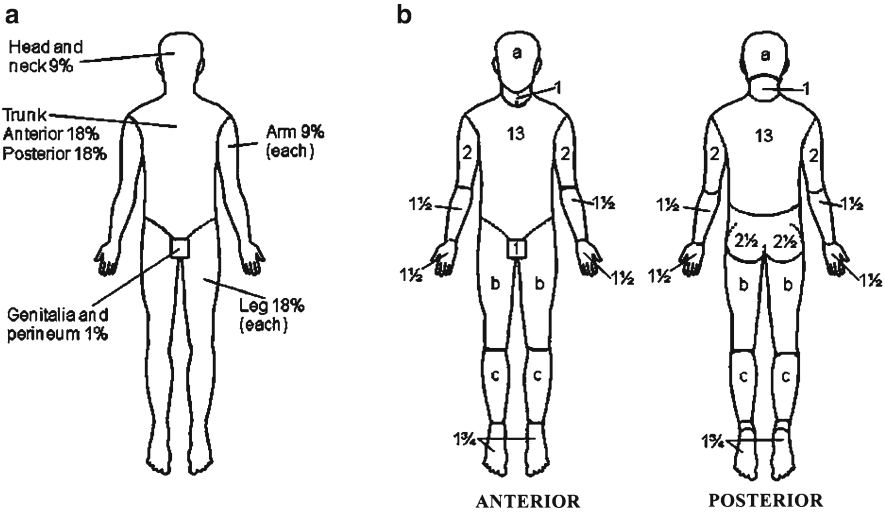
Step 3: Start supportive treatment

- The nasogastric tube (small bore) for gastric decompression and initiating early enteral nutrition
- IV analgesics
- Antacids
- Tetanus prophylaxis

Step 4: Assess severity

Burn severity is dictated by percent TBSA involvement, depth of burn, age, and associated injuries:

- Burns of 20–25% TBSA require IV fluid resuscitation.
- Burns of 30–40% TBSA may be fatal without treatment.
- In adults, rule of "nines" is used as a rough indicator of percent TBSA (Table 67.2 and Fig. 67.1).



Relative percentage of body surface areas (% BSA) affected by growth

	0 yr	1 yr	5 yr	10 yr	15 yr
a-½ of head	9½	8½	6½	5½	4½
b- ½ of 1 thigh	2¾	3¼	4	4¼	4½
c- ½ of 1 lower leg	2½	2½	2¾	3	3¼

Fig. 67.1 (**a**) Rule of "nines" and (**b**) Lund–Browder diagram for estimating extent of burns (Adapted from Artz CP, Moncrief JA. The treatment of burns. 2nd ed. Philadelphia: WB Saunders Company; 1969)

- In children, adjust percents because they have proportionally larger heads (up to 20%) and smaller legs (13% in infants) than adults.
- Lund–Browder diagrams improve the accuracy of the percent TBSA for children.
- Palmar surface of the hand is approximately 1% TBSA helps in estimating percent total body surface area in children affected by burns.

Depth of burn injury

A. Superficial burns (first-degree and superficial second-degree burns):
   - First-degree burns
     - Damage above the basal layer of epidermis.
     - Dry, red, painful ("sunburn").
   - Second-degree burns
     - Damage into dermis.
     - Skin adnexa (hair follicles, oil glands, etc.) remain intact.
     - Heal by reepithelialization from skin adnexa.
     - The deeper the second-degree burn, the slower the healing (fewer adnexa for reepithelialization).
     - Moist, red, blanching, blisters, extremely painful.

- Superficial burns heal by reepithelialization and usually do not scar if healed within 2 weeks.

B. Deep burns (deep second-degree to fourth-degree burns):

- Deep second-degree burns (deep partial thickness)
  - Damage to deeper dermis
  - Less moist, less blanching, less pain
  - Heal by scar deposition, contraction, and limited reepithelialization
- Third-degree burns (full thickness)
  - Entire thickness of skin destroyed (into fat)
  - Any color (white, black, red, brown), dry, less painful (dermal plexus of nerves destroyed)
  - Heal by contraction and scar deposition (no epithelium left in middle of wound)
- Fourth-degree burns
  - Burn into muscle, tendon, and bone.
  - Need specialized care.
  - Deep burns usually need skin grafts to optimize results and lead to hypertrophic (raised) scars if not grafted.

Age

- Mortality for any given burn size increases with age.
- Children/young adults can survive massive burns.
- Children require more fluid per TBSA burns.
- The elderly may die from small (<15% TBSA) burns.

Associated injuries

- Other trauma increases severity of injury.

Use of alcohol or drugs

- It makes assessment of the patient more difficult.

Role of antibiotics

- It can be started later on when signs/symptoms of infection are present.

Step 5: Burn wound care and control of infection

Burn wound care: Current therapy for burn wounds can be divided into the following three stages: assessment, management, and rehabilitation:

- Once the extent and depth of the wounds have been assessed and the wounds are thoroughly cleaned and debrided, each wound should be dressed with an appropriate covering that serves three functions. First, it protects the damaged epithelium. Second, the dressing should be occlusive to reduce evaporative heat loss. Third, the dressing should provide comfort over the painful wound.
- The choice of dressing should be individualized based on the characteristics of the treated wound:
- First-degree wounds are minor with minimal loss of barrier function. These wounds require no dressing and are treated with topical agents to decrease pain and keep the skin moist.

- Second-degree wounds can be treated by daily dressing changes with an antibiotic ointment such as silver sulfadiazine covered with several layers of gauze under elastic wraps. Alternatively, the wounds can be covered with a temporary biologic or synthetic covering to close the wound. These coverings eventually slough as the wound reepithelializes underneath.
- Deep second- and third-degree burns will not heal in a timely fashion without autografting. These burned tissues serve as a nidus for inflammation and infection that can lead to death of the patient. Early excision and grafting of these wounds is preferred in terms of survival, less blood loss, and decreased length of hospitalization.
- Early excision should be reserved for third-degree wounds typically caused by flame. A deep second-degree burn can appear clinically to be a third-degree wound at 24–48 h after injury, particularly if it has been treated with topical antimicrobials that combine with wound drainage to form a pseudoeschar.
- *Escharotomy*: With circumferential deep second- and third-degree burns to an extremity, peripheral circulation to the limb can be compromised. The entire constricting eschar must be incised to relieve the obstruction to blood flow. Increased pressures in the underlying musculofascial compartments are treated with standard fasciotomies to avoid compartment syndrome.
- *Control of infection*: Decreasing invasive infections in the burn wound is due to early excision and closure and the timely and effective use of antimicrobials. The antimicrobials that are used can be divided into those given topically and those given systemically. Topical antibiotic includes 11% mafenide acetate, 1% silver sulfadiazine, polymyxin B, neomycin, bacitracin, and mupirocin:
  - Mafenide acetate has a broad spectrum of activity, particularly for *Pseudomonas* and *Enterococcus* species. Mafenide sulfate is typically reserved for small full-thickness injuries and ear burns to prevent chondritis.
  - Silver sulfadiazine, the most frequently used topical agent, has a broad spectrum of activity from its silver and sulfa moieties that cover Gram-positive organisms, most Gram-negative organisms, and some fungi. It is painless upon application, has a high patient acceptance, and is easy to use.
  - Petroleum-based antimicrobial ointments with polymyxin B, neomycin, and bacitracin are clear on application, are painless, and allow for observation of the wound. These agents are commonly used for the treatment of facial burns, graft sites, healing donor sites, and small partial-thickness burns.
  - Mupirocin has improved activity against Gram-positive bacteria, particularly methicillin-resistant *Staphylococcus aureus*, and selected Gram-negative bacteria.
  - Nystatin in the powder form can be applied to wounds to control fungal growth, and nystatin powder can be combined with topical agents such as polymyxin B to decrease colonization of both bacteria and fungi.
  - Available agents for application as a soak include 0.5% silver nitrate solution, 0.5% sodium hypochlorite, 5% acetic acid, and 5% mafenide acetate solution.

– The use of perioperative systemic antimicrobials also has a role in decreasing sepsis in the burn wound until it is healed. Common organisms that must be considered when choosing a broad-spectrum perioperative regimen include *S. aureus* and *Pseudomonas* species, which are prevalent in wounds. After massive burns, gut flora are often found in the wounds mandating coverage of these species as well.

Step 6: Fluid of choice on the second day

- Dextrose 5% in water is fluid of choice.

Step 7: Supportive treatment—nutrition

- Nutritional support is best accomplished by early enteral nutrition that can abate the hypermetabolic response to a burn. Therefore, duodenal or jejunal tube feeding should be commenced as early as within the first 6 h after burn.
- The caloric requirements are needed to gain weight and achieve nitrogen balance and have been calculated from linear regression analysis of weight change versus predicted dietary intakes in adults at 25 kcal/kg plus 40 kcal/% TBSA burn for 24 h (Table 67.3). Protein needs are approximately 2.5 g/kg. Estimation of 24-h urinary urea nitrogen for calculating nitrogen balance should be obtained (see Chap. 43 on nutrition).

  The pediatric formulas have been derived from retrospective analyses of dietary intake, which is associated with maintenance of average body weight over hospital stay (Table 67.4).

  Ulcer prophylaxis and deep venous thrombosis prophylaxis should be started along with the rest of the management unless there are contraindications.

Table 67.3 Curreri formula for estimating caloric requirements for adult burn patients

Age	Formulas
6–60 years	25 kcal/kg/day + 40 kcal/percent burn/day
>60 years	25 kcal/kg/day + 65 kcal/percent burn/day

Table 67.4 Formulas for estimating caloric requirements for pediatric burn patients

Age	Formulas
0–1 years	2,100 kcal/m^2 TBSA/day + 1,000 kcal/m^2 TBSA burn/day
1–11 years	1,800 kcal/m^2 TBSA/day + 1,300 kcal/m^2 TBSA burn/day
12–18 years	1,500 kcal/m^2 TBSA/day + 1,500 kcal/m^2 TBSA burn/day

Shriners Hospitals for Children at Galveston, Texas

Step 8: Manage complications

Successful management of burns involves management of predicted complications.

Suggested Reading

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   This paper outlines nine key steps in the initial management of burn patients in the prehospital environment.
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   The treatment of partial-thickness burns with Biobrane is superior to topical therapy with 1% silver sulfadiazine. Pain, pain medication requirements, wound healing time, and length of hospital stay are significantly reduced.
7. Artz CP, Moncrief JA. The treatment of burns. 2nd ed. Philadelphia: WB Saunders Company; 1969.
   Provides the rule of nines for establishing extent of burned body surface.

Part X

Toxicology, Envenomation and Thermo Dysregulation

Omender Singh and Dhruva Chaudhry

General Poisoning Management

68

Omender Singh and Prashant Nasa

A 24-year-old lady was admitted to the hospital, with history of consumption of some liquid at home followed by vomiting, altered mental status, and labored breathing. She was brought to the triage in the comatose state with pinpoint pupils, frothy secretions from her mouth, heart rate 58/min, and blood pressure 90/48 mmHg.

High index of suspicion for intoxication is warranted in the practice of critical care medicine. The majorities of drug overdoses are polypharmacological and respond to general supportive measures and specific antidotes.

Step 1: Initiate resuscitation and assessment

- Initiate resuscitation as mentioned in Chap. 78.

Airway

- Management of airways is very important in poisoning. Some toxins (acid or alkali ingestion) require extra care during airway management. When intubation is necessary, rapid sequence induction is indicated using short-acting paralytic agents.
- Urine toxicology screening should be obtained before any sedatives or hypnotics are administered.

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Table 68.1 Physiologic grading of the severity of poisoning—signs and symptoms

Severity	Stimulant poisoning	Depressant poisoning
Grade 1	Agitation, anxiety, diaphoresis, hyperreflexia, mydriasis, tremors	Ataxia, confusion, lethargy, weakness, verbal, able to follow commands
Grade 2	Confusion, fever, hyperactivity, hypertension, tachycardia, tachypnea	Mild coma (nonverbal but responsive to pain); brainstem and deep tendon reflexes intact
Grade 3	Delirium, hallucinations, hyperpyrexia, tachyarrhythmias	Moderate coma (respiratory depression, unresponsive to pain); some but not all reflexes absent
Grade 4	Coma, cardiovascular collapse, seizures	Deep coma (apnea, cardiovascular depression); all reflexes absent

Breathing

- A patient's oxygenation status can be monitored with a bedside pulse oximeter. However, in carbon monoxide poisoning, pulse oximeter is unreliable in detecting carboxyhemoglobin.
- Give oxygen by the nasal cannula or face mask to maintain SpO_2 more than 95%.
- When the patient is in respiratory distress and not able to maintain oxygenation, assisted ventilation should be started.

Circulation

- Monitor pulse and blood pressure. Do an ECG. Obtain a good peripheral line and start intravenous fluids.

The "coma cocktail" of dextrose, naloxone, and thiamine can be considered in unknown poisoning with unconsciousness and coma.

Step 2: Take detailed history

- Detailed and targeted history from the family members and friends including the past medical treatment and occupational environment is important for making the diagnosis of poisoning.
- The history should include the type of toxin or toxins, time of exposure (acute versus chronic), amount taken, and route of administration (i.e., ingestion, intravenous, and inhalation).
- The patient should be asked about over-the-counter medications, vitamins, and herbal preparations.
- The patient or accompanying attendants should be asked about all drugs taken, including prescription drugs and empty bottles/containers, and the physician can also perform "pill count" to ascertain the number of consumed pills.
- Remember the history from the patient may not always be reliable.
- The clinical diagnosis of the type of poisoning can be identified by the clinical manifestations that may fit into a particular toxidrome. Toxic overdose can present with a wide array of symptoms, including abdominal pain, vomiting, tremor, altered mental status, seizures, cardiac dysrhythmias, and respiratory depression, which may be the only clues to diagnosis (Table 68.1).

Table 68.2 Common causes of abnormal anion gap

Elevated anion gap	Decreased anion gap
Lactic acidosis (type A)	Increased unmeasured cation
Uremia	Hyperkalemia
Sepsis	Hypercalcemia
Rhabdomyolysis	Hypermagnesemia
Ketoacidosis	Acute lithium intoxication
Diabetic	Elevated IgG (myeloma in alcoholic; cationic paraprotein)
Starvation	Unmeasured decreased anion
	Hypoalbuminemia
Toxic ingestions	Drugs
Ethylene glycol	Bromide
Methanol	Iodide
Paraldehyde	Lithium
Salicylate	Polymyxin B
Metabolic alkalosis with	Tromethamine
Volume depletion	Analytical artifact
	Hypernatremia
	Hyperlipidemia

- Symptoms are often nonspecific (as in early acetaminophen poisoning) or masked by other conditions (e.g., myocardial ischemia in the setting of carbon monoxide poisoning).

Step 3: Perform physical examination

- The patient stabilization will take precedence over the detailed physical examination.
- Once the patient is stable, a more comprehensive physical and systemic examination should be performed.
- Serial examinations are even more important to assess dynamic change in clinical appearance. The systematic neurological evaluation is particularly important in patients with altered mental status. Alert/verbal/painful/unresponsive scale (AVPU) is a simple, rapid method of assessing consciousness in most poisoned patients.

Step 4: Order investigations

A basic metabolic panel should be obtained in all suicidal poisoned patients:

- Complete blood count
- Serum electrolytes
- Blood urea nitrogen and creatinine
- Blood glucose and bicarbonate level
- Liver functions test
- Arterial blood gases
- ECG
- If the patient is a female of child-bearing age, a pregnancy test is essential.
- The anion gap, serum osmolality, and osmolal gap should be measured in each patient as it can help in finding the cause (Table 68.2).

Specific investigations:

- Sample for urine toxicology screening for common drugs must be taken before giving any sort of sedation to these patients.
- The cholinesterase level for organophosphorus poisoning: Specific levels of cholinesterase can guide treatment.
- Oxygen saturation gap (SaO_2–SpO_2): An oxygen saturation gap is present when there is more than a 5% difference between the saturation calculated from an arterial blood gas (SaO_2) and the saturation measured by CO-oximetry (SpO_2). An elevated oxygen saturation gap is found in carbon monoxide, methemoglobinemia, cyanide, and hydrogen sulfide poisoning.

Step 5: Admit to the ICU

Admit in ICU if any of the following is present:

- Respiratory depression ($PaCO_2$ > 45 mmHg)
- Emergency intubation
- Seizures
- Cardiac arrhythmia (QT prolongation, preferably corrected QTc)
- QRS duration more than 0.12 ms
- Second- or third-degree atrioventricular block
- Systolic BP less than 80 mmHg
- Unresponsiveness to verbal stimuli
- Glasgow coma scale score less than 12
- Need for emergency dialysis, hemoperfusion, or extracorporeal membrane oxygenation
- Increasing metabolic acidosis
- Pulmonary edema induced by toxins (including inhalation) or drugs
- Tricyclic or phenothiazine overdose manifesting anticholinergic signs, neurologic abnormalities, QRS duration more than 0.12 s, or QT more than 0.5 s
- Administration of pralidoxime in organophosphate toxicity
- Antivenom administration in envenomation
- Need for continuous infusion of naloxone

Step 6: Management

- The management of any clinically significant poisoning should begin with basic supportive measures. The first priority after airway, breathing, and circulation approach is to prevent and manage life-threatening complications.

Step 7: Decontamination

- The clothing should be removed in suspected or confirmed dermal exposures, and the skin should be copiously irrigated and washed with a mild soap and water in organophosphorus poisoning.
- The eye should be copiously irrigated in ocular exposure to acids and alkali.
- Gastric lavage: The place of gastric lavage in acute poisoning is debatable and is only of benefit in the hyperacute phase of poisoning (<1 h). Caution: Patients must be awake with a preserved gag reflex.

- Charcoal: Charcoal aspiration has a high morbidity and mortality. This should not be attempted in patients without a safe or protected airway.
- Administer 50-g charcoal as soon as possible and another 50 g every 4 h thereafter while indication persists. Coadministration with sorbitol has not been shown to increase efficacy.
- Charcoal administration is most effective when it is given within 1 h of ingestion.
- Contraindications to charcoal administration are as follows:
  - Elemental metals (lithium, iron)
  - Pesticides
  - Strong acids or alkalis
  - Cyanide
  - Late presentations (>4–6 h post-ingestion)

Table 68.3 Indication of dialysis and hemoperfusion

Hemodialysis	Hemoperfusion
Methanol	Theophylline
Ethylene glycol	Phenobarbital
Boric acid	Phenytoin
Salicylates	Carbamazepine
Lithium	Paraquat
	Glutethimide

Table 68.4 Common poisons and their antidotes

Poison	Antidote
Acetaminophen	*N*-Acetylcysteine
Anticholinergics	Physostigmine
Anticoagulants (warfarin/coumadin, heparin)	Vitamin K, protamine respectively
Benzodiazepines	Supportive care, flumazenil[a]
Botulism	Botulinum antitoxin
β-Blockers	Glucagon
Calcium channel blockers	Calcium, glucagon
Cholinergics (i.e., organophosphorus)	Atropine, pralidoxime in organophosphate overdose
Carbon monoxide	Oxygen, hyperbaric oxygen
Cyanide	Amyl nitrate, sodium nitrate, sodium thiosulfate, hydroxocobalamin (available in Europe)
Digoxin	Digoxin Fab antibodies
Iron	Desferrioxamine
Isoniazid	Pyridoxine
Lead	BAL, EDTA, DMSA
Methemoglobinemia	Methylene blue
Opioids	Naloxone
Toxic alcohols	Ethanol drip, dialysis (experimental trials underway on enzyme inhibitors)
Tricyclic antidepressants	Sodium bicarbonate

[a]Use of flumazenil should be contraindicated in many situations including tricyclic overdose or in chronically habituated benzodiazepine users, as this may precipitate seizures

Step 8: Enhanced elimination

- Alkalinization of urine may help in excretion of drug in the urine in poisonings such as salicylates, phenobarbital, and chlorpropamide.
- Dialysis and charcoal hemoperfusion should be considered in severe poisoning if the toxin can be removed by dialysis (Table 68.3).

Step 9: Use antidotes to common poisons

- Antidotes should be used early in the course in which the effects of poisoning can be counteracted (Table 68.4).

Suggested Reading

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   This article reviews the general approach and management of the critically poisoned patient and also specific toxin class and its complications.
2. Linden CH. General considerations in the evaluation and treatment of poisoning. In: Irwin RS, Cerra FB, Rippe JM, editors. Intensive Care Medicine. New York: Lippincott Williams & Wilkins; 2008.
   The book discusses the principles in the evaluation and management of general poisoning and specific poisoning.
3. Brent J, Wallace KL, Burkhart KK, editors, et al. Critical care toxicology: diagnosis and management of the critically poisoned patient. Philadelphia: Elsevier Mosby; 2005.
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4. Mokhlesi B, Leiken JB, Murray P, Corbridge TC. Adult toxicology in critical care. Chest. 2003;123:577–92.
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   The review discusses the symptomatic effects of drug abuse that are a result of alterations in the functioning of the various neurotransmitters or their receptors such as acetylcholine, dopamine, gamma-aminobutyric acid, norepinephrine, opioids, and serotonin.

Syndromic Approach to Poisoning

69

Praveen Aggarwal

A 45-year-old male patient presented to the emergency department with altered mental status. According to the relatives, patient had ingested unknown liquid about half an hour ago. His pulse was 110/min, blood pressure was 90/69 mmHg, and pupils were small. His breath had a garlic-like odor. He had profuse sweating and incontinence of urine. Chest auscultation revealed bilateral rhonchi and crepitations.

Toxidromes are constellations of symptoms commonly encountered with certain drug classes. Evaluation of possible poisoning should include laboratory studies with complete metabolic profiles, electrolyte estimation, and liver and renal functions.

Step 1: Initial resuscitation

- The initial approach in any emergency in an unconscious patient includes standard resuscitation with care of circulation, airway and breathing along with cervical spine immobilization (as the patient is in altered mental status, which could be due to trauma).
- High-flow oxygen and intravenous fluids should be administered, and blood should be sent for urgent blood glucose, urea and electrolytes, and arterial blood gases.
- Once the patient has been stabilized, the physician must consider how to minimize the bioavailability of toxin not yet absorbed, which antidotes (if any) to administer, and other measures to enhance elimination.

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Table 69.1 Toxidromes

Toxidrome	Clinical features	Toxins
Cholinergic	Muscarinic features (DUMBELS): D—diarrhea U—urination M—miosis B—bronchorrhea, bronchoconstriction, bradycardia E—emesis L—lacrimation S—salivation, sweating	Organophosphate and carbamate insecticides, nerve agents (Soman, Tabun, sarin, VX), nicotine
	Nicotinic features: mydriasis (uncommon), hypertension, muscle weakness, tachycardia, fasciculations	
	CNS features: confusion, coma, convulsion	
Anticholinergic	Constipation, retention of urine, mydriasis, dry lungs, dry and hot skin, dry mouth, hypertension, abnormal movements, tachycardia, hyperthermia, hallucinations, delirium	Atropine, Datura, antihistamines, tricyclic antidepressants, gyromitrin (found in a mushroom)
Opioid	Coma, pinpoint pupils, respiratory depression, bradycardia, hypotension, hypothermia	Opiates (heroin, pethidine, morphine, dextropropoxyphene, loperamide, opium)
Sympathomimetic	Sweating, tremors, tachycardia, hypertension, hyperthermia, mydriasis, tachypnea, agitation, hyper-alert, seizures	Caffeine, theophylline, amphetamines, cocaine, phencyclidine (PCP), sedative/hypnotic withdrawal
Hallucinogenic	Hallucinations, depersonalization, agitation, hyperthermia, tachycardia, hypertension, nystagmus, mydriasis	Lysergic acid diethylamide, PCP, gamma-hydroxybutyrate (GHB), psilocybin (found in a mushroom)
Hypnotic–sedative	CNS depression, confusion, stupor, coma, bradycardia, hypotension, hypopnea, miosis, hyporeflexia	Barbiturates, methaqualone, meprobamate

Table 69.2 Commonly encountered features and likely toxins

Features	Toxins/causes
Bradycardia	β-Blockers, cholinergic agents, clonidine, calcium channel blockers, ethanol, digoxin, opiates, cholinergics
Tachycardia	Sympathomimetics (cocaine, caffeine, theophylline, amphetamines), anticholinergics, reflex tachycardia due to hypotension
Hypothermia	Carbon monoxide, opiates, hypoglycemic agents, alcohol, sedative hypnotics
Hyperthermia	Nicotine, antihistamines, anticholinergics, sympathomimetics, aspirin, antidepressants, neuroleptic malignant syndrome
Hypotension	Antihypertensive drugs, aluminum phosphide, cholinergics, digoxin, antidepressants, phenothiazines, sedative hypnotics, opiates
Hypertension	Cocaine, theophylline, sympathomimetics, caffeine, anticholinergics, nicotine
Hypoventilation	Narcotics, sedative hypnotics, alcohol, GHB, botulism, clonidine
Hyperventilation	Salicylates, amphetamines, theophylline, metabolic acidosis (respiratory compensation)
Coma	Sedative hypnotics, opiates, alcohols, clonidine, carbon monoxide, antidepressants
Mydriasis	Sympathomimetics, anticholinergics, antidepressants, withdrawal (alcohol, opiate, sedative hypnotic)
Miosis	Organophosphates and carbamates, clonidine, opiates, phenothiazines, sedative hypnotics
Seizures	Organophosphates, antidepressants, INH, sympathomimetics, camphor, cocaine, amphetamines, theophylline, PCP, withdrawal (ethanol, benzodiazepines), lithium, lidocaine, lead, organochlorines (e.g., lindane, DDT), hypoglycemia
Breath odor	Garlic: organophosphate and carbamate insecticides, aluminum phosphide, arsenic, phosphorus
	Rotten eggs: hydrogen sulfide
	Moth ball: naphthalene
	Bitter almonds: cyanides
Prolonged QT interval on ECG	Carbamazepine, propoxyphene, quinidine, procainamide, terfenadine, astemizole, tricyclic antidepressants, cocaine, phenothiazines
Noncardiogenic pulmonary edema on chest X-ray	Opiates, barbiturates, salicylates, irritant gases
Radio-opaque toxins on abdominal X-ray (absence of radio-opaque shadow does not exclude poisoning by listed toxins)	Chloral hydrate, heavy metals (lead, arsenic, mercury), iron, phenothiazines, body packers, sustained-release medicines
Elevated anion gap (normal 8–12 mEq/L) [Anion gap = Na^+–(HCO_3 + Cl^-)]	Alcoholic ketoacidosis, cyanide, carbon monoxide, aspirin, toluene, methanol, ethylene glycol, metformin, uremia (due to renal toxicity), iron, INH, lactic acidosis (due to hypotension or hypoxia)
Elevated osmolar gap (>10 mOsmol/L) [Osmolar gap = measured osmolality–calculated osmolarity] [Calculated osmolarity = 2Na^++BUN/2.8 + glucose/18]	Ethanol, methanol, ethylene glycol, isopropanol

Step 2: Diagnosis by toxidromic approach
After initial stabilization, it is important to diagnose the type of poison ingested by the patient. This can be done by detailed history, examination, and simple laboratory tests, which include blood glucose, electrolytes, acid–base analysis, urine exam, and ECG. Based on history and examination, it may be possible to define a constellation of signs and symptoms or toxidromes, which may help in diagnosing the unknown poison. Common toxidromes are listed in Table 69.1. Antidotal and supportive treatment can then be provided.

Step 3: Diagnosis of the type of poison if clinical features not suggestive of a toxidrome
In many cases, a clear-cut toxidrome cannot be defined based on presenting clinical features. In such cases, prominent features may be used to diagnose the type of poison involved. Table 69.2 lists some of the commonly encountered features and the likely toxins.

Step 4: Decontamination, enhancing excretion, antidotal, and supportive treatment
Based on the likely poison, antidotal treatment should be instituted. However, supportive treatment is the most vital treatment in such patients. These topics have been discussed in Chap. 68.

Suggested Reading

1. Hill GE, Ogunnaike B, Nasir D. Patients presenting with acute toxin ingestion. Anesthesiol Clin. 2010;28:117–37.
This review of drug/toxin-induced injury discusses drug or toxin-induced pathology that the clinician may encounter and therapeutic approaches to these syndromes.
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5. Erickson TB, Thompson TM, Lu JJ. An approach to the patient with an unknown overdose. Emerg Clin North Am. 2007;25:249–81.
This article reviews the management of unknown poisoning.
6. Koren G. A primer of paediatric toxic syndromes or 'toxidromes'. Paediatr Child Health. 2007;12:457–9.

Websites

1. http://www.uic.edu/com/er/toxikon/toxidro.htm
2. www.pitt.edu/~super7/6011–7001/6331.ppt
3. http://www.sjtrem.com/content/17/1/29
4. http://openmed.nic.in/1823/01/gupta.pdf

Drug Abuse

70

Omender Singh and Prashant Nasa

A 38-year-old male known alcohol abuser, chronic smoker, and IV drug abuser came to the emergency department in inebriated state. On examination, he was cachectic, stuporous with bilateral pin-point pupils. There were multiple black erythematous patches on forearm with multiple injection marks. His pulse rate was 46/min and blood pressure was 82/60 mmHg, and on auscultation, there were bilateral crepts.

Substance abuse may be persistent or sporadic use of a drug / substance, inconsistent with or unrelated to acceptable medical practice. This subset of patients may present to the hospital with acute intoxication, withdrawal, or infectious and other chronic complications related to drug abuse. They have overall better prognosis as compared to other critically ill patients if diagnosed and managed timely.

Step 1: Initiate resuscitation

- Initial resuscitation should be done as mentioned in Chap. 78.

Airway

- Management of airways is very important in poisoning. When intubation is necessary, rapid sequence induction is indicated using short-acting paralytic agents.
- Urine toxicology screening should be obtained before administering any sedatives or hypnotics.

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Breathing
- A patient's oxygenation status can be monitored with a bedside pulse oximeter.
- Give oxygen by the nasal cannula or facemask to maintain SpO_2 more than 95%.
- The patient should be started on assisted ventilation if unable to maintain oxygenation or ventilation.

Circulation
- Monitor pulse and blood pressure and do ECG.
- Obtain a good peripheral line and start intravenous fluids.

Step 2: Initial assessment
- This subset of patients may present to the hospital with acute intoxication, withdrawal, or infectious and other chronic complications related to drug abuse.
  The drugs of abuse can be classified into major groups (Table 70.1)
  The initial evaluation of these patients has multiple physical, social, emotional, and medicolegal issues that should be addressed.

History
- Complete and focused history should be taken from the patient, family, accompanying physician, or police, as mentioned in Chap. 68.
- Do detailed examination (Fig. 70.1, 70.2):
  - Once the patient is stable, a more comprehensive physical and systemic examination should be performed.
  - Serial examinations are even more important to assess dynamic change in clinical appearance.
  - The systematic neurological evaluation is particularly important, in patients with altered mental status. Alert/verbal/painful/unresponsive scale (AVPU) is a simple rapid method of assessing consciousness in most poisoned patients.

Table 70.1 Classification of drugs of abuse

Group	Commonly abused drugs
Cannabinoids	Hashish, ganja, marijuana
Opioids	Opium, heroin, morphine, fentanyl, codeine, oxycodone
Stimulants	Amphetamines, cocaine, MDMA (ecstasy), nicotine
Hallucinogens	Lysergic acid diethylamide, mescaline
Dissociative anesthetics	Ketamine, phencyclidine analogs
Depressants	Barbiturates, nonbarbiturates (benzodiazepines, gamma-hydroxybutyrate, antihistaminics)
Others	Alcohol, anabolic steroids, dextromethorphan

Step 3: Diagnosis by toxidromic approach
The signs and symptoms of drugs of abuse are organized around the activity of six neurotransmitters (Table 70.2), with this activity being sufficiently unique to permit rapid identification of the specific drug responsible for a given clinical situation.

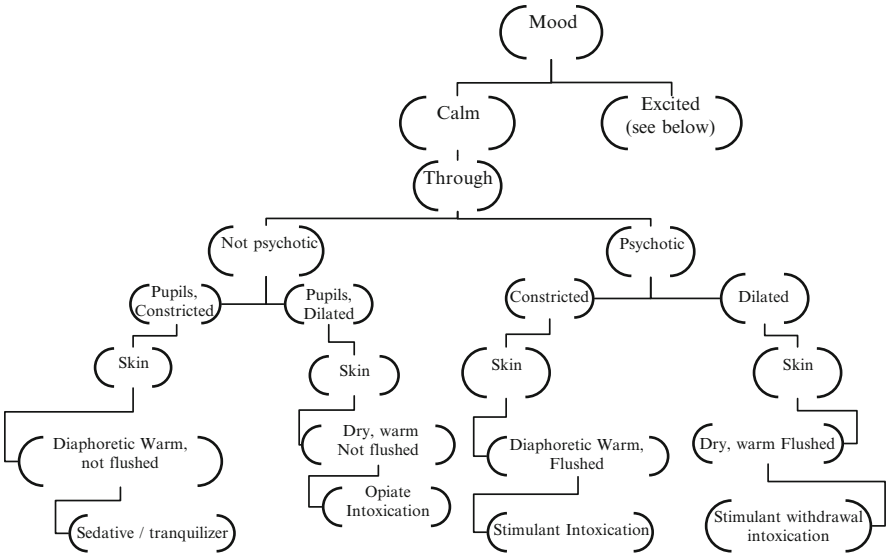

Fig. 70.1 Algorithm for the diagnosis of drug intoxication and withdrawal

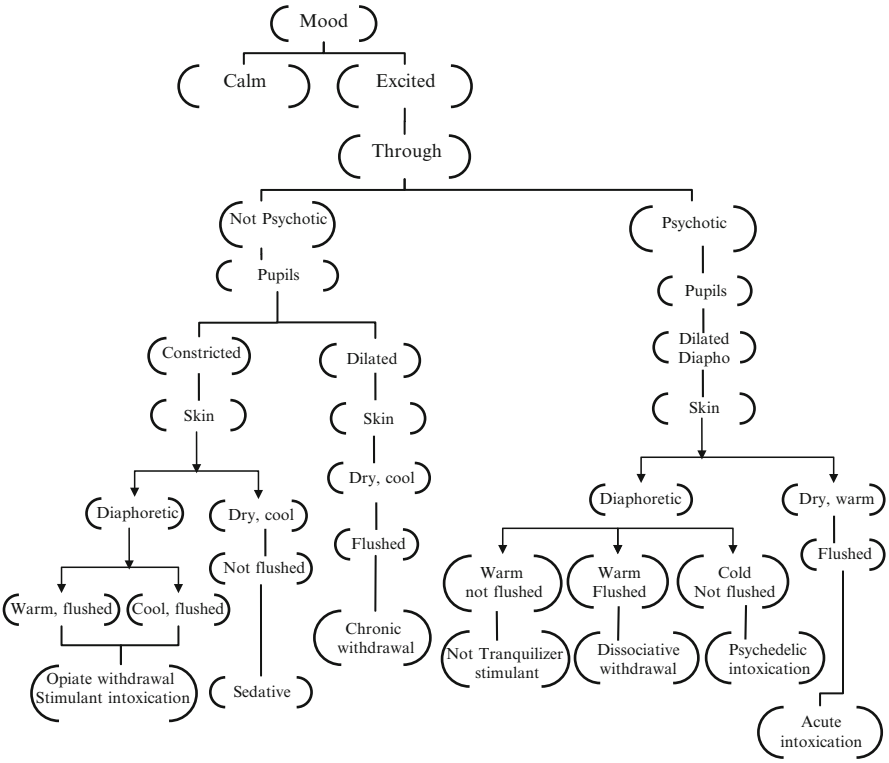

Fig. 70.2 Algorithm for the diagnosis of drug intoxication and withdrawal (continued)

Table 70.2 Specific treatment for intoxication, overdose, and withdrawal based on the affected neurotransmitter

Neurotransmitter intoxication and overdose	Treatment
Acetylcholine (anticholinergic)	Physostigmine (Antilirium)
β-Endorphin	Naloxone (Narcan)
Dopamine	Benzodiazepine
	Butyrophenone
GABA	Mechanical support
Norepinephrine	β-Blocker
	Benzodiazepine
Serotonin	Benzodiazepine
Withdrawal	
β-Endorphin	Methadone, clonidine (Catapres)
Dopamine	Bromocriptine (Parlodel)
GABA	Barbiturate or benzodiazepine replacement
Norepinephrine	Desipramine (Norpramin)
Serotonin	Fluoxetine (Prozac)

GABA gamma-aminobutyric acid

- Based on history and examination, it may be possible to define a constellation of signs and symptoms or toxidromes, which may help in diagnosing the unknown poison. Common toxidromes are listed in Chap. 69.

Step 4: Diagnose common drug abuse

A. Alcohol
- Acute effects:
  - CNS depressant.
  - In low doses, alcohol depresses inhibitory centers and resultant disinhibition (out-of-character activities).
  - At higher doses, alcohol inhibits excitatory centers.
- Signs of chronic alcohol abuse:
  - Gastrointestinal—cirrhosis of the liver, peptic ulcer disease, gastritis, pancreatitis, and carcinoma
  - Cardiovascular—hypertension, cardiomyopathy, atrial fibrillation ("holiday heart syndrome")
  - Neurological—peripheral neuropathy leading to ataxia, Wernicke encephalopathy, Korsakoff psychosis, and structural changes in the brain leading to dementia
  - Immunologic—suppression of neutrophil function and cell-mediated immunity
  - Endocrine—in males, increase in estrogen and decrease in testosterone, leading to impotence, testicular atrophy, and gynecomastia
  - Psychiatric—depression or anxiety disorders

B. Opiates
   - Acute intoxication—decreased respiratory rate and pinpoint pupils, with complications including noncardiogenic pulmonary edema and respiratory failure.
   - Complications of chronic abuse are primarily infectious and include skin abscess at an injection site, cellulitis, mycotic aneurysms, endocarditis, talcosis, HIV, and hepatitis.

C. Cocaine
   Cocaine may be smoked, inhaled, used topically, or injected:
   - Acute cocaine intoxication may present with agitation, paranoia, tachycardia, tachypnea, hypertension, and diaphoresis.
   - Complications of acute and chronic use can include myocardial ischemia or infarction, stroke, pulmonary edema, and rhabdomyolysis.

D. Amphetamines
   Acute intoxication with amphetamines presents with signs of sympathetic nervous system stimulation, tachycardia, hypertension, anorexia, insomnia, and occasionally seizures.

E. Hallucinogens
   - Different hallucinogens present with a variety of organ system effects.
   - Phencyclidine (PCP) has been known to cause muscle rigidity, seizures, rhabdomyolysis, and coma.
   - Anticholinergics have been associated with delirium, supraventricular tachycardia, hypertension, and seizures.

Other hallucinogens (e.g., lysergic acid diethylamide, peyote, marijuana, and nutmeg) rarely cause significant physical complications.

Step 5: Send investigations

A basic metabolic panel should be obtained in all suicidal poisoned patients:
- Complete blood count
- Serum electrolytes
- Blood urea nitrogen, creatinine
- Liver functions tests
- Blood glucose, bicarbonate level
- Arterial blood gases
- ECG
- Echocardiography

Special investigations:
- Urine toxicology screening: In the patient with acute intoxication, urine screening for substances of abuse and a blood or breath alcohol level may be considered, but these generally do not alter management. Urine toxicology screening is needed for the following:
  – Amphetamines
  – Barbiturates
  – Benzodiazepines

  - Cannabinoids
  - Cocaine
  - Opioids
  - Phencyclidine
- Caution: A single negative urine toxicology screening or urine immunoassay is not reliable, and repeat tests should be done after a few hours especially if clinical suspicion is high:
  - Blood toxicology profile—if available.
  - If the patient is a female of child-bearing age, a pregnancy test is essential.
  - Serum ethanol level, the anion gap, serum osmolality, and osmolal gap should be performed for alcohol intoxication.
  - A CT scan of the head is advised—if altered mental status is not explained or in the presence of new focal neurological deficit.

Step 6: General management

- The general principle of management of patients with suspected drug overdose or withdrawal is supportive and includes standard resuscitative measures, as mentioned in Chap. 68.
- Once the patient has been stabilized, the physician must consider how to minimize the bioavailability of toxin not yet absorbed, which antidotes (if any) to administer, and what other measures should be undertaken to enhance elimination.
- After initial resuscitation, use the specific antidote when available.

The management of acute intoxication and withdrawal again will depend on the particular neurotransmitters involved (Table 70.2).

Step 7: Manage as per specific class

A. Dissociative drugs
   - *Acute intoxication*: Haloperidol, a presynaptic dopamine antagonist, is useful for blocking significant symptoms of dissociative intoxication.
   - *Dose*: 1 mg IV every 15–20 min up to maximum 10 mg can be given orally or intramuscularly, too.
     Alternative to haloperidol is risperidone.
   - *Chronic intoxication*: Desipramine for postwithdrawal depression.

B. Opiates
   - *Specific antidote* (naloxone, naltrexone, naltrefene): Naloxone, at a dose of 0.1–0.4 mg or 0.01 mg/kg IV, may have to be repeated every 1–2 min.
   - Naloxone should not be used in patients with chronic abuse as it can precipitate seizures or withdrawal.
   - *Withdrawal:* Methadone is the drug of choice, but not easily available. Clonidine orally/Ryle's tube 17 μg/kg/day in three to four doses can be used.

C. Hallucinogens
   - *Acute intoxication*: Benzodiazepines (midazolam, diazepam, alprazolam) are the drug of choice.
   - *Withdrawal*: Fluoxetine can be given orally.

D. Sedative–hypnotic drugs
   - *Acute intoxication*: For supportive management, flumazenil is the specific antidote for benzodiazepines but can precipitate seizures or withdrawal in patients with chronic abuse.
   - *Chronic intoxication/withdrawal:*
     Barbiturates: The equivalent dose of phenobarbitone for a period, which depends on the duration of action of the abused drug for withdrawl effect flumazenil can cause seizure in chronic intoxication of barbiturates.
     Benzodiazepines: Long-acting like chlordiazepoxide (Librium) orally/Ryle's tube maximum up to 25 mg, three to four times a day, or lorazepam 1–2 mg three to four times a day
     Alcohol: Same as benzodiazepines

E. Stimulant drugs
   - *Acute intoxication*: Benzodiazepines (lorazepam) are the drug of choice.
   - *Chronic abuse*: Bromocriptine and/or desipramine can be given orally.

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   This article discusses the various aspects of alcohol and other substance abuse in the emergency department.
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   Subjects who received desipramine showed a decrease in depressive symptoms after a 20- to 40-day period regardless of whether they abused PCP or cocaine.

Snakebite

71

Dhruva Chaudhry, Inder Paul Singh, and Surcharita Ray

A 20-year-old male patient presented with history of diffuse abdominal pain, myalgias, difficulty in swallowing, and pooling of secretions. He also complained of difficulty in breathing and diplopia with acute onset drooping of eyes. He was conscious, oriented to time and space, with a respiratory rate of 12/min and a single breath count of 12. The power in all limbs was 4/5, but all reflexes were absent. He had ptosis, and the rest of the general and systemic examination was normal. He was absolutely normal the previous night, when he had slept on the floor.

Some snakebites result in envenomation. Most of the snakes are nonvenomous. The outcome of snakebite depends on numerous factors which include species of snake, the area of the body bitten, and the amount of venom injected.

Step 1: Initial resuscitation and assessment

Airway

- Management of airway is very important in snakebite.
- The patient should be assessed for any pooling of secretions or respiratory depression with a single breath count of less than 10 and if present should be immediately intubated following the general indications of intubation.

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Breathing

- The patient's oxygenation status can be monitored with a bedside pulse oximeter.
- When the patient is in respiratory distress and not able to maintain oxygenation, he/she should be put on assisted ventilation.

Circulation

- Obtain a good peripheral line and start intravenous fluids.
- Be careful while venipuncturing in patients with coagulopathy.

Step 2: Take detailed history

- Detailed history such as the type of the snake color, length, timing of bite, provoked or unprovoked bite, and first-aid measures done should be taken.
- Patients with snakebite usually present with history of sudden onset of generalized weakness, with diplopia, difficulty in swallowing, pooling of secretions, ptosis, abdominal pain, and diffuse myalgias.
- Ask for local swelling or pain in the body and bleeding from any site including cardiovascular collapse.

Step 3: Perform physical examination

- A comprehensive general physical and neurological examination should be performed in all patients with suspected snakebite.
- The examination may reveal generalized motor weakness with sluggish deep tendon reflexes.
- There may be ptosis and both internal and external ophthalmoplegia giving a false impression of brain stem dysfunction. However, the patient responds to commands by using the frontalis muscle and orbicularis oculi.
- Usually, there are no local reactions in neuroparalytic snake envenomation (krait); however, in cobra bite, severe local reaction can be seen.
- The differential diagnosis of any patient presenting with sudden onset of neurological deficit with respiratory compromise is enumerated in Table 71.1.

Table 71.1 Differential diagnosis of acute neurological weakness

Acute inflammatory demyelinating polyradiculoneuropathy (AIDP, i.e., LGB syndrome)
Transverse myelitis
Periodic paralysis (hypokalemic, hyperkalemic, normokalemic)
Acute myasthenic crisis
Organophosphorus poisoning
Hypomagnesemia and hypophosphatemia
Hypoglycemia
Acute intermittent porphyrias
Polymyositis/dermatomyositis
Tick paralysis
Head/spinalcord injury

Table 71.2 Severity of snakebite

Severity	Local findings	Systemic findings
Nonenvenomation (dry bite)	None or puncture wounds only	None
Mild	Puncture wounds, pain, soft tissue swelling confined to the bite site	None
Moderate	Swelling beyond bite site	Mild nausea, vomiting or fasciculations, paraesthesia, microscopic hematuria
Severe	Severe pain and swelling	Respiratory failure or hypotension or bleeding

- Look for features of local inflammation and if present on the status of circulation.
- Bleeding from the site may be the first manifestation of envenomation.
- Look for hematuria, epistaxis, hematemesis, and ecchymosis.
- Look for blood pressure and carefully follow and monitor.

Step 4: Severity of snakebite
Once a diagnosis of snakebite is made, the patient should be assessed for the severity, as enumerated in Table 71.2.

Step 5: Order investigations
- Complete hemogram with platelet counts, bleeding time (BT), coagulation time (CT), and clot retraction time (CRT) at 20 min or alternately slide test for observing coagulation of blood.
- Urine examination—RBCs in the absence of gross hematuria.
- Prothrombin time, INR, PTTK, fibrinogen level, creatinine kinase, fibrin degradation product, D-dimer.
- If urine is smoky and RBCs absent, look for myoglobulin to rule out myoglobinuria.
- Blood urea and serum creatinine levels should be regularly monitored in patients with renal failure.
- Serum electrolytes and blood gas analysis.

Step 6: Admit to the ICU
- Indications of ICU admission are mentioned in Table 71.3.

Step 7: General management
- All the patients should receive antitetanus toxoid, and the local wound should be cleansed with soap and water.
- The limb with the bite mark should be immobilized; however, no tourniquet should be tied.
- Keep the bitten limb lower than the heart as far as possible.
- Open the tourniquet, if applied outside, only when resuscitative measures are underway.
- Patients with mild features should be observed for at least 24 h.

- Do not apply ice to the bite site.
- Routine use of antibiotics is not recommended.

Step 8: Specific management

Antisnake venom
- Antisnake venom (ASV) is prepared from horses' serum.
- It can be monovalent or polyvalent.
- One milliliter of reconstituted antivenin neutralizes 0.6-mg venom of Indian cobra and Russell's viper and 0.45 mg of common krait and saw-scaled viper.
- If the patient tolerates the ASV, then patients are usually given 50–100 mL of reconstituted ASV in serious envenomation as an infusion over 1 h, after premedication with chlorpheniramine maleate (5 mg) and ranitidine (50 mg).
- It can also be given as push especially when the patient is bleeding profusely at the rate not more than 2 mL/min.
- Patients with moderate and severe envenomation should be given a test dose of ASV intradermally.
- Patients should be observed for any reaction to the ASV.
- ASV will not have a dramatic effect in neuroparalysis. Low-dose ASV is as effective as high dosage in neuroparalytic snake envenomation.
- ASV will however have dramatic effect in stopping bleeding in coagulation abnormalities.
- The patient should be regularly assessed for any signs of reaction to ASV.
- ASV should be given till the patient has no bleeding manifestation or platelet counts rise above 50,000 and resolution of paralysis.

Step 9: Watch for reaction
- ASV is a foreign protein. Therefore, allergic reactions including anaphylaxis are not unknown.
- An adrenaline syringe should always be kept ready before infusing ASV.
- In case the patient is sensitive to ASV or develops reaction to ASV during infusion, first stop the infusion of ASV.
- It should be followed by adrenaline—usual recommended dosage is 0.5 mg of 1:1,000 dilutions subcutaneously.
- Additional dosages of H_1 (chlorpheniramine maleate) and H_2 (ranitidine) blockers with hydrocortisone 100 mg, though later will take 4–6 h to act, should be given simultaneously.
- If needed, adrenaline can be repeated up to two to three dosages or an infusion can be started in dilution of 1:50,000.
- Hypotension is treated with fluids. Inotropes may be required in patients who had overt myocardial dysfunction.

Step 10: ICU management
- Initiate mechanical ventilation at appropriate time as it reduces the mortality significantly in neuroparalytic envenomation.

- Anticholinesterase drugs such as edrophonium and neostigmine have also been recommended for the treatment of neuroparalytic snake envenomation. They should be given with atropine to take care of their harmful effect.
- Ten milligram of edrophonium or 0.5 mg of neostigmine should be given over 2–3 min with atropine (0.6 mg). In case the patient improves, he/she should be managed with neostigmine/atropine over the next 24–48 h.
- General ICU management—propped up nursing, ulcer prophylaxis, DVT prophylaxis, glucose control and appropriate sedation, and analgesia.
- Majority of patients usually recover within 48 h.

Step 11: Manage complications

- Patients who develop complications should be managed in the ICU till they are resolved (Table 71.3).
- Consider fasciotomy and wound debridement if local swelling and necrosis is severe enough to threaten viability of the limb and life.

Table 71.3 Admission to the ICU

Circulatory shock, cardiac dysfunction, pulmonary edema
Hemorrhage, hypovolemia
Coagulopathy, disseminated intravascular coagulation
Coma, seizures, intracranial hemorrhage
Cranial nerve dysfunction
Rhabdomyolysis, renal failure, hyperkalemia
Gastrointestinal bleeding
Respiratory failure
Anaphylaxis (component of venom or antivenom)

Step 12: Discharge from the ICU

The patient can be discharged from the ICU if the following conditions are present:

- Resolution of paralysis more than 24 h
- Fifty percent improvement in creatine phosphokinase and potassium
- Peak expiratory flow rate (PEFR) more than 100 L/min
- Normal oximetry and blood gas analysis on room air
- Normalization of BT, CT, CRT, and platelets more than 50,000
- Stable or improved urine output

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Heat Stroke and Hypothermia

72

Jagdish Dureja and Harpreet Singh

72.1 Heat Stroke

It was the month of July; a 55-year-old male laborer became unconscious at work. On examination, he was found to be obtunded with minimal response to painful stimulus. His skin was hot and flushed. He was tachypneic, tachycardiac, hypotensive, and hyperthermic (core temperature 107°F).

Normal temperature is a balance between heat production and dissipation. High fever can have serious consequences such as renal failure, disseminated intravascular coagulation, and death. Prompt and appropriate management can improve the outcome in these patients.

Step 1: Initiate resuscitation

- These patients should be resuscitated as mentioned in Chap. 78.
- Administer IV fluids promptly as these patients are dehydrated. The type and amount of fluid should be guided by volume status, electrolytes, and cardiac functions.

Step 2: Assess the type of hyperthermia by history and examination

- Hyperthermia is a core temperature greater than 104°F. The most common causes are heat stroke and adverse reactions to drugs.

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Heat stroke is caused commonly by prolonged exposure to excessive heat:

- Exertional heat stroke occurs in young, healthy individuals engaged in heavy exercise during periods of high ambient temperature and humidity.
- Nonexertional heat stroke is precipitated by various conditions. Vasodilation, sweating, and other heat-loss mechanisms are reduced by medications, such as anticholinergic drugs, antihistaminics, and diuretics, antipsychotics (e.g., MAO inhibitors and tricyclic antidepressants), neuroleptic agents, and illicit drugs (amphetamines, cocaine, LSD, MDMA), brain hemorrhage, status epilepticus, and damage to the hypothalamus can also cause hyperthermia. Thyrotoxicosis and pheochromocytoma cause hyperthermia by increased heat production. Malignant hyperthermia is a rare complication of general anesthetics such as succinylcholine and halothane.
- A patient with heat stroke usually has a body temperature above 104°F.
- A high core temperature with appropriate history (e.g., environmental heat exposure, anticholinergics, neuroleptics, tricyclic antidepressants, succinylcholine, and halothane) is needed to diagnose heat stroke.
- Signs and symptoms include altered mentation or seizures, possible hallucinations, delirium, dry skin, rapid pulse, tachypnea, rales due to noncardiogenic pulmonary edema, pupil dilation, muscle rigidity, hypotension, arrhythmias, rhabdomyolysis, dyselectrolytemia, and coma. Disseminated intravascular coagulation and mixed acidosis can accompany the elevated temperature.
- Malignant hyperthermia: This should be suspected if there is sudden rise of $EtCo_2$ in a patient undergoing surgery under general anesthesia.

Step 3: Send investigations

- Hemogram
- Creatine phosphokinase—elevated levels suggest hyperthermia.
- Renal functions
- Urine for myoglobin
- When indicated, coagulation studies, toxicologic screening, CT head, and lumbar puncture should be carried out.
- Diagnosis of malignant hyperthermia is confirmed by in vitro muscle contracture test.

Step 4: General management

- Ask the patient to rest, preferably in a cool place.
- If the patient is conscious, offer fluids but avoid alcohol and caffeine.
- Confirm the diagnosis with a calibrated thermometer to measure high temperature (40–47°C).
- Encourage him/her to shower and bath, or sponge off with cool water.
- There is no role of antipyretics (acetaminophen/acetylsalicylic acid).
- Monitor core temperature continuously with a rectal or esophageal probe.
- In order to avoid iatrogenic hypothermia, stop cooling at 39.5°C (103°F).

- *Cooling measures:* The biggest predictor of outcome is the degree and duration of hyperthermia.
  External cooling techniques are easier to implement and are effective, well-tolerated, and include the following:
  - Conductive cooling—direct application of sources such as hypothermic blanket, ice bath, or ice packs to neck, axillae, and groins. Ice packs are effective but poorly tolerated by the awake patient. Avoid vasoconstriction and shivering as vasoconstriction impedes the heat loss and shivering creates heat.
  - Convective techniques include removal of clothing and use of fans and air conditioners.
  - Evaporative cooling can be accelerated by removing clothing and using a fan in conjunction with misting the skin with tepid water or applying a single-layer wet sheet to bare skin. Shivering may be suppressed with IV benzodiazepines such as diazepam (5 mg) or lorazepam (1–2 mg).
    - Immersing the patient in ice water is the most effective method of rapid cooling but complicates monitoring and access to the patient.
- *Internal cooling techniques* such as ice water gastric or rectal lavage, thoracic lavage, and extracorporeal blood cooling are effective, but they are difficult to manage and are associated with complications. Cold peritoneal lavage results in rapid cooling but is an invasive technique contraindicated in pregnant patients or those with previous abdominal surgery.
- Cold O_2 and cold IV fluids are useful adjuncts.

Step 5: Specific management: Malignant hyperthermia and neuroleptic malignant syndrome

- Dantrolene, a nonspecific skeletal muscle relaxant, is the mainstay of treatment. It acts by blocking the release of calcium from the sarcoplasmic reticulum, thereby decreasing the myoplasmic concentration of free calcium, and diminishes the myocyte hypermetabolism that causes the symptoms.
- It is most effective if given early in the illness, when maximal calcium can be retained within the sarcoplasmic reticulum.
- There is associated risk of hepatotoxicity with dantrolene, so it should be avoided if liver function tests are abnormal (see Fig. 72.1 for detail).

Step 6: Manage complications

- *Rhabdomyolysis*
  - Expand the intravascular volume with normal saline and administer mannitol and sodium bicarbonate.
  - Alkalinization of urine prevents the precipitation of myoglobin in the renal tubules.
  - The goal is to prevent myoglobin-induced renal injury by promoting renal blood flow, diuresis, and urinary alkalinization. Monitor serum electrolytes to prevent life-threatening arrhythmias.

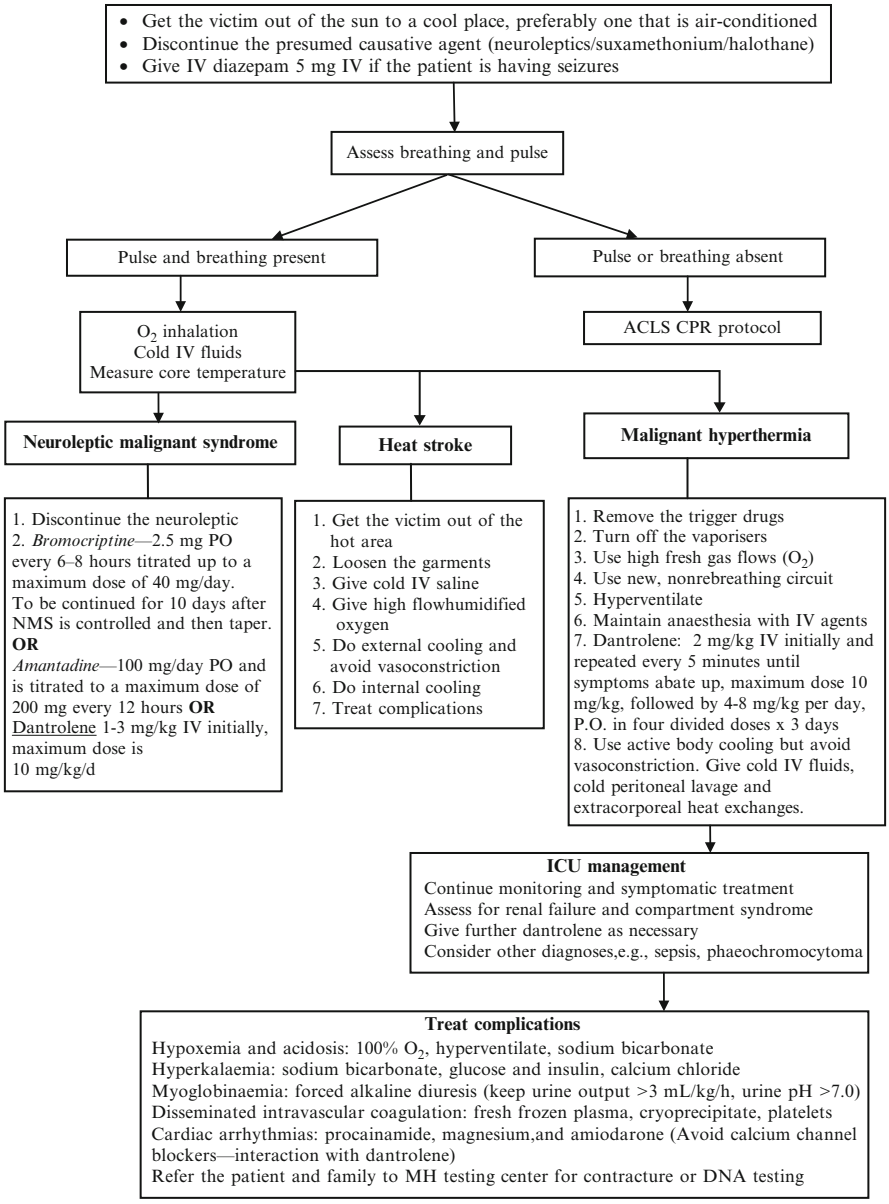

Fig. 72.1 Management of hyperthermia

- *Hypotension:* To sustain organ perfusion, maintain mean arterial pressure of more than 65 mmHg by fluid administration, consider vasopressors, and monitor central venous pressure.
- *Seizures* should be controlled by IV benzodiazepines and barbiturates.
- *Multiorgan failure*: Give supportive therapy until organ function recovers.

Stepwise management of hyperthermia is shown in Fig. 72.1.

Step 7: Prevention

- **Hyperthermia, caused by physical exertion or hot environment, can be prevented by taking frequent rest breaks and staying hydrated.**
- Genetic testing for known mutations of the SKM ryanodine receptor in conjunction with in vitro muscle contracture test can be used to evaluate individual susceptibility in patients from families with a history of malignant hyperthermia.

72.2 Hypothermia

An 82-year-old man, a known case of Alzheimer's disease and hypothyroidism, was found unresponsive on his backyard lawns. He had been taking aspirin, olanzapine, and levothyroxine for the past 3 years. Examination revealed femoral pulse 35/min, blood pressure (BP) unrecordable, Glasgow Coma Scale 3, and temperature 28°C.

Step 1: Initiate resuscitation

Initiate resuscitation as mentioned in Chap. 78:

- The management should start with removal of wet clothing if any and replacing it with warm, dry sheet.
- In severe hypothermia, if indicated, the patient is intubated gently and ventilated with warmed humidified O_2 while closely monitoring cardiac rhythm.
- One should be prepared to treat ventricular fibrillation with DC shock (200 J) and cardiopulmonary resuscitation.
- Start IV line and infuse normal saline at 43°C.

Step 2: Diagnose types and severity of hypothermia

Primary

- Normal thermoregulation
- Overwhelming cold exposure

Table 72.1 Severity of hypothermia

Mild (34–36°C)	Shivering, amnesia/dysarthria, loss of coordination, tachycardia, tachypnea, normal BP
Moderate (30–34°C)	Absent shivering, bradycardia/atrial fibrillation, ↓ BP, ↓ respiratory rate, and stupor
Severe (<30°C)	Coma, absent corneal and oculocephalic reflexes, ↓↓ BP, ventricular fibrillation, apnea, areflexia, dilated and fixed pupils, flat EEG, asystole

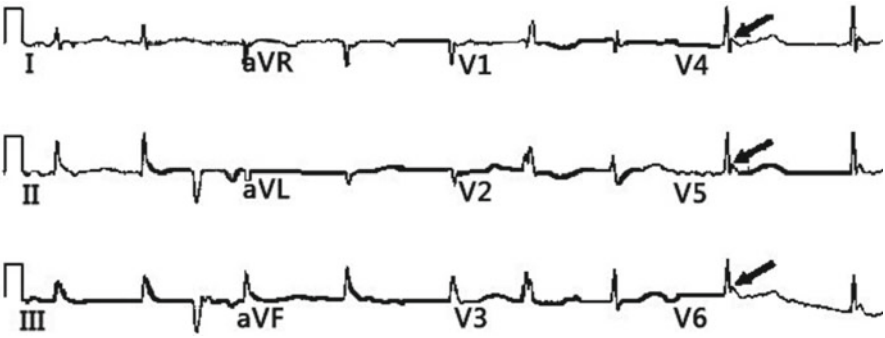

Fig. 72.2 Osborn (J) waves (Marked with arrows)

Secondary

- Abnormal thermogenesis
- Multiple causes (hypothyroidism, burns, hypothalamic abnormalities, sepsis)

Hypothermia is defined as temperature less than 36°C.

Severity of hypothermia with presentation is described in Table 72.1.

- ECG may show Osborn (J) waves especially when temperature is less than 33°C (Fig. 72.2).
- It is a positive deflection, and its amplitude is proportional to the degree of hypothermia, usually seen in leads V3–V6 at junction of QRS and ST segment.

Step 3: Manage hypothermia

The patient should be warmed by the following rewarming methods**:** passive, active external, and active internal.

- *Passive rewarming:* It allows endogenous heat production to increase the core temperature, but heat conserving mechanisms must be intact (e.g., shivering, metabolic rate, and sympathetic nervous system).

It also includes decreasing heat loss by removal from cold environment, removing wet clothes, and providing the blanket. Passive warming increases body temperature by 0.5–2.0°C/h. It is the rewarming method of choice for mild hypothermia and also adjuncts for moderate hypothermia.

- *Active external:* It transfers exogenous heat to the patient. It can be provided by heating blankets (fluid filled), air blankets, radiant warmers, and immersion in hot bath, water bottles, and heating pads. It is less effective than internal rewarming if the patient is vasoconstricted.

  The rewarming rate is 1–2.5°C/h. Although active external warming of extremities can lead to rewarming to some extent, the subsequent vasodilatation of the vessels in the extremities shunts cold blood to the core, resulting in an overall further decrease in body temperature. This paradoxical drop in core temperature is known as the after-drop phenomenon. Circulatory problem may be decreased by applying rewarming devices to trunk only.

  Active internal warming: It is done by the following:
  - Warm IV fluids
  - Humid oxygen
  - Peritoneal lavage
  - Gastric/esophageal lavage
  - Bladder/rectal lavage
  - Pleural lavage
  - Intermittent hemodialysis
  - Extracorporeal circulatory rewarming
  - Atrial arrhythmias should be monitored without intervention, as the ventricular response is slow, and unless preexistent, most will convert spontaneously during rewarming. Preexisting ventricular ectopy may be suppressed by hypothermia and can reappear during rewarming. If available, bretylium tosylate, the class III ventricular antiarrhythmic, is the drug of choice.
  - Electrolytes and thyroid profile should be assessed and corrected if required.
  - Cardiopulmonary bypass is a method of choice used for rewarming patients with cardiac arrest and severe hypothermia. This strategy provides circulation, oxygenation, and ventilation while core body temperature is increased. If cardiopulmonary bypass facilities are not available, a combination of invasive rewarming methods should be used. Once spontaneous circulation is returned, passive or active external rewarming methods can be used. Basic life support should be continued until core temperature is more than 30°C. Cardioactive drugs and further defibrillation should be withheld until this temperature is reached.

  Stepwise management of hypothermia is shown in Fig. 72.3.

If core body temperature does not respond to warming efforts, underlying infection or endocrine derangements must be considered.

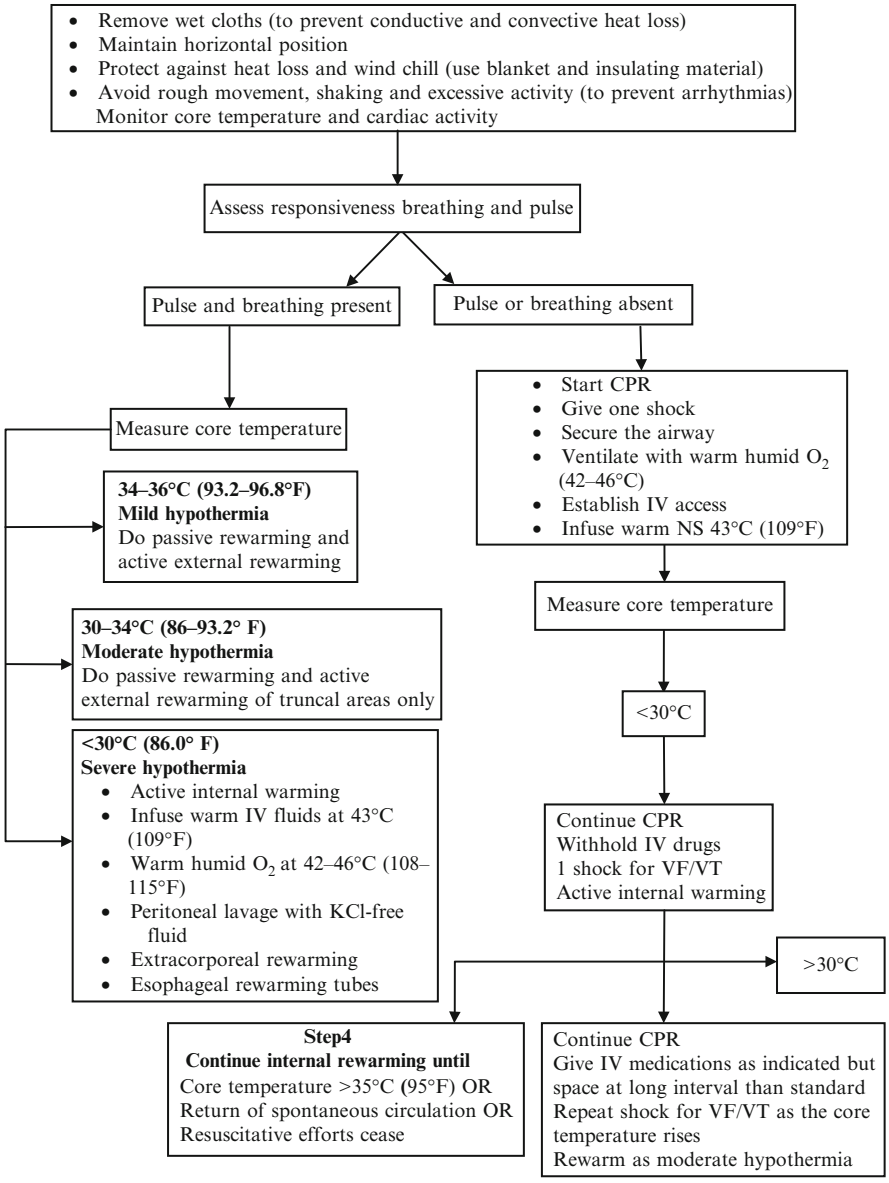

Fig. 72.3 Stepwise management of hypothermia

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Part XI

Obstetrics

Rajesh Chawla and Suninder S. Arora

Jaundice in Pregnancy

73

Rajesh Chawla and Prashant Nasa

A 25-year-old female at 34 weeks of pregnancy had been admitted to the hospital with jaundice for 5 days, altered mental status, and decreased urine output for 8 h. Her antenatal status was fine, with no history of pregnancy-induced hypertension. HBsAg and HIV were negative.

Jaundice in pregnancy can occur due to pregnancy-related and unrelated diseases.

Pregnancy-related liver diseases are real threat to the survival of the fetus and the mother.

Rapid diagnosis is needed to manage them appropriately.

Step 1: Initiate resuscitation

Airway intervention may be required in the following conditions:

- Altered mental status and seizures.
- Acute respiratory failure not responding to conservative measures.
- Cesarean section under general anesthesia.
- Shock – to reduce work of breathing.
- Always anticipate difficult airway in pregnant patients.
- Endotracheal intubation should be performed sooner rather than later to protect the airway.
- Intubation must be performed by the senior intensivist.

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- Difficult airway equipment for airway management must be thoroughly checked before proceeding to intubation, and the alternative plan for definitive airway including surgical access should be identified.
- Raised intracranial pressure (ICP) in the jaundiced pregnant patient is a serious concern, and therefore, proper sedation should be ensured with minimal manipulation during intubation.
- Supplemental oxygen may be required in some patients depending on their oxygen saturation, target SpO_2 more than 95%.

Circulation
- Two large-bore intravenous cannulae (14G or 16G) should be placed to administer fluids.
- Be careful of associated coagulopathy.
- A Foley's catheter should be placed to monitor urine output.
- Use fluid administration judiciously to optimize preload and at the same time to avoid overload, which might increase ICP.
- Nurse in the left lateral position (30° wedge to the right hip) to prevent supine hypotension syndrome.

Disability (neurological)
- Perform a brief neurological assessment including Glasgow coma score, pupil size, and reaction to light in case of altered mental status.

Step 2: Take history and perform physical examination

Take detailed history that should cover the following:
- Details about pregnancy (trimester of pregnancy)
- Antenatal evaluation and immunization
- History of hypertension, pregnancy-induced hypertension during the previous pregnancy, complications and outcome of previous pregnancy, and family history of hypertension
- Duration of jaundice and pruritus, other constitutional symptoms such as malaise, nausea, anorexia, fever, weight loss or increased abdominal girth from ascites, and seizures
- History of abdominal surgery, medication history (amount and time of acetaminophen, herbal medications), and transfusion history
- History of alcohol consumption, HIV and hepatitis risk factors, intravenous drug abuse, exposure to travel, occupational, and recreational history
- History of hepatitis B or C in the spouse

In physical examination, also look for the signs of acute liver failure:
- Altered mental status
- Icterus, anemia
- Ecchymotic patches/bleeding from gastrointestinal tract or urinary tract
- Epigastric or right upper quadrant abdominal tenderness
- Peripheral edema, hyperreflexia, or clonus
- Seizures

Table 73.1 Stages of hepatic encephalopathy

Stage	Mental status	Neuromuscular function
1	Impaired attention, irritability, depression	Tremor, incoordination, apraxia
2	Drowsiness, behavioral changes, memory impairment, sleep disturbances	Asterixis, slowed or slurred speech, ataxia
3	Confusion, disorientation, somnolence, amnesia	Hypoactive reflexes, nystagmus, clonus, muscular rigidity
4	Stupor and coma	Dilated pupils and decerebrate posturing, oculocephalic reflex

Table 73.2 Physiological changes in liver tests during normal pregnancy

Test	Normal range
Bilirubin	Unchanged or slightly decreased
Aminotransferases	Unchanged
Prothrombin time	Unchanged
Alkaline phosphatase	Increases two to four fold
Fibrinogen	Increases by 50%
Triglycerides	Increases
Globulin	Increases in α- and β-globulins
	Decreases in gamma globulin
Cholesterol	Increases twofold
Hemoglobin	Decreases in later pregnancy
WBC	Increases

- Hypotension (hypovolemia, hemolysis, sepsis)
- Spider angioma and palmar erythema may be normal in pregnancy

Step 3: Assess the severity of hepatic encephalopathy
One should assess the severity of hepatic encephalopathy to plan the appropriate treatment (Table 73.1).

Step 4: Send investigations
- Complete blood cell count.
- Liver function tests—remember normal physiological changes in pregnancy (Table 73.2).
- Renal function tests and serum electrolytes.
- Arterial blood gas analysis and blood glucose.
- Hepatotropic virus profile (IgM anti-HEV, IgM anti-HAV, IgM anti-HCV, anti-HBc antibody, HBeAg, HBsAg).
- Coagulation profile (prothrombin time, activated partial thromboplastin time, fibrinogen, fibrin degradation product).
- Uric acid.
- The antinuclear factor—to exclude autoimmune hepatitis.
- Additional tests—peripheral smear, serum lactate dehydrogenase levels, reticulocyte count, and Coombs' test—to exclude thrombotic thrombocytopenic purpura (TTP).

Table 73.3 Classification of liver diseases in pregnancy

	Pregnancy-unrelated liver diseases	
Pregnancy-related liver diseases	Preexisting liver diseases	Liver diseases coincident with pregnancy
Intrahepatic cholestasis of pregnancy (ICP)	Hepatitis B and C	Biliary disease
Preeclampsia and eclampsia	Autoimmune liver disease	Budd–Chiari syndrome
Hemolysis, elevated liver enzymes, low platelet (HELLP) syndrome	Wilson's disease	Drug-induced hepatotoxicity
Acute fatty liver of pregnancy (AFLP)	Cirrhosis and portal hypertension	Viral hepatitis A and E
Hyperemesis gravidarum		

- Ultrasonography is considered safe and is the preferred abdominal imaging modality during pregnancy.
- MRI with contrast is preferable to CT scanning during pregnancy to avoid ionizing radiation.
- Transthoracic echocardiography.

Step 5: Differential diagnosis

The various conditions that can cause acute hepatic failure can be divided into those related to pregnancy and those unrelated to pregnancy (Tables 73.3 and 73.4).

A. *Hyperemesis gravidarum*
   - Incidence: 0.3–2.0% of all pregnancies.
   - Usually within the first trimester.
   - Symptoms: intractable vomiting, resulting in dehydration, ketosis, and weight loss of 5% or more.
   - The cause remains unclear.
   - Risk factors: obesity, psychiatric illness, molar pregnancy, preexisting diabetes, multiple pregnancies, and hyperthyroidism (60%).
   - Serum aminotransferases can rise up to 20 times, but jaundice is rare.

B. *Viral hepatitis*
   - Diagnosis of viral hepatitis in pregnancy is not different from the diagnosis in the nonpregnant state.
   - Herpes simplex virus in patients who are immunosuppressed, and in the pregnant woman, can cause fulminant hepatitis. Aminotransferases are high, and other signs of hepatic failure such as prothrombin time are elevated, but jaundice (increase in bilirubin) is rare.

Step 6: Management

A. *AFLP*
   - Prompt delivery is essential (steroids if fetal maturity in doubt).
   - Supportive treatment, control of hypertension (discussed in Chap. 19), and correction of coagulation abnormalities and hypoglycemia.

Table 73.4 Comparison of severe preeclampsia–eclampsia, intrahepatic cholestasis of pregnancy, HELLP syndrome, and AFLP

	Severe preeclampsia–eclampsia	Intrahepatic cholestasis of pregnancy	HELLP syndrome	AFLP
Trimester	Second to third	Second to third	Third	Third
Incidence (%)	1–5	0.1	0.2–0.6	0.005–0.01
Family history	Occasionally	Often	No	Occasionally
Presence of preeclampsia	Yes	No	Yes	50%
Typical clinical features	Hypertension, edema, proteinuria, neurological deficits (headaches, seizures, coma)	Pruritus, mild jaundice, elevated bile acids	Hemolysis Thrombocytopenia (<50,000 often)	Liver failure with coagulopathy, encephalopathy, hypoglycemia, disseminated intravascular coagulation
Aminotransferases	None/mild	Mild to 10- to 20-fold elevation	Mild to 10- to 20-fold elevation	300–500 typical but variable ++
Bilirubin	Normal—<5 mg/dL	<5 mg/dL	<5 mg/dL unless massive necrosis	Often <5 mg/dL, higher if severe
Hepatic imaging	Normal—hepatic infarcts	Normal	Hepatic infarcts hematomas, rupture	Fatty infiltration
Histology (usually not performed)	Periportal hemorrhage, necrosis, fibrin deposits	Normal–mild cholestasis, no necrosis	Patchy/extensive necrosis and hemorrhage	Microvesicular fat in zone 3
Recurrence in subsequent pregnancies	20% risk	45–70%	4–19%	Subunit, long-chain 3-hydroxyacyl-CoA dehydrogenase defect—yes No fatty acid oxidation defect—rare

- Manage complications:
  - Renal failure
  - Acute pulmonary edema or acute respiratory distress syndrome
  - Coagulopathy/disseminated intravascular coagulation
- Rarely, liver transplantation is indicated for liver rupture with necrosis, fulminant liver failure, hepatic encephalopathy, or worsening coagulopathy.

B. *Hyperemesis gravidarum*
- Treatment is supportive and includes intravenous rehydration and antiemetics.
- Vitamin supplementation, including thiamine, is mandatory to prevent Wernicke's encephalopathy.
- There is no role of steroids.
- Relapse and recurrence in subsequent pregnancies is common.

C. *Intrahepatic cholestasis of pregnancy*
- Treatment of choice is ursodeoxycholic acid, which helps to relieve pruritis and improve hepatitis.
- Mechanism of action is unknown.
- Other drugs are cholestyramine, dexamethasone, and vitamin K supplementation.
- Termination of pregnancy—when medical measures fail or if the patient's condition deteriorates.

D. *Management of severe preeclampsia–eclampsia and HELLP syndrome (discussed in Chap. 75)*
- Treatment of hepatic rupture should be delegated to a surgeon experienced in the management of hepatobiliary surgeries.

E. *Viral hepatitis*
- Treatment is mainly supportive and similar to nonpregnant patients.
- Course is not altered by delivery.
- Herpes simplex hepatitis can be effectively treated with acyclovir if the diagnosis is recognized promptly.

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Acute Respiratory Failure During Pregnancy

74

Rajesh Chawla, Prashant Nasa, and Aakanksha Chawla

A 25-year-old female at 36 weeks of pregnancy was admitted to hospital with complaints of breathlessness, right sided chest pain, and swelling of the left leg for 3–4 days. Her BMI was 40 kg/m^2. She was tachypneic, chest was clear, and SpO_2 on room air was 90%.

Acute respiratory failure during pregnancy can occur due to many disorders. It can result in significant maternal and fetal morbidity and mortality.

Step 1: Initiate assessment and resuscitation

Airway

- Airway evaluation and management remains the first priority in the initial resuscitation as in nonpregnant patients.
- Definitive airway (tracheal intubation) is needed in persistent hypoxemia, airway obstruction, impaired laryngeal reflexes, or in altered consciousness.
- Difficult airway equipment for airway management must be thoroughly checked before proceeding to intubation, and an alternative plan for definitive airway including surgical access should be identified.
- Intubation should be performed by a senior intensivist/anesthesiologist especially in later part of pregnancy due to upper airway edema and narrow airway caliber.

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Breathing

- Supplemental oxygen may be required in some patients depending on their oxygen saturation.
- Noninvasive ventilation (NIV) can be tried only in the controlled ICU setting. Signs of failure of NIV and requirement of intubation should also be identified sooner than later. This includes increased work of breathing, mental status deterioration, hemodynamic instability, and inability to protect the airway or manage secretions.
- Always target SpO_2 of more than 95%. For adequate fetal oxygenation, a maternal arterial oxygen tension (PaO_2) of more than 70 mmHg is required, which corresponds to an oxyhemoglobin saturation of 95%.

Circulation

- Two large-bore intravenous cannulae (14G or 16G) should be placed to administer fluids.
- Administrate fluid judiciously to optimize preload and at the same time to avoid overload.
- Maintain high cardiac output.
- Nursing in the left lateral (30° wedge to the right hip) position is needed to prevent supine hypotension syndrome.

Step 2: Take history and physical examination

- Take detailed history of pregnancy, antenatal evaluation and immunization, respiratory disease (e.g., asthma and tuberculosis), and family history of active respiratory infections.
- Detailed history of respiratory symptoms such as dyspnea, cough, expectoration, and chest pain should be evaluated.
- The physical examination includes assessment of the severity of respiratory failure by general assessment, respiratory rate, use of accessory respiratory muscles, and signs of impending respiratory arrest (e.g., fatigue, drowsy, silent chest, and bradycardia).
- Assessment of the fetus is also important. Fetal heart sounds and its variability—to ascertain the fetal well-being—should be assessed along with the maternal assessment.

Step 3: Understand physiological changes in pregnancy

- Pregnancy causes various mechanical, immunological, biochemical, and hemodynamic changes on the cardiorespiratory system (Table 74.1).
- Normal $PaCO_2$ on ABG should be interpreted as a sign of impending respiratory failure as there is a mild respiratory alkalosis in pregnancy (see Table 74.1).
- Inability to maintain a PaO_2 of more than 70 mmHg, or a SaO_2 of more than 95%, with conservative therapy should also be interpreted as a sign of respiratory compromise.

Table 74.1 Effects of pregnancy on pulmonary physiology

	Anatomical changes	Physiological alterations
Airway	Edema, mucosal friability, rhinitis	Increased respiratory drive
		Hyperventilation
Thorax including lung parenchyma	Widened diameters, widened subcostal angle, elevated diaphragm	Reduced functional residual capacity
		Increased tidal volume
		Preserved vital capacity
		Respiratory alkalosis
		Normal oxygenation
Abdomen	Enlarged uterus	Reduced chest wall compliance
Cardiovascular system	Increased left ventricular (LV) mass	Increased cardiac output
	Increased blood volume	
Arterial blood gas		7.40–7.45 pH
		28–32 mmHg $PaCO_2$
		106–110 mmHg PaO_2

Step 4: Send investigations

- Complete hemogram.
- Liver function tests.
- Renal function tests and serum electrolytes.
- Arterial blood gas.
- Coagulation profile (prothrombin time [PT], activated partial thromboplastin time [aPTT], and fibrinogen international normalized ratio).
- Sputum examination/tracheal secretions—Gram stain and aerobic culture sensitivity.
- Paired percutaneous blood cultures.
- Additional tests if indicated—D-dimer does not help in pregnancy.
- Chest X-ray only if absolutely necessary.
- Multidetector computed tomographic (MDCT) pulmonary angiography if clinical situation demands.
- Ultrasonography is used to assess the status of the fetus, to evaluate growth, and in suspected case to evaluate deep venous thrombosis.
- Transthoracic echocardiography

Step 5: Make a diagnosis of respiratory failure in pregnancy

The various causes of acute respiratory failure are summarized in Table 74.2.

A. *ARDS*
   - The criteria for diagnosis of ARDS are similar to nonpregnant women (see Chap. 5).

B. *Asthma in pregnancy*
   - Rule of thirds—one-third of patients with asthma in pregnancy improve, and one-third shows no change. One-third worsens and can present in acute severe asthma.
   - This explains the unpredictable effect of pregnancy on asthma.

Table 74.2 Differential diagnosis of acute respiratory failure during pregnancy

Conditions unique to pregnancy	Conditions can be affected by pregnancy	Conditions unaffected by pregnancy
Peripartum cardiomyopathy	Acute pulmonary edema	ARDS—direct/pulmonary
		Bacterial pneumonia
Amniotic fluid embolism	Aspiration of gastric contents	Fat embolism
Tocolytic therapy-induced acute pulmonary edema	Asthma	Inhalational injury
Severe preeclampsia	Venous thromboembolism	Indirect
Chorioamnionitis, endometritis	Bacterial and viral pneumonia	Sepsis, trauma, burns
Ovarian hyperstimulation syndrome (OHSS)	Malaria, fungal infections	Acute pancreatitis, transfusion-related acute lung injury (TRALI)

C. *Pulmonary embolism in pregnancy*
- Pregnancy itself is a hypercoagulable state and an independent risk factor for pulmonary embolism (PE).
- Clinical prediction models that are used to predict pretest probability of PE have not been validated in pregnant patients.
- D-dimers are likely to perform differently in the pregnant population as D-dimers may be falsely high in pregnant patients.
- Radiographic imaging remains the primary testing modality for diagnosing PE, and it should not be delayed because of concerns about radiation exposure.
- Multidetector computed tomography (MDCT) pulmonary angiography is currently the most preferred mode for confirming diagnosing PE in pregnant patients (Fig. 74.1).
- The main concerns with MDCT are radiation and contrast exposure to the fetus in suspected PE. It has been seen that the exposure of radiation is less to the fetus.
- Compression ultrasonography and transesophageal echocardiography (TEE) are the initial test of choice to exclude deep venous thrombosis.
- Chest radiographs involve minimal radiation; they rarely show signs suggestive of PE, which may detect other diagnosis.
- The accuracy of ventilation-perfusion scan in pregnancy is not available, and outcome studies are limited.

D. *Ovarian hyperstimulation syndrome (OHSS)*
- Gestation of 3–8 weeks.
- Increased vascular permeability—fluid shift from the intravascular to extravascular space—causing pleural or pericardial effusions, ascites, electrolyte imbalances, dyspnea, oliguria, severely enlarged polycystic ovaries, hemoconcentration, and hypercoagulability, electrolyte imbalance are the common presentations.

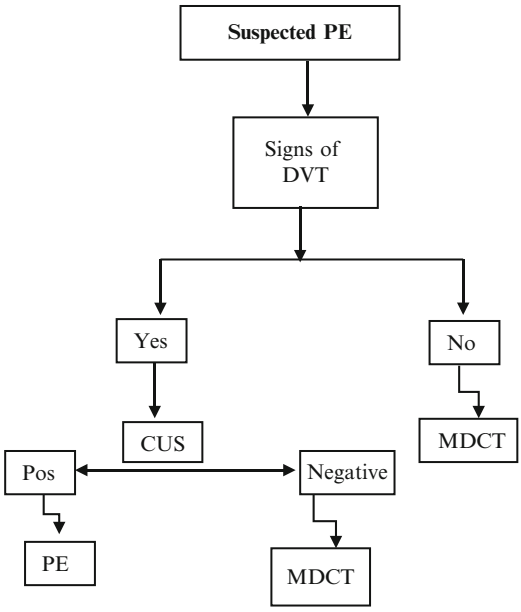

Fig. 74.1 Diagnosis of PE

Table 74.3 Criteria that define the severe and life-threatening stages of OHSS

Severe OHSS	Life-threatening OHSS
Variably enlarged ovary	Variably enlarged ovary
Massive ascites with or without hydrothorax	Tense ascites with or without hydrothorax
Hematocrit >45%	Hematocrit >55%
WBC count >15,000	WBC count >25,000
Oliguria	Oliguria
Creatinine level 1.0–1.5 mg/dL	Creatinine level ≥1.6 mg/dL
Creatinine clearance ≥50 mL/min	Creatinine clearance <50 mL/min
Liver dysfunction	Renal failure
Anasarca	Thromboembolic phenomena
	ARDS

- The common criteria for severe and life-threatening OHSS are described in Table 74.3.

E. *Peripartum cardiomyopathy (PPCM)*

- Risk factors include hypertension, preeclampsia, multiparity, multiple gestations, and older maternal age.
- Signs and symptoms are paroxysmal nocturnal dyspnea, chest pain, nocturnal cough, new regurgitant murmurs, pulmonary crackles, increased jugular venous pressure, and hepatomegaly.
- Identify other cardiac and noncardiac disorders such as coronary, rheumatic, or valvular heart disease; arrhythmias; and family history of cardiomyopathy

Table 74.4 Clinical criteria for the diagnosis of PPCM

Development of cardiac failure in the last month of pregnancy or within 5 months postpartum
Absence of another identifiable cause for the cardiac failure
Absence of recognizable heart disease before the last month of pregnancy
LV systolic dysfunction shown by echocardiographic data such as depressed shortening fraction (e.g., ejection fraction less than 45%, M-mode fractional shortening less than 30%, or both, and an LV end diastolic dimension of more than 2.7 cm/m^2)

or sudden death and other risk factors of cardiac diseases such as hypertension (chronic, gestational, preeclampsia), diabetes, dyslipidemia, thyroid disease, anemia, prior chemotherapy or mediastinal radiation, sleep disorders, current or past alcohol or drug abuse, and collagen vascular disease.

- The diagnosis of PPCM is a diagnosis of exclusion and should be made when other possible causes of acute/subacute heart failure have been ruled out (Table 74.4).

Step 6: Treat the specific cause

The general management of respiratory failure in pregnancy is similar to the management in nonpregnant women, although one should be careful about normal physiologic alterations that occur in the parturient state and effect of ventilator strategies.

A. *Management of ARDS and mechanical ventilation in pregnant patients*
   - Lung-protective strategy to avoid volutrauma, biotrauma, atelectrauma, leading to less ventilator-induced lung injury has been found to reduce mortality and improve outcome in patients with ARDS.
   - Lung-protective strategy causes hypoventilation, which is tolerated to maintain (permissive hypercapnia) the pH between 7.25 and 7.35.
   - Permissive hypercapnia can cause fetal acidosis, an increase in intracranial pressure, and a right shift in the hemoglobin dissociation curve and in first 72 h may lead to retinopathy of prematurity, so lung-protective ventilatory strategy in pregnant patients should be used with close monitoring of the fetal status with the biophysical profile.
   - Oxygen levels should be closely monitored in pregnancy and kept higher than in nonpregnant women (preferably $SpO_2 \geq 95\%$).

B. *Management of asthma in pregnancy*
   - Management of asthma in pregnancy is similar to nonpregnant women.
   - Beta-agonists bronchodilators and corticosteroids are the mainstay of the treatment.

C. *PE during pregnancy*
   - Acute treatment of PE can be done with low-molecular-weight heparin (LMWH) or unfractionated heparin (UFH) and should be started without delay whenever PE is suspected or confirmed.
   - LMWH is first-line therapy for the treatment of acute PE in the general population and in pregnancy as the risk of bleeding in pregnant women is not different from nonpregnant women.

- Thrombolysis increases the risk of obstetric and neonatal complications such as pregnancy loss, abruption, and preterm labor. Therefore, the use of thrombolytics in pregnancy should be reserved for women with PE who are hemodynamically unstable or with refractory hypoxemia.
- The American College of Chest Physicians guideline recommends the use of anticoagulation for 6 months at least in the postpartum period.
- Always give injectable heparins during the entire period of pregnancy. Start oral anticoagulants only after delivery.

D. *OHSS*
- Syndrome is self-limiting, and resolution parallels the decline in serum HCG levels: 7 days in nonpregnant patients and 10–20 days in pregnant patients.
- Monitor frequently for deterioration with physical examinations, daily weights, and periodic laboratory measurements of complete blood counts, electrolytes, and analysis of renal and hepatic function.
- Severe disease—placement of two large-bore peripheral intravenous catheters or a central venous catheter (preferred) for fluid management may be required.
- Use the Foley's catheter for close monitoring of the urine output.
- Normal saline with or without glucose is the crystalloid of choice, and potassium-containing fluids should be avoided because patients with OHSS could develop hyperkalemia.
- In more severe cases with significant hypovolemia, hemoconcentration (hematocrit >45%), hypoalbuminemia (serum albumin level <3.0 g/dL), or severe ascites, albumin can be given as a plasma expander along with diuretics (furosemide) once hematocrit is 36–38%.
- If respiratory symptoms worsen, thoracentesis/paracentesis should be performed.
- If ARDS develops and mechanical ventilation is required, lung-protective strategies must be used.

E. *PPCM*
- Diuretics are indicated for most patients because they cause symptomatic relief of pulmonary and peripheral edema and are usually used as adjuvant to other definitive therapies. Furosemide is the most commonly used diuretic.
- Aldosterone antagonists have been shown to improve survival in selected heart failure patients. These agents are still not advised in pregnancy (lack of safety data); however, they can be added postpartum.
- Hydralazine and nitrates are the vasodilators of choice for pregnant women, as angiotensin-converting enzyme inhibitors, the first-line agent for nonpregnant patients, are contraindicated for pregnant women.
- β-Blockers (sustained-release metoprolol succinate, carvedilol, and bisoprolol) have been shown to reduce mortality with current or prior heart failure and reduced ejection fraction and therefore constitute the first-line therapy for all stable patients unless contraindicated (Table 74.5).
- Digoxin improves symptoms, quality of life, and improves exercise tolerance in mild-to-moderate heart failure.

Table 74.5 Treatment of PPCM

Nonpharmacological measures	Drugs for routine use	In selected patients	Therapies avoided
Hypertension control (salt restriction)	Diuretics	Aldosterone antagonists	Angiotensin-converting enzyme inhibitors
Fluid restriction	β-Blockers	Inotropes	Angiotensin receptor blockers
	Digoxin	Anticoagulation	Many antiarrhythmic drugs
	Vasodilators	Implantable defibrillators	Nonsteroidal antiinflammatory drugs
		Biventricular pacing	Nondihydropyridine calcium channel blockers
		Cardiac transplantation	

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Severe Preeclampsia

75

Rajesh Chawla, Prashant Nasa, and Renu Chawla

A 23-year-old female at 30 weeks of pregnancy was admitted to the hospital with an episode of seizure, epigastric pain, and decreased urine output. She had pedal edema, and her blood pressure (BP) on admission was 190/110 mmHg. Her urine output was 300 mL in the past 24 h. Urine examination showed protein 4+ and hemoglobin 8 g%. Liver function test showed elevated aspartate aminotransferase and alanine aminotransferase.

Hypertensive disorders complicate 5–10% of all pregnancies. Preeclampsia either alone or superimposed on chronic hypertension may be associated with adverse outcomes.

Step 1: Initial assessment and resuscitation

- Always anticipate difficult airway in pregnant patients (Table 75.1).
- Endotracheal intubation should be performed by a senior intensivist/anesthesiologist.
- Difficult airway equipment for airway management must be thoroughly checked before proceeding to intubation, and alternative plan for definitive airway including surgical access should already be identified.

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Table 75.1 Risk factors for difficult airway during pregnancy

Progesterone-induced airway edema is further exacerbated in pregnancy-induced hypertension (PIH)
Thick neck, large breasts
Increased risk of hypoxemia—decreased cardiopulmonary reserve and increased metabolic requirements
Increased risk of aspiration of gastric contents

- Supplemental oxygen may be required in some patients depending on their oxygen saturation.
- Target SpO_2 more than 95% with oxygen or ventilation.

Circulation
- Two large-bore intravenous cannulae (14G or 16G) should be placed to administer fluids.
- The Foley catheter should be placed to monitor urine output.
- Judicious fluid administration is needed to optimize preload and at the same time to avoid overload.
- Nurse in the left lateral position (30° wedge to the right hip) to prevent supine hypotension syndrome.

Disability (neurological)
- Magnesium sulfate is a drug of choice for control of seizures.
- 4–6 g is diluted in 100 mL of IV fluid bolus over 20 min.

Step 2: Taking history and physical examination
- Detailed history should be taken about pregnancy, antenatal evaluation, immunization, hypertension, and PIH (pregnancy induced hypertension) during the previous pregnancy.
- Complications and outcome of the previous pregnancy and family history of hypertension should be required.
- History includes symptoms displaying end-organ effects to detect presence of severe preeclampsia:
  - Headache
  - Visual disturbances—blurred, scintillating scotomas
  - Altered mental status
  - Blindness
  - Dyspnea
  - Edema
  - Epigastric or right upper quadrant abdominal pain
  - Weakness or malaise—may be evidence of hemolytic anemia
- The physical examination includes the evaluation of end-organ dysfunction for diagnosis of severe preeclampsia:
  - Altered mental status
  - Decreased vision or scotomas

Table 75.2 Criteria for diagnosing severe preeclampsia

Systolic BP of 160 mmHg or higher or diastolic BP of 110 mmHg or higher on two occasions at least 6 h apart
Proteinuria of more than 5 g in a 24-h collection or more than 3+ on two random urine samples collected at least 4 h apart
Pulmonary edema or cyanosis
Oliguria (<400 mL in 24 h)
Thrombocytopenia, DIC, HELLP
Persistent headaches
Epigastric pain and/or impaired liver function
Oligohydramnios, decreased fetal growth, or placental abruption

  - Papilledema
  - Epigastric or right upper quadrant abdominal tenderness
  - Peripheral edema
  - Seizures
  - Focal neurologic deficit
- PIH (preeclampsia) is defined as presence of hypertension (BP ≥140/90 mmHg) on two occasions, at least 6 h apart in more than 20 weeks' gestation in women with previously normal BP and who have proteinuria (≥0.3 g protein in 24-h urine specimen), with or without pedal edema.
- Severe preeclampsia is defined in Table 75.2.
- Eclampsia is defined as seizures that cannot be attributable to other causes in a woman with preeclampsia.

Step 3: Send investigations
- Complete blood cell count.
- Liver function tests.
- Renal function tests and serum electrolytes.
- Arterial blood gas and blood glucose.
- Coagulation profile (prothrombin time [PT], activated partial thromboplastin time [aPTT], and fibrinogen, international normalized ratio).
- Lactate dehydrogenase.
- Uric acid.
- Urine routine microscopy, 24-h urine protein, and creatinine.
- Additional tests—peripheral smear, serum magnesium levels.
- Ultrasonography is used to assess the status of the fetus as well as to evaluate growth retardation.
- Transthoracic echocardiography.

Step 4: Make a differential diagnosis (Table 75.3)

Step 5: Admit to the ICU and monitor closely

ICU admission is indicated with:
- Obstetric hemorrhage

Table 75.3 Differential diagnosis

Severe preeclampsia (abdominal pain)
Abruptio placentae
Abdominal aneurysm
Acute appendicitis
Blunt abdominal trauma
Cholecystitis and biliary colic
Encephalitis
Hypertensive emergencies
Ovarian torsion
Status epilepticus
Thrombotic thrombocytopenic purpura
Poisoning
Eclampsia (seizure)
Cerebrovascular accidents
Brain tumors
Brain infections—meningitis, encephalitis, abscesses
Thrombotic thrombocytopenic purpura
Metabolic disorders
Hypertensive encephalopathy
Illicit drug use
Postdural puncture syndrome
Epilepsy
Posterior reversible encephalopathy syndrome

- Placental abruption
- Severe preeclampsia/eclampsia
- Hemolysis, elevated liver enzymes, and low platelet (HELLP) syndrome
- Chorioamnionitis
- Acute pulmonary edema
- Respiratory failure
- Acute respiratory distress syndrome
- Acute renal failure

Maternal monitoring is required with severe preeclampsia:

- Repeated clinical assessment including neurological examination (deep tendon reflexes for magnesium toxicity).
- ECG.
- Arterial BP—noninvasive BP can be tried initially but may be incorrect with inadequate cuff size.
- Pulse oximetry.
- Foley catheterization—urine output monitoring.
- Blood gas monitoring.
- CVP monitoring—infusion of vasopressors.
- Additional—intra-abdominal pressure during resuscitation, serum magnesium levels.

Step 6: Management of severe preeclampsia

The most important aspect in the management of severe preeclampsia is control of hypertension.

A. *BP control*

- Arterial pressure greater than 160/110 mmHg in preeclampsia can increase the risk of complication, and it should be controlled.
- BP control should only be done in the ICU, preferably with arterial line monitoring.
- BP control should also be done along with fetal monitoring. Avoid sudden fall in BP as it can result in fetal distress.
- Goal of BP control is 15–25% reduction in the mean arterial pressure, and reduction of pressure to normal levels (<140/90 mmHg) should be avoided as it may compromise placental perfusion.
- *Drugs*
  - Labetalol (IV 20 mg) can be given initially followed by doubling the dose every 10 min to a cumulative dose of 300 mg. This drug can result in severe bradycardia. A continuous infusion of labetalol at a rate of 0.5–2 mg/min can also be used.
  - Hydralazine (5–10 mg) can be given every 20 min (maximum of 40 mg) until BP is controlled.
  - Nifedipine or nicardipine can be given (sudden precipitous decrease in BP or bradycardia can occur).
  - Intravenous nitroglycerin (10–100 mg/min) or sodium nitroprusside (2–8 mg/min) can be given. Prolonged use of nitroglycerin may lead to methemoglobinemia. Cyanide toxicity in the mother and fetus may occur with sodium nitroprusside, limiting its use to less than 4 h and only as a last resort.

B. *Seizure control*

- The initial management of eclampsia includes airway, breathing, and circulation.
- The initial bolus of magnesium (4 g over 20 min) is followed by an infusion of 1–2 g/h.
- The mechanism of action of magnesium is unknown, but magnesium suppresses excitatory neurotransmitter release by replacing calcium at nerve endings.
- Monitor toxicity—loss of deep tendon reflexes; loss of patellar reflex occurs when the plasma magnesium level is more than 10 mg%. Look for respiratory muscle weakness.
- Magnesium has a relatively narrow therapeutic range, and target magnesium serum concentrations are 5–8 mg/dL.
- Infusion dose should be reduced in case of renal dysfunction. Serum magnesium level should be monitored Table 75.4.
- In recurrent seizure, additional 2 g of magnesium sulfate can be given concurrently with the magnesium sulfate infusion.
- If seizures are not controlled by repeat magnesium bolus, then diazepam or lorazepam can be administered (See chap. 28).
- Discontinue magnesium sulfate 24 h after delivery.

Table 75.4 Clinical manifestations related to serum concentration of Magnesium

Serum magnesium levels (mg/dL)	Effects
5–8	Therapeutic
8–12	Loss of deep tendon reflexes
>12	Prolonged atrioventricular conduction
15–17	Muscular paralysis and respiratory difficulties
>20	Cardiac arrest

C. *Fluid management*
- Despite the peripheral edema, patients with preeclampsia are volume depleted with high peripheral vascular resistance. Diuretics should be avoided.
- Aggressive volume resuscitation, on the other hand may lead to pulmonary edema, which is a common cause of maternal morbidity and mortality. Because volume expansion has no demonstrated benefit, patients should be fluid restricted when possible, at least until the period of postpartum diuresis.
- Central venous or pulmonary artery pressure monitoring or other hemodynamic monitoring modality may be indicated in critical cases.
- Careful measurement of fluid input and output is advisable, particularly in the immediate postpartum period.

D. *Delivery*
- Women with severe preeclampsia who are managed expectantly must be delivered under the following circumstances:
- Nonreassuring fetal heart status
- Uncontrollable BP
- Oligohydramnios, with amniotic fluid index of less than 5 cm
- Severe intrauterine growth restriction
- Oliguria (<500 mL/24 h)
- Serum creatinine level of at least 1.5 mg/dL
- Pulmonary edema
- Shortness of breath or chest pain with pulse oximetry of <94% on room air
- Headache that is persistent and severe
- Right upper quadrant tenderness with deteriorating liver function test
- Development of HELLP syndrome

Step 7: Watch for complications
- Abruptio placentae
- Disseminated intravascular coagulopathy (DIC)
- Renal insufficiency and acute renal failure
- HELLP syndrome
- Eclampsia
- Cerebral hemorrhage
- Fetal changes—intrauterine growth restriction, abruptio placentae, oligohydramnios
- Intrauterine fetal death

Step 8: Managing complications

HELLP syndrome

- HELLP syndrome can complicate 4–12% of patients with severe preeclampsia.
- Signs and symptoms are right upper quadrant or epigastric pain, nausea and vomiting, malaise, and nonspecific viral-like symptoms. Physical examination findings include right upper quadrant or epigastrium tenderness and generalized edema.
- Delivery is the definitive treatment for HELLP syndrome.
- Delivery is indicated for women with HELLP syndrome at greater than 34 weeks' gestation. During labor and for 24-h postpartum, patients should receive intravenous magnesium sulfate for seizure prophylaxis.
- If gestation is less than 34 weeks, delivery may be delayed for a steroid course of betamethasone (12 mg intramuscularly, every 24 h) in two doses, with delivery 24 h after the last dose.
- Platelets are generally transfused when the platelet count is less than 20,000/mm^3. For cesarean delivery or with any significant bleeding, platelets should be transfused if the platelet count is less than 50,000/mm^3.

Acute pulmonary edema

- Management is similar as in nonpregnant patients.
- Intravenous furosemide (bolus 20–40 mg over 2 min) is used to promote diuresis. The repeated doses of 40–60 mg are given after 30 min or infusion if there is inadequate diuretic response (maximum dose 120 mg/h).
- Careful fetal monitoring, fluid restriction, and strict fluid balance and positioning (such that the head is elevated) are required.

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Part XII

Perioperative Care

Prakash Shastri and Deepak Govil

General Issues in Perioperative Care

76

Prakash Shastri, Yogendra Pal Singh,
and Jigeeshu V. Divatia

A 45-year-old, previously healthy, female was admitted to the ICU in a state of shock. She had history of pain in the abdomen and vomiting. She had undergone vaginal hysterectomy and posterior floor repair under general anesthesia for prolapsed uterus a week back and apparently made complete recovery. After successful resuscitation, the surgeon was consulted who decided to perform an exploratory laparotomy.

Intensive care physicians are increasingly being involved in taking care of surgical patients perioperatively, due to acute physiological derangements which occurs during anesthesia and surgery and requirement for close monitoring. Principles of resuscitation and a coordinated care, essential ingredients for caring for any acutely ill patient, are equally applicable to perioperative patients.

Step 1: Assess the reason for perioperative admission to the ICU

- Perioperatively, the patient may be admitted to the ICU for the following reasons:
  - Elective preoperative admission for monitoring and optimization of hemodynamics and respiratory status in high-risk cases.
  - Elective postoperative admission for monitoring and organ support for high-risk and major surgeries

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    - Airway monitoring in major oral, head, and neck surgery
    - Flap monitoring in major plastic surgery
    - Elective ventilation after prolonged surgery
  - Emergent postoperative admission for unexpected intraoperative complications
    - Intraoperative severe blood loss
    - Hemodynamic instability due to arrhythmia and myocardial ischemia
    - Intraoperative cardiac arrest
    - Respiratory complications postextubation
- The approach in the form of initial resuscitation, monitoring, and intensity of investigation would be different in each of these situations.

Step 2: Obtain a complete and detailed handover from the anesthesia and surgical teams, take focused history, and perform physical examination

- Confirm the patient's identification
- Type of surgery
- Duration of surgery
- Anesthesia chart and postoperative notes—airway problem during intubation
- Intraoperative complications, estimated blood loss, and transfusions of blood and blood products
- Postoperative instructions
- Surgical drains placement
- Fluids, antibiotics, analgesia, antiemetic prescription
- Epidural catheters or patient-controlled analgesia (PCA) pumps
- Review of the medical records of the patient
- Drug history—aspirin, other antiplatelet agents, oral anticoagulants, and oral hypoglycemics

Step 3: Identify immediate postoperative problems

- The following are the initial general concern in immediate postoperative period in the ICU:
- *Postoperative pain*
  - Aggressive and appropriate pain relief is an essential component of any postoperative care and should be managed in consultation with the pain management team.
  - Pain should be assessed objectively with a pain scale and analgesia is titrated according to the patient's response (see Chap. 33).
  - The following modalities of pain relief are usually available:
    - Intermediate and long-acting opioid analgesics (morphine 2–4 mg) intravenously in aliquots or via PCA. During PCA, morphine is generally given without continuous infusion, and a common initial setting is 1 mg boluses on demand with a lock-out period of 10 min.
    - Nonsteroidal opioid analgesic (e.g. diclofenac intravenously/intramuscularly/rectal suppository). These should be avoided in patients at risk of renal injury, including elderly patients, and in those who have suffered intraoperative hemodynamic compromise.

  - Intravenous paracetamol.
  - Intravenous tramadol.
  - Intrathecal/epidural opioid and local anesthetic combinations (thoracic, abdominal, gynecological, and major orthopedic surgery).
  - Intra-articular infiltration with opioid/local anesthetics (joint surgery).
  - Nerve blocks.
- *Persistent sedation*
  - Review the chart for perioperative anesthetic and sedative agents administered.
  - Residual effect of anesthetic drugs is the most common cause, and treatment is expectant with close watch on airway. Rarely, reversal of opioids with naloxone is required.
  - If effect remains prolonged, other causes such as hypothermia, hypercarbia, hypoglycemia, and hyponatremia should be looked for.
  - Residual neuromuscular blockade is another important cause of hypoventilation and "delayed recovery." It can be diagnosed using a peripheral nerve stimulator.
- *Nausea and vomiting*
  - Postoperative nausea and vomiting is a troublesome complication of general anesthesia.
  - Manage with reducing doses of opioids, changing to alternative analgesics.
  - Give ondansetron 4–8 mg intravenously.
- *Altered mental state*
  - Occasionally, abnormal behavioral response during recovery from anesthesia is encountered and is usually due to medication effect and is rarely due to hypoxia, acidosis, or hypotension.
  - Reassurance, avoidance of hypnotics, and correcting underlying physiological derangements usually suffice.
- *Hypothermia and shivering*
  - This results from combined effects of inhalation of dry gases during anesthesia, convective and evaporative losses during surgery, infusion of cold intravenous fluid and blood products, medication effect, and use of muscle relaxants.
  - These may be detrimental to the cardiorespiratory system especially in patients with low cardiorespiratory reserve.
  - This may also lead to tissue ischemia with delayed wound healing, increased incidence of surgical site infection, organ hypoperfusion due to vasoconstriction, and a tendency to bleed. Patients with coronary artery disease and those with vascular anastomoses and skin grafts are particularly vulnerable.
  - Patients with core temperature below 35°C on arrival to the ICU should be actively rewarmed with warm air blankets, warm intravenous fluid, and adequate covering. All hypothermic patients should receive supplemental oxygen.

Step 4: Identify and correct fluid imbalance

- Conventional fluid intake–output charts may not reflect fluid balance in postoperative patients.

- This is due to increased antidiuretic hormone and aldosterone secretion due to pain and stress of surgery resulting in a high incidence of syndrome of inappropriate antidiuretic hormone (SIADH), fluid sequestration in the gut during abdominal surgery, and fluid leak in the interstitial space due to increased capillary permeability ("third spacing"). In such cases, a low urine output may not be indicative of hypovolemia, and other measures of volume status either clinically or with hemodynamic monitoring should be instituted.
- As postoperative patients tend to retain free water, hypotonic fluid infusion may lead to hyponatremia and should be restricted in these patients.
- In patients with chronic diuretic use, hypertension, and cardiac dysfunction, cautious use of diuretics could be tried if urine output remains low in spite of normal hemodynamics and no evidence of sepsis.

Step 5: Identify and correct circulatory problems

- Cardiovascular status should be optimized preoperatively by careful preoperative cardiovascular risk assessment and optimizing medications (Table 76.1).
- Patients on β-blockers and statins preoperatively should have these continued postoperatively. In patients with high cardiac risk factors, β-blockers should be started cautiously few weeks before surgery and continued postoperatively. Long-acting preparations are preferable to avoid complications associated with abrupt withdrawal of β-blockade. High-dose β-blockers for the first time immediately prior to surgery are discouraged. Patients receiving β-blockade should be monitored for bradycardia and hypotension as their occurrence is associated with increased incidence of cerebrovascular accident. Clopidogrel and anticoagulants should generally be stopped prior to surgery, but these need to be restarted at the earliest specially in patients with atrial fibrillation, previous history of thromboembolic disease, and with coronary drug-eluting stent. Aspirin can be continued throughout the perioperative period without increased risk of bleeding.
- Routine preoperative optimization of hemodynamics by placing a pulmonary artery catheter and attaining supranormal cardiac output and oxygen delivery is not advocated. In high-risk patients (Table 76.2), perioperative goal-directed therapy using minimally invasive cardiac output monitoring techniques has been shown to improve outcome.
- Intraoperative monitoring of volume loss and hemodynamics with minimally invasive devices like pulse contour analysis, measuring half hourly urine output and correcting volume deficit appropriately, and avoiding excessive swings of blood pressure will help in better postoperative cardiac outcome.

Table 76.1 Risk factors for postoperativecardiac complication

Age more than 70 years
Current or prior angina pectoris
"Q" wave in resting electrocardiogram
Clinical cardiac failure

Table 76.2 Shoemaker criteria for identifying the high-risk patient

Patient factors
Prior severe cardiac illness, acute myocardial infarction(AMI), stroke, congestive heart failure (CHF)
Age more than 70 years
Severe sepsis with septic shock
Severe nutritional problems
Respiratory distress, chronic obstructive pulmonary disease, requiring mechanical ventilation
Acute hepatic failure and acute renal failure
Severe CNS problem—head injury with coma (Glasgow coma score <8)
Surgical factors
Extensive ablative surgery for cancer, more than 8 h
Severe multiple trauma—three organs or two body cavities
Massive blood loss of more than 8 units
Acute abdominal catastrophe—peritonitis, perforated bowel with gangrene
Aortic aneurysm and end-stage vascular disease

- Postoperatively, the patient at high risk should be monitored for occurrence of chest discomfort, changes in ST segment, hypotension or hypertension, and features of pulmonary edema. A low threshold should be kept for performing 12-lead electrocardiogram and troponin levels, as creatinine phosphokinase may be falsely raised after surgery.

Step 6: Identify and correct pulmonary problems

- Careful preoperative risk assessment should be performed to predict likelihood of postoperative respiratory compromise (Table 76.3).
- Preoperatively, optimize respiratory status by cessation of smoking, reduction in body weight, diaphragmatic conditioning exercises with chest physiotherapy and incentive spirometry, and treating chest infection with antibiotics and

Table 76.3 Risk factors for postoperative pulmonary complications

Age more than 50 years
Obesity
Smoking
Chronic obstructive pulmonary disease
Location of incision (upper abdominal, thoracic)
FEV1 less than 1 L
FVC less than 1.5 L
FEV1/FVC less than 30%
Use of pancuronium
Surgery lasting more than 3 h
Functional dependence
Serum albumin less than 3.5 g/dL

bronchospasm aggressively with inhaled β-agonist, tiotropium, and inhaled glucocorticoids in patients with reactive airway disease.

- Postoperatively, high-risk patients are prone to develop respiratory failure due following reasons:
  - Atelectasis
  - Aspiration
  - Splinting of diaphragm due to pain and hypoventilation
  - Tracheobronchitis and pneumonia
  - Noncardiogenic pulmonary edema—due to aspiration, blood transfusion, fat emboli
- The following measures should be taken postoperatively to avoid respiratory complications:
  - Early ambulation and assisted coughing
  - Adequate hydration and humidification of inspired air and oxygen
  - Intermittent positive-pressure breathing exercises
  - Noninvasive ventilation specially in patients with chronic obstructive pulmonary disease with hypercarbia
  - Optimizing use of analgesics, epidural analgesia, and avoiding excessive sedation
  - Minimizing the use of the nasogastric tube
  - Early identification and treatment of sepsis and shock
  - Early stabilization by external fixators of long bone fractures using a damage control philosophy, with formal internal fixation undertaken later, after the acute inflammatory response has ebbed

Step 7: Provide other general measures

- Transporting patients perioperatively safely, with adequate monitoring, appropriate handover, and documentation checklist, should be performed judiciously (see Chap. 83).
- Early identification of ongoing hemorrhage by inspecting volume and type of drain, hemodynamic instability, falling hematocrit and correcting volume deficit, hypothermia, acidosis, coagulopathy, and thrombocytopenia.
- Identify the site of bleeding and prepare the patient for re-exploration if necessary in consultation with the surgical team.
- Use blood and blood products judiciously. In a hemodynamically stable patient, without active bleeding or active coronary artery disease, keep the hemoglobin level at 8 g/dL (see Chap. 61).
- Early identification of sepsis and use of antibiotics judiciously. Institutional protocol should be followed as per established guidelines for perioperative antibiotic prophylaxis (see Chap. 49).
- Perioperatively, surgical patients are in a hypercoagulable state and at increased risk for venous thromboembolic manifestations. Institutional protocols should be followed as per established guidelines for deep venous thrombosis prophylaxis. Mechanical methods (pneumatic compression or graduated compression stockings) should be used in patients who have undergone intracranial, spinal, or ocular surgery and in those at high risk of bleeding.

- Early enteral nutrition should be instituted as soon as permissible. If early enteral nutrition cannot be initiated, parenteral nutrition should be started especially in patients with established malnutrition. Consideration should be given for immunonutrition in patients with cancer surgery (see Chap. 43).
- Proper stress ulcer prophylaxis with H_2 blockers should be instituted.
- Maintain normothermia perioperatively to reduce incidence of surgical site infection.
- Frequent point of care blood sugar monitoring, keeping it below 150 mg/dL, and avoiding hypoglycemia are useful in preventing postoperative complications (see Chap. 60).
- Thyroid status should be optimized if necessary with thyroid supplementation in hypothyroid patients. Supplemental corticosteroid should be given to patients with history of chronic use of systemic steroids.

Suggested Reading

1. Silverman DG, Rosenbaum SH. Integrated assessment and consultation for the preoperative patient. Med Clin North Am. 2009;93:963–77.
   The article describes a framework for documentation, optimization, risk assessment, and planning, as well as a uniform grading of existing morbidities and anticipated perioperative disturbances, for patients requiring integrated assessment and consultation.
2. Geerts WH, Bergqvist D. Prevention of venous thromboembolism: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2008;133(6 Suppl):381S.
   Updated guidelines for perioperative thromboembolic prophylaxis.
3. Halaszynski TM, Juda R. Optimizing postoperative outcomes with efficient preoperative assessment and management. Crit Care Med. 2004;32(4 Suppl):S76–86.
   The preoperative visit is also an opportunity to perform directed laboratory testing (as opposed to across the board batteries of tests) and to carefully plan out the continuance, discontinuance, or initiation of medications in the perioperative period. It may also be beneficial to stabilize disorders such as hypertension and, when indicated, initiate preoperative optimization of patients with advanced disease.

Web Site

1. http://www.nice.org.uk
   National Institute for Health and Clinical Excellence. Reducing the risk of venous thromboembolism

Specific Issues in Perioperative Care

77

Subhash Todi, Shrikanth Srinivasan,
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A 60-year-old male patient with triple-vessel disease with reduced left ventricular function and diabetes mellitus underwent coronary artery bypass graft (CABG) with extracorporeal support. He was transferred to the ICU, and his blood pressure was 90/60 mmHg on epinephrine infusion.

A 50-year-old male patient with road traffic accident had undergone an emergency decompressive craniectomy due to an expanding intracerebral hematoma. He had arrived in the ICU postoperatively on the ventilator and was paralyzed. His blood pressure was 110/70 mmHg without any vasopressor support.

A 50-year-old male patient had undergone an emergent thoracotomy and left upper lobe resection due to massive hemoptysis not getting controlled with conventional measures. He had arrived in the ICU ventilated with a saturation of 90% on FiO_2 of 0.8.

Due to increasing specialization of intensive care, patients with organ-specific surgery (thoracic, cardiac, neurosurgery) are being managed in dedicated ICUs. As these patients have specific perioperative problems, the intensive care physician taking care of these patients should have a working knowledge of their specific perioperative critical issues and should work in close consultation with the surgical and anesthetic team.

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77.1 Cardiac Surgery

Traditionally, cardiac surgery has been performed via a median sternotomy incision with the use of a cardiopulmonary bypass (CPB) machine that maintains total body oxygenation and perfusion despite cardioplegia. After CPB is initiated, injection of hyperkalemic cardioplegic solution directly into the coronary circulation produces cardiac standstill. Cardioplegic solution also provides necessary nutrients for myocardial preservation despite the absence of cardiac blood flow. Traditional surgical approaches are associated with varying degrees of hypothermia, coagulopathy, and hemodilution. Usually the patients need varying period of mechanical ventilation postoperatively.

Minimally invasive surgery (MIS) modifies one or more of these techniques to accomplish similar surgical goals through small surgical incisions without CPB (i.e., off-pump), or both. MIS has been shown to reduce blood requirements, length of stay, and resource use.

Step 1: Take handover information from operating room staff

- Patient identification details
- Preoperative details
  - Type of coronary artery disease, valve dysfunction, left ventricular function, and pulmonary hypertension
  - Medications used—antiplatelets, diuretics, angiotensin-converting enzyme inhibitors, statins, and calcium channel blockers
  - Comorbidities—diabetes, hypertension, peripheral vascular disease, stroke, renal dysfunction, and thyroid status
  - Preoperative functional capacity
  - Previous medical records
- Operation performed (on- or off-pump, arterial, venous graft) and problems encountered
- Current drug infusions
- Pacemakers and antiarrhythmic drug information
- Estimated blood loss, blood and blood product administered, and urine output
- Intraoperative fluid balance
- Antibiotics administered and timing
- Drains (number, placement)
- Latest arterial blood gas analysis, hematocrit, blood sugar, and electrolytes

Step 2: Checklist on arrival of the patient (A to I)

- *Airway*
  - The patient is connected to the ventilator.
  - Note the size of the tube, position of fixation at the angle of mouth, and cuff pressure.
- *Breathing*
  - Look for chest movement. Auscultate and confirm air entry to both the lungs.

  - The usual initial ventilator setting are as follows:
    - Breath rate of 12–15/min
    - FiO_2 of 0.6–0.8
    - Tidal volume of 6–8 mL/kg
    - Depending on arterial blood gas (ABG) report, settings are modified subsequently
- *Circulation*
  - Set up the monitor.
  - Check
    - ECG for rate, rhythm, and ST segment changes.
    - Arterial pressure, oxygen saturation.
    - Pulmonary artery pressure/central venous pressure—measure the pulmonary artery wedge pressure (PAWP), cardiac output (CO), and systemic vascular resistance.
    - Temperature probe—if temperature is less than 37°C, warming blanket should be placed.
    - Low urine output, acidosis, and peripheral examination are not a good indicator of the low perfusion state in these patients, and direct measurement of cardiac output is preferable in unstable patients.
- *Drugs*
  - Vasoactive drugs—check infusion pumps labeled with proper drug dosing and dilutions, and calculate infusion rate (mcg/kg/min).
- *Electrolytes*
  - Maintain K^+ at 4–4.5 mmol/L.
  - Maintain Mg^+ at 0.8–1.5 mmol/L.
- *Fluids*
  - Intravenous maintenance fluids (crystalloid) are started at the rate of 1–1.5 mL/kg/h.
  - Intermittent colloid to maintain pulmonary capillary wedge pressure at 8–15 mmHg.
  - Blood transfusion to keep hematocrit at more than 25–30%.
  - Maintain urine output at 0.5–1.0 mL/kg/h.
- *Glucose control*
  - Tight glycemic control (TGC) (80–110 mg/dL) is helpful in this group of patients but runs the risk of hypoglycemia, and therefore close monitoring of blood sugar should be done if TGC policy is adopted, otherwise blood sugar should be kept below 150 mg/dL.
  - In diabetic and hyperglycemic patients, dextrose infusions should be neutralized with insulin.
- *Hemorrhage*
  - Causes of bleeding after cardiac surgery include:
    - Inadequate surgical hemostasis
    - Inadequate platelet number or function
    - Inadequate reversal of heparin
    - Dilutional coagulopathy

    - Heparin rebound
    - Hypothermia
  - Chest tubes are connected to underwater seal. If bleeding is significant, and coagulation profile is normal, the patient needs to go back to the operation theater for re-exploration.
  - In adult patients, bleeding is significant when:
    - >400 ml for 1 h
    - >300 ml/hr for 2 h
    - >200 ml/hr for 3 consecutive hours
    - >100 ml/hr for 4 consecutive hours
  - CPB may induce coagulation abnormalities in these patients and this may be the cause of excessive bleeding.
  - Anticoagulation protocols:
    - Valve surgery: Anticoagulation is maintained with intravenous heparin. With mechanical valve prosthesis, oral anticoagulants (warfarin) should be started as soon as oral intake is permitted (48–72 h). Initial overlapping therapy of warfarin with heparin is recommended for 48–72 h to prevent warfarin-induced hypercoagulability.
  - Coronary artery bypass graft—aspirin/clopidogrel in low doses is started as soon as oral feeds are started.
  - Reverse heparin effect by protamine if needed.
- *Investigations*
  - Investigations should be done within 30 min of arrival.
    - ECG
    - ABG
    - Hct and electrolytes
    - Chest X-rays—look for pneumothorax, hemothorax, position of endotracheal tubes, chest tubes, intravascular catheters, pacing wires, lung infiltrates, and cardiac size.
    - Coagulation profile (Prothrombin Time (PT), APTT, ACT)
    - Thromboelastogram (if available)

Step 3: Take general care of the patients

- Position—head end elevated at 30–45°
- Neurological assessment
  - Awake and obeying commands
  - Able to move all four limbs

Step 4: Look for and manage specific complications

- *Arrhythmias* are common, occurring in 25–60% of patients. Advanced age, prior atrial fibrillation, and combined bypass graft/valve surgery are risk factors. Exclude precipitating causes such as hypoxia, hypercarbia, lack of analgesia, and electrolyte imbalance (hypokalemia and hypomagnesemia) before instituting antiarrhythmics. Treat arrhythmias only if hemodynamically significant. Arrhythmias with signs of ischemia may signal perioperative

infarction, inadequate revascularization, and blocked graft requiring urgent reoperation.

- *Low-output state*: Urgent echocardiogram should be performed to exclude pericardial tamponade. Assess left ventricular function and volume status.
  - In cases of pericardial tamponade, the patient should be re-explored with evacuation of hematoma. The chest may have to be reopened in the ICU if tamponade is sudden and severe, leading to hemodynamic collapse.
  - In low-output states, rewarming should be gradual. Decrease metabolic demand by proper analgesia, sedation, and muscle relaxant to decrease shivering. Optimize preload by judicious use of fluid and blood (keep hematocrit 0.25–0.35) under monitoring. Add inotropes and if blood pressure permits decrease afterload by adding vasodilators. Due to ischemia reperfusion injury, a phase of stunned myocardium persists, which usually resolves over a variable period and is helped by inotropic support. This phenomenon should be distinguished from ongoing ischemia where inotropic support is detrimental.
  - An intra-aortic balloon pump is sometimes used to maintain coronary perfusion in low-output states (see Chap. 101).
- *Postoperative hypertension*: It is usually transient but may lead to left ventricular dysfunction, myocardial ischemia, graft and suture line disruption, and increased bleeding. Ensure proper analgesia and sedation. Parenteral vasodilators like nitrates may be used.
- *Atelectasis:* Ensure early mobilization and incentive spirometry.
- *Fluid overload*: Maintain strict input–output chart. Low-dose diuretics may be needed.
- *Myocardial ischemia* or *infarction* may be difficult to diagnose in postoperative settings as ECG, echocardiogram, and cardiac enzyme may not be able to detect early ischemia and may be false positive.
- *Right ventricular dysfunction*: This may occur due to pulmonary hypertension or ischemic reperfusion injury. It presents with low cardiac output syndrome, which may initially be volume responsive. The patient has high right-sided filling pressure disproportionate to left-sided pressure, low cardiac index, and low systemic blood pressure. It is managed by maintaining sinus rhythm, appropriate heart rate (by pacing if necessary), optimizing preload, reducing afterload (with pulmonary vasodilators such as inhaled nitric oxide or epoprostenol infusion), inotropic support, and mechanical assist devices if needed.
- *Significant neurological deficit:* It occurs in 2–3% of patients undergoing coronary artery bypass surgery. This can present as stroke, transient ischemic attack, or global cerebral dysfunction.

Step 5: Take a fast-track approach to extubation

- The increasing use of off-pump surgery, short anesthesia, and lower doses of sedatives has led to early liberation of patients from ventilators. Many patients can be extubated within 4 h of surgery or even in the operating room.
- The key to a successful fast-track program is proper patient selection, high-level supervision by a disciplined team, and absence of surgical complications.

77.2 Thoracic Surgery

Step 1: Take care of immediate postoperative issues

- Immediate concerns include assessment of oxygenation, volume status, cardiovascular support, provision of ventilatory support if needed to ensure adequate oxygen delivery and status of chest drains that accompany the patient from the operating room.
- Special concerns apply to pain control, which is especially important, as pain will limit respiratory effort and can also precipitate delirium and agitation.

Step 2: Be cognizant of potential problems following thoracotomy

- Poor respiratory effort and sputum retention (chest wall trauma and pain)
- Atelectasis, pneumonia, and sepsis
- Alveolar and minor bronchial air leaks
- Localized or generalized pulmonary edema
- Intercostal, pulmonary, or bronchial vessel hemorrhage
- Cardiac arrhythmias, myocardial infarction, and heart failure
- Pulmonary and systemic embolism
- Chest wall hematoma, wound infection, and wound dehiscence

Step 3: Be cognizant of potential problems following lung resection

- Respiratory insufficiency due to extensive lung resection
- Bronchopleural fistula and massive air leak
- Early and late mediastinal shift
- Atrial fibrillation and other supraventricular arrhythmias
- Torsion of lobe or segment
- Cardiac herniation (usually after pneumonectomy with a partial pericardium excision, when the heart herniates through a gap in the pericardium; may be manifested by supraventricular arrhythmias and/or severe hypotension)
- Residual venous or arterial lung infarction
- Blood loss into the pleural space, mediastinum, or bronchus
- Bronchial obstruction from accumulated secretions, blood, and pus
- Empyema following air leaks, insufficient lung volume, or overwhelming sepsis
- Paradoxical chest wall movement following extensive rib resection
- Pulmonary hypertension and acute right-sided heart failure

Step 4: Get a chest X-ray in the hypoxic patient

- In all postoperative thoracic surgery patients who are hypoxic on arrival, after a careful physical examination, urgent chest X-rays should be requested.
- A daily chest radiograph must be performed in unstable patients, to confirm endotracheal, nasogastric, and chest tube placement, as well as to identify any pneumothorax, mediastinal shift, or significant atelectasis.

Step 5: Assess chest drain sites and amount of drainage

- Hourly output from chest tubes should be recorded, and the operative team should be notified if drainage is greater than 100 mL/h for more than 4 h, or if greater than 200 mL of drainage is recorded in any 1-h observation period.
- Expected chest tube drainage from major thoracic procedures in the first 24 h is roughly 300–600 mL, tapering to less than 200 mL by the second day.
- Daily chest radiographs are usually obtained while chest tubes are in place.
- Once all air leaks resolve and drainage is minimal (<100 mL/24 h), chest tubes may be removed during the expiratory phase of ventilation or while the patient performs a Valsalva maneuver.
- After pneumonectomy, surgeons usually keep the intercostals drain on the operated side clamped so that the fluid fills the pneumonectomy space and maintains the mediastinum central.
- This drain may be occasionally unclamped for a short period to note whether there is bleeding.
- The drain may need to be unclamped if there is very rapid accumulation of fluid in the pneumonectomy space, manifested by dyspnea, mediastinal shift to the opposite side, high jugular venous pressure (JVP), or central venous pressure. This may be mistaken for congestive cardiac failure.

Step 6: Address airway concerns and plan for extubation

- Extubation can often be accomplished in the operating room, but continued ventilation may be necessary in the presence of concurrent cardiac illness, inability to protect the airway, malnutrition, or coexisting lung disease.
- Ideally, the patient should be awake and following instructions and have an adequate gag reflex (signifying airway protection) and cough (for secretion clearance).

Step 7: Control pain

- Adequate pain control is important not only to ensure patient comfort but also to avoid potential cardiac and pulmonary complications. Early pain management is also important in an effort to reduce the chances of developing long-term postthoracotomy pain.
- Various options exist for pain management. They include systemic analgesics, neuraxial opioids, and local anesthetics via the epidural route, regional anesthesia such as intercostal and paravertebral nerve blocks, and adjuvant therapies such as transcutaneous electrical nerve stimulation (TENS) or applied heat. Exercise caution when using TENS in the patient with the temporary pacemaker in situ as it may interfere with sensing function of the pacemaker.
- The mainstay of postoperative pain control is systemic analgesics in the form of opioids. Agents such as morphine and fentanyl are frequently used, with the intravenous route providing the most predictable responses. Opioid side effects remain the greatest issue, with respiratory depression, nausea, vomiting, and ileus being the most common.

- Nonopiate medications such as paracetamol and nonsteroidal anti-inflammatory drugs (NSAIDs) are reasonable adjuncts to the opioids. Because NSAIDs may exacerbate renal dysfunction, it is necessary to exercise caution when using them in the presence of underlying renal insufficiency.
- Neuraxial opioids and local anesthetics via the epidural route provide excellent regional pain control. Epidural catheters are the preferred route, and when local anesthetics, either with or without opioids, are infused in this manner, the incidence of pulmonary complications decreases relative to that with systemic opioids.
- In addition, patients requiring prolonged postoperative mechanical ventilation may benefit from the centrally acting α-adrenergic agonist, dexmedetomidine, as an analgosedative.

Step 8: Optimize fluid balance

- Fluid management in the postoperative period requires special attention due to the high risk for pulmonary edema. The choice of fluid for resuscitation is left to the discretion of the caregiver, as there is no known difference in outcome with use of either isotonic crystalloid or colloid.
- Traditional markers of perfusion help determine if a patient is adequately volume-resuscitated. These include urine output (usually >0.5 mL/kg/h), mental status, blood pressure, heart rate, blood lactate level, capillary refill time, venous oxygen saturation, filling pressures, and cardiac performance.
- Ideally, the clinician should limit crystalloid infusion to 20 mL/kg for the first 24 h.

Step 9: Start respiratory therapy

- Thoracic surgical patients often have significant underlying chronic obstructive pulmonary disease, impaired mucociliary clearance, excessive secretions, and/or increased closing volumes, all of which predispose to atelectasis.
- The respiratory therapist plays an important role in providing secretion management and performing chest physiotherapy (percussion and vibration) and incentive spirometry.
- Other modalities supporting recovery include adequate hydration, aerosolized bronchodilators, humidified oxygen, and early identification and treatment of infection of the tracheobronchial tree.
- Chest physiotherapy should begin as soon as the patient has recovered sufficiently from anesthesia to cooperate.

Step 10: Manage bronchopleural fistula

- Early postoperative bronchopleural fistula in a pneumonectomy patient is a surgical emergency. The typical presentation is sudden expectoration of copious amounts of pink, frothy sputum, which may be misdiagnosed as pulmonary

edema. Further management will likely include bronchoscopy to assess the stump closure and immediate reoperation if a leak is detected.
- A double-lumen tube may need to be introduced to prevent soiling of the opposite lung by contents of the pleural space and to prevent loss of tidal ventilation through the fistula.
- Always insert an intercostal drain on the side of the fistula and keep it draining at all times.

Step 11: Manage postoperative hypoxemia
- Postoperative hypoxemia is common and may be due to hypoventilation, atelectasis, aspiration, sepsis, acute respiratory distress syndrome, pneumonia, or pulmonary embolization.
- Noninvasive ventilation may be useful to treat respiratory failure after lung surgery.
- If pulmonary emboli are suspected, manage the patient accordingly (refer to Chap. 5).
- Systemic tumor emboli, though uncommon, may be seen after pulmonary resections for primary bronchogenic carcinomas or metastatic sarcomas.
- Meticulous attention must be given to prevent dehydration, overtransfusion, and infection.

Step 12: Address special concerns in esophageal surgery
- Patients who undergo esophageal resection for carcinoma tend to be malnourished and have complications, including atelectasis, pneumonia, aspiration, and retained secretions.
- Noninvasive ventilation should be avoided after esophageal surgery and surgery involving upper gastrointestinal anastomoses. If the patient needs ventilatory support, intubate the patient.
- One-third of patients experience respiratory complications. The most dreaded complication of esophageal surgery is leakage from the surgical site. Factors impacting the incidence include high estimated intraoperative blood loss, cervical location of the anastomosis, and the development of postoperative acute respiratory distress syndrome.
- Anastomotic dehiscence or ischemia of the gastric tube should be suspected when the following signs/symptoms appear: hydropneumothorax, bronchospasm, atrial fibrillation, dyspnea, hypotension, raised lactate levels, and tachycardia.
- Mortality associated with anastomotic leaks is historically high, but with improved surgical techniques, the patients now have a more promising outcome.
- Intraoperative nasojejunal tube placement or jejunostomy is vital to maintain enteral nutrition throughout the postoperative period.
- A multimodal approach including epidural analgesia, judicious fluid administration, early mobilization, and enteral nutrition contributes to a good outcome.

77.3 Neurosurgery

Step 1: Maintain airway, oxygenation, and ventilation

- Adequate oxygenation is mandatory for proper neuronal functioning. Hypercarbia is detrimental to the brain injury patient as it leads to rise in intracranial pressure (ICP), and therefore proper ventilation should be ensured (see Chap. 31).
- Maintain arterial oxygen saturation of more than 94% and $PaCO_2$ in the normocapnic range. Reserve hyperventilation for management of sudden increases in the ICP.

Step 2: Maintain adequate fluid balance while preventing brain swelling

- Avoid hypotonic fluids (like 5% dextrose) to prevent brain swelling. Note that lactated Ringers' solution is also mildly hypotonic.
- Use isotonic fluid like normal saline to maintain euvolemia.
- Fluid restriction and active diuresis should be avoided as it will lead to reduced circulating blood volume and hypoperfusion of the brain.
- Either isotonic saline or colloids can be used as a volume replacement.
- Maintain normal or slightly high serum sodium values (145–150 mEq/L).

Step 3: Maintain normoglycemia

- Hyperglycemia is associated with worse outcome after brain injury. This is because during low oxygen supply state intracellular sugar is converted into lactate, which causes intracellular acidosis and is detrimental to neuronal cells.
- On the other hand, for normal neuronal function, continuous supply of glucose is mandatory and hypoglycemia is equally detrimental.
- Thus, a fine balance of glucose control between 110 and 150 mg/dL should be maintained, with insulin infusion and ensuring adequate carbohydrate intake.

Step 4: Treat fever aggressively

- Fever is detrimental to brain tissues, and on the other hand, mild hypothermia is beneficial.
- Any febrile episode should be actively controlled with antipyretics and external cooling measure.

Step 5: Maintain blood pressure in the normal range

- Excessive swings of blood pressure should be avoided as autoregulation of cerebral blood flow is disrupted with the injured brain and flow will increase or decrease with changes in blood pressure leading to hyperemia with increased ICP during hypertension or hypoperfusion leading to decreased cerebral blood flow and neuronal injury during hypotension. Mean arterial pressure should be kept in the range of 65–75 mmHg in most patients.

Step 6: Decrease cerebral metabolic demand

- Judicious use of sedatives (e.g., barbiturates and propofol) and analgesics is useful in these cases.

Step 7: Prevent and treat convulsions aggressively (see Chap. 28)

- Anticonvulsant prophylactic may be given perioperatively for cortical surgeries.
- All episodes of new onset seizures should be actively managed to prevent secondary brain injury.
- In patients with persistent or fluctuating level of consciousness, nonconvulsive status should be ruled out.

Step 8: Monitor the patient for increases in ICP and neurological deterioration frequently (see Chap. 31)

- Hourly Glasgow coma score, pupillary size and reaction
- ICP monitoring where appropriate
- Maintain CPP (MAP–ICP > 65 mmHg).
- *Measurement and management of raised ICP (refer to Chap. 31)*
  - Basics
    - Normal ICP is less than 15 mmHg.
    - Raised ICP is more than 15–20 mmHg for more than 1–5 min.
    - CPP = MAP – ICP.
    - Always measure cerebral perfusion pressure (CPP) along with ICP.
    - The ICP monitor (intraventricular drain or subarachnoid bolt) is inserted if indicated.
    - Transducer (without flush system) has to be kept at midventricular level which is at the level of tragus in supine position.
    - Start treatment if ICP is more than 20–25 mmHg for more than 5 min.
  - Management of intraventricular drain (IVD)
    - Drain cerebrospinal fluid (CSF) whenever ICP is more than 15–20 mmHg.
    - Drain CSF till ICP is 10–15 mmHg.
    - Measure daily CSF drain required to maintain ICP.
    - Examine CSF every day.
    - Take full sterile precautions.
- Lumbar drain
  - If IVD is in situ, do lumbar puncture and compare opening and closing ventricular and lumbar pressures.
  - If there is comparable drop, IVD can be removed, and CSF is drained by Lumbar punctures (LPs).
  - If there is no fall in ventricular pressures, drain CSF from IVD and avoid further LPs.
- Approach to an acute rise of ICP in a previously stable patient
  - Check the transducer level and rezero.
  - Confirm waveform of ICP trace.
  - Position the head, neck, and endotracheal tube tape properly to minimize increase in ICP.
  - Check ventilation, ABG, and X-rays and increase mechanical ventilation to decrease pCO_2 if necessary.
  - Exclude anxiety, pain, or seizures.
  - Drain CSF or give mannitol bolus.
  - Perform a CT scan if appropriate.

Suggested Reading

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Part XIII

General Issues

Yatin Mehta and Shirish Prayag

Initial Assessment and Resuscitation

78

Jeetendra Sharma and Yatin Mehta

A 53-year-old female patient with history of coronary artery bypass grafting 6 years ago underwent bilateral knee replacement 7 days back. She was shifted to the ICU from the ward with fever, respiratory distress, and altered sensorium. Her heart rate was 134 beats/min with frequent ventricular ectopic beats, blood pressure 98/50 mmHg, respiratory rate 30/min, temperature 38.1°C in axilla, and SpO_2 88% on 60% oxygen by a Venturi mask.

Outcome in the ICU is predominantly determined by initial management of patients. Early identification of the patient at risk of life-threatening illness is essential to manage them appropriately and prevent further deterioration. "Time is tissue" in critically ill patients, and a prompt and protocolized resuscitation regimen will help in salvaging these patients.

Step 1: Assign responsibilities

- Quickly make a team and assign job responsibilities to every member clearly and appropriately.
- In the initial phase, the patient should be seen by a senior member of the ICU team for initial resuscitation, investigation, management planning, and family briefing.
- Assign two residents for initial resuscitation.
- Assign two nurses initially for unstable patients.
- Take early assistance whenever needed from other members of the team.

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R. Chawla and S. Todi (eds.), *ICU Protocols: A stepwise approach*,
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Step 2: Start initial assessment and resuscitation

- Initial aim is to determine immediate life-threatening problems. Time is usually short and not enough to be certain about the cause of the problem, and correcting physiological abnormalities should take precedence over arriving at an accurate diagnosis. However, a working diagnosis is essential for deciding treatment options once physiological stability is achieved.
- For the patient in cardiorespiratory arrest, follow ACLS protocol (see Chap. 19).
- History taking, physical examination, sending investigations, and resuscitation need to be carried out simultaneously rather than sequentially as time is limited.
- For hemodynamically unstable patients, resuscitation should be systematic and aimed toward assessment and management of A (airway), B (breathing), and C (circulation).
- All three components can be managed simultaneously; sequential approach is not necessary.

Airway (A)

Assess the airway. Need for definitive airway by endotracheal intubation or airway adjunct (oral/nasal airway), supralaryngeal devices, or surgical cricothyrotomy in a patient is mainly based on clinical assessment and should not be delayed.

- Ask for assistance whenever in doubt about a difficult airway.
  - Look, listen, and feel for features of airway obstruction and secure airway and intubate when necessary (for details, see Chap. 1).
  - Snoring—due to obstruction of upper airway by tongue and oropharyngeal soft tissue—insert oro-/nasopharyngeal airway.
  - Gurgling—due to obstruction of upper airway by liquid—perform suctioning.
  - Stridor—due to obstruction by foreign body or stenosis of upper airway, usually inspiratory—remove foreign body or intubate.
  - Wheeze—due to spasm in small airways—give bronchodilators.
  - Complete airway obstruction is silent—intubate.

Breathing (B)

- Assess the need for oxygen and ventilation. It can be assessed clinically along with pulse oximetry and arterial blood gas analysis:
  - Look for clinical signs of respiratory distress:
    - Breathlessness
    - Tachypnea
    - Inability to talk
    - Open-mouth breathing
    - Flaring of ala nasi
    - Use of accessory muscles of respiration
    - Paradoxical breathing (inward movement of abdomen during inspiration)

  - Look for clinical features suggestive of inadequate oxygenation or ventilation:
    - Restlessness
    - Delirium
    - Drowsiness
    - Cool extremities
    - Cyanosis
    - Tachycardia
    - Arrhythmia
    - Hypotension
    - Flapping tremor (asterixis)
- Remember that these clinical presentations are a very late feature of respiratory failure and imply impending cardiorespiratory arrest. Patients need to be identified much earlier, and appropriate management should be instituted.
- Look for features of tension pneumothorax and evidence of massive pleural effusion or hemothorax and drain immediately.
- Any evidence of massive lung collapse with desaturation requires intubation, suctioning, and positive-pressure ventilation.
- Some clinical conditions, for example, deep unconsciousness (GCS <8), severe hemodynamic instability, or severe respiratory distress, require immediate endotracheal intubation and mechanical ventilation (see Chap. 4).
- Noninvasive ventilation can be tried in relatively stable patients if they are suffering from a condition where noninvasive ventilation has been shown to be effective (see Chap. 3).
- Normal oxygen saturation does not exclude compromised airway and need for intubation and ventilation.

Circulation (C)

- Assess adequacy of circulation. Assessment and management should go side by side.
  - Examine the following:
    - Peripheral and central pulse for rate, regularity, volume, and symmetry
    - Skin temperature
    - Heart rate and rhythm
    - Blood pressure (supine and sitting for orthostatic hypotension)
    - Capillary refill
    - Jugular venous pressure
    - Urine output
    - Bedside echocardiography (see Chap. 17).
    - Consider invasive monitoring (see Chap. 16).
    - Central venous catheter insertion
    - Arterial catheter insertion
    - Advanced hemodynamic monitoring
- Judiciously use volume, inotropes, and vasopressor support (see Chap. 18).
- Early volume challenge is appropriate in most hypotensive patients.

- Identify cardiogenic shock and rapidly triage to appropriate facility.
- Look for pericardial tamponade causing hemodynamic instability requiring immediate pericardiocentesis.
- Any suspicion of pulmonary embolism should lead to urgent anticoagulation if not contraindicated, and then arrange for appropriate investigation.
- Patients presenting with features suggestive of aortic dissection should have urgent control of hypertension and heart rate and should be urgently investigated to confirm diagnosis.
- In patients with features of severe sepsis and septic shock, prompt broad-spectrum antibiotics and early goal-directed resuscitation should be started (see Chap. 50).
- *Consciousness*—frequent neurological examination needs to be performed in drowsy patients (see Chap. 30):
  - Lateralizing features like hemiplegia are usually a feature of neurological disease.
  - A depressed conscious level in the absence of a primary neurological cause is indicative of severe systemic disease.
  - Check for hypoglycemia and correct urgently.
  - Control ongoing seizures with appropriate measures.
  - Consider urgent antibiotics for patients with features suggestive of bacterial meningitis.

Step 3: Take focused history

- Obtain history from relatives and medical and nursing staff in the unstable patient.
- Review patients' clinical chart and perioperative note.
- Presenting problem in chronological order with duration and temporal profile of illness needs to be documented.
- Take history of mechanism of injury in trauma patients.
- Ask for significant comorbidities such as cardiac, pulmonary, renal diseases, previous surgery, or any other significant past medical problem.
- Enquire about previous hospitalization or use of NIV at home.
- Enquire about functional state at home—bedbound, ambulatory with support or independent.
- Enquire regarding exercise tolerance.
- In the elderly, enquire about mental state and cognition.
- Take detailed medication history with doses and duration. Enquire about any recent change of medication, drug allergies, over-the-counter medications, alternative medication, and self-administration of medications.
- Ask for any routine use of sedatives or psychiatric medication.
- Enquire about addictions such as alcohol and tobacco.
- A problem list of active and inactive problems needs to be documented in the clinical notes.
- Ascertain patients' resuscitation status as per family's wish.

Step 4: Perform focused physical examination

- Check for vital signs.
- Look for warning signs of severe illness (Table 78.1).
- Examine for any life-threatening or limb-threatening abnormalities systematically.
- Examine for pallor, cyanosis, jaundice, clubbing, or pedal edema.
- Examine skin for rash, petechiae, urticaria, and eschar.
- Examine other organ systems systematically.
- Examination needs to be repeated frequently for any new features or findings missed previously. In neurological patients, Glasgow coma score needs to be assessed frequently.
- Patients should be fully exposed with proper privacy during initial examination.
- A detailed physical examination should be performed later once the patient stabilizes after initial resuscitation.

Table 78.1 Warning features of severe illness

BP systolic <90 or mean arterial pressure <60 mmHg
Glasgow coma score <12
Pulse rate >150 or <50 beats/min
Respiratory rate >30 or <8/min
Urine output <0.5 mL/Kg/h

Step 5: Send basic investigation

- Send screening investigations during initial resuscitation.
- Complete blood count, blood sugar, sodium, potassium, urea, creatinine, aspartate transaminase (AST), alanine transaminase (ALT), PTime, APTT, arterial blood gas, and lactate level in septic patients are important initial investigation.
- Chest X-rays and a 12-lead ECG should be performed.
- Appropriate microbiology cultures should be sent.
- Further investigations should be based on finding from history and physical examination.
- In unstable patients, investigations should be performed at the bedside as much as possible.
- If transport outside the ICU is needed, the patient should be properly monitored and accompanied by qualified personnel (see Chap. 83).
- Maintain an investigation flow sheet in chronological order.
- Red flag investigations require immediate corrective actions (Table 78.2).

Table 78.2 Investigations requiring urgent corrective action

Blood sugar <80 mg/dL
Sodium <120 or >150 mmol/L
Potassium <2.5 or >6.0 mmol/L
pH < 7.2
SpO_2 < 90%
Bicarbonate < 18 mmol/L

Step 6: Recognize the patient at risk
- Take special precautions in the following group of patients:
  - The elderly and immunocompromised may not show features of decompensation such as fever and tachycardia.
  - Polytrauma patients, due to multiple injuries and effect of distracting pain, are difficult to assess.
  - In young adults, decompensation is late due to physiological reserve.

Step 7: Assess response to initial resuscitation
- Assess changes in vital signs with initial resuscitation—pulse rate, rhythm, blood pressure, oxygen saturation, urine output, and mental state.
- Continuous assessment is mandatory, and one needs to be vigilant and present at the bedside.

Step 8: Assess intensity of support
- Inspired oxygen fraction needed to maintain saturation above 90%
- Intensity of ventilatory support—positive end-expiratory pressure, minute ventilation
- Dose of vasopressor and inotrope needed to maintain mean arterial pressure above 60 mmHg
- Need for volume support to keep adequate urine output
- Need for blood transfusion to keep hemoglobin above 8 g/dL
- Need for sedation in agitated patients
- Need for dialysis support
- Worsening biochemistry

Step 9: Seek help for specific problems that might require expertise
- Cardiologist—complete heart block, acute coronary syndrome, cardiogenic shock, intra-aortic balloon pump insertion, pericardial tamponade, massive pulmonary embolism
- Nephrologist—dialysis
- Neurologist—acute stroke or undiagnosed depressed conscious level
- Neurosurgeon—intracranial hemorrhage, head injury, severe cerebral edema
- Trauma surgeon—polytrauma, abdominal trauma, thoracic trauma, compartment syndrome
- Obstetrician—ruptured ectopic pregnancy, postpartum hemorrhage

Step 10: Construct a working diagnosis and plan for further management
- After initial resuscitation, assessment, investigation, and response, a differential diagnosis should be arrived at.
- Reassess the patient frequently to modify initial plan if needed.

Step 11: Brief relatives
- After initial resuscitation, assessment, investigation, and response, the family should be briefed about the likely diagnosis, treatment plan, and approximate

prognostication, and duration of stay and consent should be taken for any invasive procedures.
- Family briefing should be documented in clinical notes.

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Comprehensive ICU Care

79

Tariq Ali, Yatin Mehta, Subhash Todi, and Rajesh Chawla

A 60-year-old male patient with urosepsis and multiple organ failure was admitted to the ICU for 10 days. He was requiring ventilator support, vasopressor, and dialysis support. He was under continuous sedation and not tolerating enteral feeding fully which was being supplemented with partial parenteral nutrition.

ICU management of the multiorgan failure patient is getting increasingly complex due to the availability of the advanced organ support system. A systematic approach to multiple critical-care-related issues encountered by these patients should be initiated by the ICU team to minimize chances of hospital-acquired complications or infections and maximize chances of recovery. For an experienced intensivist, the comprehensive ICU care begins before he/she enters the ICU. Having a plan ready for each patient and modulating it with the current condition drives confidence in both the staff and the patient.

Step 1: Perform a quick overview

- Perform a quick overview of ICU occupancy, patient–nurse ratio, and medical staff available for the day. It helps in identifying staffing problems early.

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- Check and allocate staff for remote calls (emergency department, wards, high-dependency units [HDUs], cardiac arrest).
- Planned shifts are best worked up early to accommodate the transfer in timely.
- Ensure proper allocation of residents and nurses.

Step 2: Take proper handover

- Continuity of patient care in the ICU is dependent on accurate and timely handover. Due to shift work of junior doctors, this may need to be done once or even twice in 24 h and is a common source of medical error.
- Structured method of handover has been shown to critically influence the transfer of clinical information, and this process should be implemented for a smooth and correct transfer of information.
- Only 2.5% patient information is retained in verbal handover, 85.5% is retained when using the verbal along with note-taking method, and 99% is retained when a printed handout with all clinical information of the patient is used.
- Handover should take place in an unhurried manner at a set time and place with minimal interruptions and under senior supervision. Each handover session should last 20–30 min to cover 10–15 patients.
- A structured written format like ISBAR should be maintained for all new patient handover. The essentials of this format are as follows:
  - *I*dentity of the patient—age, gender, and primary consultant.
  - *S*ituation—symptoms/problems, patient stability/the level of concern.
  - *B*ackground—the date of admission, history on presentation, diagnosis, and relevant past medical history.
  - *A*ssessment and action—what has been done so far and assessment of situation.
  - *R*esponse and rationale—response to intervention, what needs to be done, investigation, treatment pending, review by whom and when, further plan, and recommendations.
- For patients known to the ICU team, ISBAR may be shortened to SAR only.

Step 3: Take relevant history, perform clinical examination, and review investigations, nursing charts, and clinical notes

- After taking proper handover, the patients assigned should be thoroughly reviewed and examined afresh rather than relying on previous information.
- Enquire about any recent events from the duty nurse.
- Observe the patient from the bedside for a minute for any evidence of respiratory distress, restlessness, patient ventilator asynchrony, and paucity of spontaneous movements.
- After taking the bedside nurse's permission, ensuring proper hand hygiene, and maintaining patient privacy, introduce yourself and take patient's consent before examination. Examine from head to toe in a systematic way without causing any discomfort to the patient. Always thank the patient at the end of your examination and ensure proper covering.

- In the head and neck region, examine for pallor, jaundice, pupils, conjunctival hemorrhage, evidence of exposure keratitis, jugular venous pressure, carotid pulse, carotid bruit, thyromegaly, and cervical lymphadenopathy. Avoid manipulating the neck in trauma patients and ensure proper placement of cervical collar if present.
- Examine the conscious level by Glasgow coma scale scoring (see Chap. 30).
- In intubated patients, note the length of the endotracheal tube at lips and whether properly secured. Check proper placement of heat and moisture exchanger (HME) filters with dates changed and condition of the filter whether clogged with secretions. Check the ventilator circuit for not causing undue traction on the endotracheal tube, water accumulation, and attachment to heated humidifiers. Ensure proper attachment of nebulizer or metered-dose inhaler devices. Check inline suction assembly and endotracheal tube cuff pressure. In tracheotomized patients, check tracheostomy site for erythema, purulence, proper tying of the tracheostomy tube, and functioning of supraglottic suction, if present, and measure cuff pressure. In the uncuffed tube, check patency by blocking the tube and asking the patient to vocalize. Enquire about the frequency of suctioning and the amount and type of respiratory secretions.
- Check placement of orogastric or nasogastric tube position, patency, and attachment to the enteral feeding pump.
- In patients with central venous catheters at jugular or subclavian venous sites, ensure proper dressing and inspect the entry site for erythema and purulence. Palpate over the dressing for tenderness. Ensure stopcocks are properly cleaned and securely attached.
- Examine the chest systematically. Inspect for proper electrocardiograph lead placement, any skin changes, and flail chest in trauma patients. Palpate for any crepitus and percuss for dullness of effusion and hyperresonance of pneumothorax. Auscultate for breath sounds, cardiac sounds, adventitious breath sounds, and cardiac murmurs.
- Examine the abdomen for fullness, tenderness, visceromegaly, ascites, and bowel sounds. Also check the position of the gastrostomy or jejunostomy tube if any.
- Rectal examination in all patients and pelvic examination in women should not be ignored. Enquire about bowel movements, consistency, and color of stool.
- Check penile area for urinary catheter position and proper tying of the urinary bag at the thigh to avoid traction and reverse drainage. Examine the color and quantity of urine in the drainage bag.
- Examine upper extremities for radial and brachial pulse, blood pressure, hand grip, and thrombophlebitis. Check radial artery line if in place for proper functioning by performing a flush test, date of insertion, and capillary refill for ensuring hand perfusion.
- Examine lower extremities for edema, calf swelling, muscle strength, proper fitting of anti-embolism stockings, or pneumatic compression. Look for any femoral lines and if present whether properly secured and any evidence of groin hematoma.

- Roll the patient on the side with nurse's help and examine the back. Feel the back of scalp and ears for pressure areas, auscultate for basal crepitations, or diminished breath sounds. Look for decubitus ulcers at the sacral area, scrotal swelling, and any perineal soiling or evidence of candidiasis.
- In postoperative and trauma patients, look at the wound or surgical incision site for erythema and purulence, palpate for induration and tenderness, and check proper dressing. Check the drainage bag for proper labeling, amount, and type of drainage.
- Take note of bedside monitor readings of vital signs—cardiac rate and rhythm (print out a rhythm strip), any obvious ST changes, and mean arterial pressure—noninvasive or invasive, and confirm yourself by checking manually if in doubt about correct values. Check pulse oximeter plethysmograph and oxygen saturation, central venous pressure, or pulmonary arterial pressures (after printing out a pressure strip), capnograph, and core temperature readings.
- Check ventilator parameters—mode, FiO_2, positive end-expiratory pressure (PEEP), tidal volume, pressure limit, ventilator rate, inspiratory–expiratory ratio, and inspiratory flow. Monitor minute ventilation, auto-PEEP, and pause pressure. Measure lung compliance and airway resistance.
- Check intravenous infusions, volumetric infusion pumps, and syringe pumps for proper labeling and functioning.
- Review recent investigations including hematology, biochemistry, microbiology, and imaging studies and compare it with the previous reports to analyze the trend.
- Familiarize with the ICU nursing chart and review it systematically. Examine previous 24-h trend and worst values. Look for records of vital signs, hemodynamic and ventilator parameters, intake and output chart, enteral feed rate and tolerance, hourly urine output, blood or blood product transfusion in previous 24 h, and any untoward transfusion-related reaction.
- Review cumulative fluid balance till date and cumulative calories or protein deficit or excess.
- Review the medication sheet daily for proper drug dosing and stop any unnecessary medication.
- Review clinical notes for any referral input and any new major event described.
- Review patient's code status and therapeutic support level as desired by the patient and family.
- Review the payor status of the patient.

Step 4: Participate in a multidisciplinary ward round

- ICU care is a teamwork, and a typical ICU round in a tertiary care hospital consists of the ICU consultant, resident doctor, senior sister, duty nurse, physiotherapist/respiratory therapist, dietitian, clinical pharmacist, ICU technician, and social worker.
- Rounds in ICUs are different from a general ward round in many aspects. First, substantially more information is exchanged, which is essential. Second, the emphasis is on physiological derangements rather than on specific problems.

Third, the discussion is always goal-oriented so that when goals are met the patient may be transferred to a lower level of care.

- In addition to providing educational value, rounds in ICUs serve two purposes: first to communicate the patient's present status to the entire team and second to establish goals and plans for each patient.
- To ensure that each patient undergoes a comprehensive evaluation each day, think and communicate in terms of systems. These typically include neurological (including analgesia and sedative), pulmonary, cardiovascular, renal, fluid, electrolytes, nutrition, gastrointestinal, metabolic, infectious, and hematologic. Rounds will move more smoothly and efficiently if a structured and uniform format of presentation is adopted by all members.
- Each system should be analyzed and presented according to outcome and process variables. For example, in the renal system, urine output, intake/output balance, and electrolyte levels are outcome variables, and supplemental electrolytes administered, volume of intravenous fluid given, and amount of diuretic used are process variables (Table 79.1).
- Case presentation should start with identifying the patient, the day of ICU or hospital admission, reason for admission, principal diagnosis, and any significant event in the previous 24 h. For new patients, significant medical background and presenting complaint should be presented. Vital signs, pertinent physical examination findings, hemodynamic, ventilator parameters, intake and output, invasive procedures performed, major investigations done with results, and treatment initiated should be described. Area of major concern needs to be addressed; treatment goals and the plan for the day should be elaborated. A summary capsule of case should be presented at the end. The case presentation should be precise and should not take more than 5 min.

Step 5: Write proper clinical notes

- Appropriate documentation whether on paper or electronic is of paramount importance and should be done in a systematic and unhurried manner. Writing should be legible, and the proper date, time, and signature should be recorded.
- A uniform format should be maintained during daily case record documentation.
- SOAP (subjective, objective, assessment, plan) format may be utilized for case notes in short-stay cases.
- A more elaborate and comprehensive daily checklist should be utilized in complex and long-stay cases on multiple organ support (Table 79.2). This ensures that all aspects of case management have been addressed.
- Every patient should have a master problem list (active and inactive problems), which needs to be updated periodically.
- Documentation of family briefing and end-of-life care decisions should be done meticulously.

Step 6: Perform procedures under supervision

- Acquiring technical skills in different procedures is a requisite for any ICU training program.

Table 79.1 Outcome and process variables

System	Outcome variables	Process variables
Neurological	Motor function	Type/route of analgesics
	Pain level	Type/route of sedative, antiseizure medications
	Sedation level	Intracranial pressure monitors
	Glasgow coma score	
	Intracranial pressure	
	Occurrence of seizures	
Pulmonary	Presence of rales or wheezes	Ventilator settings
	Appearance of the chest X-ray	Administration of nebulized bronchodilators
	Oxygen saturation	Administration of supplemental gases such as nitric oxide
	End-tidal CO_2 concentration	Readiness for weaning and extubation daily assessment
	Arterial blood gas data	
	Spontaneous ventilation rate	
	Forced vital capacity	
	Negative inspiratory pressure	
Cardiovascular	Blood pressure	Estimates of and interventions to adjust preload, such as central venous pressure or pulmonary artery occlusion pressure
	Heart rate	Estimates of and interventions to adjust afterload, such as vasodilator therapy
	Abnormal rhythm	Estimates of and interventions to adjust contractility, such as inotropic therapy
	Presence of rales	Estimates of (e.g., drug level) and interventions to adjust antiarrhythmic
	Peripheral pulses and extremity warmth	
	Cardiac output	
	Evidence of ischemia	

Renal/fluid/electrolytes	Weight	Intravenous fluid composition and rate
	Net intake and output balance	Supplemental electrolytes
	Current electrolytes	Sites of unusual loss of volume
	Blood urea nitrogen, creatinine, ABG	Sites of unexpected loss of specific electrolytes
Gastrointestinal/metabolic/nutrition	Bowel sounds, function	Route/rate/composition of nutritional support
	Absorption of enteral feedings	Use of prokinetic or antiemetic agents
	Fraction of caloric goal attained	Prophylaxis against gastrointestinal bleeding
	Nitrogen balance	Insulin requirements
	Hyper- or hypoglycemia	Hormone replacement therapy (e.g., thyroid)
Hematologic/infections disease	New findings on physical examination suggestive of bleeding	Transfusion requirements
	Hematocrit, platelet count, and coagulation parameters	Deep venous thrombosis prophylaxis
	Temperature; findings suggestive of infection on physical examination; gram stain and culture data, including antimicrobial and sensitivity	Procedures to diagnose and/or control infection
	Leukocyte count and differential count	Antimicrobial prescription, including drug levels where appropriate

Adapted from www.sccm.org
Medical students' guide to intensive care medicine

Table 79.2 Daily checklist

I Hug Fast	Continuous Quality Improvement (CQI) checklist
I = Infection control	What needs to be done for the patient to be discharged from the ICU?
H = Hand hygiene and head of bed elevation	What is the patient's greatest safety risk? How can we reduce that risk?
U = Ulcer prophylaxis	Pain management/sedation
G = Glycemic control	Cardiac/volume status
F = Feeding	Pulmonary/ventilator (plateau pressure, elevate head of bed 30–45°)
A = Analgesia	Mobilization
S = Sedation	Infectious disease issues, cultures, drug levels
T = Thromboprophylaxis	Gastrointestinal issues, nutrition
	Medication changes (can any be discontinued?)
	Tests/procedures
	Review morning laboratory results and the chest X-ray
	Consultations
	Communication with primary service
	Family communication
	Can catheters tubes be removed?

Adapted from Vincent (2005) and Pronovost et al. (2003)

- Acquire factual knowledge about the common procedures performed in the ICU with indications, contraindications, complications, and steps of procedure (see Sect. XV).
- Familiarize yourself with procedures performed by observing seniors in ICUs.
- Initial procedures should be performed under elective conditions under proper supervision.
- Take informed consent in elective procedure, explain procedure to the patient, and always remember "do no harm."
- Procedure performed should be documented, and any complication should be recorded and countersigned by the supervisor. An individual logbook of procedures should be maintained to acquire sufficient experience to have privileges of unsupervised procedures.

Step 7: Follow infection control practices (see Chap. 48)

- Take leadership and exemplary role in maintaining proper infection control practices.
- Maintain and teach hand hygiene procedures to juniors and nonmedical members of the ICU team.
- Practice isolation practices wherever applicable.
- Be vigilant in detecting and reporting nosocomial infection to the infection control nurse.
- Practice antibiotic stewardship.

- Take proper preventive measures during invasive procedures and during maintenance of invasive devices.

Step 8: Counsel family members
- Be observant and listen to seniors discussing a patient with family members and clarify any doubts.
- Start participating in group discussion with the family and document discussions in clinical notes.
- Be sensitive about discussion of end-of-life care (see Chap. 81).
- Above all, be compassionate.

Step 9: Be a productive member of the ICU team
- ICU care is a teamwork where each member of the team has a defined responsibility.
- Many of the ICU tasks are interdependent, and therefore effective communication among team members is essential.
- Familiarize yourself with policies and protocols of the ICU, which may vary between ICUs.
- Create a safe work culture, avoid distractions, and keep ICU environment clean, calm, and acceptable to patients and family members.
- Punctuality, following a dress code if present, and proper mannerism reflect a professional approach.
- Attend departmental meeting regularly.
- Take an active role in quality control programs of the ICU.

Step 10: Keep yourself updated
- Actively participate in academic and research activities of the ICU.
- Keep a reference ICU handbook with you and refer to it whenever in doubt.
- Keep hospital drug formulary in the ICU and communicate with pharmacists regarding drug dosing.
- Attend simulation workshop for proper training in ICU skills.
- Participate in e-learning programs available on the web.
- Be familiar with ICU syllabus (see Appendix).
- Work towards gaining an accreditation at the end of your training period.

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Website

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Quality Control

80

Subhash Todi and Ashit Bhagwati

Case 1

A 70-year-old male patient with dementia and Parkinson's disease was admitted to the ICU with the confusional state. He fell from his bed on the night of admission and suffered scalp injuries. How would you ensure that similar accidents do not happen in the future?

Case 2

A 60-year-old male patient was admitted to hospital with hypertensive intracerebral bleed and required ventilatory support. On the fourth day of admission, he developed features of ventilator-associated pneumonia. What measures should have been in place to avoid this complication?

Case 3

A 30-year-old male patient was admitted to hospital with gastroenteritis and severe hypokalemia. He was inadvertently administered high concentration of potassium in intravenous infusion through the central line and suffered a cardiac arrest. How could you have prevented such errors?

In a landmark publication, *To Err Is Human: Building a Safer Health System*, a decade ago by the Institute of Medicine USA, it was described that human error was one of the common causes of morbidity, mortality, and increased health care cost in hospitalized patients worldwide. Experts estimate that as many as 98,000 people die

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every year due to medical errors in hospitals. This number is more than the number of deaths due to motor vehicle accidents, breast cancer, and AIDS—three causes that receive far more public attention. This error is more evident in the critically ill patients in the ICU. Increasing accountability and demand from public and accrediting agencies have led to a movement of quality care in ICUs.

Step 1: Understand the concept of quality and safety

- Quality and safety are two sides of the same coin. Quality reflects measures that should have been taken or errors of omission, and safety reflects actions that were taken inappropriately or errors of commission.
- Case 1 may be taken as quality issue as proper precautions were not taken, which led to compromise in patient safety.
- Case 2 reflects need for preventive protocols for ventilator-associated pneumonia to be in place, another quality control issue.
- Case 3 reflects not only an error of commission, clearly a safety issue, but also lack of protocol for intravenous potassium infusion, a quality issue.

Step 2: Understand Donabedian's theory on quality control

- Three important ingredients are as follows:
  1. Structure (what we have)
  2. Process (what we do)
  3. Outcome (what we get)
- Structural issues consist of organizational elements, personnel, and finance and are predominantly under administrative control.
- Process issues are the care given to the patient by health care providers. Daily checklists of such issues are always helpful.
- Outcome reflects what happens to the patient from morbidity and mortality point of view, given the structure in place and processes being implemented (Tables 80.1).

Step 3: Implement standardized data collecting and reporting system

- This should be done for all the three elements: structure, process, and outcome.
- It should follow SMART principle (specific, measurable, achievable, reliable, and time bound). A well-trained data collector is the backbone of any quality control program (Fig. 80.1).

Step 4: Understand principles of data collection

- Any data should have a numerator (affected persons) and a denominator (persons at risk) (Table 80.2).

Step 5: Prioritize

- Identify important elements for which data need to be collected (Table 80.3).

Step 6: Identify team members

- This should be done for data collection, data entry, data analysis, and data reporting.

Table 80.1 Donabedian's model of quality control

Structure	Process	Outcome
Closed model of ICU care	Compliance with hand hygiene	Crude ICU mortality
Critical care consultant availability	Family conference	Risk-adjusted ICU mortality
24 × 7 intensivist coverage	End-of-life support policies	Standardized mortality ratio = crude mortality/ predicted mortality
Ward design	Compliance with ventilator bundle	Hospital mortality
Nurse–patient ratio	Compliance with central line insertion bundle	ICU length of stay
Doctor–patient ratio	Antibiotic consumption	Hospital length of stay
Policies and protocols	Implementation of catheter-related blood stream infection prevention policies	Family satisfaction
Infectious disease consultant	Implementation of urinary tract infection prevention policies	Cost of care
Infection control nurse		Resource utilization
Multidisciplinary ward round		
Infection control committee		
Daily goal sheet		
Antibiotic form		
Adequate equipment		

Step 7: Identify benchmarks

- This should be done for comparison of data.
- There are national and international benchmarks for various quality control processes and outcomes.
- In the absence of a comparative benchmark, one can follow one's own trend and performance over time.

Step 8: Adopt the plan-do-study-act cycle for quality control

- After identifying specific elements for data collection, collect, analyze, and compare reliable data with benchmark, take corrective action, and revisit the same process periodically to maintain a standard of care.

Step 9: Understand terminology for reporting of safety issues

- Patient safety data should be reported in the format including error, incident, near miss, adverse event, and preventable adverse event (Table 80.4).

Step 10: Implement

- One of the measures for evaluating patient safety such as incident report, root cause analysis, and failure mode effect analysis should be implemented:

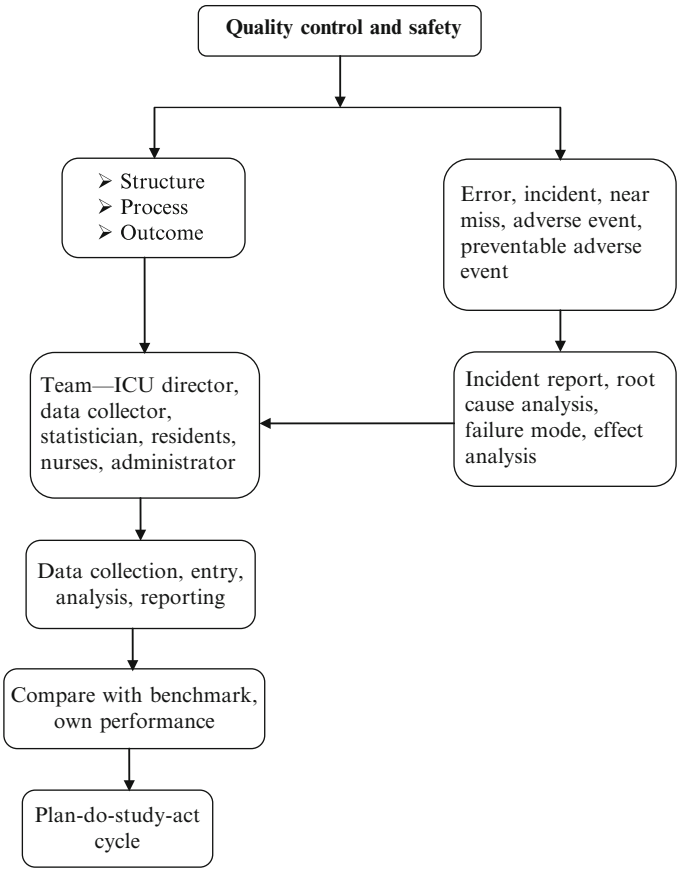

Fig. 80.1 Quality control approach in the ICU

Table 80.2 Formulae for urinary tract infections, central line-associated blood stream infections, and ventilator-associated pneumonia

$\frac{\text{Number of catheter - associated urinary tract infections}}{\text{Number of urinary catheter - days}} \times 1{,}000$
$\frac{\text{Number of central line - associated blood stream infections}}{\text{Number of central line - days}} \times 1{,}000$
$\frac{\text{Number of ventilator - associated pneumonias}}{\text{Number of ventilator - days}} \times 1{,}000$

– *Incident report*: It evaluates how a single patient comes to a harm. An incident reporting system should be voluntary, anonymous, and not linked with any form of punitive measures.
– *Root cause analysis*: This is a more focused enquiry on certain incidents deemed to be important for patient safety. A sentinel event is identified, and

Table 80.3 Fundamental quality indicators

(a) Early administration of acetylsalicylic acid in acute coronary syndrome
(b) Early reperfusion techniques in ST-elevation myocardial infarction
(c) Semirecumbent position in patients undergoing invasive mechanical ventilation
(d) Prevention of thromboembolism
(e) Surgical intervention in traumatic brain injury with subdural and/or epidural hematoma
(f) Monitorization of intracranial pressure in severe traumatic brain injury with pathologic CT findings
(g) Pneumonia associated to mechanical ventilation
(h) Early management of severe sepsis/septic shock
(i) Early enteral nutrition
(j) Prophylaxis against gastrointestinal hemorrhage in patients undergoing invasive mechanical ventilation
(k) Appropriate sedation
(l) Pain management in unsedated patients
(m) Inappropriate transfusion of packed red blood cells
(n) Organ donors
(o) Compliance with hand-washing protocols
(p) Information of patients' families in the ICU
(q) Withholding and withdrawing life support
(r) Perceived quality survey at discharge from the ICU
(s) Presence of an intensivist in the ICU 24 h/day
(t) Adverse events register

Adapted from Spanish quality control guideline

Table 80.4 Terminology for reporting adverse events

Patient safety	Absence of the potential for, or occurrence of, health care-associated injury to patients
Error	It is defined as mistakes made in the process of care that result in, or have the potential to result in, harm to patients. Mistakes include the failure of a planned action to be completed as intended or the use of a wrong plan to achieve an aim. These can be the result of an action that is taken (error of commission) or an action that is not taken (error of omission)
Incident	Unexpected or unanticipated events or circumstances not consistent with the routine care of a particular patient, which could have, or did lead to, an unintended or unnecessary harm to a person, or a complaint, loss, or damage
Near miss	An occurrence of an error that did not result in harm
Adverse event	An injury resulting from a medical intervention
Preventable adverse event	Harm that could be avoided through reasonable planning or proper execution of an action

important preventive aspects of this event are discussed by the safety team, and safeguards are implemented.

– *Failure mode and effects analysis*: An error-prone process is identified, and a multidisciplinary team is formed to analyze prospectively the process from multiple perspectives before a sentinel event has occurred.

Step 11: Initiate safety and quality culture

- This has to come from a strong leadership, primarily from the ICU director, backed by a willing management.
- This has to be backed up by full support and motivation of ICU staff.
- Adequate budget needs to be provided by the administration.
- Computerized physician order entry system goes a long way in ensuring safety in the ICU by reducing human error.

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Ethical Principles in End-of-Life Care

81

Subhash Todi and Rajesh Chawla

A 70-year-old male patient was admitted with massive intracerebral bleed to the ICU for 6 days. He was on a ventilatory support, with a Glasgow Coma Score of 6. According to the treating physician and neurologist, his survival chances were poor, and even if he survived, he would be fully dependent functionally. His eldest son requested withdrawal of the ventilatory support to provide comfort measures only and transfer out of the ICU.

Optimizing comfort care for critically ill patients during the terminal stage according to patient and family's wishes is an obligation for all critical care physicians. With increasing complexity of organ support, increasing age, and multiple comorbidities of critically ill patients, prolonged life-sustaining treatment is very commonly observed in modern ICU care. Limitations of such treatment in selected individuals need to be realized early, and clinical skills need to be developed for managing end-of-life (EOL) issues in these patients.

Step 1: Identify situations when EOL support needs to be initiated

Identifying these situations needs expertise and experience. The following checklist, though not exhaustive, should help the physician to recognize when to start discussions on EOL issues:

- Advanced age coupled with a poor premorbid state due to chronic debilitating diseases, for example, advanced chronic obstructive pulmonary disease requiring

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home oxygen and/or bi-level pressure support or severe impairment of quality of life, advanced interstitial lung disease on oxygen therapy with failed medical treatment, chronic renal failure requiring long-term dialysis, chronic liver disease, and advanced congestive heart failure.
- Catastrophic illnesses with multiple organ dysfunctions unresponsive to a reasonable period of aggressive treatment.
- Prolonged coma (in the absence of brain death) due to acute nonreversible causes or chronic vegetative state.
- Incurable chronic severe neurological states rendering meaningful life unlikely, for example, progressive dementia or quadriplegia with ventilator dependency.
- Progressive metastatic cancer where treatment has failed or the patient refuses treatment.
- Post-cardiorespiratory arrest, situations with non-restoration of comprehension after a few days.
- Comparable clinical situations coupled with a physician's prediction of low probability of survival.

Step 2: Discuss with other team members including nurses regarding EOL decision
- Ensure that all members of health care team are on board and agree on initiating this discussion.
- The overall responsibility for the decision rests with the attending physician/intensivist of the patient, who must ensure that all members of the caregiver team including the medical and nursing staff follow the same approach.

Step 3: Identify a surrogate decision maker
Majority of patients in the ICU are not competent to participate in EOL discussion. In these circumstances, the following approaches may be adopted:
- *Living will or advanced directive*: A duly processed legal document, which states patient's explicit wishes while he/she was campus mentis (in full sense), should be honored. This situation is met very rarely.
- *Durable power of attorney*: The patient has legally designated a surrogate to take decisions on his/her behalf during period of incompetency.
- *Surrogate decision maker*: This means spouse, children, parents, siblings, the next of kin who is available, or even a trusted friend. Existing laws for hierarchy of surrogates for EOL decision making, if present, should be applied in these situations.

Step 4: Understand ethical principles about withdrawing life-support measures in the ICU
- *Autonomy*
  - Right to self-determination: The properly informed patient has a right to choose the manner of his/her treatment.
  - Competency: The patient should be competent to make decisions and choices. This competency is assessed clinically by the physician and a psychiatrist if necessary.

- *Beneficence*
  - It means doing what is (or judged to be) in patient's best interest.
  - In this context, the physician's expanded goals include facilitating (neither hastening nor delaying) the natural dying process, avoiding or reducing the sufferings of the patient and the family, providing emotional support, and protecting the family from undue financial loss.
- *Non-maleficence*
  - It means doing no harm and avoiding the imposition of unnecessary or unacceptable burdens on the patient and the family.
- *Distributive justice*
  - It means that patients in similar circumstances should receive same care.

Step 5: Initiate discussion on EOL with the surrogate decision maker

- The intensivist should initiate this process.
- This should be done in an empathic manner, in an unhurried way, with due time given for discussion. The environment should preferably be a quiet room, ensuring privacy and without any interim disturbance.
- A senior nurse or other members of health care team including family physician may be present during discussion.
- Other senior family members apart from the surrogate can also participate in the process, though total number should be restricted.
- Discussions should be carried out in a language and in terms that the family can understand.
- His/her present understanding of the disease process, expectations, and areas of uncertainties need to be identified. Attentive listening during this process is the key in reaching a consensus.
- The present clinical situation needs to be explained in simple nonclinical terms.
- The diagnosis, prognosis, and the range of therapeutic interventions available, including their risks, benefits, costs, and consequences, as well as the option of no therapy, should be explained clearly.
- As accurate a prognosis as is possible should be given, clarifying that uncertainty is inherent in the treatment of critical illness.
- Family's wish for a second opinion needs to be clarified and if requested should be complied with.
- The possibility of death should be discussed along with the medical and palliative treatment options.
- Any previously stated terminal care wishes or preferences directly or indirectly expressed by the patient should be enquired.
- The discussions should include the relevant economical, ethical, and legal issues.
- The family should be counseled that withdrawal of support does not mean withdrawal of care, and all measures will be taken to ensure that the patient is free of pain and discomfort during EOL care.
- It should be made clear to the family that the decision is not binding and they are at liberty to change their mind if needed later (Fig. 81.1).

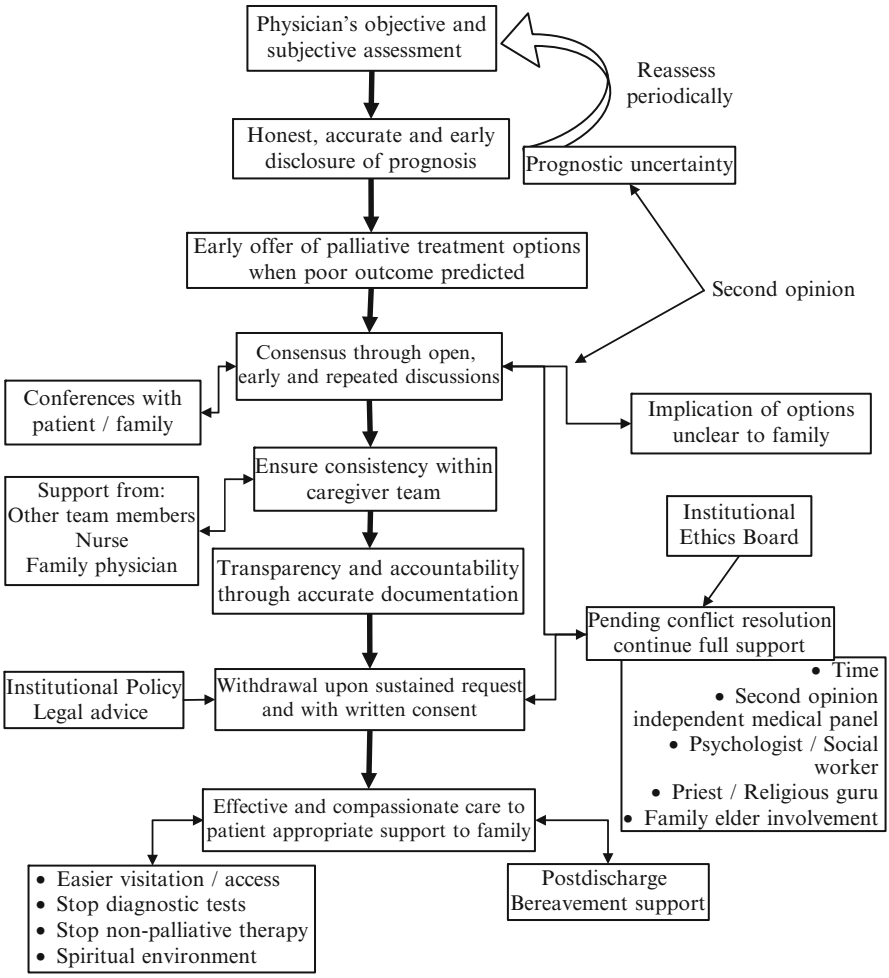

Fig. 81.1 Pathway to end-of-life decision making

Step 6: Hold multiple counseling sessions

- As EOL decisions are very sensitive, these should not be taken in haste. The family should be given adequate time and opportunity to ask questions and to express their views and emotions and to come to term with the situation and make an informed decision.
- There should be multiple counseling sessions of adequate duration.
- Pending consensus decisions or in the event of conflicts between the physician's approach and the patient's/family's wishes, all existing supportive interventions should continue.

Step 7: Reach a consensus and discuss modalities of palliative care

- If the family consistently desires that life support should be withdrawn and when the treating physician also considers aggressive treatment non-beneficial, it is ethically justifiable to consider withdrawal of life support within the limits of existing laws of the country.
- The physician should explicitly communicate the available modalities of limiting life-sustaining interventions as follows:
- Do not intubate/resuscitate (DNI/DNR)
  - Aggressive ICU management but not including intubation (DNI) or attempts at cardiopulmonary resuscitation (DNR)
- Do not escalate
  - Not to escalate some or all existing life-support modalities (intubation, inotropes, vasopressors, mechanical ventilation, dialysis, antibiotics, intravenous fluids, enteral or parenteral nutrition) in case of clinical deterioration with the understanding that the patient will probably die from the underlying condition.
- *Withdrawal of life support*
  - All or specific life-support systems such as dialysis or ventilators may be withdrawn.
  - Decision not to institute new life-support treatment.
  - Ethically, there is no difference between withholding and withdrawing life-support therapy.

Step 8: Document discussion in case notes

- The proceedings of the counseling sessions, the decision-making process, name of health care members and family members present during discussion, and the final decision should be clearly documented in the case records, to ensure transparency and to avoid future misunderstandings.
- Details of the communications between the medical team and the family should be documented accurately and completely.
- The signature of a family representative is not a mandatory requirement but may be kept optional.

Step 9: Institute palliative care

- Ensure proper sedation and analgesia (e.g., midazolam/fentanyl), preferably as an infusion. Give proper dose to ensure comfort and analgesia. Avoid excessive doses leading to respiratory depression or hypotension. Document doses and intention of palliation in the case notes.
- Neuromuscular blockers should be stopped. Ventilators may be disconnected, and the patient may be left on T piece for suctioning or extubated if family desires.
- Family members should be allowed at the bedside and given adequate time to spend with the patient. Monitors may be switched off, and blood draws should be stopped to avoid distraction.
- The patient may be shifted out of the ICU if the family wishes and if permitted within the laws of the country.

Step 10: Resolve areas of conflict

When the family may be pursuing unrealistic demands of continuing futile care as deemed by the treating senior physician, or the physician may be seeking to impose his/her wishes on the family in contradictions to their wishes, conflicts may arise. The proposed course of action in these situations may be as follows:

- A second opinion from another physician not hitherto involved in the care of the patient.
- Multiple counseling sessions explicitly informing the family the hopeless prognosis of the patient and the futility of continuing life support.
- If the family is intransigent, then suggest transfer to another treating team willing to continue support.
- With the help of the hospital administration, set up a committee of doctors to counsel the family. The committee may also take the help of a social worker, psychologist, or a religious person identified by the family to help resolve barriers to understanding.
- Seek a judicial review.

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ICU Organization and Training

82

Narendra Rungta, Manish Munjal, and Kundan Mittal

A 50-year-old male patient was brought to the emergency department in a shock state. After initial resuscitation, the emergency physician wanted to admit this patient in the intensive care unit (ICU), but there were no beds available. The duty resident in the ICU was unable to shift any patient to make room for the patient in the emergency department.

Organizational issues, anticipating problem areas, and prior planning are of utmost importance for smooth functioning of any intensive care unit (ICU). These organizational aspects may be looked from human resources, infrastructure, and processes of care viewpoint (Table 82.1).

Step 1: Designate the level of care that can be provided by the ICU

- ICUs are usually designated by three levels of care provided, with a varying nomenclature for these levels.
- In essence, they are the basic, intermediate, and advanced level of ICU care.
- Minimum requirements for a basic level ICU care:
  - Resuscitation and short-term cardiorespiratory support including mechanical ventilation
  - Noninvasive ventilation

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Table 82.1 Important considerations in organizing an ICU

ICU design
Assessing cost-effectiveness in the ICU
Improving the quality of care in the ICU
Infection control and surveillance in the ICU
Outreach services
Legal issues in critical care
Assessment of severity of illness and likely outcome
Physiotherapy in intensive care
Critical care nursing
Common problems after ICU care
Clinical information system
Clinical trials in critical care
Transportation of the critically ill patients
Telemedicine
Preparedness for catastrophe

  - Facilities for transport to higher centers
  - Basic laboratory, radiology, blood bank outsourcing
  - 24-h coverage by a physician trained in fundamentals of ICU care
  - Adequate support staff
- Minimum requirements for an intermediate level ICU care:
  - All requisites for the basic level ICU.
  - Intermediate or long-term cardiorespiratory support.
  - Expert consultation available on call.
  - The intensivist should be in charge of ICU care.
  - Duty doctors and nurses should have intensive care training.
  - Onsite blood bank facility.
  - Comprehensive ICU care facility.
  - Policies and protocols for the ICU are followed.
- Minimum requirement for an advanced level ICU care:
  - All requisites for an intermediate level ICU
  - Fulltime multidisciplinary critical care team, led by an ICU director
  - A nursing director
  - Subspecialty services such as neurosurgery, cardiothoracic surgery, interventional cardiology, and radiology available round-the-clock
  - Preferably a closed model of ICU care delivery
  - Bedside endoscopy, bronchoscopy, and dialysis facilities
  - Extracorporeal support available
  - A step-down unit
  - Academic program for ICU training

Step 2: Identify the model of ICU care delivery

- Pattern of delivery of care in the ICU varies globally. In essence, it can be described as closed, open, or transitional ICU care.

  - *Closed ICU care*: Patient care is transferred to consultant intensivist, who makes all major decisions including transferring out of patients. Once the patient is transferred out of ICU, the primary physician takes over the care.
  - *Open ICU care*: Patient care remains under the primary physician who may not be an intensivist. Intensivist, if available, consults only on request and can suggest treatment which is not binding.
  - *Semiclosed or transitional ICU care*: This is a hybrid model where the consultant intensivist rounds on every patient as a mandatory consultation. Patient management is a shared decision between the primary physician and the intensivist.
- There is an increasing body of literature that the closed ICU system is a better model of delivery of care in the ICU.

Step 3: Construct a multidisciplinary team

- The principal ingredients of a multidisciplinary team in an advanced ICU should consist of the following:
  - Consultant intensivists
    - Conduct daily rounds of all ICU patients preferably twice
    - Available on call or in-house for emergencies
    - Supervise residents in writing clinical notes and during procedures
    - Coordinate admissions and discharges
    - Coordinate with the primary physician
    - Communicate with the patient and the family
    - Coordinate end-of-life decisions (see Chap. 81)
    - Maintain policies and protocols (see Chap. 80)
    - Perform quality control and audit (see Chap. 84)
    - Play an active role in teaching and research
  - Resident doctors
    - One qualified resident doctor for five ICU beds
    - Rotate at 8- or 12-h shift
    - Present cases in rounds, write clinical notes, and perform procedures and proper handover (see Chap. 79)
  - Nurses
    - 1:1 Nursing for patients on the ventilator
    - 1:2 or 1:3 Nursing for less sicker patients
  - Health assistants
    - Assist nurses in patient care activities such as feeding, giving bath, bed making, etc.
  - Respiratory/physiotherapists
    - Help in early mobilization
  - Nutritionists
    - Assess calories and protein goal every day and ensure adequacy of nutrition delivery
    - Coordinate with the physician and nurses to ensure early enteral nutrition delivery

  - Biomedical technicians
    - Maintain, calibrate, and troubleshoot different biomedical devices such as monitors and defibrillators
    - Ensure safe transport of these equipments
    - Ensure proper disinfection of the equipments
  - Clinical pharmacists
    - Coordinate with nurses and doctors to identify adverse drug reaction, drug dosing, and drug–drug interaction
    - Ensures compliance with the hospital antibiotic policy
  - Social workers
    - Liaise with family members and coordinate between them and ICU staff
  - Secretarial staff
    - Keep proper medical records, billing, computer entry of drugs, etc.
    - Answer phone calls and check the laboratory and radiology report.
  - Cleaning and housekeeping personnel
    - Clean the ICU (see Chap. 48)
    - Help in transporting the patient and blood samples
    - Help with catering services

Step 4: Understand important elements of an ICU design

- Location
  - The ICU should be located ideally near the emergency department and operation theater.
- Number of beds
  - General recommendation for number of ICU beds is usually 10 ICU beds per 100 hospital beds.
  - Bed strength in one ICU should be between 8 and 12.
- Layout
  - The ICU could have separate rooms, two or four bed cubicles, or an open ward with curtains or partition between patients.
  - The isolation room should be present for immunosuppressed patients (positive pressure) or infectious patients (negative pressure).
  - Space per bed has been recommended from 125 to 150 square feet.
  - Each bed should have compressed air, oxygen, vacuum source, and adequate electrical sockets for power source.
  - Beds should have removable headboards and adjustable position ideally motorized.
  - Beds should be equipped with the cardiopulmonary resuscitation (CPR) facility knob.
- Adequate lighting, preferably natural light, and minimum noise level should be maintained.
- Bedside hemodialysis facility should be available in some beds.
- There should be ample storage area and clean and dirty utility rooms.
- Proper hand hygiene, waste disposal, and adequate CSSD facilities should be available.

- Disaster preparedness should be maintained.
- Family counseling room and doctors and nurse resting rooms should be provided.
- Adequate toilet facilities for the patient and staff should be provided.

Step 5: Equip the ICU with the following services

- Continuous electrocardiogram monitoring (with high/low alarm) in all beds
- Pulse oximetry monitoring capability in all beds
- Continuous arterial pressure monitoring (noninvasive and invasive)
- Continuous central venous pressure monitoring
- Emergency resuscitative equipment including defibrillators
- Airway maintenance equipment including laryngoscopes and endotracheal tubes
- Adequate number of ventilators depending on case mix
- Equipment to support hemodynamically unstable patients including infusion pumps, blood warmers, pressure bags, and blood filters
- Hypo-/hyperthermia blankets
- Core temperature monitoring devices
- Temporary pacemakers
- Cardiac output monitoring facility
- Pulmonary artery pressure monitoring
- Glucometer
- Continuous or intermittent hemodialysis
- Peritoneal dialysis
- Capnography
- Fiber-optic bronchoscopy
- Intracranial pressure monitoring
- Continuous EEG monitoring
- Portable X-ray facilities
- Computerized access to laboratories, pharmacy, and imaging
- Immediate access to information—paging numbers, hospital directory, duty roster, online search facility, medical textbooks and journal, and poison center contact number

Step 6: Define ICU policies and protocols

- An updated policy and protocol of the ICU should be available to all ICU personnel.
- These policies should be formed with consultation of all stakeholders and approved by the ICU director and hospital management.
- A few examples of such policies are as follows:
  - Interhospital and intrahospital transport
  - End-of-life policies
  - Guidelines for determining brain death
  - Restraint and sedation protocols
  - Organ donation policies
  - Infection control policies
  - Antibiotic policies

Step 7: Make an organogram

- All ICUs should have a structured organogram depicting various activities carried out by the critical care department, personnel involved, and hierarchal structure.

Step 8: Organize training curriculum

- Training ICU residents and fellows should be an integral part of services provided by advanced ICUs.
- Nursing, physiotherapy, and technician training should also proceed in parallel.
- There is a wide variation in credentialing for intensive care training globally with variation in basic specialty requirement, duration of training, etc.
- All residents in training should keep a logbook of procedures performed under supervision and get it signed by the supervisor.
- They should acquire factual knowledge of core critical care syllabus during their training period (see Appendix). These can be obtained through hospital library or over internet.
- Simulation training in ICUs has been found to be the most effective way of training where various ICU scenarios can be simulated and various aspects of critical care training requirements apart from factual knowledge may be evaluated.

Suggested Reading

1. Haupt MT, Bekes CE. Guidelines on critical care services and personnel: recommendations based on a system of categorization of three levels of care. Crit Care Med. 2003;31:2677–83.
   North American guidelines for optimal ICU services and personnel for hospitals with varying resources.
2. Brilli RJ, Spevetz A. Critical care delivery in the intensive care unit: defining clinical roles and the best practice model. Crit Care Med. 2001;29:2007–19.
   Guidelines on different models of critical care delivery with pros and cons. These are being updated.
3. Task Force of the American College of Critical Care Medicine, Society of Critical Care Medicine. Guidelines for intensive care unit admission, discharge, and triage. Crit Care Med. 1999;27:633–8.
   A comprehensive guideline on policies and protocols for ICU triage, currently under revision.
4. Society of Critical Care Medicine. Guidelines for intensive care unit design. Crit Care Med. 1995;23:582–8.
   ICU designing details with recommendations, currently under revision.

Website

1. www.isccm.org
   Intensive care unit planning and designing in India, guidelines (2010)—defining the functions, roles, and responsibilities of a consultant intensivist.

Transportation of Critically Ill Patients

83

Amit Varma and Sandeep Dewan

A 57-year-old male patient was admitted to the emergency department with complaints of abdominal pain and recurrent vomiting. He was found to be in a state of septic shock. After the initial resuscitation, his abdominal examination was remarkable for abdominal distension with absent bowel sounds. The ultrasonography report of the abdomen was inconclusive, and he was shifted to the radiology department for a contrast-enhanced CT scan of the abdomen. He was still on inotropic and vasopressor support.

The ideal way to consider transport of a critically ill patient is as a "mobile ICU environment." Attention to details during transport ensures patient safety.

83.1 Intrahospital Transport

Step 1: Evaluate the need for transfer

- The most important initial step is to evaluate the potential benefit which may be derived by shifting the patient against the risks involved.
- The aim or purpose and the justification to transport should be noted in the case record.
- The potential risks can be minimized by careful planning of the procedure and utilization of available equipment and personnel.
- A multidisciplinary team of the physician, nurses, paramedical staff, and transport coordinator is required to plan and coordinate the process.

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- Transport of the patient should not be undertaken in the following circumstances:
  - Inability to provide adequate oxygenation and ventilation during transport or at destination, either by the manual resuscitator bag, portable ventilator, or standard intensive care unit ventilator.
  - Inability to maintain acceptable hemodynamic parameters during transport or at destination.
  - Inability to adequately monitor the patient's cardiopulmonary status during transport.
  - Inability to maintain airway control during transport or at destination.
  - All the necessary members of the transport team are not present.
  - Receiving team is not ready.

Step 2: Pretransport coordination and communication
- A physician-to-physician and nurse-to-nurse communication is required to plan the transport.
- The team ensures that the receiving location is ready to receive the patient for immediate procedure and testing.
- Documentation in the medical record should be done, which includes the indication of transport and the clinical status of the patient.

Step 3: Accompanying personnel
- Minimum of two people, preferably one of them from the treating ICU team, should accompany a critically ill patient.
- It is strongly recommended that a physician with training in airway management and advance cardiac life support accompanies the unstable patient.
- The transport personnel should remain with the patient until return to the ICU.

Step 4: Equipment requirement
- The equipment to be used during transport should be dedicated and should not be used anywhere else.
  - A blood pressure monitor, a pulse oximeter, invasive and noninvasive ventilators, and defibrillators.
  - Basic resuscitation drugs including epinephrine, nor epinephrine, antiarrhythmic drugs, vasopressin, muscle relaxants, sedatives, narcotics, analgesics, dextrose ampoule, and appropriate IV fluids.
  - Drip medications must accompany the patient.
  - All battery-operated equipments must be fully charged and should have adequate battery backup provision.
- In mechanically ventilated patients, endotracheal tube position is noted and secured before and during transport and the adequacy of oxygenation and ventilation is reconfirmed.
- No equipment or drugs should be placed over the patient. Most units will have custom-made shelves, which will fit on the beds or trolleys.
- The monitors and/or ventilators should be properly secured with straps to the bed or shelves so that they do not fall on the patient.

Step 5: Identifying high-risk patients
Patients in the following categories are at particularly high risk for deterioration during or after transport:
- The mechanically ventilated patients, particularly those with requirement of high positive end-expiratory pressure and FiO_2 more than 0.5. Extra oxygen reserve for patients with high oxygen requirement should be kept.
- Patients with high therapeutic injury severity score
- Head-injured patients
- Hemodynamically unstable patients requiring continuous infusion of dobutamine, or a continuous infusion of norepinephrine or other potent vasoactive agents

Step 6: Monitoring during transport includes the followings
- ECG monitoring
- Pulse oximetry
- Periodic measurement of the blood pressure, pulse rate, and respiratory rate
- Selective patients may benefit from capnography, continuous intra-arterial blood pressure monitoring, and intracranial pressure monitoring if required.

Step 7: Care during transport
- Ideally, the patient should receive the same level of care as in the pretransport area.
- Vital signs should be monitored and recorded at fixed intervals.
- Use of memory-capable monitors should be used. This will allow documentation of data during transport.
- Any adverse events should be noted and immediately acted upon.
- There should be a designated senior physician available for consult in case of an adverse or critical event during transport.
- Ideally, he/she should be available on-site and should be able to arrive at the destination area if required.
- The transport team should be able to communicate with the designated person during transit as well as upon arrival at the destination in case of an emergency.

83.2 Interhospital Transport

When a critical care patient requires resources, which are not available in the existing hospital, the patient will be transferred to a facility that has the required resources. Interhospital patient transfer will occur only when the benefits exceed the efforts. If needed, the resuscitation and stabilization of the patient should be carried out before the transport.

Basic requirements are the same for intra- or interhospital transport. Interhospital transport requires more planning, more personnel, vehicle availability, consideration of altitude effects in air transport, weather condition, battery life of equipments,

backup equipment, oxygen supply, power supply, contingency plan in case of breakdown, and more documentation for medicolegal purposes.

Step 1: Take informed consent

- An informed consent for interhospital transport must be taken from a competent patient, guardian, or legally authorized representative, if the patient is incompetent.
- It includes a discussion of the risks and benefits of transfer.
- It should be documented in the medical records before the transfer is done.
- In case of life-threatening emergencies when an informed consent cannot be taken, the indication of transfer and the reason for not obtaining consent must be documented in the medical record.

Step 2: Communicate and coordinate prior to transport

- The referring physician will contact the receiving physician and will explain the clinical condition to him/her.
- The mode of transportation (ground/air) will be determined by the transferring physician based on the medical condition, the time savings, facilities available, and the medical interventions required.
- The transport service will then be contacted to confirm its availability and coordinate the timing. A copy of the medical record including case summary and all relevant laboratory and radiographic data will accompany the patient.

Step 3: Decide on accompanying personnel

- It is recommended that minimum of two people should accompany a critically ill patient.
- The transport team leader should be a treating physician/intensivist/anesthesiologist with additional training in transport medicine.
- It is strongly recommended that a physician with training in airway management and advance cardiac life support accompanies the unstable patient.
- The transport personnel will remain with the patient until reaching the ICU.
- There must be a clear chain of responsibility throughout the transfer. A proper handover from referring physician to transfer physician and then to receiving facility physician is essential.

Step 4: Choose transport equipment and medicines

- When choosing the equipment, the following should be considered: size, weight, battery life, ability to fit to trolley railings, ability to function under condition of vibration, ease of use in poor light, and placement in restricted space.
- Equipments should be adequately restrained and should be easily accessible to the operator.
- Backup equipment may be desirable in some situation.
- The recommended minimum transport equipments and medications are given in Tables 83.1 and 83.2.

Table 83.1 Recommended minimum transport equipments

Adult/pediatric bags—valve systems and oxygen reservoir
Adult and pediatric masks
Flexible adaptors to connect the bag valve system to the endotracheal/tracheostomy tube
End-tidal carbon dioxide monitors (pediatric and adult)
Infant medium- and high-concentration masks with tubing
Laryngoscope with blades with extra batteries
Endotracheal tubes with stylets
Magill forceps
Nasopharyngeal airways
Oral airways
Scalpel with the blade for cricothyroidotomy kit
Needle cricothyroidotomy kit
Water-soluble lubricant
Nasal cannulae
Oxygen tubings
Adhesive tape
Aerosol medication delivery system
Alcohol swabs
Arm boards
Arterial line tubings
Intraoseous needle
Blood pressure cuffs
Butterfly needles
Communications backups
ECG monitor/defibrillator with electrolyte pads and jelly
Flashlights with extra batteries
Heimlich valve
Infusion Pumps
IV fluid administration tubing
Y fluid administration tubing
Extension tubing
Three-way stopcocks
IV catheter (14–24G)
Intravenous solutions (1,000 mL, 500 mL of normal saline)
Irrigating syringe (60 mL), catheter tip
Kelley clamp
Hypodermic needles and syringes, assorted sizes
Normal saline for irrigation
Pressure bags for fluid administration
Pulse oximeter with multiple site adhesive or reusable sensors
Soft restraints for upper and lower extremities
Stethoscope
Suction apparatus and catheters
Surgical dressings and tourniquets
Trauma scissors
The followings are considered as needed: neonatal/pediatric isolette, spinal immobilization device, and transport ventilator

Table 83.2 Recommended minimum transport medication

Adenosine (6 mg/2 mL)
Amiodarone (150 mg/3 mL)
Atropine (0.6 mg/mL)
Calcium chloride (1 g/10 mL)
Dextrose (25%/50%)
Digoxin (0.5 mg/2 mL)
Diltiazem (25 mg/5 mL)
Diphenhydramine (50 mg/1 mL)
Dopamine (200 mg/5 mL)
Epinephrine (1 mg/10 mL)
Furosemide (100 mg/10 mL)
Glucagon (1 mg vial)
Heparin (1,000 units)
Isoproterenol (1 mg/5 mL)
Labetalol (40 mg/8 mL)
Lidocaine (100 mg/10 mL)
Mannitol (50 g/50 mL)
Magnesium sulfate (1 g/2 mL)
Metroprolol (5 mg/5 mL)
Naloxone (2 mg/2 mL)
Nitroglycerine injection (50 mg/10 mL)
Nitroglycerine tablets (0.4 mg)
Nitroprusside (50 mg/2 mL)
Normal saline (30 mL) for injection Nor epinephrine (2 mL)
Phenobarbital (65 mg/mL or 130 mg/mL)
Potassium chloride (20 mEq/10 mL)
Procainamide (1,000 mg/10 mL)
Sodium bicarbonate (50 mEq/50 mL)
Sterile water (30 mL) for injection
Terbutaline (1 mg/1 mL)
Verapamil (5 mg/2 mL)

The following specialized/controlled medications are added immediately before transport as indicated:

- Narcotic analgesics (e.g., morphine and fentanyl)
- Sedatives/hypnotics (e.g., lorazepam, midazolam, propofol, and ketamine)
- Neuromuscular blocking agents (e.g., succinylcholine, pancuronium, atracurium, and rocuronium)

Additional drugs should be added depending on specific circumstances (antiarrhythmic or antibiotics that need to be dosed during transport).

Step 5: Monitoring during transport

This includes followings:

- ECG monitoring
- Pulse oximetry
- Periodic measurement of blood pressure, pulse rate, and respiratory rate
- Selective patients may benefits from capnography, continuous intra-arterial blood pressure monitoring, and intracranial pressure monitoring.

Step 6: Preparing intravenous access and airway before transport

- If peripheral venous access is unavailable, central venous access is established. If needed, fluid resuscitation and inotropic support are initiated, with all intravenous fluids and medications maintained in plastic (not glass) containers.
- A patient should not be transported before airway stabilization if it is judged likely that airway intervention will be needed en route (a process made more difficult in a moving vehicle).
- The airway must be evaluated before transport and secured. Finally, the patient's medical record—laboratory and radiological data—is copied for the receiving unit.
- Use appropriate physical restraint.
- Particular attention has to be focused on the personnel, equipment, and monitoring in use to prevent adverse events during transportation of critically ill patients.
- Detailed planning of the process goes a long way in preventing the adverse events related to patient, equipment, and transport personnel.

Suggested Reading

1. Warren J, Fromm RE Jr., Orr RA, Rotello LC, Horst HM, American College of Critical Care Medicine. Guidelines for the inter and intra hospital transport of critically ill patients. Crit Care Med. 2004;32:256–62.
   These guidelines promote measures to ensure safe patient transport during both intra- and interhospital transport and give minimum standard regulations to ensure patient safety during transport by establishing an organized, efficient process supported by appropriate equipment and personnel.
2. Waydhas C. Intrahospital transfer of critically ill patients. Crit Care. 1999;3:R83–9.
   This review addresses the type and incidence of adverse effects, risk factors and risk assessment, and the available information on efficiency and cost-effectiveness of transferring such patients for diagnostic or therapeutic interventions within hospital.

Scoring Systems

84

Jigeeshu V. Divatia

A 60-year-old male patient with cirrhosis of the liver and portal hypertension was admitted to the hospital with pneumonia. He developed septic shock and became encephalopathic and anuric. The family wanted to know the chances of survival. Can a scoring system be used to predict the chances of survival?

The annual mortality in the ICU patients of hospital A is 5% and of hospital B is 15%. Can it be concluded that the ICU patients of hospital B are poorly managed compared to that of hospital A?

Performance measures of ICU care are usually subjective and difficult to compare. An objective measure of the structure, processes, and outcome by prognosticating in a cohort of ICU patients makes it more meaningful and easier to compare. This also helps on rational allocation of resources. A severity scoring system also helps in controlling risk factors in intervention and control groups in clinical trials.

Step 1: Understand the type of scoring systems used in ICU population

- General risk-prognostication scores (severity of illness scores)
  - Acute physiology and chronic health evaluation (APACHE II, III, and IV)
  - Simplified acute physiology score (SAPS II and III)
  - Mortality prediction model (MPM II0 and MPM II24)
- Disease and organ-specific risk-prognostication scores
  - Ranson's score for acute pancreatitis
  - RIFLE and AKIN classification for acute kidney injury
  - Trauma scores
  - Glasgow coma score

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  - KILLIP—heart failure
  - CURB—pneumonia
  - CAM-ICU—delirium
- Organ dysfunction score—sequential organ failure assessment (SOFA)
- Nursing workload measurement—therapeutic intensity scoring systems (TISS)
- Population-specific—pediatrics—APGAR score
- Postoperative—PRISM

Step 2: Understand general ICU scoring systems

- All scoring systems are developed from large databases of ICU patients.
- Statistical modeling is used to determine the variables that are likely to impact survival.
- A summary score is derived from these variables, and the predicted mortality is calculated using predictive equations.
- The performance of the scoring system depends on the size and case mix of patients in the reference database and the methodology used to assign weights to different elements of the scoring system.
- APACHE II and SAPS II scoring systems were derived from datasets of patients in North American and European ICUs in the mid-1980s and early 1990s.
- The APACHE II scoring system assigns points to age, acute physiological observations based on the worst values in the first 24 h after admission for 12 variables, and specified preexisting chronic diseases. It also requires selection of a single diagnostic category for each patient. The predicted mortality is based on the APACHE II score and the diagnostic category (Table 84.1).
- The SAPS scoring system does not require ICU admission diagnosis for calculating the score.
- Both APACHE II and SAPS II did not account for lead-time bias (i.e., the time lag between the onset of critical illness and admission to the ICU).
- APACHE III was developed as a further refinement of APACHE II, but its mortality prediction equations are not in the public domain.
- The APACHE IV system (2006) is based on 110,558 patients in 104 North American intensive care and coronary care units between 2003 and 2004.
- SAPS III, published in 2005, was based on 16,784 patients aged 16 years or more from all continents. Three subscores—namely, patient characteristics before admission (5 variables), circumstances of admission (5 variables), and acute physiology (10 variables)—are summed up to produce the SAPS III score. A diagnostic category is essential for estimating mortality.
- Both APACHE IV and SAPS III account for lead-time bias, but have not been tested and validated as extensively as APACHE II and SAPS II.
- MPM II0, published in 1985, was the first general severity model to assess risk of death based on parameters assessed at ICU admission. Prediction models for assessment at admission and after 24 h (MPM II24) were developed originally. The models consist mainly of dichotomous variables.

Table 84.1 The SOFA score

SOFA score					
	0	1	2	3	4
Respiration	>400	≤400	≤300	≤200 with respiratory support	≤100 with respiratory support
PaO_2/FiO_2					
Coagulation	>150	≤150	≤100	≤50	≤20
Platelets ($10^3/mm^3$)					
Liver					
Bilirubin (mg/dL)	1.2	1.2–1.9	2.0–5.9	6.0–11.9	>12.0
(μmol/L)	<20	20–32	33–101	102–204	>204
Cardiovascular					
Hypotension	No hypotension	MAP <70 mmHg	Dopamine ≤5 or dobutamine (any dose)[a]	Dopamine ≥5 or epi 0.1 (or norepi ≤0.1)[a]	Dopamine >15 or epi 0.1 (or norepi ≥0.1)[a]
Central nervous system					
Glasgow coma score	15	13–14	10–12	6–9	<6
Renal					
Creatinine (mg/dL)	<1.2	1.2–1.9	2.0–3.4	3.5–4.9	>5.0
(μmol/L)	<110	110–170	171–299	300–400	>400
or urine output				or <500 mL/day	or <200 mL/day

Epi, epinephrine; norepi, norepinephrine

[a]Adrenergic agents administered for at least 1 h (doses given are in μg/kg/min)

Step 3: Understand organ failure scoring system

- The SOFA score is a descriptive score that uses routinely collected data for the calculation of a score of 0–4 for each organ, the higher number meaning more severe failure (Table 84.2).
- Daily scoring enables monitoring of the progress of organ dysfunction or failure.
- There are no equations to estimate mortality. However, high initial SOFA scores and worsening of SOFA scores over time correlate with increased mortality.
- The logistic organ dysfunction system (LODS) was developed for the evaluation of organ dysfunction on the first day of the ICU.
- It provides probability of hospital mortality, distinguishing it from merely descriptive models such as SOFA.

Step 4: Evaluate the scoring system

- The ability of the model to distinguish between patients who survive and patients who do not survive is termed discrimination.
- The area under the receiver operating characteristic curve (AUC) is used to give a graphical and numerical estimate of discrimination. If AUC is 0.5, it means the system is only as good as flipping a coin, and if AUC is 1, this indicates excellent discrimination.
- Calibration of a system examines the difference between the observed and expected deaths in patients grouped into different severity of illness.
- This can be evaluated graphically as well as by goodness-of-fit statistics using the Hosmer-Lemeshow test. If the p value is more than 0.05, the model provides a good fit for the data.
- The standardized mortality ratio (SMR = actual mortality/predicted mortality) also takes into account severity of illness and evaluates risk-adjusted ICU performance.

Step 5: Understand limitations of the scoring system

- None of the scoring systems are accurate enough to make predictions in individual patients and hence cannot be used to predict outcomes of individual patients.
- Most systems require data to be collected in the first 24 h after ICU admission; hence, the severity score cannot be used to decide whether to admit a patient to the ICU.
- Erroneous conclusions can be drawn if data are not collected correctly according to the original database and definitions of the scoring system.
- The score cannot be applied to patients excluded from the original database (e.g., patients younger than 16 or 18 years and patients with burns).
- Missing data and interobserver variability can affect accuracy.
- These scores may not be accurate in geographical regions, and case mix significantly different from that in the original database.
- All the scoring systems can only predict the behavior of a group of patients that matches the patients in the original database population.
- The commonly used APACHE II and SAPS II do not account for lead-time bias.

Table 84.2 The APACHE II scoring system

	High abnormal range					Low abnormal range			
Physical variable	+4	+3	+2	+1	0	+1	+2	+3	+4
Temperature—rectal (°C)	>4	39–40.9		38.5–38.9	36–38.4	34–35.9	32–33.9	30–31.9	<29. 9
Mean arterial pressure (mmHg)	≥160	130–159	110–129		70–109		50–69		≤49
Heart rate (ventricular response)	≥180	140–179	110–139		70–109		55–69	40–54	≤39
Respiratory rate (nonventilated or ventilated)	≥50	35–49		25–34	12–24	10–11	6–9		≤5
Oxygenation: A-aDO_2 or PaO_2 (mmHg)									
(a) FiO_2 ≥0.5 record A-aDO_2	≥500	350–499	200–349		<200				PO_2
(b) FiO_2 <0.5 record PaO_2					PO_2 >70	PO_2 61–70		PO_2 55–60	PO_2 <55
Arterial pH	≥7.7	7.6–7.69		7.5–7.59	7.33–7.49		7.25–7.32	7.15–7.24	<7.15
Serum sodium (mMol/L)	≥180	160–179	155–159	150–154	130–149		120–129	111–119	≤110
Serum potassium (mMol/L)	≥7	6–6.9		5.5–5.9	3.5–5.4	3–3.4	2.5–2.9		<2.5
Serum creatinine (mg/100 mL) (double-point score for acute renal failure)	≥3.5	2–3.4	1.5–1.9		0.6–1.4		<0.6		
Hematocrit (%)	≥60		50–59.9	46–49.9	30–45.9		20–29.9		<20
White blood count (total/mm^3) (in 1,000 s)	≥40		20–39.9	15–19.9	3–14.9		1–2.9		<1
Glasgow coma score (GCS) Score = 15 minus actual GCS									
[A] Total acute physiology score (APS) Sum of the 12 individual variable points									
Serum HCO_3 (venous mMol/L) (not preferred, use if no ABGs)	≥52	41–51.9		32–40.9	22–31.9		16–21.9	15–17.9	≤15

(continued)

Table 84.2 (continued)

[B] Age points	
Assign points to age as follows:	
Age (years)	Points
≤44	0
45–54	2
55–64	3
65–74	5
≥75	6
[C] Chronic health points	
If the patient has a history of severe organ system insufficiency or is immunocompromised, assign points as follows:	
(a) For nonoperative or emergency postoperative patients, 5 points	
(b) For elective postoperative patients, 2 points	
Definitions	
Organ insufficiency or immunocompromised state must have been evident prior to this hospital admission and conform to the following criteria:	
Liver: Biopsy-proven cirrhosis and documented portal hypertension, episodes of past upper GI bleeding attributed to portal hypertension, or prior episodes of hepatic failure/encephalopathy/coma.	
Cardiovascular: New York Heart Association Class IV.	
Respiratory: Chronic restrictive, obstructive, or vascular disease resulting in severe exercise restriction (i.e., unable to climb stairs or perform household duties, or documented chronic hypoxia, hypercapnia, secondary polycythemia, severe pulmonary hypertension (>40 mmHg), or respirator dependency).	
Renal: Receiving chronic dialysis.	
Immunocompromised: The patient has received therapy that suppresses resistance to infection (e.g., immunosuppression, chemotherapy, radiation, long-term or recent high-dose steroids), or has a disease that is sufficiently advanced to suppress resistance to infection (e.g., leukemia, lymphoma, and AIDS).	
APACHE II score	
Sum of **[A]**+**[B]**+**[C]**	
A ASP Points_____	
B Age points_____	
C Chronic health points_____	
Total APACHE II_____	

Step 6: Understand utility of scoring system

- Scoring systems may be used to evaluate the performance of an ICU using the SMR.
  - The SMR of 1 implies that mortality in the ICU is equal to what is predicted by the system. The SMR of less than 1 indicates that ICU performance is better than predicted, while the SMR of more than 1 implies poor performance.
  - The SMR may be used to compare different ICUs, or the performance of the same ICU over a period. Differences in the SMR may represent differences in case mix, or differences in ICU practices between observed ICUs and the ICUs that contributed patients to the derivation dataset, or differences in quality of care.
  - The trend of SMRs can be used to evaluate ICU performance over time, or to compare ICUs.
- Scoring systems have been used in clinical trials to ensure similarity of study groups in terms of severity of illness at baseline.
- APACHE IV gives predictions for ICU mortality as well as hospital length of stay.
- TISS can be used to quantify and optimize nursing workload, staffing patterns, and costs.
- The daily SOFA score is useful to monitor progress of organ dysfunction. If an ICU treats a large number of patients belonging to a specific group (e.g., trauma, cancer, and coronary), specific scoring systems may be used.

Suggested Reading

1. Vincent JL, Bruzzi de Carvalho F. Severity of illness. Semin Respir Crit Care Med. 2010; 31:31–8.
   This article reviews the most commonly used severity-of-illness scoring systems and discusses some of their uses and limitations.
2. Vincent JL, Moreno R. Clinical review: scoring systems in the critically ill. Crit Care. 2010;14(2):207.
   The different types of scores should be seen as complementary, rather than competitive and mutually exclusive. It is possible that their combined use could provide a more accurate indication of disease severity and prognosis. All these scoring systems will need to be updated with time as ICU populations change and new diagnostic, therapeutic, and prognostic techniques become available.
3. Khwannimit B. Serial evaluation of the MODS, SOFA and LOD scores to predict ICU mortality in mixed critically ill patients. J Med Assoc Thai. 2008;91(9):1336–42.
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4. Zimmerman JE, Kramer AA, McNair DS, et al. Acute physiology and chronic health evaluation (APACHE) IV: hospital mortality assessment for today's critically ill patients. Crit Care Med. 2006;34:1297–310.
   APACHE IV predictions of hospital mortality have good discrimination and calibration and are useful for benchmarking performance in US ICUs. The accuracy of predictive models is dynamic and should be periodically retested. When accuracy deteriorates they should be revised and updated.

5. Moreno RP, Metnitz PG, Almeida E, et al. SAPS 3 investigators. SAPS 3—from evaluation of the patient to evaluation of the intensive care unit. Part 2: development of a prognostic model for hospital mortality at ICU admission. Intensive Care Med. 2005;31:1345–55.
The SAPS III admission score is able to predict vital status at hospital discharge with use of data recorded at ICU admission. Furthermore, SAPS III conceptually dissociates evaluation of the individual patient from evaluation of the ICU and thus allows them to be assessed at their respective reference levels.

Websites

1. http://www.sfar.org/article/316/scoring-systems-for-icu-and-surgical-patients
   For calculation of various scores
2. http://www.medcalc.be/manual/roc.php
   Understand the ROC curve

Part XIV

Pediatrics

Praveen Khilnani and Krishan Chugh

Mechanical Ventilation

85

Praveen Khilnani and Rajiv Uttam

A 2-year-old girl with fever and cough for the past 4 days was admitted to the hospital with worsening respiratory distress and tachypnea. Her SpO_2 on room air was 83%. She was put on oxygen at 12 L/min. In spite of high flow of oxygen, SpO_2 was still 85–88%. Chest X-ray showed fluffy shadows bilaterally. In view of clinical exhaustion, severe hypoxemia, and evidence of respiratory acidosis on blood gas, she was intubated.

Mechanical ventilation is the process of delivery of tidal volume with a set FiO_2 at a certain rate by presetting the peak inspiratory pressure (pressure ventilation) or tidal volume (volume ventilation) on the ventilator, with a purpose to remove CO_2 from lungs and deliver oxygen to the pulmonary capillaries. This is based on gradient of mean airway pressure in the alveoli resulting from delivery of peak inspiratory pressure (PIP) and positive end-expiratory pressure (PEEP) for the entire duration of the respiratory cycle (inspiratory time and expiratory time).

Step 1: Initial resuscitation

- Patient is resuscitated and rapid sequence intubation (RSI) is planned within 1 min (Table 85.1 and Fig. 85.1).
- The main purpose of RSI is to avoid positive-pressure ventilation by bag and mask and prevent gastric inflation in patients at risk of aspiration.

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Table 85.1 The eight "P"s of RSI

Time	Action
Zero minus 10 min	Preparation
Zero minus 5 min	Preoxygenation
Zero minus 3 min	Pretreatment
Time zero	Paralysis with induction
Zero plus 20–30 s	Protection and positioning
Zero plus 45 s	Placement
Zero plus 45 s	Proof
Zero plus 1 min	Postintubation management

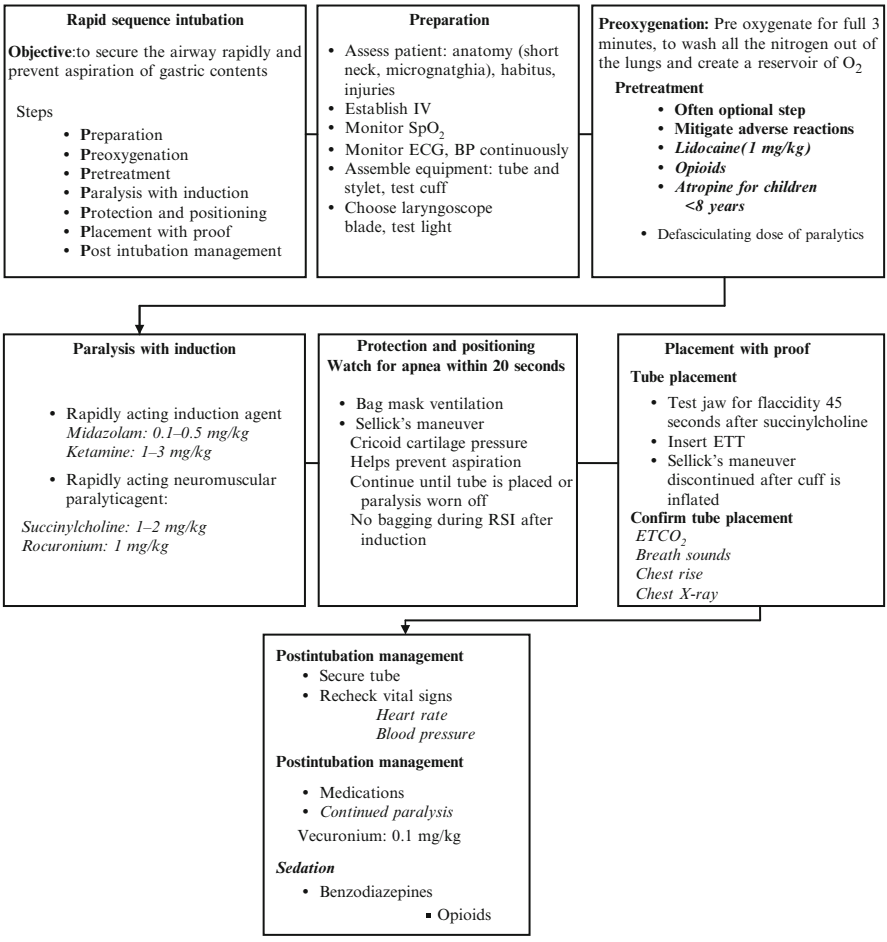

Fig. 85.1 Rapid sequence intubation protocol

- Bag-and-mask ventilation may be necessary in apneic patients or those with ineffective spontaneous breathing.
- In such patients, Sellick's maneuver is performed to prevent air entering into stomach, and gentle AMBU bagging can be done.

Step 2: Initiation and ventilator management

Monitor the status of oxygenation and ventilation and titrate ventilator parameters accordingly (Fig. 85.2).

A. *Initial ventilator settings: pressure limited*
   - Mode—pressure control.
   - FiO_2—start with 1 and wean down to get good SpO_2 (>90%).
   - Optimal positive end-expiratory pressure (PEEP)—to achieve adequate alveolar recruitment so that saturations are maintained at minimum FiO_2 (<0.6) and compliance is best with no hemodynamic compromise.
   - Respiratory rate—normal for age (adjust if there is air trapping).
   - Pressure control above PEEP (peak inspiratory pressure [PIP]-PEEP)—so that tidal volume equal to 6–8 mL/kg is delivered with adequate chest rise.
   - Inspiratory time—normal for age, 0.4 s for neonates, 0.5–0.6 s for infants, 0.6–0.8 s for toddlers, and 0.9–1.0 s for older children (adjust in case of air trapping or severe acute respiratory distress syndrome [ARDS]).

B. *Volume limited*
- Mode—volume control
- Tidal volume—6–8 mL/kg of ideal body weight, look for adequate chest rise
- Inspiratory time—normal for age (adjust in case of air trapping or severe ARDS)
- Optimal PEEP—adequate alveolar recruitment so that saturations are maintained at minimum FiO_2 (<0.6) and compliance is best with no hemodynamic compromise
- Respiratory rate—normal for age (adjust if there is air trapping)
- FiO_2—to get good SpO_2 (>90%)

C. *Sedation and analgesia*
   - Most patients can be managed with adequate sedation and analgesia without muscle relaxants. Muscle relaxants should never be started without adequate sedation.
   - Midazolam and morphine or fentanyl are used for most of the cases. In case of specific scenarios, other agents can be tried.
   - Morphine is not preferred in hemodynamic instability and wheezing. Ketamine can be used.
   - Midazolam is not preferred in severe hemodynamic instability and liver failure.
   - Ketamine is preferred in shock and wheezing. Ketamine is not used in raised intracranial pressure.

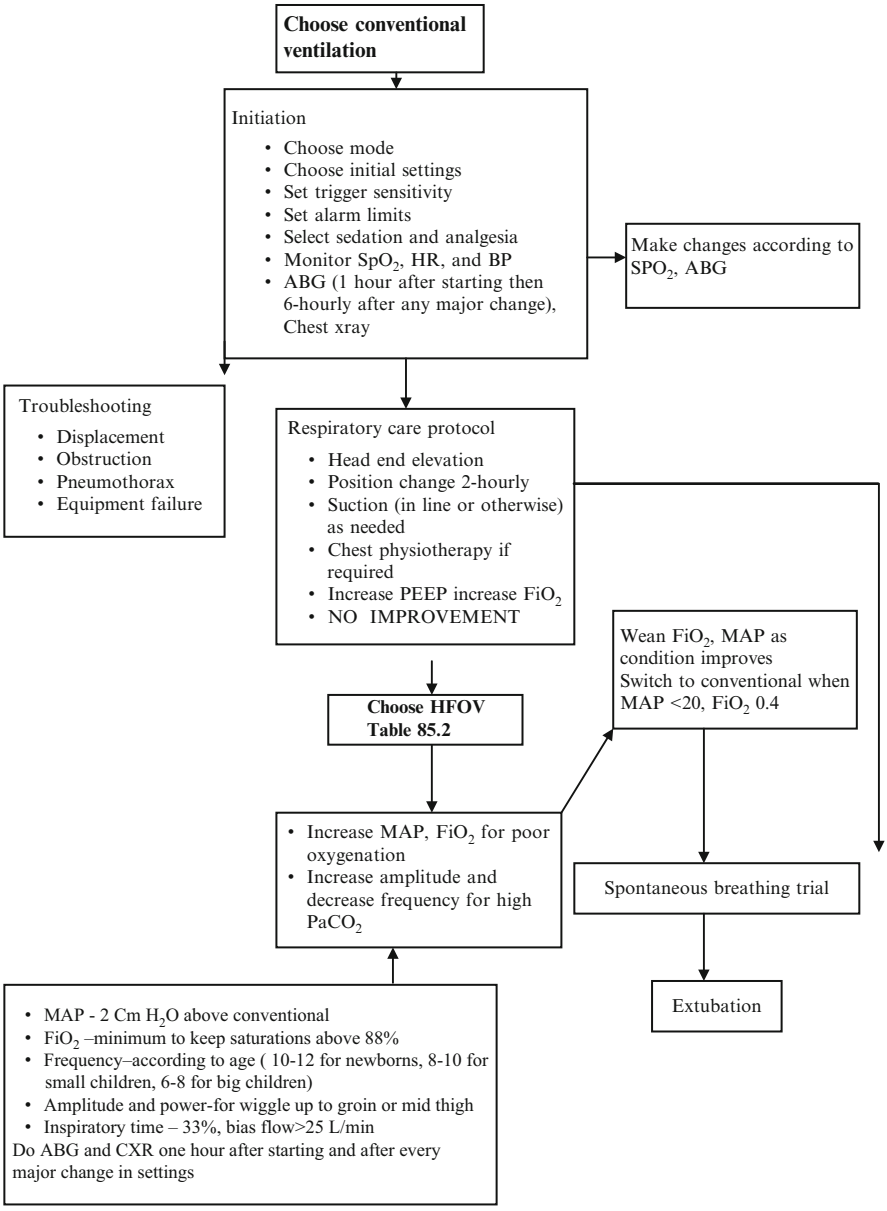

Fig. 85.2 Ventilator management protocol

Step 3: Change settings according to arterial blood gas

- Poor oxygenation—increase FiO_2, optimize PEEP, increase inspiratory pressure or tidal volume(Vt) if chest rise is not adequate, increase inspiratory time(Ti), and try inverse ratio ventilation if severe ARDS.

Table 85.2 Indications for high-frequency oscillatory ventilation

Requiring mean airway pressure more than 20
Not maintaining saturations with PEEP more than 14, FiO_2 more than 0.6
Oxygenation index more than 16 (oxygenation index = mean airway pressure × FiO_2 × 100/PaO_2)
Consider early use rather than as a rescue therapy

- High $PaCO_2$—ignore if pH is acceptable (>7.2) unless there is increased intracranial pressure or severe pulmonary hypertension (permissive hypercapnia).
- To decrease $PaCO_2$, increase rate or increase PIP or Vt. In bronchospasm, decrease rate and increase expiratory time to prevent air trapping.
- High PaO_2—decrease FiO_2.
- Low $PaCO_2$—decrease rate and decrease Vt.

Step 4: Weaning

Ventilatory settings are reduced once the primary pathology or condition that led to ventilation is improving. There are no set protocols for weaning. Different protocols are followed by different institutions. Generally, the following pattern is adopted:

- FiO_2 is weaned first to 0.4, maintaining saturation in acceptable range.
- Mode is changed to Synchronized intermittent mandatory ventilation (SIMV) with pressure support mode or pressure support mode.
- PEEP is decreased gradually in steps of 2 cm H_2O to 4–5 cm H_2O.
- SIMV rate is decreased to 5–10.
- The patient is reassessed after each change in the settings, and if the oxygen requirement goes up or the patient develops respiratory distress or is hypercarbic on blood gas, weaning process is paused and the support level is increased.

Some patients (especially when the lung is normal or short ventilation for neurological indications) can be directly given a spontaneous breathing trial after stopping sedation and extubated without weaning.

Step 5: Spontaneous breathing trial

- Spontaneous breathing trial is done before extubation to assess extubation readiness. It can be done with a T piece after disconnecting ventilator, endotracheal continuous positive airway pressure (CPAP), or minimal pressure support with CPAP.
- Usually the pressure support (PS) level is adjusted to the size of endotracheal tube (ETT) (6 cm H_2O PS for ETT >5 mm, 8 cm for ETT 4–5 mm, and 10 cm for ETT 3–4 mm).

Duration of the trial ranges from 30 min to 2 h. The following are the criteria for terminating a spontaneous breathing trial.

- Inability to maintain gas exchange (needing more than 0.5 FiO_2 for saturations greater than 95%)
- Inability to maintain effective ventilation (measured exhaled tidal volume <5 mL/kg; $PaCO_2$ >50 mmHg or increase >10 mmHg above baseline)

- Increased work of breathing (tachypnea or use of accessory muscles or paradoxical breathing pattern)
- Other signs of distress (e.g., diaphoresis, anxiety, rise in heart rate, change in mental status, and hypotension)

If the patient tolerates the spontaneous breathing trial, we can proceed to extubate.

Step 6: Extubation

The following criteria should be met before extubation:

- Alert or easily arousable
- Presence of airway reflexes, manageable secretions
- Minimal oxygen requirement less than 0.4 and PEEP less than 5 with saturations above 94%
- Good spontaneous tidal volume with minimal pressure support (5–10 above PEEP depending on the tube size) during spontaneous breathing trial
- Nil orally for at least 4 h before extubation
- Hemodynamically stable (dopamine requirement <5 mic/kg/min)
- $PaCO_2$ less than 50 mmHg
- pH 7.3–7.47
- Core temperature below 38.5°C
- Leak around the endotracheal tube is good but not a prerequisite for extubation
- No major metabolic derangements

Injection dexamethasone (0.2 mg/kg) q6h can be given prior to extubation, the first dose given 12 h before extubation. It can be continued 48 h after extubation. It decreases postextubation stridor.

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Acute Severe Asthma

86

Krishan Chugh

A 6-year-old girl developed worsening of her asthma symptoms one early morning. Her mother administered her two puffs of salbutamol with spacer. Not seeing any improvement after 15 min, she gave her two more puffs and moved her to the neighborhood nursing home. At arrival there the pediatrician found her to be dyspnoeic, diaphoretic, and unable to talk in full sentences. Auscultation of the chest revealed B/L ronchi. Her SpO_2 was 90%.

Acute severe asthma results from reversible airway obstruction mostly expiratory, with main reason of obstruction being bronchospasm due to various trigger factors (such as allergens or viral respiratory infection) and inflammation of the bronchi and smaller airways. This leads to progressive hypoxemia and hypercarbia requiring bronchodilator nebulizer therapy, systemically administered anti-inflammatory agents (steroids), and sometimes mechanical ventilation.

Step 1: Initial resuscitation

Assess airway, breathing, and circulation and take resuscitative measures as described in Chap. 78.

Step 2: Assess severity of the asthmatic attack (Table 86.1)

- The rapid assessment of a child with status asthmaticus should focus on determining the severity of airway obstruction.
- Wheezing, which reflects turbulent airflow in obstructed airways, is usually equally audible on both hemithoraces. Asymmetric wheezing may imply unilateral atelectasis, pneumothorax, or foreign body. Expiratory wheezing alone is

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Table 86.1 Severity of asthma exacerbations

	Mild	Moderate	Severe	Respiratory arrest imminent
Breathing difficulty	On walking	On talking	At rest	
		Infant softer		
		Shorter cry	Infant stops feeding	
		Difficult feeding		
	Can lie down	Prefers sitting	Hunched forward	
Talk in	Sentences	Phrases	Words	
Alertness	May be agitated	Usually agitated	Usually agitated	Drowsy or confused
Respiratory rate	Increased	Increased	Increased	
	Normal rate of breathing in awake children:			
	Age	Normal rate		
	<2 months	<60/min		
	2–12 months	<50/min		
	1–5 years	<40/min		
	6–8 years	<30/min		
Accessory muscles and suprasternal retractions	Usually present	Usually present	Usually present	Paradoxical thoracoabdominal movement
Wheeze	Moderate, often only end expiratory	Loud	Usually loud	Absence of wheeze
Pulse/min	Mild tachycardia	Moderate tachycardia	Severe tachycardia	Bradycardia

	Guide to limits of normal pulse rate in children:			
	Age	Normal rate		
	2–12 months	<160/min		
	1–2 years	<120/min		
	2–8 years	<110/min		
Pulsus paradoxus (can be observed on SpO_2 monitor waveform)	Absent	May be present	Often present	Absence suggests respiratory muscle fatigue
	<10 mmHg	10–20 mmHg	20–40 mmHg	
Peak expiratory flow rate (PEFR)	>80%	~60–80%	<60% predicted or personal best or response lasts <2 h	
After initial bronchodilator % Predicted or % personal best				
PaO_2 (on air)	Normal	>60 mmHg	<60 mmHg	
			Possible cyanosis	
And/or $PaCO_2$	<45 mmHg	<45 mmHg	>45 mmHg	
			Possible respiratory failure	
SaO_2% (on air)	>95%	91–95%	<90%	

Hypercapnia (hypoventilation) develops more readily in young children than in adults and adolescents

found in mild-to-moderate illness, whereas expiratory plus inspiratory wheezing is present in moderate-to-severe status asthmaticus.
- The silent chest is an ominous sign and may indicate either pneumothorax or the complete absence of airflow due to severe airway obstruction and imminent respiratory failure.
- Blood gas analysis may support the clinical judgment of severity; an increasing level of CO_2 is an ominous sign. During a moderate asthma attack, a capillary blood gas analysis may be sufficient; in patients admitted to an intensive care unit, arterial blood gas analyses should be a routine. Sequential measurements are important as respiratory alkalosis with hypocarbia is common during the early phases of an asthma attack, while normalization and a subsequent increase in the $PaCO_2$ may be important indicators of clinical deterioration. Thus, a normal $PaCO_2$ with even borderline low PaO_2 indicates a phase of rising $PaCO_2$, hence, need for more intensive therapy.
- A chest X-ray may be relevant in search for underlying complications such as pneumonia or air leakages.

Step 3: Review ongoing treatment
- Take into consideration the treatment that the child may have received in the past few hours. This helps us in deciding where in the treatment algorithm (Fig. 86.1) we should start. For example, in a child who has received several doses of salbutamol in the past 1 h, it may be futile to begin treatment at the top end of the algorithm.

Step 4: Start treatment (Fig. 86.1)
- Follow the algorithm for treatment.
- Generally children tolerate repeated doses of salbutamol very well and tachycardia as a side effect is less worrisome.

Step 5: Monitor closely
- At all stages, the child should be constantly monitored and escalation or de-escalation of therapy should be done accordingly. For example, a child who is showing signs of exhaustion may have to be intubated straightaway even if IV β-agonist or aminophylline has not yet been tried.

Step 6: Further treatment
- Intravenous ketamine can be tried in children who are not improving on intravenous β-agonist, intravenous steroids, and supportive therapy. It is a sedative that has bronchodilator properties. Generally, it is started in the dose of 1 mg/kg/h after a loading dose of 1 mg/kg. The infusion can be increased to 3 mg/kg/h. However, all preparations should have been made for intubation and ventilation before starting IV ketamine.

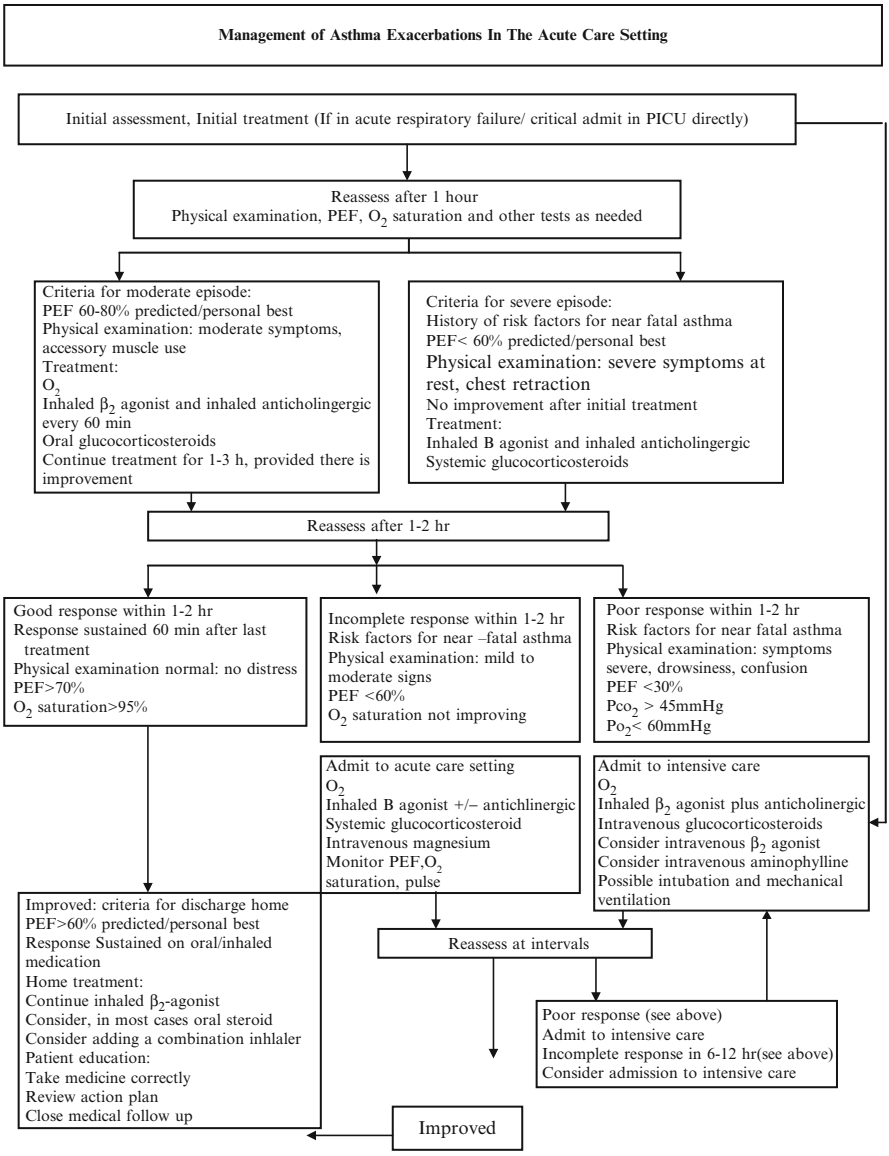

Fig. 86.1 Management of asthma exacerbations in the acute care setting

Step 7: Assess the need for intubation and ventilation

- Generally, decision to intubate and ventilate an asthmatic child is made on clinical grounds.
- Thus, cardiac arrest, respiratory arrest or severe bradypnea, extreme physical exhaustion, and altered sensorium are taken as absolute indications.

- Blood gas analysis and worsening pulsus paradoxus as assessed on the bedside monitors can be additional parameters in making a decision for intubation and ventilation.

Step 8: Initiate ventilation

- Rapid sequence intubation should be done and avoid overventilation with Ambu bag during preoxygenation.
- Ventilation is started in the controlled mode. Both pressure- and volume-controlled modes (or the combined modes like pressure-regulated volume control) can be used initially. As soon as possible, the child is shifted to assist/synchronized intermittent mandatory ventilation modes. Experience with pressure-support mode in the initial stages of ventilation is very limited in pediatrics.
- Standard rules of sedation and muscle relaxation are followed with some preferring to use ketamine.
- Noninvasive ventilation for status asthmaticus in children is not generally recommended, although a few units had encouraging experience with this modality.
- Permissive hypoventilation is an accepted strategy to ventilate asthmatic children.

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Status Epilepticus

87

Soonu Udani

A 3-year-old boy with a known seizure disorder was brought to the emergency department with generalized tonic–clonic seizures for the past 30 min. He was unresponsive with a temperature of 99°F, heart rate 140/min, systolic blood pressure 100 mmHg, respiratory rate 30 breaths/min, and SpO_2 94% on room air. Both pupils were equal and reactive.

Status epilepticus involves the following main issues besides controlling the seizures in status epilepticus: to prevent or treat airway compromise, hypoxemia and hypercarbia, and any further neurological dysfunction. Mechanical ventilation may be necessary to save the patient's life.

Step 1: Identify status epilepticus and resuscitate

- Status epilepticus may be defined as follows:
  - A child having a seizure lasting for more than 10 min
  - A child brought to hospital with a seizure
  - A child having a series of seizures without return to baseline mental status between attack
- For purposes of quick identification and timely treatment to prevent brain damage, the second definition is used as the working one in practice.
- The initial priority in an ongoing seizure is airway protection. This can be achieved by proper positioning, oral suctioning, and an oral airway device. If necessary, the patient should be intubated.
- Urgent peripheral intravenous access (preferably two) should be established.

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Step 2: Terminate seizures

- While monitoring heart rate, blood pressure, and respiratory rate, give a benzodiazepine.
- Give lorazepam 0.1 mg/kg, maximum 2 mg, slow IV. The same dose can be given via the intraosseous, per rectal or buccal route.
  Or
- Diazepam or midazolam (MDZ) 0.2 mg/kg can be given, slow IV. The same dose can be given by intraosseous route. Rectal dose is 0.3–0.5 mg/kg.
- Respiratory depression or hypotension can occur, and this needs to be monitored closely.
- Out-of-hospital intranasal or buccal MDZ is an easily available option. The intranasal easy calculation is 1 puff for every 2 Kg weight.
- If the seizures do not stop in another 10 min, go to the next step.

Step 3: Treat resistant seizure

- Give phenytoin 20 mg/kg IV by slow push over 20 min.
- Or
- Fosphenytoin 20 mg/kg (of phenytoin equivalents) IV can be given by slow push over 10–15 min. This dose can also be given by the intraosseous route.
- If seizure does not stop within 5 min after dose completion, go to next step
- This is also to be used if diazepam is the first benzodiazepine used but not if lorazepam is used.
- Phenobarbitone should be given 20 mg/kg IV. It can cause respiratory depression and hypotension, particularly if given with benzodiazepines. If required, secure airway with endotracheal intubation. This would be the first choice in neonates and infants.
- If seizures continue, then go to step 4—the patient is in refractory status epilepticus. One of the discussed drugs could be given depending on the patient's evaluation and availability of resources.
- A general caveat is that it is best to optimize the levels of one drug before adding another, and hence a repeated dose of these may be given.

Step 4: Manage refractory status epilepticus (RSE) 30–45 minutes have passed

- IV valproic acid (VPA) 30–35 mg/kg diluted with normal saline is administered over 20 min as profound hypotension can occur.
- Levetiracetam (LEV) at a dose of 20 mg/kg loading infusion and then 10 mg/kg 12-hourly can also be tried where intubation and ventilation need to be deferred for transport.

However, by now 3/4 to 1 h may have passed and the clock is ticking, so if seizures are not aborted, coma-producing therapies need to be started.

- *Midazolam (MDZ) infusion*
  - A loading dose of 0.2 mg/kg is followed by infusion of 2–6 mcg/kg/min. MDZ 3 mg/kg added to 50 cm^3 N saline when given 1 cm^3/kg will deliver 1 mcg/kg/min.

  - Start at low dose and increase by 1 mcg/kg/min every 15 min until control is achieved.
  - Maximum rate, 20 mcg/kg/min, is recommended or till hemodynamic instability is a problem to manage.
  - Once control is achieved, maintain the same dose for 24 h and then wean by 1 mcg/kg/min every 2–3 h.
  - Transfer to a center capable of long-term life support is needed as the respiratory depression and hemodynamic instability is unpredictable and varies from patient to patient.
- An accelerated protocol can be used here where the step of an additional drug in step 3 is now not advocated as it is deemed a waste of precious time and the drugs in step 4 are given together. i.e VPA or LEV + MDZ infusion started simultaneously.
- Propofol: Start with 2–4 mg/kg bolus and then 1–5 mg/kg/h. This is not recommended for children younger than 12 years. Approval for this drug is for usage for 12 h only, so informed consent before usage is advised. (Vigilance for the propofol infusion syndrome is required).
- *Thiopentone infusion (cautionary warning for non-intensivists)*
  - This general anesthesia drug is reserved for severe refractory status.
  - The patient should be intubated and ventilated prior to starting the infusion, and inotropes should be put on standby.
  - Invasive BP monitoring and real-time EEG monitoring will be needed, at least intermittently if not continuously.
  - A separate IV line is needed. The loading dose is 3–5 mg/kg slowly immediately, followed by an infusion of 1–5 mg/kg/min.
  - Hemodynamic support in terms of extra fluids, vasopressors, and inotropes may be required. Hence, this needs to be done within a fully equipped PICU.
  - Burst suppression with 6–8 bursts/min is the target, and hence it is foolhardy to try this without EEG monitoring.

Step 5: Anesthetic agents

- Once this stage is reached, the mortality and morbidity of refractory status epilepticus are more than 50%.
- These agents need to be delivered through a proper circuit and monitoring done by an anesthetist who understands the drug.
- Aborting the seizures is usually easy, but maintenance and survival are a universal issue.
- In addition to these drugs, oral drugs like topiramate can be started. Other drugs that have been tried with success are as follows:
  - Give lidocaine 1.5–2 mg/kg IV over 2 min and then give a drip at 3–4 mg/min—same class of drugs as phenytoin and an excellent membrane stabilizer. Neonatal studies have shown this drug to be effective.
  - MDZ infusion as in older children should also be used in neonates because the same principles of quick resolution apply.

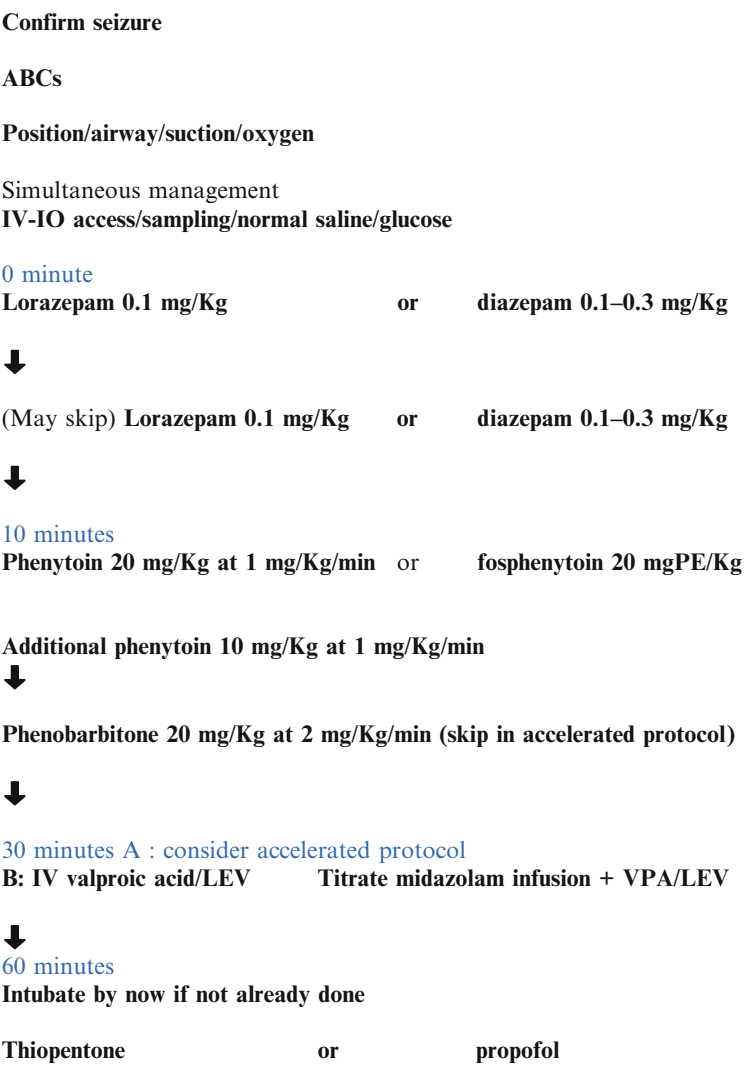

Fig. 87.1 Algorithm for seizure control

– Pyridoxine (vitamin B6) should be given to all neonates and infants with resistant seizures (B6-responsive seizures). Dose is 100 mg IV.

Step 6: Tapering of infusion

- Tapering of any infusion should only be done after complete electrical seizure freedom for at least more than 24 h.
- Very gradual tapering should be done as seizures will return and will often be nonconvulsive and only be caught by EEG monitoring.
- The most toxic drug or last introduced should be removed first.

- Hence, long-term agents should be on board and all levels are well maintained before new drugs are added or tapering is begun (F ig. 87.1).

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Severe Sepsis and Septic Shock

88

Praveen Khilnani

A 2-year-old boy was brought to the emergency department with lethargy, poor feeding, fever for the past 24 h, cold extremities, mild respiratory distress for the past 3 h, and no urine output for the past 8 h. He was lethargic but arousable. His rectal temperature was 104°F, with heart rate 170/min, blood pressure 60 mmHg, respiratory rate 45 breaths/min, and SpO_2 92% at room air. Capillary refill time was 5 s, and extremities were cold with palpable but feeble pulses.

Severe sepsis and septic shock involve clinical SIRS (systemic inflammatory response syndrome) with suspected or proven infection (blood culture not always positive) with cardiovascular involvement and dysfunction (septic shock) or multiple organ involvement (severe sepsis with multiple organ dysfunction syndrome). This chapter describes the step-by-step management of severe sepsis and septic shock.

Step 1: Initial resuscitation

- This includes fast recognition and action done almost simultaneously.
- Shock should be clinically diagnosed before hypotension occurs by clinical signs, which include the following:
  - Hypothermia or hyperthermia
  - Altered mental status
  - Peripheral vasodilation (warm shock) or vasoconstriction with capillary refill more than 2 s (cold shock)
  - Tachycardia
  - Tachypnea out of range for age and level of fever or anxiety

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Zero minutes
Recognize decreased mental status and perfusion
Maintain and establish vascular access—use intraosseous if IV fails in 90 s
5–15 min: Push 20 mL/kg normal saline/colloid × 3 up to 60 mL/kg
Assess between each push
Correct hypoglycemia and hypocalcemia

- There should be no time wasted in gaining access. If access is not easily obtained in about 90 s, the interosseous route is a must, as almost everything can go in by that route including inotropes.
- Because mortality goes up with delay in time to inotrope drug use, now it is recommended to use the peripheral line for inotropes—dopamine and dobutamine (not vasopressors)—until central access is attained.
- *Optimizing fluids in the first 15 min or as soon as possible*: Pediatric septic shock is associated with severe intravascular volume depletion, and children frequently respond well to aggressive volume resuscitation.
- The continued emphasis is on the first-hour fluid resuscitation, and appropriate inotrope drug therapy is directed to achieve the following goals:
  - Reducing heart rate to the threshold level for age
  - Getting peripheral pulse to match central pulse volume
  - Improving mentation
  - Improving urine output to at least 1 mL/kg/h
  - Reducing clot retraction time to less than 3 s.

  This assessment for quick check for overload is done after each bolus of fluid.
- Rapid expansion of the liver span
- Rales and increased work of breathing
- Enlargement of the cardiac silhouette on chest X-ray
- Drop in SPO_2

Step 2: Manage 15-min fluid-refractory shock
- Establish central venous access.
- Start dopamine 10 mcg/kg/min.
- Establish arterial access.
- Continue maintenance fluids 4 mL/kg/h and boluses of .9% normal saline/colloid as needed.
- Thirty to sixty minutes have passed—fluid-refractory, dopamine-resistant shock.

Scenarios
1. When pediatric patients are normotensive with a low cardiac output (CO) and high systemic vascular resistance (SVR), initial treatment of fluid-refractory patients consists of the use of an inotropic agent such as dobutamine. Dopamine at a dose of 10–15 μ/kg/min should be administered at this time.

However, fluid-refractory, dopamine-resistant shock is an important defining step as the mortality changes when the patient fails to respond to fluids and dopamine.

2. When pediatric patients are hypotensive with a low CO and high SVR (cold shock), EPI (epinephrine) is started at a dose of 0.1 μg/kg and titrated to effect. When BP improves, an inodilator (dobutamine, milrinone, and nitroglycerine) is added to improve tissue perfusion. This can be done using the same clinical parameters described above or additional laboratory data such as base excess of more than 5 or increasing lactate levels.
3. When pediatric patients are hypotensive with a high CO and low SVR (warm shock), then norepinephrine is the vasopressor of choice. Since the pulse pressure is wide and diastolic pressures are usually low, the need is to increase the mean arterial pressure (MAP). Here, a vasodilator can be added.

There is no magic formula for inotrope or fluid titration. The guidelines are there to give a framework for initiating and adding drugs based on clinical examining and parameter readings of central venous pressure (CVP), BP, etc. Many children by now may be on more than three agents including vasopressors and vasodilators.

Step 3: Early goal-directed therapy

- It restores the balance between delivery and demand quickly by manipulating preload, afterload, and contractility using fluids, inotropes, and vasodilators to enhance delivery and PRBCs to deliver more oxygen by increasing O_2 content (Table 88.1).
- All four goals to be met for success

Table 88.1 Early goal-directed therapy

1. Normal MAP (>60 mmHg)
2. Mixed venous saturation >70%
3. Urine output >1 mL/kg/h
4. CVP >8–12 cm H_2O

Step 4: Give antibiotics within the first hour and control the source

- An increased mortality rate due to delay in the administration of an appropriate antibiotic has been clearly shown in several pediatric and adult studies. Therefore, every attempt should be made to get appropriate cultures earlier, but this should not hold up the administration of the drug.
- The choice should be on the basis of the site of infection and local patterns. A broad-spectrum antibiotic like a third-generation cephalosporin should be used. De-escalate antibiotics once the culture results are available.
- Along with this, there must be an active search for a source of infection, and immediate action for source control should be taken wherever possible.

Step 5: Mechanical ventilation and sedation

- There are many reasons to ventilate patients with septic shock. This step should be considered in any patient who is not rapidly stabilized with fluid resuscitation and peripherally administered inotropes.

Step 6: Give steroids

- If a child is at risk of absolute adrenal insufficiency (e.g., purpura fulminans, congenital adrenal hyperplasia, prior recent steroid exposure as in asthma, or nephrotic syndrome) and remains in shock despite epinephrine or norepinephrine infusion, fluids and inotropes are optimized for an hour (catecholamine-resistant shock) and then hydrocortisone can be administered.
- Hydrocortisone may be administered as an intermittent or continuous infusion at a dosage of 50 mg/m^2/day (2 mg/kg 6-hourly) till hemodynamic stability is achieved.

Step 7: Glucose control

- Glucose-containing fluids D5 or D10 along with insulin should be used for maintenance, and insulin is titrated to keep blood glucose between 100 and 150 mg/dL. This prevents catabolism as well as the ill effects of hyperglycemia.
- Tight glucose control leads to hypoglycemia and this can be brain damaging, so avoid this and maintain higher glucose value. Hyperglycemia should not be treated by reducing fluid concentrations to glucose-free fluids and removing insulin as there is poor glucose utilization and insulin is needed.

Summary of guidelines for pediatric septic shock management in resource-limited environment

- Immediate recognition of shock state from decreased perfusion state and altered mental status.
- Airway, breathing, and circulation approach with high-flow O_2.
- Rapid intraosseous access immediately, if IV is not available.
- Up to 60 mL/kg isotonic nonglucose-containing fluid can be given for 0–15 min.
- Clinical evaluation of improvement of shock by decreasing heart rate, clot retraction time less than 2 s, improved mental status, improved peripheral pulse and central pulse, improved urine output, warmer extremities, and MAP more than 60 mmHg (age-related values).
- Evaluate for fluid overload.
- Rapid decision to start dopamine/dobutamine by the peripheral line, not wait for the central line.
- Start appropriate antibiotics in first hour.
- Continue fluid boluses as needed throughout the process—in the first few hours—and continue maintenance fluids.
- Mechanical ventilation with sedation and analgesia.
- If fluid-refractory, dopamine-resistant shock, insert CVP and arterial line.
- Epinephrine for cold shock, norepinephrine for warm shock ± vasodilators.
- Steroids for catecholamine-resistant shock at 2 mg/kg/day q8.
- Early goal-directed therapy with $ScVO_2$ more than 70%, hemoglobin 10 g/dL, CVP 8–12 cm H_2O, and MAP more than 60 mmHg.
- Source control as soon as possible.
- Glucose control with insulin if needed (<150 mg/dL).

Suggested Reading

1. Khilnani P, Singhi S, Lodha R, et al. Pediatric sepsis guidelines: summary for resource- limited countries. Indian J Crit Care Med. 2010;14(1):41–52.
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2. Brierley J, Carcillo JA. Clinical practice parameters for hemodynamic support of pediatric and neonatal septic shock: 2007 update from the American College of Critical Care Medicine. Crit Care Med. 2009;37:666–88.
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Early recognition and aggressive resuscitation of pediatric and neonatal septic shock by community physicians can save lives.
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Early goal-directed therapy provides significant benefits with respect to outcome in patients with severe sepsis and septic shock.

Acute Intracranial Hypertension

89

Sunit Singhi

A 2-year-old unconscious child was brought to the emergency department following fall from the first floor of a building. Initical Glasgow coma score was 6. Both pupils were reactive, blood pressure was 95 mmHg systolic, and heart rate was 120/min. Head CT on admission revealed multiple contusions with cerebral edema. Within 30 min of admission, blood pressure shot up to 130 mmHg, heart rate dropped to 70/min, and the right pupil got dilated.

Acute intracranial hypertension is a medical emergency requiring prompt diagnosis and management. Appropriate and timely management strategies result in better patient's outcome in an otherwise severely debilitating or fatal disease process.

Step 1: Initiate resuscitation

- Airway (A): Secure airway, do rapid sequence intubation, and maintain/induce sedation with midazolam and/or diazepam.
- Breathing (B): Perform hyperventilation using Ambu bag while waiting for intubation, and maintain $PaCO_2$ of 30–35 mmHg.
- Circulation (C): Assess for euvolemia, give normal saline bolus if central venous pressure is less than 8–10 or systolic blood pressure is less than 5th percentile prior to instituting osmotic therapy.

Step 2: Understand intracranial hypertension

A. *Monro–Kellie doctrine*

The pathophysiology and management of AIH is based on the Monro–Kellie doctrine. Intracranial pressure (ICP) is the sum total of pressure exerted by the

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brain tissue (≈80%), blood volume (≈10%), and cerebrospinal fluid (≈10%) in the noncompliant cranial vault.

B. *Normal value*
ICP is not a constant value but is variable with various activities such as coughing, sneezing, and age. Single measurement is not a true representation of ICP; it needs to be measured over the period (24–72 h). Usually normal limits are taken as 5–15 mmHg.

C. *Acute intracranial hypertension*
AIH is a clinical condition defined as the persistent elevation of ICP of more than 20 mmHg for more than 5 min in a patient who is not being stimulated and as a threshold to define intracranial hypertension requiring treatment. Sustained ICP values of more than 40 mmHg indicate severe, life-threatening intracranial hypertension.
- An algorithmic approach to management of ICP (Fig. 89.1) helps put things into perspective so that all aspects of care are attended to.
- Maximize oxygenation and ventilation.
- In an ICP-based therapy, the primary goal is reduction of ICP to less than 20 mmHg.
- In a cerebral perfusion pressure (CPP)-based therapy, systolic blood pressure and mean arterial pressure (MAP) should be maintained to keep CPP more than 60 mmHg.
- CPP = MAP–ICP; MAP = one-third systolic pressure plus two-thirds diastolic pressure.
- Avoid factors that aggravate or precipitate elevated ICP.
- Decrease cerebral metabolic rate.

Step 3: Start general measures
- Keep temperature below 38°C (around-the-clock oral acetaminophen 15 mg/kg 6 hourly).
- Glucose control—keep blood glucose between 80 and 140 mg/dL.
- Avoidance of jugular venous outflow obstruction (head in midline and elevated to 30°).
- Normoxia (PaO_2 80–120 mmHg and SpO_2 >90%) and normocarbia ($PaCO_2$ 35–40 mmHg).
- Preservation of adequate sedation–analgesia.
- Seizure prophylaxis (Phenytoin 20 mg/kg loading, then 5–8 mg/kg/d), for patients at high risk.
- Nutrition—enteral (preferred) to be started within 72 h.

Step 4: Start first-tier ICP-specific treatments
- Ventilate to normocarbia (PCO_2 35 mmHg).
- Sedation and pharmacologic paralysis.
- Hyperventilate to $PaCO_2$ of 30–35 mmHg (moderate and transient only, do not prolong, >6 h, and prophylactic hyperventilation).
- Increase MAP.

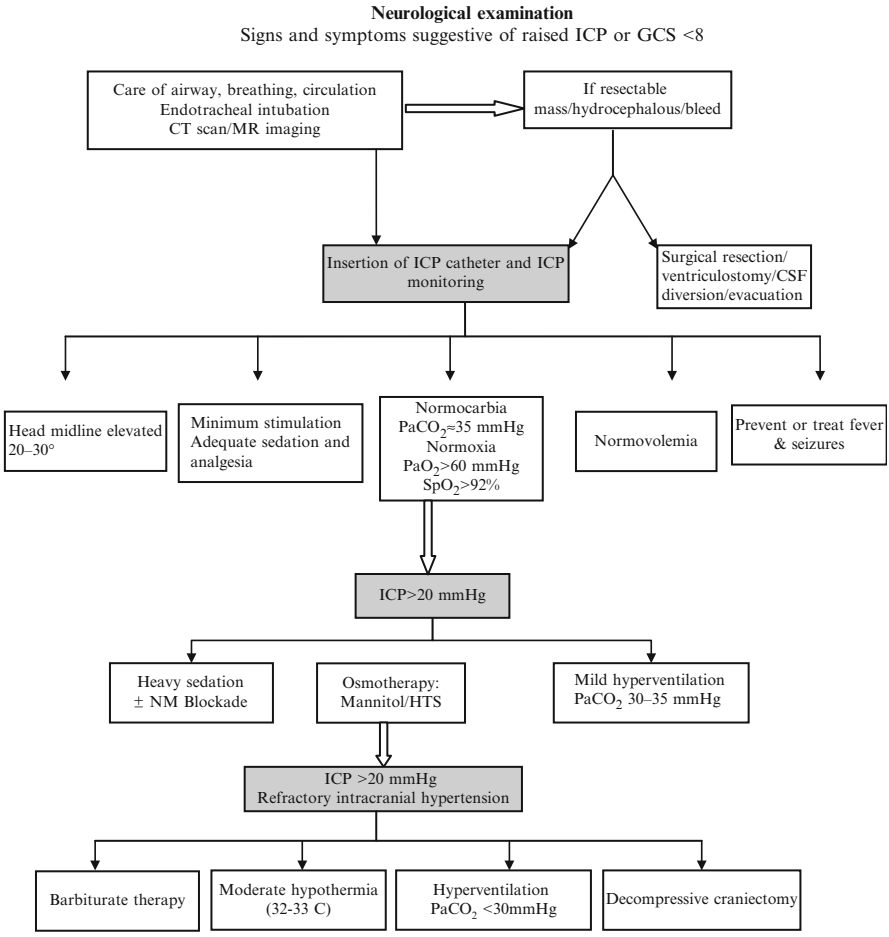

Fig. 89.1 An approach to the management of intracranial hypertension. *ICP* Intracranial pressure, *GCS* Glasgow coma score, *HTS* hypertonic saline

- Mannitol (0.25–2 g/kg IV bolus every 4–6 h; serum osmolality not >320 mOsmol/kg).
- Saline infusion (3%) (loading 10 mL/kg; 0.1–1 mL/kg/h infusion; serum osmolality not >360 mOsmol/kg).
- Consider ventriculostomy—drain 3–5 mL cerebrospinal fluid.

Step 5: Consider second-tier therapy if ICP is persistently high

- Barbiturates coma (thiopental loading 1–5 mg/kg IV; if complete response [ICP <20 mmHg], return to first-tier agents or repeat bolus doses as necessary; if incomplete response [ICP >20 mmHg but reduction <25%], start IV 1–5 mg/kg/h infusion or until burst suppression EEG pattern at 1–2 bursts/min).

- Moderate hypothermia (32–34°C with surface or endovascular cooling method for 24–72 h, followed by passive rewarming over 12–24 h).

Step 6: Consider third-tier therapy

- Decompressive craniectomy or temporal lobectomy (if medical AIH management has failed but the patient does not have overt herniation syndrome yet).
- Hyperventilation for acutely symptomatic patients may be lifesaving.
- Two osmotic agents are currently in use: mannitol and hypertonic saline (3%).
- Induced hypothermia is effective in reducing ICP by suppressing all cerebral metabolic activities.

Suggested Reading

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   There is a paucity of information regarding nonpharmacological acute management of patients with ABI. This review found strong levels of evidence for only four interventions (decompressive craniectomy, cerebrospinal fluid drainage, hypothermia, and hyperbaric oxygen).
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Multiorgan Failure

90

Sajith Kesavan and Bala Ramachandran

A 1-year-old infant was admitted to pediatric intensive care unit (PICU) with fever, shock, and lethargy. After administering fluid boluses and starting on inotropes, he was intubated and shifted to PICU. Investigations showed leukocytosis and thrombocytopenia with severe metabolic acidosis. Within 6 h of admission, urine output decreased, and he started bleeding from the nasogastric tube. He had persistent tachycardia with cold extremities. Investigations showed persistent metabolic acidosis, elevated liver enzymes, and severe coagulopathy (both prothrombin and partial thromboplastin time were prolonged) with rising serum creatinine.

Multiple organ failure (MOF) defined as dysfunction of more than two organs, is quite frequently seen in the PICU associated with high mortality. Mortality increases as the number of organ involved increases. Early and appropriate management involving multiorgan support improves outcome in these patients.

Step 1: Initial resuscitation

The patient should be resuscitated, taking care of airway, breathing, and circulation.

Step 2: Assess renal function

- Renal dysfunction is defined as serum creatinine more than two times the upper limit of normal for age or twofold increase in baseline creatinine.

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Table 90.1 Modified pediatric RIFLE criteria

	Serum creatinine criteria	Urine output criteria
Risk	eCCL decreased by 25%	Urine output <0.5 mL/Kg/h × 8 h
Injury	eCCL decreased by 50%	Urine output <0.5 mL/Kg/h × 16 h
Failure	eCCL decreased by 75% or eCCL < 35 mL/min/1.73 m^2	Urine output <0.3 mL/Kg/h × 24 h or anuria × 12 h
Loss	Persistent failure (>4 weeks)	
End-stage kidney disease	End-stage kidney disease (>3 months)	

eCCL estimated creatinine clearance

Table 90.2 Classification using renal failure indices

	Prerenal	Renal
Urine sediment	Bland	Broad, brownish granular casts
Urine sodium (mEq/L)	<20	>30
Urine osmolality (mosm/L)	>400	<350
Fractional excretion of Na	<1	>1

- Intensivists prefer the modified pediatric RIFLE criteria to define and classify acute kidney injury.
- The acronym RIFLE stands for the increasing severity classes—risk, injury, and failure—and the two outcome classes—loss and end-stage kidney disease (Table 90.1).

Renal failure can also be classified into prerenal and renal causes by using renal failure indices (Table 90.2).

$$\text{Fractional excretion of Na} = \frac{\text{urine sodium} \times \text{plasma creatinine}}{\text{plasma sodium} \times \text{urine creatinine}} \times 100$$

Step 3: Send investigations

- Urine routine examination
- Renal function test with electrolytes
- Urine sodium
- Urine osmolality
- Urine-specific gravity
- Arterial blood gas analysis
- ECG

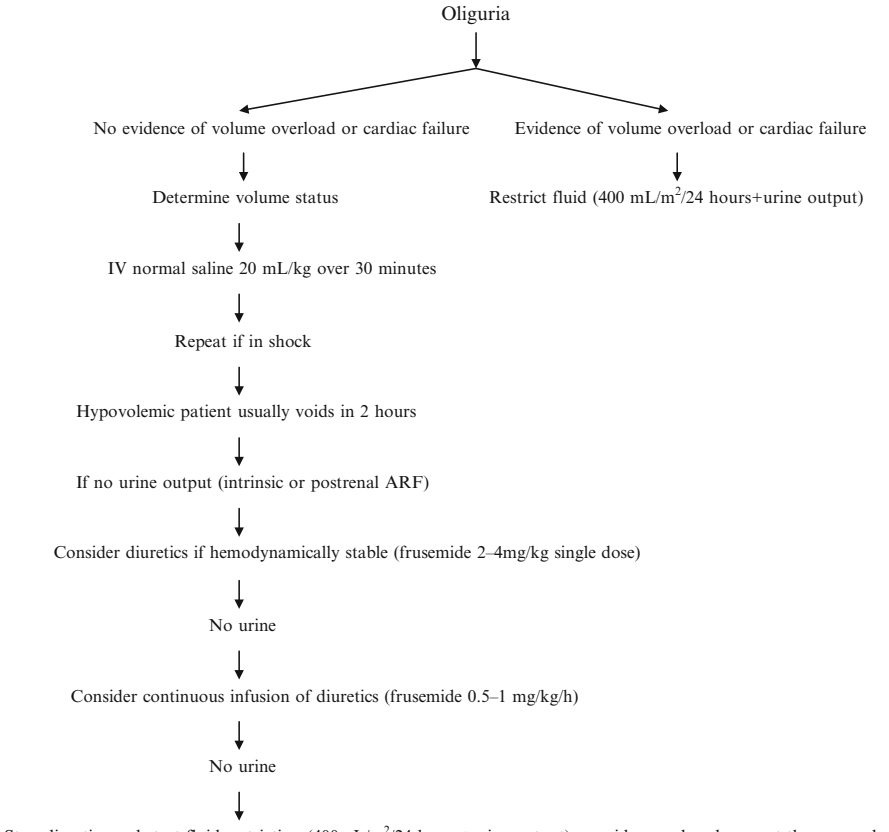

Fig. 90.1 Algorithm for oliguria

Step 4: Manage renal failure

- Follow oliguria algorithm (Fig. 90.1).
- Avoid nephrotoxic drugs.
- Maintain kidney perfusion with fluids and inotropes—judicious use of fluids to prevent fluid overload and further ischemic damage to the kidney.
- Adjust drug dosages according to eCCL.
- Use Schwartz formula for calculating glomerular filtration rate (GFR):

$$\text{GFR}\left(\text{mL}/\text{min}/1.73\text{m}^2\right) = \text{k} \times \frac{\text{height in centimeters}}{\text{serum creatinine}}$$

where k is 0.33 in preterm infants, 0.45 in infants, and 0.55 in older children.

Table 90.3 Types of dialysis

Type	Complexity	Use in hypotension	Efficiency	Volume control	Anticoagulation
Peritoneal dialysis	Low	Yes	Moderate	Moderate	No
Intermittent hemodialysis	Moderate	No	High	Moderate	Yes
CVVH	Moderate	Yes	Moderate	Good	Yes
CVVHDF	High	Yes	High	Good	Yes

- Schwartz formula is not accurate in a sick child with rapidly changing physiological status. Measuring creatinine clearance directly by using the following formula is better estimate of GFR:

$$\frac{\text{urine creatinine} \times \text{volume of urine in mL/min}}{\text{plasma creatinine}} \times \frac{1.73}{\text{body surface area in m}^2}$$

- In a sick child with oliguria and kidney injury, it is better to assume GFR less than 10 while dosing.
- Early nutritional support—high-calorie enteral diet with adequate protein is started early.
- Try to convert hemodynamically stable oliguric into nonoliguric renal failure if possible by using diuretics.
- Start renal replacement therapy early.

Step 5: Monitor
- Hourly intake–output chart, daily weight if possible
- Hemodynamic monitoring
- 6th-hourly serum electrolytes, daily renal function test

Step 6: Renal replacement therapy

Indications of renal replacement therapy are as follows:
- Oliguria/anuria with fluid overload, refractory to diuretic therapy
- Persistent hyperkalemia not responding to other measures
- Severe metabolic acidosis unresponsive to medical management
- Severe electrolyte abnormality

Types of dialysis (Table 90.3)
- Intermittent hemodialysis
- Peritoneal dialysis
- Continuous renal replacement therapy (CRRT)—continuous venovenous hemofiltration (CVVH) or continuous venovenous hemodiafiltration (CVVHDF)

The choice of renal replacement therapy depends on the clinical circumstances, availability of expertise, good vascular access, size of the child and hemodynamic stability.

A. Peritoneal dialysis is the easiest and most widely used modality.
   - Solute clearance is achieved by diffusion and solvent drag. Fluid removal happens by osmosis.
   - It can be done through a catheter placed at the bedside or the surgically placed Tenckhoff catheter. Dialysate volume of 10–20 mL/Kg with dwell time of 30 min to 1 h is a good starting prescription.
   - Increasing the dextrose concentration of the dialysate, increasing dwell volume, shortening the dwell time and doing more cycles help in more ultrafiltrate.
   - Hypertonic dialysate fluid may cause hyperglycemia and rapid ultrafiltration. Heparin (500 units/mL) may be added to the dialysate fluid to prevent catheter blockage.
   - Potassium can be added to the PD fluid to a maximum of 4 mEq/L of PD fluid if there is hypokalemia.
   - Dialysate can be changed to bicarbonate-based instead of lactate-based if there is severe lactic acidosis.

B. Intermittent hemodialysis is done in hemodynamically stable children.
   - Children with multiorgan dysfunction and shock may not be good candidates for it. The advantage of hemodialysis is the rapid removal of toxins and ultrafiltration of fluid.

C. CVVH is preferred in hemodynamically unstable children.
   - Care should be taken to minimize the amount of blood in the extracorporeal circuit and blood priming of the hemofiltration circuit may be necessary at the outset.
   - Fluid removal is adjusted according to the patient's clinical state during the treatment.
   - The extracorporeal circuit requires good central venous access, usually via a dual-lumen catheter, to allow the high blood flows necessary to prevent clotting in the hemofilter.
   - Blood volume in the extracorporeal circuit should be less than 10% of the patient's circulatory volume. Blood flow of 6–9 mL/Kg/min or 8% of circulating blood volume prevents excessive hemoconcentration in the filter.
   - Automated machines with appropriate accuracy are recommended for children for delivering the CRRT prescription safely and have replaced pump-assisted hemofiltration using volumetric pumps.
   - If only fluid removal is required, then relatively low rates of filtration are needed, often referred to as slow continuous ultrafiltration. There will be negligible solute removal under these circumstances.

When more solute clearance is needed in addition to fluid removal, dialysis component is added to the CVVH to make it CVVHDF.

90.1 Concurrent Management of Hepatic Dysfunction

Step 1: Make a diagnosis
Total bilirubin of more than 4 mg/dL or ALT two times, normal for age, signifies hepatic dysfunction. The Pediatric Acute Liver Failure Study Group defined acute liver failure as follows:
- Biochemical evidence of liver injury
- No history of known chronic liver disease
- Coagulopathy not corrected by vitamin K administration
- International normalized ratio (INR) greater than 1.5 if the patient has encephalopathy or greater than 2.0 if the patient does not have encephalopathy

Step 2: Laboratory evaluation
- Liver function test
  - Bilirubin is not usually high
  - ALT/AST can be in 10,000 IU/L (AST is usually more than ALT)
  - Prothrombin time and INR
- Serum electrolytes
- Hourly Blood glucose
- Serum ammonia

Step 3: Treatment
- Prevent further hepatic injury by avoiding hepatotoxic drugs.
- Prevent and treat hypoglycemia and electrolyte abnormality.
- Early nutrition should be with low-protein and high-calorie (120–150% requirement) enteral feeding.
- Correct coagulopathy with blood products, only when there is bleeding or for invasive procedures.
- Look for and treat raised intracranial hypertension as a part of hepatic encephalopathy:
  - Head end elevation should be 30°.
  - Adequate sedation and analgesia is needed for children with hepatic encephalopathy and grade 3 or 4 encephalopathy.
  - Intracranial pressure monitoring is considered for patients who are listed for liver transplantation.
  - Mannitol can be given for acute rise in intracranial pressure.
  - 3% saline is a better option in a child with shock and coexistent renal failure.
    - *N*-acetylcysteine—there is evidence favoring the use of *N*-acetylcysteine infusion in children with nonparacetamol liver failure, but the use in septic shock and ischemic hepatic dysfunction has not been studied. Ischemic hepatic dysfunction usually responds well to correction of the shock.
    - Lactulose, branched chain amino acids, enteral rifaximin and bowel wash have insufficient evidence for routine use.
    - Liver-support devices may be used as a bridge to transplantation or to help recovery of the ailing liver. They have limited role outside the

clinical trials. Two main categories of support devices are bioartificial and artificial (MARS).

- Consider liver transplant if no improvement and where prognostic factors indicate a high likelihood of death. Liver dysfunction as the part of septic shock and MODS improves on correction of shock and rarely requires transplant.

Suggested Readings

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   This article discusses guidelines for renal replacement therapy in children.

Part XV

ICU Procedures

Rajesh Chawla and Sudha Kansal

Central Line Placement

91

Rajesh Chawla, Vishakh Varma, and Sudha Kansal

A 55-year-old diabetic female patient was brought to the emergency department with history of fever with chills and rigors for the past 3 days. She also had altered sensorium for the past few hours. On arrival she was found to have tachycardia and hypotension.

Central line catheterization is a commonly performed procedure in any ICU. It is now recommended to be performed under ultrasound guidance. This is a fairly safe procedure in expert hands.

Step 1: Assess the need for central line placement

Insert a central line only for patients in whom it is indicated (as mentioned below) after ruling out contraindications (as mentioned in Step 2):

- For appropriate fluid management
  - Severe sepsis and septic shock
  - Low urine output
  - Intraoperative
  - For patients in shock
- Concentrated vasoactive agent administration
- Difficult peripheral vascular access
- Multiple drug administration

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- Concentrated electrolytes (e.g., potassium)
- Total parenteral nutrition
- Chemotherapy
- Agents irritating to peripheral veins (e.g. Amiodarone, Phenytoin, mannitol)
- Prolonged antibiotic therapy (e.g., endocarditis)
- Temporary hemodialysis
- During cardiopulmonary resuscitation
- Large-bore venous access for rapid administration of fluids

Step 2: Check for any contraindications

There are no absolute contraindications to central line placement. Relative contraindications are as follows:

- Local site infections or burns
- Anatomic abnormalities
- Coagulopathy (ultrasound guidance will help)

Step 3: Choose the appropriate site

The central venous cannulation site can be decided on the basis of the patient's requirement and the comorbid conditions:

- Coagulopathy: Prefer—femoral > internal jugular > subclavian
- To decrease risk of infection: Prefer—subclavian > internal jugular > femoral

Step 4: Choose the appropriate catheter

1. Single-lumen or multilumen catheters*:* The more is the number of lumens, the smaller is their diameter.
   - If rapid fluid infusion is required—as in trauma—single- or double-lumen catheters are preferred.
   - If the number of infusions is substantial, three- or four-lumen catheters are preferred.
   - The infection risk is directly proportional to the number of lumens, so the more the number of lumens, the more is the risk of infection associated with it.
2. Antimicrobial-impregnated catheters*:* Can use a chlorhexidine/silver sulfadiazine or minocycline/rifampin-impregnated CVC in patients:
   - When catheter is expected to remain in place for more than 5 days
   - If the catheter infection rates are high in the ICU even after successful implementation of a comprehensive strategy to reduce rates of infection
3. Tunneled catheters*:* Tunneling is ineffective in decreasing infection rate in short-term CVCs.

Step 5: Know the relevant anatomy

A. *The subclavian vein*: It crosses under the clavicle just medial to the midclavicular point. It lies underneath the clavicle at the insertion of the lateral head of the sternocleidomastoid on the clavicle. It is separated from the subclavian artery by the anterior scalene muscle, which lies deep to the vein. The vein lies in proximity to the dome of the pleura.

B. *The internal jugular vein*: It is located in the neck at the apex of the triangle formed by the two heads of the sternocleidomastoid muscle and the clavicle. At the apex, the carotid artery is medial and posterior to the vein.
C. *The femoral vein*: It lies 1–1.5 cm medial to the femoral artery at the inguinal ligament. If the inguinal ligament cannot be identified as in obese patients, then the femoral artery lies approximately at the centre of the pubic tubercle and the anterior superior iliac spine.

Step 6: Take informed consent
- Communicate with the patient or their surrogate.
- Explain the detailed procedure, the benefit, the risk and the alternative in the language they understand.
- Reply to all the queries and concerns.
- Document the consent and get it signed.

Have a peripheral venous access before attempting central cannulation except probably during cardiopulmonary resuscitation.

Step 7: Keep all equipment ready for cannulation and pressure transducing system
- Turn up the volume on the monitor so that it can be heard.
- ECG, pulse oximetry and BP monitoring instruments.
- Material for sterile preparation—cap, mask, sterile gown, gloves and drapes.
- 2% chlorhexidine with alcohol.
- Shoulder roll.
- A 25-gauge needle and a syringe with 2% lignocaine.
- Sterile saline flush.
- A sterile cannulation set with CVCs, a guidewire, and a locator needle with the syringe.
- A needle holder with suture material.
- Sterile dressing.
- The pressure transducing system.

Step 8: Set up the pressure transducing system
This consists of a pressure transducing assembly with a flushing system. Details have been discussed in Chap. 92.

Step 9: Obtain a procedure-directed history and do physical examination
- Location and number of previous CVCs
- Location of any known venous thrombi
- History of clavicle fracture
- History of IVC filter placement or pacemaker insertion
- History of any bleeding disorder or current use of anticoagulants
- History of allergy to chlorhexidine, povidone-iodine, or lidocaine

Table 91.1 Approaches to subclavian vein cannulation

	Infraclavicular (common)	Supraclavicular
Insertion landmark	2 cm inferior to midportion of the clavicle and walk down the clavicle	Just above the clavicle, lateral to the clavicular head of sternocleidomastoid
Angle with skin	0°	45°
Aim toward	Sternal notch	Contralateral nipple
Depth from skin	Just deep to the clavicle	1–2 cm, just under the clavicle

Step10: Central line placement

- Wear the cap and the mask.
- Wash hands with alcohol-based hand rub for 3–5 min and minimum three applications.
- Put on a sterile gown and gloves.
- Clean the skin of the patient with 2% chlorhexidine in alcohol preparation.
- Give a frictional scrub in a circular manner to at least 10 cm area from the insertion site.
- Do not shave if hair is present.
- Place large sterile drapes over the insertion site. Do not occlude the air supply or field of vision when draping neck areas of conscious patients.
- Use Seldinger technique for cannulation
  - The desired vessel is punctured with a sharp, hollow needle called a trocar.
  - A round-tipped (J-tipped), long guidewire is then advanced through the lumen of the trocar into the vessel.
  - The trocar is withdrawn, leaving the guidewire in the vessel.
  - The tract is dilated with a dilator introduced in rotating motion.
  - A hollow catheter can now be passed over the guidewire into the vessel.
  - The guidewire is then withdrawn and the catheter remains in situ.
  - Never lose control of the guidewire.
    1. *Subclavian vein cannulation*
       - Position should be Trendelenburg with the head turned toward the opposite side and a shoulder roll placed along the spine.
       - Stand on the side of the patient, where the procedure is planned.
       - Ensure maximum sterile barrier precautions.
       - Locate the landmarks, namely, the clavicle, sternal notch, sternocleidomastoid muscle, and its insertion on the clavicle, lateral end of the clavicle (Table 91.1).
       - Apply generous local anesthesia.
       - Insert the needle and syringe (filled with 1–2 mL saline), constantly aspirating for venous blood (Fig. 91.1).
       - If the rapid flush of blood does not appear during insertion of the needle, gradually withdraw the needle constantly aspirating. Blood may now appear.
       - If the first attempt is unsuccessful, then withdraw the needle up to the skin and reposition the needle.

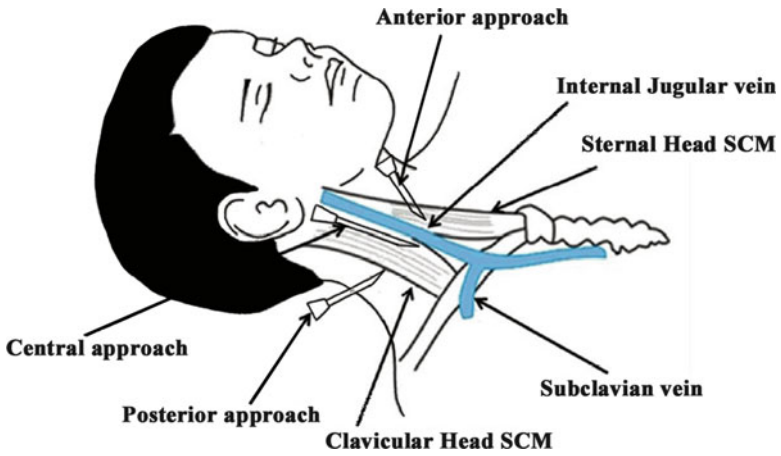

Fig. 91.1 Internal jugular vein cannulation

Table 91.2 Approaches to the internal jugular vein (Fig. 91.1)

	Central	Anterior	Posterior
Insertion landmark	Apex of the triangle formed in the neck by the two heads of the sternocleidomastoid muscle and the clavicle[a]	Medial edge of the sternocleidomastoid muscle at level of thyroid cartilage	Lateral edge of sternocleidomastoid muscle, one-third of the way from the clavicle to the mastoid process
Angle with skin	45°	45°	30–45°, dive under the border of the sterno-cleidomastoid muscle
Aim toward	Ipsilateral nipple	Ipsilateral nipple	Sternal notch
Depth from skin	Within 3 cm	Within 3 cm	Within 5 cm

[a]If the vein is not encountered, then enter the skin slightly more medially and retry (Fig. 91.2)

- Cannulate the vein using Seldinger technique as described above.
- Ensure backflow in all ports and flush all the ports.
- Ensure local hemostasis.
- Fix the catheter appropriately.
- Apply sterile dressing.

2. *Internal jugular vein cannulation*
   - Position should be Trendelenburg with the head turned toward the opposite side.
   - Stand at the head end of the patient.
   - Feel for the carotid and always keep it under your fingers.
   - Insert the needle at the following landmark and cannulate in a similar manner to subclavian vein (Table 91.2).
   - It is preferable to first locate the vein with a 25-gauge needle (finder needle) and then puncture with the larger needle.

- Cannulate using Seldinger technique.
- Obtain the chest X-ray after cannulation.

3. *Femoral vein cannulation*
   - Position should be supine with the leg slightly abducted and externally rotated.
   - Stand on the side of the patient.
   - Insert the needle 45° angle to the skin at a point 1–1.5 cm medial to the femoral arterial pulsation and about 2–3 cm below the inguinal ligament.
   - Direct the needle cephalad.
   - Cannulate using Seldinger technique.
4. *Ultrasound use for vascular access*
   A. *Advantages*
      - Fewer complications
      - Fewer attempts for successful cannulation
      - Fewer failed procedure
      - Shorter time for procedure (can be used in emergency situations)
      - Can be used in patient with contraindication to blind technique; patient with coagulopathy
      - Can be used in "difficult access" category; obesity, short neck, swollen neck, burns/postradiotherapy/postsurgical contracture, etc.
      - Decrease need of postprocedure radiological confirmation

   B. *B mode ultrasound*
      - B mode ultrasound allows for detailed evaluation of vascular anatomy.

   C. *Transducer selection*
      - For central venous cannulation, high-frequency transducer (5–7 MHz) is ideal. Though in obese patients you may require low-frequency transducer.

   D. *Technique*
      - USG guidance can be:
        – Static guidance: better than landmark approach and inferior to dynamic guidance. USG is used to localize the venipuncture site.
        – Dynamic guidance: here the procedure is performed under real-time guidance, i.e., while doing the puncture, needle is seen puncturing the vessel wall, however more difficult clinically.

   E. *View*
      - Transverse view: here cross section view of vessel is obtained.
      - Longitudinal view: here longitudinal view of the vessel is obtained.

   F. *Method of orientation*
      The transducer has an identification mark on one side which corresponds to mark displayed on one side of image, or alternatively finger can be rubbed on one side of transducer surface to produce an image and confirm orientation.

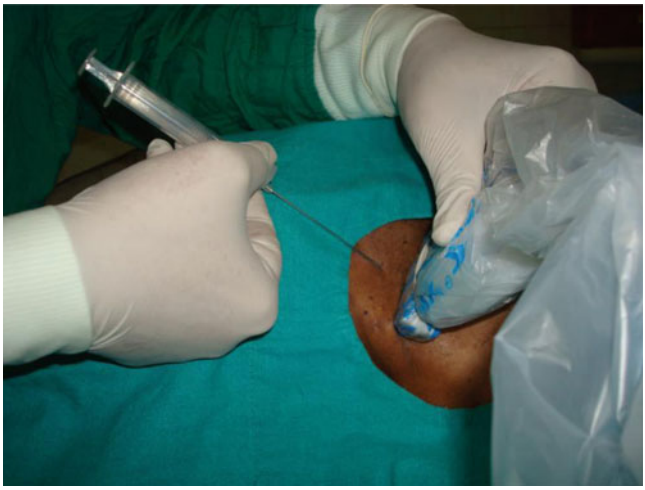

Fig. 91.2 Central line cannulation under USG guidance

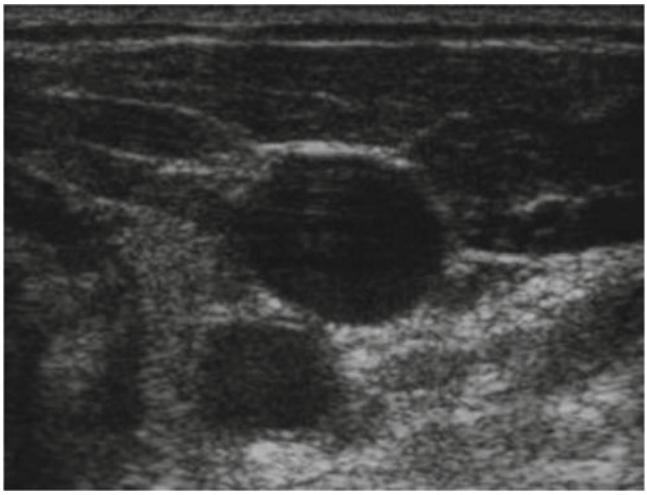

Fig. 91.3 Ultasonographic transverse view of internal jugular vein (*above*) and common carotid artery (*below*)

G. *Procedure IJV (Figs. 91.2 and 91.3)*
- Position the patient in supine Trendelenburg position.
- Turn head to other side.
- Identify the landmark and select the site of puncture.
- Place the USG machine on ipsilateral side.
- Confirm the site puncture with ultrasound.

- Use transverse and longitudinal view to identify the structure around the vein.
- Can use Doppler to differentiate between vein and artery (depending on the flow velocity).
- The procedure should be performed under strict aseptic protocol (as described).
- Skin is prepared as described.
- The assistant holds the transducer and applies ultrasound gel over it.
- A sterile sheath (camera cover; used in laparoscopy) is placed on the sterile field.
- The operator takes the transducer from the assistant, ensuring that the transducer is covered in the sterile sheath. To maintain sterility, sterile sheath is also stretched over the cord. Then apply band available with the sheath over the transducer to secure the sheath.
- Reconfirm the site of puncture. Can apply chlorhexidine over the transducer if image is not clear.
- Ensure that the vessel to be punctured is in the center of screen so that the vessel is lying just deep to the center of transducer.
- A dummy poke can be done by laying the needle on the skin surface and then pressure is applied near the tip of the needle, and visualize acoustic disturbance in the subcutaneous tissue due to this to ensure that it is positioned directly over the needle.
- Perform the skin puncture proximal to transducer, and while puncturing the subcutaneous tissue, ensure that the needle tip is seen advancing. If the tip is not seen, move the probe along the axis of the vein.
- Advance the needle further and visualize the needle tip entering the vessel lumen. Aspirate with the syringe to confirm the flash of blood.
- Reconfirm the needle position on the ultrasound.
- Now keep the probe aside in sterile environment.
- Proceed as before with placement of guidewire (Seldinger technique).
- Once the line is placed, reconfirm the position of line with the transducer by scanning distally.
- Examine with the probe for any pneumothorax.

Disadvantages

1. Cost and maintenance of equipment
2. Special USG training for operator
3. Difficulty to maintain sterility during procedure

Step 11: Check the post-central-line chest X-ray

The chest X-ray should be done after a subclavian and internal jugular cannulation. The following points should be noted in the X-ray:

- Catheter tip location
  - Catheter tips located within the heart or below the pericardial reflection of the superior vena cava increase the risk of cardiac perforation and fatal cardiac tamponade.

Table 91.3 Management of mechanical complication

Complication		Management
I. Vascular		
1.	Arterial puncture	Press the artery for at least 15 min or until bleeding stops
2.	Venous bleeding	Compress till bleeding stops
3.	Hematoma	
4.	Hemothorax	Correct coagulopathy, if any; may need drainage if massive
5.	Cardiac tamponade	
	Cardiac perforation	Surgical intervention
6.	Thoracic duct injury, chylothorax	Usually conservative
II. Pneumothorax		Always put an intercostal tube drainage if the patient is on positive-pressure ventilation
		If tension pneumothorax is present, release immediately with the needle thoracocentesis and follow with tube drainage
		Small pneumothorax in the spontaneously breathing patient can be kept under close observation
III. Air embolism		Always position the patient flat if the head is not down while inserting the line
		Never leave the lumen of the catheter uncapped
		If suspected, place the patient the right side up and the head down and aspirate blood mixed with air
IV. Nerve injuries		Conservative management
V. Tracheal/laryngeal injury		May need intubation
VI. Arrhythmia		Pull out the catheter till it is in the superior vena cava
VII. Malposition		May need repositioning

  - Ideally, the catheter tip should lie within the superior vena cava, parallel to the vessel walls, and be positioned below the inferior border of the clavicle and above the level of the third rib, the T4 to T5 interspace or the tracheal carina.
- Pneumothorax
- Pleural fluid / hemothorax

Step 12: Remove the line
- As soon as it is not required
- Induration, redness or frank pus discharge from insertion site
- Suspected or confirmed catheter-related infection
- Catheter occlusion/thrombosis
- Vascular erosion caused by the catheter

Step 13: Manage complications

I. *Mechanical complications (Table 91.3)*
- Never force the guidewire or the catheter; it may cause rupture of the vessel or injury to nearby structures.
- Do not overdilate—dilating the skin and subcutaneous tissue may be enough.

- During internal jugular vein and femoral vein puncture, always keep one hand over the artery to prevent arterial puncture.
- Never lose control of the guidewire, and hold it in one hand.
- When there is increased risk of bleeding, internal jugular vein route is preferable (with ultrasound guidance).

II. *Infectious complications*

1. Insertion site infection 2. Catheter related blood stream infection (CRBSI) 3. Endocarditis	Remove the line and treat the infection

The following methods are required to prevent infectious complications:

1. Use the line only when necessary and remove it as soon as it is not required.
2. Use the subclavian vein and avoid femoral or internal jugular vein cannulation.
3. Use a CVC with the minimum number of ports or lumens essential.
4. Hand hygiene and maximal sterile barrier precautions are needed at all times.
5. Use sterile gauze or sterile, transparent, semipermeable dressing to cover the catheter site.
6. If the patient is diaphoretic or if the site is bleeding or oozing, use a gauze dressing until this is resolved.
7. Replace dressings used on short-term CVC sites every 2 days for gauze dressings and every 7 days for transparent dressings.
8. Use a chlorhexidine-impregnated sponge dressing if the infection rate is not decreasing despite adherence to basic prevention measures.
9. Use a 2% chlorhexidine wash for patients' daily skin cleansing, not the insertion site.
10. Evaluate the catheter insertion site daily for signs of infection.
11. Use a sutureless securement device.
12. Use a chlorhexidine/silver sulfadiazine or minocycline/rifampin-impregnated CVC in patients whose catheter is expected to remain in place for more than 5 days or if the high infection rate is expected.
13. Use povidone-iodine antiseptic ointment or bacitracin/polymyxin B ointment at the hemodialysis catheter exit site after catheter insertion and at the end of each dialysis session.
14. Do not use guidewire exchanges to replace a catheter suspected of being source of infection.

III. *Misinterpretation of data*

Suggested Reading

1. O'Grady NP, Alexander M, Burns LA, et al. Guidelines for the prevention of intravascular catheter-related infections. Am J Infect Control. 2011;39(4 Suppl 1):S1–34.

The latest version of the CDC guidelines for the prevention of intravascular catheter-related infections discusses in detail and provides recommendations on all aspects of catheter care and CRBSI reduction.

2. Biffi R, Orsi F, Pozzi S, Pace U, et al. Best choice of central venous insertion site for the prevention of catheter-related complications in adult patients who need cancer therapy: a randomized trial. Ann Oncol. 2009;20(5):935–40.
   Central venous insertion modality and sites had no impact on either early or late complication rate, but US-guided subclavian insertion showed the lowest proportion of failures.
3. McGee DC, Gould MK. Preventing complications of central venous catheterization. N Engl J Med. 2003;348(12):1123–33.
   NEJM current concepts series—a lucid description of the insertion maintenance and complications of central venous catheters.
4. Hind D, Calvert N, McWilliams R, et al. Ultrasonic locating devices for central venous cannulation: meta-analysis. BMJ. 2003;327(7411):361.
   A real-time two-dimensional ultrasound guidance for cannulating the internal jugular vein in adults was associated with a significantly lower failure rate both overall and on the first attempt.
5. Ruesch S, Walder B, Tramèr MR. Complications of central venous catheters: internal jugular versus subclavian access—a systematic review. Crit Care Med. 2000;30(2):454–60.
   This study shows significantly more arterial punctures with jugular catheters compared with subclavian. There are significantly less malpositions with the jugular access. They further show that the incidence of bloodstream infection is less with subclavian.

Internal jugular vein cannulation using dynamic guidance of ultrasound in the transverse view

Arterial Catheterization

92

Sheila Nainan Myatra, Parvez Ali Khan,
and Jigeeshu V. Divatia

A 65-year-old diabetic male patient was admitted to the ICU with a right lobar pneumonia. He was started on antibiotic therapy. He was receiving oxygen by a mask at 8 L/min and maintaining an SpO_2 of 94%. His blood pressure was being monitored every 10 min using noninvasive blood pressure measurement. By evening his blood pressure started to drop. Noninvasive blood pressure reading was 80/50 mmHg at 8 PM, which was not responding to fluid boluses.

Invasive arterial pressure monitoring, using arterial catheterization, is one of the commonly performed bedside procedures in the ICU during shock, when noninvasive blood pressure monitoring becomes unreliable. This chapter describes the indications, contraindications, preparation, procedural details, and maintenance of the catheter in detail along with the complications that can arise from arterial catheterization.

Step 1: Assess the need for intra-arterial pressure monitoring indications

- Hemodynamic instability
- Need for frequent blood pressure monitoring during vasopressor therapy
- Need for frequent arterial blood gas analysis

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R. Chawla and S. Todi (eds.), *ICU Protocols: A stepwise approach*,
DOI 10.1007/978-81-322-0535-7_92, © Springer India 2012

Step 2: Check for any contraindications

- Inadequate circulation to the extremity
- Uncontrolled coagulopathy
- Extremities with full-thickness burn or trauma
- Skin infection over the insertion site
- Raynaud's phenomenon
- Thromboangiitis obliterans (Buerger's disease)
- Locations near arteriovenous fistulas

Step 3: Choose the appropriate site

- The radial artery at the wrist is the most preferred site as the hand has usually good collateral supply, and it is easy to access and maintain.
- Acceptable alternate sites commonly used in adult patients include the femoral, axillary, brachial, and dorsalis pedis arteries.
- All sites are at a risk of ischemic complications due to their small caliber (radial and dorsalis pedis), lack of good collateral supply (brachial and axillary), and presence of atherosclerotic vascular disease (femoral and dorsalis).
- Although infectious complications may be higher with the femoral artery, this may be the only palpable artery amenable to cannulation during severe hypotension. Ultrasound guidance may be useful in locating and cannulating the femoral artery.
- Keeping in mind the above, always choose an artery you are familiar with cannulating.

Step 4: Check perfusion of the extremity

- Both the necessity and the optimal method to assess adequacy of collateral blood flow to the hand before radial artery cannulation are controversial.
- To perform an Allen's test:
  - The patient's hand should be elevated above his or her heart.
  - The patient should be asked to make a fist.
  - Pressure should be applied to both the radial and the ulnar artery until distal blood flow is occluded.
  - While maintaining the elevated hand position, the patient should then open the hand. The hand should appear pale and have limited capillary refills.
  - The ulnar arterial pressure should be released (while maintaining enough pressure to occlude the radial artery).
  - The hand should return to normal color within 5–7 s.
  - Delayed return suggests poor collateral circulation
  - The test should then be performed on the radial artery circulation in the same manner.
- There is lack of evidence that these tests can predict hand ischemia after radial artery cannulation. Although the value of these tests has not been established, it may provide some qualitative assessment of collateral circulation.
- To make the interpretation more objective, pulse oximetry, plethysmography, or Doppler ultrasound examination may be used along with the modified Allen's test.
- The operator should document the impression of collateral circulation in the procedure note.

Step 5: Keep all equipment ready for arterial cannulation and pressure transducing

- Material for sterile preparation
- A wrist board or roller pad under the wrist, 25-gauge needles, and syringes with 1% lidocaine
- An arterial catheter and wire set/arterial cannulae (cannulae for arterial placement should be without an injection port and preferably have an eye to take a stitch)
- A needle holder with suture material
- Sterile dressing
- An arterial connector
- A pressure transducing system

Step 6: Set up the pressure transducing system

This consists of a pressure transducing assembly with a flushing system. The accuracy of the intra-arterial blood pressure measurement will depend on the proper setup and function of the pressure transducing system.

- *The pressure transducing assembly* consists of a coupling system, pressure transducer, amplifier, signal conditioner, analog to digital converter, and microprocessor that converts the signal received from the artery into a waveform on the a bedside monitor.
- *The flushing system* is set up using a 500-mL saline bottle encased in a bag pressurized to 300 mmHg. At this pressure, the catheter will be flushed with 3 mL saline per hour and help keep the catheter patent. Using the flushing device helps flush the assembly as required.

  Before connecting flush the pressure transducing system with saline using the flushing device, remove all air bubbles, and keep it ready to connect to the arterial catheter. Heparinized saline is no longer routinely used in view of concerns about heparin-induced thrombocytopenia. Also, continuous heparin flush solution has been shown to affect coagulation studies if the sample is drawn via the arterial line.

Step 7: Positioning and preparation prior to radial artery cannulation

- Inform the patient about the procedure (if conscious) and take the informed consent.
- Don the mask, cap, sterile gown, and gloves.
- Position the wrist in dorsiflexion. This brings the radial artery in closer approximation to the skin and can be instrumental in success of the procedure.
- This position can be maintained using a roll of gauze below the wrist or with a specially designed arm board and securing the arm with tape.
- The field can be sterilely prepared and draped using towels. In all invasive procedures, meticulous care should be taken to minimize the risk of infection.
- A small wheal of 1% lidocaine should be raised in the conscious patient to decrease the pain during cannulation.

Step 8: Radial arterial cannulation

Two types of arterial catheters are used commonly:

- Catheter with needle
- Catheter with needle and a guidewire

The radial artery is palpated between the distal radius and the flexor carpi ulnaris tendon. The arterial catheter with needle is inserted at a 30- to 45-degree angle toward the artery.

Over-the-Needle Technique

Once there is blood return, the needle is advanced slightly further to ensure the catheter has entered the vessel. The needle angle is then lowered to 10–15°, and the catheter is guided over the needle and advanced into the vessel.

Over-the-Wire Technique

- When blood return is noted, the catheter is advanced further, and the needle is then removed. The guidewire is then kept ready, and the catheter is withdrawn till there is pulsatile blood flow. The guidewire is inserted into the vessel, the catheter is advanced over it, and then the guidewire is removed.
- A commonly used variant of this technique is to initially insert only the introducer needle without catheter and then advance guidewire through the needle when in position and finally thread arterial catheter over the guidewire.

Anticipated Difficulties During Cannulation

- In the over-the-needle technique, sometimes there is a blood return, but the artery cannot be cannulated. This may be because the needle has entered the vessel, but the catheter is still outside it. This can be overcome by advancing the needle further and then guiding the catheter over it or removing the needle and passing a guidewire into the vessel over which the catheter can be advanced easily.
- Sometimes the catheter may not easily pass through the skin. To overcome this, make a small nick on the skin with a needle or a blade at the insertion site.
- After multiple attempts at cannulation, the artery may go into spasm. Change the site for arterial line placement at this point.

After cannulation, pressure is given on the artery proximal to the catheter tip to reduce bleeding while the pressure transuding assembly is connected.

Step 9: Secure the catheter and check perfusion

- Great care should be taken to make sure the catheter stays in place. Although there are various ways of fixing the catheter with adhesive tape, the best method of securing it is to suture it in place. A moderate-diameter, nonabsorbable suture material can be used.
- Place a clear dressing over the catheter, which will not only secure it further but also allow inspection of the insertion site.
- Label and date the arterial line.
- Immediately after cannulation, check perfusion of the extremity. This should also be checked periodically when the arterial catheter is in place.

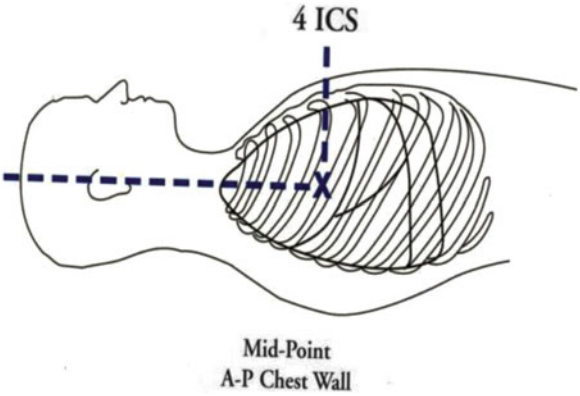

Fig. 92.1 Phlebostatic axis

Step 10: Zero and level the transducer (static calibration)

- To obtain accurate pressure measurements, the air-fluid interface must be aligned with the chamber or vessel being measured.
- The reference point is usually at the level of the heart. Use the phlebostatic axis (junction of the fourth intercostal space and midpoint between the anterior and posterior chest walls—Fig. 92.1).
- A spirit level should be used to level this point with the stopcock of the pressure transducing system, which is used for zeroing.
- The transducer is opened to air and the recorded pressure (atmospheric pressure) is used by convention as 0 mmHg reference value.

Step 11: Check if the system is optimally damped (dynamic calibration)

- Damping indicates the tendency of an oscillating system to return to its resting state. Anything that takes energy out of the system results in a progressive diminution of amplitude of oscillations.
- *Underdamped waveforms* (will be narrow and peaked tracing and will record higher systolic and lower diastolic pressure) are seen when long tubing is used or with increased vascular resistance.
- *Overdamped waveforms* (will record lower systolic and higher diastolic pressure) are commonly seen when there are air bubbles or blood clots, overly compliant tubing, catheter kinks, stopcocks, no fluid in the flush bag, or low flush bag pressure.
- In both the above, the mean arterial pressure (MAP) will not change. Hence, always rely on the MAP, especially when you are not sure whether the system is optimally damped.
- Damping can be checked by doing a "square wave test" (Fig. 92.2). Activate the flush device, quickly release it, and observe the waveform on the monitor. The waveform will sharply rise and "square off" at the top when the flush is activated and then the tracing returns to the baseline after it is released (Fig. 92.2). Check the number of oscillations:

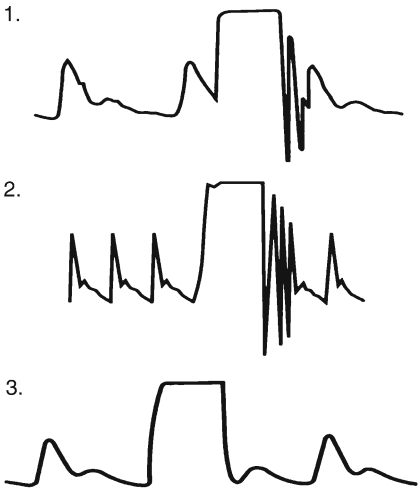

Fig. 92.2 Square wave test

1. Optimally damped—one or two oscillations before return to tracing
2. Underdamped—more than two oscillations before return to tracing
3. Overdamped—less than one oscillation before return to tracing

Repeat the square wave test every 8–12 h, whenever the waveform looks over- or underdamped, when the accuracy of the measurement is doubtful, especially when you are implementing some interventions based on intra-arterial pressure values.

Step 12: Check the arterial waveform and MAP (Fig. 92.3)

- Arterial pressure waveforms differ from site to site. As the arterial pressure is recorded more distally, the trace gets progressively more peaked and the dicrotic notch migrates away from the peak. The MAP however does not vary widely as one measures more distally.
- An under- or overdamped tracing can either under- or overestimate the systolic and diastolic pressures. However, the MAP always remains the same.
- Considering the above, always use and rely on only the MAP rather than the systolic or diastolic pressure recorded during intra-arterial blood pressure monitoring.

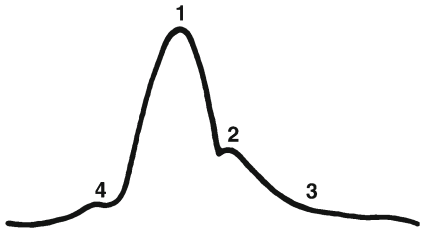

Fig. 92.3 Components of the arterial waveform (*1*—peak systolic pressure, *2*—dicrotic notch, *3*—diastolic pressure, and *4*—anacrotic notch)

Step 13: Make other interpretations from the arterial waveform

Besides more accurate and real-time recording of arterial pressure, a lot of hemodynamic interpretations can be made from the arterial waveform:

- Systolic blood pressure variations (swing in the waveform) can be seen during hypovolemia.
- Steep slope of upstroke means good contractility and vice versa.
- Area under the curve represents the stroke volume.
- Position of the dicrotic notch—low (low systemic vascular resistance) and high (high afterload).
- Slope of the decent—steep (low systemic vascular resistance).

Step 14: Optimize the natural frequency of the system to improve accuracy

- Use a wide-bore, high-pressure tubing no longer than 122 cm (48 in.).
- Avoid tubing extensions and stopcocks.
- All connections should be tight.
- Eliminate air bubbles.
- Ensure that the flush bag external pressure is 300 mmHg.
- Keep cannulated extremity in neutral or slightly extended position.

Step 15: Ensure proper maintenance of the Arterial catheter

- Ensure that the catheter is labeled and has an insertion date at all times.
- Check perfusion of the extremity at regular intervals.
- Check the insertion site daily through the clear dressing for signs of inflammation and infection.
- Change dressing only if it is not well coated, very dirty, or there is collection under it.
- Whenever the arterial catheter is not being transduced, block it using an arterial connector (not venous connectors /stopcocks). These provide high resistance to the blood flow into the catheter and prevent them from getting blocked.

Step 16: Watch for complications

- *Vascular complications* of clinical significance are rare but can be devastating. Attention to the adequacy of distal perfusion is of great importance.
- Absent pulse, dampened waveform, blanched or mottled skin, delayed capillary refill, and painful and cold hands or fingers with motor weakness are presentations of hand ischemia.
- *Infections complications*: Arterial catheters can be responsible for both local and catheter-related bloodstream infections, though the incidence is low. The arterial catheter should be given the same degree of importance as the central venous catheter as a potential source of sepsis. Remove the catheter if it is suspected to be the cause of infection.
- Bleeding, hematoma.
- Nerve damage.
- Pseudoaneurysm.

Step 17: Treat ischemic complications if they occur

- Hand ischemic—remove the cannula.
- Monitor patient's condition and use splinting.
- If the patient is on vasopressors, stop therapy if possible.
- If the patient's condition is medically stable, consider the following:
  - Arterial duplex sonography
  - Angiography
- Operative intervention. if the patient's condition is medically unstable, consider the following:
  - Arterial duplex sonography
  - Sympathetic block
  - Use of thrombolytics

Step 18: Remove the arterial catheter at the earliest

There is no fixed number of days after which the arterial catheter should be removed. Catheter colonization increases with dwell time. Hence, assess the need for the arterial catheter daily and remove it as soon as it is no longer required or earlier if there are any complications.

Suggested Reading

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   Consistent anatomic accessibility, ease of cannulation, and a low rate of complications have made the radial artery the preferred site for arterial cannulation. Radial artery catheterization is a relatively safe procedure with an incidence of permanent ischemic complications of 0.09%.
2. Wallach SG. Cannulation injury of the radial artery: diagnosis and treatment. Algorithm Am J Crit Care. 2004;13(4):315–9.
   Cannulation of the radial artery can result in complications ranging from arterial thrombosis, arterial aneurysm, compartment syndrome, infection, nerve injury, and skin necrosis to possible thumb or even hand necrosis if not recognized and treated early.
3. Koh DB, Gowardman JR, Rickard CM, Robertson IK, Brown A. Prospective study of peripheral arterial catheter infection and comparison with concurrently sited central venous catheters. Crit Care Med. 2008;36(2):397–402.
   In this study, arterial catheter colonization and rates of catheter-related bloodstream infection were found similar to those in concurrently sited and identically managed central venous catheters. By inference, the arterial catheter should be given the same degree of importance as the central venous catheter as a potential source of sepsis.
4. Del Cotillo M, Grane N, Llavore M, Quintana S. Heparinized solution vs. saline solution in the maintenance of arterial catheters: a double blind randomized clinical trial. Intensive Care Med. 2008;34:339–43.
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5. Hoste EA, Roels NR, Decruyenaere JM, Colardyn FA. Significant increase of activated partial thromboplastin time by heparinization of the radial artery catheter flush solution with a closed arterial catheter system. Crit Care Med. 2002;30:1030–4.
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Pulmonary Artery Catheterization

93

Rajesh Chawla, Vishakh Varma, and Atul Kulkarni

A 65-year-old male patient, a known case of chronic obstructive pulmonary disease with cor pulmonale, hypertension, and coronary artery disease with chronic congestive heart failure, was admitted to the ICU with right lower lobe pneumonia. He was in respiratory failure and in shock. On the second day, he developed renal failure and azotemia. A pulmonary arterial catheter (PAC) was inserted.

The pulmonary artery catheterization (PAC) provides direct pressure measurements from the right atrium, right ventricle, pulmonary artery, and pulmonary artery occlusion pressure. It is also a mean of measuring cardiac output and mixed venous oxygen saturation. Routine use of this should be avoided, but it has still a role in expert hands in cardiac surgery, difficult to treat heart failure, congenital heart disease, and complex fluid management situations.

Step 1: Assess the need for PAC—indications

- PAC is used in situations where right-sided pressures (i.e., central venous pressure [CVP]) may not reflect the changes in pressures in the left side of the heart. Right-sided filling pressures are disproportionately elevated compared to the left-sided filling pressures.

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- PAC should be used in centers with nursing expertise in the management of catheters and sufficient physician experience in the interpretation of data in the following conditions:
  - For management of heart failure
    - Patients with refractory shock not responding to noninvasive management
    - Patients with significant azotemia on diuretic therapy and are clinically volume overloaded
    - As part of workup or bridge to cardiac transplant or the left ventricular assist device
  - Complex fluid management (shock, burns, acute renal failure, major surgery) in patients with poor left or right ventricular function
  - Cardiac surgery patients on cardiopulmonary bypass or patients with complex cardiac lesions
  - High-risk obstetric cases such as severe preeclampsia and abruptio placentae
  - Surgical procedures such as liver transplant and aortic cross clamping

Step 2: Check for the contraindications

Relative contraindications are as follows:

- Complete left bundle branch block may convert to complete heart block.
- Wolff–Parkinson–White syndrome and Ebstein's malformation because of possible tachyarrhythmias. A catheter with pacing capability is preferred in these situations.
- Coagulopathy.
- Severe pulmonary hypertension.
- It should not be used in centers that do not have experience and expertise in its use.

Step 3: Know the PAC

- Circumference should be 7–9 Fr.
- Length is 110 cm, marked at 10 cm intervals.
- The distal port (yellow colored) at the catheter tip is used for monitoring of pulmonary artery pressure.
- The second port (blue colored) is 30 cm proximal from the tip and is used for monitoring of CVP and injecting fluid bolus for computing cardiac output with bolus technique.
- The third lumen (red colored) leads to a balloon near the tip, with a locking port.
- The fourth lumen houses wires for a temperature thermistor, the end of which lies just proximal to the balloon. This attaches to the interface cable from the cardiac output monitor.
- The continuous cardiac output PAC has a copper thermal filament embedded in the catheter at 30 cm. Once inserted and connected to the monitor, this filament heats up every few seconds, warms blood around it, and thermistor in the pulmonary artery detects the change in temperature and calculates cardiac output.

The PAC set also contains the following:
- Large-bore introducer sheath with a one-way valve at its outer end and a side arm extension for intravenous access. (The PAC is introduced through the one-way valve. Some sets may not contain this sheath, but is also available separately.)
- Stiff dilator
- Plastic sheath to cover the catheter
- A 1.5-mL syringe for balloon inflation
- Guidewire
- Puncture needles and syringes
- Three ways and connectors
- A disposable knife

Step 4: Obtain informed consent
This has been explained in detail in Chap. 91.

Step 5: Select the appropriate PAC for insertion
- Select the PAC which is appropriate for that patient.
- Catheters are available, which can perform the following additional functions:
  - An extra venous infusion port.
  - Pacing capability.
  - Continuous mixed venous oximetry: Special fiber-optic PACs can be used to monitor mixed venous oxygen saturation (SvO_2) continuously, initially developed as a surrogate for continuous cardiac output.
  - An ejection fraction catheter has a faster thermistor response time so that it can calculate RV ejection fraction in addition to the cardiac output.
  - Continuous cardiac output.

Step 6: Prerequisites
- Establish monitoring of ECG, noninvasive blood pressure, and pulse oximetry.
- Keep ready all emergency medication and transcutaneous pacing equipment.
- Provide sedation in a conscious patient.
- Supply oxygen through the nasal cannula.
- Secure a peripheral venous access.
- Assemble the pressure transducer and flush it.
- An assistant is needed who can prepare the set and closely monitor the patient.
- The patient should be in supine position with the head slightly down and turned toward the opposite side.
- Make use of maximum sterile barrier precautions, described Chap. 91.

Step 7: Choose the site of insertion
- Generally the right internal jugular vein or left subclavian is selected.
- Alternatively any other site used for central venous cannulation can be selected keeping in mind the distance from the puncture site to the right atrium.
- An extra distance of 5–10 cm from the left internal jugular, 15 cm from the femoral veins, and 30–35 cm from the antecubital veins is required. But accurate placement rates are lower from these sites.

Step 8: Prepare the cannulation set

With maximum sterile precautions do the following:

- Pass the catheter through the sterile sheet.
- Flush the catheter with heparinized saline.
- Inflate the balloon with 1.5 mL air and check for its shape and any leakage.
- Zero and level the transducer and connect to the saline-filled catheter.
- Place the tip of the catheter at the heart level; pressure on the monitor should read zero.
- Next, raise the catheter tip to 30 cm height; the monitor should show a pressure of 22 mmHg (equivalent to 30 cm H_2O).

Step 9: Insertion of PAC through internal jugular vein

- Use maximum sterile barrier precautions.
- Apply generous local anesthesia.
- Locate the internal jugular vein.
- Puncture the vein with the puncture needle preferably under ultrasound guidance.
- Pass the guidewire through the needle and remove the needle.
- Dilate the skin and subcutaneous tissue with the dilator. This is generally done with the dilator loaded inside the introducer sheath. A small incision is often needed.
- Pass the large-bore sheath using Seldinger technique.
- Confirm placement by aspirating blood, flush it, and secure it with stitches.
- Introduce the prepared catheter through the introducer up to a distance of 20 cm with the balloon deflated. Note the waveform on the monitor—CVP tracing should be seen.
- Rotate the catheter so that curvature is at 11 o'clock position from patient's head end.
- Inflate the balloon gently with 1.5 cc of air and lock it. During pulmonary artery occlusion pressure (PAOP) measurement if the balloon is left inflated, you may cause a pulmonary infarct.
- Advance slowly and keep looking at the monitor for RV waveform with systolic peaks of 25–35 mmHg. Note that the diastolic pressure is close to zero. This is reached at around 30–35 cm length.
- If the RV or PA is difficult to enter:
  - Have the patient take deep breath.
  - Raise the head end of the bed or tilt the table to left or right.
  - Flush the PA port with 1–2 mL cold sterile saline so that the catheter becomes stiff.
- Keep inserting further; PA is reached at 40–45 cm. At PA, there is an increase in the diastolic pressure (Fig. 93.1).
- Now advance another 5–10 cm or so very gradually keeping an eye on the monitor to look for wedging. When it is wedged, the waveform becomes similar to that of CVP tracing at a pressure near to the PA diastolic pressure. This is the pulmonary artery occlusion pressure PAOP, and it is always lower than the pulmonary artery diastolic pressure (Fig. 93.1).

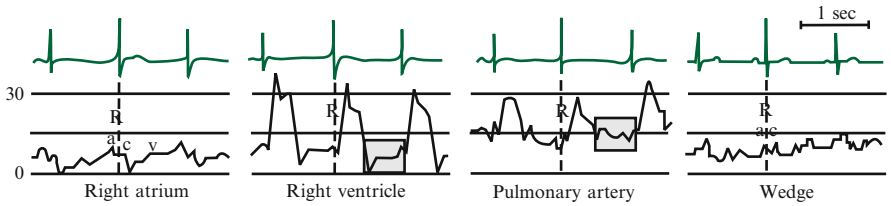

Fig. 93.1 Pressure tracings recorded from the right atrium, right ventricle, pulmonary catheter, and on pulmonary artery occlusion

- Do not advance any further; deflate the balloon.
- Now inflate the balloon with 0.5 cc increments and look for wedging. If it wedges before 1.5 cc, pull the catheter back 3–4 cm. Do not pull with the inflated balloon.
- Fix the catheter at that length. Note the length of the catheter that led to a good PAOP tracing in the case chart.
- Never keep the PAC wedged continuously; deflate the balloon after taking the readings.
- Measured and derived hemodynamic indices values are mentioned in Tables 93.2 and 93.3.

Step 10: Manage complications

- Minor complications are seen in up to 50% of patients, but major complications are seen in only 0.1–0.5% of patients.

Besides all the complications of insertion and maintenance of central venous lines, there are a few unique complications of the use of the PAC (Table 93.1).

Step 11: Interpretation of data obtained (Tables 93.2, 93.3 and 93.4)

Measuring Cardiac Output

- Enter the catheter constant into the monitor; this is generally written on the pack of the set or the insert.
- 10 mL of cold or room temperature saline is smoothly injected from the proximal (blue) port in the right atrium. In small children or patients with volume overload, smaller volumes (2 and 5 mL) may be used.
- A cable from the cardiac output monitor is dipped into the same bottle saline from which the injectant volume was aspirated.
- The temperature of the blood mixed and cooled with the cold saline is measured at the end of the catheter by a thermistor.
- This produces a thermodilution curve, from which the cardiac output is calculated by the monitor. Usually three measurements are made.
- These measurements may have a variability of up to 10%.
- There are various factors that influence the accuracy that include intracardiac shunts, tricuspid regurgitation, pulmonary valve regurgitation, respiratory cycle influences, and rapid injection of saline.

Table 93.1 Complications of the PAC

Complication	Description	Treatment
I. Catheterization		
a. Arrhythmias, ventricular fibrillation	Self-limited arrhythmias extremely common during passage	3.1% of patients require treatment, mostly withdrawal of catheter or guidewire
b. Right bundle branch block, complete heart block	Transient during passage in 5%	May need transcutaneous or transvenous pacing
	Permanent in 0.9%	
	Should rule out ischemia	
II. Catheter resistance		
a. Mechanical, catheter knots	Suspect if the catheter is blocked or difficulty in withdrawing	Radiological maneuver
	Confirm on a chest X-ray	Surgery
b. Thromboembolism	Clots seen within hours	The heparin-coated catheter reduces risk
	Thromboembolism rare	
c. Pulmonary infarction	Opacity on a chest X-ray	Removal of the catheter
d. Infection, endocarditis	Significant risk after 72 h especially in septic patients	Should be removed as soon as feasible
e. Endocardial damage, cardiac valve injury	53% in autopsy series, but clinically significant regurgitation does not occur	Removal of the catheter
f. Pulmonary artery rupture	0.02–0.2% of patients	One-lung ventilation to isolate normal lung
	Mortality is 50%	Positive end-expiratory pressure to the affected lung
	Cause:	Reverse anticoagulation
	Excessive insertion depth	May try to reinflate to cause tamponade
	Persistent wedging	May need surgical intervention
	Frequent manipulations	
	Inflation with liquid	
	Presents as hemoptysis and desaturation	
g. Pulmonary artery pseudoaneurysm	Sequelae of PA rupture	Surgery may be needed
	May cause secondary hemorrhage	
III. Misinterpretation of data		May be widespread
		Use requires expertise and experience
IV. Misuse of equipment		

Table 93.2 Normal cardiovascular pressures

	Pressure	
	Average (mmHg)	Range (mmHg)
Right ventricle		
Peak systolic	25	15–30
End-diastolic	6	1–7
Pulmonary artery		
Peak systolic	25	15–30
End-diastolic	9	4–12
Mean	15	9–19
Pulmonary artery wedge		
Mean	9	4–12
Left ventricle		
Peak systolic	130	90–140
End-diastolic	8	5–12
Central aorta		
Peak systolic	130	90–140
End-diastolic	70	60–90
Mean	90	70–105

Continuous Thermodilution Cardiac Output

- Near-continuous cardiac output can be measured by a specially designed pulmonary artery catheter.
- The RV portion of the catheter has a thermal filament that releases a small amount of heat in a pulsatile manner.
- This temperature variation is measured at the tip of the catheter. It has a measurement delay of 5–15 min, but the measurement is quite reliable.
- Acute changes in cardiac output are detected more slowly, but it has the advantage of ease of operation, minimal handling, and reduced risk of fluid overload.

Pulmonary Capillary Wedge Pressure

- Imagine that the vessel in which the pulmonary artery catheter lies is like a tube connected to the left atrium.
- When there is no flow of blood through the tube, the pressure at the tip of the tube will be the same as the pressure at the left atrium. So, we stop the blood flow by inflating the balloon and measure the pressure at the tip of the pulmonary artery catheter and call it the pulmonary capillary wedge pressure (PCWP), but technically the correct term is pulmonary artery occlusion pressure (PAOP) as PCWP is actually lower than PAOP.
- Pulmonary artery diastolic pressure can be used as an alternative to PCWP to measure left ventricular filling pressure, which we assume predicts left ventricular volume.

Table 93.3 Derived hemodynamic indices

Parameter	Physiologic significance	Formula	Normal value
Systemic vascular resistance	Reflects impedance of the systemic vasculature	80 × (MAP–CVP)/CO	700–1,600 dyne·s·cm^{-5}
Pulmonary vacular resistance	Reflects impedance of pulmonary circuit	80 × (PAM–PCWP)/CO	20–130 dynes·cm^{-5}
Cardiac index	Allows for meaningful comparison between patients	CO/BSA	2.5–4.2 L·min^{-1}·m^{-2}
Stroke volume index	Reflects fluid status and ventricular performance	CI/HR × 1,000	40–60 mL·beat^{-1}·m^{-2}
Left ventricular stroke work index	Estimates work of the left ventricle, reflects contractile state	(MAP − PCWP) × SVI × 0.0136	45–60 gm·m^{-2}
Right ventricular stroke work index	Estimates work done by the right entricle and RV performance	(PAM − CVP) × SVI × 0.0136	5–10 gm·m^{-2}

CI cardiac index, *CO* cardiac output, *CVP* central venous pressure, *HR* heart rate, *MAP* mean arterial pressure, *PAM* pulmonary artery mean pressure, *PCWP* pulmonary capillary wedge pressure, *SVI* stroke volume index

Table 93.4 Oxygen transport parameters

Parameter	Symbol	Formula	Normal value
Mixed venous oxygen saturation	SvO_2		70–75%
Oxygen delivery	DO_2	$1.34 \times Hb \times SaO_2 \times CO$	520–570 mL/min/m^2
Oxygen uptake	VO_2	$1.34 \times Hb \times (SaO_2 - SvO_2) \times CO$	110–160 mL/min/m^2
Oxygen–extraction ratio	O_2ER	VO_2/DO_2	20–30%

Checklist to Follow Before PCWP Can Reliably Reflect the LV Filling Pressure

- The tip of the PAC should be in west zone 3 in the lung. The airway pressure fluctuations are minimum in this zone. On the chest X-ray, the tip of the PAC should be below the level of the left atrium within 2 cm of cardiac silhouette.
- Correct pulmonary artery and wedge pressure waveforms: Pulmonary artery pressure upstroke slightly precedes the radial artery pressure upstroke.
- Rule out abnormal waveforms: There should be no air, clots, or motion-related artifacts (distinguished from normal by their shape and timing). If the balloon is overinflated and occludes the lumen orifice or forces the catheter tip against the vessel wall—or if there is distal catheter migration—overwedging may result. Overwedged pressure is devoid of pulsatility and is higher than expected.
- Measure the pressures only at end expiration. This is because end-expiratory pressure is closest to the atmospheric pressure. This is done by freezing the waveform on the monitor and observing the movement of the trace up or down along with the phases of respiration or on a paper printout.
- Wedge pressure will underestimate the left ventricular end-diastolic pressure if the patient has diastolic dysfunction, aortic regurgitation, pulmonary regurgitation, right bundle branch block, or postpneumonectomy.
- Wedge pressure will overestimate the left ventricular end-diastolic pressure if the patient has pulmonary arterial hypertension, pulmonary veno-occlusive disease, tachycardia, mitral stenosis, or mitral regurgitation.
- Always remember that wedge pressure is a reflection of LV end-diastolic pressure, whereas it is the end-diastolic volume that determines preload. The two measurements may not correlate in up to 58% of measurements.

Suggested Reading

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4. Connors AF Jr, Speroff T, Dawson NV et al. The effectiveness of right heart catheterization in the initial care of critically ill patients. SUPPORT Investigators. JAMA. 1996;276(11):889–97.
PAC use was associated with increased mortality and increased utilization of resources. Subgroup analysis did not reveal any patient group or site for which the PAC was associated with improved outcomes. This study started the outcome controversies on PAC use.
5. Swan HJC, Ganz W, Forrester JS, Marcus H, Diamond G, Chonette D. Catheterization of the heart in man with use of a flow-directed balloon-tipped catheter. N Engl J Med. 1970;283:447–51.
The landmark article that completely changed the way people monitored patients in the ICUs. Since its introduction the catheter has hardly undergone change in size or structure. It was at one time the most widely used equipment in the ICU.

Website

1. www.pacep.org
A free online multiorganization effort to provide educational tools for the use of the pulmonary artery catheter in clinical practice

Defibrillation and Cardioversion

94

Rajesh Chawla and Sananta K. Dash

A 70-year-old diabetic, hypertensive, and coronary artery disease male patient was admitted to the hospital with acute myocardial infarction. His pulse was 120/min, and blood pressure was 100/60 mmHg. He was on dopamine and dobutamine infusion. He was being prepared for primary angioplasty. While being shifted to the catheterization laboratory, he collapsed. The cardiac monitor showed ventricular fibrillation (VF).

Electrical shock therapies are capable of terminating arrhythmias due to reentry. Reentry is the predominant mechanism of majorities of arrhythmias in ICUs.

Step 1: Be familiar with the device

1. *Types of Defibrillators*
   A. Manual external defibrillators
      - These defibrillators have electrocardiogram (ECG) readers, which the health care provider uses to diagnose a cardiac rhythm. The health care provider will then decide what charge (in joules) to use, based on proven guidelines (ACLS) and experience, and will deliver the shock through paddles or pads on the patient's chest.
      - As they require detailed medical knowledge, these units are generally only found in hospitals and on some ambulances.

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B. Automated external defibrillators (AEDs)
- AEDs are sophisticated, reliable computerized devices that use voice and visual prompt to guide lay users and health care providers to safely defibrillate the appropriate rhythm.
- They are not designed to deliver synchronized shock (i.e., cardioversion of ventricular tachycardia (VT) with pulse). They will rather recommend a nonsynchronized shock for both monomorphic and polymorphic VTs if the rate and morphology exceed the preset value.
- The AEDs take time (~10–20 s) to diagnose the rhythm. On the other hand, a professional can diagnose and treat the condition far more quickly with a manual unit. This valuable time gap between analysis and application of shock, where the chest compression has to be withheld, is unavoidable for the AEDs.
- These time intervals for analysis, which require stopping of chest compressions, have been shown in a number of studies to have a significant negative effect on shock success. This effect led to the change in the AHA defibrillation guideline (calling for 2 min of cardiopulmonary resuscitation (CPR) after each shock without analyzing the cardiac rhythm), and some recommend that AEDs should not be used when manual defibrillators and trained operators are available.
- There are two types of AEDs: fully automated and semiautomated. Most AEDs are semiautomated. A semiautomated AED automatically diagnoses heart rhythms and determines if a shock is necessary. If a shock is advised, the user must then push a button to administer the shock.
- A fully automated AED automatically diagnoses the heart rhythm and advises the user to stand back while the shock is automatically given. Also, some types of AEDs come with advanced features, such as a manual override or an ECG display.

C. Implantable cardioverter defibrillators *(ICD)*
ICDs analyze the rhythm based on an internal program and shocks appropriately.

2. *Types of Shocks*

A. Monophasic
A monophasic shock delivers current in one polarity and is classified again according to the rate at which the current pulse decreases to 0.

B. Biphasic shocks
- A biphasic shock delivers current that reverses course during the pulse.
- Defibrillation with biphasic waveform improves short-term outcome of terminating VF.
- It is safe and has equivalent or higher efficacy in terminating VF than the monophasic.
- Recommendation is 120–200 J according to manufacturer's recommendation. If not known, then defibrillate at the maximum dose.

Table 94.1 Indication of cardioversion and defibrillation

Type	Indications
Immediate	Hemodynamic instability due to tachyarrhythmia of shockable variety
	Congestive heart failure and angina due to shockable tachyarrhythmia
Elective	Hemodynamically stable
	No significant symptoms

Caution: Patients with digitalis toxicity, electrolyte imbalance (more prone to ventricular fibrillation (VF) and ventricular tachycardia (VT) after shock), chronic atrial fibrillation (AF), and atrial flutter (AFL) of more than 48 h who are not adequately anticoagulated

3. *The Modes (Defibrillation and Cardioversion)*
   A. *Defibrillation*
      Defibrillation is a method of introduction of unsynchronized electrical shock that stuns the heart briefly and terminates all electrical activities including VF and rapid VT, and if the heart is still viable then its pacemakers will eventually resume its normal rhythm, which ultimately results in a perfusing rhythm. It is not synchronized with the R wave in ECG.
   B. *Cardioversion*
      Here, the shock delivery is synchronized with QRS complexes. It prevents shock delivery during the relative refractory portion of the cardiac cycle (i.e., ventricular vulnerable period, between 60 and 80 ms before and 20–30 ms after peak of the T wave) when shock could produce VF.
4. *Electrodes*
   A. *Types*
      - Handheld paddles (pediatric and adult)
      - Self-adhesive pads (pediatric and adult)
   B. *Size*
      - 8–12 cm for the adult and child (≥8 years)

Step 2: Assess the need for cardioversion and defibrillation—indications and contraindications (Tables 94.1, 94.2 and 94.3)

Step 3.1: Method for cardioversion

A. Patient preparation for elective cardioversion
   - It should be done in hospital areas equipped with cardiac monitoring, airway management, and cardiopulmonary resuscitation.
   - Ensure nil by mouth (NBM) status.
   - Patient counseling is required in detail about the procedure.
   - Obtain valid informed consent from the patient or legal surrogate.
   - Confirm adequacy of anticoagulation in chronic AF.
   - If digoxin is given, measure the serum level.
   - Consider starting antiarrhythmics 24–48 h preprocedure.
   - Pre- and postprocedure ECG.

Table 94.2 Tachyarrhythmias responsive to electrical therapy

Responsive to cardioversion		Responsive to defibrillation
Supraventricular	Ventricular	Pulseless VT
		VF
Atrial fibrillation	Monomorphic VT with pulse	Unstable polymorphic VT with or without pulse
Atrial flutter		
Sinoatrial nodal reentrant tachycardia		
Atrioventricular nodal reentrant tachycardia		
Atrioventricular reciprocating tachycardia		

Table 94.3 Tachyarrhythmias unresponsive to electrical therapy

Unresponsive to cardioversion/defibrillation	
Supraventricular	Ventricular
Sinus tachycardia	Idiopathic monomorphic VT
Focal atrial tachycardia	
Junctional tachycardia	Accelerated idioventricular rhythm

B. Preprocedural sedation protocol
- If the patient requires oxygen or is currently receiving oxygen, the delivery of oxygen should be directed away from the chest.
- Continuous monitoring—ECG, SPO_2, and noninvasive blood pressure (NIBP).
- Give sedation and analgesia.
  - Agents—propofol, midazolam, and etomidate
  - Propofol is the best option for its early awakening time and better safety profile. Short-acting agents are preferred.
  - Opioid analgesics, such as fentanyl, are used for analgesia.
- Conscious sedation
  - Goal—maintain consciousness but in a somnolent state. It can be done by a trained physician without anesthesiologist's supervision. Midazolam is the preferred agent here.

C. Turn the defibrillator on (monophasic or biphasic shock)
It simultaneously switches the monitor on.

D. Suggested electrode position
1. Anterolateral (most common): An anterior paddle is placed in right infraclavicular area, and the lateral paddle is placed lateral to the left breast in longitudinal alignment.
2. Anteroposterior: The anterior paddle is same as before, and the posterior paddle is on the left side of the spine at the level of lower end of the scapula.
   - Other two positions include anterior-left infrascapular and anterior-right infrascapular. Anteroposterior placement is found to be more successful in cardioversion of AF with monophasic shock.
   - Apply jelly (water-based conducting jelly). Place the negative electrode closer to the heart with both the electrodes adequately separated.

Table 94.4 Specific energy levels

Rhythm	Mode	Monophasic (initial and consecutive shocks)	Biphasic shock
VF, pulseless VT	Defibrillation	360	120–200
Stable, monomorphic VT with pulse	Cardioversion	100, 200, 300, 360	70, 120, 150, and 170[a]
AF	Cardioversion	100–200, 300, 360	100–120
Atrial flutter, Supravetricular tachycardia (SVT)	Cardioversion	50, 100, 200, 300, 360 (MDS)	70, 120, 150, and 170[a]

[a]The biphasic waveform using the lower energy level is acceptable if documented to be clinically equivalent or superior to reports of monophasic shock success. Initial biphasic dose of 100–200 J with escalation depending on the need is recommended (evidence extrapolated from cardioversion of atrial fibrillation). For specific recommendation consultation from the device, manufacturer is advised

- The conducting jelly should be restricted to the pad area and should not be spread all over the chest.

E. Synchronization (for synchronized cardioversion)
- The device should be in the synchronized mode as most AEDs have a default unsynchronized mode.
- For each subsequent defibrillation, one needs to reset to synchronized mode. Confirm synchronization by looking at markers on the R wave. It may be necessary to adjust the gain of the monitor to remark the R wave correctly.

F. Announce "charging-stand clear"

G. Charge
Press the charge button (present on the paddle as well as on the monitor) to select the level of charge (Table 94.4). Hear the audible sound/alarm when charging is completed.

H. Clearing
Say "I am going to shock on three; one, I am clear; two, you are clear; three, everybody is clear." Check and look around after each step and confirm safety.

I. Shock
Check to see the synchronized mode prior to giving a synchronized shock.

Step 3.2: Method for defibrillation

A. Analyze the rhythm
A bedside cardiac monitor or ECG display of the defibrillator is needed, if already attached.

B. Sedation protocol
As most often patients with pulseless VT and VF present in an emergent condition with unstable hemodynamics and impending cardiac arrest, sedation in such cases is not required.

C. Turn the defibrillator on
In most defibrillators, the default mode is the asynchronized mode.

D. Same as step D for cardioversion

Table 94.5 Complications and their prevention/treatment

Complications	Prevention/treatment
Thermal burns	The lowest accepted energy level
	Biphasic shock requires less energy
Thromboembolism	More common with AF (incidence in 1–7% patients who are not receiving anticoagulation)
	Ensure adequate anticoagulation
	Exclude left atrial clots with transesophageal echocardiography
Arrhythmia	For expected sinus bradycardia and sinus arrest, prophylactic placement of the pacemaker (transvenous/transcutaneous) in patients with AF with slow ventricular rate
	VT and VF—in patients with digitalis toxicity or hypokalemia, better to avoid cardioversion; if necessary to perform, then be prepared for a more refractory ventricular arrhythmia
Myocardial damage	Clinically insignificant but recommended to give two shocks at least 1 min apart
Loss of airway	Mostly sedation related
	Complications such as aspiration can be reduced by ensuring nil by mouth (in elective cases), supervised cardioversion preferable
Pulmonary edema	Supportive measures and gradual improvement expected
Fire hazard	Reported when shock is given in an oxygen-rich environment
	Avoid direct blowing of oxygen across the chest in the oxygen-rich environment

E. No need for synchronization
F. Same as cardioversion up to step H
G. Shock (asynchronized)
H. Post-shock
Resume CPR for five cycles, check rhythm, and proceed according to ACLS guidelines.

Step 4: Manage complications (Table 94.5)

Step 5: Special circumstances

A. *Anticoagulation for reverting atrial fibrillation and flutter*
- Anticoagulation is indicated in atrial fibrillation and flutter lasting more than 48–72 h.
- Recommendation is 3–4 weeks of anticoagulation prior to attempt cardioversion. It should be continued for at least 4 weeks post-cardioversion.
- This approach has an inherent risk of increased bleeding. So, in patients at the higher risk of bleeding, transesophageal echocardiography can be performed to exclude intracardiac thrombus and proceed with cardioversion without adequate prior anticoagulation. In any case, at least 4 weeks of anticoagulation is mandatory in post-cardioversion period.

B. *External defibrillation with the ICD/pacemaker in situ*
   - If the ICD is currently delivering shock (as evidenced by external muscle contraction similar to external defibrillation), allow 30–60 s for the ICD to complete the treatment cycle.
   - Place the pads at least 8 cm away from the ICD/pacemaker, but placing the paddle should not be delayed in defibrillation.
   - It is not desirable to place the pads or paddles directly over the device.

C. *Pregnancy*
   Cardioversion and defibrillation have been performed in all trimesters of pregnancy. It has been found to have no obvious adverse fetal effects or premature labor. Fetal heart rhythm monitoring is recommended.

D. *Pediatric age group*
   - The lowest energy dose for effective defibrillation is not known. The lower and upper limits to safe defibrillation are not known for infants and children.
   - Biphasic shocks appear to be at least as effective as monophasic shocks and are less harmful than monophasic shocks.
   - It is recommended to use an initial dose of 2–4 J/kg, and for refractory VF, increase the dose to 4 J/kg. Subsequent energy levels should be at least 4 J/kg, and higher energy levels may be considered, but not to exceed 10 J/kg or the adult maximum dose.
   - For infants (<1 year of age), a manual defibrillator is preferred. If a manual defibrillator is not available, an AED with pediatric attenuation is desirable. If neither is available, an AED without a dose attenuator may be used.

E. *Drowning*
   - Removal of the patient from water and thorough wiping of the chest and the patient is prerequisite before attempting electrical therapy.

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Temporary Pacemaker Insertion

95

Rajesh Chawla and Vipul Roy

A 70-year-old male patient—a case of coronary artery disease on regular treatment—was admitted to the hospital with chief complaints of syncope and giddiness. His heart rate was 38/min and blood pressure was 90/60 mmHg. ECG showed complete heart block. Insertion of temporary pacemaker was planned.

Pacemakers provide electrical stimuli which cause cardiac contraction when the intrinsic myocardial electrical activity is slow or absent. Temporary pacemakers use an external pulse generator with leads placed either transcutaneously or transvenously. During emergency resuscitation, transcutaneous leads are the easiest and most convenient method of choice. Transcutaneous pacing requires mild sedation. For transvenous pacing, a semirigid catheter is placed through central access. ECG monitoring is used for tracking catheter positioning.

Step 1: Assess the need for the temporary pacemaker (Tables 95.1 and 95.2)

Step 2: Be familiar with the device (Table 95.3)

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Table 95.1 Indications of temporary pacing in the absence of acute myocardial infarction

1. Symptomatic bradycardia refractory to medical treatment
(a) Sinus node dysfunction
(b) Second- or third-degree atrioventricular (AV) block
2. Third-degree AV block with wide QRS escape or ventricular rate <40 bpm
3. Prophylactic

Table 95.2 Indications of temporary pacing in acute myocardial infarction

Class I
1. Asystole
2. Symptomatic bradycardia (includes sinus bradycardia with hypotension and type I second-degree AV block with hypotension not responsive to atropine)
3. Bilateral bundle-branch block [BBB; alternating BBB or right BBB (RBBB) with alternating left anterior fascicular block (LAFB)/left posterior fascicular block (LPFB)] (any age)
4. New bundle-branch block with Mobitz II second-degree AV block
5. RBBB plus fascicular block with Mobitz II second-degree AV block
Class IIa
1. Narrow QRS plus Mobitz II second-degree AV block
2. Old or new fascicular block with Mobitz II second-degree AV block and anterior myocardial infarction
3. Old bundle-branch block and Mobitz II second-degree AV block
4. New bundle-branch block plus first-degree AV block
5. New bundle-branch block plus Mobitz I second-degree AV block
6. RBBB plus LAFB or LPFB (new or indeterminate) with first-degree AV block
7. RBBB plus LAFB or LPFB (new or indeterminate) with Mobitz I second-degree AV block

Step 3: Transvenous pacemaker—procedure

A. *Obtain a central venous access*
   1. The preferred route: Internal jugular (most common and most preferred), subclavian, and femoral veins, preferably right-sided veins, should be used when possible. Local anesthesia is always indicated.
   2. Access blind or ultrasound-guided intracardiac placement of the pacing wire.

B. Intracardiac placement of the pacing wire
   1. This should only be inserted by experienced practitioners.
   2. Preparation:
      (a) A defibrillator and other resuscitation equipments should be immediately accessible.
      (b) Strict aseptic technique.
      (c) ECG monitoring.
   3. Cannulate the suitable vein (internal jugular, subclavian, or femoral veins preferably on the right side) using Seldinger's technique of guidewire and dilators to place a sheath of the correct size.
   4. Bend the tip of the electrode to give a 20–30° curve for the correct positioning in the heart.

Table 95.3 Temporary pacemaker method and device details

Device	Parts	Current	Benefits	Drawback	Uses
Transcutaneous external pacemakers	1. External patch electrodes	Higher current (up to 200 mA) and longer pulse duration (20–40 ms)	1. Less time-consuming	Require sedation	1. Cardiac arrest
	2. Pulse generator (usually a defibrillator)		2. Risks of central venous access avoided	Pacing limited to ventricle and minimal capacity for atrial pacing	2. Symptomatic bradyarrhythmia
					3. Overdrive pacing
					4. Prophylactically for arrhythmia in myocardial infarction
					5. Unavailability or contraindication to transvenous pacing (prehospital setting during thrombolytic therapy for acute myocardial infarction)
Transvenous pacing	1. Transvenous pacing catheters (4–7 F)	Threshold for vent.	Different modes (ventricular, arterial, sequential)	Inherent risk with central venous line	Indications as per Table 95.1
	2. Pulse generator	Pacing (<1 mA), atrial pacing (<2 mA)			
		Output three to four times of threshold			

Transcutaneous needle temporary pacemaker should not be used in current technology as it has serious complications

5. Advance the electrode under ultrasound or fluoroscopic guidance until it lies vertically in the right atrium with its tip pointing toward the free wall on the right side.
6. Rotate the wire between the index finger and the thumb so that it points toward the patient's left side; advance the wire steadily through the tricuspid valve and along the floor of the right ventricle to the apex.
7. If blind technique is used, the V1 lead is connected to the distal port (cathode). Endocardial contact is indicated by prominent ST-segment elevation. Placement is facilitated by balloon inflation and floatation in the superior vena cava. Position is confirmed by successful capturing. For placement in the right ventricular apex, the balloon is deflated and the catheter is advanced a few centimeters. This technique is practiced in the emergency department where fluoroscopy and ultrasonography is unavailable instantly.
8. The anteroposterior and lateral X-ray after placement is always indicated.
9. If AV sequential pacing is desired, the atrial J-shaped pacing catheter should be advanced into the right atrium and rotated anteromedially to achieve a stable position in the right atrial appendage; positioning the atrial catheter usually requires fluoroscopy.

C. *Setting the Pacemaker*

1. Keep the pacemaker box in off position and attach the leads to the ventricular output position.
2. Turn the pacemaker into asynchronous mode and set the ventricular rate 10–20 beats/min higher than the patient's intrinsic rate.
3. Set the threshold current for ventricular pacing at 5–0 mA and switch the pacemaker on. See for ventricular pacing as evidenced by a wide QRS complex, with ST-segment depression and T-wave inversion, following each pacemaker depolarization (spike). (Right ventricular apex pacing presents as a pattern of left bundle-branch block on the surface ECG.)
4. Output current is slowly reduced and the threshold current (the lowest current at which consistent ventricular capture occurs) is determined. Recommended pacing threshold of less than 0.5–1.0 mA should be achieved.
5. If the threshold is high, then consider relative endocardial refractoriness due to fibrosis (rare) or a malposition of the electrode (more common). In any case, the tip of the pacing electrode should be repositioned in the region of the ventricular apex until satisfactory ventricular capture at a current of less than 1.0 mA is consistently maintained.
   - The ventricular output is set to exceed the threshold current at least threefold. The pacemaker is now in VOO mode.
   - After insertion of the lead and before stitching the lead, withdraw the sheath as it reduces infection rate.
   - For blind pacing without the balloon-tipped lead, use left subclavian access.

Step 4: Know the modes

Modes	Paced (A, atrium; V, ventricle; D, dual)	Sensed (A, atrium; V, ventricle; D, dual)	Response (I, inhibit; T, trigger)	Programmability (R, programmable; O, nonprogrammable; M, multiprogrammable)	Multisite pacing (A, multisite pacing; O, nonmultisite pacing)
VVI	Ventricle	Ventricle	A sensed event in the ventricle inhibits the pacemaker from pacing or producing any output	None	None
AAI	Atrium	Atrium	The sensing of an event (e.g., sensing atrial activity within 1 s) inhibits the pacemaker from pacing	None	None
DDD	Both	Both	Response can be both triggering and inhibitory	None	None

Set the mode according to the need and device

Step 5: Know the complication and management

Complications

1. *Complications as with any route*—pericardial friction rub, arrhythmia, right ventricular perforation, cardiac tamponade, infection, arterial injury, diaphragmatic stimulation, phlebitis, and pneumothorax
2. *Complications of internal jugular venous and subclavian access*—pneumothorax, carotid arterial injury, venous thrombosis, and pulmonary embolism
3. *Complication of antecubital venous access*—dislodgement of the pacing electrode from a stable ventricular or atrial position (movement of the arm) and infection (more with this approach than others)
4. *Complication of femoral access*—deep venous thrombosis and infection

Management

1. Optimum knowledge about the anatomy and the procedure
2. Ability to evaluate the correct placement and the desired rhythm
3. Strict intra- and postprocedural asepsis.

Step 6: Troubleshooting

1. *Satisfactory pacing not achieved*: Withdraw the wire into the right atrium and repeat the attempt to cross the tricuspid valve.
2. *Difficulty in positioning the wire at the apex of the right ventricle*: Pass the tip of the wire into the right ventricular outflow tract and withdraw gently while rotating

between the index finger and the thumb. When the tip is at a downward angle, advance toward the apex.
3. *No spikes seen and no output*: Suspect failure of the battery or generator or a loose connection.
4. *Spikes seen but no capture*:
Suspect a loose connection but may be due to exit block causing a high threshold. Check the position of the pacing wire and consider repositioning.

Step 7: How to monitor

Assess rhythm for appropriate pacemaker function:
1. *Capture*: Is there a QRS complex for every ventricular pacing?
2. *Rate*: Is the rate at or above the pacemaker rate if in the demand mode?
3. *Sensing*: Does the sensitivity light indicate that every QRS complex is sensed?

Step 8: Postprocedural investigations and precautions

1. A chest X-ray is needed to confirm a satisfactory position of the wire and to exclude a pneumothorax.
2. Ensure the pacing wire is secured.
3. Check and document all connections, battery, and control settings every 4 h and document.
4. Sterile precaution is required as in handling a central line.
5. Keep the pulse generator dry and the controls protected from mishandling.
6. Protect the patient from electromicroshock and electromagnetic interference by covering the exposed wires and the pulse generator, wearing gloves when handling exposed wires; avoid any patient contact with electrical apparatus.

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Percutaneous Tracheostomy

96

Rajesh Chawla and Munish Chauhan

A 50-year-old male patient, a known case of chronic obstructive pulmonary disease with ischemic cardiomyopathy and renal failure, was admitted to hospital with acute breathlessness. He was drowsy and unable to maintain oxygenation on noninvasive ventilation. He was put on invasive ventilation and he got better. Spontaneous breathing trial was tried a number of times, but he could not be weaned off the ventilator for 10 days. Percutaneous tracheostomy (PCT) was planned.

PCT is a bedside procedure performed usually in an ICU setting. This uses Seldinger technique and is associated with lesser postoperative complications.

Step 1: Assess the need for tracheostomy and advantage of PCT

A. *Indications*

- Securing the airway
  - Temporary—to aid weaning after long-term mechanical ventilation
  - Permanent—airway protection in neurological patients
- Tracheal toileting and airway protection
  - In the patient with excess or thick secretions who is not able to expectorate
  - Generalized weakness—neuromuscular disease or central cause
  - Altered mentation—unable to maintain airways

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- Relief of nonemergent upper airway obstruction
  - Once initial airway stabilization has been done via translaryngeal intubation/emergency cricothyroidotomy

B. *Advantages of PCT over surgical tracheostomy*
- Blunt dilatation causes less tissue trauma and devitalization than sharp dissection.
- It may lead to lower rates of hemorrhage, stomatitis, and cosmetic deformity.
- The tracheostomy tube is fitted tightly against the stoma.
- Interval between decision and actual procedure is shorter.
- It can be done at the bedside in the ICU, avoiding a potentially hazardous transfer of critically ill patients to the operating room.
- Savings in cost of operating room personnel and equipment can be achieved.

Step 2: Select patient for PCT
- The patient should be hemodynamically stable as much as possible.
- FiO_2 should be below 0.6
- Positive end-expiratory pressure should be less than 10 cm H_2O.
- History of uncomplicated translaryngeal intubation is obtained.
- Cricoid cartilage is palpable at least 3 cm above the sternal angle during appropriate neck extension.

Step 3: Check for the contraindications

There are no absolute contraindications. Suggested contraindications are not supported by adequate data but are decided on merit depending on the operator experience and protocols of the center involved (Table 96.1).

Table 96.1 Contraindications to PCT

Inability to identify anatomical landmarks	Surgical skin site infection
Previous major neck surgery completely obscuring the anatomy	Midline neck mass
Emergency airway control	High positive end-expiratory pressure (>10–20 cm H_2O)
Repeat tracheostomy	Severe coagulopathy
Age less than 15 years	Tracheomalacia
Cervical fixation/injury/fracture	Obese/thick neck

Step 4: Decide timing
- The decision about tracheostomy requires anticipation of the duration of expected mechanical ventilation and the expected benefits and risks of the procedure.
- Time of PCT could be 7–14 days of intubation or less than 7 days for anticipated prolonged ventilation.

Step 5: Obtain informed consent
- Discuss the prognosis of the patient and the need for the procedure.
- Explain the advantages and disadvantages of the procedure and the available options in detail. Communicate with the patients or their surrogates.
- Explain the detailed procedure, the benefits, the risks, and the alternatives in the language they understand.
- Document the consent and get it signed.
- In case of emergency, when the patient is unconscious and the surrogates are not available, document the situation clearly and perform the procedure.

Step 6: Form your team
- The operating physician.
- One physician, managing the upper airway and bronchoscope, manipulates the tube to allow PCT.
- The paramedical staff/technician who assists with the bronchoscope and handling of the endotracheal tube.
- Another paramedical staff monitoring the vitals and administering medication.

Step 7: Prepare for the procedure
- A PCT set as per the type decided by the physician
- A bronchoscope and its attachments
- Continuous monitoring of ECG, blood pressure, and oximetry
- Functioning intravenous access
- A sterile setup with enough sterile linen and instruments
- A crash cart with a laryngoscope and endotracheal tubes and emergency drugs
- Suction equipment
- Medications
  - 1% Xylocaine with epinephrine
  - Sedating and paralyzing agents

Step 8: Identify anatomy (Fig. 96.1)
- Tracheostomy is carried out at least one to two rings beyond the cricoid.
- The tracheostomy tube is entered between the second and third cartilage rings or between the third and fourth cartilage rings.
- In a too high tracheostomy (close to cricoid), there is a risk of a subglottic stenosis.
- In a too low tracheotomy, there is a risk of bleeding from the brachiocephalic trunk.

Step 9: Perform percutaneous tracheostomy
- *Ciaglia method (Blue Rhino PCT kit—Cook Critical Care Inc, Bloomington, IN)* (Figs. 96.2, 96.3, 96.4, 96.5, 96.6, 96.7, and 96.8)
  1. Continuously monitor vital signs, pulse oximetry, and complete ventilatory parameters.
  2. Ventilate with 100% oxygen during the procedure.

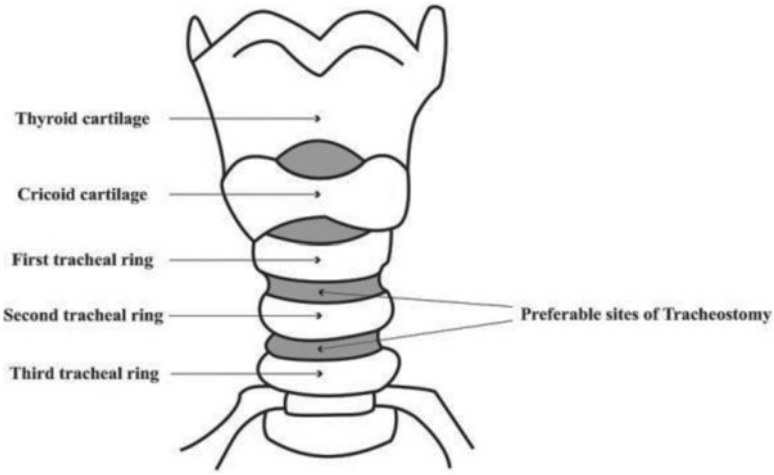
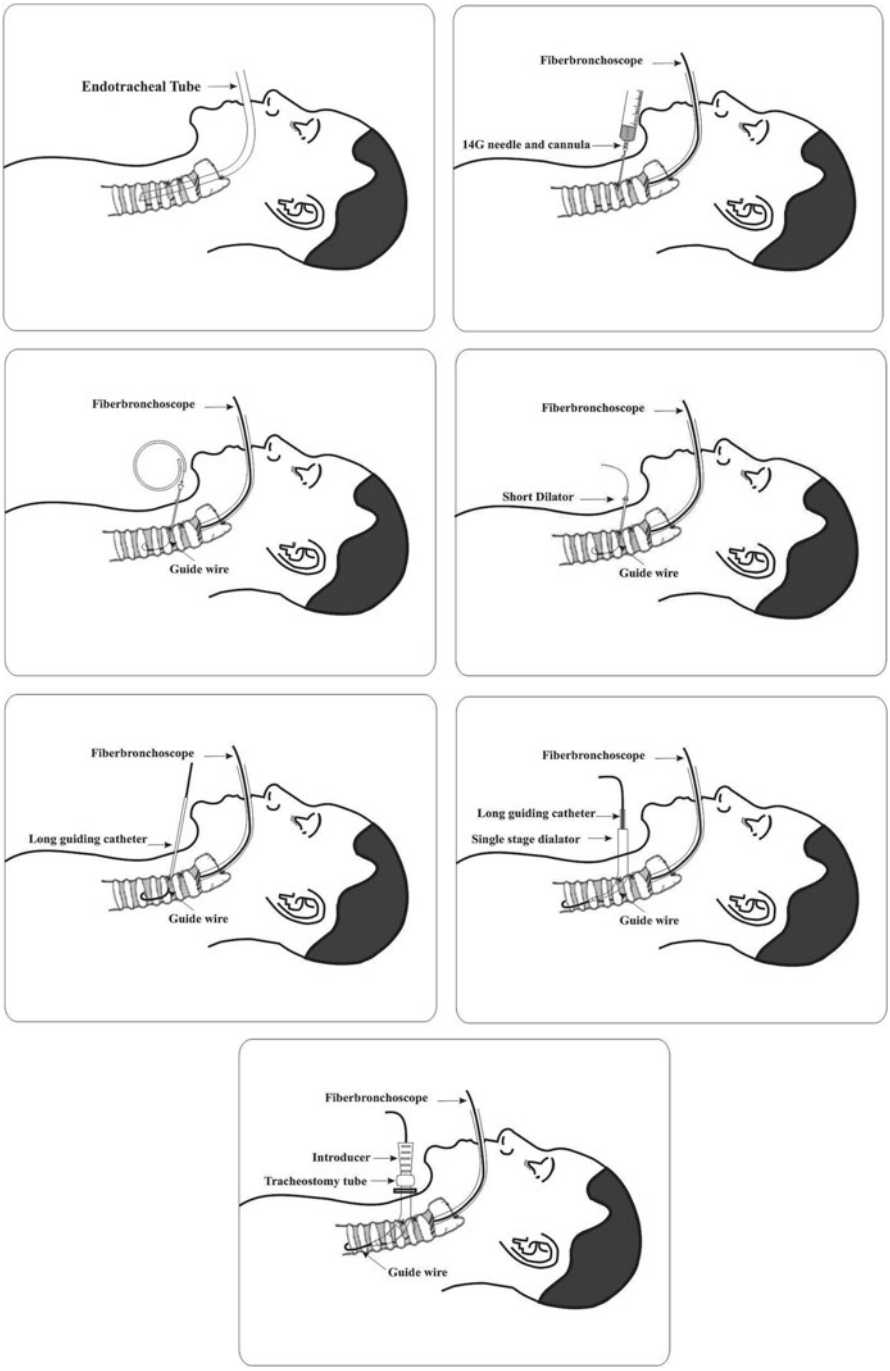


Fig. 96.1 Tracheal anatomy

3. Counsel and comfort the patient if he/she is conscious.
4. Sedate and paralyze the patient before positioning.
5. Extend the neck to open the tracheal interspaces, carefully supporting the vertex using a sand bag beneath the shoulders and the head ring.
6. Prepare the surgical field with alcohol-containing solution and drape it.
7. Verify the anatomy and identify the neck structures and landmarks. A pre-procedure ultrasound may be done if anatomy is not clear (e.g., morbid obesity).
8. The local anesthetic with epinephrine is infiltrated into the surgical site.
9. Check all parts of the tracheostomy set. Check the tracheostomy balloon by inflating and collapsing it.
10. Make a transverse skin incision approximately 2 cm over the first and second tracheal interspace, approximately two fingers' breadth above the sternal notch.
11. Dissect the wound bluntly with a hemostat through the subcutaneous fascia.
12. Withdraw the endotracheal tube into a position above the first tracheal interspace under bronchoscopic guidance.
13. Insert a 14-gauge cannula over the needle through the skin incision between either the first and second or the second and third tracheal rings under bronchoscopic guidance, aspirating for air (Fig. 96.3).
14. Withdraw the needle leaving the cannula in place.
15. Advance a J-tipped guidewire through the cannula toward the carina and withdraw the cannula (Fig. 96.4).
16. Dilate the opening using a small dilator (Fig. 96.5).
17. Insert a stiffer guide cannula over the guidewire after withdrawing the cannula (Fig. 96.6).



Figs. 96.2, 96.3, 96.4, 96.5, 96.6, 96.7, and 96.8 Ciaglia method

18. Use a single, sharply tapered dilator with a hydrophilic coating and dipped in water-based jelly, for complete dilatation in one step (Fig. 96.7).
19. Withdraw the dilator leaving the guidewire and the stiff white guide cannula assembly in place.
20. Once the tracheostoma has been dilated to the appropriate size, a tracheostomy tube is introduced into the trachea over the same guidewire using introducer dilators as an obturator (Fig. 96.8).
21. The guidewire assembly is removed leaving the tracheostomy tube in place.
22. Position is confirmed by bronchoscopic visualization.
23. The tube is sutured to the skin and also fixed with the provided thread around the neck.
    - **Griggs guidewire dilating forceps**
      - Steps 1–15 as above.
      - The cannula is removed leaving the guidewire in place.
      - The Griggs guidewire dilating forceps are threaded over the guidewire into the soft tissue.
      - Open the forceps "dilating" the soft tissue and advance the forceps into the trachea.
      - The trachea is dilated to an aperture sufficient enough to accommodate the tracheotomy tube.
      - An obturator is used to insert the tube over the guidewire.
      - The rest of the steps of fixation of the tube are same as above (Fig. 96.3).
    - **PercuTwist technique**. (It contains a J-tipped guidewire, a scalpel, a large-bore introducer needle, the hydrophilically coated PercuTwist dilator, a specially designed 9.0-mm internal diameter PercuTwist tracheotomy cannula, and an insertion dilator.)
      - Steps 1–15 as above.
      - The PercuTwist single dilator is moistened to activate the hydrophilic coating.
      - Advance it over the guidewire into the soft tissue using a clockwise rotation.
      - Further rotation of the device engages the anterior tracheal wall and enlarges the aperture.
      - Once dilated adequately, the device is removed and replaced with the 9.0-mm tracheotomy tube fitted with the insertion dilator.

Step 10: Postoperative care of the tracheostomy tube

- Wound and dressing care
  - Daily examination of the stoma is needed to identify infections or excoriations of the skin.
  - Keep the wound clean and free of blood and secretions, especially in the immediate posttracheostomy period.

  - Dressing changes should be performed at least twice a day and when the dressings are soiled.
  - When changing dressings and tapes, special care is needed to avoid accidental dislodgement of the tracheostomy tube.
  - The inner cannula if used is changed daily or more frequently if necessary.
- Humidification
  - Humidification of inspired gases prevents obstruction of the tube by inspissated secretions and maintains mucociliary clearance and cough reflex.
  - Heat and moisture exchangers are preferred over heated humidifiers.
- Suctioning
  - Airways should be cleared of excess secretions to decrease the risk of lung infection and airway plugging.
  - Suctioning is frequently required in patients with poor or ineffective cough.
  - Suctioning should remove the maximal amount of secretions and cause the least amount of airway trauma. Thus, practice slow suctioning.
    1. Routine suctioning, however, is not recommended.
    2. Upper airway suctioning should also be done periodically to remove oral secretions and to minimize stasis of pooled secretions above the tracheotomy cuff with subsequent potential aspiration into the lower airways.
- Change tracheostomy tube
  - In case of a functional problem with the tube, such as an air leak.
  - If the lumen is narrowed due to the buildup of dried secretions.
  - Switching to a new type of the tube.
  - May downsize the tube prior to decannulation.
  - Do not change the outer cannula, unless the cuff is damaged, in the initial 5–7 days as the tract is not stable.
- Tube cuff pressure
  - Tracheotomy tube cuffs require monitoring to maintain pressures in a range of 20–25 mmHg.
  - Cuff pressures should be monitored with calibrated devices.
  - Record at least once every nursing shift and after manipulation of the tracheotomy tubes.
  - Maintain the tube in a central position, avoiding angling and contact between tracheal mucosa and the tube to avoid damage by the distal end.
  - Avoid traction as well as unnecessary movement of the tube.
- Nutrition
  - Feeding may become complicated because of tube interference with normal swallowing and airway control.
  - It decreases laryngeal elevation during swallowing and an inflated cuff may compress the esophagus. So it may deflate a little.
  - Keep the head end elevated to 45° during periods of tube feeding.
  - Before attempting oral feedings, several objective criteria must be met.
    - The patient must be consistently alert and able to follow complex commands.

- Adequate cough and swallowing reflexes.
- Adequate oral motor strength.
- A significant respiratory reserve.
- Assess swallowing function.
- Oral feeding is done under supervision of a caregiver and carefully assessed for aspiration or regurgitation.

Step 11: Manage complications

- Early complications (until 7 days)
  1. Tube displacement
     - Management—endotracheal intubation to establish airway. Replace the tracheostomy tube under less urgent conditions, always under fiber-optic guidance as there is a danger of entering a false tract. If it fails, intubate orally.
     - Prevention— proper placement of the stoma, avoid excessive neck hyperextension and/or tracheal traction, apply sufficiently tight tracheostomy tube retention tapes, and suture tracheostomy tube flange to the skin.
     - Displacements after 7 days are managed by simply replacing the tube as the tract is well formed.
  2. Tube obstruction
     - By mucus, blood clots, displacement into surrounding soft tissues, or abutment of the tube's open tip against the tracheal wall.
     - Reposition or suction thoroughly; deflate cuff as a temporizing measure.
     - If it fails, replace the tube immediately or intubate orally.
  3. Pneumothorax/pneumomediastinum
     - Pleura can be damaged during tracheostomy.
     - The incidence of pneumothorax after tracheostomy ranges from 0% to 5%.
     - Many surgeons routinely obtain a postoperative chest radiograph though optional.
     - Immediate tube thoracostomy.
  4. Subcutaneous emphysema
     - Positive-pressure ventilation or coughing against a tightly sutured or packed wound causes this.
     - It can be prevented by not suturing the wound around the tube.
     - It resolves spontaneously within a few days.
     - A chest radiograph should be done to rule out a pneumothorax.
  5. Hemorrhage
     - Usually, minor postoperative venous ooze is the most common complication.
     - Elevate the head of the bed, pack the wound, and/or use homeostatic materials.
     - Major bleeding can occur in up to 5% of tracheotomies.
       - Hemorrhage from the isthmus of the thyroid gland
       - Injury to the transverse jugular vein
       - May require an exploration

6. Stomal infections
   - Good stoma care
   - Early use of antibiotics but do not use prophylactic antibiotics
7. Others
   - Arrhythmia
   - Hypotension
   - Hypoxia/hypercapnia
   - Loss of airway control
   - Bacteremia
   - Esophageal injury
   - Cardiorespiratory arrest
   - Tracheolaryngeal injury

- Late complications (>7 days)
  1. Tracheoinnominate artery fistula (<0.7% cases)
     - Occurs due to erosion through the trachea into the artery due to excessive cuff pressure or by angulation of the tube tip against the anterior trachea
     - Risk increased by the following:
       – Low placement of tracheotomy
       – High-pressure cuffs
       – Excessive head or tracheostomy tube movement
       – Malnourishment
     - Management
       – Evaluate even minor bleeds
       – Hyperinflation of the cuff; lower neck incision with blind digital compression on the artery may be attempted in a resuscitative effort
       – Operative intervention
  2. Dysphagia and aspiration
     - Due to causes discussed under "nutrition"
  3. Tracheal stenosis
     - Approximately 1–2% cases
     - Caused by
       – Ischemia
       – Devascularization
       – Chemical erosion
       – Infection
     - Due to high-pressure cuffs
     - Forced angulation of a stiff tube
     - Hyperinflation of the cuff which results in tracheal damage
     - Site of stenosis may occur at the:
       – Stoma
       – Cuff
       – Tip of the tracheotomy tube
  4. Tracheoesophageal fistula
     - Less than 1% of patients
     - Mostly iatrogenic during procedure

- Erosion by the tracheotomy cuff
- Tube angulation with pressure against the posterior tracheal wall
- More common with a nasogastric tube in place as well
- Suspect if:
  - Cuff leaks
  - Abdominal distention
  - Recurrent aspiration pneumonia
  - Reflux of gastric fluids through the tracheostomy site
- Diagnosed by endoscopy or contrast studies
- Requires surgery or esophageal and tracheal stent

5. Granuloma formation
   - A foreign body reaction to the tracheotomy tube or part.
   - Treated with the YAG laser.
   - Granulomas at the lower end of the tracheotomy tube require bronchoscopic removal providing temporary relief.
6. Persistent tracheocutaneous stoma
   - Can occur when tube has been left in position for a prolonged period.
   - Surgical closure is required.
7. Tracheomalacia
   - Weakening of the tracheal wall
     - Ischemic injury to the trachea
     - Followed by chondritis
     - Then destruction and necrosis of the tracheal cartilage
   - Collapse of the affected portion of the trachea with expiration
     - Airflow limitation
     - Air trapping
     - Retention of airway secretions
   - Cause of weaning failure from mechanical ventilation.
   - A short-term therapeutic approach to tracheomalacia is to place a longer tracheostomy tube to bypass the area of malacia.
   - Long-term treatment options include stenting, tracheal resection, or tracheoplasty.

Step 12: Decannulation

1. Criteria
   - Stable arterial blood gases
   - Absence of distress
   - Hemodynamic stability
   - Absence of fever or active infection
   - $PaCO_2 < 60$ mmHg
   - Absence of delirium or psychiatric disorder
   - Normal endoscopic examination or revealing stenotic lesion occupying less than 30% of the airway
   - Adequate swallowing
   - Able to expectorate

2. Procedure
   - The deflated-cuff tracheotomy occlusion procedure
     – Occlude the opening of the tube with the cuff deflated by a gloved finger observing the patient for objective signs of respiratory distress.
     – In case of problems, promptly return the patient to breathing through the tracheotomy tube and perform a fiberendoscopic examination to check for upper airway obstruction.
     – If no lesions are present, consider whether the tube is not too large and try again after changing the tube.

     The tube can be removed, and the opening is covered with sterile dressings. The wound spontaneously heals in 10 days in most cases.
   - Use tracheotomy button or speech valve in patients with prolonged tracheotomy.

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Thoracentesis

97

Rajesh Chawla and Ashish Jain

A 65-year-old diabetic male patient was admitted to the hospital with severe community-acquired pneumonia and respiratory failure. He was started on antibiotics and other supportive medication. On the second day of admission, his breathlessness increased and he became hypoxic despite oxygen therapy. His chest X-ray showed blunting of the right costophrenic angle. USG chest showed presence of 400 mL of pleural fluid on the right side.

Thoracentesis is the aspiration of fluid or air from pleural space. This can be done with or without ultrasound guidance; however, ultrasound guidance is preferred in critically ill patient. Bedside ultrasonography can be used before the procedure to determine the presence and size of pleural effusion, to assess for loculations, and to guide needle placement.

Step 1: Assess the need of thoracentesis

Diagnostic

- Any undiagnosed pleural effusion of any amount

Therapeutic

- Massive pleural effusion and the patient in respiratory distress
- Suspected hemothorax

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- Suspected parapneumonic infection and empyema
- Small unresolved pneumothorax

Step 2: Rule out contraindications
- No absolute contraindications
- Relative contraindications include the following:
  - Uncorrected bleeding diathesis
  - Chest wall cellulitis at the site of puncture
  - Lack of expertise

Step 3: Arrange all equipments
- A thoracentesis device (This typically consists of an 8F catheter over an 18-gauge, 7.5-in. (19-cm) needle with a three-way stopcock and, ideally, a self-sealing valve.)
- A self-assembled device, if the thoracentesis device is unavailable (It includes using an 18-gauge needle or 12- to 14-gauge intravenous cannula connected to a 50-mL syringe through stopcock.)
- Injection needles—18, 20, 22, and 25 gauge
- Syringes—5, 10, and 50 mL
- A tubing set
- Antiseptic (preferably, 2% chlorhexidine solution)
- Lidocaine 1% or 2% solution
- The specimen cap for the 60-mL syringe
- Heparin 1,000 IU
- Specimen collecting vials or vacutainers
- A drainage bag or vacuum bottle
- Drape (24 in.×30 in.)
- Sterile towels
- Adhesive dressing (7.6 cm×2.5 cm)
- Gauze pads (4 in.×4 in.)

Step 4: Place the patient in proper position
- Ensure proper written consent of the patient or surrrogate.
- Collect equipment, and preprocedure diagnostic laboratory studies, as necessary.
- Alert and cooperative patients are most comfortable in a seated position leaning slightly forward, resting their head on their arms on a pillow, which is placed on an adjustable bedside table.
- This position facilitates access to 6–9th rib space in the posterior axillary line, which is the most dependent part of the thorax.
- Unstable patients and those who are unable to sit up may be in the supine position for the procedure with slight head elevation.
- The patient is moved to the extreme side of the bed, the ipsilateral hand is placed behind the head, and a towel roll is placed under the contralateral shoulder to facilitate dependent drainage.

Step 5: Procedure

1. *Needle thoracentesis*
   - This procedure is preferably done for diagnostic pleural aspiration.
   - Position the patient appropriately as already discussed.
   - After positioning the patient and prior to preparing, ideally perform ultrasonography to confirm the pleural effusion, assess its size, look for loculations, and determine the optimal puncture site.
   - Determine the optimal puncture site by searching for the largest pocket of fluid superficial to the lung.
   - If ultrasonography machine is not available, then identify the correct site of aspiration as a site of maximum dullness on percussion of the chest.
   - Ideally, the site is between the 7th and 9th rib spaces in the middle and posterior axillary line.
   - Use standard aseptic technique for the remaining steps of the procedure.
   - Clean a wide area with an antiseptic bacteriostatic solution such as chlorhexidine.
   - Place a sterile drape over the puncture site and use sterile towels on the bed to establish a large sterile field within which to work.
   - Lidocaine 2% solution should be used for local anesthesia. The skin, subcutaneous tissue, rib periosteum, intercostal muscle, and parietal pleura should all be well infiltrated with local anesthetics.
   - The needle is inserted to the periosteum of the lower rib and is moved up and over the lower rib with frequent injection of small amounts (0.1–0.2 mL) of lidocaine.
   - Once this needle is superior to the rib, it is slowly advanced toward the pleural space with aspiration, followed by the injection of 0.1–0.2 mL of lidocaine every 1–2 mm.
   - As soon as pleural fluid is aspirated through this needle into the syringe containing lidocaine, the needle should be withdrawn from the pleural space and reattached to a 50- to 60-mL syringe through a stopcock.
   - The same needle or large needle (20 gauge) is reintroduced along the same tract slowly with constant aspiration until pleural fluid is obtained.
   - Aspiration is then continued until the syringe is filled with pleural fluid.
   - Avoid draining more than a liter in one sitting.
   - Stop aspirating if the patient coughs and gets dyspneic.
   - The needle is then withdrawn, and the procedure is stopped.
   - Carefully remove the needle and dress the wound.
   - Label the pleural fluid and send it for diagnostic analysis.
   - If the effusion is small and contains a large amount of blood, place it in an anticoagulant (heparin) so that it does not clot.
   - Reposition the patient appropriately based on his or her comfort and respiratory status.
   - Write a procedure note and comment specifically on the descriptive characteristics of the pleural fluid.

2. *Thoracentesis with intravenous cannula*
   - Follow the similar procedure as pleural aspiration with the needle up to anesthetizing the desired intercostal space.
   - Then, arrange a 12G intravenous cannula with a needle and a three-way stopcock and 50-mL syringe.
   - While aspirating, introduce this cannula with the same track up to the pleural space till pleural fluid fills in the syringe.
   - Remove the inner needle from the outer cannula and reattach the three-way stopcock and syringe.
   - Then using the manual syringe pump method or vacuum bottle, aspirate the desired amount of fluid. Follow the rest of steps as described above.
3. *Thoracentesis with commercial kits*
   - Follow the similar procedure as pleural aspiration with the needle up to anesthetizing the desired intercostal space.
   - Initially nick the skin with a No. 11 scalpel blade to reduce skin drag.
   - While aspirating, advance the device over the superior aspect of the lower rib until pleural fluid is obtained.
   - When a free flow of fluid is encountered, the catheter is advanced approximately 1 cm and the needle is withdrawn completely.
   - There is a self-sealing valve so that air does not leak into the pleural space when the needle is withdrawn; however, the needle cannot be reinserted through the catheter.
   - Using either a syringe pump method or a vacuum bottle, drain the pleural effusion until the desired volume has been removed for symptomatic relief or diagnostic analysis.

Step 6: Manage complications

Major complications
- Pneumothorax (3–11%)
- Tension pneumothorax
- Hemothorax (0.8%)
- Laceration of the artery, liver, or spleen (0.8%)
- Diaphragmatic injury
- Empyema
- Hypotension
- Reexpansion pulmonary edema

Minor complications
- Pain (22%)
- Dry tap (13%)
- Cough (11%)
- Subcutaneous hematoma (2%)
- Subcutaneous seroma (0.8%)
- Vasovagal syncope
- Tumor seeding

Step 7: Send pleural fluid for the laboratory tests

Routine investigations

- Biochemical analysis—pH level (in heparinised syringe), glucose levels, protein levels, albumin, lactic acid dehydrogenase levels, and adenosine deaminase
- Microbiology examination—Gram stain, fungal stain, AFB stain and culture, and aerobic culture
- Total cell count and differential cell count
- Cytology

Special investigation

- Creatinine levels and pH for urinothorax
- Amylase levels—if there is a pretest suspicion of acute pancreatitis, chronic pancreatic disease, or esophageal rupture
- Triglyceride levels for chylothorax
- Rheumatoid factor for rheumatic lung disease
- Pro-BNP levels for congestive heart failure
- Hematocrit levels for hemothorax

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Chest Tube Placement

98

Rajesh Chawla, Ashish Jain, and Sudha Kansal

A 60-year-old male patient—a known case of chronic obstructive pulmonary disease—was admitted to the hospital with sudden onset of breathlessness. On examination he was found to be tachypneic and had cyanosis. His chest skiagram showed pneumothorax on the right side.

A chest tube placement (tube thoracostomy) is a method to insert a flexible, hollow tube into pleural space to extract air, fluid blood, or pus. It helps in maintaining negative intrapleural pressure and expansion of the lung.

Step 1: Assess the need of chest tube insertion

- Pneumothorax in any mechanically ventilated patient
- Pneumothorax after initial relief with needle aspiration
- Bilateral pneumothoraces
- Persistent or recurrent pneumothorax after simple aspiration
- Large secondary spontaneous pneumothorax
- Malignant pleural effusion
- Empyema and complicated parapneumonic pleural effusion
- Traumatic hemopneumothorax
- Chylothorax
- Postoperative—for example, thoracotomy, esophagectomy, and cardiac surgery

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Step 2: Rule out contraindications

There is no absolute contraindication in emergency situation:

- Bleeding diathesis (prothrombin time or partial thromboplastin time more than two times normal, platelets <50,000/ml) should be corrected in nonemergency settings.
- Inability to aspirate pleural fluid or air to confirm correct pleural space before chest drain insertion.
- Caution is required when there is a history of thoracic surgery or pleurodesis on the side of proposed chest tube insertion.
- The lung densely adherent to the chest wall throughout the hemithorax is an absolute contraindication to chest drain insertion.

Step 3: Pre-drainage risk assessments

- Risk of hemorrhage, any coagulopathy, or platelet defect should be corrected prior to chest drain insertion in nonemergency situations.
- Routine measurement of the platelet count and prothrombin time is only recommended in patients with known risk factors.
- A careful radiological differentiation between pneumothorax and bullous disease, collapse and a pleural effusion, is required.
- The drainage of a postpneumonectomy space should only be carried out by or after consultation with a cardiothoracic surgeon.

Step 4: Preparation

- Sterile gloves and gown
- Skin antiseptic solution, for example, Betadine or chlorhexidine in alcohol
- Sterile drapes, eye protection, mask, and caps
- Gauze swabs
- Intravenous catheters, tubing
- Supplemental oxygen
- Monitors (cardiac, pulse oximeter)
- A selection of syringes and needles (16–25 gauge)
- Local anesthetic, for example, lignocaine (lidocaine) 1% or 2%
- Scalpel and #10 or #15 blade
- Suture (e.g., "1–0" silk)
- Instrument for blunt dissection (e.g., curved clamp)
- Forceps and the needle holder
- The guidewire with dilators (for intercostal drainage catheter placement)
- Chest tube (No 24–40 French)
- Connecting tubing
- Closed drainage system (including sterile water if underwater seal being used)
- Dressing and adhesive
- Antiseptic ointment
- Resuscitation cart
- Drugs—benzodiazepine, anticholinergics

Step 5: Consent and premedication
- Written and informed consent should be taken before doing the procedures.
- Intravenous analgesics or mild sedation (benzodiazepine or narcotic) and anticholinergics should be administered.

Step 6: Patient position
- The preferred position for drain insertion is the patient lying on the bed with the head up, slightly rotated, with the arm on the side of the procedure behind his/her head to expose the axillary area.
- Procedure can also be done while the patient is sitting upright leaning over an adjacent table with a pillow or in the lateral decubitus position.

Step 7: Site selection
- Careful identification of the correct patient, correct side, and correct site should be checked immediately before the procedure. Confirm the indication of chest tube insertion by reviewing the clinical signs and the chest radiograph.
- Ultrasonography can be used as adjunctive guides to the site of tube placement.
- A chest radiograph must be available at the time of drain insertion except in the case of tension pneumothorax.
- The chest tube should be inserted in the fourth to sixth intercostal space in the midaxillary line in the safe triangle.
- The safe triangle is bordered by the anterior border of the latissimus dorsi, the lateral border of the pectoralis major muscle, a line superior to the horizontal level of the nipple, and an apex below the axilla.
- This position minimizes risk to underlying structures such as the internal mammary artery and avoids damage to muscle and breast tissue resulting in unsightly scarring.
- A more posterior position may be chosen if suggested by the presence of a loculated effusion or air. While this is safe, it is not the preferred site as it is more uncomfortable for the patient to lie down after insertion and there is a risk of the drain kinking.
- For apical pneumothoraces, the second intercostal space in the midclavicular line is sometimes selected but is not recommended routinely as it may be uncomfortable for the patient and may leave an unsightly scar. This site can be chosen for needle thoracostomy in tension pneumothorax.

Step 8: Select the drain size

Drain size depends on the underlying pathology:
- Small-bore drains are recommended as they are more comfortable than large-bore tubes, but there is no evidence that either is therapeutically superior. These are put in patients with pneumothorax or pleural effusion.
- Large-bore drains are recommended for drainage of acute hemothorax and empyema.

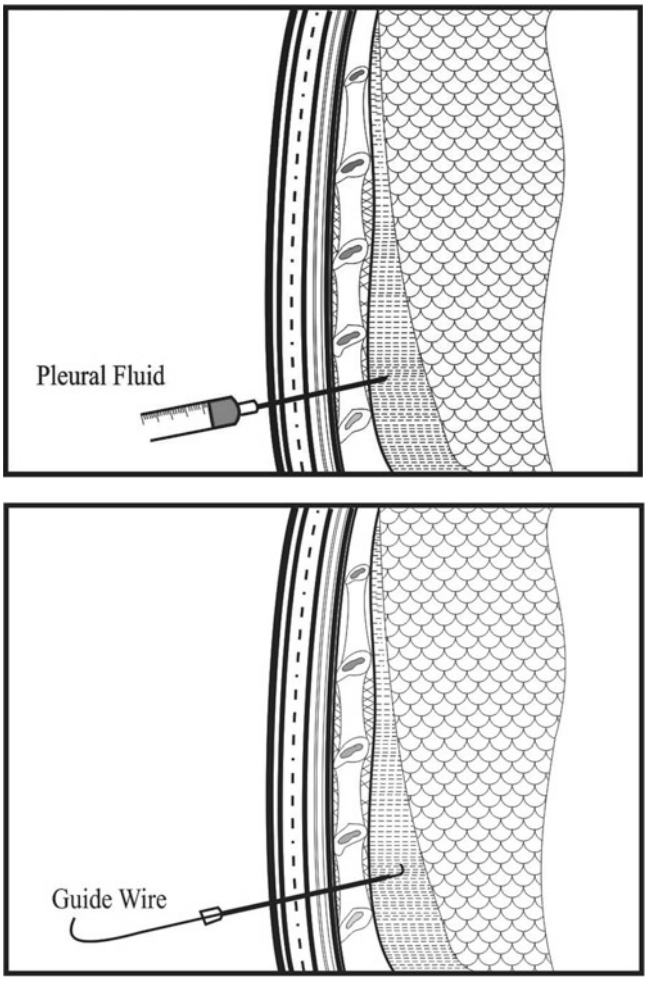
Step 9: Procedure

Four methods are described:

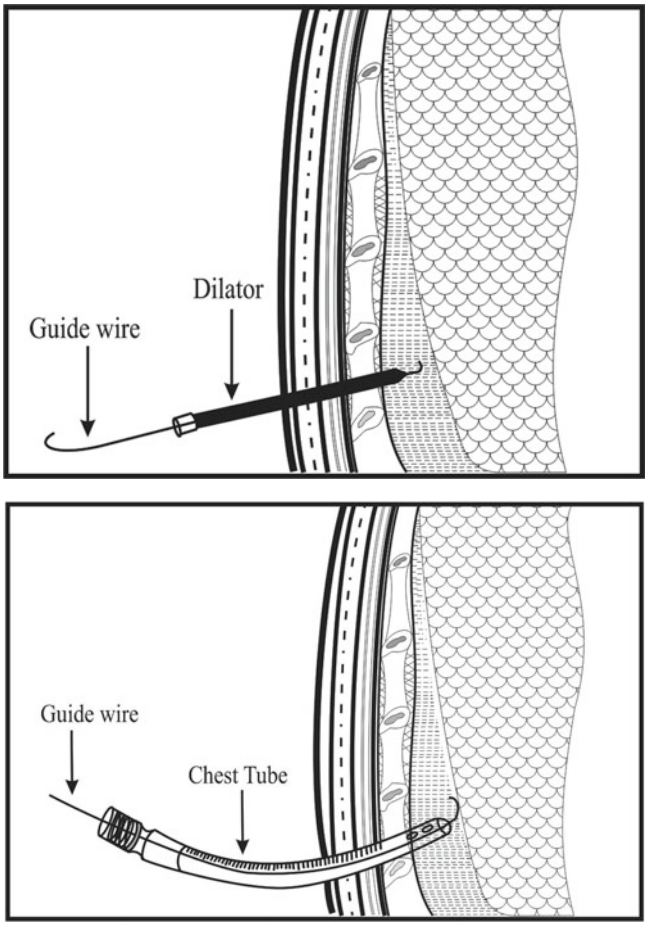
1. Guidewire tube thoracostomy
2. Trocar tube thoracostomy
3. Operative tube thoracostomy
4. Single-port thoracoscopy

A. *Guidewire tube thoracostomy* (Figs. 98.1, 98.2, 98.3 and 98.4)

- Explain procedure to the patient.
- Take written consent.



Figs. 98.1 to 98.2 Guidewire tube thoracostomy



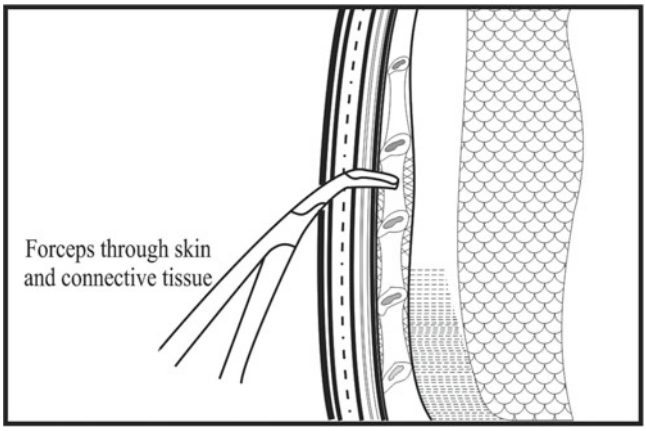
Figs. 98.3 to 98.4 Guidewire tube thoracostomy

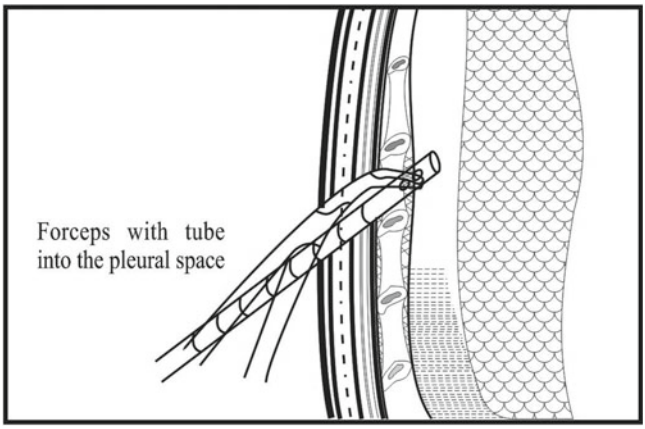
- Give proper position to the patient.
- Wear the cap and mask, perform hand hygiene, and wear personal protective equipment (PPE) with sterile gloves.
- Provide supplemental oxygen, secure intravenous access, and attach all monitors.
- Ensure adequate lighting.
- Arrange all equipments on a sterile workplace.
  - Clean the skin of the patient with 2% chlorhexidine in alcohol preparation.
  - Give a frictional scrub in a circular manner to at least 10-cm area from the insertion site.

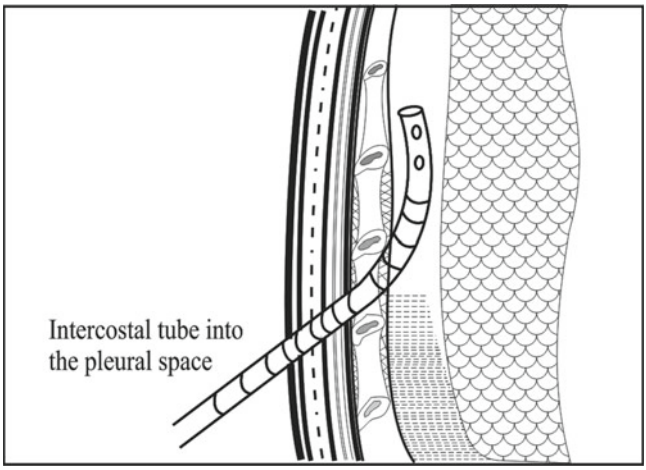
  - The field can be draped using towels. In all invasive procedures, meticulous care should be taken to minimize the risk of infection.
  - After locating intercostal space, infiltrate local anesthesia into the skin raising the cutaneous wheel at incision site and subcutaneous tissue.
- Anesthetize rib and pleural space in selected intercostal space.
- Insert the introducer needle just superior to the appropriate rib. Stop just at the point where air or fluid is aspirated (Fig. 98.1).
- Remove the syringe keeping the needle in situ, covering the needle opening with fingers to prevent entry of air.
- Introduce the guidewire through the needle into pleural space and then remove the needle from pleural space while keeping the guidewire in situ (Fig. 98.2).
- Make a small nick at the entry site to allow introduction of dilators and the chest tube.
- Use dilators to dilate the tract over the guidewire (Fig. 98.3).
- Introduce the chest tube over the guidewire into the pleural space. Confirm that all openings are in pleural space. Remove wire.(Fig. 98.4).
- Connect the chest tube to the drainage system.
- Suture the tube in place and dress with gauze and tape.

B. *Trocar tube thoracostomy*
- Take written consent.
- Give local anesthesia with 2% Xylocaine.
- This method initially requires a 2–4-cm incision parallel to the superior border of the lower rib through the skin and subcutaneous tissues after local anesthesia.
- This method uses a chest tube with a trocar positioned inside the tube.
- The chest tube with the trocar can then be inserted between the ribs into the pleural cavity, directed toward the opposite shoulder with the flat edge of the stylet tip cephalad to prevent damage to the intercostal vessels.
- Because significant force is often required to insert the trocar, the hand not applying the force should be placed next to the patient's chest wall to control the depth of penetration.
- Once the pleural cavity is entered, the inner trocar is gradually removed from the chest tube. When the proximal end of the trocar clears the chest wall, a clamp is placed between the trocar and the chest wall until the trocar can be completely withdrawn and the tube attached to a water-seal drainage system.
- In critically ill patients, one should avoid the trocar tube thoracostomy.

C. *Operative tube thoracostomy*
- Explain the procedure.
- Position the patient in a semi-recumbent position with the head and shoulder about 30° off the bed.
- The ipsilateral arm is placed above the head for exposure of the axilla and to increase distance between the ribs.
- Follow the first few steps as in the guidewire method.







Figs. 98.5 to 98.7 Operative tube thoracostomy

- After locating intercostal space, infiltrate local anesthesia into the skin raising the cutaneous wheel at incision site and subcutaneous tissue.
- Generously anesthetize parietal pleura and confirm entry into pleural space by aspiration of air or fluid. Then, withdraw syringes and needles.
- Make a skin incision above and parallel to the upper border of the lower rib, one space below the desired site, in intercostals space wide enough to insert a finger.
- The incision should be made down to the fascia overlying the intercostal muscle. This fascia is then incised throughout the length of the incision, with care taken not to cut the muscle.
- Once the fascia has been incised, the muscle fibers are spread with a blunt-tipped hemostat tracking upward until the upper desired intercostal interspace is identified. This will make a tunnel, which helps in keeping the tube in the right place (Fig. 98.5).
- An incision is made in the intercostal fascia just above the superior border of the rib over which the tube will pass.
- Again infiltrate muscle and pleura with the local anesthetic agent.
- Advance the needle into the pleural space while aspirating fluid or air to confirm the correct location.
- The parietal pleura is then dissected with a blunt-tipped hemostat, ensuring that the tip of hemostat remains on the superior aspect of the lower rib. The hole is then enlarged by means of the operator's index finger.
- At this time, the operator should palpate the adjacent pleural space to detect any adhesions in the pleura.
- Clamp the end of the chest tube with a Kelly clamp and guide into the pleural space with its distal end clamped. Direction is anteroapical for air and inferoposterior for fluid drainage (Figs. 98.6 and 98.7).
- Attach to the external drainage system.
- Suture the tube securely with a purse-string suture to prevent tube displacement.
- Use occlusive gauze to seal the skin around the tube.
- Dress area with a generous amount of gauze and tape.

D. *Single-port thoracoscopy*

Chest tubes can be inserted through a single-port thoracoscopy. Then under direct visualization, the chest tube is placed into the costodiaphragmatic gutter or in the upper part of thoracic cavity.

The great advantage is the visualization of the place where the tube will be placed.

Step 10: Verification of chest tube placement

- After the chest tube has been inserted and connected to a drainage system, a chest radiograph should be obtained to verify the correctness of its position.
- Ideally, both a posteroanterior view (PA) and a lateral view should be obtained because certain ectopic locations may not be apparent on the PA view alone.

- A CT scan should be obtained when the chest tube does not drain adequately and the chest radiograph is noncontributory.
- With CT, the tube can be visualized over its entire course with accurate location. If there are undrained locules of fluid, additional chest tubes can be inserted.

Drainage system

One-bottle collection system

- This system consists of one bottle that serves as both a collection container and a water seal.
- The chest tube is connected to a rigid straw inserted through a stopper into a sterile bottle.
- Enough sterile saline solution is instilled into the bottle so that the tip of the rigid straw is approximately 2 cm below the surface of the saline solution.
- The bottle's stopper must have a vent to prevent pressure from building up when air or fluid coming from the pleural space enters the bottle.
- This one-bottle system works well for uncomplicated pneumothorax.
- If substantial amount of fluid is draining from the patient's pleural space, the level of fluid will rise in the one-bottle system, and therefore, the pressure will have to be higher and higher in the rigid straw to allow additional air or fluid to exit from the pleural space. So, in such a case, two-bottle collection system is advised.

Two-bottle collection system **(Fig. 98.8)**

- This system is preferred to the one-bottle collection system when substantial amounts of liquid are draining from the pleural space.

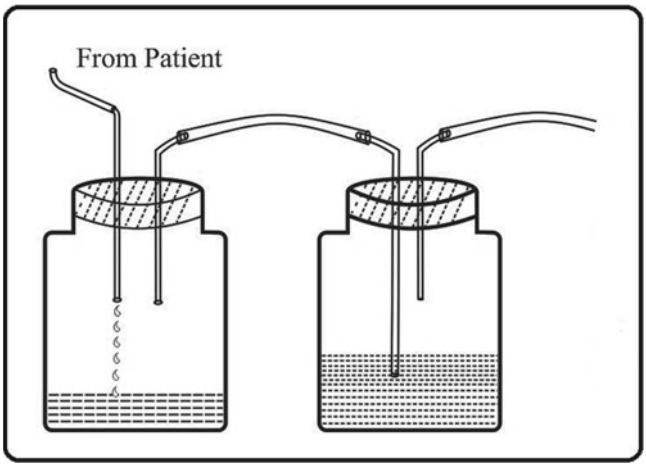


Fig. 98.8 Two-bottle collection system

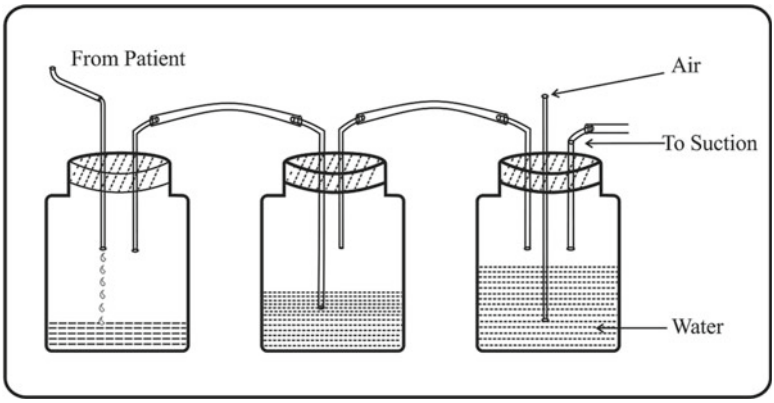


Fig. 98.9 Three-bottle drainage system

- With this system, the bottle adjacent to the patient acts as a collection bottle for the drainage, and the second bottle provides the water seal and the air vent.
- The degree of water seal does not increase as the drainage accumulates. The water-seal bottle functions identically in both the one- and two-bottle systems.

Suction and three-bottle collection systems (Fig. 98.9)

- Controlled amounts of suction (usually 15–20 cm H_2O) can be readily applied to the system if a third bottle, the suction-control bottle, is added to the system.
- The amount of negative pressure in the system is equal to the depth to which the rigid straw in the suction-control bottle is submerged below the surface of water.
- It is desirable to apply negative pressure to the pleural space to facilitate reexpansion of the underlying lung or to expedite the removal of air or fluid from the pleural space.

Step 11: Care of the chest tube

Always see the following things:

- Is there bubbling through the water-seal bottle or the water-seal chamber on the disposable unit?
- Is the tube functioning? Always check for air column movement.
- What is the amount and type of drainage from the tube?

Step 12: Guidelines for removal

- Fully expanded lung
- Resolution of air leak for 24 h
- For pleural effusion, drainage less or up to 50 mL/day for 3 consecutive days

Step 13: How to remove

- The chest tube should be removed either while the patient performs Valsalva maneuver or during expiration with a brisk firm movement while an assistant ties the previously placed closure suture.
- Obtain an early chest radiograph.

Step 14: Complications

- Local site bleeding
- Hematoma
- Hemothorax from intercostals vessel injury
- The tube misplaced
- The nonfunctional tube
- Laceration of the lung, liver, and heart
- Intra-abdominal placement
- Pneumothorax
- Infection-site cellulitis, track infection, empyema
- Subcutaneous emphysema
- Clamping a chest tube with presence of air leak may result in tension pneumothorax
- Persistent leak at the site of infection and around the tube

Suggested Reading

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3. Gayer G, Rozenman J, Hoffmann C, et al. CT diagnosis of malpositioned chest tubes. Br J Radiol. 2000;73:786–90.
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   A review article on chest tube management.

Pericardiocentesis

99

Rajesh Chawla, Sananta K. Dash, and Vipul Roy

A 60-year-old patient—a case of non-Hodgkin's lymphoma—presented in the emergency department with acute breathlessness. His pulse was 80/min, and blood pressure was 80/60 mmHg. Neck veins were prominent and heart sounds were feeble. ECG showed low voltage and echocardiogram showed massive pericardial effusion. A pericardiocentesis was planned.

The removal of fluid from the pericardial space is called pericardiocentesis. The abrupt collection of fluid raises intrapericardial pressure, compresses the heart, and decreases cardiac output. This condition is called cardiac tamponade. Echocardiography is recommended to make urgent diagnosis and look for diastolic collapse of the right atrium and ventricle due to cardiac tamponade. Immediate aspiration of fluid is recommended in such a case.

Step 1: Assess the patient

Assessment of a patient of excessive pericardial fluid is done clinically based on the clinical signs, ECG, and echocardiography (Table 99.1).

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Table 99.1 Differentiating cardiac tamponade and constrictive pericarditis

Clinical signs	Tamponade	Constrictive pericarditis
Pulsus paradoxus	Common	Usually absent
Jugular veins		
Prominent *y* descent	Absent	Usually present
Prominent *x* descent	Present	Usually present
Electrocardiogram		
Low ECG voltage	May be present	May be present
Electrical alternans	May be present	Absent
Echocardiography		
Thickened pericardium	Absent	Present
Pericardial calcification	Absent	Often present
Pericardial effusion	Present	Absent
Right ventricle size	Usually small	Usually normal
Myocardial thickness	Normal	Normal
Right atrial collapse and right ventricular diastolic collapse	Present	Absent
Exaggerated respiratory variation in flow velocity	Present	Present
CT/MRI		
Thickened/calcific pericardium	Absent	Present
Cardiac catheterization		
Equalization of diastolic pressures	Usually present	Usually present

Step 2: Assess the need of needle pericardiocentesis and contraindications

A. *Indications*

Emergency

I. Evidence of cardiac tamponade:
   (a) Hypotension (refractory to fluid resuscitation and vasopressors)
   (b) Distended neck veins with cyanosis
   (c) Central venous pressure more than 20 mmHg
   (d) Narrowed pulse pressure
   (e) No other explanation of hypotension (e.g., pneumothorax)

II. Penetrating injury to the chest between the nipples

Elective

Purely diagnostic pericardiocentesis should be limited to selective cases:

I. Cytologic evaluation (discriminate a bacterial, traumatic, neoplastic, or idiopathic cause)
II. Removal of chronic pericardial effusion, which may also produce immediate clinical improvement
III. Placement of a catheter for repeated pericardial drainage and lavage
IV. Instillation of antimicrobial agents into the pericardial space
V. Suspicion of purulent pericarditis

B. *Contraindications*
   (i) Septic pleuritis (may introduce infection into pericardial space).
   (ii) External wounds overlying the site of centesis (The approach for the procedure can be from either side of thorax.)
   (iii) Thrombocytopenia (<50,000/mm^3), bleeding disorders, and anticoagulant therapy (for elective pericardiocentesis).

Step 3: Know the options

1. Needle pericardiocentesis: It is decompression of pericardial tamponade by needle aspiration of blood or fluid from the pericardial space.
2. Intrapericardial catheterization: This is a nonsurgical, usually done in a catheterization laboratory under fluoroscopic or echocardiography guidance using dilatational technique.

Step 4: Procedure

- Aggressive resuscitation measures should continue along with preparation for emergency pericardiocentesis.
- Vasopressor and inotropic support should be considered in fluid unresponsive shock.
- The required preprocedure investigations include complete hemogram, prothrombin time, activated partial thromboplastin time, renal functions tests (RFT), and liver functions tests (LFT).
- Blind pericardiocentesis is no longer recommended. Echocardiography-guided procedure is safe and desirable (Table 99.2)

  A. *Percutaneous blind technique*
     1. Take written informed consent.
     2. *Patient preparation*: Monitor vital signs and attach cardiac monitor. Keep the head of the bed elevated to approximately 45°. The patient should be placed at a comfortable height for the physician. A central venous catheter is essential for monitoring of right heart pressure and rapid infusion of saline and drugs. Invasive arterial pressure monitoring is indicated. Oxygen supplementation is essential:
        - *Localizing the entry site*: Locate the patient's xiphoid process and the border of the left costal margin using inspection and careful palpation. The needle entry site should be 0.5 cm to the (patient's) left of the xiphoid process and 0.5–1.0 cm inferior to the costal margin.
        - *Skin preparation*: Strict asepsis is required with povidone iodine preparation. Local anesthesia is required (lidocaine 2%) prior to the puncture.
        - *Puncture*: Puncture at a 45° angle to the skin with the needle toward the inferior tip of the left scapula.
        - *Advancement*: Advance the needle posteriorly (while initially pressing the liver hard with the other hand to avoid a tear of the liver) with intermittent aspiration and injection of lidocaine through the path. Pass the tip beyond the posterior border of the bony thorax (usually lies within

Table 99.2 Equipment for pericardiocentesis

Equipments for needle pericardiocentesis	Equipments for intrapericardial catheterization
Preparation of the site	***Catheter placement***
Antiseptic	Teflon-coated, flexible J-curved guidewire
Gauze, sterile drapes, and towels	5F or other system
Sterile gloves, masks, gowns, caps	A 35-cm flexible pigtail catheter with multiple fenestrations (end and side holes)
A 5-mL or 10-mL syringe with a 25-gauge needle	
1% or 2% lidocaine (without epinephrine)	
Emergency drugs	
Procedure	***Drainage system***
No. 11 blade	A three-way stopcock
A 20-mL syringe with 10 mL of 1% lidocaine (without epinephrine)	Sterile IV tubing
An 18-gauge, 8-cm, thin-walled needle with the blunt tip	A 500-mL sterile-collecting bag (or bottle)
Multiple 20- and 50-mL syringes	Sterile gauze and adhesive bag (or bottle)
Hemostat	Suture material
Electrocardiogram machine	
Three red top tubes	
Two purple top (heparinized) tubes	
Culture bottles	
Postprocedure	
Suture material	
Scissors	
Sterile gauze and bandage	

2.5 cm of the skin surface). If bone contact occurs, then walk the needle behind the posterior (costal) margin. Reduce the angle of contact to 15° once the tip has passed the posterior margin of the bony thorax, and continue in the same direction.

- Further advancement is done with continuous aspiration. If electrocardiographic guidance is used, the sterile alligator clip is applied to the needle hub. Monitor continuous ECG throughout the procedure. Look for ST-segment elevation or premature ventricular contractions (evidence of epicardial contact) as the needle is advanced.
- *End point*:
  - Advance the needle along this extrapleural path until a definite give-way is felt and fluid is aspirated from the pericardial space (usually 6.0–7.5 cm from the skin). Some patients may experience a vasovagal response at this point and require atropine intravenously to increase their blood pressure and heart rate.
  - If ST-segment elevation or premature ventricular complexes occur (i.e., the needle in contact with pericardium), withdraw the needle

toward the skin surface while aspirating, and if unsuccessful, then retry in the same way (caution is not to do any lateral motion as it can damage the epicardial vessels).
  - Collect the samples and send investigations accordingly.
- *Evidence of successful decompression*
- Decreased intrapericardial pressure to levels between −3 and +3 mmHg:
  - Fall in right atrial pressure and separation between the right and left ventricular diastolic pressures
  - Increased cardiac output
  - Increased systemic blood pressure
  - Reduced pulsus paradoxus to physiologic levels (≤10 mmHg)

Please note that these blind techniques have a high incidence of morbidity and mortality, and they are no longer justified without echocardiography.

B. *Echocardiography-guided intrapericardial catheterization pericardiocentesis*
- Take an informed consent.
- The patient is placed in the semi-reclining position, slightly rotated leftward to enhance the fluid collection in the inferoanterior part.
- Define the site of entry and needle trajectory. The site of needle insertion is the place where the pericardial space is closest to the probe and the fluid accumulation is maximum.
- Local site preparation is the same as that for the percutaneous blind technique.
- A straight trajectory that avoids puncture of vital organs is chosen. The site should be 3–5 cm from the parasternal border to avoid puncture of the internal mammary artery. The optimal needle trajectory has to be preimagined by the operator.
- A 14–16-gauge Teflon sheath needle attached with a saline-filled syringe is used. On entering the fluid, a further advancement of 2 mm is advised; the sheath is advanced over the needle and the needle is withdrawn. Confirmation of the needle position is done by 5 mL of agitated saline and seen by echocardiography in the pericardial space.
- Seldinger technique is used to place a guidewire through the sheath, and then, sheath is removed. A series of skin dilation is then performed to finally allow an 8F, 35-cm flexible pigtail catheter to be guided over the guidewire into the pericardial space.
- Maintenance of the system—secure the pigtail with suture and connect it to a reservoir. Flush the drain every 4–6 h with 10–15 mL saline to maintain the patency.
- Other different methods and kits are now available as possible alternate techniques.

Step 5: Manage complications (Table 99.3)

Table 99.3 Management of complications

	Complications	Prevention/treatment
Structural damage	Cardiac puncture with hemopericardium	Careful procedure, urgent thoracotomy, and repair
	Coronary artery laceration (hemopericardium or myocardial infarction)	Careful procedure, urgent thoracotomy, and repair
	Fistula formation	Surgical correction
Rhythm disturbance	Arrhythmias, bradycardia, ventricular tachycardia/ventricular fibrillation	Often spontaneously revert, may need cardioversion/defibrillation/ cardiopulmonary resuscitation
	Cardiac arrest (precipitated by pulseless electrical activity, tachyarrhythmia, or bradyarrhythmia)	Cardiopulmonary resuscitation according to ACLS protocol
Dysfunction (cardiopulmonary)	Transient biventricular dysfunction	Often reverts, vasopressors, and inotropes
	Pulmonary edema	Manage according to standard practice
Extracardiac	Hemothorax	Intercostal tube drainage (ICD)
	Pneumothorax	ICD insertion
	Trauma to abdominal organs (liver, gastrointestinal tract)	Careful procedure, better to do under sonological guidance
	Infection	Standard therapy

Step 6: Send investigations of pericardial fluid

Investigations
Hematocrit
White blood cell count with differential count
Glucose, protein, cholesterol, triglyceride
Amylase, lactate dehydrogenase
Gram's stain
Routine aerobic and anaerobic cultures
Smear and culture for acid-fast bacilli
Cytology
Special cultures (viral, parasite, fungal)
Antinuclear antibody
Rheumatoid factor
Total complement, C3

Suggested Reading

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Lumbar Puncture

100

Rajesh Chawla and Charu Gauba

A 40-year-old male patient was admitted to hospital with altered sensorium, headache, vomiting, high-grade fever and rash. He was drowsy. His pulse was 120/min and blood pressure was 110/80 mmHg. Neck rigidity was positive and CT scan report of the head was normal. A lumbar puncture (LP) was planned.

Lumbar puncture is a commonly performed procedure to obtain cerebrospinal fluid (CSF) for diagnosis of various neurological disorders.

Step 1: Assess the need for lumbar puncture

A. *Diagnostic indications*

- Infectious disease
  - Meningitis
    - Tubercular
    - Viral
    - Bacterial
    - Fungal
  - Encephalitis
- Subarachnoid hemorrhage (SAH)
- Demyelinating/inflammatory diseases
  - Multiple sclerosis/acute disseminated encephalomyelitis
  - Guillain–Barré syndrome/chronic inflammatory demyelinating polyneuropathy
  - Neurosarcoid

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- Neurodiagnostic imaging
  - Myelography
  - Cisternography
- CSF pressure (opening pressure)
  - Normal pressure hydrocephalus (NPH)
  - Idiopathic intracranial hypertension (IIH)
- Oncologic procedures
- Carcinomatous meningitis
- Central nervous system lymphoma

B. *Therapeutic indications*
- Neuraxial analgesia and anesthesia
  - Narcotics
  - Local anesthetics
- Ventriculitis and post-instrumentation meningitis
  - Antibiotic administration
- Leukemias and lymphomas with cerebrospinal involvement
  - Chemotherapy
  - Methotrexate
- Draining CSF in NPH and IIH

Step 2: Be familiar with the CSF analysis

Tests on CSF are determined by:
- Age
- Clinical history
- Differential diagnosis

Basic investigations
- Biochemical
  - Glucose
    - Approximately two-third of serum glucose or higher.
    - Decreased levels below 40–50% of serum glucose generally imply a bacterial infection.
    - Simultaneously random blood sugar must be checked.
  - Protein (<0.5% of plasma)
    - CSF total protein: 15–45 mg/100 mL
    - Approximately 1,000 RBCs = 1 mg% protein (in a bloody tap)
    - Increased protein
      - Infective and post-infective state
      - Demyelinating polyneuropathies
- Hematology
  - Cell counts
    - Total
      - Maximum 5 WBCs/mL; RBCs nil
      - In bloody tap 1, WBC per approximately 700 RBCs can exist
    - Differential

- Microbiology
  - Stains: gram/fungal/acid fast/India ink
  - Cultures: aerobic/fungal/tubercular
- Immunology
  - Cryptococcal antigen
  - Bacterial antigens
  - Viral (e.g., herpes simplex PCR)
  - Mycobacterial (TB PCR)
  - Immunoglobulins
  - Oligoclonal band
  - Cysticercus antibody
  - VDRL
- Cytology
  - Malignancies

Step 3: Rule out the contraindications

A. *Absolute*

- Infected skin over the needle entry site
- Risk/signs of cerebral herniation
  - Intracranial lesions especially posterior fossa tumors
  - Intraspinal mass, especially intramedullary
  - Focal neurological signs
  - Brain stem signs
    - Pupillary changes
    - Decerebrate posturing
    - Altered respiration

B. *Relative*

- Raised intracranial pressure (ICP)
- Cardiorespiratory compromise: position related
- Coagulopathy/thrombocytopenia (platelet count <50,000 or INR >1.5): risk of spinal hematoma
- Previous lumbar surgery/congenital defects/degeneration: may require radiology guidance

Step 4: Order CT head before lumbar puncture

- In all patients to rule out mass effect/frank bleeding, especially if there is:
  - Age > 60 years
  - Immunocompromised patient with known CNS lesions
  - Altered sensorium
  - Focal neurological deficit
  - Seizure within past 1 week
  - Papilledema
  - Suspicion of raised ICP

  CT does not always rule out the risk of herniation completely.

Step 5: Informed consent

- Discuss the prognosis of the patient and the need for the procedure.
- Explain in detail the advantages and disadvantages of the procedure and the available options.
- Obtain an informed consent.

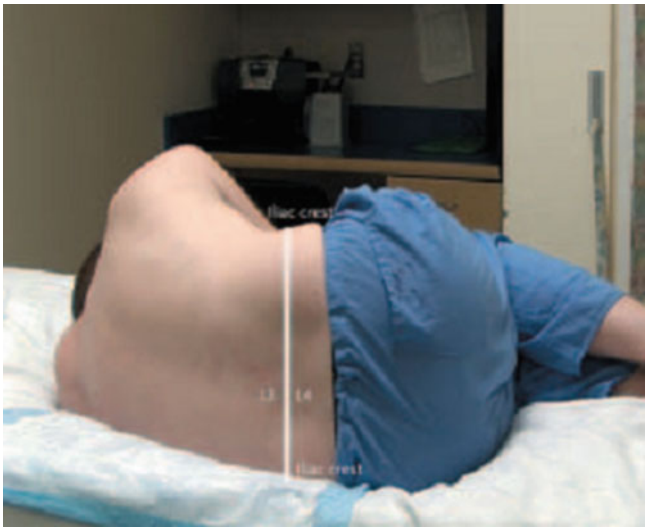
Step 6: Prepare for the procedure

- A spinal needle (20G commonly)
- Sterile sheets and instruments
- A manometer
- Antiseptic cleansing agents, Lignocaine 2%
- Numbered collection tubes (at least 4)
- Functioning intravenous access
- Crash cart
- Vital monitoring depending on the patient condition

Step 7: Position the patient

Explain the procedure to the patient if he/she is conscious.
Take informed consent
Lateral recumbent position

- Preferred for an accurate opening pressure.
- Less incidence of post-puncture headache.
- Make the patient acquire a fetal position with the back flexed, to widen the gap between the spinous processes.
- The head flexed, chin close to the chest.
- Hips flexed.
- Knees flexed and as close to the chest as possible.
- Keep the back perpendicular to the bed and close to the edge.



Sitting position
- Lumbar spine should be perpendicular to the bed, leaning forward on a bedside table
- Preferred for obese/elderly/degenerative spine

Step 8: Know landmarks and anatomy

Skin-marking pencils should be used to mark before skin preparation:
- Determine the superior point of iliac crests.
- Connect both crests with the imaginary line.
- This line crosses the midline at L4 spine level (spinal cord ends at lower border of L1 in adults).
- Walk the fingers down over the spinous process to palpate L4-L5 and L5-S1 interspaces
- Layers encountered during LP are the following:
  - Skin
  - Superficial fascia
  - Supraspinous ligament
  - Interspinous ligament
  - Ligamentum flavum
  - Epidural space
  - Dura
  - Arachnoid membrane

Step 9: Procedure

A. *Preparation*
- Wear the cap, masks, and goggles.
- Scrub appropriately.
- Wear the sterile gown and gloves.
- Prepare the skin:
  - Use povidone-iodine or chlorhexidine.
  - Cover several interspaces.
- Drape with the sterile fenestrated sheet with the opening over the intended area.
- Cover the iliac crest with the sheet.

B. *The procedure*
- Apply local anesthesia (2% lignocaine), use a 25-gauge needle, and infiltrate subcutaneously. Use a 20-gauge needle for deeper tissue and aspirate to see that no blood is aspirated before injecting. Inject while withdrawing the needle. Cover a broad area to allow manipulation.
- Systemic sedatives and analgesics can be used under close monitoring.
- Reconfirm the landmarks and interspaces by palpation.
- Insert the spinal needle with stylet in place at superior aspect of inferior spinous process.
- Stay in the midline.

- Angle 15–30° cephalad; aim for the umbilicus.
- If the needle is bevel tipped, then keep bevel in sagittal plane. Feel the layers as the needle passes through:
  - Popping sensation is felt as the needle passes through the ligamentum flavum.
  - Another feeling of giveaway is felt on puncturing the dura.
  - Feeling of the layers becomes more consistent with practice.
- Withdraw the stylet to check for flow: if none present, rotate by 90° or advance by 2 mm and recheck.
- If flow is poor, rotate by 90°.
- If bone is encountered, withdraw the needle upto the subcutaneous tissue and redirect the needle superiorly or inferiorly.
- Once the flow is adequate, do the following:
  - Measure opening pressure as the height of the fluid via the flexible tube connected to the manometer and needle hub.
  - Relax the legs for accurate measurement.
  - Measure in recumbent position only (normal pressure 70–180 mm H_2O).
  - Collect samples and do not aspirate—it may cause hemorrhage.
- Once minimum amount is collected, replace stylet and withdraw the needle.
- Apply pressure at the puncture site, use tincture benzoin to seal, and apply bandage.
- Keep the patient supine for 1–3 h to reduce severity of postdural puncture headache.

Step 10: Know the complications and their management

- Postdural puncture headache
  - Most common
  - Excessive CSF leak
    - Intracranial hypotension
    - Stretch on pain-sensitive veins
  - Linked to previous history of headaches and psychological factors
  - Risk decreased by
    - Thinner needles
    - Paramedian approach
    - Pencil-point needles (controversial)
    - Bevel parallel to sagittal dural fibers: to split, not cut
    - Replacing the stylet before withdrawing
  - Features
    - Typically occurs within 72 h and lasts 3–5 days
    - Increases on sitting up, better on lying down
    - Usually frontal
  - Treatment
    - Bed rest.
    - Hydration.

    - Analgesics.
    - Methylxanthines—caffeine (most effective), theophylline.
    - Epidural blood patch is most effective.
    - Epidural injection of saline, dextran, or adrenocorticotropic hormone has been described.
- Hemorrhage (uncommon)
  - More risk with bleeding tendency.
  - Spinal SAH: radicular pain, paraparesis, sphincter disturbances.
  - Spinal subdural hematoma (rare): early surgical intervention, else irreversible neurological damage may occur.
- Difficulty in identifying landmarks or subarachnoid space
  - Obesity
  - Ankylosing spondylitis
  - Kyphoscoliosis
  - Lumbar surgery
  - Disk degeneration
  - Calcification of ligaments

Request for an anesthesiologist or interventional radiologist.

- Dry tap
  - The misplaced needle tip
  - Dehydration
  - Low CSF volume
- Infection (uncommon)
  - Seeding of skin flora: preventable by aseptic technique
  - More risk with repeated procedures or lumbar drains
- Hemodynamic disturbances
- Cerebral/spinal herniation (see steps 3 and 4)
  - Raised ICP
  - Cerebrospinal pressure gradient
  - Intramedullary/intracerebral mass lesions
- Hearing loss (rare)
  - Decreased ICP transmitted to cochlear apparatus
  - Reversible
  - Underreported
- Sixth nerve palsy
  - Reversible
  - Traction injury with decreased ICP
- Injury to spinal nerves
  - Usually neuropraxia
  - Local or referred pain
- Subarachnoid epidermal cysts
  - Seeding with skin tissue
  - Avoided by a needle with stylet

Step 11: Managing the anticoagulated patient and timing of LP

Antiplatelets

- NSAIDs: No contraindication
- Ticlopidine: Discontinue 14 days prior
- Clopidogrel: Hold 7 days prior
- GP IIb/IIIa inhibitors: Hold 8–48 h prior

Unfractionated heparin

- Subcutaneous
  - If the total dose is less than 10,000 units/day, twice daily, there is no contraindication.
  - If the total dose is more than 10,000 units/day, more than twice daily, safety is not established.
- Intravenous
  - One hour prior and 2–4 h after heparin dose.
  - No change in next dose timing even if traumatic.

Low-molecular-weight heparin

- Therapeutic dosing
  - 24 h after the last dose
- Single daily dosing
  - 10–12 h after the last dose
  - Next dose 4 h after the procedure

Warfarin

- International normalized ratio 1.5 or less

Fondaparinux

Direct thrombin inhibitors

- Insufficient evidence should be avoided.
- If still necessary
  - 8–10 h after the last dose
  - 2–4 h after needle placement

Thrombolytics

- Absolute contraindication

Suggested Reading

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3. Ellenby MS, Tegtmeyer K, Lai S, et al. Lumbar puncture. N Engl J Med. 2006;355:e12.
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This textbook outlines the preparation and technique adopted for successful and safe execution of lumbar puncture in a crisp and to the point way.

Website

1. http://emedicine.medscape.com/article/80773-overview#a01

Intra-aortic Balloon Pump

101

Khusrav Bajan

A 55-year-old male patient was admitted to hospital with a history of chest pain for about 3 h. He was drowsy, extremities were cold, and his blood pressure was 84/60 mmHg. He was started on inotropic and vasopressor support, but he remained hypotensive.

Intra-aortic balloon pump (IABP) is a mechanical support device to support cardiac pump function by increasing coronary perfusion and decreasing afterload and used as a salvage therapy in cardiogenic shock. IABP therapy should only be considered for use in patients who have the potential for left ventricular recovery or to support those awaiting cardiac transplantation.

Step 1: Assess the need for IABP—indications

Since the balloon counterpulsation helps to improve myocardial oxygen supply and decrease oxygen demand, the IABP is indicated for conditions with decreased myocardial oxygen supply–demand ratio:

- Cardiogenic shock
- Acute myocardial infarction with pulmonary edema
- Mechanical complications of myocardial infarction (ventricular septal defect, acute mitral regurgitation)
- High-risk angioplasty
- Unstable angina refractory to medical treatment
- In conjunction with thrombolysis in myocardial infarction
- Bridge to cardiac transplant

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- Ventricular arrhythmias secondary to ischemia
- High-risk cardiac surgeries
- Patients undergoing noncardiac surgery with high cardiac risk
- Postoperative low cardiac output syndrome
- Weaning from bypass open heart surgery
- Stunned myocardium
- Drug-induced cardiac failure
- Myocardial contusion
- Aortic stenosis

Step 2: Check for any contraindications

- *Absolute*
  - Irreversible brain damage
  - Chronic end-stage heart disease without the possibility of heart transplant
  - Dissecting aortic aneurysms
- *Relative*
  - Aortic incompetence
  - Severe peripheral vascular disease where the decision is based on patient risk–benefit ratio

Step 3: Understand principles of IABP

- The IABP is positioned in the descending thoracic aorta just distal to the left subclavian artery.
- It is connected to an IABP console, which shuttles helium in and out of the balloon, and is timed to inflate and deflate in synchronization with the mechanical cardiac cycle; i.e. the balloon inflates during cardiac diastole and deflates during cardiac systole.
- Inflation at the onset of diastole results in proximal and distal displacement of blood volume in the aorta. This displacement creates elevated pressures by which the coronary artery and systemic perfusion is increased.
- Deflation occurs just prior to the onset of systole. This leads to reduction in the systolic pressure thus decreasing the afterload. Myocardial oxygen demand is decreased as a result of the reduction in systolic pressure and thus improving cardiac output.

Step 4: Techniques and sites of insertion

- It consists of two principal parts:
  - The first part is a catheter with two lumens, one for flushing and pressure monitoring and another for delivery of helium gas in a closed balloon (20–50 cm^3).
  - The second part is a mobile console for delivering helium, controlling balloon inflation and deflation cycling, and displaying pressure waveform and alarms.
- The balloon is inserted from the femoral artery using a Seldinger technique.
- In rare cases, it may be inserted through the axillary artery in patients with severe peripheral arterial disease with bilateral femoral artery occlusion or graft.

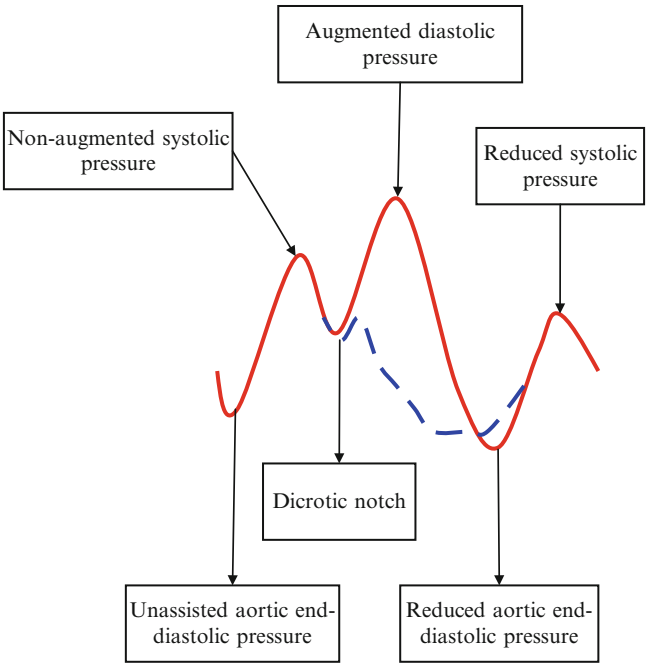

Fig. 101.1 IABP waveform (From www.aic.cuhk.edu.hk)

Step 5: Position the balloon

- The tip of the balloon should lie 2–3 cm below the left subclavian artery so that the entire length of the balloon lies in the descending thoracic aorta.
- The tip of the balloon catheter is radiopaque, and hence, a check X-ray should always be taken after insertion to ensure correct balloon placement.
- The balloon should not be too high, so as to avoid blocking the branches of the arch of aorta, especially the left subclavian artery, and should not be too low, so as to avoid blocking the renal arteries.

Step 6: Set cycling time for IABP (Fig. 101.1)

- The mechanical cardiac cycle represented by the arterial pressure waveform is observed to assess appropriate timing.
- Electrocardiographic synchronization may also be done for cycling.
- Inflation of the intra-aortic balloon occurs at the onset of diastole noted by the dicrotic notch on the arterial waveform.
- A sharp deep "V" should be observed when the balloon inflates. As balloon inflates, aortic diastolic pressure is augmented and a second peak is observed. This peak is referred to as diastolic augmentation.
- Diastolic augmentation (30%) is ideally higher than the patient's systolic pressure and is generated by the displacement of blood volume within the aorta.

- Deflation occurs at end-diastole prior to the next systole. The precise timing of deflation is found by observing the arterial pressure tracing. The optimal deflation point is selected to achieve the greatest reduction (20%) in the next unassisted systole.
- An effective IABP cycling will result in increase of mean arterial pressure, decrease in heart rate, decrease in pulmonary capillary wedge pressure, and increase in cardiac output.

Step 7: Beware of complications
- Trauma to the arterial wall incurred while inserting and advancing the guidewire or balloon (laceration, dissection, subadventitial hematoma) (1–5%)
- Limb ischemia associated with the position of the balloon catheter, which disappears with catheter removal (5–11%)
- Dislodged thrombus created during balloon removal, resulting in distal embolization (peripheral, renal) (1–5%)
- Hematologic (thrombocytopenia, red blood cell hemolysis, hemorrhage) (1–5%)
- Balloon leak/rupture (1–4%)
- Infection (2–4%)
- Cholesterol embolization—presents with fever, thrombocytopenia, livedo reticularis

Step 8: Know the factors affecting IABP complications
- The following factors increase IABP complications:
  - Peripheral artery disease
  - Old age
  - Female sex
  - Diabetes mellitus
  - Hypertension
  - Prolonged support
  - Large catheter size (>9.5 Fr)
  - Low cardiac index
  - Low body surface area
- The following factors are associated with less IABP complications:
  - Decrease in balloon size
  - Sheathless technique

Step 9: Take routine care of IABP
- Specialized nursing care with 1:1 nursing every shift is needed to take care of patients.
- The chest X-ray to document position of the catheter tip, which should be at the bifurcation of the left and right main bronchi.
- Three times daily documentation of peripheral pulses.
- Daily measurement of hematocrit, platelet count, and creatinine.
- Anticoagulation parameters.

Step 10: Wean off IABP

- The patient can be weaned if the following criteria are satisfied:
  - Urine output is more than 40 mL/h without the use of diuretics
  - Improved mentation
  - Extremities are warm
  - Hemodynamics appear to be getting better and stable on little or no inotropes
  - No evidence of ongoing ischemia

Suggested Reading

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Appendices

Appendix A

Table A.1 Drugs and Doses

Drug class/prototypes	Dosing	Common toxicities
ABCD (amphotericin B cholesteryl sulfate complex)	3–4 mg/kg IV q24h	Hypotension, hypokalemia, thrombocytopenia, hypomagnesemia, hepatotoxicity, renal failure allergic reactions
Abacavir	300 mg PO q12h or 600 mg q24h	
Abciximab	0.25 mg/kg IV bolus, and then 0.125 mcg/kg/min	Hypotension, chest pain, nausea, minor bleeding, back pain
ABLC (amphotericin B lipid complex)	5 mg/kg IV q24h	Hypotension, hypokalemia, thrombocytopenia, hepatotoxicity, renal failure, allergic reactions
Acetaminophen	325–1,000 mg PO/IV q4–6h PRN	Rash, anemia, blood dyscrasias, hepatotoxicity
Acetazolamide	250–500 PO/IV mg given q8h	Metabolic acidosis, hypokalemia, hyponatremia, abnormal LFT
Activated charcoal	25–100 g PO	Vomiting, constipation, fecal discoloration (black)
Acetylcysteine	Acetaminophen poisoning	Anaphylactoid reaction, angioedema, vasodilatation, hypotension, tachycardia, urticaria, nausea, vomiting, bronchospasm
	Oral: 140 mg/kg followed by 17 doses of 70 mg/kg q4h	
	IV: 150 mg/kg over 60 min f/b 300 mg/kg over 21 h	

(continued)

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Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
	Nebulization: 3–5 mL of 20% solution three to four times a day, administer before chest physiotherapy	
	Prevention of radiocontrast-induced renal injury: 600 mg PO q12h for 3 days starting 1 day before procedure, may be given intravenously	
Acyclovir	10–15 mg/kg/dose q8h IV (HSV encephalitis) 800 mg PO every 4 hrs (Herpes Zoster)	Malaise, headache, nausea, vomiting, diarrhea, renal, and hepatic toxicity
Adenosine	6 mg IV, if not effective in 1–2 min, can give 12 mg, may repeat 12 mg	Flushing, light headedness, headache, nervousness/anxiety
Adrenaline (see epinephrine)		
Albumin	0.5–1 g/kg/dose (5% in hypovolemia)	Hypervolemia, anaphylaxis, chills, fever, tachycardia, bronchospasm
Albuterol	5–10 mg nebulized over 30–60 min	Arrhythmias, chest discomfort, palpitation, CNS stimulation, drowsiness, diarrhea, dry mouth, micturition difficulty
Alfentanil	IV bolus 500 mcg every 10 min as necessary	Respiratory depression, apnea, bradycardia, delayed gastric emptying, chest wall rigidity
	IV infusion: 1 mcg/kg/min	
Allopurinol	600–800 mg/day in two to three divided doses	Rash
Alteplase	15 mg bolus, then 0.75 mg/kg (up to 50 mg)×30 min, then 0.5 mg/kg (up to 35 mg)×60 min (maximum 100 mg over 90 min)	Hypotension, bleeding, allergic reactions
	Pulmonary embolism: 100 mg IV over 2 h	
	Stroke: 0.9 mg/kg 10% bolus, rest over 60 min (Max 90 mg)	
Amantadine	100 mg PO q12h	Nausea, vomiting, anorexia, xerostomia
Amikacin	15–20 mg/kg once a day	Ototoxicity, neurotoxicity, nephrotoxicity
Aminophylline	Loading dose; 5 mg/kg IV over 30 min	Tachycardia, arrhythmia, convulsions
	Maintenance: 0.1–0.8 mg/kg/h	

(continued)

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Amiodarone	150–300 mg bolus, then 1 mg/min for 6 h, then 0.5 mg/min for 18 h Oral 200 mg 8 hourly, then titrate down to 200 mg q24h	Bradycardia, hypotension, AV block, nausea, photosensitivity, hypothyroidism, hyperthyroidism, coagulation abnormalities, hepatitis, visual disturbance, pulmonary fibrosis
Amitryptiline	25–75 mg PO q24h	Confusion, dry mouth, retention of urine
Amlodipine	5–10 mg PO q24h	Pedal edema, headache, nausea, vomiting
Amoxicillin/clavulanate	625 mg PO q12h/q8h	Nausea, vomiting, diarrhea, allergic reaction
Amphotericin B deoxycholate	0.3–1.5 mg/kg IV q24h	Hypotension, hypokalemia, thrombocytopenia, hepatotoxicity, creatinine increase, allergic reactions
Ampicillin	250–500 mg IV q4–6h	Fever, allergic reaction, penicillin encephalopathy, diarrhea, pseudomembranous colitis, agranulocytosis, anemia
Ampicillin/sulbactam	1.5–3 g IVq6h	Fever, allergic reaction, penicillin encephalopathy, diarrhea, pseudomembranous colitis, agranulocytosis, anemia
Anidulafungin	200 mg IV bolus, then 100 mg IV q24h	Elevated LFT
Aqueous penicillin G	2–4 million U IV q4h	Fever, allergic reaction, penicillin encephalopathy, diarrhea
Argatroban	350 mcg/kg bolus, then 25 mcg/kg/min adjust based on aPTT (For PCI) Initial 2 mcg/Kg/min, adjust based on aPTT measurements (For prophylaxis in heparin induced thrombocytopenia)	Bleeding, cardiac arrest, dyspnea
Aspirin	160–325 mg PO q24h	Bleeding, dyspepsia
Atropine	1 mg IV q3–5 min	Dry eyes, dry mouth, urinary retention, tachycardia
Atracurium	0.5 mg/kg IV Bolus then 0.08–0.12 mg/Kg bolus every 20–30 min or 5–10 mcg/kg/min infusion	Flushing, allergic reactions, bradycardia, hypotension, bronchospasm, laryngospasm, seizures
Azithromycin	250–500 mg IV/PO q24h	Headache, nausea, vomiting, diarrhea, allergic reactions, fungal infection

(continued)

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Bivalirudin	1 mg/kg IV bolus, then 1.75 mg/kg/h	Hypotension, hemorrhage, pain, headache, nausea, back pain
Bosentan	62.5 mg PO q12h × 1 month, then 125 mg PO q12h, as tolerated	Headache, anemia, transaminase increase, nasopharyngitis, flushing, pruritus
Bromocriptine	2.5–5 mg PO q8h (Max 45 mg for Neuroleptic Malignant syndrome)	Headache, dizziness, nausea, hypotension, nasal congestion
Bumetanide	0.5–2 mg/dose PO q24h	Hyperuricemia, hypochloremia, hypokalemia, azotemia, hyponatremia, hyperglycemia, muscle cramps, creatinine increase
Calcitonin	Initial 4 U/kg IM q12h, up to 8 U/kg IM q6h	Facial flushing, nausea, vomiting
Calcium gluconate/chloride (10 ml of 10%)	1 g IV over 2–5 min	Hypercalcemia, constipation (oral)
Captopril	6.25–50 mg PO q8h	Hypotension, dizziness, abnormal taste, cough, worsening renal function
Carvedilol	6.25 mg PO q12h, maximum 25 mg PO q12h	Hypotension, dizziness, fatigue, hyperglycemia, weight gain, diarrhea, bradycardia, syncope, deranged LFT, bronchospasm
Caspofungin	70 mg IV bolus, then 50 mg IV q24h	Headache, fever, chills, hypokalemia, flushing, tachycardia, anemia, eosinophilia, neutropenia, nephrotoxicity
Cefazolin	1–2 g IV q8h	Allergic reaction, fever, Stevens–Johnson syndrome, nephrotoxicity, diarrhea, nausea, vomiting
Cefepime	500 mg to 2 g IV q8–12h	Positive Coombs test, fever, headache, rash, pruritus, diarrhea, nausea, vomiting, agranulocytosis
Cefoxitin	1–2 g IV q6–8h	Diarrhea, anaphylaxis, nausea, vomiting, headache, rash, pruritus, diarrhea, agranulocytosis, pseudomembranous colitis

(continued)

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Ceftazidime	500 mg IV to 2 g q8–12h	Diarrhea, hypersensitivity reactions, candidiasis, nephrotoxicity, encephalopathy, headache, fever
Ceftriaxone	1–2 g IV q12–24h	headache, rash, pruritus, diarrhea, nausea, vomiting, agranulocytosis
Cefuroxime	0.75–1.5 g IV 6–8 hourly	*C. difficile* diarrhea
		Hypersensitivity
		Transient rise in liver function test
Chlordiazepoxide	10–30 mg PO q8h to q6h	Muscle weakness, ataxia, confusion, hypotension
Cyclosporine	IV: 1–5 mg/kg/day	Increased urea, creatinine
	Oral: 1.5 times IV dose q12h	Hypertension
		Hirsutism, gingival hypertrophy
		Hyperuricemia, tremor
Cidofovir	5 mg/kg IV weekly plus probenecid 2 g PO 3 h before the infusion and then 1 g at 2 and 8 h after the infusion	Nephrotoxicity, uveitis/iritis, nausea, vomiting
Ciprofloxacin	500–750 mg PO q12h or 400 mg IV q8–12h	Dizziness, insomnia, restlessness, fever, rash, nausea, vomiting, diarrhea, ALT/AST increase, rhinitis
Clarithromycin	500 mg IV/PO q12h	Headache, nausea, vomiting, diarrhea, abdominal pain, rash
Clindamycin	600–1,200 mg IV q8h to q6h, maximum 4.8 g/day PO 150–450 mg/dose every 6–8 hours, maximum dose 1.8 g/day	Diarrhea, abdominal pain, hypotension, urticaria, rash, pseudomembranous colitis
Clonidine	0.1–0.3 mg PO q12h/8h	Drowsiness, dizziness, hypotension, bradycardia, dry mouth
Clopidogrel	75 mg PO q24h	Nausea, vomiting, diarrhea, bleeding
Codeine phosphate	30–60 mg PO q4h/q6h	Drowsiness, constipation, respiratory depression
Colistimethate	IV: 1–2 million units (80–160 mg) q8h	Fever, headache, pruritus, rash, GI upset, paresthesia, weakness, apnea, respiratory arrest, renal dysfunction, myopathy
	Nebulization: 1 million units q8h	
Conivaptan	20 mg IV bolus, then 0.8–1.6 mg/h IV continuous infusion	Diarrhea, hypokalemia

(continued)

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Co-trimoxazole (trimethoprim: sulfamethoxazole 1:5)	PCP pneumonia treatment: 15–20 mg/kg/day of trimethoprim IV for 14 days, followed orally for further 7 days	Rash, nausea, vomiting, diarrhea, agranulocytosis, thrombocytopenia, hemolysis in G6PD deficiency, rash, allergic myocarditis, peripheral neuritis, aseptic meningitis, hyperkalemia, interstitial nephritis, Steven Johnson
	PCP prophylaxis: 80 mg trimethoprim orally daily	
Dalteparin	120 U/kg SC q12h	Bleeding, wound hematoma, pain at injection site, thrombocytopenia, allergic reactions, alopecia
Dantrolene	1–2.5 mg/kg IV; may repeat q5–10 min to maximum cumulative dose 10 mg/kg	Drowsiness, dizziness, diarrhea, nausea, vomiting
Daptomycin	4–6 mg/kg IV q24h	Anemia, diarrhea, vomiting, peripheral edema, rash, insomnia, UTI, rise in CPK
DDAVP	0.3 mcg/kg slow IV/SC/IM	Facial flushing
	Intranasally: 5–20 mcg daily	
Deferoxamine	1 g IV bolus, then 500 mg IV q4h × 2 doses	Urine discoloration (orange–red)
Dexamethasone	10 mg IV prior to ACTH stimulation test, 4–6 mg IV q6h/q8h	Same as hydrocortisone
Dexmedetomidine	0.2–0.7 mcg/kg/h IV	Hypotension, bradycardia
Dextran (40)	Maximum 20 mL/kg, 20–40 mL/min IV	Allergic reaction, fluid overload, platelet dysfunction
Diazepam	5–10 mg IV over 2 min	Apnea, respiratory depression, drowsiness, hypotension, bradycardia
Diclofenac	75 mg IM	
	50 mg PO q8h	
Digoxin	Load: 10–15 mcg/kg; give 50% of load in initial dose, then 25% at 6–12 h intervals × 2	Bradycardia, heart block, arrhythmias, yellow vision, rash, muscle weakness
	Maintenance:	
	0.125–0.5 mg/day (dose should be reduced by 20–25% when changing from oral to IV)	
Diltiazem	0.25 mg/kg bolus (may repeat 0.35 mg/kg bolus after 15 min), then 5–15 mg/h (PO (extended release) 60–120 mg q12h)	Bradycardia, hypotension, constipation (verapamil > diltiazem), headache, flushing, edema
Dobutamine	2.5–20 mcg/kg/min	Tachycardia, hypertension, ventricular ectopics, headache, palpitations

(continued)

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Dopamine	5–20 mcg/kg/min	Ectopic beats, tachycardia, arrhythmia, palpitations, angina, headache, dyspnea
Dopexamine	0.25–6 mcg/kg/min	Tachycardia, hypotension, angina, hypokalemia, hyperglycemia
Doxycycline	100 mg PO/IV q12h	Intracranial hypertension, pericarditis, angioneurotic edema, skin hyperpigmentation, bone marrow depression, hepatotoxicity
Enalapril	2.5–20 mg PO q12h	Hypotension, dizziness, abnormal taste, cough, worsening renal function
Enoxaparin	1 mg/kg SC q12h	Bleeding, thrombocytopenia
Epinephrine	1 mg IV q3–5 min in cardiac arrest (10 mL of 1 in 10,000 solution)	Tachycardia, hypertension, angina, arrhythmia, sudden death, dry throat, nausea, vomiting, anxiety, headache, dyspnea, urinary retention
	0.01–0.3 mcg/kg/min IV	
	Infuse via central vein in shock	
	Anaphylaxis: 0.5–1.0 mL of 1 in 1,000 solution (50–100 mcg) may be given subcutaneously	
	Bronchospasm: 0.5–1.0 mL of 1:1,000 (0.5–1 mg) diluted with normal saline 2.5 mL and nebulized	
Epoprostenol	2–50 ng/kg/min IV	Flushing, headache, nausea vomiting, hypotension, chest pain, palpitation, diarrhea, weight loss, weakness, myalgia
	5,000–20,000 ng/mL continuous nebulization	
Eptifibatide	180 mcg/kg bolus, then 2 mcg/kg/min	Bleeding, hypotension, thrombocytopenia
Ertapenem	1 g IV q24h	Edema, chest pain, tachycardia, headache, fever, rash, diarrhea, nausea, abdominal pain, hepatic enzyme increase
Erythromycin	250–500 mg PO q6h or 0.5–1 g IV q6h	QTc prolongation, torsades de pointes, pruritus, rash, abdominal pain, anorexia, cholestatic jaundice, neuromuscular weakness, hearing loss

(continued)

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Erythropoietin (recombinant human)	50–300 units/kg weekly in 2–3 divided doses subcutaneously	Hypertension, thrombocytosis, flu-like symptoms, hyperkalemia, shunt, thrombosis
Esmolol	500 mcg/kg bolus, then 50–300 mcg/kg/min	Hypotension, diaphoresis, dizziness, nausea, vomiting
Esomeprazole	20–40 mg PO q24h	Headache, dizziness, pruritus, flatulence, diarrhea
Factor VIIa (recombinant)	Hemorrhagic stroke: (Warfarin related) 10–100 mcg/kg IV: Bleeding episode: 90 mcg/kg every 2 hrs	Hypertension
Fentanyl	1–2 mcg/kg/dose Infusion: 1–3 mcg/kg/h	Hypotension, bradycardia, CNS depression, confusion, chest wall rigidity, respiratory depression
Fluconazole	100–800 mg PO/IV q24h	Headache, seizure, rash, angioedema, hypercholesterolemia, hypokalemia, hepatitis, cholestasis
Fondaparinux	2.5 mg SC q24h	Bleeding, fever, nausea, anemia
Flucytosine	25–37.5 mg/kg PO q6h	Nausea, vomiting, diarrhea, rash
Fludrocortisone	50–200 mcg PO q24h	Hypertension, edema, acne, hypokalemic alkalosis, hyperglycemia, peptic ulcer
Flumazenil	0.2–0.5 mg IV q1min, up to 3 mg	Vasodilatation, headache, agitation, dizziness, blurred vision, dyspnea, hyperventilation
Fomepizole	15 mg/kg/IV bolus, then 10 mg/kg IV q12h × 4 doses, then 15 mg/kg IV q12h until ethylene glycol or methanol level <20	Headache, nausea, bradycardia, hypotension, dizziness, metallic taste
Foscarnet	60 mg/kg IV q8h or 90 mg/kg IV q12h	Nephrotoxicity, electrolyte abnormalities (hypocalcemia, hypomagnesemia, hypokalemia, hypophosphatemia), nausea, vomiting, diarrhea, headache
Fosphenytoin 75 mg of fosphenytoin = 50 mg of phenytoin	Loading dose; 15–20 mgPE/kg IV Maintenance; 4–6 mg phenytoin equivalent (PE)/kg/day in two to three divided doses	IV form: hypotension, bradycardia, phlebitis, nystagmus, rash

(continued)

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Furosemide	20–80 mg/day IV/PO in two to three divided doses	Hypotension, blurred vision, cutaneous vasculitis, gout, hyperglycemia, anorexia, allergic interstitial nephritis, fall in GFR, increased blood urea
Ganciclovir	5 mg/kg IV q12h	Fever, rash, abdominal pain, nausea, vomiting, anemia, leucopenia, thrombocytopenia, confusion, neuropathy, pruritus, paresthesia, retinal detachment
Gemifloxacin	320 mg PO q24h	Headache, dizziness, rash
Gentamicin	3 mg/kg bolus, then 2 mg/kg IV q8h or 5–7 mg/kg extended interval (q24h to q12h or divided dose)	Vertigo, ataxia, gait instability, ototoxicity, nephrotoxicity, edema, pruritus
Glutamine	5 g 6 hourly orally	Increase in AST and ALT
	0.3–0.4 g/kg body weight IV	
Haloperidol	0.5–5 mg 2–3 times/day/max 30 mg IV/PO 2–10 mg IV bolus, repeat bolus every 15–30 mins with sequential doubling of dose	CNS depression, orthostatic hypotension, arrhythmia, alopecia, extrapyramidal symptoms, neuroleptic malignant syndrome, cholestatic jaundice
Heparin	Prophylaxis: 5,000 units 8–12 hourly	Bleeding, hyperkalemia, cutaneous necrosis, elevated liver enzymes, peripheral neuropathy
	Therapeutic: 60 units/kg bolus f/b 12 units/kg/h infusion maximum 1,000 units/h	
Hydralazine	10–40 mg IV q4–6h or 10–75 mg PO q8h/q6h	Hypotension, tachycardia, flushing, headache
Hydrocortisone	Septic shock: 200–300 mg/day in three to four divided doses or as continuous infusion	Hyperglycemia, mood changes, insomnia, gastrointestinal irritation, increased appetite, GI bleed, hypokalemia,
		Long-term: osteoporosis, acne, fat redistribution, muscle wasting, cataracts, increased blood pressure, infection
Hypertonic saline (23.4% NaCl)	For mannitol refractory patients: 3–50 mL q3–6h as needed (central line only), 0.686 mL of 23.4% saline is equimolar to 1 g of mannitol	Hypernatremia, hyperchloremia, fluid overload, pulmonary edema

(continued)

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Ibuprofen	200–800 mg PO q3–6h	Edema, dizziness, itching, fluid retention, dyspepsia, tinnitus, hypocalcemia
Ilioprost	2.5–5 mcg inhaled six to nine times daily	Flushing, hypotension, headache, nausea, trismus, cough, flu-like syndrome, jaw pain, syncope, hemoptysis
Imipenem + cilastatin	500 mg to 1 g IV q6–8h	Tachycardia, seizure, oliguria, nausea, diarrhea
Immune globulin (intravenous)	IV 0.4 g/kg/day for 5 days	Allergic reaction, anaphylaxis, chest tightness, edema, flushing, anxiety, chills, pruritus, bronchitis, abnormal liver function tests
Ipratropium	2–4 puffs (15 mcg/actuation) q12h to q6h Nebulised: 500 mcg 3–4 times/day	Bronchitis, upper respiratory tract infection, palpitation, dizziness, rash, nausea
Isoprenaline	Up to 20 mcg/min IV infusion, titrate according to heart rate	Tachycardia, arrhythmia, angina, hypotension
Isosorbide dinitrate	5–40 mg PO q8h	Hypotension, headache, dizziness, flushing
Isosorbide mononitrate (Extended Release)	30–120 mg PO q24h	Hypotension, headache, dizziness, flushing
Itraconazole	200 mg IV/PO q24h	Pruritus, nausea, vomiting, chills
Ketorolac	15–30 mg IV q6h 20 mg PO f/b 10 mg q6–8h	Headache, abdominal pain, dyspepsia, nausea, edema, drowsiness, diarrhea
Labetalol	100–400 mg PO q8–12h (max 2.4 gm/day) 20–40 mg IV (maximum 80 mg) as bolus at 10–20 min intervals (Max 300 mg), then 0.5–2 mg/min infusion if needed	Dizziness, hypotension, bradycardia, nausea, vomiting, transaminase increase, paresthesia, flushing, headache
Lactulose	20–30 g (30–45 mL) PO q2h until initial stool, then adjust to maintain two to three soft stools/day	Diarrhea, flatulence, nausea
Lansoprazole	30–60 mg PO q12–24h	Headache, abdominal pain, nausea, diarrhea
Lepirudin	0.5 mg/kg IV loading over 5 min as a loading dose (0.2 mg in renal failure) 0.15 mg/kg/h continuous IV infusion adjust based on aPPT measurements	Bleeding

(continued)

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Levalbuterol	adjust based on aPPT measurements 0.63–0.125 mg q8h 2–4 puff TID (45 mcg/actuation)	Hyperglycemia, hypokalemia, tremors, rhinitis, viral infection, headache, migraine, rash, abdominal cramps
Levetiracetam	500–1,000 mg IV/PO q12h	Behavior changes, somnolence, nausea, vomiting, anorexia, weakness, cough, facial edema, bruising
Levofloxacin	500–750 mg IV/PO q24h	Chest, pain, edema, nausea, vomiting, dyspnea, pharyngitis, rash, CNS stimulation, seizure, dizziness, somnolence
Levosimendan	Loading dose (may be omitted) 6–12 mcg/kg given over 10 min	
	0.1 mcg/kg/min continuous infusion	
Levothyroxine	50–100 mcg IV	Angina, arrhythmia, MI, palpitations, tachycardia, anxiety, headache, hyperactivity, insomnia, alopecia, tremors
	Q6–8h × 24 h, then 100 mcg IV q24h	
Lidocaine	1–1.5 mg/kg IV bolus (may repeat doses 0.5–0.75 mg/kg in 5–10 min up to maximum 3 mg/kg), then 1–4 mg/min	Arrhythmia, bradycardia, heart block, hypotension, edema, flushing, anxiety, hallucinations, seizures
Linezolid	600 mg IV/PO q12h	Headache, diarrhea, insomnia, rash, nausea, constipation, thrombocytopenia, anemia, leucopenia, abnormal liver tests
Liothyronine	200–500 mcg (in myxedema coma)	Tachycardia, arrhythmia
Lisinopril	2.5–40 mg PO q24h	Hypotension, dizziness, abnormal taste, cough, worsening renal function
Lorazepam	Status epilepticus: 4 mg IV bolus, 0.5–4 mg/h	Sedation, hypotension, confusion, dermatitis, rash
	Sedation: 0.02–0.06 mg/kg bolus	
	Infusion: 0.01–0.1 mg/kg/h	
Magnesium sulphate	4–6 g IV over 15–20 min, then 2 g/h infusion (1 gm of Mg So_4 = 98.6 mg of elemental Mg = 8.12 meq of elemental magnesium)	Hypermagnesemia, diarrhea (oral)
Mannitol (10–20%)	1–1.5 g/kg IV bolus, then 0.25–1 g/kg q3–6h as needed	Hypotension, acute renal failure, fluid and electrolyte imbalances

(continued)

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Meropenem	1 g IV q8h	Headache, rash, diarrhea, anemia, phlebitis, agranulocytosis, TEN, glossitis
Methimazole	Initial 30–60 mg/day in three divided doses q8h, maintenance 5–30 mg/day PO	Vasculitis, CNS stimulation, alopecia, agranulocytosis
Methylprednisolone	Pulse therapy: 15–30 mg/kg/day for 3 days IV Spinal cord injury: 30 mg/kg over 15 min IV f/b 5.4 mg/kg/h for 23 h (Unlabelled use)	Hypertension, arrhythmia, insomnia, seizure, psychosis, hirsutism, adrenal suppression, diabetes mellitus, hypokalemia, hyperglycemia, peptic ulcer, pancreatitis, osteoporosis, muscle weakness
Metoclopramide	10 mg PO/IV q8h to q6h	Bradycardia, AV block, CHF, drowsiness, dystonic reaction, rash, agranulocytosis, bronchospasm
Metoprolol	IV: 5 mg every 2 min for three doses f/b 50 mg orally q6h for 48 h, then 100 mg q12h	Bradycardia, hypotension, syncopy, Raynaud's disease, dizziness, fatigue, bronchospasm, diarrhea, rash
Metronidazole	500 mg IV/PO q8h	Nausea, vomiting, metallic taste, disulfiram-like reaction
Micafungin	50–150 mg IV q24h	Headache, hypokalemia, hypocalcemia, leucopenia, neutropenia, transaminase increase, rigors
Midazolam	1–5 mg bolus, 1–10 mg/h, 0.2 mg/kg bolus, then 0.75–10 mcg/kg/min	Sedation, hypotension, confusion, dermatitis, rash
Milrinone	50 mcg/kg/bolus, then 0.25–0.75 mcg/kg/min	Hypotension, arrhythmia
Morphine sulphate	2.5 mg IV q3–4h Infusion: 1–10 mg/hr	Constipation, dyspepsia, nausea, drowsiness, dizziness
Moxifloxacin	400 mg IV/PO q24h	
Naloxone	0.4–2 mg IV q2min, up to 10 mg	Narcotic withdrawal
Neomycin	500–2,000 mg PO q6–12h	Nausea, vomiting, diarrhea, irritation or soreness of mouth or rectal area
Neostigmine	2.5 mg IV bolus, may be repeated in 3 h	Sweating, salivation, abdominal cramps, diarrhea, bradycardia
Nesiritide	2 mcg/kg bolus, then 0.01–0.03 mcg/kg/min	Hypotension, increased serum creatinine, arrhythmia

(continued)

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Nicardipine	3–15 mg/h IV infusion PO: 20 mg q8h	Hypotension, tachycardia, headache, flushing, peripheral edema
Nifedipine (Immediate release) Extended Release	30 mg once daily PO up to 30 mg q8h 30–120 mg PO q24h	Hypotension, tachycardia, headache, flushing, peripheral edema
Nimodipine	60 mg q6h to q4h orally in subarachnoid hemorrhage	Hypotension Elevated liver enzyme
	1–2 mg/h in hypertensive emergencies.	
Nitric oxide	5–40 ppm inhalation	Hypotension, flushing, rashes, withdrawal syndrome
Nitroglycerin	10–200 mcg/min IV infusion	Nausea, vomiting, headache, hypotension, tachycardia, thiocyanate and cyanide toxicity
Nitroprusside	Usual, 0.25–3 mcg/kg/min, maximum 10 mcg/kg/min	Nausea, vomiting, hypotension, tachycardia, thiocyanate and cyanide toxicity
Norepinephrine	0.02–3 mcg/kg/min IV infusion	Hyperglycemia, bradycardia, skin necrosis, arrhythmia
Octreotide	25–50 mcg IV bolus, then 25–50 mcg/h infusion	Diarrhea, flatulence, nausea, abdominal cramps, bradycardia, dysglycemia
	50–100 mcg SC q8h	
Ofloxacin	200–400 mg PO q12h	Chest pain, headache, rash, diarrhea, visual disturbance, pharyngitis
Omeprazole	20–40 mg PO/IV q12–24h/IV infusion 8 mg/hr	Headache, dizziness, rash, vomiting, taste perversion
Ondansetron	8–10 mg PO/q24h/q12h	Headache, malaise, drowsiness, fever, pruritus, diarrhea
Oseltamivir	Prophylaxis: 75 mg PO q24h	Vomiting, nausea, abdominal pain, allergy, anaphylaxis
	Treatment: 75 mg PO q12h	
Oxacillin	2 g IV q4–5h	Headache, rash, diarrhea, anemia, phlebitis, agranulocytosis, TEN, glossitis
Pamidronate	60–90 mg IV	Renal failure, allergic reaction, hypotension
Pancuronium	50–100 mcg/kg IV bolus f/b 1–2 mcg/kg/min IV infusion	Tachycardia, hypertension
Pantoprazole	20–40 mg PO q12–24h, 80 mg IV bolus, then 8 mg/h × 72 h	Chest pain, headache, rash, diarrhea, visual disturbance, pharyngitis

(continued)

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Pentamidine	Treatment PCP: 4 mg/kg IV q24h for 14–21 days Prophylaxis PCP: 300 mg/dose monthly inhalation	Renal failure, leucopenia, thrombocytopenia, pancreatitis, hypoglycemia
Phenobarbital	20 mg/kg IV bolus	Sedation, nystagmus, ataxia, nausea, vomiting
		IV form: hypotension, bradycardia, respiratory depression
Phentolamine	2–5 mg IV bolus	Hypotension, tachycardia, dizziness
	0.1–2 mg/min IV infusion	
Phenylephrine	0.5–10 mcg/kg/min	Arrhythmia, hypertension, chest pain
Phenytoin	20 mg/kg IV bolus, then 5–6 mg/kg/day PO/IV	Concentration-dependent: nystagmus, diplopia, ataxia, sedation, lethargy, mood/behavior changes, coma, seizures
Phosphate salts (over 6 hours IV infusion)	0.08–0.16 mmol/kg	Hyperphosphatemia
Vitamin K	1–10 mg PO, SQ, or IV q24h	Hemolysis in G6PD deficiency
Piperacillin/tazobactam	3.375–4.5 g IV q6h	Diarrhea, hypertension, insomnia, rash, transaminase increase, moniliasis, fever
Polymyxin B	15,000–25,000 units/kg/day in two divided doses	Neurotoxicity, nephrotoxicity, neuromuscular blockade, respiratory arrest
Potassium chloride	Daily requirement: 40–80 mEq/day	Rash, hyperkalemia, thrombophlebitis, abdominal pain, constipation (oral)
	Deficiency correction: 10 mEq/h infusion, maximum 40 mEq/h for first 3–4 h	
Potassium iodide	50–100 mg 1–2 drops or 0.05–0.1 ml PO q8–12h	Metallic taste, nausea, stomach upset, diarrhea, salivary gland swelling
Procainamide	15–18 mg/kg bolus, then 1–4 mg/min infusion	Hypotension, rash, diarrhea, nausea, vomiting
Propofol	Bolus: 0.5–3 mg/kg over 3–5 min f/b 5–50 mcg/kg/min infusion	Hypotension, bradycardia, arrhythmia, CNS depression, apnea, hypertriglyceridemia, thrombophlebitis
Propranolol	40 mg PO q12h, maximum 640 mg/day	AV conduction disturbance, cardiogenic shock, Raynaud's syndrome, psychosis, alopecia, anorexia, impotence, agranulocytosis

(continued)

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Propylthiouracil	Initial 300 mg PO in three divided doses q8h, maintenance 50–300 mg/day	Vasculitis, CNS stimulation, alopecia, agranulocytosis
Prostacyclins Epoprostenol	1–20 ng/kg/min	Jaw pain, nausea, headache, flushing, hypotension, infusion-site pain
Protamine	10 mg IV is required to neutralize 1,000 units of unfractionated heparin in previous 15 min	Hypersensitivity, hypotension
Pyridostigmine	60–240 mg PO q4h to q6h	Sweating, salivation, abdominal cramps
Quinupristin/dalfopristin	7.5 mg/kg IV q12hr	Hyperbilirubinemia, arthralgia, myalgia
Ramipril	1.25–5 mg PO q12h	Hypotension, dizziness, abnormal taste, cough, worsening renal function
Ranitidine	50 mg IV q8h	Hypersensitivity, bradycardia, thrombocytopenia, leucopenia reversible, transient rise in LFT
Rasburicase	0.2 mg/kg IV q24h × 5days	Nausea, vomiting, fever, headache, rash, diarrhea, constipation
Remifentanil	0.5–1 mcg/kg/min (Induction of anaesthesia)	Hypomagnesemia, bradycardia, hypotension
Reteplase	10 mg IV, then 10 mg IV 30 min after the first dose	Hypotension, bleeding, allergic reactions
Rifampicin	10 mg/kg/day PO q24h, maximum 600 mg/day	Edema, flushing, ataxia, pemphigoid reaction, adrenal insufficiency, agranulocytosis, hepatitis, myalgias, acute renal failure
Rocuronium	Intubation: 0.6–1.2 mg/kg Maintenance: 0.01–0.012 mg/kg/min infusion	Hypotension/hypertension, arrhythmia, acute quadriparetic myopathy, bronchospasm
Rifaximin	400 mg PO q8h	Headache
Sildenafil	20 mg PO q8h (Pulmonary hypertension)	Headache, dyspepsia, flushing, dizziness, diarrhea, anemia, leucopenia, abnormal vision
Sodium bicarbonate (7.5–8.4%)	0.3 × weight (kg) × base deficit (meq/L) = desired increase in sodium bicarbonate 7.5% (8.92 meq/10 ml) 8.4 % (10 meq/10ml)	Metabolic alkalosis, hypernatremia, hypokalemia, fluid overload, tetany

(continued)

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Sodium valproate	10 mg/kg IV bolus, then IV infusion 1–4 mg/kg/hour up to 2.5 g/day	
	Oral: 20–30 mg/kg/day in 2–4 divided doses	
Spironolactone	12.5–200 mg PO q24h	Hyperkalemia
Streptokinase	1.5 million units over 2 h IV infusion	Allergic reactions, hypersensitivity reactions, hypotension, bleeding
Suxamethonium	1.0–1.5 mg/kg IV bolus Rapid sequence intubation	Hyperpyrexia, muscle pain, hyperkalemia
Teicoplanin	400 mg 12 hourly for three doses IV, then 400 mg q24h IV	Raised LFT, hypersensitivity
Tenecteplase	One-time bolus over 5 seconds:	Hypotension, bleeding, allergic reactions
	≤60 kg = 30 mg	
	61–70 kg = 35 mg	
	71–80 kg = 40 mg	
	81–90 kg = 45 mg	
	≥90 kg = 50 mg	
Terlipressin	Hepatorenal syndrome: 0.5–1 mg q6h IV	Hypertension, abdominal cramps
	Varices: 2 mg IV bolus, then 1–2 mg q4–6h IV	
Theophylline	Bolus: 5 mg/kg if no theophylline received in the previous 24 hours	Arrhythmia, headache, seizure, nervousness, nausea, diarrhea, tremor, muscle cramp
	Maintenance: 0.7 mg/kg/h	
Thiopental	2.5–4 mg/kg IV bolus for seizure control	Apnea, bronchospasm, hypersensitivity
Thiourea drugs	Initial 300–600 mg q24h PO	Rash, arthralgias, fever, leucopenia, nausea, vomiting
Ticarcillin/clavulanate	3.1 g IV q4–6h	Diarrhea, hypertension, insomnia, rash, transaminase increase, moniliasis, fever
Tigecycline	100 mg bolus, then 50 mg IV q12h	Nausea, hypertension, peripheral edema, phlebitis, fever, headache, insomnia, pruritus, hyperglycemia, hyperproteinemia, hyperkalemia, thrombocytopenia, leukocytosis, hepatic dysfunction, neuromuscular weakness
Tirofiban	0.4 mcg/kg/min × 30 min, then 0.1 mcg/kg/min (In unstable angina) 0.4 mcg/kg/min × 3 min, then 0.1 mcg/kg/min (In PCI)	Bleeding, bradycardia, coronary artery dissection, dizziness, vasovagal reaction, thrombocytopenia

(continued)

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Torsemide	10–20 mg IV/PO daily Maximum: 200 mg (PO, IV)	Arrhythmia, chest pain, headache, ototoxicity, dizziness, hyperglycemia, hyperuricemia, hypokalemia
Valproate	1,000–2,500 mg/day IV/PO q12h to q6h Maintenance Loading (in status epilepticus): 15–45 mg/kg IV at <6 mg/kg/min Infusion (in status epilepticus): 1–4 mg/kg/hr	Somnolence, diplopia, nausea, vomiting, diarrhea
Vancomycin	Loading (In severe infection): 25–30 mg/kg f/b 15–20 mg/kg IV q8–12h 125–500 mg PO in C. difficile diarrhea	Bitter taste, nausea, vomiting, chills, fever, eosinophilia, interstitial nephritis, vasculitis, thrombocytopenia, red man syndrome
Vasopressin	40 units IV bolus 0.01–0.04 U/min IV infusion (in refractory septic shock) 0.2–0.4 U/min IV infusion (in variceal hemorrhage)	Arrhythmia, asystole, decreased cardiac output, chest pain, MI, peripheral ischemia, venous thrombosis, urticaria, mesenteric ischemia
Verapamil	5 mg bolus (may repeat up to total 20 mg)	Gingival hyperplasia, constipation, bradycardia, heart block, hypotension, rash, alopecia, bronchospasm
Voriconazole	6 mg/kg for two doses q12h, fist day f/b 4 mg/kg IV q12h	Photophobia, agranulocytosis, thrombocytopenia, anemia, diarrhea, vomiting, hallucinations, tachycardia, hyper/hypotension, raised liver enzymes, cholestatic jaundice
Warfarin	Initial 1–5 mg PO q24h, adjust based on INR measurements	Bleeding, angina, chest pain, hypotension, alopecia, skin necrosis, agranulocytosis, purple toe syndrome

Table A.2 Dosage modification in renal failure

Medication	Dose for normal renal function	Dose with impaired renal function (GFR mL/min/1.73 m^2)			Supplemental dose in dialysis	
		30–50	10–29	<10	Hemodialysis (HD)	Peritoneal dialysis (PD)
Antimicrobials						
Acyclovir	PO: 80 mg/kg/day, divided q6h IV: 30 mg/kg/day	10 mg/kg, q12h	10 mg/kg, q24h	5 mg/kg, q24h	Yes CVVHD/CVVHDF: 10 mg/kg q12–24h	No
Amikacin	5–7.5 mg/kg/dose, q8–12h or 15–20 mg/kg IV OD	5–7.5 mg/kg, q12–18h	5–7.5 mg/kg, q24h	5–7.5 mg/kg, q48–72h	Yes CVVHD/DF: Loading dose 10 mg/kg f/b maintenance 7.5 mg/kg q24–48h	Yes
Amphotericin B (conventional)	0.5–1.5 mg/kg IV, q24h	No change	No change	No change	No	No
Ampicillin	100–200 mg/kg/day, divided q6h	No change	Usual dose q6–12h	Usual dose q12–24h	Yes CVVHD/DF: Loading Dose 2 gm followed by 1–2 gm q6–8h	No
Amoxicillin	20–50 mg/kg/day IV/PO, divided q8h	No change	10–20 mg/kg/dose, q12h	10–20 mg/kg/dose, q24h	Yes	No
Azathioprine	1–3 mg/kg, q24h PO	Reduce dose by 25%	Reduce dose by 25%	Reduce dose by 50%	Yes	Yes
Azithromycin	10 mg/kg/day PO/IV	No change	No change	No change	No	No
Caspofungin	70 mg on day 1, then 50 mg IV, q24h	No change	No change	No change	No	No
Co-amoxiclav	IV/PO: 10–20 mg/kg, q8h	No change	Increase interval, q12h	Increase interval, q24h	Yes	No
Cefaclor	20–40 mg/kg/day IV, divided q8–12h	No change	No change	Reduce dose by 50%; divided q12h	Yes	No
Cefepime	50 mg/kg/dose IV, q12h	50 mg/kg/dose, q24h	50 mg/kg/dose, q24h	50 mg/kg/dose, q48h	Yes CVVHD/DF: Loading dose 2 gm f/b 2 gm q12h	No
Cefixime	8–10 mg/kg/day, divided q12h PO	No change	Reduce daily dose by 25%	Reduce daily dose by 50%	Yes	No

Cefotaxime	100–200 mg/kg/day IV, divided 6–8 h	50 mg/kg/dose q8–12h	50 mg/kg/dose, q12h	50 mg/kg/dose, q24h	Yes CVVHD/DF: 1–2 gm q6–8h	No
Ceftazidime	100–150 mg/kg/day IV, divided 8 h	50 mg/kg/dose, q12h	50 mg/kg/dose, q24h	50 mg/kg/dose, q48–72h	Yes CVVHD/DF: loading dose 2 gm f/b 2gm q12h	Yes
Ceftriaxone	75–100 mg/kg/day IV, divided q12–24h	No change	No change	No change	No	No
Cefuroxime	PO: 20–30 mg/kg/day, divided q12h IV: 50–100 mg/kg/day, divided q8h	No change	50 mg/kg/dose, q12h	50 mg/kg/dose, q24h	Yes CRRT 1 gm q12h	No
Cephalexin	30–50 mg/kg/day PO, divided q6h	5–10 mg/kg/dose, q8h	5–10 mg/kg/dose, q12h	5–10 mg/kg/dose, q24h	Yes	No
Cefoperazone	100 mg/kg/day IV, divided 12 h	No change	No change	No change	Yes	No
Cefoperazone/ sulbactam	30–60 mg/kg/day (total), 10–20 mg/kg/day of sulbactam IV	No change	50% dose of sulbactam	25% dose of sulbactam	Yes	No
Ciprofloxacin	PO: 20 mg/kg/day, divided q12h IV: 10 mg/kg/day, divided q12h	No change	q12–24h	q24h	Yes CVVHD/DF: 200–400 mg q12–24h	Yes
Co-trimoxazole	6–10 mg/kg/day (TMP), IV/PO divided q12h	No change	5–10 mg/kg/dose, q12h	Not recommended	Yes	No
Daptomycin	6 mg/kg/dose IV, q24h	No change	4 PO/IV/kg/dose, q24h	4 mg/kg/dose, q48h	No CVVHD: 8 mg/kg q48h	No
Erythromycin	30–50 mg/kg/day IV/PO, q6–8h	No change	No change	50% dose	No	No
Fluconazole	6–12 mg/kg IV/PO, q24h	Reduce dose by 50%	Reduce dose by 50%	Reduce dose by 50%	Yes CVVHD/DF Loading Dose: 400–800 mg f/b 400–800 mg q24h	No

(continued)

Table A.2 (continued)

Medication	Dose for normal renal function	Dose with impaired renal function (GFR mL/min/1.73 m^2)			Supplemental dose in dialysis	
		30–50	10–29	<10	Hemodialysis (HD)	Peritoneal dialysis (PD)
Gentamicin	2–2.5 mg/kg IV, q8h	q12h	q18–24h	q24–48h	Yes CVVHD/DF 1.5–2.5 mg/kg q24–48h (9 redose when concentration <3–5 mg/l)	Yes
Imipenem Cilastatin	60–100 mg/kg/day IV, divided q6h; maximum daily dose 4 g	20 mg/kg, q8h	10 mg/kg, q12h	10 mg/kg, q12h	Yes CRRT: Loading dose 1 gm f/b 500 mg q6h	No
Itraconazole	3–10 mg/kg/day PO, q24h	No change	No change	No change	No	No
Linezolid	10 mg/kg/dose PO/IV, q8h	No change	No change	No change	Yes	Yes
Lamivudine	4 mg/kg, q12h PO	4 mg/kg, q24h	2 mg/kg, q24h	1 mg/kg, q24h	Yes	No
Metronidazole	20–25 mg/kg/day IV/PO, divided q8h	No change	No change	Reduce daily dose by 50%	No	No
Meropenem	60–120 mg/kg/day IV, divided q8h	20–40 mg/kg, q12h	10–20 mg/kg, q12h	10–20 mg/kg, q24h	Yes CRRT: Loading dose of 1 gm f/b 1 gm q8–12h	10–20 mg/kg q24h
Netilmicin	4–7.5 mg/kg IV, divided q8–12h	2 mg/kg, q12h	2 mg/kg, q12h	2 mg/kg, q24–48h	Yes	Yes
Ofloxacin	15 mg/kg/day IV/PO, q12h	7.5 mg/kg/dose, q24h	7.5 mg/kg/dose, q24h	7.5 mg/kg/dose, q48h	Yes	No
Penicillin G	50,000–200,000 U/kg/day IV, divided q4–6h	No change	Reduce daily dose by 25%, divided q8–12h	Reduce daily dose by 50%, divided q12–16h	Yes	No
Piperacillin/tazobactam	150–300 mg/kg/day IV, divided q6–8h	Reduce dose by 30%, q6h	Reduce dose by 30%, q8h	Reduce dose by 30%, q8h	Yes CRRT: 2.25–3.375 gm q6h	No
Teicoplanin	10 mg/kg IV, q12h for 3 doses IV, then 10 mg/kg IV, q24h	Normal loading dose, then 1–4 mg/kg, q24h	Normal loading dose, then 1–4 mg/kg, q24h	Normal loading dose, then 1 mg/kg, q24h	No	No
Tobramycin	2.5 mg/kg/dose, q8h	q12h	q24h	q48h	Yes	Yes
Valganciclovir	450 mg/m^2/day or 30 mg/kg/day q24h	50%	25%	25%		Yes
Vancomycin	10–15 mg/kg IV, q6–8h	10 mg/kg, q12h	10 mg/kg, q24h	10 mg/kg, q48–72h	No	No

Voriconazole	6 mg/kg/dose IV/PO, q12h on day 1, then 4 mg/kg, q12h	No change	No change	No change		Yes
Miscellaneous						
Allopurinol	10 mg/kg/dose PO, q24h	Reduce dose by 50%	Reduce dose by 50%	Reduce dose by 75%	Yes	Yes
Amlodipine	0.05–0.15 mg/kg/day PO	No change	No change	No change	No	No
Aspirin	1–5 mg/kg/day PO	No change	No change	Avoid	Yes	Yes
Atenolol	1–3 mg/kg PO, q24h	Normal dose	50% dose, q24h	50% dose, q48h	Yes	No
Cyclosporine	3–6 mg/kg/day	No change	No change	No change	No	No
Digoxin	6–10 μg/kg/day	75% dose	50% dose	25% dose	No	No
Enalapril	0.1–1 mg/kg/day	75% dose	75% dose	50% dose	Yes	No
Enoxaparin	1 mg/kg/day, q12–24h	No change	70% dose	50% dose, q24h	No	No
Furosemide	1–6 mg/kg/day divided PO 6–12 h	No change	No change	No change	No	No
Heparin	50–200 U bolus f/b 20 U/kg/h	No change	No change	50% dose	No	No
Hydrochlorothiazide	2 mg/kg/day, q12h	No change	Avoid	Avoid	Avoid	Avoid
Labetalol	5–20 mg/kg/day, q12h PO	No change	No change	No change	No	No
Metoclopramide	0.2–0.8 mg/kg/day, divided q6–8h	Reduce dose by 25%	Reduce dose by 50%	Reduce dose by 75%	Yes	No
Mycophenolate mofetil	600–1,200 mg/m^2/day	No change	No change	No change	No	No
Nitroprusside	0.3–8 μg/kg/min	No change	No change	No change	Yes	Yes
Prazosin	50–500 μg/kg/day	No change	No change	75% dose	No	No
Propanolol	0.5–4 mg/kg/day divided q6–8h	No change	No change	No change	No	No
Ramipril	6 mg/m^2, q24h	No change	50% dose	25% dose	No	NA
Ranitidine	PO: 3–6 mg/kg/day, divided q12h	Reduce dose by 25%	Reduce dose by 25%	Reduce dose by 50%	No	No
	IV: 2–4 mg/kg/day, divided q8h					

(continued)

Table A.2 (continued)

Medication	Dose for normal renal function	Dose with impaired renal function (GFR mL/min/1.73 m²)			Supplemental dose in dialysis	
		30–50	10–29	<10	Hemodialysis (HD)	Peritoneal dialysis (PD)
Tacrolimus	0.15 mg/kg/day	No change	No change	No change	No	No
Warfarin	0.1–0.3 mg/kg/day	No change	No change	No change	No	No
Antitubercular drugs						
Ethambutol	15–25 mg/kg, q24h	No change	Increase interval, q36h	Increase interval, q48h	Yes	No
Isoniazid	10–15 mg/kg/day, q12–24h	No change	No change	No change	Yes	Yes
Pyrazinamide	30 mg/kg, q24h	No change	50% dose	normal dose after HD, 3 weeks	Yes	Yes
Rifampicin	10–20 mg/kg/day, q12–24h	No change	No change	No change	No	No
Streptomycin	20–40 mg/kg, q12–24h IM	q24–72h	q24–72h	q24–72h	Yes	Yes
Anticonvulsants						
Carbamazepine	10–30 mg/kg/day, divided 8 h	No change	No change	No change	No	No
Clonazepam	0.05–0.5 mg/kg/day	No change	No change	75% dose	No	No
Lamotrigine	2 mg/kg/day in two single doses for 2 weeks, then 5 mg/kg for 2 weeks, then 5–15 mg/kg/day	No change	No change	75% dose	No	No
Levetiracetam	10–60 mg/kg/day, divided 8 h	50% dose	50% dose	50% dose	Yes	Yes
Phenobarbitone	5–8 mg/kg/day	No change	No change	50% dose	Yes	Yes
Phenytoin	5–8 mg/kg/day	No change	No change	No change	No	No
Topiramate	3–9 mg/kg/day, divided 8–12 h	50% dose	50% dose	25% dose	Yes	NA
Valproate sodium	10–60 mg/kg/day	No change	No change	No change	No	No

Appendix B

Common ICU Formulae

A. *Pulmonary equations*

1. *Arterial oxygen tension (PaO_2)*
   On room air = 100 − 1/3 (age)
   On supplemental oxygen = FiO_2 (in decimals) × 500, Room air FiO_2 = 21% (0.21), FiO_2 increases by approximately 4% for each litre increase in Supplemental Oxygen
2. *Alveolar gas equation*

$$PAO_2 = (FiO_2 \times [Patm - PH_2O]) - \left(\frac{PaCO_2}{R}\right)$$

$$PAO_2 = 150 - (1.25 \times PaCO_2)$$

   Normal = 100 mmHg (room air, at sea level)
   where PAO_2 = alveolar partial pressure of oxygen
   FiO_2 = fraction of inspired oxygen (in decimals)
   Patm = barometric pressure (760 mmHg at sea level)
   PH_2O = water vapor pressure (47 mmHg at normal body temperature 37°C)
   $PaCO_2$ = partial pressure of carbon dioxide in the blood
   R = respiratory quotient, assumed to be 0.8
3. *Alveolar–arterial oxygen gradient*
   $PAO_2 - PaO_2$
   A-a gradient (on room air) = 2.5 + 0.21 × age in years
   Normal value = 3–15 mmHg
   Varies with FiO_2
   For FiO_2 = 21%; A-a gradient = 5–15 mmHg
   For FiO_2 = 100%; A-a gradient = <150 mmHg
4. *PaO_2/FiO_2 ratio*
   Normal = 300–500 mmHg
   <300 = acute lung injury (previous definition)
   <200 = ARDS (previous definition)
   Berlin definition:
   200–300 (with PEEP/CPAP >5) = Mild ARDS
   <200 (with PEEP >5) = Moderate ARDS
   <100 (With PEEP >5) = Severe ARDS
5. *Arteriolar–alveolar oxygen ratio = PaO_2/PAO_2*
   Normal = 0.77–0.82 (most reliable when FiO_2 <0.5)
6. Oxygenation index =

$$\left[\text{mean airway pressure (cm } H_2O) \times \frac{FiO_{2(\text{fraction of inspired } O_2)}}{PaO_{2(\text{mm Hg})}}\right] \times 100,$$

   0 − 25 = Good outcome

   >25–40 = severe hypoxemia

7. *Static lung compliance (Crs stat)*

$$\text{Compliance}_{\text{static}} = \frac{\text{Tidal volume}}{\text{Plateau pressure} - \text{PEEP(positive end - expiratory pressure)}}$$

Normal compliance in an intubated patient = 57–85 mL/cm H_2O

8. *Dynamic lung compliance (Crs dynamic)*

$$\text{Compliance}_{\text{dynamic}} = \frac{\text{Tidal volume}}{\text{Peek pressure} - \text{PEEP(positive end - expiratory pressure)}}$$

Variable depending on peak pressure in an intubated patient
Lung + Thoracic wall compliance = 0.1 L (100 ml)/cm H_2O

9. *Airway resistance*

$$\text{Airway resistance} = \frac{\text{Peak inspiratory pressure} - \text{plateau pressure}}{\text{Peak inspiratory flow}}$$

Normal resistance in an intubated patient is 4–6 cm H_2O/L/s

10. ***$PaCO_2$–$PetCO_2$ gradient***
Normal = 4–5 mmHg

11. *Dead space ventilation* $\frac{V_D}{V_T} = \frac{PaCO_2 - PetCO_2}{PaCO_2}$

V_D = Dead Space Ventilation = 1ml/lb (2.2 kg) of ideal body wt = 150 ml
V_T = Tidal Volume

$PetCO_2$ = end-tidal CO_2 measured by capnography
Normal V_D/V_T = 0.5 (50%) in mechanically ventilated patients
0.3 (30%) in spontaneously breathing patients

12. *Shunt equation (right to left shunt)* $\text{Qs}/\text{Qt} = \frac{(CcO_2 - CaO_2)}{(CcO_2 - CvO_2)}$

Qs/Qt = shunt fraction
CcO_2 is the end-capillary oxygen content (estimated from the PAO_2)
CaO_2 is the arterial oxygen content
CvO_2 is the mixed venous oxygen content
Normal = 5%

Alternate equation (in patients breathing 100% oxygen for 20 min)

$$\text{Qs}/\text{Qt} = 100 \times (0.0031 \times \text{AaG}) / ((.0031 \times \text{AaG}) + 5)$$

13. *$PaO_2 + PaCO_2 < 150$ mmHg at sea level breathing room air*

B. *Hemodynamic equations*
(See Chap. 16)

Parameter	Formula	Normal range
Pulse pressure	Systolic – diastolic BP	40 mmHg
Mean arterial pressure (MAP)	1/3 pulse pressure + diastolic BP	65 mmHg
Cardiac output (CO)	SV × HR	4–7 L/min
Cardiac index (CI)	CO/BSA	3.5–4.5 L/min/m^2
Stroke volume (SV)	CO/HR × 1,000 End diastolic volume (EDV) (120 ml) – End systolic volume (ESV) (50 ml)	60–80 mL
Stroke volume index (SVI)	CI/HR × 1,000, SV/BSA	33–47 mL/m^2/beat
Systemic vascular resistance (SVR)	[(MAP – CVP)/CO] × 80	900–1,200 dyn.s/cm^5
Systemic vascular resistance index (SVRI)	(MAP – CVP) 80/CI	1,970–2,390 dyn.s/cm^5/m^2
Pulmonary vascular resistance	[(MPAP – PAOP)/CO] × 80	80–120 dyn.s/cm^5
Pulmonary vascular resistance index	[(MPAP – PAOP)/CI] × 80	255–285 dyn.s/cm^5/m^2
Oxygen delivery (DO_2)	CO (L) × CaO_2 (ml/dl) × 10	700–1,400 mL/min
Oxygen delivery index (DO_2I)	CaO_2 × CI × 10	500–600 mL/min/m^2
Oxygen consumption (VO_2)	CO (L) × (CaO_2 – CvO_2) × 10	180–280 mL/min
Oxygen consumption index (VO_2I)	CI × (CaO_2 – CvO_2) × 10	120–160 mL/min/m^2
Oxygen extraction ratio (O_2ER)	VO_2/DO_2 × 100	25%
Oxygen extraction index (O_2EI)	[(SaO_2 – SvO_2)/SaO_2] × 100	20–25%
Arterial oxygen content (CaO_2)	(1.39 × Hb SaO_2) + (0.003 × PaO_2)	17–20 mL/dL
Mixed venous oxygen content (CvO_2)	(1.39 × Hb × SvO_2) + (0.003 × PvO_2)	12–15 mL/dL
A-V oxygen content difference ($C(a\text{-}v)O_2$)	CaO_2 – CvO_2	4–6 mL/dL
Systolic pressure variation (SPV)	[(SPmax – SPmin)/(SPmax + SPmin)/2] × 100	<5 mmHg unlikely to be preload responsive >5 mmHg likely to be preload responsive
Pulse pressure variation (PPV)	(SVmax – SVmin)/[(SVmax + SVmin)/2] × 100	<10% unlikely to be preload responsive >13–15% likely to be preload responsive
Stroke volume variation (SVV)	SV × (MAP – PAWP) × 0.0136	<10% unlikely to be preload responsive >13–15% likely to be preload responsive
Left ventricular stroke work (LVSW)	SVI × (MAP – PAWP) × 0.0136	58–104 g m/beat

(continued)

Parameter	Formula	Normal range
Left ventricular stroke work index (LVSWI)	SV × (MPAP − RAP) × 0.0136	50–62 g m/m^2/beat
Right ventricular stroke work (RVSW)	SVI × (MPAP − RAP) × 0.0136	8–16 g m/beat
Right ventricular stroke work index (RVSWI)	Diastolic BP − PAWP	5–10 g m/m^2/beat
Coronary artery perfusion pressure (CPP)		60–80 mmHg

CVP central venous pressure, *MPAP* mean pulmonary artery pressure, *HR* heart rate, *BP* blood pressure, *PAOP* pulmonary artery occlusion pressure, SaO_2 arterial oxygen saturation, SvO_2 mixed venous oxygen saturation, PaO_2 arterial oxygen partial pressure, PvO_2, mixed venous oxygen partial pressure

C. *Acid–base equations*

1. *Validity of the data*
   Henderson's equation

$$\frac{H^+ \times HCO_3}{PaCO_2} = 24$$

H^+ = hydrogen ion
HCO_3 = Bicarbonate
$PaCO_2$ = Partial pressure of carbon dioxide

pH	[H^+] (mmol/L)
7.60	25
7.55	28
7.50	32
7.45	35
7.40	40
7.35	45
7.30	50
7.25	56
7.20	63
7.15	71

Rule of thumb: H^+ = 80 minus the last two digits of pH after decimal (for pH 7.20–7.50)
For example, pH 7.35: H^+ = 80–35 = 45

2. *Respiratory acidosis or respiratory alkalosis*
   - Acute respiratory acidosis or alkalosis: $\Delta pH = 0.008 \times \Delta PaCO_2$ (from 40)
   - Chronic respiratory acidosis or alkalosis: $\Delta pH = 0.003 \times \Delta PaCO_2$ (from 40)
   - Acute respiratory acidosis = $\uparrow PaCO_2$ 10 mmHg = $\uparrow HCO_3$ 1 mmol/L
   - Chronic respiratory acidosis = $\uparrow PaCO_2$ 10 mmHg = $\uparrow HCO_3$ 3 mmol/L
   - Acute respiratory alkalosis = $\downarrow PaCO_2$ 10 mmHg = $\downarrow HCO_3$ 2 mmol/L
   - Chronic respiratory alkalosis = $\downarrow PaCO_2$ 10 mmHg = $\downarrow HCO_3$ 4 mmol/L
   - Acute respiratory acidosis or alkalosis: SBE (standard base excess) = zero
   - Chronic respiratory acidosis or alkalosis: Change in bicarbonate = 0.4 × SBE

3. *Metabolic acidosis*
   - Predicted $PaCO_2 = 1.5 \times [HCO_3^- + 8] \pm 2$
   - Change in bicarbonate = change in standard base excess (SBE)
   - 1 mEq/L fall in HCO_3 = 1.2 mmHg fall in $PaCO_2$
   - Bicarbonate deficit (mEq/L) = [0.5 × body weight (kg) × (24 − $[HCO_3^-]$)]

   Rule of thumb: Expected $PaCO_2$ = the last two digits of pH after decimal
4. *Metabolic alkalosis*
   - Predicted $PaCO_2 = 0.7 \times [HCO_3 + 21] \pm 2$
   - Change in bicarbonate = 0.6 × standard base excess (SBE)
   - 1 mEq/L rise in HCO_3 = 0.7 mmHg rise in $PaCO_2$
   - Bicarbonate excess [0.4 × body weight (kg) × ($[HCO_3^-]$ − 24)]

   Rule of thumb: Expected $PaCO_2$ = the last two digits of pH after decimal
5. *Blood anion gap*
   - Anion gap (AG) = $Na^+ - (Cl^- + HCO_3^-)$
     - Normal value: 10 ± 4 mmol/L
   - Correction for albumin: For every change (increased or decreased) of 1 g/dL in albumin, a change of 2.5 mmol/L in the anion gap
   - Correction for pH: In acidosis, decrease by 2 mmol/L; in alkalosis, increase by 2 mmol/L
6. *Delta gap/Delta ratio*
   - Delta gap = *delta* AG − *delta* HCO_3^-
   - Delta ratio = *delta* AG/*delta* HCO_3
   - Where *Delta* AG = patient's AG − 12 mEq/L {normal AG}
   - *Delta* HCO_3^- = 24 mEq/L {normal HCO_3^-} − patient's HCO_3
   - Normal delta gap (in pure anion gap metabolic acidosis) = 0 ± 6
   - Normal delta ratio = 1.1
     - High delta gap/delta ratio > 1 signifies a concomitant metabolic alkalosis or chronic respiratory acidosis.
     - Low delta gap/delta ratio < 1 signifies a concomitant normal anion gap metabolic acidosis or chronic respiratory alkalosis.
7. *Urine anion gap (UAG)*
   - UAG (mmol/L) = urine [(Na + K) − Cl]
     - Normal: usually zero or positive
     - Nonanion gap metabolic acidosis due to gastrointestinal loss: UAG negative
     - Nonanion gap metabolic acidosis due to renal cause (renal tubular acidosis): UAG positive
8. *Stewarts approach*
   - Strong ion difference (SID): $[Na^+] + [K^+] + [Ca^{2+}] + [Mg^{2+}] - [Cl^-] - [lactate]$
     - Normal value: 40 mEq/L
     - Increase in SID = alkalosis (increase in pH)
     - Decrease in SID = acidosis (decrease in pH)
   - Strong ion gap (SIG): $SID - SID_{eff}$
     - SID_{eff} = effective strong ion difference (depends on pH, albumin, phosphate)

- $12.2 \times PCO_2/(10 - pH) + [albumin] \times (0.123 \times pH - 0.631) + [PO^{4-}] \times (0.309 \times pH - 0.469)$
- Normal SIG = 0
- Positive SIG = Increase in organic acid

D. *Electrolyte equations*

1. *Hyponatremia*
   - Sodium deficit = (desired $[Na^+]$ − current $[Na^+]$) × 0.6 × body weight in kg
   - Increase in serum sodium = (infusate sodium − serum sodium)/[(0.6 × body weight) + 1]

     Rule of thumb:
     - For hypertonic (3%) saline, infusion rate (mL/h) = weight (kg) × desired rate of correction (mEq/h)
     - e.g. to correct sodium by 0.5 meq/l/hr, the desired rate of 3% saline infusion in a 60 kg man would be = 60 × 0.5 = 30 ml/hr
     - 0.9% NaCl corrects at 1–2 mmol/L for every 1 L NaCl
   - Calculated urine osmolarity = the last two digits of urine-specific gravity × 30
2. *Hypernatremia*
   - $\text{Free water deficit (L)} = 0.4 \times \text{body weight} \times \left(\frac{\text{plasma Na}^+}{140} - 1 \right)$
3. *Correction sodium for hyperglycemia*
   - For each 100 mg/dL increase in blood glucose above 200 mg/dL, serum sodium decreases by 2.4 mEq/L.
4. *Serum osmolality*
   - Calculated Sosm = (2 × serum [Na]) + [glucose, in mg/dL]/18 + [blood urea nitrogen, in mg/dL]/2.8
   - Calculated Sosm with standard units (mmol/L) = (2 × serum [Na]) + [glucose] + [urea]
     - Normal value = 270 and 290 mOsm/kg H_2O
   - Osmolar gap = measured osmolality − calculated osmolality
     - Normal value = <10 mOsm/kg H_2O
5. *Corrected calcium*
   - Corrected calcium (mg/dL) = measured total calcium (mg/dL) + [0.8 × (4.0 − albumin)]
   - Corrected calcium (mmol/L) = measured total calcium (mmol/L)+ [0.02 × (Normal albumin [40 g/l] − patients albumin)]

E. *Renal equations*

1. *Measured creatinine clearance (CCr) L/day*
   - [24-h urine creatinine (mg/dL) × 24-h urine volume (L/day)]/serum creatinine (mg/dL)
   - CCr ml/min = [(CCr L/day × 1000 ml/L)]/1440 min/day
   - CCr ml/min × 1.73/BSA = CCr ml/min/1.73 sq.m
     - Normal values = 95 ± 20 mL/min per 1.73 m^2 in women and 120 ± 25 mL/min per 1.73 m^2 in men

2. *Estimated creatinine clearance (Cockroft–Gault equation)*
   - (140 - Age in years × Weight in kg) / Serum creatinine in mg/dl × 72
   - For female patient multiply with 0.85
3. *Fractional excretion of sodium ($FENa^+$)*

$$\frac{[\text{Urine}Na^+] \times [\text{plasma creatinine}]}{[\text{Urine creatinine}] \times [\text{plasma}Na^+]}$$

   – Normal value = <1
4. *Fractional excretion of urea (FEurea)*

$$\frac{[\text{Urineurea}] \times [\text{plasma creatinine}]}{[\text{BUN}] \times [\text{urinecreatinine}]}$$

   – <35 in prerenal azotemia, 50–65 in acute tubular necrosis

F. *Nutrition equations*
1. *Ideal or predicted body weight (IBW)*
   - Male IBW (kg) = 50 + (0.91 × (height in cm − 152.4))
   - Male IBW (kg) = 50 kg for 5 ft; add 2.3 kg for every 1 in. above 5 ft
   - Female IBW (kg) = 45.5 + (0.91 × (height in cm − 152.4))
   - Female IBW (kg) = 45.5 kg for 5 ft; add 2.3 kg for every 1 in. above 5 ft
2. *Harris–Benedict equation with Long's modification (calories requirement)*
   - For women, basal metabolic rate (BMR) = 65.5 + (9.6 × weight in kg) + (1.8 × height in cm) − (4.7 × age in years)
   - For men, BMR = 66 + (13.7 × weight in kg) + (5 × height in cm) − (6.8 × age in years)
   - Actual energy needs = BMR × AF × IF (AF, activity factor; IF, injury factor)
   - Activity factor (AF): Confined to bed = 1.2; out of bed = 1.3
   - Injury factor (IF): Minor surgery = 1.2; skeletal trauma = 1.3; major sepsis = 1.6; severe burn = 2.1
   - Normal calories requirement = 25–30 kcal/kg of predicted body weight
3. *Protein requirement*
   - 1 g of nitrogen = 6.25 g of protein
   - Non-protein calories (NPC)–nitrogen ratio = 150:1
   - Nitrogen balance = (protein intake/6.25) − (24-h urinary urea nitrogen + 4)
   - Negative nitrogen balance >5 = severe stress
   - 1 g of nitrogen loss = 30 g lean body mass lost
   - 1 g of glucose = 4 kcal
   - 1 g of protein = 4 kcal
   - 1 g of lipid = 9 kcal
   - Protein loss in dialysis = 4–6 g/h in hemodialysis; 40–60 g in peritoneal dialysis
4. *Respiratory quotient (RQ):*
   - Carbon dioxide production (VCO_2)/oxygen consumption (VO_2)
   - Normal value on balanced diet = 0.7–1.0
   - > 1: Excess carbohydrate
   - <0.7: Excess fat

G. *Intra-abdominal pressure equation*
- Abdominal perfusion pressure (APP) = mean arterial pressure (MAP) − IAP (intra-abdominal pressure)
- Normal intra-abdominal pressure = 5–7 mmHg
- Filtration gradient (FG) = glomerular filtration pressure (GFP) − proximal tubular pressure (PTP) = MAP − 2 × IAP

H. *Statistical equations*
- Sensitivity: True positives/(true positive [TP] + false negative [FN])
- Specificity: True negative/(true negative [TN] + false positive [FP])
- Positive predictive value: True positive/ (true positive + false positive)
- Negative predictive value: True negative/(true negative + false negative)
- Positive likelihood ratio (LR^+): sensitivity/(1 − specificity)
- Negative likelihood ratio (LR^-): (1 − sensitivity)/specificity
- Prevalence (pretest probability): (TP + FN)/(TP + FP + TN + FN)
- Pretest odds: Prevalence/(1 − prevalence)
- Posttest odds: Pretest odds × LR
- Posttest probability: Posttest odds/(posttest odds + 1)
- Event rate (ER): Total events/total subjects (event + nonevent)
- Absolute risk reduction (ARR): Control event rate (CER) − experimental event rate (EER)
- Relative risk reduction (RRR): (CER − EER)/CER
- Relative risk (RR): EER/CER
- Odds ratio: (experimental event [EE]/experimental nonevent [EN])/(control event [CE]/control nonevent [CN])
- Number needed to treat (NNT): 1/ARR
- Number needed to harm (NNH): 1/(CER − EER)
- Rate of Type I error = Number of False positives = Alpha
- Rate of Type II error = Number of False negatives = Beta
- Power of a test = (1-Beta)

I. *Neurology equations*
- CBF = (CAP − JVP) ÷ CVR
  (CBF, cerebral blood flow; CAP, carotid artery pressure; JVP, jugular venous pressure; CVR, cerebrovascular resistance)
- CPP = MAP − ICP
  (CPP, cerebral perfusion pressure; MAP, mean arterial pressure; ICP, intracranial pressure)
  – Keep CPP between 60 and 75 mmHg
- Increased WBC in traumatic tap:

Rule of thumb: Subtract one WBC for every 500–1,500 RBCs (if peripheral WBC is normal)

J. *Hematology equation*
- ANC = WBC × [(segs/100) + (bands/100)]
  (ANC, absolute neutrophil count)
- Corrected reticulocyte count $\left(\text{CRC}\right) = \dfrac{\text{reticulocytes (\%)}}{0.45\ \text{L/L}} \times \text{Hct}\ \left(\text{L / L}\right)$

Appendix C

Reference ranges for selected clinical laboratory tests

Substance	Fluid[a]	Traditional units	×	k	=	SI units
Acetoacetate	P, S	0.3–3.0 mg/dL		97.95		3–30 μmol/L
Alanine aminotransferase (ALT, SGPT)	S	7–41 U/L		0.016		0.12–0.70 μkat/L
Albumin	S					
Female Albumin	S	4.1–5.3 g/dL		10		41–53 g/L
Male Albumin	S	4.0–5.0 g/L		10		40–50 g/L
Albumin	CSF	11–48 mg/dL		0.01		0.11–0.48 g/L
Aldolase	S	1.5–8.1 U/L		17.33		26–138 nkat/L
Alkaline phosphate	S	(F) 30–100 U/L		0.016		0.5–1.92 μkat/L
		(M) 45–115 U/L				0.75–1.92 μkat/L
Alpha fetoprotein (adult)	S	0–8.5 ng/mL		1		0–8.5 μg/L
Ammonia, as NH_3	P	19–60 μg/dL		0.587		11–35 μmol/L
Amylase (method dependent)	S	20–96 U/L		0.016		0.34–1.6 μkat/L
Anion gap	S	7–16 mmol/L		1		7–16 mmol/L
Arterial blood gases						
$[HCO_3^-]$		22–30 mEq/L		1		22–30 mmol/L
PCO_2		32–45 mmHg		0.134		4.3–6.0 kPa
Ph		7.35–7.45		1		7.35–7.45
PO_2		72–104 mmHg		0.134		9.6–13.8 kPa
Aspartate aminotransferase (AST, SGOT)	S	12–38 U/L		0.016		0.20–0.65 μkat/L
B-type natriuretic peptide (BNP)	P	Age and gender specific: <167 pg/mL		1		Age and gender specific: <167 ng/L
Bilirubin	S					
Total (Bilirubin)		0.3–1.3 mg/dL		17.1		5.1–22 μmol/L
Direct (Bilirubin)		0.1–0.4 mg/dL		17.1		1.7–6.8 μmol/L
Indirect (Bilirubin)		0.2–0.9 mg/dL		17.1		3.4–15.2 μmol/L
β-Hydroxybutyrate	S	<1.0 mg/dL		96.05		<100 μmol/L
Bicarbonate	S	22–26 mEq/L		1		22–26 mmol/L
Blood urea nitrogen (BUN)	P, S	8–18 mg/dL		0.367		3.0–6.5 mmol/L
Calcium-Total	S	8.7–10.2 mg/dL		0.252		2.2–2.6 mmol/L
Calcium Ionized	WB	4.5–5.3 mg/dL		0.25		1.12–1.32 mmol/L
Carboxyhemoglobin (carbon monoxide content)	WB	>20%		0.01		>0.2 proportion of 1
– Nonsmokers		0–4%		0.01		0–0.04
– Smokers		4–9%		0.01		0.04–0.09
– Onset of symptoms		15–20%		0.01		0.15–0.20
– Loss of consciousness and death		>50%		0.01		>0.50

Reference ranges for selected clinical laboratory tests (continued)

Substance	Fluid[a]	Traditional units	×	k	=	SI units
Chloride	S	102–109 mEq/L		1		102–109 mmol/L
	CSF	120–130 mEq/L		1		120–130 mmol/L
	U	10–200 mEq/L		1		10–200 mmol/L
Cholinesterase	S	5–12 U/mL		1		5–12 kU/L
Complement						
C3	S	83–177 mg/dL		0.01		0.83–1.77 g/L
C4	S	16–47 mg/dL		0.01		0.16–0.47 g/L
Cortisol Fasting, 8 a.m.–12 noon 12 noon–8 p.m. 8 p.m.–8 a.m.	S	 5–25 μg/dL 5–15 μg/dL 0–10 μg/dL		 27.588 27.588 27.588		 138–690 nmol/L 138–414 nmol/L 0–276 nmol/L
Cortisol, free	U	20–70 μg/24 h		2.758		55–193 nmol/24 h
C-reactive protein	S	0.2–3.0 mg/L		1		0.2–3.0 mg/L
Creatine kinase (total) Females Males	S	 39–238 U/L 51–294 U/L		 0.017 0.017		 0.66–4.0 μkat/L 0.87–5.0 μkat/L
Creatine kinase-MB	S					
Mass		0.0–5.5 ng/mL		1		0.0–5.5 g/L
Fraction of total activity (by electrophoresis)		0–4.0%		0.01		0–0.04
Creatinine Female Male	S	 0.5–0.9 ng/mL 0.6–1.2 ng/mL		 88.4 88.4		 44–80 μmol/L 53–106 μmol/L
Creatinine	U	15–25 mg/kg/24 h		0.009		0.13–0.22 mmol/kg/24 h
Cyanide: Nontoxic	WB	<μg/dL		3.8		<19 μmol/L
Cyanide: Lethal		>30 μg/dL				>114 μmol/L
Erythropoietin	S	4–27 U/L		1		4–27 U/L
Fatty acids, free (nonesterified)	P	<8–25 mg/dL		0.0355		<0.28–0.89 mmol/L
Ferritin Female Male	S	 10–150 ng/dL 29–248 ng/mL		 1 1		 10–150 μg/dL 29–248 μg/L
Fibrinogen	P	150–350 mg/dL		0.01		1.5–3.5 g/L
Fibrin split products	S	<10 μg/mL		1		<10 mg/L
Glucose	P					
Glucose (fasting)	P	70–100 mg/dL		0.06		3.9–6.1 mmol/L
Glucose	CSF	50–80 mg/dL		0.06		2.8–4.4 mmol/L
Impaired glucose tolerance		111–125 mg/dL		0.056		6.2–6.9 mmol/L
Diabetes mellitus		>125 mg/dL		0.056		>7.0 mmol/L
Glucose, 2 h postprandial	P	70–120 mg/dL		0.056		3.9–6.7 mmol/L
Hemoglobin (Hb)	P	0.6–5.0 mg/dL		10		6–50 mg/L
Adult males (Hb)	WB	13.3–16.2 g/dL		10		133–162 g/L
Adult females (Hb)	WB	12–15.8 g/dL		10		120–158 g/dL

Reference ranges for selected clinical laboratory tests (continued)

Substance	Fluid[a]	Traditional units	×	k	=	SI units
Mean corpuscular hemoglobin (MCH)	WB	26–34 pg/cell		1		26–34 pg/cell
Mean corpuscular hemoglobin concentration (MCHC)	WB	33–37 g/dL		10		330–370 g/L
Mean corpuscular volume (MCV)	WB	80–100 μm^3		1		80–100 fL
Hemoglobin A_{1c}	WB	4.0–6.0%		0.01		0.04–0.06 Hb fraction
Homocysteine	P	4.4–10.8 µmol/L		1		4.4–10.8 µmol/L
Iron	S	41–141 µg/dL		0.178		7–25 µmol/L
Iron-binding capacity	S	251–406 µg/dL		0.179		45–73 µmol/L
Lactate	P, arterial	4.5–14.4 mg/dL		0.111		0.5–1.6 mmol/L
	P, venous	4.5–19.8 mg/dL		0.111		0.5–2.2 mmol/L
Lactate: Resting	P	<2.0 mEq/L		1		<2 mmol/L
Exercise		<4.0 mEq/L				<4 mmol/L
Lactate dehydrogenase	S	115–221 U/L		0.0171		2.0–3.8 µkat/L
Lipase	S	3–43 U/L		0.166		0.5–0.73 µkat/L
Magnesium	S	1.5–2.3 mg/dL		0.413		0.62–0.95 mmol/L
Methemoglobin	WB	0–1% of total Hb		0.01		0.0–0.01 proportion of total Hb
Microalbumin urine 24-h urine Spot urine	U	 0–30 mg/24 h 0–30 µg/mg creatinine		 0.001 0.001		 0.0–0.03 g/day 0.0–0.03 g/g creatinine
Myoglobin Male Female	S	 19–92 µg/L 12–76 µg/L		 1 1		 19–92 µg/L 12–76 µg/L
Osmolality	P	275–295 mOsm/kg serum water		1		275–295 mOsm/kg serum water
	U	500–800 mOsm/kg water		1		500–800 mOsm/kg water
Phosphatase, alkaline	S	33–96 U/L		0.0169		0.56–1.63 µkat/L
Phosphorus, inorganic	S	2.5–4.3 mg/dL		0.324		0.81–1.4 mmol/L
Potassium	S	3.5–5.0 mEq/L		1		3.5–5.0 mmol/L
Prealbumin	S	17–34 mg/dL		10		170–340 mg/L
Prolactin	S	0–20 ng/mL		1		0–20 g/L
Prostate-specific antigen (PSA) <40 years male >40 years male	S	 0.0–2.0 ng/mL 0.0–0.40 ng/mL		 1 1		 0.0–2.0 µg/L 0.0–0.4 µg/L
PSA, free; in males 45–75 years, with PSA values between 4 and 20 g/mL	S	>25% associated with benign prostatic hyperplasia		0.01		>0.25% associated with benign prostatic hyperplasia

Reference ranges for selected clinical laboratory tests (continued)

Substance	Fluid[a]	Traditional units	×	k	=	SI units
Protein fractions	S					
Albumin		3.5–5.5 g/dL (50–60%)		10		35–55 g/L
Globulin		2.0–3.5 g/dL (40–50%)		10		20–35 g/L
$Alpha_1$		0.2–0.4 g/dL (4.2–7.2%)		10		2–4 g/L
$Alpha_2$		0.5–0.9 g/dL (6.8–12%)		10		5–9 g/L
Beta		0.6–1.1 g/dL (9.3–15%)		10		6–11 g/L
Gamma		0.7–1.7 g/dL (13–23%)		10		7–17 g/L
Total protein	P, S	6.0–8.0 g/dl/L		10		60–80 g/L
	CSF	<40 mg/dL		0.01		<0.40 g/L
	U	<150 mg/24 h		0.01		<1.5 g/24 h
Sodium	S	136–146 mEq/L		1		136–146 mmol/L
Thyroid-stimulating hormone	S	0.34–4.25 μIU/mL		1		0.34–4.25 mIU/L
Thyroxine, free (fT_4)	S	0.8–1.7 ng/dL		12.871		10.3–21.9 pmol/L
Thyroxine, total (T_4)	S	5.4–11.7 μg/dL		12.871		70–151 nmol/L
Triiodothyronine (T_3)	S	75–220 pg/dL		0.015		12–3.4 pmol/L
Troponin I Normal population, 99% tile Cutoff for MI	S	 0–0.08 ng/mL >0.4 ng/mL		 1 1		 0–0.08 μg/L >0.4 μg/L
Troponin T Normal population, 99% tile Cutoff for MI	S	 0–0.01 ng/mL 0–0.1 ng/mL		 0.1 1		 0–0.1 μg/L 0–0.1 μg/L
Urea nitrogen	S	7–20 mg/dL		0.357		2.5–7.1 mmol/L
Uric acid Females Males	S	 2.5–5.6 mg/dL 3.1–7.0 mg/dL		 0.06 0.06		 0.15–0.33 μmol/L 0.18–0.41 μmol/L
Urobilinogen	U	1–3.5 mg/24 h		1.7		1.7–5.9 μmol/d

Adapted from the New England Journal of Medicine SI Unit Conversion Guide. Waltham, MA: Massachusetts Medical Society, 1992

[a]*P* plasma, *S* serum, *U* urine, *WB* whole blood, *CSF* cerebrospinal fluid, *RBC* red blood cell

Reference ranges for vitamins and trace elements

Substance	Fluid[a]	Traditional units	×	k	=	SI units
Chromium	S	0.14–0.15 ng/mL		17.85		2.5–2.7 nmol/L
Copper	S	70–140 μg/dL		0.16		11–22 μmol/L
Folate	RBC	140–960 ng/mL		2.26		317–2,196 nmol/L
Iron	S	(M) 80–180 μg/dL		0.18		(M) 14–32 μmol/L
		(F) 60–160 μg/dL				(F) 11–29 μmol/L

Reference ranges for vitamins and trace elements (continued)

Substance	Fluid[a]	Traditional units	×	k	=	SI units
Ferritin	P, S	(M) 20–250 ng/mL		1		(M) 20–250 μg/L
		(F) 10–120 ng/mL				(F) 10–120 μg/L
Manganese	WB	0.4–2.0 μg/dL		0.018		0.7–3.6 μmol/L
Pyridoxine	P	20–90 ng/mL		5.98		120–540 nmol/L
Riboflavin	S	2.6–3.7 μg/dL		26.57		70–100 nmol/L
Selenium	WB	58–234 μg/dL		0.012		0.7–2.5 μmol/L
Thiamine (total)	P	3.4–4.8 μg/dL		0.003		98.6–139 μmol/L
Vitamin A	P, S	10–50 μg/dL		0.349		0.35–1.75 μmol/L
Vitamin B_{12}	S	200–1,000 pg/mL		0.737		150–750 pmol/L
Vitamin C	S	0.6–2 mg/dL		56.78		30–100 μmol/L
Vitamin D	S	24–40 ng/mL		2.599		60–105 nmol/L
Vitamin E	P, S	0.78–1.25 mg/dL		23.22		18–29 μmol/L
Zinc	S	70–120 μg/dL		0.153		11.5–18.5 μmol/L

Adapted from the New England Journal of Medicine SI Unit Conversion Guide. Waltham, MA: Massachusetts Medical Society, 1992

[a]*P* plasma, *S* serum, *U* urine, *WB* whole blood, *CSF* cerebrospinal fluid, *RBC* red blood cell

Appendix D: Syllabus for ICU Training

Narendra Rungta and Arvind Kumar Baronia

1. General
   (a) ICU infrastructure: building, equipments and manpower
   (b) Organization of critical care services: models of intensive care and outreach services
   (c) Critical care physiology (system-wise)
   (d) Assessment of critically ill patients
   (e) Monitoring in the ICU
   (f) Principles of critical care pharmacology, Drug interactions and toxicity, Pharmacology of sedatives, hypnotic agents, analgesics and neuromuscular blocking agents
   (g) Pain management
   (h) Scoring system in the ICU
   (i) Enteral and parenteral nutrition
   (j) Care of ICU equipment-electrical safety, calibration, decontamination and maintenance
   (k) Intra and inter-hospital transport of critically ill patients
   (l) Basics of imaging modalities including ultrasound, x-ray, CT, MRI and Angiography in the ICU patients
   (m) Systemic disorders in critical illness
   (n) Obesity-hypoventilation syndrome and obstructive sleep apnea syndrome
2. Fluid and electrolytes
   (a) Fluid requirements in critically ill patients
   (b) Monitoring of fluid therapy and diagnosis of inappropriate fluid therapy i.e. fluid overload and hypovolemia

(c) Colloid versus crystalloid
(d) Electrolyte disturbances (calcium, magnesium, potassium, sodium and phosphorus) in ICU
(e) Hyperosmolar therapies-Hypertonic saline
(f) Acid-base disorders-Bicarbonate and Anion Gap, Base Deficit, Stewart approach
(g) Fluid therapy in children

3. Renal disorders
   (a) Acute kidney injury
   (b) Renal tubular acidosis
   (c) Hepatorenal syndrome
   (d) Peritoneal dialysis, plasmapheresis and apheresis
   (e) Renal replacement therapy
   (f) Drugs in renal failure
4. Nervous system
   (a) Seizure disorders and status epileptics
   (b) Cerebrovascular accident (CVA)
   (c) Acute CNS infections
   (d) Intra-arterial pressure: Physiology, Intracranial hypertension, ICP monitoring
   (e) Coma
   (f) Traumatic brain injury
   (g) Neuromuscular diseases
   (h) Acute Flaccid Paralysis-Guillain-Barré syndrome and other disorders
   (i) Tetanus
   (j) CNS drugs
   (k) Brain death
   (l) EEG in the ICU
5. Cardiovascular system
   (a) Acute coronary syndrome
   (b) Acute heart failure
   (c) ACLS guidelines
   (d) Rhythm disorders
   (e) Basics of echocardiography in the ICU
   (f) Valvular heart diseases
   (g) Cardiomyopathies
   (h) Postoperative cardiac care
   (i) Cardiogenic shock
   (j) Myocarditis
   (k) Hypertensive emergencies
   (l) Cardioversion
   (m) Cardiac drugs
6. Environmental disorders
   (a) Near-drowning
   (b) Thermal injuries
   (c) Biochemical hazards

(d) Radiation hazards
(e) Polytrauma
(f) Disaster management guidelines
(g) Envenomation
(h) Acute poisoning

7. Endocrinal disorders
   (a) Thyroid storm and other thyroid disorder in critical care
   (b) Diabetic ketoacidosis (DKA)
   (c) Adrenal insufficiency
   (d) Cerebral salt wasting
   (e) Hyperglycemia and hypoglycemia in the ICU
8. Gastrointestinal disorders
   (a) Upper gastrointestinal bleeding
   (b) Lower gastrointestinal bleeding
   (c) Acute liver failure
   (d) Acute pancreatitis
   (e) Acute abdomen-medical and surgical emergencies
   (f) Stress ulcer prophylaxis
   (g) Postoperative care
   (h) Liver transplant: Basics
9. Respiratory disorders
   (a) Oxygen therapy
   (b) Airway adjuncts
   (c) Basics of mechanical ventilation and applied physiology
   (d) Disease-specific ventilation
   (e) Ventilator-Graphics, monitoring and Troubleshooting
   (f) High-frequency oscillation ventilation
   (g) Acute respiratory distress syndrome
   (h) Pulmonary thromboembolism
   (i) Pneumonias
   (j) Chronic obstructive pulmonary disease
   (k) Noninvasive ventilation
   (l) Chest physiotherapy
   (m) Pulmonary function test (PFT)
   (n) Extracorporeal membrane oxygenation (ECMO) + $ECCO_2$ Elimination: Basics
10. Infections
   (a) Hand hygiene
   (b) Asepsis guidelines
   (c) Sepsis syndrome: SIRS, sepsis, severe sepsis, septic shock and multiorgan dysfunction syndrome (MODS)
   (d) Immunocompromised hosts
   (e) HIV and AIDS
   (f) Ventilator-associated pneumonia (VAP)
   (g) New outset fever in the ICU

(h) Severe Tropical infections: Malaria, Typhoid, Scrub typhus and zoonosis
(i) Nosocomial infections
(j) Viral hemorrhagic fevers
(k) Endocarditis
(l) Opportunistic infections in the ICU
(m) Fungal infections
(n) Infection control measures in the ICU
(o) Antimicrobial therapy
(p) Prevention of Antibiotic Resistance in the ICU
(q) Antibiotic resistance and MDR pathogens

11. Obstetric disorders
    (a) Pregnancy-induced hypertension
    (b) Acute haemorrhage
    (c) Trauma in pregnancy
    (d) HELPP syndrome
    (e) Cardiomyopathy in pregnancy
    (f) Amniotic fluid embolism
12. Procedures
    (a) Endotracheal Intubation
    (b) Percutaneous tracheostomy
    (c) Flexible bronchoscopy
    (d) Intercostal drainage
    (e) Intracranial pressure monitoring
    (f) EEG interpretation
    (g) Peritoneal dialysis
    (h) Continuous renal replacement therapy
    (i) Cardiac pacing
    (j) ECG
    (k) CPR
    (l) Defibrillation
    (m) Pericardiocentesis
    (n) Central venous access
    (o) Echo cardiography(ECHO)
    (p) Emergency ultrasonography
    (q) Emergency radiology
    (r) Percutaneous endoscopic gastrostomy (PEG)
    (s) Intra-abdominal pressure monitoring
13. Hematology
    (a) Blood component therapy
    (b) Thrombocytopenia in the ICU
    (c) Oncology-related life threatening issues in critical care
    (d) Laboratory tests: Interpretation
14. Research
    (a) Basics-statistical definitions
    (b) Sample size calculations, study designs, data collection

(c) Generation of research ideas and hypotheses
(d) Interpretation of results
(e) Understanding evidence-based medicine in critical care

15. Miscellaneous
(a) Do not attempt resuscitation (DNAR)
(b) Medical ethics
(c) Withholding and withdrawing care
(d) Organ donation
(e) Legal issues-Laws related to ICU
(f) Anxiety and stress management in health care providers in ICU
(g) Communication skills in acute care
(h) Critical Care nursing-education
(i) Quality care in the ICU-Bench marking

16. Skills
(a) Endotracheal intubation
(b) Difficult airway management
(c) Flexible bronchoscopy
(d) Surgical airway
(e) Percutaneous tracheostomy
(f) Needle thoracotomy
(g) Chest tube insertion
(h) Initiation of ventilation
(i) Care of equipment
(j) Central venous access
(k) Intra-arterial pressure monitoring
(l) Defibrillation
(m) Pacing
(n) Cardiac output measurement
(o) Gastric tonometry
(p) Peritoneal dialysis
(q) Continuous renal replacement therapy
(r) Intra-abdominal pressure monitoring
(s) Interpretation of ECG/arterial blood gas/Ventilator waveforms
(t) Chest physiotherapy
(u) Lumbar puncture
(v) Intracranial pressure monitoring
(w) Intraosseous insertion

Index

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D

I