Pulmonary Disorders

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Learning Objectives

1. Synthesize a holistic treatment plan for a patient with acute respiratory distress syndrome that includes nonpharmacologic and pharmacologic therapies.
2. Recommend agents used for endotracheal intubation including premedications, induction agents, and neuromuscular blocking agents.
3. Recognize key parameters and commonly used modes for treatment with mechanical ventilation.
4. Identify pertinent therapies for the treatment of a cystic fibrosis exacerbation.
5. Formulate a treatment plan for a patient with pulmonary hypertension.
6. Describe a treatment plan for patients with severe asthma exacerbations and acute respiratory failure from chronic obstructive pulmonary disease.

Abbreviations in This Chapter

AC/VC	Assist control/volume control
ARDS	Acute respiratory distress syndrome
CF	Cystic fibrosis
COPD	Chronic obstructive pulmonary disease
CTEPH	Chronic thromboembolic pulmonary hypertension
CVP	Central venous pressure
ED	Emergency department
ICU	Intensive care unit
MAP	Mean arterial pressure
MDI	Metered dose inhaler
mPAP	Mean pulmonary arterial pressure
MV	Mechanical ventilation
NMBA	Neuromuscular blocking agent
PAH	Pulmonary arterial hypertension
PEEP	Positive end-expiratory pressure
PH	Pulmonary hypertension
PS	Pressure support
RSI	Rapid sequence intubation
RV	Right ventricular
SIMV	Synchronized intermittent mechanical ventilation

Self-Assessment Questions

Answers and explanations to these questions may be found at the end of this chapter.

1. A 65-year-old man presents to the emergency department (ED) with severe shortness of breath, tachypnea, altered mental status, and diaphoresis. A chest radiograph reveals diffuse, bilateral opacities. Vital signs are as follows: blood pressure (BP) 94/54 mm Hg, respiratory rate (RR) 26 breaths/minute, heart rate (HR) 120 beats/minute, pain score 2/10, and temperature 41.0°C. The patient's wife states that his symptoms began about 2 days ago and gradually worsened during the past day. The decision is made to transfer the patient to the intensive care unit (ICU), where he is intubated. An arterial blood gas shows pH 7.30, $Paco_2$ 50 mm Hg, Pao_2 50 mm Hg, and oxygen saturation Sao_2 85% while receiving Fio_2 100%. Which is the best therapy plan for the next 24 hours?
   A. Empiric antibiotic therapy, intravenous fluid resuscitation, and vasopressors for shock; low tidal volume (4–6 mL/kg) ventilation strategy; deep sedation to achieve a Richmond Agitation Sedation Scale (RASS) score of -4; and prone positioning.
   B. Empiric antibiotic therapy, intravenous fluid resuscitation, and vasopressors for shock; low tidal volume (4–6 mL/kg) ventilation strategy; deep sedation to achieve a RASS score of -5 and cisatracurium administration to limit plateau pressures; and prone positioning.
   C. Empiric antibiotic therapy, aggressive diuresis (goal central venous pressure [CVP] less than 4 mm Hg), and vasopressors for shock; low tidal volume (4–6 mL/kg) ventilation strategy; deep sedation to achieve a RASS score of -4; and prone positioning.
   D. Empiric antibiotic therapy, intravenous fluid resuscitation, and vasopressors for shock; low tidal volume (4–6 mL/kg) ventilation strategy; deep sedation to achieve a RASS score of -4; and supine positioning.

2. Which best describes the category of acute respiratory distress syndrome (ARDS) that most benefits from prone positioning and cisatracurium administration?
   A. Acute lung injury.
   B. Severe.
   C. Moderate.
   D. Mild.

3. Which sequence of medication administration would be most appropriate for a 34-year-old woman with no significant medical history receiving rapid sequence intubation (RSI)?
   A. Rocuronium, etomidate, midazolam.
   B. Fentanyl, succinylcholine, propofol.
   C. Atropine, rocuronium, etomidate.
   D. Fentanyl, etomidate, succinylcholine.

4. A 78-year-old man presents to the ICU after being intubated for a severe chronic obstructive pulmonary disease (COPD) exacerbation. His current ventilator settings are as follows: assist control/volume control (AC/VC) mode, tidal volume 700 mL (10 mL/kg), RR 20 breaths/minute, F_{IO_2} 50%, positive end-expiratory pressure (PEEP) 5 cm H_2O, and pressure support (PS) 10 cm H_2O. The first arterial blood gas reveals pH 7.25, Pa_{CO_2} 65 mm Hg, HCO_3- 15 mmol/L, Pa_{O_2} 65 mm Hg, and Sa_{O_2} 90%. Which is the most appropriate setting to adjust on the ventilator?
   A. Reduce the tidal volume.
   B. Increase the RR.
   C. Increase the F_{IO_2}.
   D. Increase the PEEP.

5. A 21-year-old woman (height 62 inches, weight 50 kg) with a history significant for cystic fibrosis (CF) is admitted to the ICU with acute respiratory failure requiring mechanical ventilation (MV). After intubation, her arterial blood gas results are as follows: pH 7.27, Pa_{CO_2} 45 mm Hg, HCO_3- 22 mmol/L, Pa_{O_2} 55 mm Hg, and Sa_{O_2} 88%. Ventilator settings are as follows: AC/VC mode, tidal volume 300 mL (6 mL/kg), RR 20 breaths/minute, F_{IO_2} 60%, PS 5 cm H_2O, and PEEP 5 cm H_2O. Her BP is 110/70 mm Hg with an HR of 95 beats/minute. Which is the best option for a holistic therapy plan?
   A. Initiate cefepime 2 g intravenously every 8 hours, tobramycin 150 mg intravenously every 8 hours; intravenous fluid resuscitation to maintain a CVP goal of 10–14 mm Hg; dornase alfa and hypertonic saline 7% nebulizations.
   B. Initiate cefepime 2 g intravenously every 8 hours, tobramycin 500 mg intravenously every 8 hours; intravenous fluid resuscitation to maintain a CVP goal of 10–14 mm Hg; dornase alfa and hypertonic saline 7% nebulizations.
   C. Initiate cefepime 2 g intravenously every 8 hours, tobramycin 150 mg intravenously every 8 hours; intravenous fluid resuscitation to maintain a CVP goal of 10–14 mm Hg.
   D. Initiate cefepime 2 g intravenously every 8 hours and tobramycin 500 mg intravenously every 24 hours; diuresis to maintain a CVP goal less than 4 mm Hg while mean arterial pressure (MAP) is greater than 65 mm Hg; dornase alfa and hypertonic saline 7% nebulizations.

6. A 55-year-old woman with pulmonary arterial hypertension (PAH) is admitted to the ICU for severe respiratory failure. She reports increased work of breathing for the past 5 days and full adherence to her PAH medication regimen, which includes macitentan 10 mg daily and sildenafil 40 mg three times daily. Current vital signs are as follows: BP 76/60 mm Hg, HR 140 beats/minute, RR 30 breaths/minute, and 85% Sa_{O_2} on 6 L nasal cannula. Right heart catheterization reveals the following: mean pulmonary arterial pressure (mPAP) 50 mm Hg, right arterial pressure of 25 mm Hg, cardiac index 1.9 L/minute/m^2, and pulmonary capillary wedge pressure 16 mm Hg. A transthoracic echocardiogram reveals an ejection fraction of 60% with severe right ventricular (RV) dilatation. Which would be the most appropriate regimen to initiate for this patient?
   A. Dopamine infusion.
   B. Epoprostenol infusion.
   C. Phenylephrine infusion.
   D. Furosemide.

7. A 42-year-old man presents to the ED anxious and short of breath. Auscultation reveals audible wheezing. He has trouble speaking full sentences. He has used his albuterol metered dose inhaler (MDI) at home for the past several hours without resolution of symptoms. His forced expiratory volume in 1 second (FEV_1) is 35% of predicted. Which is the best classification of this patient's asthma?

   A. Mild.
   B. Moderate.
   C. Severe.
   D. Near-fatal.

8. A 66-year-old man presents to the ICU with acute respiratory failure from a COPD exacerbation. He has had no exacerbations in the past 2 years. His home medications include albuterol HFA (hydrofluoroalkane) 2 puffs four times daily as needed and tiotropium 1 puff once daily. The patient denies any recent sick contacts or changes in sputum production. He has no known drug allergies. The patient is placed on 3 L nasal cannula ($Sa0_2$ 97%) and inhaled albuterol and ipratropium by nebulization. Which other therapy would be most appropriate for this patient?

   A. Azithromycin 500 mg intravenously daily.
   B. Prednisone 40 mg orally daily.
   C. Levofloxacin 500 mg orally daily.
   D. Methylprednisolone 125 mg intravenously every 6 hours.

I. ACUTE RESPIRATORY DISTRESS SYNDROME

A. Definition and Epidemiology
1. First described in 1967, a consensus definition for ARDS was proposed in 1994 with the American-European Consensus Conference (AECC). Acute onset (not defined); Pa_{O_2}/F_{IO_2} of 200 mm Hg or less; bilateral infiltrates on chest radiography; absence of left atrial hypertension (pulmonary artery wedge pressure of 18 mm Hg or less). Acute lung injury fulfills the same criteria except for a milder pathology for hypoxemia (Pa_{O_2}/F_{IO_2} of 300 mm Hg or less).
2. AECC definition refined into the Berlin Definition of ARDS. Notable differences in the revised definition (JAMA 2012;307:2526-33)

Table 1. Berlin Definition of ARDS

Variable	Definition
Timing	Onset within 1 week of a known clinical insult or new or worsening respiratory symptoms
Chest imaging	Bilateral opacities not fully explained by effusions, lobar/lung collapse, or nodules
Origin of edema	Respiratory failure not fully explained by cardiac failure or fluid overload Need objective assessment (ECHO) to exclude hydrostatic edema if no risk factor present
Oxygenation	
Mild	200 mm Hg < Pa_{O_2}/F_{IO_2} ≤ 300 mm Hg with PEEP or CPAP ≥ 5 mm Hg
Moderate	100 mm Hg < Pa_{O_2}/F_{IO_2} ≤ 200 mm Hg with PEEP or CPAP ≥ 5 mm Hg
Severe	Pa_{O_2}/F_{IO_2} ≤ 100 mm Hg with PEEP ≥ 5 mm Hg

CPAP = continuous positive airway pressure; ECHO = echocardiogram.

3. The reported incidence of ARDS in the United States is 59 per 100,000 person-years.
4. Estimated mortality ranges from 27% to 45% (Berlin Definition). Six variables are associated with increased mortality: age, immunocompromised state, multiorgan dysfunction score, acidemia, barotrauma, and presence of major organ dysfunction on admission (N Engl J Med 2005;353:1685-93).

B. Etiology and Pathophysiology
1. Direct and indirect causes of lung injury
   a. Direct: Pneumonia, aspiration, and trauma
   b. Indirect: Sepsis, transfusion injury, pancreatitis, burn injury, trauma
2. Hypoxemia develops because of the destruction of alveoli at the cellular level. Destruction of the alveolar epithelium and type I and type II cells causes impaired lymphatic drainage, disruption of the osmotic gradient, accumulation of cellular debris, reduced surfactant production, and microthrombi.
   a. The pathophysiologic cellular changes manifest with pulmonary edema, impaired oxygenation, and organ failure.
   b. Clinical hallmark of ARDS is hypoxemia.

C. Nonpharmacologic Therapy
1. The primary goals of nonpharmacologic therapy (e.g., MV, prone positioning) are to support oxygenation and minimize further organ dysfunction.
2. Lung-protective ventilation in the form of a low tidal volume strategy (4–6 mL/kg of ideal body weight) is the standard of care (N Engl J Med 2000;342:1301-8).
   a. Targeting a plateau pressure of 30 cm H_2O or less is recommended.
   b. Permissive hypercapnia (P_{CO_2} 50–55 mm Hg) is acceptable to optimize tidal volume strategy.

3. Prone positioning for the treatment of early ARDS (less than 36 hours) in moderate to severe ARDS (Pa_{O_2}/F_{IO_2} of 150 mm Hg or less) has been shown to reduce 28-day mortality compared with supine positioning (16% vs. 32.8%, p<0.0001; hazard ratio 0.44; 95% confidence interval [CI], 0.29–0.67) (N Engl J Med 2013;368:2159-68).

D. Pharmacologic Therapy
   1. In a randomized trial comparing the optimal fluid management strategy, a conservative fluid management strategy (CVP less than 4 mm Hg) compared with a liberal fluid management strategy (CVP 10–14 mm Hg) in patients with ARDS and hemodynamic stability (not requiring vasopressors or MAP greater than 60 mm Hg) increased ventilator-free days (14.6 ± 0.5 vs. 12.1 ± 0.5, p<0.001) (N Engl J Med 2006;354:2564-75). Patients with concomitant shock were enrolled in the study and randomized to both treatment arms. If shock was present for patients randomized to the fluid-conservative strategy, diuretics were withheld and administered once the patient established hemodynamic stability (discontinuation of vasopressors or MAP greater than 60 mm Hg).
   2. Early administration of cisatracurium (less than 48 hours) has been shown to reduce mortality in a cohort of patients with moderate to severe ARDS (Pa_{O_2}/F_{IO_2} less than 150 mm Hg) compared with placebo (hazard ratio 0.68; 95% CI, 0.48–0.98; p=0.04) (N Engl J Med 2010;363:1107-16).
   3. Corticosteroids are presupposed to mediate the inflammatory cytokines and mitigate fibrotic alveolar changes during ARDS.
      a. Several studies tested the effects of administering corticosteroids during early ARDS and found no benefit.
      b. A multicenter study of 24 patients with ARDS for more than 7 days reported mortality benefit. Limitations of this study include unbalanced groups (treatment = 16 patients vs. placebo = 8 patients). In addition, four patients were crossed over from the placebo arm to the corticosteroid arm.
      c. A multicenter study by the Acute Respiratory Distress Syndrome Network (ARDSNet) tested corticosteroid administration in late ARDS and reported no survival benefit.
         i. Increased mortality in the subgroup of patients receiving corticosteroids after day 14
         ii. However, corticosteroid treatment was associated with an improvement in ventilator-free and shock-free days during the first 28 days of treatment.

Patient Cases

1. A 56-year-old man is admitted to the ICU with ARDS after experiencing increasing dyspnea during the past 24 hours, culminating in cardiopulmonary arrest. His medical history is significant for alcoholism and hypertension. Results of the initial arterial blood gas are as follows: pH 7.24, $Paco_2$ 58 mm Hg, HCO_3- 24 mmol/L, Pao_2 50 mm Hg, and Sao_2 84% while receiving MV AC mode with Fio_2 100%. Chest radiography reveals diffuse bilateral infiltrates. The patient has BP 108/40 mm Hg (MAP 62 mm Hg), HR 142 beats/minute, and CVP 8 mm Hg while receiving a norepinephrine (10 mcg/minute) infusion after intravenous fluid resuscitation. Ceftriaxone 1 g intravenously every 24 hours and levofloxacin 750 mg intravenously every 24 hours have been initiated for the treatment of community-acquired pneumonia. Which is the best therapeutic plan for management of ARDS and septic shock?
   A. Continue fluid resuscitation to maintain a CVP of 10–14 mm Hg; low tidal volume strategy of 4–6 mL/kg of ideal body weight; prone positioning; and administration of sedatives to target deep sedation and cisatracurium infusion.
   B. Diuresis to target a CVP less than 4 mm Hg; low tidal volume strategy of 4–6 mL/kg of ideal body weight; supine positioning; and administration of sedatives to target deep sedation and cisatracurium infusion.
   C. Diuresis to target a CVP less than 4 mm Hg; low tidal volume strategy of 4–6 mL/kg of ideal body weight; supine positioning; and administration of sedatives to target deep sedation.
   D. Discontinue fluid resuscitation and norepinephrine infusion, and begin diuresis to target a CVP less than 4 mm Hg while maintaining MAP greater than 65 mm Hg; low tidal volume strategy of 4–6 mL/kg of ideal body weight; prone positioning; and administration of sedatives to target deep sedation and cisatracurium infusion.

2. A 70-year-old woman (height 63 inches, weight 65 kg) is transferred to your ICU from an outside hospital after outside hospital admission for hypoxic respiratory failure. She had been treated at the outside hospital for ARDS for 3 days before transfer after a request from her son for hospital transfer. On admission, the patient is receiving MV with the following settings: synchronized intermittent mechanical ventilation (SIMV) mode, tidal volume 600 mL (12 mL/kg), RR 12 breaths/minute, PS 10 mm Hg, and PEEP 10 mm Hg. Which option represents the best therapy plan for treatment of her ARDS?
   A. AC/VC mode, tidal volume 300 mL (6 mL/kg), RR 20 breaths/minute, PS 10 mm Hg, PEEP 5 mm Hg; supine positioning.
   B. AC/VC mode, tidal volume 300 mL (6 mL/kg), RR 20 breaths/minute, PS 10 mm Hg, PEEP 5 mm Hg; prone positioning; cisatracurium administration.
   C. SIMV mode, tidal volume 300 mL (6 mL/kg), RR 20 breaths/minute, PS 10 mm Hg, PEEP 5 mm Hg; supine positioning; cisatracurium administration.
   D. AC/VC mode, tidal volume 300 mL (6 mL/kg), RR 20 breaths/minute, PS 10 mm Hg, PEEP 5 mm Hg; prone positioning.

II. INTUBATION

A. Endotracheal Intubation
   1. Provides access for suctioning of tracheobronchial secretions, maintains a patent airway, and allows administration of medications.
   2. Indications include airway protection, facilitation of ventilation and oxygenation, assurance of airway patency, and anesthesia and surgery.

3. Orotracheal intubation is preferred for elective and emergency cases.
4. Nasotracheal intubation is beneficial for patients undergoing maxillofacial surgery or dental procedures or for patients with limited mouth opening. May be associated with increased risk of bleeding and sinusitis and should be avoided in patients with severe nasal or midface trauma.
5. Complications include insertion trauma, gastric aspiration, hypoxemia, laryngospasm, esophageal intubation, right main bronchus intubation, cardiac arrhythmias, and hemodynamic impairment.

B. Rapid Sequence Intubation
1. Rapid and simultaneous administration of a rapid-acting induction agent and a neuromuscular blocking agent (NMBA) to facilitate intubation and decrease the risk of aspiration.
2. Series of seven distinct steps (7 ps): preparation, preoxygenation, pretreatment, paralysis with induction, protection and positioning, placement of the tube in the trachea, and postintubation management.

C. Pretreatment
1. Occurs 3 minutes before the administration of any induction agent or NMBA.
2. The purpose of pretreatment is to attenuate the sympathetic and parasympathetic response (catecholamine release, hypertension, tachycardia, potentially increased intracranial pressure in patients with impaired cerebral autoregulation) to laryngoscopy.
3. Fentanyl or lidocaine are recommended for pretreatment (Table 2).
4. Atropine and defasciculating doses of non-depolarizing NMBAs are not recommended for routine use in RSI for adult patients.

Table 2. Pretreatment Agents

Agent	Dose	Onset	Duration	Advantages	Disadvantages
Fentanyl (Sublimaze)	1–3 mcg/kg IV	< 30 s	0.5–1 hr	• Blunts hypertensive response from intubation • Recommended over other opioids because of its rapid onset and short duration of action	• Chest wall rigidity (doses greater than 100 mcg/kg) • Hypotension, bradycardia, and respiratory depression
Lidocaine (Xylocaine)	1.5 mg/kg IV	45–90 s	10–20 min	• Prevents rise in ICP through blunting cough reflex; lack of evidence of improved outcomes in patients at risk • May reduce bronchospasm in patients with reactive airway disease	• Contra-indicated in patients with an amide anesthetic allergy, bradycardia, or severe heart block

hr = hour; ICP = intracranial pressure; IV = intravenously; min = minutes; s = second(s).

D. Induction Agents
1. Given as rapid intravenous push immediately before paralyzing agent to help achieve optimal conditions for intubation.
2. Agents should provide rapid loss of consciousness, analgesia, amnesia, and stable hemodynamics.
3. Agents used for induction during RSI include barbiturates, benzodiazepines (midazolam), etomidate, ketamine, and propofol (Table 3).

4. Barbiturates
   a. Thiopental is no longer available in the United States.
   b. Methohexital is rarely used because of its adverse effect profile, which includes respiratory depression, hypotension, and histamine release.
5. Etomidate
   a. Etomidate is a nonbarbiturate, imidazole derivative with a rapid onset of action and a very short elimination half-life.
   b. Enhances the effects of γ-aminobutyric acid, thereby blocking neuroexcitation and inducing unconsciousness (does not provide analgesia).
   c. Etomidate transiently inhibits the conversion of cholesterol to cortisol by inhibiting 11-β-hydroxylase, leading to adrenal suppression. Negative outcomes associated with this effect remain elusive:
      i. Etomidate administration in patients with sepsis or septic shock was an independent predictor of mortality in an a priori subgroup analysis of the CORTICUS study (Intensive Care Med 2009;35:1868-76).
      ii. A meta-analysis observed a higher mortality rate when used in patients with septic shock compared with other induction agents (Intensive Care Med 2011;37:901-10). The results from this systematic review should be interpreted cautiously. The studies included were of low quality, including mostly retrospective reviews, and had small sample sizes; also, clinical illness scores were not matched.
      iii. There is no convincing or consistent evidence to suggest that etomidate is associated with an increased risk of death. Large prospective studies are needed to clarify the clinical significance of etomidate in patients at risk of adrenal insufficiency.

Table 3. Induction Agents

Agent	Dose	Onset	Duration	Advantages	Disadvantages
Etomidate (Amidate)	0.3 mg/kg IV	15–45 s	4–10 min	• Minimal cardiovascular effects • Decreased ICP with minimal effects on cerebral perfusion	• Myoclonic jerks • Transient decrease in cortisol production
Ketamine (Ketalar)	1–2 mg/kg IV, 4–10 mg/kg IM	10–15 s	5–15 min	• Catecholamine reuptake inhibition (transient rise in BP and HR) • Respiration and airway reflexes maintained • Does not increase ICP • Relieves bronchospasm • Has both amnestic and analgesic effects	• Negative inotropic/chronotropic effects (in catecholamine-depleted patients) • Emergence delirium, nightmares, and hallucinations (pre-medication with a benzodiazepine does not reduce the incidence)
Midazolam (Versed)	0.2–0.3 mg/kg IV or IM	60–90 s	1–4 hr	• Recommended over other benzodiazepines because of its relatively faster onset of action	• Compared with other agents, slow onset and longer duration • Dose-dependent respiratory depression and hypotension

Table 3. Induction Agents *(continued)*

Agent	Dose	Onset	Duration	Advantages	Disadvantages
Propofol (Diprivan)	0.5–1.2 mg/kg IV	15–45 s	3–10 min	• Decreases ICP; however, may also decrease CPP • Mild bronchodilating effects • Drug of choice in pregnancy	• Hypotension and bradycardia • Negative inotropic effects

CPP = cerebral perfusion pressure; hr = hour(s); ICP = intracranial pressure; IM = intramuscular(ly); IV = intravenously; min = minutes; s = seconds.

E. Neuromuscular Blocking Agents
   1. Quaternary ammonium compounds that mimic the structure of acetylcholine.
   2. Blockade of the impulse transmission at the neuromuscular junction results in skeletal muscle paralysis.
   3. Used immediately after induction agents to help achieve optimal conditions for intubation.
   4. Do not possess any sedative, analgesic, or amnestic properties.
   5. Problematic in patients with a difficult or failed airway.
   6. Depolarizing NMBAs
      a. Succinylcholine: Noncompetitively binds to acetylcholine receptors, leading to sustained depolarization of the neuromuscular junction and prevention of muscle contraction
      b. Best agent for RSI
   7. Non-depolarizing NMBAs
      a. Rocuronium and vecuronium: Competitive antagonists of acetylcholine at the neuromuscular junction leading to the prevention of muscle contraction
      b. Intermediate-acting non-depolarizing agents are alternatives when succinylcholine is contraindicated
      c. Usually have a slower onset of action and a longer duration of action

Table 4. Common Neuromuscular Blocking Agents

Agent	Dose	Onset	Duration	Cautions
Succinylcholine (Anectine)	1–2 mg/kg IV or 3–4 mg/kg IM (max IM dose 150 mg)	1 min (delayed with IM administration)	3–5 min	• Prolonged effects in pseudocholinesterase deficiency • Hyperkalemia or patients at risk of hyperkalemia (prolonged immobilization, crush injuries, myopathies, burns, muscular dystrophy, stroke, and spinal cord injuries) • Malignant hyperthermia • Bradycardia/hypotension with repeated doses • Mild increase in intracranial pressure
Rocuronium (Zemuron)	1 mg/kg IV	1–2 min	30–60 min	• Moderate increase in duration with liver dysfunction, minimal increase in duration with renal dysfunction
Vecuronium (Norcuron)	0.08–0.1 mg/kg IV	2–3 min	20–60 min	• Prolonged duration in renal and liver dysfunction

IM = intramuscular(ly); IV = intravenously; min = minute(s).

F. Postintubation Management
   1. Provide continued sedation/analgesia as needed to assist in adequate oxygenation and ventilation. If patient received rocuronium or vecuronium, provide adequate sedation/analgesia because these agents have a longer duration than succinylcholine.
   2. Minimize long-term use of analgesics and sedatives.
   3. Maintain the head of the bed elevated 30–45 degrees.
   4. Mouth and eye care.
   5. Bowel regimen.
   6. Stress ulcer and DVT (deep venous thromboembolism) prophylaxis.

Patient Cases

3. A 55-year-old, 75-kg man is admitted to the burn ICU after sustaining a 65% total body surface area burn to the abdomen, back, and lower extremities from a house fire. He is unconscious and unable to protect his airway. His medical history is significant for hypertension and hyperlipidemia. He is currently on high-dose norepinephrine and vasopressin to maintain a MAP of 65 mm Hg. His current laboratory data show the following: sodium 130 mEq/L, potassium 5.9 mEq/L, chloride 122 mEq/L, carbon dioxide 15 mg/dL, BUN 10 mg/dL, and SCr 1.3 mg/dL. Which medications would be most appropriate to use for RSI?
   A. Propofol, fentanyl, rocuronium.
   B. Ketamine, fentanyl, succinylcholine.
   C. Etomidate, fentanyl, rocuronium.
   D. Propofol, fentanyl, succinylcholine.

4. A 39-year-old, 70-kg homeless man was admitted to the neurosciences ICU with a traumatic head injury after falling off a 3-foot ladder while intoxicated. Imaging reveals a subdural hematoma. The team decides to intubate this patient. His current laboratory values are as follows: sodium 133 mEq/L, potassium 4.5 mEq/L, chloride 97 mEq/L, carbon dioxide 28 mg/dL, BUN 13 mg/dL, SCr 0.7 mg/dL, and glucose 140 mg/dL. Which induction medication would be most appropriate to use for RSI?
   A. Propofol 90 mg intravenous push.
   B. Ketamine 100 mg intravenous push.
   C. Midazolam 15 mg intravenous push.
   D. Etomidate 150 mg intravenous push.

III. MECHANICAL VENTILATION

A. Critical to Understanding How MV Works: A fundamental knowledge of acid-base disorders and normal respiratory physiology

B. Two Essential Categories of Respiratory Failure: Hypercapnic and hypoxic. Derangements in Pa_{O_2} or Pa_{CO_2} will help determine the etiology of respiratory failure. (Table 2 provides the context for normal oxygenation and ventilation values.)

C. Modes
   1. AC ventilation
      a. Volume control
         i. The patient receives a predetermined RR and tidal volume, with additional patient-initiated breaths provided at the preset tidal volume. Patient-initiated respiration generates a negative pressure within the ventilator circuit, which is sensed by the ventilator, and a full tidal volume breath is provided.
         ii. Potential for ventilator dyssynchrony, "double-stacking," and respiratory alkalosis
         iii. Mode used in the ARDSNet study of tidal volume strategy to limit spontaneous tidal volumes (N Engl J Med 2000;342:1301-8)
      b. Pressure control
         i. Patient will receive a breath at a fixed rate until a predetermined peak pressure limit is reached. The tidal volume is variable and limited by the peak pressure limit.
         ii. Not ideal for patients with low minute ventilation and may lead to hypoventilation and further hypoxia
   2. SIMV: Patient will receive predetermined RR and tidal volume plus additional spontaneous, self-generated breaths at whatever tidal volume the patient is able to generate. Not ideal for the treatment of ARDS given the ability of patients to exceed the present tidal volume for spontaneous breaths in excess of 6 mL/kg
   3. PS ventilation
      a. Usually used as a weaning mode of MV from a more intensive mode of MV (i.e., AC ventilation)
      b. Patient initiates each breath with assistance from the ventilator in the form of a preset pressure value. The ventilator is set to provide a set amount of pressure to assist each inspiratory effort. The tidal volume and RR depend on the patient.

D. Ventilator Parameters
   1. Fractional inspired oxygen
      a. The amount of oxygen that is delivered with each breath, ranging from 21% to 100%
      b. F_{IO_2} is generally titrated to a P_{aO_2} greater than 55 mm Hg. Amount of F_{IO_2} delivered is limited by concerns for oxygen toxicity.
   2. Tidal volume
      a. The volume of air inspired in a breath (delivered by MV or spontaneous)
      b. Tidal volume is set according to oxygenation and ventilation needs. Patients with ARDS will be treated with a low tidal volume strategy, whereas most other patients will have their tidal volume titrated to P_{aCO_2} and pH.
   3. Respiratory rate
      a. The RR is set to provide a minimal number of breaths from the ventilator at the set tidal volume.
      b. The RR is titrated minute ventilation, P_{aCO_2}, and pH. Minute ventilation (liters per minute) = tidal volume (L) x RR (breaths per minute). 6.0 L/minute = 0.5 (L) x 12 (breaths per minute)
   4. Flow rate: Describes the velocity of air delivered. The velocity is greatest initially on inspiration and decelerates toward the end of the inspiratory effort.
   5. PEEP
      a. Positive pressure in the alveoli during expiration
      b. Provides greater surface area at the alveolar epithelial surface to promote diffusion of oxygen and improve ventilation/perfusion matching
      c. Titrated to meet oxygenation needs

Table 5. Normal Respiratory Physiology Values

Value	Normal Range
Tidal volume (mL/kg)	5–10
RR (breaths/minute)	12–20
Minute ventilation (L/minute)	5–10
$Paco_2$ (mm Hg)	35–45
Pao_2 (mm Hg)	80–100
Sao_2 (%)	95–100

Patient Case

5. A 74-year-old woman (height 63 inches, weight 65 kg) is transferred to your ICU from an outside hospital after admission there for hypoxic respiratory failure. She had been treated there for ARDS for 3 days before transfer after a request from her son for hospital transfer. On receiving the patient in your ICU, she is receiving MV with the following settings: SIMV mode, tidal volume 600 mL/kg (12 mL/kg), RR 12 breaths/minute, PS 10 mm Hg, and PEEP 10 mm Hg. Which option represents the best ventilator plan for treatment of her ARDS?

   A. AC/VC mode, tidal volume 300 mL (6 mL/kg), RR 20 breaths/minute, PS 10 mm Hg, PEEP 5 mm Hg.
   B. SIMV mode, tidal volume 300 mL (6 mL/kg), RR 20 breaths/minute, PS 10 mm Hg, PEEP 5 mm Hg.
   C. PS mode, PS 10 mm Hg, PEEP 5 mm Hg.
   D. SIMV mode, tidal volume 300 mL (6 mL/kg), RR 10 breaths/minute, PS 10 mm Hg, PEEP 5 mm Hg.

IV. CYSTIC FIBROSIS

A. Cystis Fibrosis – A chronic disease process affecting many organs, including the pancreas, liver, and intestine, but primarily the lung (Chest 2004;125:1-39)
   1. CF fibrosis is a recessive disorder that is caused by a mutation of the CFTR (cystic fibrosis transmembrane conductance regulator).
   2. Acute exacerbations include symptoms of increased cough, sputum production, shortness of breath, weight loss, and a decline in lung function.
   3. The lungs become colonized with bacteria, and chronic infections become common. Gradually, the formation of a thick mucus ("mucoid") harboring *Pseudomonas aeruginosa* becomes common.

B. Antibiotic Therapy
   1. Because of the high incidence of resistance, initial treatment with two antipseudomonal agents is recommended (Am J Respir Crit Care Med 2009;180:802-8). Aggressive dosing of β-lactam antibiotics is recommended to optimize time above the minimum inhibitory concentration.
   2. Antibiotic dosing is challenging because of the altered pharmacokinetics in patients with CF. Patients with CF are distinguished for their large volume of distribution and increased renal clearance.
   3. Once-daily dosing of tobramycin (10 mg/kg) to target a peak concentration of 20–30 mg/L and a trough concentration of less than 1 mg/L was shown to be as effective as conventional dosing (Lancet 2005;365:573-8).

C. Adjunctive Therapies for CF Exacerbations
   1. Adjunctive therapies for CF exacerbations are key to improving outcomes and mucous clearance.
      a. Aggressive chest physical therapy
      b. Dornase alfa administered as a nebulized therapy
      c. Hypertonic saline (7%)
   2. Nutrition
      a. The provision of nutrition during acute exacerbations is key to maintaining metabolic function and promoting optimal outcomes for lung transplantation, should the situation arise.
      b. Administration of pancreatic enzymes to assist with digestion

Patient Case

6. A 20-year-old woman is admitted to the ICU for an acute exacerbation of her CF. Before admission, the patient was doing well. The patient had maintained her ideal body weight and had just completed a home regimen of suppressive antibiotics. The patient requires MV for management of her hypoxic respiratory failure. She is initiated on AC/VC mode with a lung-protective strategy (4–6 mL/kg tidal volume). Which represents the best option for managing her acute CF exacerbation?
   A. Tobramycin nebulization; hypertonic saline 7% nebulization; and tube feedings to target a hypocaloric goal during her acute illness (15 kcal/kg/day).
   B. Ceftriaxone 2 g intravenously every 24 hours; tobramycin nebulization; normal saline 0.9% nebulization; and tube feedings to target her goal caloric intake (25 kcal/kg/day).
   C. Piperacillin/tazobactam 4.5 g intravenously every 6 hours; tobramycin 10 mg/kg intravenously once daily; hypertonic saline 7% nebulization; and tube feedings to target her goal caloric intake (25 kcal/kg/day).
   D. Piperacillin/tazobactam 3.375 g intravenously every 6 hours; tobramycin 10 mg/kg intravenously every 8 hours; hypertonic saline 7% nebulization; and tube feedings to target her goal caloric intake (25 kcal/kg/day).

V. PULMONARY HYPERTENSION

A. Definition
   1. Pulmonary hypertension (PH) is defined as a mPAP of 25 mm Hg or greater at rest as assessed by right heart catheterization.
   2. No definition of PH is currently accepted during exercise.

B. Clinical Classification of PH by the World Health Organization: Updated at the 2013 World Conference on Pulmonary Hypertension (J Am Coll Cardiol 2013;62:D34-41):
   1. Group 1: pulmonary arterial hypertension
   2. Group 1': pulmonary veno-occlusive disease and/or pulmonary capillary hemangiomatosis
   3. Group 2: pulmonary hypertension caused by left heart disease
   4. Group 3: pulmonary hypertension caused by chronic lung disease and/or hypoxia
   5. Group 4: chronic thromboembolic pulmonary hypertension
   6. Group 5: unclear multifactorial mechanisms

C. Functional Classification
   1. Developed in 2004 by the World Health Organization (Table 6).
   2. Used to determine the baseline functional status of the patient and throughout the disease.

Table 6. World Health Organization of Functional Class Assessment

Class	Definition
I	No symptoms (dyspnea, fatigue, syncope, chest pain) with normal activities
II	Symptoms with strenuous normal daily activities that slightly limit functional status and activity level
III	Symptoms of dyspnea, fatigue, syncope, and chest pain with normal daily activities that severely limit functional status and activity level
IV	Symptoms at rest; cannot perform normal daily activities without symptoms

D. Pathophysiology
   1. In PH, vascular changes occur, including vasoconstriction, cellular proliferation, and thrombosis.
   2. Levels of thromboxane A2 (potent vasoconstrictor) are increased, whereas prostacyclin levels are decreased (potent vasodilator, inhibitor of platelet aggregation, and antiproliferative properties).
   3. Increased endothelin-1 levels lead to potent vasoconstriction and mitogenic activity on pulmonary artery smooth muscle cells. Nitric oxide is a potent vasodilator, an inhibitor of platelet activation, and an inhibitor of vascular smooth muscle cell proliferation. Decreased levels are observed in PH.

E. Treatment Goals for PH
   1. Achieve and maintain World Health Organization of Functional Class Assessment (WHO-FC) I or II.
   2. Preserve 6-minute walk distance to 380 m or more.
   3. Preserve RV size and function (right arterial pressure less than 8 mm Hg and cardiac index greater than 2.5–3.0 L/minute/m^2).
   4. Normalize B-type natriuretic peptide.
   5. Sustain cardiopulmonary exercise testing, including peak oxygen consumption greater than 15 mL/minute/kg and ventilator equivalent for carbon dioxide less than 45 L/minute.

F. Management of PAH
   1. Supportive therapy
      a. Oxygen: Maintain Sa_{O_2} 90% or greater and Pa_{O_2} 60 mm Hg or greater.
      b. Diuretics should be used for the symptomatic management of RV dysfunction and signs of fluid overload; choice of diuretic is variable.
      c. Digoxin will increase cardiac output; consider in patients who develop atrial tachyarrhythmias.
      d. Anticoagulation should be considered in idiopathic PAH, heritable PAH, and PAH secondary to anorexigenic use (goal INR [international normalized ratio] 1.5–2.5).
   2. Vasodilator therapy with calcium channel blockers (diltiazem, amlodipine, nifedipine)
      a. Considered only for patients who have a positive response to acute vasoreactivity testing (reduction in mPAP of 10 mm Hg or greater to a mPAP of 40 mm Hg or less with unchanged or increased cardiac output (N Engl J Med 1992;327:76-81)).
      b. Patients should not be considered candidates for calcium channel blocker therapy if they have RV dysfunction, depressed cardiac output, or WHO-FC IV symptoms.
   3. Targeted therapies include prostacyclin derivatives, endothelin receptor antagonists, phosphodiesterase type 5 inhibitors, and soluble guanylate cyclase (sGC) stimulators.

G. Prostacyclins
   1. Parenteral prostacyclins
      a. Considered first-line therapy in patients with PAH with WHO-FC III or IV symptoms.
      b. Continuous-infusion epoprostenol is the most thoroughly studied of the medications approved for the treatment of PAH and significantly prolongs survival.
         i. 12-week survival: 100% with intravenous epoprostenol compared with 80% in the conventional group (N Engl J Med 1996;334:296-301)
         ii. 1-year survival: 88% with intravenous epoprostenol compared with 80% historical controls (Circulation 2002;106:1477-82)
         iii. 5-year survival: 55% with intravenous epoprostenol compared with 34% historical controls (J Am Coll Cardiol 2002;40:780-8)
      c. Complications related to delivery include the need for a dedicated intravenous line, local catheter infections/bloodstream infections, and catheter-related thrombosis.
   2. Inhaled prostacyclins
      a. Advantages over intravenous route:
         i. Selective pulmonary vasodilation
         ii. Short elimination half-life and minimal systemic effects
         iii. Improves ventilation-perfusion mismatch
      b. Eleven studies evaluated the use of inhaled epoprostenol (not FDA [U.S. Food and Drug Administration] approved) in critically ill patients with PH (Pharmacotherapy 2010;30:728-40)
         i. Studies included patients undergoing cardiac surgery or lung or heart transplantation, as well as non-specific ICU patients
         ii. Most studies showed a significant decrease in pulmonary pressures; however, significance with improving outcomes is unknown
         iii. Minimal adverse effects reported
      c. Inhaled iloprost
         i. Small studies of critically ill patients with PH
         ii. Not diluted in glycine buffer and no need for continuous administration

Table 7. Available Prostacyclins

Agent	**Epoprostenol IV**		**Treprostinil IV**	**Treprostinil SC**	**Treprostinil Inhaled**	**Iloprost Inhaled**	**Treprostinil Oral**
	Flolan	**Veletri**	**Remodulin**	**Remodulin**	**Tyvaso**	**Ventavis**	**Orenitram**
WHO-FC	III–IV		II–IV		III	III–IV	II–III
Initial dose	1–4 ng/kg/minute IV; based on dry dosing weight		1.25 ng/kg/minute IV or SC; based on dry dosing weight; dose adjustments in hepatic impairment		18 mcg every 4 hours 4x/day	2.5–5 mcg six to nine times daily	0.25 mg every 12 hr or 0.125 mg every 8 hours; caution with strong CYP2C8 inhibitors and severe hepatic dysfunction
Elimination half-life	6 min		4 hr			25 min	4 hr

Table 7. Available Prostacyclins *(continued)*

Agent	Epoprostenol IV		Treprostinil IV	Treprostinil SC	Treprostinil Inhaled	Iloprost Inhaled	Treprostinil Oral
	Flolan	**Veletri**	**Remodulin**	**Remodulin**	**Tyvaso**	**Ventavis**	**Orenitram**
Stability	Protect from light		48 hr at room temp	72 hr at room temp	Do not mix with other medications		—
	8 hr at room temp; 24 hr with cold packs	48 hr at room temp					
Adverse effects	Flushing, headache, diarrhea nausea/vomiting, jaw pain, thrombocytopenia				Cough, throat irritation, bronchospasm, hypotension		Headache, diarrhea, nausea, flushing, jaw pain, and abdominal discomfort
Cautions	Rebound PH with abrupt discontinuation						

CYP = cytochrome P450; hr = hour(s); IV = intravenously; PH = pulmonary hypertension; min = minutes; SC = subcutaneously; WHO-FC = World Health Organization of Functional Class.

H. Endothelin Receptor Antagonists
   1. Recommended for patients with WHO-FC II–IV symptoms.
   2. Minimal place in therapy for critically ill ICU patients.
   3. Macitentan is the only drug in this class with long-term data on morbidity and mortality; pooled primary end point (worsening PAH to mortality) occurred in 31% of patients receiving macitentan compared with 46% in patients receiving placebo ($p<0.001$) (N Engl J Med 2013;369:809-18).

Table 8. ET Receptor Antagonists

	Bosentan (Tracleer) – Oral	**Ambrisentan (Letairis) – Oral**	**Macitentan (Opsumit) – Oral**
WHO-FC	II–IV	II–III	II–IV
Receptor affinity	Blocks ET_A & ET_B	Blocks ET_A	Blocks ET_A & ET_B
Elimination half-life	5 hr	9 hr	16 hr
Approved dose	62.5–125 mg BID	5–10 mg daily	10 mg daily
Outcomes	Improved hemodynamics and functional capacity		
Adverse effects	Hepatotoxicity, peripheral edema, anemia		
Drug interactions	Glyburide (increased LFTs) and cyclosporine (decreased effects of both cyclosporine and bosentan), CYP2C8/9 and CYP3A4 inhibitors and inducers	Caution with cyclosporine (maximum dose of ambrisentan is 5 mg daily)	CYP2C19 and CYP3A4 inhibitors and inducers

BID = twice daily; ET = endothelin; hr = hours; LFT = liver function test.

I. Phosphodiesterase Type 5 Inhibitors: Their role in the critically ill patient:
   1. Intravenous formulation used in patients who temporarily cannot ingest tablets; however, limited by hemodynamic effects.
   2. Improvement in RV contractility by increasing cyclic guanosine monophosphate inhibiting downstream phosphodiesterase type 3, exerting an inotropic effect (Br J Clin Pharmacol 2011;71:289-92).

Table 9. Phosphodiesterase Type 5 Inhibitors

	Sildenafil (Revatio) – Oral	**Sildenafil (Revatio) – IV**	**Tadalafil (Adcirca) – Oral**
WHO-FC	II–IV	II–IV	II–IV
Elimination half-life	4 hr		15 hr
Approved dose	20 mg three times daily	10 mg three times daily	40 mg daily; dose adjustment necessary for renal impairment
Outcomes	Improved hemodynamics and functional capacity		
Adverse effects	Headache, epistaxis, flushing, dyspepsia, hypotension visual alterations (nonischemic arteritic optic neuropathy)		
Drug interactions	Contraindicated in patients receiving nitrates; avoid with strong CYP3A4 inhibitors and inducers		

hr = hours; IV = intravenously.

J. sGC Stimulator
   1. Riociguat (Adempas) sensitizes sGC to endogenous nitric oxide (NO) by stabilizing the NO-sGC binding while directly stimulating sGC independent of the NO pathway.
   2. Also approved for the treatment of group 4 PH in patients with residual chronic thromboembolic pulmonary hypertension (CTEPH) after surgical treatment or inoperable CTEPH to improve exercise capacity.
   3. Currently, riociguat is the only medication approved for patients with group 4 PH (N Engl J Med 2013;369:319-29).
   4. Elimination half-life is 12 hours.
   5. Approved dose is 1–2.5 mg three times daily.
   6. Outcomes include improved hemodynamics and functional capacity.
   7. Adverse effects include hypotension, hemoptysis, headache, dizziness, dyspepsia, nausea, diarrhea, vomiting, and anemia.
   8. Contraindicated in patients receiving nitrates and phosphodiesterase inhibitors; avoid with strong cytochrome P450 (CYP) 3A4/2C8 inhibitors and inducers and with P-glycoprotein/breast cancer resistance protein inhibitors.

K. Managing Decompensated PH
   1. Control contributing factors such as infections, arrhythmias, rebound PH (noncompliance or ineffective dosing), hypoxemia, acidosis, and metabolic abnormalities.
   2. Supportive therapies include optimizing RV preload, maintaining aortic root pressure, improving RV contractility, and reducing RV afterload.

3. Hemodynamic support
    a. Maintaining aortic root pressure and minimizing RV ischemia can be accomplished using vasopressors, which increase the systemic vascular resistance and ultimately improve RV perfusion (Crit Care Med 2007;35:2037-50).
    b. Direct effects on the pulmonary circulation from vasopressors may increase the pulmonary vascular resistance, potentially leading to further clinical decompensation.
    c. Few studies published to help guide the optimal vasopressor in patients with PH; recommendations are essentially extrapolations from other patient populations.
    d. Inotropes are used to further augment the cardiac output of the RV and may improve pulmonary vascular resistance; because of systemic vasodilatory properties from inotropes, anticipate possible systemic hypotension and need for vasopressors.
4. Unloading the RV with pulmonary vasodilators is essential to controlling decompensated PH and RV failure.

Table 10. Agents Used for Hemodynamic Support for Decompensated PH

Drug	Actions	Effects on PVR	Effects on CO	Comments
Dopamine	Dose-dependent dopaminergic effects; β_1- and α_1-agonists	↔	↑	May not improve RV ejection fraction; arrhythmias
Norepinephrine	$\alpha_1 >> \beta_1$-adrenergic receptors	↑	↑ or ↔	Decreased mortality in subgroup of cardiogenic shock and decreased rate of arrhythmias compared with dopamine in a randomized trial[a]
Phenylephrine	α_1-adrenergic receptors	↑	↑ or ↔	Reflex bradycardia may have detrimental effects in the setting of RV failure
Epinephrine	α- and β-adrenergic receptors	↑ or ↔	↑	Arrhythmias, hypoglycemia, increased lactate concentrations
Vasopressin	V_1 receptors	↑ or ↔	↔ or ↓	Use low dose (0.03 unit/min or less); favorable effects on urine output
Dobutamine	$\beta_1 >> \beta_2$	↓	↑	Combine with peripheral vasoconstrictor to attenuate systemic vasodilation
Milrinone	PDE-3 inhibitor	↓	↑	Combine with peripheral vasoconstrictor to attenuate systemic vasodilation

[a]N Engl J Med 2010;362:779-89.

CO = cardiac output; min = minute; PDE = phosphodiesterase; PH = pulmonary hypertension; PVR = pulmonary vascular resistance; RV = right ventricular.

L. Limitations of Targeted Therapies
    1. Indicated only for patients with PAH
    2. May result in worsening fluid retention, pulmonary edema, and gas exchange in other PH groups
    3. Limited data describing efficacy and safety in other PH groups
    4. Small population size, primarily surrogate markers as outcomes measures; limited data in hospitalized and/or critically ill patients; sparse long-term data
    5. Outcomes from combination therapy remain elusive

Patient Case

7. A 44-year-old man is transferred to the medical ICU for treatment of his worsening PAH. He is currently on no treatment for PAH. The patient reports having increased dyspnea on exertion for the past 6 months with exercise, but for the past 3 days, he has had severe shortness of breath at rest. His physical examination is remarkable for a BP of 105/64 mm Hg and a HR of 85 beats/minute. Lung examination is clear, and extremities are notable for trace edema. An echocardiogram reveals an elevated pulmonary systolic pressure and a normal ejection fraction. The patient does not have a favorable response to vasodilator challenge. Pertinent laboratory data are BUN 10 mg/dL, SCr 0.6 mg/dL, AST 160 IU/L, and ALT 100 IU/L. Which would be the most appropriate regimen to initiate for this patient?

   A. Epoprostenol infusion at 2 ng/kg/minute.
   B. Diltiazem 180 mg orally daily.
   C. Macitentan 10 mg orally daily.
   D. Sildenafil 10 mg intravenously three times daily.

VI. SEVERE ASTHMA EXACERBATION

A. Classification of Asthma Exacerbations in the Urgent or Emergency Care Setting
   1. Asthma is a chronic inflammatory disorder of the airways causing recurrent episodes of wheezing, cough, chest tightness, or breathlessness that is often reversible spontaneously or with treatment.
   2. Severe refractory asthma defined as one major and two minor criteria (Am J Respir Crit Care Med 2000;162:2341-51):
      a. Major criteria: Treatment with high-dose inhaled corticosteroids or treatment with oral corticosteroids for 50% or more of the year
      b. Minor criteria: (1) requirement for additional daily controller treatments (long-acting β_2-agonists, theophylline, omalizumab, leukotriene receptor antagonists); (2) asthma symptoms requiring albuterol on a daily basis; (3) persistent airway obstruction (FEV_1 of 80% or less, peak expiratory flow rate of 20% or less; (4) one or more urgent care visits per year; (5) three or more oral corticosteroid bursts per year; and (6) near-fatal asthma event in the past (requiring noninvasive or invasive ventilator support)
   3. Asthma exacerbations are characterized by decreases in expiratory airflow that can be quantified by measuring lung function such as spirometry or peak expiratory flow.
   4. Objective measures more reliably denote the severity of an exacerbation than the severity of symptoms.
   5. Status asthmaticus is an acute, severe asthma exacerbation that does not respond to initial intensive therapy.
   6. Near-fatal asthma is status asthmaticus that progresses to respiratory failure.
   7. Patterns of near-fatal asthma:
      a. Type 1: Subacute worsening (up to 85% of cases)
         i. Slow onset of symptoms in days to weeks
         ii. Poor response to inhaled bronchodilators
         iii. Copious mucous, eosinophilic infiltration
      b. Type 2: Acute deterioration (up to 20% of cases)
         i. Onset over minutes to hours
         ii. Marked response to bronchodilators
         iii. Absence of secretions, neutrophilic infiltration

Table 11. Classification of Asthma Exacerbations in the Urgent or Emergency Care Setting

	Symptoms	**Initial PEF or FEV_1**	**Clinical Course**
Mild	Dyspnea only with activity	≥ 70% of predicted or personal best	• Usually cared for at home • Prompt relief with inhaled SABA • Possible short course of oral CS
Moderate	Dyspnea interferes with or limits usual activity	40%–69% of predicted or personal best	• Usually requires office or ED visit • Relief from frequent inhaled SABA • Oral CS; some symptoms last 1–2 days after treatment is initiated
Severe	Dyspnea at rest; interferes with conversation	< 40% of predicted or personal best	• Usually requires ED visit and likely hospitalization • Partial relief from frequent inhaled SABA • Oral CS; some symptoms last > 3 days after treatment is begun • Adjunctive therapies are helpful (see below)
Near-fatal	Too dyspneic to speak; perspiring	< 25% of predicted or personal best	• Requires ED/hospitalization; possible ICU • Minimal or no relief from frequent inhaled SABA • Intravenous CS • Adjunctive therapies are helpful (see below)

CS = corticosteroid(s); FEV_1 = forced expiratory volume in 1 second; PEF = peak expiratory flow; SABA = short-acting β_2-agonist.

Adapted from: National Institutes of Health National Heart, Lung, and Blood Institute. National Asthma Education and Prevention Program Guidelines (NAEPP). NAEPP Expert Panel Report 3. Available at www.nhlbi.nih.gov/health-pro/guidelines/current/asthma-guidelines/index.htm. Accessed August 15, 2014.

B. Mortality Risk Factors
   1. Prior episode of near-fatal asthma
   2. Two or more hospitalizations in the previous year
   3. Three or more ED visits in the previous year
   4. Hospitalization or ED visit for asthma in the past month
   5. Use of more than 2 canisters of short-acting β-agonists in the past month
   6. Social history that includes major psychosocial problems, illicit drug use, low socioeconomic status
   7. Concomitant illnesses including cardiovascular diseases, psychiatric illness, or other chronic lung diseases

C. Alternative Causes (mimic severe asthma exacerbation)
   1. Upper airway: Vocal cord dysfunction, anaphylaxis, laryngeal stenosis
   2. Central airway: Tracheomalacia, tracheal stenosis mucus plugging
   3. Lower airway: Bronchiolitis, COPD, valvular heart disease, diastolic heart dysfunction

D. Arterial Blood Gas Assessment
   1. Acute, severe asthma typically presents as a respiratory alkalosis.
   2. As respiratory status worsens, arterial carbon dioxide increases (patient exhaustion, inadequate alveolar ventilation and/or an increase in physiologic dead space), leading to respiratory acidosis.
   3. Metabolic (lactic) acidosis may coexist. Lactate production presumably stems from the use of high-dose β_2-agonists, increased work of breathing resulting in anaerobic metabolism of the ventilatory muscles, and tissue hypoxia.

E. Mechanical Ventilation
   1. Indications
      a. Apnea, coma, or respiratory arrest
      b. Inability to speak
      c. Worsening hypoxia
      d. Hypercapnia
      e. Exhaustion
      f. Drowsiness or altered mental status
      g. Worsening acidosis
   2. Low minute ventilation (by reduced tidal volume and/or RR), high inspiratory flow rate, and minimal PEEP on the ventilator will help minimize dynamic hyperinflation.

F. β-Agonist and Anticholinergic Therapy
   1. Rapid-acting β_2-agonists are the cornerstone in the management of acute, severe asthma.
   2. Long-acting β_2-agonists and anticholinergic agents are not recommended in the acute treatment of a severe asthma exacerbation.
   3. Adverse effects of β-agonists include tremor, tachyarrhythmias, hypokalemia, tachyphylaxis, hyperglycemia, and type B lactic acidosis.
   4. Adverse effects of anticholinergic agents include headache, flushed skin, blurred vision, tachycardia, palpitations, and urinary retention.

Table 12. Commonly Used β-Agonists and Anticholinergics

Generic	Brand	Dose[a]	Comments
Albuterol MDI 90 mcg/puff	Proventil HFA Ventolin HFA ProAir HFA	4–8 puffs every 20 min up to 4 hr; then every 1–4 hr as needed	• The canister must be removed from the actuator and connected to the inspiratory limb of the ventilator circuit with spacer • The actuation of an MDI must be synchronized with the onset of inspiratory airflow from the ventilator • A longer inspiratory time and slower inspiratory flow improve aerosol delivery in ventilated patients • Wait 15 s between actuations
Albuterol sulfate 0.5% (2.5 mg/mL) or 0.083% (2.5 mg/3 mL)	Only brand name is the preservative-free product (AccuNeb [DSC])	2.5–5 mg every 20 min for three doses; then 2.5–10 mg every 1–4 hr as needed, or 10–15 mg/hr continuously	• Continuous nebulization (slight benefit in severely obstructed patients) or intermittent nebulization is the safest and most effective approach to reverse airflow obstruction

Table 12. Commonly Used β-Agonists and Anticholinergics *(continued)*

Generic	Brand	Dose[a]	Comments
Levalbuterol tartrate MDI 45 mcg/puff	Xopenex HFA	4–8 puffs every 20 minutes for up to 4 hr; then every 1–4 hr as needed	• *R*-enantiomer of albuterol • MDI not studied in adults receiving mechanical ventilation
Levalbuterol solution 0.01% (0.31 mg/3 mL); 0.02% (0.63 mg/3 mL); 0.04% (1.25 mg/3 mL); 0.25% (1.25 mg/0.5 mL)	Xopenex	1.25–2.5 mg every 20 min for three doses; then 1.25–5 mg every 1–4 hr as needed	
Terbutaline injection 1 mg/mL	(generic only)	0.25 mg SC every 20 min up to three doses	• May be considered if the patient does not respond to inhaled therapy after several hours • No proven advantage over inhaled β_2-agonist therapy • Contraindicated in patients with coronary artery disease
Epinephrine injection 1 mg/mL	Adrenalin	0.3–0.5 mg or 1:1000 solution SC every 20 min up to three doses	
Ipratropium bromide MDI 17 mcg/puff	Atrovent HFA	Eight inhalations every 20 min as needed for up to 3 hr	• Should be given in combination with a rapid-acting β_2-agonist • The addition of ipratropium to inhaled albuterol compared with albuterol alone in patients with severe asthma resulted in improved response; however, outcomes with this combination in status asthmaticus or near-fatal asthma remain elusive (Am J Respir Crit Care Med 2000;161:1862-8) • See above (albuterol MDI) for administration technique on the ventilator
Ipratropium bromide 0.5 mg/3 mL	(generic only)	0.5 mg every 20 min for three doses; then as needed	

[a]Doses based on recommendations from the National Institutes of Health National Heart, Lung, and Blood Institute. National Asthma Education and Prevention Program Guidelines (NAEPP). NAEPP Expert Panel Report 3. Available at www.nhlbi.nih.gov/health-pro/guidelines/current/asthma-guidelines/index.htm. Accessed August 15, 2014.

HFA = hydrofluoroalkane; hr = hours; MDI = metered dose inhaler; min = minutes; s = seconds; SC = subcutaneously.

G. Corticosteroid Therapy
   1. Systemic corticosteroids should be administered to patients admitted to the hospital to hasten the resolution of an asthma exacerbation (Am J Med 1983;74:845-51).
   2. Typically, there is a 6- to 8-hour delay in the response to corticosteroids in status asthmaticus or near-fatal asthma; therefore, administration should be considered early in the course.
   3. Oral prednisone is as effective as parenteral corticosteroids; however, it may not be beneficial in the critically ill patient with impaired gastric absorption.
   4. Methylprednisolone 40–80 mg per day (or equivalent) in one or two divided doses until peak expiratory flow reaches 70% of predicted or personal best.

5. The duration of systemic corticosteroids for a severe asthma exacerbation requiring hospitalization may range from 3 to 10 days.
   a. For corticosteroid courses less than 1 week, tapering is not necessary.
   b. For longer courses (up to 10 days), there is probably no need to taper, especially if patients are concurrently using an inhaled corticosteroid.
6. Inhaled corticosteroids can be initiated any time in the treatment of an asthma exacerbation.

H. Adjunctive Therapies
1. Oxygen should be administered to maintain arterial Sao_2 values of 90% or greater.
2. Helium-oxygen (heliox) blended gas may delay the need for intubation by allowing other therapies to work.
3. Magnesium sulfate infusions may be considered in patients who have life-threatening exacerbations and are unresponsive to conventional therapies after 1 hour.

I. Treatments Not Recommended
1. Methylxanthines do not improve lung function or other outcomes in hospitalized adults.
2. Antimicrobials are not generally recommended for the treatment of acute asthma exacerbations; however, consider using them if there is evidence of concurrent infection.
3. Mucolytics may worsen cough or airflow obstruction.

Patient Cases

8. A 30-year-old, 115-kg woman with status asthmaticus is admitted to the ICU. She has a history of severe refractory asthma that has required endotracheal intubation on three occasions in the past 6 months. Her medical history includes hypertension, diabetes mellitus, obesity, and bipolar disease. She reports that she has used at least 3 canisters of albuterol per month for the past 2 months to manage her symptoms. Which best represents the patient's risk factors that put her at risk of a higher mortality?

   A. Three hospitalizations in the past 6 months and bipolar disorder.
   B. Use of more than 2 canisters of short-acting β-agonists in the past month and obesity.
   C. Hospitalization for asthma in the past month and diabetes mellitus.
   D. Prior episode of near-fatal asthma and hypertension.

9. The patient is endotracheally intubated and placed on MV. Which would be the most appropriate initial therapy for this patient with near-fatal asthma?

   A. Inhaled albuterol by nebulization 2.5 mg every 4 hours.
   B. Inhaled albuterol by nebulization 2.5 mg every 4 hours and inhaled ipratropium by nebulization 0.5 mg every 6 hours.
   C. Inhaled albuterol by nebulization 2.5 mg every 4 hours, inhaled ipratropium by nebulization 0.5 mg every 6 hours, and methylprednisolone 40 mg intravenously twice daily.
   D. Inhaled albuterol by nebulization 2.5 mg every 4 hours, inhaled ipratropium by nebulization 0.5 mg every 6 hours, and methylprednisolone 125 mg intravenously every 6 hours.

VII. ACUTE RESPIRATORY FAILURE IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

A. Definitions
   1. COPD is characterized by a chronic limitation in expiratory airflow that is not fully reversible. Chronic airflow limitation results from a combination of small-airway disease (emphysema) and parenchymal destruction caused by inflammatory processes (chronic bronchitis).
   2. A COPD exacerbation can be defined as an acute worsening in the patient's baseline status (increase in dyspnea, cough, and/or sputum production), necessitating a change in medications.
   3. General criteria for diagnosis are based on clinical presentation:
      a. Spirometry is not accurate during an exacerbation and is not recommended.
      b. Arterial blood gas should be measured.
      c. Pulse oximetry can be used to determine the need for supplemental oxygen.

Table 13. Classification of COPD Severity

Stage	Spirometric GOLD Classification	Characteristics
GOLD 1: Mild	$FEV_1 \geq 80\%$ predicted	0 or 1 exacerbation per year AND no hospitalizations for exacerbation
GOLD 2: Moderate	$50\% \leq FEV_1 < 80\%$ predicted	
GOLD 3: Severe	$30\% \leq FEV_1 < 50\%$ predicted	≥ 2 exacerbations per year OR ≥ 1 hospitalizations for exacerbation (patients in GOLD classifications 3 and 4 are at increased risk of hospital admission and death)
GOLD 4: Very Severe	$FEV_1 < 30\%$ predicted	

COPD = chronic obstructive pulmonary disease; FEV_1 = forced expiratory volume in 1 second.

Adapted from: Global Initiative for Chronic Obstructive Lung Disease. Global Strategy for Diagnosis, Management and Prevention of COPD. Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2014 Update. Available at www.goldcopd.org/uploads/users/files/GOLD_Report_2014_Jun11.pdf. Accessed August 15, 2014.

B. Causes of Acute COPD Exacerbation
   1. New infection
      a. Bacterial
         i. *S. pneumoniae, H. influenzae, M. Catarrhalis* are the most common organisms.
         ii. *P. aeruginosa* is common in patients with GOLD (Global Initiative for Chronic Obstructive Lung Disease) 3 and 4 severities.
      b. Viral (influenza, rhinovirus, respiratory syncytial virus)
   2. Pulmonary embolism
   3. Pneumothorax
   4. Respiratory depression (may be a result of the injudicious use of sedatives and/or analgesic medications)
   5. Surgery (especially of chest and upper abdomen)
   6. Noncompliance
   7. Temperature change and air pollution

C. Indications for MV
   1. Severe dyspnea
   2. Severe acidosis or hypercapnia
   3. RR greater than 35 breaths/minute
   4. Severe hypoxemia

5. Failure of noninvasive ventilation
6. Hemodynamic instability

D. Pharmacotherapy
   1. Inhaled short-acting β_2-agonists (nebulized or MDI) with or without a short-acting anticholinergic.
   2. Systemic corticosteroids (N Engl J Med 1999;340:1941-7; Chest 2001;119:726-30)
      a. Shorten recovery time, improve FEV_1, and improve hypoxemia
      b. May lower the risk of treatment failure, early relapse rate, and hospital length of stay
      c. Prednisone 40 mg orally once daily for 5 days
      d. If oral administration is not an option, equivalent doses of intravenous hydrocortisone or methylprednisolone or nebulized budesonide may be administered.
   3. Antimicrobials
      a. Should be administered if one of the following are met:
         i. All three cardinal symptoms of a COPD exacerbation (increased dyspnea, increased sputum production, and increased sputum purulence) are present (supported by clinical trials, but limited literature)
         ii. Two of the three cardinal signs are present, with increased sputum purulence as one of the symptoms (supported by nonrandomized and observational trials)
         iii. Require noninvasive or invasive ventilation (supported by clinical trials, but limited literature)
      b. Recommended duration of antimicrobials is 5–10 days.
      c. Optimal antimicrobial therapy is not established; however, should be based on local resistance patterns.

Patient Case

10. A 79-year-old, 70-kg woman is admitted to the ICU for management of hypercapnic respiratory failure related to a COPD exacerbation. Two days before admission, the patient experienced dyspnea, for which she was prescribed prednisone 40 mg daily as an outpatient. Today, the patient presents with profound dyspnea, increased sputum production (thick and purulent), and confusion. She has a history of anaphylaxis to penicillin. Her BP is currently 190/100 mm Hg, HR is 110 beats/minute, and RR is 22 breaths/minute. Her chest is hyperinflated and has poor entry bilaterally. Her blood gas is as follows: pH 7.20, P_{CO_2} 85 mm Hg, and P_{O_2} 44 mm Hg on 6 L nasal cannula. The patient is intubated and placed on MV. Which would be the most appropriate medications to treat this patient's severe COPD exacerbation?

    A. Methylprednisolone 1 mg/kg intravenously administered as two divided doses, inhaled albuterol by nebulization, ampicillin/sulbactam 3 g intravenously every 6 hours for 7 days, and azithromycin 500 mg intravenously daily for 5 days.
    B. Prednisone 40 mg by nasogastric tube (NGT) daily x 5 days, inhaled albuterol and ipratropium by nebulization, ampicillin/sulbactam 3 g intravenously every 6 hours for 10 days, and azithromycin 500 mg daily intravenously for 5 days.
    C. Methylprednisolone 1 mg/kg intravenously administered as two divided doses, inhaled albuterol and ipratropium by nebulization, and levofloxacin 500 mg by NGT daily for 7 days.
    D. Prednisone 40 mg by NGT daily x 5 days, inhaled albuterol and ipratropium by nebulization, and levofloxacin 500 mg intravenously daily for 10 days.

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ANSWERS AND EXPLANATIONS TO PATIENT CASES

1. Answer: D

The patient has early, severe ARDS (for less than 48 hours and Pao_2/Fio_2 less than 150 mm Hg) and hemodynamic stability (post-resuscitation MAP greater than 65 mm Hg). According to the findings of a multicenter trial sponsored by the Acute Respiratory Distress Syndrome Network, this patient would qualify for a conservative fluid management strategy (CVP less than 4 mm Hg). In addition, vasopressors should be discontinued and diuresis initiated to achieve a target CVP of less than 4 mm Hg (Answer A incorrect). Given the timing and the severity of the patient's ARDS, he should be placed in the prone position (Answers B and C incorrect). In addition, this patient would qualify for administration of a cisatracurium infusion. In light of the timing and severity of this patient's ARDS, he qualifies to receive a lung-protective ventilation strategy (tidal volume 4–6 mL/kg of ideal body weight) and diuresis to a CVP of less than 4 mm Hg (hemodynamically stable if weaned off vasopressors) while placed in prone position and administered a cisatracurium infusion (Answer D correct).

2. Answer: A

The patient presents to your ICU after 3 days of care. Therefore, the patient does not currently meet the criteria for being administered cisatracurium or being placed in the prone position (Answer B, C, and D incorrect). Currently, the applicable therapy to apply is a lung-protective ventilation strategy (tidal volume 4–6 mL/kg of ideal body weight) (Answer A correct).

3. Answer: C

Propofol, ketamine, and etomidate may all be used for induction. Propofol may worsen hypotension because this patient is already on vasoactive medications to maintain his BP (Answer A incorrect). Succinylcholine causes the up-regulation of acetylcholine receptors, predisposing the muscle fibers to release excess potassium as they are depolarized, subsequently leading to significant dysrhythmias or cardiac arrest (Answers B and D incorrect). Appropriate induction and neuromuscular blockade in this patient would be to administer etomidate (indicated for hemodynamically unstable patients), fentanyl (providing adequate analgesia), and rocuronium (does not increase serum potassium) (Answer C correct).

4. Answer: B

Although propofol may promptly lower intracranial pressure (ICP), it may also induce hypotension and thus decrease cerebral perfusion pressure (Answer A incorrect). Midazolam could be used as an induction agent; however, it is not the best agent for RSI because of its delayed onset of action (Answer C incorrect). Etomidate may be considered in the setting of increased ICP; however, the dose in this case is too high (Answer D incorrect). Ketamine not only decreases ICP, but also prevents fluctuations in ICP (Answer B correct).

5. Answer: A

After recognizing that the patient has ARDS, it is important to implement a lung-protective ventilation strategy (tidal volume 4–6 mL/kg). Choosing a PS or SIMV mode would allow the patient to initiate spontaneous breaths in excess of the goal tidal volume (Answers B, C, and D incorrect). In the ARDSNet study of tidal volume strategy, the AC mode was most commonly used to promote the application of low tidal volumes (Answer A correct).

6. Answer: C

The patient presents with an exacerbation of CF, most likely caused by an infection. The most likely causative organism of her infection is *P. aeruginosa*; therefore, therapy directed to treat *P. aeruginosa* is imperative (Answer B incorrect). In addition, antibiotic treatment should include the empiric selection of two antibacterial agents, ideally a β-lactam and an aminoglycoside, dosed to effectively treat the infection (Answers A and D incorrect). The ideal regimen should include a β-lactam dosed to treat *P. aeruginosa*—in this case, piperacillin/tazobactam at the recommended dose—and an aminoglycoside dosed once daily (Answer C correct).

7. Answer: A

Symptoms and physical findings would place him in WHO-FC IV. An unfavorable response to the vasodilator challenge makes calcium channel blockers an undesirable class of medications for this patient (Answer B incorrect). Epoprostenol continuous infusion is indicated for patients with PAH WHO-FC IV to improve symptoms, exercise capacity, and hemodynamics, In addition, it is the only treatment shown to reduce mortality in PAH (Answer A correct). Macitentan and sildenafil could be considered

in this patient; however, the patient's elevated liver enzymes do not make macitentan an ideal agent (Answer C incorrect). Intravenous sildenafil is also not the most ideal agent because of the hypotension associated with the intravenous formulation (Answer D incorrect).

8. Answer: A

All of the following are risk factors for increased mortality in patients with asthma: (1) prior episode of near-fatal asthma; (2) two or more hospitalizations in the previous year; (3) three or more ED visits in the previous year; (4) hospitalization or ED visit for asthma in the past month; (5) use of more than 2 canisters of short-acting β-agonists in the past month; (6) social history that includes major psychosocial problems, illicit drug use, low socioeconomic status; (7) prior episode of near-fatal asthma; and (8) concomitant illnesses, including cardiovascular diseases, psychiatric illness, and other chronic lung diseases. The patient's history of obesity, hypertension, and diabetes mellitus are not risk factors (Answers B, C, and D incorrect).

9. Answer: C

For near-fatal asthma exacerbations, rapid-acting β_2-agonists and intravenous corticosteroids are recommended (Answers A and B incorrect). The recommended dose for intravenous corticosteroids is methylprednisolone 40–80 mg intravenously per day administered early in the course of the exacerbation (Answer C correct; Answer D incorrect).

10. Answer: D

The latest GOLD (Global Initiative for Chronic Obstructive Lung Disease) guidelines recommend systemic corticosteroids to shorten recovery time, improve FEV_1, and improve hypoxemia. The recommended dose is prednisone 40 mg orally once daily (or equivalent) for 5 days. There is no evidence to suggest that higher doses of corticosteroids would be beneficial, and higher doses may in fact be associated with more adverse effects (Answers A and C incorrect). Adding inhaled short-acting β_2-agonists (nebulized or MDI) with or without a short-acting anticholinergic is the preferred treatment in a COPD exacerbation. Antibiotic treatment for 5–10 days is also indicated because the patient has all three cardinal symptoms of infection. This patient has a history of anaphylactic reaction to penicillin (Answers A and B incorrect); therefore, levofloxacin would be the best recommendation (Answer D correct).

ANSWERS AND EXPLANATIONS TO SELF-ASSESSMENT QUESTIONS

1. Answer: B

It is important to recognize that this patient has both ARDS and septic shock. In addition, the patient has likely had ARDS less than 48 hours; therefore, the time-to-initiation of several treatments is essential. The patient is actively in shock, thus making a fluid-conservative strategy (CVP less than 4 mm Hg) not possible (Answer C incorrect). Because the time to presentation is less than 48 hours and the patient has severe ARDS, he meets the criteria for cisatracurium administration and prone positioning, and a treatment plan should include these two therapies (Answers A and D incorrect). A therapy plan should include shock resuscitation (fluid-liberal strategy, CVP 10–14 mm Hg), lung-protective ventilation (tidal volume 4–6 mL/kg of ideal body weight), prone positioning, and cisatracurium administration (Answer B correct).

2. Answer: B

According to the Berlin Definition for ARDS, acute lung injury was removed in favor of categorizing the severity of ARDS (Pao_2/Fio_2 less than 200 mm Hg) (Answer A incorrect). Because of the relative difference in mortality rates, mild and moderate ARDS are less likely to benefit from therapeutic interventions, given the number needed to treat to show an effective intervention (Answers C and D incorrect). In the trials evaluating prone positioning and cisatracurium, patients with severe ARDS were most likely to benefit. Although the criteria used for severe ARDS in these studies differed from the Berlin Definition (both studies were initiated before publication of the Berlin Definition), a post hoc analysis shows a survival benefit in favor of the group with the highest mortality rate.

3. Answer: D

Neuromuscular blocking agents should always be administered after induction agents (Answers A, B, and C incorrect). In addition, atropine is not routinely recommended (Answer C incorrect) in adult patients for RSI. Atropine should be kept nearby for patients who are at an increased risk of bradycardia during RSI (use of β-blockers, calcium channel blockers, digoxin, or amiodarone). Induction agents (and pretreatment medications) should be administered before NMBAs (Answer D correct).

4. Answer: B

The patient has hypercarbic respiratory failure, for which the primary treatment goals are to restore normalized ventilation parameters and acid-base status. A reduction in tidal volume will only exacerbate the problem of hypercarbia (Answer A incorrect). Increasing the Fio_2 and PEEP will improve oxygenation; however, this will not help improve ventilation (Answers C and D incorrect).

5. Answer: D

It is imperative to recognize that this patient has ARDS caused by a CF exacerbation. Therefore, an inclusive therapy plan will include appropriate treatments for ARDS and CF. Regarding the treatment of ARDS, a lung-protective ventilation strategy (tidal volume 4–6 mL/kg) and a fluid-conservative strategy (CVP less than 4 mm Hg if not in shock) are of utmost importance (Answers A and C incorrect because of the CVP goal). Appropriate treatment of the CF exacerbation includes empiric therapy for *P. aeruginosa* in the form of optimal doses of β-lactam and aminoglycoside (Answer B incorrect because of the inappropriate dose of tobramycin).

6. Answer: D

This patient presents with severe right heart failure. The primary goal would be to optimize RV preload by maintaining a net negative fluid balance with the use of gentle diuresis and BP monitoring (Answer D correct). Dopamine would increase BP; however, it might worsen the patient's tachycardia, thereby worsening the patient's already tenuous clinical status (Answer A incorrect). Epoprostenol would help decrease pulmonary pressures; however, it would lead to potential worsening of the patient's BP because of the drug's peripheral vasodilating effects (Answer B incorrect). Phenylephrine would not be optimal because this vasopressor might worsen RV function, further elevate pulmonary artery pressure by the α1-receptors in the pulmonary vasculature, and potentially induce a reflex bradycardia (Answer C incorrect).

7. Answer: C

This patient is experiencing shortness of breath at rest that is interfering with his conversational ability, and his FEV_1 is less than 40% of predicted; therefore, the

patient's asthma would be classified as severe (Answer C correct). In near-fatal asthma, the FEV_1 would have been less than 25% of predicted (Answer D incorrect). In mild asthma, patients experience dyspnea with activity and an FEV_1 of 70% or greater of predicted (Answer A incorrect). In moderate asthma, dyspnea interferes with or limits usual activity, and patients have an FEV_1 of 40%–60% of predicted (Answer B incorrect).

8. Answer: B

The recommended dose of corticosteroids for a COPD exacerbation is prednisone 40 mg orally once daily (Answer D incorrect; Answer B correct). Antimicrobial treatment should be initiated if (1) all three cardinal symptoms of a COPD exacerbation (increased dyspnea, increased sputum production, and increased sputum purulence) are present; (2) two of the three cardinal signs are present, with increased sputum purulence as one of the symptoms; or (3) the patient needs noninvasive or invasive ventilation. This patient has no indication for antimicrobials (Answers A and C incorrect).