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Part 1:

Renal, Endocrine, and Metabolism Disorders in the ICU

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Instructions: For each question, select the most correct answer.

1. A 24-year-old woman was recently started on valproic acid for new-onset seizures. She is otherwise healthy and takes sports supplements, including

steroids for heavy weight lifting. She is brought to the emergency department with acute altered mental status and subsequently intubated for worsening lethargy. Laboratory results show the following: hematocrit 38%, platelets 250,000/µL, INR 1.2, albumin 4.2 g/dL, alanine aminotransferase 32 U/L, aspartate aminotransferase 35 U/L, total bilirubin 1.2 mg/dL, creatinine 1.0 mg/dL, ammonia 440 µg/dL, sodium 132 mEq/L, potassium 4.0 mEq/L, bicarbonate 18 mEq/L. Toxicology screen is negative. Head CT without contrast shows diffuse cerebral edema. Doppler ultrasonography of the liver is normal. She is started on lactulose, rifaximin, and dialysis. Serum ammonia level continues to be high. Further testing shows elevated urine orotic acid, elevated serum glutamine, a low citrulline level, and a normal arginine level.

Which of the following treatments might help decrease her cerebral edema?

A. Oral vancomycin
B. Protein-rich diet
C. Sodium benzoate
D. Sodium polystyrene sulfonate

2. A 34-year-old woman with a history of Graves disease and one week of illness is admitted to the ICU with altered mental status. She is vomiting, tremulous, and diaphoretic. She has a temperature of 40°C (104°F), heart rate 140 beats/min, blood pressure 90/45 mm Hg, and respiratory rate 28 breaths/min.

   Which of the following sequences of medication administration is the most appropriate initial treatment?

   A. Propylthiouracil (PTU), propranolol, cholestyramine, iodine
   B. Cholestyramine, iodine, PTU, propranolol
   C. Propranolol, iodine, PTU, cholestyramine
   D. Iodine, PTU, dexamethasone, propranolol

3. After a high-speed motor vehicle collision resulting in multiple injuries, a 35-year-old, otherwise healthy patient is admitted to the ICU after operative fixation of a right femur and a left tibial fracture. Postoperative laboratory results are significant for acidosis, hyperkalemia, and hypocalcaemia. Because the patient's urine is a dark brown, a creatine kinase level is ordered, with a result of 18,000 U/L.

   Which of the following is correct with regard to treatment of rhabdomyolysis?

   A. Administration of bicarbonate and mannitol will reduce the incidence of renal failure.
   B. Administration of Ringer lactated solution, 200 mL/hr, is recommended over the administration of normal saline.
   C. Administration of loop diuretics is beneficial and generally recommended in patients with oliguria following traumatic rhabdomyolysis in the absence of preexisting renal failure.

D. Administration of normal saline, 200-1,000 mL/hr, is recommended in the absence of contraindications for administration of significant volume load.

4. A 65-year-old man is status post three-vessel coronary artery bypass graft. His medical history is significant for hypertension treated with lisinopril, congestive heart failure, for which he takes furosemide, 20 mg twice daily, and diabetes mellitus that is controlleld with metformin. He is currently on continuous infusions of dopamine, 3 µg/kg/min, and nitroglycerine, 20 µg/min.

   Which of the following medications will lead to the greatest increase in glomerular filtration rate by its effects on renal plasma flow?

   A. Furosemide
   B. Dopamine
   C. Lisinopril
   D. Metformin
   E. Metoprolol

5. A 56-year-old man with a 10-year history of type 2 diabetes mellitus and end-stage liver disease secondary to hepatits C is admitted to the ICU with respiratory failure secondary to increasing ascites, which has been treated with furosemide and spironolactone, with poor results. His laboratory values are: serum creatinine 2.4 mg/dL (increased from 1.3 mg/dL), bilirubin 8 mg/dL, INR 2.3, albumin 2.5 g/dL, hemoglobin 9 g/dL, and platelet count 40,000/µL. Antibiotics were started for a recent diagnosis of spontaneous bacterial peritonitis. His condition further deteriorated with the development of tense ascites and oliguria (daily urine output 300 mL) with a further rise in creatinine to 3 mg/dL. A diagnosis of hepatorenal syndrome is made.

   Which of the following is the best alternative treatment for this patient?

   A. Dopamine
   B. Fenoldopam and albumin
   C. Isoproterenol
   D. Octreotide and albumin

6. A 55-year-old woman with a history of end-stage renal disease presents to the emergency department (ED) after missing her last two outpatient hemodialysis sessions. Her main symptom is severe lower extremity weakness without clinical evidence of volume overload. Her urine output has been minimal since the initiation of renal replacement therapy four years ago. Laboratory results indicate the following serum values: sodium 126 mEq/L, potassium 8.5 mEq/L, chloride 93 mEq/L, carbon dioxide 17 mEq/L, blood urea nitrogen 65 mg/dL, creatinine 5.8 mg/dL. An ECG performed in the ED indicates peaked T waves. There is a two-hour delay in the initiation of emergent hemodialysis.

   Which of the following agents will reduce the serum potassium most rapidly?

A. IV furosemide
B. Insulin and glucose
C. Albuterol nebulizer
D. IV calcium gluconate

7. A 79-year-old woman with a history of hypertension, insulin-dependent diabetes mellitus, and coronary artery disease presents with acute coronary syndrome. She undergoes percutaneous coronary angiography. At 24 hours after the procedure, her serum creatinine rises from 1.0 mg/dL to 1.5 mg/dL. At 72 hours after the procedure, it returns to 1.0 mg/dL. She is discharged on hospital day four. Two weeks later, she returns to the emergency department with severe bilateral lower extremity neuropathic pain. Laboratory results revealed the following serum values: sodium 140 mEq/L, potassium 5.1 mEq/L, chloride 97 mEq/L, carbon dioxide 17 mEq/L, blood urea nitrogen 45 mg/dL, creatinine 3.5 mg/dL, creatine kinase 520 U/L; and the following urine values: specific gravity 1.015, blood 2+, protein 2+, red blood cells 10-15 cells per high-power field. Granular casts are seen.

   Which of the following is the most likely etiology of this patient's acute kidney injury?

   A. Diabetic nephropathy
   B. Contrast-induced nephropathy
   C. Pigment nephropathy
   D. Atheroembolic renal disease

8. A 20-year-old male college student is evaluated in the emergency department (ED) after a head-on motor vehicle collision. His right lower extremity sustained a crush injury after being pinned in the car. It took emergency medical services (EMS) three hours to extricate him. Creatinine phosphokinase of 145,000 U/L was noted on arrival in the ED.

   While in the field, EMS should have instituted which of the following IV therapies to prevent the risk of acute kidney injury?

   A. Colloid
   B. Crystalloid
   C. Furosemide
   D. Low-dose dopamine infusion
   E. Mannitol

9. A 40-year-old, disheveled man with a history of alcohol abuse is brought to the emergency department with altered mental status. He was picked up by prehospital personnel on the street after a pedestrian found him passed out on the ground. On arrival, he is arousable to voice and denies any toxic ingestion, but becomes agitated quickly during questioning. Vitals signs are: heart rate 130

beats/min, blood pressure 120/60 mm Hg, respiratory rate 34 breaths/min, temperature 38°C (100.4°F), oxygen saturation 90% on room air. Physical examination is notable for temporal wasting, a protuberant abdomen with a fluid wave, caput medusae, scleral icterus, and crackles in the right lung base. Laboratory analysis shows white blood cell count of 15,000/μL, mild anemia and thrombocytopenia, sodium 131 mEq/L, creatinine 1.5 mg/dL, glucose 70 mg/dL, anion gap 22 mEq/L, osmolar gap 8 mOsm/kg, lactate 2.5 mmol/L, urinalysis 3+ ketones, and undetectable ethanol level. Arterial blood gas analysis reveals a pH of 7.28, partial arterial carbon dioxide pressure 30 mm Hg, partial arterial oxygen pressure 80 mm Hg, and bicarbonate 15 mEq/L. Chest radiograph shows right lower lobe infiltrate. Head CT is unremarkable.

Which of the following is the most likely cause of the patient's metabolic disturbance?

A. Ethylene glycol poisoning
B. Isopropyl alcohol intoxication
C. Diabetic ketoacidosis
D. Alcoholic ketoacidosis and lactic acidosis

10. A 36-year-old man is evaluated in the emergency department for right flank pain. His only medical history is the donation of his left kidney to his brother eight years ago. He is in considerable distress and has difficulty sitting on the stretcher. The pain is associated with intense nausea and vomiting; he also reports a subjective low-grade fever. Vital signs are: heart rate 130 beats/min, blood pressure 30/70 mm Hg, temperature 38°C (100.4°F), respiratory rate 26 breaths/min, oxygen saturation 100% on room air. Physical examination is notable for a soft abdomen and pain localized to the right flank and back. Laboratory analysis shows white blood cells 20,000/μL, creatinine 4.0 mg/dL, lactate 4 mmol/L, urinalysis positive for nitrite, and leukocyte esterase 3+. Bedside ultrasound shows moderate right-sided hydronephrosis.

    Which of the following is the most appropriate next step in management?

    A. Abdominal CT and noncontrast pelvic CT
    B. Blood and urine cultures, IV antibiotics and fluids, and pain medication
    C. Blood and urine cultures, IV antibiotics, and nephrology consultation for dialysis
    D. IV fluids, pain control, and tamsulosin

11. A 67-year-old man with hypertension and type 2 diabetes undergoes a transurethral resection of a bladder tumor under general anesthesia. After the procedure, he is slow to awaken and subsequently has a grand mal seizure. He is given lorazepam, 4 mg, and transferred to the ICU. On arrival, he is unarousable, with a heart rate of 91 beats/min, blood pressure of 160/81 mm Hg, oxygen saturation as measured by pulse oximetry 100% on face mask, sodium 118 mEq/L, potassium 5.4 mEq/L, chloride 89 mEq/L, bicarbonate 14 mEq/L,

creatinine 1.1 mg/dL, blood urea nitrogen 21 mg/dL. An emergent repair of the bladder is performed after a cystourogram reveals intraperitoneal extravasation of contrast.

Which of the following is the most appropriate approach for correction of electrolyte abnormalities?

A. Administer 3% sodium chloride with attempt to achieve a sodium level of 126 mEq/L in six hours.
B. Administer 3% sodium chloride with attempt to achieve a sodium level of 126 mEq/L in 24 hours.
C. Initiate fluid restriction diet.
D. Administer desmopressin.

12. A 54-year-old man is admitted to the ICU after presenting with lower back pain radiating to the abdomen, sudden weakness of his lower extremities, hypertension (210/105 mm Hg) and tachycardia (heart rate 113 beats/min). Contrast CT of chest and abdomen shows acute type B thoracic aortic dissection extending into the abdomen with occlusion of the abdominal aorta below the level of the celiac artery. He undergoes transthoracic endovascular repair. A spinal catheter is placed in the lumbar region before induction of general anesthesia. At the end of the procedure he develops a wide-complex arrhythmia with elevated T waves subsequently followed by ST elevations in leads II and V and is quickly returned to the ICU for further treatment.

    Which of the following is the most likely reason for this acute change in cardiac function?

    A. Acute coronary ischemia
    B. Dissection of the ascending aorta
    C. Mesenteric ischemia
    D. Reperfusion
    E. Pulmonary embolism

13. Which of the following is correct about the endothelial glycocalyx?
    A. It has positively charged membrane glycoproteins.
    B. It has a fixed composition across all tissue beds.
    C. It mediates colloid osmotic pressure.
    D. It can be damaged by hypervolemia.

14. A 67-year-old, 84-kg (184-lb) man is postoperative day one after exploratory laparotomy for a perforated intestinal viscus with gross spillage of bowel contents. His medical history includes hypertension, tobacco abuse, and colon cancer. After localization of the perforation and adequate intra-abdominal washout, his bowels were placed back in continuity and the peritoneum was closed. He remains sedated on mechanical ventilation, and is receiving adequate

antimicrobial therapy. He has been adequately resuscitated, weaned off vasoactive medications, and remains on maintenance IV fluids, consisting of Ringer lactated solution, 120 mL/hr.

The use of maintenance IV fluids is associated most with which of the following outcomes?

A. Mortality benefit in the postoperative surgical patient population
B. Increased length of ventilatory support
C. Reduction in the incidence of acute renal failure
D. Increased association with mortality

15. A 70-year-old woman with a history of a prior ventral hernia repair with mesh is admitted to the ICU for a small bowel obstruction requiring serial examinations, nasogastic tube decompression, IV hydration, and correction of electrolyte abnormalities. During the next 24 hours, her pain worsens and there is significant bilious drainage from the nasogastric tube. Laboratory results reveal: sodium 149 mEq/L, potassium 3.3 mEq/L, chloride 105 mEq/L, bicarbonate 17 mEq/L, blood urea nitrogen 55 mg/dL, creatinine 2.3 mg/dL, calcium 8.0 mg/dL, albumin 4.0 g/dL, white blood cell count 18,000/µL, hematocrit 30%. Arterial blood gas analysis shows a pH of 7.50, partial pressure of carbon dioxide 24 mm Hg, partial pressure of oxygen of 90 mm Hg and bicarbonate of 17 mEq/L.

Which of the following acid-base disorder is most likely?

A. Acute respiratory alkalosis with elevated anion gap metabolic acidosis and metabolic alkalosis
B. Metabolic alkalosis and elevated anion gap metabolic acidosis
C. Acute respiratory alkalosis with elevated anion gap acidosis
D. Acute respiratory alkalosis with elevated anion gap acidosis and a non-anion gap acidosis
E. Metabolic alkalosis and non-anion gap metabolic acidosis

16. A 57-year-old man with a history of type 1 diabetes mellitus is evaluated in the emergency department for severe abdominal pain, nausea, and vomiting. Ketones are detected in his urine. After establishing IV access and beginning IV hydration with 0.9% normal saline, he is admitted to the ICU. Shortly after admission, arterial blood gas analysis reveals pH 7.12, partial arterial carbon dioxide pressure 40 mm Hg, bicarbonate 17 mEq/L. Chemistry results are: sodium 145 mEq/L, potassium 3.1 mEq/L, chloride 95 mEq/L, bicarbonate 17 mEq/L, blood urea nitrogen 25 mg/dL, creatinine 1.65 mg/dL, albumin 2.5 g/dL.

Which of the following scenarios best fits these laboratory findings?

A. Anion gap metabolic acidosis with respiratory compensation
B. Anion gap metabolic acidosis with metabolic alkalosis and respiratory acidosis

C. Non-anion gap metabolic acidosis with respiratory acidosis
D. Anion and non-anion gap acidosis with respiratory alkalosis

17. A 64-year-old man is transferred to the ICU from a hospital floor two weeks after a bone marrow transplant. He has a temperature of 39.4°C (103°F), a heart rate of 125 beats/min, tachypnea, and an oxygen saturation of 95% on room air. His arterial blood gas analysis reveals pH 7.45, carbon dioxide 23 mm Hg, and oxygen 63 mm Hg. Sodium 133 mEq/L, potassium 3.5 mEq/L, chloride 104 mEq/L, bicarbonate 18 mEq/L, blood urea nitrogen 7.0 mg/dL, creatinine of 0.9 mg/dL, with an albumin of 1.4 g/dL.

    Which of the following best describes his metabolic status?

    A. Non-anion gap metabolic acidosis with respiratory compensation
    B. Primary respiratory alkalosis and metabolic alkalosis
    C. Mixed respiratory alkalosis and non-anion gap acidosis
    D. Mixed respiratory alkalosis and anion gap acidosis

18. A man presents to the emergency department in a postictal state after a witnessed seizure. Five minutes after arrival, he has another tonic-clonic seizure that is difficult to control with antiseizure drugs. He is given benzodiazepines followed by phenytoin and remains in status epilepticus. There is concern that he may need an infusion of phenobarbital or propofol. Because of concerns for airway protection, he is successfully intubated. He is monitored with continuous EEG, and control of his seizure activity is obtained with a propofol infusion. Laboratory testing and imaging studies are obtained. Arterial blood gas analysis is pending. The bedside nurse reports that the continuous end-tidal carbon dioxide monitor alarm is sounding, with a value of 22 mm Hg. There have been no issues with hypoxia.

    Which of the following is the best immediate next step?

    A. Increase the set positive end-expiratory pressure to 10 mm Hg.
    B. Ignore the alarm because this is within the physiologic normal end-tidal carbon dioxide range for a patient receiving positive-pressure ventilation and sedated with propofol.
    C. Wait for laboratory results.
    D. Decrease the respiratory rate.
    E. Add dead space to the ventilator circuit.

19. A 22-year-old woman is brought to the hospital by emergency medical services after being found on the floor of her apartment by her boyfriend. He says that he last spoke to her 24 hours ago and discloses that she has type 1 diabetes. She is somnolent upon arrival and has tachypneia, diaphoresis, and tachycardia. Her boyfriend denies that she had any cold-like symptoms during the past week. She is allergic to nonsteroidal antiinflammatory drugs and takes an over-the-counter

medication daily for severe headaches. Her boyfriend says that she has been extremely depressed since the death of her child. She drinks six cans of beer daily and occasionally injects heroin. Two doses of naloxone are administered, but she remains obtunded.

Laboratory results reveal white blood cell count 20,500/μL, hemoglobin 12.1 g/dL, glucose 134 mg/dL, sodium 145 mEq/L, potassium 4.0 mEq/L, chloride 106 mEq/L, carbon dioxide 4 mEq/L, blood urea nitrogen 20 mg/dL, creatinine 2.36 mg/dL, AST 160 U/L, ALT 200 U/L, alkaline phosphate 20 U/L, troponin 0.01 ng/ml. Arterial blood gas analysis reveals: pH 7.14, carbon dioxide 18 mm Hg, partial pressure of oxygen 106 mm Hg, bicarbonate 10 mEq/L, lactate 1 mmol/L, ethanol less than 5, acetylsalicylic acid negative.

After the patient is intubated, which of the following initial treatments is most appropriate?

A. Administer 2 L normal saline bolus, 10 units of insulin, and start IV insulin at 0.5 mL/kg/hr.
B. Obtain blood cultures and start broad-spectrum antibiotics.
C. Start N-acetylcystine and trend liver enzymes.
D. Start IV naloxone and order a urine toxicology screen.

20. A 65-year-old woman with chronic obstructive pulmonary disorder is evaluated in the emergency department for fever, cough, and increased sputum production. Her symptoms began 48 hours ago and have progressively worsened. Her baseline arterial blood gas (ABG) results are pH 7.34, carbon dioxide 60 mm Hg, oxygen 81 mm Hg, and bicarbonate 32 mEq/L. A current ABG shows a partial pressure of carbon dioxide 72 mm Hg, partial arterial oxygen pressure 80 mm Hg.

Which of the following is closest to her expected pH?

A. 7.3
B. 7.25
C. 7.2
D. 7.15

21. After cardiopulmonary bypass, a patient who is on a long-term standing dose of digoxin receives additional digoxin, 0.5 mg, in error. An ECG shows sinus bradycardia with intermittent sinus arrest, with blood pressure of 90/60 mm Hg.

Which of the following drugs is contraindicated in this patient?

A. Atropine
B. Calcium chloride
C. Ephedrine
D. Magnesium sulfate

22. A 24-year-old woman is brought to the emergency department by her boyfriend, who says that she has not been acting like herself. He says that she has no previous medical issues and does not take any medications. She is afebrile, with blood pressure 100/62 mm Hg and pulse 110 beats/min, and she appears confused. Physical examination is notable for dry mucosa. A head CT shows no acute abnormalities, and a urine toxicology screen is negative. Complete blood count is unremarkable. A basic metabolic panel reveals the following: sodium 140 mEq/L, potassium 4.3 mEq/L, chloride 110 mEq/L, bicarbonate 20 mEq/L, blood urea nitrogen 40 mg/dL, creatinine 2.0 mg/dL, and calcium 18 mg/dL.

    Which of the following is the most appropriate treatment at this time?

    A. Cinacalcet
    B. Isotonic saline
    C. Prednisone
    D. Zoledronate

23. A 50-year-old woman with a history of hypertension treated with lisinopril, and depression currently being treated with a selective serotonin reuptake inhibitor, presents to the emergency department with right lower quadrant abdominal pain. She also reports weight loss, fatigue, poor appetite, and palpitations. She has not seen her primary care provider in years. Vitals signs are: temperature 38.5°C (101.3°F), heart rate 130 beats/min, respiratory rate 24 breaths/min, blood pressure 150/90 mm Hg, oxygen saturation 100% on room air. CT reveals appendicitis, and she undergoes an urgent appendectomy. At the end of the procedure she develops atrial fibrillation at a ventricular rate of 150 beats/min. After treatment with metoprolol, 5 mg, the rate decreases to 120 beats/min, then converts to sinus rhythm, and she is moved to the ICU for observation. In the ICU she is confused, diaphoretic, mildly agitated, and has one or two episodes of emesis. Vitals signs are: temperature 40°C (104°F), heart rate 120 beats/min, respiratory rate 30 breaths/min, blood pressure 195/95 mm Hg, oxygen saturation 95% on room air. Physical examination is notable for a supple neck, soft abdomen, and warm extremities without rigidity or clonus. Laboratory results are pending.

    Which of the following is the most appropriate next pharmacologic intervention?

    A. Cyproheptadine and IV benzodiazepines
    B. IV dantrolene
    C. Enalaprilat
    D. IV propranolol, propylthiouracil, and dexamethasone

24. A 35-year-old woman with a history of diabetes, hypertension, and lupus is admitted to the ICU with concern for pneumonia and severe sepsis. Her home medications include methotrexate, hydroxychloroquine, prednisone, esomeprazole, lisinopril, and metformin. Her initial lactate level in the emergency department is 5 mmol/L. She is started on broad-spectrum antibiotics and given 3

liters of IV normal saline. Despite continued aggressive fluid resuscitation in the ICU, her blood pressure decreases and she is started on norepinephrine and low-dose vasopressin. She is on 6 L nasal cannula with oxygen saturations of 95%, blood pressure 80/40 mm Hg, pulse 120 beats/min, respiratory rate 22 breaths/min, and is afebrile. Laboratory assessment shows a lactate of 3 mmol/L, hemoglobin 10, and a central venous oxygen saturation of 70. Central venous pressure is 12 mm Hg and urine output is adequate.

Which of the following is the best next step in management?

A. Order an additional 2 L IV crystalloid bolus.
B. Add antifungal coverage.
C. Start IV stress-dose steroids.
D. Start epinephrine.

25. A woman with Burkitt lymphoma is admitted to the ICU 48 hours after initiation of cytotoxic chemotherapy. She is febrile, vomiting and lethargic. Tumor lysis syndrome is suspected, with hyperkalemia, hyperphosphatemia, hypocalcemia, and hyperuricemia.

    Which of the following medications is used to prevent hyperuricemia as a complication of cytotoxic chemotherapy in high-risk patients?

    A. Phosphate binder
    B. Recombinant urate oxidase
    C. Xanthine oxidase inhibitor
    D. Purine analog

26. A 64-year-old man is admitted to the ICU with hypotension, bronchospasm, and diarrhea that resolves with IV fluid resuscitation. CT reveals a tumor in the small bowel metastatic to the liver. Shortly after arrival in the ICU and after the lesions are biopsied, he becomes hypotensive, with sinus tachycardia, wheezing, and severe facial flushing. Examination reveals jugular venous distention and a systolic murmur along the left sternal border. His central venous pressure waveform demonstrated a prominent v-wave.

    Which of the following immediate interventions is most appropriate?

    A. Administer IV furosemide.
    B. Administer an antihistamine.
    C. Begin an octreotide infusion.
    D. Begin a norepinephrine infusion.

27. A 75-year-old man with diabetes mellitus, hypertension, and peripheral vascular disease is scheduled to undergo endovascular repair of an 8-cm abdominal aortic aneurysm. Administration of iodinated contrast will be used during the procedure. Which of the following is the best method for prevention of postoperative acute

kidney injury?

A. Administration of N-acetylcysteine before the procedure
B. Goal-directed fluid therapy and avoidance of hypotension during the procedure
C. Use of IV mannitol intraoperatively to maintain urine output
D. Use of an isotonic bicarbonate infusion started before the procedure and continued for six hours

28. A 30-year-old man was severely burned in a house fire and explosion caused by a gas leak. He sustained third-degree burns over 70% of his body and remains in the ICU seven days later in respiratory failure and shock. He has no other injuries. Overnight, his urine output decreases to 10 mL/hr and he has increasing vasopressor requirements to maintain a mean arterial pressure above 65 mm Hg. On examination, his temperature is 39°C (102.2°F), heart rate 96 beats/min, blood pressure 130/75 mm Hg (mean arterial pressure 70 mm Hg), and oxygen saturation 100% on 40% fraction of inspired oxygen. Pulse pressure variation is 6%, and central venous pressure is 13 mm Hg. He remains intubated and sedated on fentanyl and low-dose propofol, has equal breath sounds bilaterally, and a firm and distended abdomen with edematous arms and legs. On pressure-control ventilation, his tidal volume is 300 mL, down from 500 mL earlier in the day. His urine is dark in color, with a recent creatinine kinase level down-trending from 2,500 to 1,000 U/L. His evening laboratory results show evidence of acute kidney injury, with a creatinine level of 2.05 mg/dL.

    Which of the following is the most appropriate next step in management?

    A. Administer 1 liter normal saline bolus.
    B. Check bladder pressure.
    C. Check urine electrolytes.
    D. Administer IV furosemide, 40 mg.

29. A 72-year-old man with a history of chronic obstructive pulmonary disease, hypertension, and colon cancer, who is status post partial colectomy four years ago presents with symptoms of a small bowel obstruction with transition point noted on CT. He undergoes urgent small bowel resection with primary anastamosis. The repair is difficult, and the patient receives 7 liters of crystalloid and 1 liter of albumin, with an estimated blood loss of 300 mL. He produces 700 mL of urine during the repair. He is given ciprofloxacin and metronidazole intraoperatively. The abdomen is closed at the conclusion of the repair. He is brought to the ICU intubated and on nitroprusside for intraoperative hypertension. Over the next 12 hours, he becomes febrile to 39.4°C (103°F) and develops atrial fibrillation with a rate in the 130s beats/min. His blood pressure remains stable at 120/80 mm Hg, and his oxygen saturation is 96% on 70% fraction of inspired oxygen with peak airway pressures of 30 cmH_2O (up from 20 cmH_2O in the operating room). Urine output for the past hour is 5 mL. On examination, he is sedated, with a distended abdomen, and the exploratory laparotomy incision site

appears clean. His laboratory results show the following values: sodium 145 mEq/L, potassium 3.8 mEq/L, chloride 109 mEq/L, bicarbonate 13 mEq/L, blood urea nitrogen: 45 mg/dL, creatinine 2.34 mg/dL (up from baseline of 1.2 mg/dL), albumin 4 g/dL.

Which of the following is the most likely cause of this patient's renal failure?

A. Intravascular depletion and hypovolemia
B. Ureteral compression by increased abdominal pressure
C. Decreased cardiac output due to increased abdominal pressures
D. Renal vein compression by increased abdominal pressure

30. A 57-year-old man presents to the emergency department in septic shock. Abdominal CT reveals cecal volvulus and perforation. The intensivist initiates appropriate antimicrobial coverage, obtains adequate venous access, and orders cultures and laboratory testing. The patient is scheduled for emergent surgical intervention to obtain source control. The intensivist then initiates aggressive resuscitation for the patient's wide-gap metabolic acidosis. The patient initially receives a two-liter bolus of normal saline (NS). His lactate remains elevated on an interval check, and the bedside nurse asks the intensivist what type of resuscitative fluid should be used at that point.

    Compared to low-chloride resuscitative fluids (ie, balanced saline solutions), the use of high-chloride resuscitative fluids (ie, NS) for septic patients requiring abdominal surgery is associated with

    A. a higher rate of in-hospital mortality
    B. a higher rate of metabolic alkalosis
    C. a lower rate of acute kidney injury
    D. fewer blood product transfusions
    E. fewer postoperative course infections

31. A 34-year-old man sustained a severe traumatic brain injury; splenic, multiple right rib fractures; pulmonary contusion; right femoral fracture; and thoracic lumbar fractures. He underwent an emergency craniotomy and splenectomy. He is now intubated on mechanical ventilation, and on enteric nutrition through a post-pyloric feeding tube. On hospital day 3, he is scheduled for femoral fracture internal fixation.

    Which of the following is the most appropriate preoperative preparation?

    A. Withhold tube feeding at midnight on the day of surgery.
    B. Withhold tube feeding six to eight hours before surgery.
    C. Withhold tube feeding two hours before surgery and administer metoclopramide on call to the operating room.
    D. Continue tube feeding until surgery.

32. A 55-year-old man with a history of morbid obesity is admitted to the ICU with septic shock five days after undergoing a partial colectomy for colon cancer. Fluid resuscitation, vasopressor support, and antibiotics are immediately initiated. An abdominal CT reveals an abdominal abscess; two percutaneous drains are inserted.

    Which of the following is the best predictor of daily energy needs for this patient?

    A. Indirect calorimetry
    B. Harris-Benedict equation
    C. Nutrition Risk in Critically Ill (NUTRIC) score
    D. Sequential Organ Failure Assessment (SOFA) score

33. A 52-year-old man with known HIV infection presents to the emergency department with progressively worsening shortness of breath and productive cough. He is diagnosed with pneumonia and is emergently intubated due to respiratory failure. While in the ICU, he is given volume resuscitation and started on empiric antibiotics. On day three, he is started on enteral feeding via orogastric tube. He is having persistent residuals of 150 to 200 mL.

    Which of the following is the most appropriate next step in management?

    A. Discontinue enteral feeding.
    B. Reduce rate of enteral feeding to half.
    C. Continue current rate of enteral feeding.
    D. Change enteral feeding to low-volume elemental feeding.
    E. Start a pro-motility agent.

Part 1 Answers:
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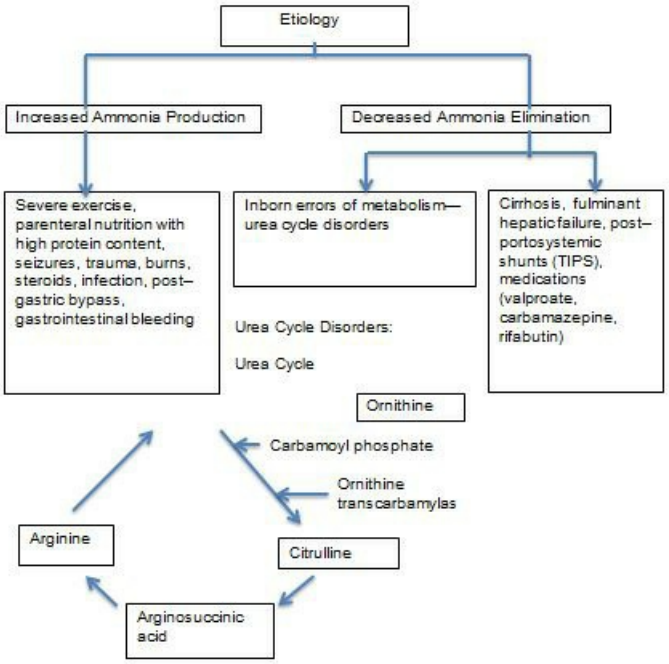
1. Rationale

Answer: C

Urea cycle disorders (UCDs) secondary to enzyme defects include carbamoyl phosphate synthetase 1, ornithine transcarbamylase (OTC), argininosuccinate synthetase, argininosuccinate lyase, and arginase 1 deficiencies. The most common UCD in adults is OTC deficiency, an X-linked disease. Female heterozygotes may not develop the condition until they are adults. Patients present with hyperammonemia, typically when they are exposed to precipitants such as increased protein intake, drugs, or infection. In adults, UCD diagnosis should especially be sought after refractory hyperammonemia with no acidosis, after excluding common etiologies. In suspected UCDs, serum glutamine, citrulline, and urine orotic acid should be checked. In OTC deficiency there is increased glutamine level, low citrulline level, and increased urine orotic acid level. A combined preparation of sodium phenylacetate/sodium benzoate is approved by the U.S. Food and Drug Administration for the treatment of hyperammonemic crisis in patients with inborn errors of metabolism. Arterial ammonia level greater than 200 μg/dL is strongly associated with cerebral edema and cerebral herniation. Decreasing the ammonia levels will help with decreasing the cerebral edema and intracranial pressure. Oral vancomycin can be used for the treatment of hepatic encephalopathy. The patient has hyperammonemia from UCD and is already on lactulose and rifaximin. She would benefit more from sodium benzoate to increase the urea clearance and decrease the ammonia. Sodium polystyrene sulfonate is useful for treating hyperkalemia, and a protein-rich diet would worsen the hyperammonemia.



References:

1. Clay AS, Hainline BE. Hyperammonemia in the ICU. *Chest.* 2007 Oct;132(4):1368-1378.
2. Häberle J, Boddaert N, Burlina A, et al. Suggested guidelines for the diagnosis and management of urea cycle disorders. *Orphanet J Rare Dis.* 2012 May 29;7:32.
3. Clemmesen JO, Larsen FS, Kondrup J, Hansen BA, Ott P. Cerebral herniation in patients with acute liver failure is correlated with arterial ammonia concentration. *Hepatology.* 1999 Mar;29(3):648-653.

2. Rationale

Answer: A

This patient has thyroid storm. While diagnostic criteria remain controversial, her history of Graves diseases, combined with the clinical features, is strongly suggestive, and treatment should be initiated immediately, even before laboratory results are available.

Treatment involves several components:

1) Inhibition of new hormone synthesis with propylthiouracil (PTUs) or imidazoles (methimazole and carbimazole). PTU blocks the enzyme thyroidal peroxidase to inhibit thyroid hormone synthesis. It is generally preferred over methimazole because it also inhibits the peripheral conversion of thyroxine to triiodothyronine. The dosage of PTU is a 500-1000 mg loading dose, followed by 250 mg every four hours. Methimazole is dosed 60-80 mg/day in divided doses.

2) Blockade of release with iodine or lithium. Blocking release of thyroid hormone is

best accomplished with iodine, but lithium can be used in iodine-allergic patients. It is important not to administer iodine until after the synthetic pathways have been blocked with PTU (at least 30 minutes); otherwise administration of iodine might cause more thyroid hormone to be formed. Options B, C, and D each have iodine being given before PTU, which make them incorrect.

3) Inhibition of peripheral effects with beta-adrenergic agents. Propranolol is the preferred treatment to block peripheral effects of thyroid hormone because of its nonselective effects and the additional benefit of inhibiting peripheral conversion of thyroxine to triiodothyronine. If a contraindication to propranolol exists (eg, asthma, congestive heart failure), then an agent such as diltiazem could be considered. Furthermore, possible inciting events should be addressed (eg, infection, diabetic ketoacidosis, trauma, etc.). Administration of glucocorticoids is recommended because thyroid storm can precipitate adrenal crisis (relative adrenal insufficiency), with similar dosing regimens. Dexamethasone may be preferred, since it also blocks the peripheral conversion of thyroxine to triiodothyronine. Antipyretics and external cooling methods may be considered, but salicylates should be avoided because they may increase free hormone levels. Most patients will benefit from IV fluids to replace significant volume loss from hyperthermia and gastrointestinal losses.

4) Inhibition of enterohepatic circulation of thyroid hormone, which is metabolized in the liver where it is conjugated to glucuronides and sulfates and excreted into the intestine in bile, while unconjugated free hormones are reabsorbed into circulation. Cholestyramine, by binding conjugated products, promotes their excretion, thereby lowering thyroid hormone levels. The recommended dose is 1-4 g twice daily.

Reference:

1. Asare K. Diagnosis and treatment of adrenal insufficiency in the critically ill patient. *Pharmacotherapy.* 2007 Nov;27(11):1512-1528.

3. Rationale

Answer: D

Posttraumatic rhabdomyolysis is common and associated with significant morbidity and mortality. In earthquake survivors, it is the second most important cause of mortality. Nontraumatic causes of rhabdomyolysis include extreme exertion, grand mal seizures, delirium, drugs, toxins, infections, and endocrine disorders. Prolonged anesthetics can be associated with rhabdomyolysis, especially in young muscular patients. A common feature of both traumatic and nontraumatic rhabdomyolysis is massive necrosis resulting in limb weakness, myalgia, and gross pigmenturia.

The pathophysiologic process involves sarcolemmic injury as well as depletion of ATP within the myocyte. This leads to a detrimental increase in intracellular calcium. Tight calcium regulation is necessary in order to ensure proper contractile function (low concentrations at rest and increasing concentrations during a state of activation facilitate proper actin myosin-binding and contraction). Channels and pumps that regulate this calcium concentration are ATP dependent and, once ATP depletion occurs, are no longer able to maintain calcium homeostasis. The muscle persistently

contracts, and calcium-dependent proteases and phospholipases are activated, eventually leading to destruction of the myocyte. Kidney injury commonly results as a consequence of renal vasoconstriction, direct and ischemic tubule injury, and tubular obstruction.

After identification and treatment of the cause of rhabdomyolysis, the important steps to prevent acute kidney injury include aggressive volume administration with the goal of maintaining and enhancing renal perfusion to minimize cast formation and/or to flush out casts that have already formed. Another goal is enhancement of urinary potassium excretion, since death from hyperkalemia is a major complication of traumatic rhabdomyolysis. Although the optimal type of fluid and rate of repletion is unclear, potassium-containing fluids should be avoided, especially in the initial phase, and administration of normal saline at 1-2 L/hr is generally recommended initially.

Despite the theoretical benefits of bicarbonate administration (prevention of nephrotoxic effects of myoglobinuria such as heme protein precipitation with Tamm-Horsfall protein, decrease of release of free iron from myoglobin and prevention of formation of uric acid crystals), the administration of bicarbonate plus mannitol over normal saline alone has not been shown to prevent renal failure, reduce the need for dialysis or prevent death in trauma patients. There was, however, a trend towards better outcome in patients with CK values over 30,000 U/L.

The use of loop diuretics remains controversial. No study has shown a clear benefit to patients with rhabdomyolysis. The use of loop diuretics therefore is recommended in the same manner as that for acute kidney injury that is due to other causes.

References:

1. Better OS, Abassi ZA. Early fluid resuscitation in patients with rhabdomyolysis. *Nat Rev Nephrol.* 2011 May 17;7(7):416-422.
2. Bosch X, Poch E, Grau JM. Rhabdomyolysis and acute kidney injury. *N Engl J Med.* 2009 Jul 2;361(1):62-72.
3. Warren JD, Blumbergs PC, Thompson PD. Rhabdomyolysis: a review. *Muscle Nerve.* 2002 Mar;25(3):332-347.
4. Brown CV, Rhee P, Chan L, Evans K, Demetriades D, Velmahos GC. Preventing renal failure in patients with rhabdomyolysis: do bicarbonate and mannitol make a difference? *J Trauma.* 2004.

4. Rationale

Answer: B

Glomerular filtration rate (GFR) is the total amount of plasma filtered at the glomerulus. Inulin is used to estimate GFR because it is freely filterable and not secreted or absorbed by the kidneys. Creatinine can be used as an approximation but is both filtered and secreted.

Renal plasma flow is the amount of plasma that flows through the kidneys per unit of time. This is difficult to measure and is instead estimated from the effective renal

plasma flow (ERPF), which is the amount of plasma cleared of para-aminohippuric acid (PAH) per unit time. PAH is primarily secreted rather than filtered, but can be used to estimate ERPF.

At a level of 3 µg/kg/min, dopamine theoretically acts solely on the D1 receptor, causing dilation of the afferent and efferent arterioles of the glomerulus, leading to increased renal plasma flow and glomerular filtration rate. Dose response studies demonstrated that the dopamine-induced increase in ERPF reaches its maximum at 3 mcg/kg/min. The increase in ERPF remained unchanged by pretreatment with metoprolol, and a comparison of dopamine and dobutamine in doses producing similar increases in cardiac output showed that only dopamine increased ERPF. These findings indicate that indirect hemodynamic effects secondary to increases in cardiac contractility and cardiac output do not contribute significantly to the increase in renal perfusion caused by dopamine in doses lower than 3 mcg/kg/min. It is important to note that, despite this mechanism of action, dopamine has not been shown to prevent renal failure.

Furosemide is a loop diuretic that acts in the ascending limb of the loop of Henle. It inhibits the cotransport of sodium, potassium and chloride out of the nephron, making the ultrafiltrate more tonic and leading to a less hypertonic interstitium. With a less hypertonic interstitium, free water is retained in the collecting duct and thus excreted. Furosemide does not affect filtration at the glomerulus by direct effects on renal plasma flow.

Lisinopril is an angiotensin-converting enzyme inhibitor (ACEI). Normally, in the setting of sympathetic stimulation or decreased afferent blood flow, the renin-angiotensin-aldosterone system (RAAS) is activated, leading to increased release of angiotensin II, which acts both to increase aldosterone secretion from the adrenal cortex and directly causes constriction of the efferent arteriole to decrease ERPF and increase GFR. By inhibiting the formation of angiotensin II, ACEIs prevent efferent arteriolar constriction and therefore decrease GFR.

Metformin has no appreciable affects on ERPF or GFR.

References:

1. Olsen NV. Effects of dopamine on renal haemodynamics tubular function and sodium excretion in normal humans. *Dan Med Bull.* 1998 Jun;45(3):282-297.
2. Le T, Bhushan V. *First Aid for the USMLE Step 1.* New York, NY: McGraw-Hill; 2009: 438, 450-452.

5. Rationale

Answer: D

Hepatorenal syndrome (HRS) is a well-described entity in patients with end-stage liver disease, and is believed to be caused mainly by functional factors. HRS type 1 is characterized by a rapid decline of renal function over a period of several weeks whereas HRS type 2 is considered to be a more chronic disease. Pathophysiology is mostly believed to be due to arterial vasodilation with reduced systemic vascular

resistance and cardiac output that cannot compensate for this vasodilation. Secondary phenomenon is activation of the renal angiotensin-aldosterone system and increase secretion of arginine vasopressin to maintain blood pressure. The problem is multifactorial, and lately an increase in an inflammatory state has been described as yet another factor potentiating this problem. The treatment of HRS is in part preventive, by administration of concentrated albumin and treatment of spontaneous bacterial peritonitis, so D is the correct answer. In some patients dual transplant of liver and kidney can be considered but this is a controversial issue since we cannot predict which patients will recover their kidney function after liver transplant.

Reference:

1. Durand F, Graupera I, Ginès P, Olson JC, Nadim MK. Pathogenesis of hepatorenal syndrome: implications for therapy. *Am J Kidney Dis.* 2016 Feb;67(2):318-328.

6. Rationale

Answer: B

Beta-adrenergic agents can be effective in rapidly lowering potassium. However, they are relatively contraindicated in patients with coronary artery disease. Although IV furosemide can lower serum potassium, it is ineffective in patients with end-stage renal disease and no urine output at baseline. IV calcium gluconate is the therapy of choice in patients with ECG changes secondary to hyperkalemia to stabilize the cardiac membrane against the hyperkalemia-induced depolarization of resting cardiac membrane potential. It has no direct effect in lowering serum potassium. Finally, treatment with glucose and insulin lowers serum potassium within minutes. IV insulin promotes potassium uptake intracellularly by enhancing the sodium-potassium-ATPase transporter. Onset of insulin action occurs within 10 to 20 minutes and peaks at 30 to 60 minutes. The duration of insulin in the setting of normal creatinine clearance is between 4 to 6 hours. The range of potassium lowering after insulin and glucose therapy is between 0.5 to 1.2 meq/L.

References:

1. Lens XM, Montoliu J, Cases A, Campistol JM, Revert L. Treatment of hyperkalaemia in renal failure: salbutamol v. insulin. *Nephrol Dial Transplant.* 1989;4(3):228-232.
2. Emmett M. Non-dialytic treatment of acute hyperkalemia in the dialysis patient. *Semin Dial.* 2000 Sep-Oct;13(5):279-280.

7. Rationale

Answer: D

The delayed onset in acute kidney injury after percutaneous angiography is suggestive of atheroembolic disease. Atheroemboli contributing to renal failure typically occurs weeks after the procedure and contrast-induced nephropathy. Rhabdomyolysis from

myoglobin-induced pigment nephropathy is unlikely, given the red blood cells in the urine with a mild rise in creatine kinase. Diabetic nephropathy may be present in a patient with long-standing diabetes mellitus and may contribute to chronic kidney disease. However, diabetic nephropathy does not cause an acute worsening in renal function as in this case.

References:

1. Haas M, Spargo BH, Wit EJ, Meehan SM. Etiologies and outcome of acute renal insufficiency in older adults: a renal biopsy study of 259 cases. *Am J Kidney Dis.* 2000 Mar;35(3):433-447.
2. Richards AM, Eliot RS, Kanjuh VI, Bloemendaal RD, Edwards JE. Cholesterol embolism: a multiple-system disease masquerading as polyarteritis nodosa. *Am J Cardiol.* 1965 May;15:696-707.

8. Rationale

Answer: B

IV crystalloid therapy should be administered immediately and aggressively to prevent myoglobin-induced pigment nephropathy. Aggressive fluid resuscitation with crystalloid therapy has been demonstrated to enhance renal perfusion and improve urine flow rate to prevent obstruction from renal casts. Also, volume resuscitation is required to prevent hypovolemia that may result from site of crush injury. If overt alkalosis is ruled out, alkaline crystalloid solution is preferred for volume resuscitation. If there is no evidence of volume overload, loop diuretics are not recommended, and may also increase the likelihood of volume depletion. No benefit has been demonstrated with IV colloid therapy or low-dose dopamine infusion.

References:

1. Gunal AI, Celiker H, Dogukan A, et al. Early and vigorous fluid resuscitation prevents acute renal failure in the crush victims of catastrophic earthquakes. *J Am Soc Nephrol.* 2004 Jul;15(7):1862-1867.
2. Ron D, Taitelman U, Michaelson M, Bar-Joseph G, Bursztein S, Better OS. Prevention of acute renal failure in traumatic rhabdomyolysis. *Arch Intern Med.* 1984 Feb;144(2):277-280.

9. Rationale

Answer: D

The metabolic disturbance causing the anion gap acidosis is a combination of alcoholic ketoacidosis and lactic acidosis. This combination is often seen in patients with alcohol abuse who binge drink and are concurrently malnourished due to excessive alcohol intake and/or gastritis leading to food intolerance. The elevated anion gap is a result of ketone body production due to suppressed insulin secretion and lipolysis, due in part to the alcohol metabolism and starvation state. In addition, a mild lactic acidosis is present due to volume depletion or possibly early sepsis

secondary to aspiration pneumonia.

Distinguishing toxic alcohol ingestions, such as from ethylene glycol and isopropanol, from alcoholic ketoacidosis is challenging, and may not be feasible in the acute setting. Often empiric treatment with fomepizole may be needed until further laboratory testing can be conducted. History is usually the most important clue in suspecting toxic alcohol ingestion, in addition to detecting an anion gap acidosis with an elevated osmolar gap. Relying exclusively on an elevated anion gap and osmolar gap is ill advised, however, since there are many instances in which this will not hold true. Isopropyl alcohol ingestion does not cause acidosis and can be eliminated from the differential diagnosis. Similarly, with no history of diabetes and a normal blood sugar level, diabetic ketoacidosis is less likely in this scenario.

References:

1. Wrenn, KD, Slovis CM, Minion GE, Rutkowski R. The syndrome of alcoholic ketoacidosis. *Am J Med*. 1991 Aug;91(2):119-128.
2. Jenkins, DW, Eckle RE, Craig JW. Alcoholic ketoacidosis. *JAMA.* 1971 Jul 12;217(2):177-183.

10. Rationale

Answer: B

This patient has evidence of acute renal failure, most likely post-obstructive from nephrolithiasis. This is a medical emergency given that he has a solitary kidney, as well as evidence of severe sepsis due to the urinary tract obstruction. Bedside ultrasound was used to determine this diagnosis, showing moderate right-sided hydronephrosis. A CT may eventually be requested by the urologist to plan the intervention, but the most critical next step is to begin management for severe sepsis while consulting urology for source control and obstruction relief. Given the findings of severe sepsis and a solitary kidney, treating this patient as uncomplicated nephrolithiasis with pain management alone is inappropriate. Similarly, the patient may eventually require dialysis and nephrology consultation, but in the acute time period, treatment of the obstructive nephrolithiasis with associated severe sepsis takes precedence in hopes that dialysis may be avoided.

Reference:

1. Portis AJ, Sundaram CP. Diagnosis and initial management of kidney stones. *Am Fam Physician*. 2001 Apr 1;63(7):1329-1338.

11. Rationale

Answer: A

The patient has acute severe hyponatremia in the setting of transurethral resection of bladder tumor (TURBT) syndrome, which develops from bladder perforation with subsequent absorption of large amount of irrigation fluids (typically glycine, sorbitol, or free water) that results in circulatory overload, hemolysis, hyponatremia, and acute

renal failure. Small subclinical perforations can occur in more than 50% of patients. The hallmarks of TURBT syndrome are acute hyponatremia, hemolysis, and metabolic acidosis.

Absorption of large amounts of hypotonic fluid leads to significant plasma hypotonicity and hyponatremia. The central nervous system and brain are most susceptible to devastating changes secondary to acute hyponatremia. A rapid drop in plasma sodium concentration leads to brain swelling, increase in intracranial pressure, and potential herniation. In response to hypotonicity, astrocytes activate cell-to-cell transfer of taurine (organic osmolyte) that protects neurons from swelling at the expense of astrocytes swelling. Within 24 to 48 hours, astrocytes normalize in volume due to slow loss of taurine and glutamate. In addition to loss of organic osmolytes, the downregulation of osmolyte-accumulating transporters (taurine and myo-inositol transporters) takes place. As results of these changes, astrocytes are extremely susceptible to hypertonic injury in cases of rapid correction of hyponatremia. Hypertonic injury triggers apoptosis, disruption of the blood-brain barrier, and demyelination. Demyelination syndrome manifests as altered mental status, seizure and movement disorders, and behavioral abnormalities. Central pontine dimyelination presents with locked-in syndrome.

It is very important to distinguish the chronicity of hyponatremia. Fast correction of chronic hypernatremia (greater than 24-48 hours in duration) will lead to hypertonic injury of astrocytes, since their osmolar adjustment mechanism are exhausted. In the setting of acute (less than 24 hours in duration) and severe symptomatic hyponatremia, aggressive correction of hyponatremia is necessary to prevent fatal cerebral edema, and will not cause demyelinating injury.

In the case of acute severe hyponatremia, administration of several boluses (1-2 mL/kg) of 3% sodium chloride is indicated with the goal of raising the sodium concentration by 4 to 6 mEq/L in the first 6 hours. This approach hastens the development of acute cerebral edema. Correction of chronic hyponatremia should not exceed 8 mEq/L/day to prevent the development of demyelination. Fluid restriction is not suitable for patients with acute severe symptomatic hyponatremia. Desmopressin leads to increased reabsorption of free water and decrease of free water loss with urine.

References:

1. Golan S, Baniel J, Lask D, Livne PM, Yossepowitch O. Transurethral resection of bladder tumour complicated by perforation requiring open surgical repair—clinical characteristics and oncological outcomes. *BJU Int.* 2011 Apr;107(7):1065-1068.
2. Sterns RH. Disorders of plasma sodium—causes, consequences, and correction. *N Engl J Med.* 2015 Jan 1;372(1):55-65.
3. Sterns RH, Nigwekar SU, Hix JK. The treatment of hyponatremia. *Semin Nephrol.* 2009 May;29:282-299.
4. Sood L, Sterns RH, Hix JK, Silver SM, Chen L. Hypertonic saline and desmopressin: a simple strategy for safe correction of severe hyponatremia. *Am J Kidney Dis.* 2013 Apr;61(4):571-578.

12. Rationale

Answer: D

The patient presents with leg weakness as a surrogate of acute ischemia of the distal spinal cord. The initial CT showed interruption of aortic flow below the celiac artery. The ischemic cells have released potassium to the extracellular space concomitantly with an underlying severe metabolic acidosis. Although metabolic acidosis has repeatedly been implicated as a causative factor of hyperkalemia via transcellular shift of potassium from the intracellular to extracellular compartment, this paradigm has been challenged. The significant elevation of potassium is secondary to reperfusion distal to the celiac artery, which explains the occurrence of a wide complex arrhythmia, peak T waves/ST elevations, and eventually asystole.

An acute coronary syndrome could have explained some of the ECG changes since most vascular patients have undetected coronary artery disease. A retrograde dissection of the aorta compromising the ascending segment, even when possible, is not a frequent presentation for a type B dissection; however, many investigators have reported the transformation to type A dissection after stent graft placement for type B dissection with an estimated rate of 2%. Mesenteric ischemia is possible but it would not be manifested so acutely.

References:

1. Golledge J, Eagle KA. Acute aortic dissection. *Lancet.* 2008 Jul 5;372(9632):55-66.
2. Eggebrecht H, Nienaber CA, Neuhäuser M, et al. Endovascular stent-graft placement in aortic dissection: a meta-analysis. *Eur Heart J.* 2006 Feb;27(4):489-498.

13. Rationale

Answer: D

The endothelial glycocalyx is located on the luminal side of endothelial cells and serves as the active interface between blood and the capillary wall. Traditionally, the Starling principle has been taught as a model of semipermeable capillaries subject to hydrostatic and oncotic pressure gradients. This model employed the classic compartments of plasma, interstitial, and intracellular as locations where resuscitative fluids would filter, depending on the balance between hydrostatic and oncotic pressure gradients. Recent research has shown that the endothelial glycocalyx layer appears to have a major role in fluid exchange and volume of distribution. The glycocalyx model, an acellular layer lining the endothelium, is a paradigm shift in our understanding of the interface between the blood and the endothelial cells. It is a key determinant of vascular permeability. The glycocalyx layer has varying membrane permeability across organ systems, which changes based on timing and severity of the ongoing disease process, as well as treatment. Extravasation of fluid from the capillaries is predominately dependent on capillary hydrostatic pressure and not on decreased intravascular colloid osmotic pressure, as once thought. Various disease states (ie, sepsis and trauma) as well as over-resuscitation (leading to the release of

atrial natriuretic peptide) can damage the glycocalyx layer.

References:

1. Myburgh JA and Mythen MG. Resuscitation fluids. *N Engl J Med.* 2013 Sep 26;369(13):1243-1251.
2. Woodcock TE, Woodcock TM. Revised Starling equation and the glycocalyx model of transvascular fluid exchange: an improved paradigm for prescribing intravenous fluid therapy. *Brt J Anaesth.* 2012 Mar;108(3):384-394.
3. Chappell D, Bruegger D, Potzel J, et al. Hypervolemia increases release of atrial natriuretic peptide and shedding of the endothelial glycocalyx. *Crit Care.* 2014 Oct 13;18(5):538.

14. Rationale

Answer: D

Fluid resuscitation is a ubiquitous intervention in critical care medicine, and the provision of maintenance fluids is a common cornerstone of this therapy. The rationale for maintenance fluids is that they assist in fluid resuscitation and prevent preload-dependant hypoperfusion. This has not been proven. What is known is that approximately 80% of isotonic crystalloid infusions are not maintained in the vascular space, maintenance fluids contribute to volume overload, and volume overload is increasingly recognized as a direct contributor to organ failure in critically ill patients.

Intravascular circulating volume is important for patients with markers of poor perfusion or end-organ damage. There appears to be an optimal circulating fluid volume to prevent shock and multisystem organ failure. Liberal fluid strategies have shown such complications as peripheral edema, respiratory failure/lung injury, dilutional anemia and coagulopathy, neutrophil activation, poor wound healing, and delayed bowel recovery. Intravascular volume should be restored on an individualized basis with care given to the type of fluid used for resuscitation and the amount of fluid provided.

References:

1. Myburgh JA and Mythen MG. Resuscitation fluids. *N Engl J Med.* 2013 Sep 26;369(13):1243-1251.
2. Raghunathan K, Shaw A, Nathanson B, et al. Association between the choice of IV crystalloid and in-hospital mortality among critically ill adults with sepsis. *Crit Care Med.* 2014 Jul;42(7):1585-1591.
3. Hilton AK, Pellegrino VA, Scheinkestel CD. Avoiding common problems associated with intravenous fluid therapy. *Med J Aust.* 2008 Nov 3;189(9):509-513.

15. Rationale

Answer: A

This patient has a mixed acid-base disorder. She has worsening sepsis from an ischemic small bowel obstruction leading to a metabolic lactic acidosis. There is an underlying metabolic alkalosis from vomiting and nasogastric tube drainage. The respiratory alkalosis develops with her abdominal pain and she becomes tachypneic.

Discerning acid-base problems requires a systematic approach. Here is one of several methods that can be used. Step 1: Look at the pH. The process that caused the shift to either side of 7.40 is the primary abnormality. This patient's pH is 7.50, with a partial pressure of carbon dioxide of 24 mm Hg, consistent with acute respiratory alkalosis. Step 2: Calculate the anion gap. The body will never generate a large anion gap to compensate for the primary disorder. In this case the anion gap is 27 mEq/L. Of note, the albumin level is normal, but if less than 4.0 g/dL, the anion gap would require correction by 2.5 mEq/L for every 1 below 4.0 g/dL. Step 3: Calculate the delta-delta gap to see if there is an underlying non-anion gap acidosis or metabolic alkalosis in addition to the anion gap acidosis. In this case the delta gap is greater than 2.0, indicating a concurrent metabolic alkalosis.

References:

1. Haber, Richard. A practical approach to acid-base disorders. *West J Med.* 1991 Aug;155(2):146-151.
2. Adrogué HJ. Mixed acid-base disturbances. *J Nephrol.* 2006 Mar-Apr;19 Suppl 9:S97-S103.

16. Rationale

Answer: B

When solving acid/base problems, the first step is examining the pH. A normal pH is between 7.35 and 7.45. Acidemia is present when serum pH is less than 7.35, while alkalemia is present when serum pH is more than 7.45. In this case, the pH is 7.12, indicating academia.

The second step is examining the partial arterial carbon dioxide pressure ($Paco_2$) to determine whether the academia is respiratory in nature or not. A normal $Paco_2$ is 35-45 mm Hg. In this case, the $Paco_2$ is 40 mm Hg, indicating that the low pH is due to a metabolic, rather than respiratory, component. This is further validated by the low bicarbonate level (17 mEq/L).

The third step is to see whether or not there is respiratory compensation. With a metabolic acidosis, the body attempts to compensate by hyperventilating in order to remove carbon dioxide. In this case, the $Paco_2$ is 40 mm Hg. In order to be appropriately compensated, for every 1 mEq/L decrease in bicarbonate from 24 mEq/L, the $Paco_2$ should decrease by 1 mm Hg from 40 mm Hg. In this case, the bicarbonate decreases by 7 mEq/L (from 24 mEq/L to 17 mEq/L) but the $Paco_2$ does not decrease at all from 40 mm Hg.

Alternatively, the Winters formula can be used to predict the appropriate $Paco_2$ for a

given bicarbonate. The Winters formula is $Paco_2$ = (1.5 x bicarbonate) + 8 ± 2. For the given question, the expected $Paco_2$ would be 33 ± 2 mm Hg. The actual $Paco_2$ is 40 mm Hg, which is too high given the level of acidosis; therefore, a concomitant respiratory acidosis is present.

When dealing with a metabolic acidosis, it is imperative to next calculate the anion gap using the anion gap formula: Anion gap = sodium - (bicarbonate + chloride); normal 10-12. In this case, the anion gap is 33 so an anion gap metabolic acidosis must be present.

Finally one must determine if there is a mixed picture present. In order to determine this, the delta anion gap must be calculated: Delta anion gap = (anion gap - 12)/(24 - bicarbonate). In this case, the delta anion gap is 3: (33-12)/(24-17) = 3.

Delta ratio assessment guidelines specify that a value less than 0.4 = hyperchloremic normal anion gap acidosis. If 0.4-0.8, consider combined high anion gap and normal anion gap acidosis but note that the ratio is often less than 1 in acidosis associated with renal failure. A value of 1-2 is usual for uncomplicated high anion gap acidosis. Lactic acidosis yields an average value of 1.6. Diabetic ketoacidosis is more likely to yield a ratio closer to 1 due to urine ketone loss (especially if the patient is not dehydrated). A value of greater than 2 suggests a preexisting elevated bicarbonate level. Consider a concurrent metabolic alkalosis or a preexisting compensated respiratory acidosis.

Since this value is greater than 2, a concomitant metabolic alkalosis is also present. The bicarbonate is too high given the current anion gap. In this case, the patient was admitted for nausea and vomiting, which could lead to a mixed picture, including a metabolic alkalosis. Other potential causes of metabolic alkalosis include iatrogenic administration of bicarbonate or excessive diuretic use.

It is also important to note how hypoalbuminemia can affect acid/base status. Since albumin is a negatively charged anion that greatly contributes to the anion gap, when albumin levels are decreased, the anion gap may be falsely decreased. It is important then to be aware of the albumin corrected anion gap: Albumin corrected anion gap = observed anion gap + 2.5 (normal albumin-observed albumin) where the normal albumin is 4 g/dL. In this case, the albumin corrected anion gap = 33 + 2.5 (4-2.5) = 36.75.

References:

1. Matthes K, Urman R, Ehrenfeld J, eds. *Anesthesiology: A Comprehensive Board Review for Primary and Maintenance of Certification.* Oxford: Oxford University Press; 2013:51-52.
2. Marini JJ, Wheeler AP. *Critical Care Medicine: The Essentials.* 4th ed. Baltimore, MD: Lippincott Williams & Wilkins; 2012:236-237.

17. Rationale

Answer: D

The patient has mild alkelemia, with a pH of 7.45. His carbon dioxide level is 23 mm Hg, consistent with respiratory alkalosis. However, the pH is lower than would be expected for a carbon dioxide value of 23 mm Hg, indicating a mixed process. Bicarbonate level is 18 mEq/L, indicating a metabolic acidosis. The anion gap is calculated to be 11 mEq/L (133 - (104 +18)). However, albumin is only 1.4 g/dL, as opposed to the normal level of 4 g/dL. For every 1 g/dL decrease in albumin, the anion gap should be raised by approximately 2.5 mEq/L, leading to a final value of 17.5 mEq/L.

References:

1. Berend K, de Vries AP, Gans RO. Physiological approach to assessment of acid-base disturbances. *N Engl J Med.* 2014 Oct 9;371(15):1434-1445.
2. Seifter JL. Integration of acid-base and electrolyte disorders. *N Engl J Med.* 2014 Nov 6;371(19):1821-1831.

18. Rationale

Answer: C

Proper assessment and management of the airway of the status epilepticus patient with ongoing convulsions can be difficult. Most patients will have a profound metabolic acidosis (as severe as arterial pH < 7.0) with attempted respiratory compensation. Patients in status epilepticus continue to breathe with appropriate gas exchange as long as the airway remains clear. This metabolic acidosis will correct itself once the seizures are controlled. Antiseizure drugs with sedating side effects can impede the drive for respiratory compensation, creating a secondary acid-base disturbance (worsening the overall acidosis) with a respiratory acidosis. This respiratory compensation is of paramount importance as a patient is placed on the ventilator, and clinicians should plan on a high minute ventilation requirement. This patient has no oxygenation issues, and increasing positive end-expiratory pressure is not the correct intervention for increasing ventilation. Propofol is a sedating medication that usually impedes respiratory drive, leading to an increase in carbon dioxide levels. Decreasing the set respiratory rate could worsen respiratory acidosis, negatively impacting the clinical situation. Dead space is calculated from correlating the measured expiatory carbon dioxide and the blood gas measurement that is still pending; however, this end-tidal carbon dioxide value is not consistent with a dead space issue.

References:

1. Brophy GM, Bell R, Claassen J, et al. Guidelines for the evaluation and management of status epilepticus. *Neurocrit Care.* 2012 Aug;17(1):3-23.
2. Lowenstein DH, Alldredge BK. Status epilepticus. *N Engl J Med.* 1988 April 2;338(14):970-976.

19. Rationale

Answer: C

This patient has elevated anion gap metabolic acidosis, which is often caused by methanol, ethanol, uremia, diabetic ketoacidosis, propylene glycol, oxoproline, lactate, or salicylates. A normal anion gap ranges from 8 to 16 mEq/L, with a value over 16 mEq/L considered an elevated anion gap. In this case, the anion gap is calculated to be 35 mEq/L (145 - (106 + 4)). The patient is nonadherent with her insulin, but her blood glucose on arrival is 134, making diabetic ketoacidosis less likely. Intoxication from vast quantities of ethanol is similarly unlikely since her ethanol level was less than 5 on admission. Salicylates such as aspirin can cause an elevated anion gap metabolic acidosis and a respiratory alkalosis, but her aspirin level is negative and she has a compensated metabolic acidosis.

Acetaminophen overdose is the most common cause of acute liver failure in the United States. Signs and symptoms of an overdose include nausea, vomiting, sweating, lethargy, and elevated liver enzymes. Aside from causing an elevation in liver enzymes, ingesting a large quantity of acetaminophen also causes an elevation in 5-oxoproline. 5-Oxoproline is a metabolite of acetaminophen, and if it accumulates in the body it can cause an elevated anion gap metabolic acidosis. 5-Oxoproline is an intermediate in the gamma-glutamyl pathway, which is the metabolic cycle responsible for creating glutathione and pushing amino acids into the cytosol. When glutathione levels are diminished, feedback inhibition ceases, causing an overproduction of gamma-glutamylcysteine, which is then metabolized to 5-oxoproline. Treatment with N-acetylcysteine should be initiated and referral to a liver transplant center should be considered.

References:

1. Pitt JJ, Hauser S. Transient 5-oxoprolinuria and high anion gap metabolic acidosis: clinical and biochemical findings in eleven subjects. *Clin Chem.* 1998 Jul;44(7):1497-1503.
2. Fenves AZ, Kirkpatrick HM 3rd, Patel VV, Sweetman L, Emmett M. Increased anion gap metabolic acidosis as a result of 5-oxoproline (pyroglutamic acid): a role for acetaminophen. *Clin J Am Soc Nephrol.* 2006 May;1(3):441-447.
3. Tokatli A, Kalkanoglu-Sivri HS, Yüce A, Coskun T. Acetaminophen-induced hepatotoxicity in a glutathione synthetase-deficient patient. *Turk J Pediatr.* 2007 Jan-Mar;49(1):75-76.
4. Lawrence DT, Bechtel LK, Charlton NP, Holstege CP. 5-oxoproline-induced anion gap metabolic acidosis after an acute acetaminophen overdose. *J Am Osteopath Assoc.* 2010 Sep; 110(9):545-551.

20. Rationale

Answer: C

This patient at baseline has a compensated chronic respiratory acidosis; her baseline partial pressure of carbon dioxide (pCO_2) is 60 mm Hg with a relatively normal pH (7.35-7.45) and bicarbonate of 32 mEq/L. This can be explained by this equation:

Expected [bicarbonate] = 24 + 4 {(Actual pCO_2 - 40)/10} or 32 = 24 + 4(60-40)/10).

She is experiencing a chronic obstructive pulmonary disease exacerbation, mostly likely due to an underlying respiratory infection. This has led to an acute rise in pCO_2 12 mm Hg, without time for metabolic compensation, which takes 48 hours. Her pH can be calculated as follows:

Change in pH = .008 x (new pCO_2 - baseline pCO_2), or .008 x (72-60) = 0.096, or 7.34, which is the patient's current pH. 0.096 = 7.24.

References:

1. Berend K, de Vries AP, Gans RO. Physiological approach to assessment of acid-base disturbances. *N Engl J Med Med.* 2014 Oct 9;371(15):1434-1445.
2. Dorman PJ, Sullivan WJ, Pitts RF. The renal response to acute respiratory acidosis. *J Clin Invest.* 1954 Jan;33(1):82-90.
3. Rose B, Post T. *Clinical Physiology of Acid-Base and Electrolyte Disorders.* 5th ed. New York, NY: McGraw-Hill; 2001.
4. Nichols G Jr. Serial changes in tissue carbon dioxide content during acute respiratory acidosis. *J Clin Invest.* 1958 Aug;37(8):1111-1122.

21. Rationale

Answer: B

In a case of digitalis toxicity, during the patient's stabilization and transport, it is possible to use atropine to attempt to reverse the pronounced bradyarrythmia. Ephedrine and, eventually, epinephrine in small doses can be considered as well. Electrolytes should be corrected quickly, especially in the case of hypokalemia and hypomagnesemia. Hypercalcemia enhances digitalis-induced increases in intracellular calcium, which can lead to calcium overload and increased susceptibility to digitalis-induced arrhythmias.

References:

1. Gheorghiade M, van Veldhuisen DJ, Colucci WS. Contemporary use of digoxin in the management of cardiovascular disorders. *Circulation.* 2006 May 30;113(21):2556-2564.
2. Chan AL, Wang MT, Su CY, Tsai FH. Risk of digoxin intoxication caused by clarithromycin-digoxin interactions in heart failure patients: a population-based study. *Eur J Clin Pharmacol.* 2009 Dec;65(12):1237-1243.
3. Kelly RA, Smith TW. Recognition and management of digitalis toxicity. *Am J Cardiol.* 1992 Jun 4;69(18):108G-118G; disc 118G-119G.

22. Rationale

Answer: B

Hypercalcemic crisis is an endocrine disorder that is seen in the ICU, most often in the setting of malignancy or hyperparathyroidism. This young, relatively healthy patient is

found to have hypercalcemia, along with renal dysfunction. In this setting, the clinician must be concerned about hyperparathyroidism, with a main goal of restoring her volume status. IV resuscitation in the acute setting would have the most benefit for the patient because she is probably dehydrated from hypercalcemia-induced urinary salt wasting. Calcimimetic agents, such as cincalcet, reduce calcium levels by activating the calcium-sensing receptor in the parathyroid gland, thereby inhibiting parathyroid hormone secretion. They have shown clinical benefit in secondary hyperparathyroidism associated with renal failure and in parathyroid carcinoma.

Glucocorticoids, such as prednisone, reduce serum calcium concentrations by decreasing calcitriol production by activated mononuclear cells. Clinical studies have shown the most benefit in hypercalcemia secondary to granulomatous disease; they take effect in two days. Bisphosphonates, such as zoledronate, act by inhibiting calcium release by interfering with osteoclast-mediated bone resorption, and have shown clinical benefit in hypercalcemia secondary to malignancy. Although bisphosphonates may be used in conjunction with isotonic solution, their maximal effect usually takes two to four days.

References:

1. Basso SM, Lumachi F, Nascimben F, Luisetto G, Camozzi V. Treatment of acute hypercalcemia. *Med Chem.* 2012 Jul;8(4):564-568.
2. Silverberg SJ, Bone HG 3rd, Marriott TB, et al. Short-term inhibition of parathyroid hormone secretion by a calcium-receptor agonist in patients with primary hyperparathyroidism. *N Engl J Med.* 1997 Nov 20;337(21):1506-1510.
3. Mirrakhimov AE. Hypercalcemia of malignancy: an update on pathogenesis and management. *N Am J Med Sci.* 2015 Nov;7(11):483-493.

23. Rationale

Answer: D

Thyroid storm is a challenging diagnosis to make, especially without prior history of disease and other confounding factors. This patient had undiagnosed hyperthyroidism as evidenced by her preoperative weakness, fatigue, and palpitations. She subsequently developed appendicitis, and the stress of the infection as well as the surgery, sent her into thyroid storm.

Thyroid storm is a rare but potentially life threatening complication of hyperthyroidism that is often triggered by a stress to the body, such as infection. Symptoms include high fever, tachycardia, mental status changes, gastrointestinal symptoms, and potentially high-output heart failure. Treatment must be immediately initiated, often before laboratory results are available, to achieve the best outcome. IV beta-blockers, such as propranolol, are effective for rate control and help block peripheral thyroxine to triiodothyronine conversion. Antithyroid drugs such as propylthiouracil and methimazole are also needed to block production of thyroid hormone. Steroids are given to protect against concomitant adrenal insufficiency and prevent peripheral thyroid conversion. Iodine may be added only after antithyroid drugs are started.

Malignant hyperthermia and serotonin syndrome may look similar to thyroid storm, but there are some subtle differences. In malignant hyperthermia, a more rapid onset after induction might be expected as well as muscle rigidity and respiratory acidosis. Serotonin syndrome is also associated with muscle rigidity and often clonus. The hypertension can be controlled with the IV ACE inhibitor enalaprilat, but the intitial treatment of her thyroid storm will treat the underlying cause of her increased blood pressure.

Reference:

1. Chiha M, Samarasinghe S, Kabaker AS. Thyroid storm: an updated review. *J Intensive Care Med.* 2015 Mar;30(3):131-140.

24. Rationale

Answer: C

Critical illness-related corticosteroid insufficiency (CIRCI) is encountered in the ICU. This patient was on prednisone for lupus before being hospitalized and had a suppressed hypothalamic-pituitary-adrenal axis that prevented an appropriate response to the severe infection. As a result, despite appropriate fluid resuscitation, antibiotics, and vasopressor support, she remained in refractory shock requiring IV stress-dose steroids to support her blood pressure.

CIRCI is a form of relative adrenal insufficiency in which blood corticosteroid levels are inadequate for the stress imparted during critical illness. Features include refractory shock as well as electrolyte abnormalities including hypoglycemia, hyperkalemia, and hyponatremia. The diagnosis is often challenging based on laboratory test parameters, with no agreed-upon values in the literature. Conflicting results from trials such as Annane's and the CORTICUS study (albeit with different patient populations) have led to a Surviving Sepsis Guideline recommendation to treat CIRCI on clinical grounds alone, if it is suspected. Exact dosing and duration of steroids is undefined, but lower, intermittent dosing of IV hydrocortisone is often used and weaned once shock is resolved.

Adding antifungal coverage could be considered, although it is less likely to be of benefit in this scenario. The patient has received more than adequate resuscitation and does not meet any hard criteria for starting epinephrine.

References:

1. Annane D, Sébille V, Charpentier C, et al. Effect of treatment with low doses of hydrocortisone and fludrocortisone on mortality in patients with septic shock. *JAMA.* 2002 Aug 21;288(7):862-871.
2. Sprung CL, Annane D, Keh D, et al; CORTICUS Study Group. Hydrocortisone therapy for patients with septic shock. *N Engl J Med.* 2008 Jan 10;358(2):111-124.

25. Rationale

Answer: B

Tumor lysis syndrome (TLS) describes the physiologic disturbances that can occur after initiation of cancer treatment. Spontaneous cases of TLS may also occur. The potential to develop TLS exists with any cancer, but is more common with hematologic malignancies or when a large cancer burden is present. In TLS, rapid cancer cell lysis releases intracellular contents and metabolites (potassium, phosphate, purines, and cytokines) beyond the body's ability to manage, leading to hyperkalemia, hyperphosphatemia, hypocalcemia, and hyperuricemia.

Signs and symptoms may develop at any time, but commonly within the first few days of starting cytotoxic medication. Examples include nausea, emesis, cramps, tetany, or seizures due to hypocalcemia. Cardiac dysrhythmias may occur due to hyperkalemia and hypocalcemia. Uremia can lead to metallic taste, pruritus, restless legs, ecchymoses or pericarditis. Hypotension and inflammation may occur with release of cytokines. Acute kidney injury can develop as a result of the precipitation of uric acid crystals and calcium phosphate crystals, and can be exacerbated by dehydration and acidosis.

Uric acid is a product of the metabolic breakdown of purine nucleotides, the building blocks of DNA and RNA. After cell lysis, enzymes break down DNA and RNA, leading to the release of purines, which are then broken down to hypoxanthine through purine catabolism. The enzyme xanthine oxidase catalyzes the formation of uric acid from xanthine and hypoxanthine. Uric acid is excreted in the urine, but higher levels lead to precipitation and crystal-induced nephropathy. Urate oxidase is an enzyme that does not exist in humans, but exists in other animals, and is used as a therapeutic drug target to further break down uric acid into the water-soluble molecule allantoin, which is excreted in the urine.

Identifying patients at high risk for TLS before initiation of cancer therapy and early recognition of these metabolic complications is important. Hydration is essential to prevent hypotension and improve renal perfusion. There are two main mechanisms for treating elevated uric acid levels: xanthine oxidase inhibitors and recombinant urate oxidase. Xanthine oxidase inhibitors (allopurinol, febuxostat) prevent the formation of uric acid; however, existing uric acid still must be cleared and can take several days to improve. Furthermore, xanthine levels can increase and lead to nephropathy secondary to xanthine precipitation. Therefore, allopurinol is recommended only for patients at low risk for TLS or in combination with rasburicase.

Rasburicase is a recombinant urate oxidase, converting uric acid to water-soluble allantoin, which is excreted in the urine. Because rasburicase does not increase xanthine levels and directly reduces uric acid levels, it is recommended as the first-line agent for patients at high risk for TLS. In severe situations, hemodialysis may be used.

Although urinary alkalinization increases uric acid solubility, it decreases calcium phosphate solubility. Because it is more difficult to correct hyperphosphatemia than hyperuricemia, urinary alkalinization is approached with caution in TLS. Purine analogs are antimetabolites that mimic the structure of metabolic purines. They act as inhibitors of DNA synthesis and are used to treat certain cancers and autoimmune

disorders. Phosphate binders are medications used to reduce the absorption of phosphate and are typically used in people with chronic kidney failure. They are taken with meals, binding to phosphate in the gastrointestinal tract and excreted, preventing phosphate absorption.

References:

1. Howard SC, Jones DP, Pui CH. The tumor lysis syndrome. *N Engl J Med.* 2011 May 12;364(19):1844-1854.
2. Abu-alfa AK, Younes A. Tumor lysis syndrome and acute kidney injury: evaluation, prevention, and management. *Am J Kidney Dis.* 2010 May;55(5 Suppl 3):S1-S13.
3. Coiffier B, Altman A, Pui CH, Younes A, Cairo MS. Guidelines for the management of pediatric and adult tumor lysis syndrome: an evidence-based review. *J Clin Oncol.* 2008 Jun 1;26(16):2767-2778.

26. Rationale

Answer: C

Carcinoids are neuroendocrine tumors that originate mainly in the gastrointestinal (GI) tract and lungs. They synthesize and release a variety of bioactive substances (mainly serotonin, histamine, tachykinins, kallikreins, and prostaglandins), which are responsible for the symptoms and manifestations known as carcinoid syndrome. Most GI carcinoid tumors do not initially manifest with these symptoms, however, because their humoral substances are released into the portal circulation and inactivated by the liver. Carcinoid syndrome develops in patients with gastrointestinal carcinoid tumors that have metastasized to the liver. Once liver disease is present, the liver is unable to protect the body from the actions of these substances.

The most significant long-term sequela of chronic exposure to these bioactive chemicals is carcinoid heart disease, which consists of pathognomonic plaque-like fibrous deposits on the heart valves, chambers, and intima of the great vessels. Typically only the right side of the heart is affected due to inactivation of these substances by the lungs. Surgical resection is the primary treatment for carcinoid tumors. Before resection, symptom management is controlled mainly with the somatostatin analogs, such as octreotide. Somatostatin is an endogenous peptide that inhibits the release of a broad range of hormones, including many of those released by carcinoid tumors. The majority of carcinoid tumors express somatostatin receptors and, therefore, its administration will inhibit the release of its bioactive substances. Carcinoid crisis is a life-threatening form of this syndrome that may be triggered by tumor manipulation, as in this patient. The somatostatin analogs are the primary treatment since the administration of catecholamines can worsen the situation by potentiating further hormone release from the tumors. Therefore, systemic catecholamines are recommended only in life-threatening situations or sustained vasodilatory shock following administration of a somatostatin analog. IV furosemide in the setting of hypotension is not recommended and, furthermore, the findings of jugular venous distention and right-sided regurgitant murmurs in this patient likely reflect primary valvular carcinoid heart disease rather than fluid overload. Histamine

blockers will not do much to treat the hypotension in this disease, which is due not just to histamine, but to a number of substances.

References:

1. Fox DJ, Khattar RS. Carcinoid heart disease: presentation, diagnosis, and management. *Heart.* 2004 Oct;90(10):1224-1228.
2. Mancuso K, Kaye AD, Boudreaux JP, et al. Carcinoid syndrome and perioperative anesthetic considerations. *J Clin Anesth.* 2011 Jun;23(4):329-341.
3. Bhattacharyya S, Davar J, Dreyfus G, Caplin ME. Carcinoid heart disease. *Circulation.* 2007 Dec 11;116(24):2860-2865.
4. Strosberg JR. Treatment of the carcinoid syndrome. *UpToDate.* Last updated Nov 12, 2015.

27. Rationale

Answer: B

Risk factors for acute kidney injury (AKI) in the postoperative period include age older than 70, history of diabetes melllitus, high-risk surgical procedures, and use of IV contrast dye. Many agents have been evaluated for prevention of AKI; however no agent has been shown to be more effective than maintaining optimal volume status and hemodynamics. Avoidance of hypotension is important in order to maintain renal perfusion pressure. N-acetylcysteine, mannitol, and isotonic bicarbonate have all been studied for their efficacy in prevention and have shown benefit in some studies. However, none of these interventions has proven to be more efficacious than maintaining optimal hydration and blood pressure.

Reference:

1. Kidney Disease: Improving Global Outcomes. Acute Kidney Injury Work Group. KDIGO clinical practice guideline for acute kidney injury. *Kidney Int Suppl.* 2012;2:1-138.

28. Rationale

Answer: B

This patient has abdominal compartment syndrome (ACS) due to extensive volume resuscitation in the setting of severe burns. Bladder pressure should be urgently checked to formally diagnose this condition and expedite further management. ACS is often under-recognized in critically ill patients because organ failure is often multifactorial and attributed to the underlying disease process. When abdominal pressures are found to be greater than 20 mm Hg with associated organ failure, criteria are met for a diagnosis of ACS. Organ failure can be manifested as hypotension due to pressure on the vena cava and a decrease in venous return and subsequent drop in cardiac output. Patients on mechanical ventilation often have high peak airway pressures due to a distended abdomen. However, this patient was on pressure-control ventilation, in which airway pressures are regulated, and thus ACS

manifests as a reduction in tidal volume on this mode of ventilation. Renal failure is another common finding, and thought to be secondary to decreased renal perfusion from renal vein compression and diminished cardiac output. Management is abdominal decompression. Providing more IV fluids is likely to worsen compartment pressures. With a low pulse pressure variation, it is highly unlikely that he will respond to more fluid boluses. Acute tubular necrosis from rhabdomyolysis is possible, but less likely given the time frame from the contrast bolus and the relatively low creatinine kinase level.

References:

1. Kirkpatrick AW, ROberts DJ, De Waele J, et al; Pediatric Guidelines Sub-Committee for the World Society of the Abdominal Compartment Syndrome. Intra-abdominal hypertension and the abdominal compartment syndrome: updated consensus definitions and clinical practice guidelines from the World Society of the Abdominal Compartment Syndrome. *Intensive Care Med.* 2013 Jul;39(7):1190-1206.
2. Mirrakhimov AE, Voore P, Halytskyy O, Khan M, Ali AM. Propofol infusion syndrome in adults: a clinical update. *Crit Care Res Pract.* 2015;2015:260385.
3. Bosch X, Poch E, Grau JM. Rhabdomyolysis and acute kidney injury. *N Engl J Med.* 2009 Jul 2;361(1):62-72.

29. Rationale

Answer: D

Intra-abdominal hypertension is defined as intra-abdominal pressure (IAP) of greater than 10 mm Hg. Abdominal compartment syndrome (ACS) is the effective end-organ hypoperfusion that results from prolonged intra-abdominal hypertension. IAP higher than 20 to 25 mm Hg may cause ACS and, in this way, acute functional loss of various abdominal and extra-abdominal organs. Inflammatory and hemodynamic factors caused by intra-abdominal hypertension may affect pelvic, thoracic, cranial and muscular areas beside abdominal organs. Urinary bladder pressure is the gold standard for measuring IAP and is valid up to an IAP of 70 mm Hg. Factors affecting its reliability include pregnancy, obesity, and ascites.

Option A is incorrect because the patient has remained normotensive throughout his hospitalization and we can assume that after 7 liters of crystalloid, he is close to intravascularly replete. Furthermore, administration of IV fluids in this situation is be appropriate given the evidence of increased abdominal pressures. Oliguria progressing to anuria, and prerenal azotemia unresponsive to volume expansion characterize the renal dysfunction of ACS.

Ureteral compression by increased IAP was felt to at one time be the cause of renal failure in ACS but this has since been disproven because ureteral stents do not prevent the development of renal failure in this setting. In 1947, studies examined subjects undergoing external compression to 20 mm Hg. In these models, measurements of renal vein pressure, inferior vena cava pressure, renal plasma flow and glomerular filtration rate were studied. The effective renal plasma flow and

glomerular filtration rate dropped by 24.4% and 27.5%, respectively. All patients became oliguric and the absence of a sudden increase in urine flow on release of pressure suggested that ureteral compression was unlikely to be the cause of oliguria. Instead, it was discovered that elevations in renal vein pressure was probably the culprit, making option D the correct answer.

Intra-abdominal hypertension causing venous congestion and decreased preload can certainly impact cardiac output, especially when pressures enter the range to cause ACS; however, this is not felt to be the primary cause of renal failure because correcting cardiac output with fluid and inotropes has not shown to be of benefit in this instance. It is important to note that, when fluid is administered, it should be done through an internal jugular vein rather than a femoral line given the likely impedement in venous return below the diaphragm.

Reference:

1. Gurel A. Acute kidney injury due to abdominal compartment syndrome caused by duodenal metastases of prostate cancer. *Clin Case Rep.* 2015 Jul;3(7):629-631.

30. Rationale

Answer: A

Unfortunately, there is no such thing as an ideal resuscitation fluid; all resuscitative fluids have some physiologic impact as parenteral medications. Saline's designation as "normal" was based on an erroneous calculation of the salt concentration in blood as 0.9% in the 1800s (the actual salt concentration of blood is closer to 0.6%). Saline frequently causes a hyperchloremic metabolic acidosis with large-volume resuscitation. While this is a transient effect, the acidosis has been associated with immune suppression and coagulopathy. Saline has also been found to be associated with renal injury; both in humans and animal models, the data suggests that the increased chloride load decreases renal perfusion and may interfere with renal hemostasis. High-chloride loads have also been associated with increased renal replacement therapy requirements. Individual studies looking at both septic patients and abdominal surgery patients have shown increased all-cause in-hospital mortality in high-chloride resuscitative strategies.

References:

1. Shaw AD, Bagshaw SM, Goldstein SL, et al. Major complications, mortality, and resource utilization after open abdominal surgery: 0.9% saline compared to Plasma-Lyte. *Ann Surg.* 2012 May;255(5):821-829.
2. Yunos NM, Bellomo R, Hegarty C, Story D, Ho L, Bailey M. Association between a chloride-liberal vs chloride-restrictive intravenous fluid administration strategy and kidney injury in critically ill adults. *JAMA.* 2012 Oct 17;308(15):1566-1572.
3. Krajewski ML, Raghunathan K, Paluszkiewicz SM, Schermer CR, Shaw AD. Meta-analysis of high- versus low-chloride content in perioperative and critical care fluid resuscitation. *Br J Surg.* 2015 Jan;102(1):24-36.
4. Neyra, JA, Canepa-Escaro F, Li X, et al. Association of hyperchloremia with

hospital mortality in critically ill septic patients. *Crit Care Med.* 2015 Sept;43(9):1938-1944.

31. Rationale

Answer: D

Adequate nutrition is recognized as an important component of critical care and is believed to improve clinical outcomes. Temporary cessation of enteric tube feeding occurs in as many as 68% to 83% of surgical patients admitted to the ICU and accounts for up to 32% of potential feeding time. The purpose of nothing-by-mouth status is to prevent gastric aspiration during the induction of anesthesia. However, for mechanically intubated patients who are scheduled to undergo procedures in the supine position, there will be no airway manipulation. Enteric feeding may be continued up until or even during the procedure. Although the practice of reducing the duration of nothing-by-mouth status or providing compensatory nutrition is already being practiced at some centers, there is little published literature on this topic. The Society of Critical Care Medicine and American Society for Parenteral and Enteral Nutrition recommend that nothing-by-mouth status surrounding the duration of diagnostic tests or procedures should be minimized to prevent inadequate delivery of nutrients and prolonged periods of ileus.

References:

1. Peev MP, Yeh DD, Quraishi SA, et al. Causes and consequences of interrupted enteral nutrition: a prospective observational study in critically ill surgical patients. *JPEN J Parenter Enteral Nutr.* 2015 Jan;39(1):21-27.
2. McClave SA, Martindale RG, Vanek VW, et al; A.S.P.E.N. Board of Directors; American College of Critical Care Medicine; Society of Critical Care Medicine. Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N). *JPEN J Parenter Enteral Nutr.* 2009 May-Jun;33(3):277-316.

32. Rationale

Answer: A

The metabolic response of critical illness is characterized by an increase in resting energy expenditure (REE). Energy needs of the critically ill patient are dynamic, changing throughout the ICU stay. Nutrition may affect clinical outcomes in critically ill patients, and providing either fewer or more calories than the patient needs can adversely affect outcomes. It is therefore essential to have a precise measurements of energy needs in these patients in order to avoid underfeeding and overfeeding, loss of critical lean body mass, and worsening of any existing nutrient deficiencies.

In clinical practice, energy needs are determined either by using predictive equations (eg, Harris-Benedict) or by actual measurement using indirect calorimetry (IC). Although many equations exist for predicting resting energy expenditure, most studies

have reached the conclusion that current predictive equations do not accurately predict required energy needs in the critically ill population. The epidemic of obesity further renders the calculations of requirements by predictive equations increasingly inaccurate at extremes of body mass index. The IC technique most accurately reflects the exact rate of energy production and substrate oxidation in critically ill patients in the clinical practice setting. IC calculates REE by measuring whole-body oxygen and carbon dioxide gas exchange. This concept is based on the strong correlation between intake of oxygen and release of carbon dioxide with energy production. It is estimated that approximately 80% of energy expenditure is due to oxygen consumption, and the remaining 20% is due to carbon dioxide production.

The Nutrition Risk in Critically Ill (NUTRIC) score is a recently developed tool to help discriminate which ICU patients will benefit more (or less) from aggressive protein-energy provision. The score, ranging from 1-10, is based on six variables (age, Acute Physiologic and Chronic Health Evaluation [APACHE] II score, Sequential Organ Failure Assessment [SOFA] score, number of comorbidities, days from hospital to ICU admission and interleukin 6 levels). Patients with a score greater than 5 are most likely to benefit from aggressive nutrition therapy.

The SOFA score allows for calculation of both the amount and severity of organ dysfunction in six organ systems (respiratory, coagulatory, liver, cardiovascular, renal, and neurologic). It is used to quantify the severity of the patient's illness based on the degree of organ dysfunction serially over time.

References:

1. Heyland DK, Dhaliwal R, Jiang X, Day AG. Identifying critically ill patients who benefit the most from nutrition therapy: the development and initial validation of a novel risk assessment tool. *Crit Care.* 2011;15(6):R268.
2. Lev S, Cohen J, Singer P. Indirect calorimetry measurements in the ventilated critically ill patient: facts and controversies—the heat is on. *Crit Care Clin.* 2010 Oct;26(4):e1-e9.
3. McClave SA, Martindale RG, Kiraly L. The use of indirect calorimetry in the intensive care unit. *Curr Opin Clin Nutr Metab Care.* 2013 Mar;16(2):202-208.
4. Schlein KM, Coulter SP. Best practices for determining resting energy expenditure in critically ill adults. *Nutr Clin Pract.* 2014 Feb;29(1):44-55.

33. Rationale

Answer: C

A major problem in the ICU is malnutrition. One of the reasons for this is that most critically ill patients are in a catabolic state due to a proinflammatory state and thus have increased caloric demands. Current guidelines promote early enteral nutrition due to the benefits of decreased gut atrophy, as well as preserving normal gut flora. Initiating enteral feeding compared to parenteral nutrition has also been shown to result in less infection. Multiple clinical trials have shown that gastric residual volumes are unnecessary and may contribute to malnutrition. Therefore, reducing or discontinuing enteral feeding would prevent patients from meeting their increased

caloric demands No evidence exists that low-volume elemental feeding has clinical benefit compared to full enteral feeding. Pro-motility agents may decrease gastric residuals, but have no effect on mortality.

References:

1. Reignier J, Mercier E, Le Gouge A, et al; Clinical Research in Intensive Care and Sepsis (CRICS) Group. Effect of not monitoring residual gastric volume on risk of ventilator-associated pneumonia in adults receiving mechanical ventilation and early enteral feeding: a randomized controlled trial. *JAMA.* 2013 Jan 16;309(3):249-256.
2. McClave SA, Martindale RG, Vanek VW, et al; A.S.P.E.N. Board of Directors; American College of Critical Care Medicine; Society of Critical Care Medicine. Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N). *JPEN J Parenter Enteral Nutr.* 2009 May-Jun;33(3):277-316.
3. Khalid I, Doshi P, DiGiovine B. Early enteral nutrition and outcomes of critically ill patients treated with vasopressors and mechanical ventilation. *Am J Crit Care.* 2010 May;19(3):261-268.
4. Yavagal DR, Karnad DR, Oak JL. Metoclopramide for preventing pneumonia in critically ill patients receiving enteral tube feeding: a randomized controlled trial. *Crit Care Med.* 2000 May;28(5):1408-1411.

Part 2:

Cardiovascular Critical Care

Part 2:
Cardiovascular Critical Care

Instructions: For each question, select the most correct answer.

1. A 65-year-old woman admitted for aneurysmal subarachnoid hemorrhage has dyspnea and substernal chest pain two days after admission. ECG shows

anterior lead ST elevations. Troponin is mildly elevated. However, there is no angiographic evidence of obstructive coronary disease or acute plaque rupture. She then develops hypotension (blood pressure 80/60 mm Hg) and is found to have a moderate left ventricular outflow tract obstruction.

Which of the following treatments is contraindicated for this patient?

A. Alpha-agonists
B. Beta-blockers
C. Inotropic agents
D. Intra-aortic balloon pump

2. A 53-year-old man with a history of IV drug abuse is admitted to the ICU after a Whipple procedure. He regularly takes methadone. Acutely, he takes hydromorphone for acute analgesia and antibiotic prophylaxis with cefazolin. The QTc from the morning 12-lead ECG is 510 ms. Later that morning, the rhythm shown below is observed.

Which of the following is the most appropriate next intervention?

A. Discontinue methadone.
B. Continue all current drugs and monitor ECG twice daily.
C. Start amiodarone.
D. Administer bicarbonate.

3. A 65-year-old woman with a history of diabetes, hypertension, depression, and anxiety is evaluated in the emergency department for severe substernal chest pain with nausea and vomiting. She recently lost her husband to cancer and just found out that her son was killed in a car accident this morning. On arrival, vital signs are: temperature 37°C (98.6°F), heart rate 120 beats/min, blood pressure

90/60 mm Hg, respiratory rate 24 breaths/min, oxygen saturation 92% on 6 liters/min nasal cannula. Physical examination is notable for crackles in the lung bases and cool extremities. ECG shows ST elevation in leads V1-V3 with T wave inversions in leads I and aVL. Chest radiograph shows mild pulmonary edema.

She is started on aspirin, clopidogrel, and a heparin infusion, while being given a 1-liter IV normal saline bolus as she is taken up to the catheterization laboratory for a percutaneous coronary intervention. She is noted to have small amounts of plaque with less than 30% stenosis in her left anterior descending and right coronary arteries. Left ventriculography reveals apical ballooning with vigorous contraction of the basal segment. Echocardiography shows evidence of left ventricular outflow tract obstruction (see below). During the procedure, her oxygen saturations drop to 70% despite a nonrebreather mask, and her blood pressure is now 70/40 mm Hg, with a heart rate of 130 beats/min, and she is confused.

Which of the following is the most appropriate hemdynamic support strategy for this patient?

A. Intubate and start dobutamine and norepinephrine.
B. Intubate and start IV esmolol and phenylephrine.
C. Intubate and give a 1-liter IV normal saline bolus.
D. Begin bilevel positive airway pressure, and start dobutamine and norepinephrine.

4. A 54-year-old man presents with advanced heart failure. He had a left ventricular assist device placed two days ago as a bridge to transplantation. His intraoperative course was uneventful and he was extubated 24 hours ago. His pump speed has remained at 9,600 revolutions/min. Power has remained at 5.7 watts. His last documented flow was 4.8 L/min. His heart has remained in normal

sinus rhythm. The on-duty physician is called to the bedside by the nurse, who has now noted an acute decrease in cardiac output (pump flow). There have been no complications with the left ventricular assist device machinery or connections.

Which of the following findings would be consistent with the emergent situation of cardiac tamponade?

	CVP	PAP	PAOP	MAP	Echocardiography
A.	Low	Low	Low	Low	LV underfilled
B.	High	Low	Low	Low	RV compression
C.	High	High	Low	Low	RA/RV dilated
D.	High	High	High	Low	LA/LV dilated
E.	High	High	High	Low	RV dilated

Abbreviations: CVP = central venous pressure, PAP = pulmonary artery pressure, PAOP = pulmonary artery occlusion pressure, MAP = mean arterial pressure, LV = left ventricle, RV = right ventricle, LA = left atrium, RA = right atrium

5. Two hours after a right carotid endarterectomy, a 75-year-old man is increasingly somnolent and has a right-sided headache when aroused. His blood pressure is 180/100 mm Hg, heart rate 70 beats/min, and respiratory rate 18 breaths/min.

   Which of the following is the most appropriate intervention?

   A. Administer labetolol to control hypertension.
   B. Obtain a head CT to rule out intracranial bleeding.
   C. Administer a narcotic for analgesia.
   D. Obtain transcranial Doppler study to assess possible vasospasm.

6. A 55-year-old man with hypertension has chest pain and is brought to the emergency department by his wife, where he has a cardiac arrest, and cardiopulmonary resuscitation (CPR) is immediately initiated with compressions and masked ventilation. An endotracheal intubation is performed, and colorimetric end-tidal carbon dioxide (CO_2) testing is used to aid in confirmation of endotracheal tube placement. There is mild color change on the end-tidal CO_2 detector. On auscultation of the chest, breath sounds can be heard in bilateral lung fields during manual ventilation with no rush of air heard over the stomach. Chest compressions are continued. He is ventilated via the endotracheal tube for a full round of CPR, and the color change does not go away.

   Which of the following most likely accounts for the low-level color variation on the end-tidal CO_2 tester?

   A. Severe acidosis
   B. Venous hyperoxia post-cardiac arrest
   C. Hypoventilation with the bag ventilation

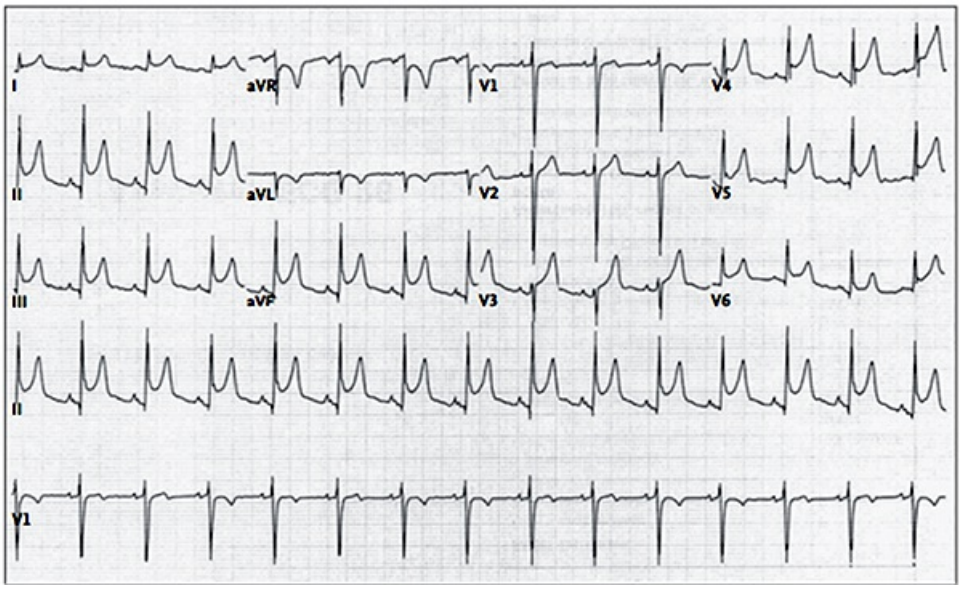
D. Low cardiac output

7. A 30-year-old man is placed on peripheral venoarterial extracorporeal membrane oxygenation (ECMO) using femoral artery and vein catheters for worsening cardiogenic shock due to viral myocarditis. During the following week his native cardiac function appears to be improving, although he develops ventilator-associated pneumonia and is being treated with broad-spectrum antibiotics. Arterial blood gas (ABG) analysis drawn from the right radial arterial line is pH 7.48, partial arterial carbon dioxide pressure ($PaCO_2$) 32 mm Hg, partial arterial oxygen pressure (PaO_2) 60 mm Hg. Oxygen saturation is 90% on 60% fraction of inspired oxygen (FIO_2) and 7.5 cm H_2O positive end-expiratory pressure, tidal volume 450 mL, respiratory rate 18 breaths/min. Chest radiograph shows a right middle lobe and left lower lobe infiltrate. Post-oxygenator ABG readings are pH 7.40, $PaCO_2$ 40, PaO_2 300. The nurse alerts the attending physician to the patient's declining oxygen saturations throughout the day and the low partial arterial oxygen pressure.

   Which of the following is the most appropriate next step in management?

   A. Change out the oxygenator.
   B. Add a second oxygenator to the circuit.
   C. Consider changing to central venoarterial ECMO or increasing circuit flow.
   D. Increase the ventilator FIO_2.
   E. Convert to venovenous ECMO.

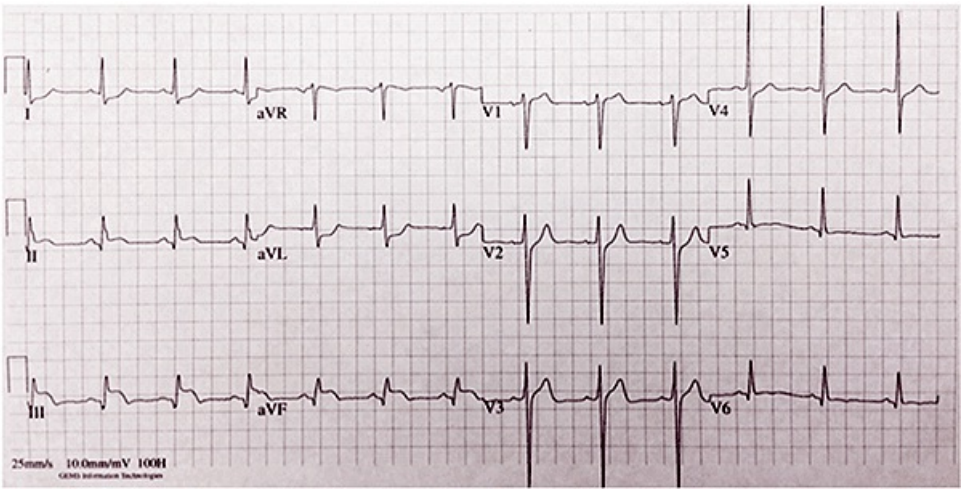
8. A 74-year-old man is being treated in the ICU for severe community-acquired pneumonia. In the evening, he has been reporting severe, sharp, substernal chest pain with radiation of his symptoms. Vital signs are: blood pressure 132/68 mm Hg, heart rate 113 beats/min, respiratory rate 22 breaths/min, oxygen saturation 94% on 2 liters, and initial troponin T level 0.03 ng/dL. On physical examination, he is moderately distressed and sitting upright. The rest of the examination is significant for flat neck veins, bibasilar rales on lung examination, and distal, harsh, heart sounds. His ECG is shown below.



Which of the following is/are the most appropriate next step(s) in management?

A. Emergent percutaneous coronary intervention
B. Chest CT angiography and heparin infusion
C. Aggressive diuresis
D. Nonsteroidal anti-inflammatory therapy and reassurance

9. An 82-year-old man is transferred to the ICU two days after a total hip replacement with chest pain and new hypotension. He is afebrile, with a heart rate of 75 beats/min, blood pressure 88/67 mm Hg, respiratory rate 22 breaths/min, and oxygen saturation 98% on room air. He is clammy and confused, but is able to state that his chest pain is 9 out of 10. The ECG obtained on ICU admission is shown below.



Which of the following medications should be administered while awaiting arrival of the cardiology team?

A. Nitroglycerin to reduce his chest pain, with a goal of 0 out of 10

B. Aspirin, 162-325 mg, immediately
C. IV diltiazem to target a heart rate of 60 beats/min
D. IV morphine, 4 mg

10. Which of the following is true about perioperative 5-lead telemetry monitoring in noncardiac surgery patients?
    A. Leads II and V5 have equivalent sensitivity for myocardial ischemia.
    B. Leads II, V4, and V5, when used together, have superior sensitivity to detect myocardial ischemia.
    C. Lead II has superior sensitivity for myocardial ischemia compared to lead V5.
    D. Lead V5 has superior sensitivity for rate and rhythm disturbances compared to lead II.
    E. Lead V4 has less sensitivity than lead V2 for myocardial ischemia.

11. Which of the following agents is most appropriate to administer should the patient with the ECG shown below develop atrial fibrillation with rapid ventricular rate?

    A. Procainamide
    B. Metoprolol
    C. Verapamil
    D. Adenosine
    E. Digoxin

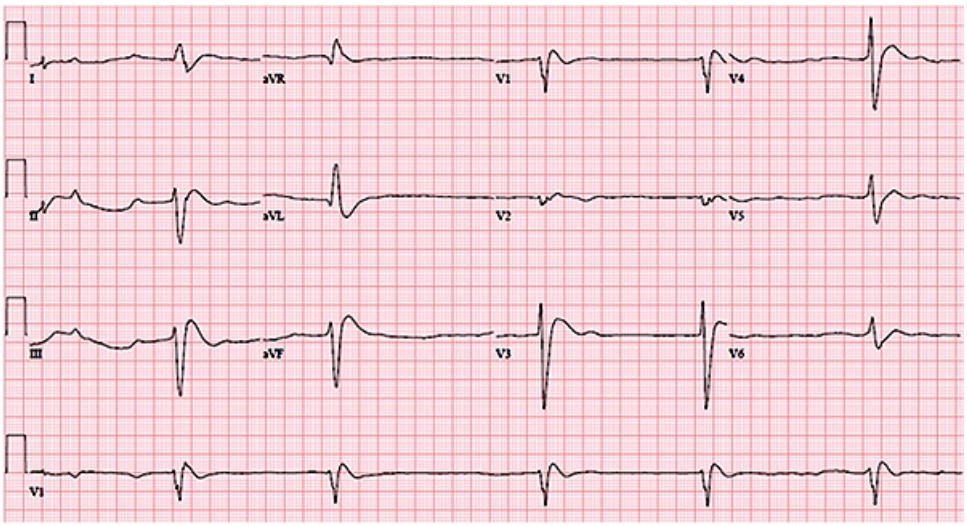
12. A 66-year-old man with aortic stenosis arrives in the ICU after repair of an abdominal aortic aneurysm. Shortly after admission, his ECG shows a change from normal sinus rhythm to atrial fibrillation at a ventricular rate of 84 beats/min. His blood pressure shows a slight change from 110/60 mm Hg to 100/52 mm Hg. Pulmonary artery occlusion pressure (PAOP) increased from 16 to 22 mm Hg with prominent a waves noted.

    Which of the following is the most appropriate course of action?

    A. Increase myocardial contractility with inotropic support.
    B. Maintain PAOP below 20 mm Hg with diuresis.
    C. Attempt conversion to sinus rhythm with amiodarone.
    D. Decrease peripheral vascular resistance with vasodilator therapy.

13. An 86-year-old woman with a history of hypertension, heart failure, and atrial

fibrillation has had weakness, abdominal pain, blurry vision, and vomiting for two days. Her blood pressure is 92/55 mm Hg. She takes metoprolol, digoxin, aspirin, and lisinopril. Her ECG on ICU admission is shown below.



Which of the following is the most appropriate treatment at this time?

A. Calcium chloride
B. Digoxin immune Fab
C. Activated charcoal
D. Potassium repletion
E. Dialysis

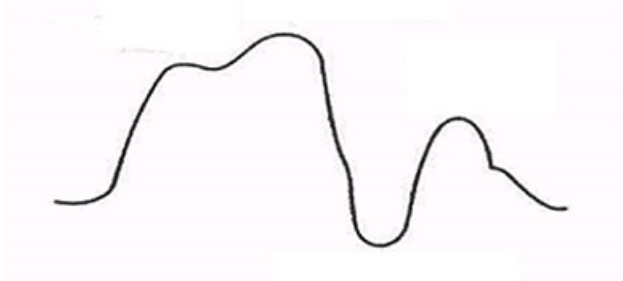
14. A 70-year-old woman with a history of nephrolithiasis and myocardial infarction is admitted to the ICU with hypotension and urosepsis. She is treated with fluid resuscitation, antibiotics, and vasopressor support. While being admitted, she develops atrial fibrillation with rapid ventricular rate, which is controlled with a diltiazem infusion. An echocardiogram shows mild systolic impairment, normal left atrial size, and normal valves. Thyroid function tests are are normal. Three days later, the urosepsis has resolved and she undergoes diuresis but remains in atrial fibrillation with ventricular rate controlled on an oral medication regimen. An oral anticoagulation is being considered, given the ongoing atrial fibrillation.

    Which of the following is the best risk-benefit analysis of thrombosis and bleeding?

    A. Thrombosis risk: high, bleeding risk: high
    B. Thrombosis risk: high, bleeding risk: low
    C. Thrombosis risk: low, bleeding risk: high
    D. Thrombosis risk: low, bleeding risk: low

15. A 68-year-old man is undergoing a mitral valve replacement for severe mitral regurgitation. He is unable to be weaned from cardiopulmonary bypass. An intra-aortic balloon pump (IABP) is placed and he is able to separate from the heart-

lung machine. The IABP pressure tracing in the ICU is shown below.



Which of the following is the necessary correction?

A. No adjustment is necessary; the IABP is augmenting correctly.
B. Set the balloon pump to trigger later; the tracing suggests early balloon inflation.
C. Set the balloon pump to trigger earlier; the tracing suggests late balloon inflation.
D. Set the balloon pump to deflate earlier; the tracing suggests late balloon deflation.

16. A 76-year-old man develops right ventricular failure on postoperative day three after implantation of a left ventricular assist device. Furosemide, 120 mg IV every 6 hours, is administered and, initially, the patient's response is vigorous, but after four days, his response is significantly diminished.

    Which of the following most likey explains the patient's decreased response to the furosemide?

    A. Atrophy of cells in the distal convoluted tubule
    B. Increased protein binding of furosemide
    C. Competitive inhibition of furosimide transport
    D. Decreased stimulation of the renin-angiotensin-aldosterone system

17. A 67-year-old man is admitted to the ICU after implantation of a continuous flow left ventricular assist device. Three days later, his device monitor displays a gradual increase in pump power from 4.3 to 6.7 watts, and the pulsatility index has decreased from 6.2 to 4.3. The speed set on the device is unchanged. Repeated laboratory values demonstrate an increased serum lactate dehydrogenase, increased serum total bilirubin, and a mixed venous oxygen saturation that has decreased from 62% to 49%.

    Which of the following is the most likely explanation for these findings?

    A. Popliteal vein thrombosis
    B. Acute mitral regurgitation
    C. Impeller thrombosis
    D. Right ventricular failure

18. A 70-year-old woman with chronic ischemic heart failure and ejection fraction of 15% is in the ICU for acute exacerbation of heart failure. She has no valvular abnormalities and is being evaluated for possible revascularization. She has had previous cardiac catheterizations, which demonstrated multiple proximal left-sided lesions that were not amenable to percutaneous revascularization and stenting. Past medical history also includes diabetes mellitus, chronic obstructive pulmonary disease, obesity, and hypertension. Chest radiograph demonstrates bilateral infiltrates. She is intubated and placed on mechanical ventilation. She becomes hypotensive; pulmonary artery and radial artery catheters are inserted. The cardiac index (CI) is 1.1 L/min/m^2 and dobutamine is started without commensurate increase in CI. She becomes hypotensive, and her heart rate increases from 85 to 110 beats/min with ST changes

    Which of the following is the most appropriate next step in management?

    A. Give 2 liters of IV fluids rapidly to increase mean arterial pressure (MAP).
    B. Start esmolol infusion to decrease heart rate.
    C. Insert intra-aortic balloon pump to unload left ventricle and increase coronary perfusion pressure.
    D. Start phenylephrine infusion to increase MAP.

19. A 43-year-old man is admitted to the ICU with nausea, vomiting, and jaundice. He says that the symptoms have been progressing over the past two months. His medical history is significant for end-stage non-ischemic cardiomyopathy, and he has a HeartMate II left ventricular assist device (LVAD). Current vital signs are: blood pressure 121/83 mm Hg, heart rate 98 beats/min, respiratory rate 14 breaths/min. His hemoglobin is 8.3 g/dL; four months ago it was 12.1 g/dL. His current lactate dehydrogenase is 2,123 U/L. His LVAD setting is 9,000 RPM, pulsatility index 1.3, and pump power 8.4 watts with occasional increases to 13 watts. Transthoracic echocardiography shows a well-filled left ventricular cavity and a ventricular septum with a slight rightward bow. His INR is 2.8.

    Which of the following is the best treatment for this patient?

    A. Continue observation.
    B. Increase the RPM speed.
    C. Increase anticoagulation therapy with a goal of raising INR to 4.
    D. Initiate pump exchange.

20. Despite the decreased use of pulmonary artery catheters (PAC) in the ICU because of controversy regarding their benefit, in which of the following clinical situations is a PAC most useful?
    A. Acute respiratory distress syndrome
    B. Septic shock
    C. Severe pulmonary hypertension
    D. Traumatic brain injury

21. A 72-year-old woman with a history of atrial fibrillation is intubated for respiratory distress secondary to septic shock. She receives a 30 mL/kg IV fluid bolus and her lactate decreases from 5.0 to 3.0 mmol/L in two hours. She has a right subclavian central line and a right radial arterial line. Her central venous pressure (CVP) is 12 mm Hg. Her vital signs, relevant laboratory results, and ventilator settings are as follows: sodium 135 mEql/L, potassium 3.7 mEql/L, chloride 100 mEql/L, carbon dioxide 18 mmol/L, blood urea nitrogen 22 mg/dL, creatinine 1.5 mg/dL. Ventilator tidal volume: 7 mL/kg (patient is dysynchronous with ventilator), respiratory rate 12 breaths/min (set), patient is breathing 15 breaths/min, positive end-expiratory pressure 5 cm H_2O, fraction of inspired oxygen 65%.

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

    A. Pulse pressure variation can accurately predict her fluid responsiveness.
    B. An increase in CVP (from 12 to 15 mm Hg) will predict her fluid responsiveness.
    C. A positive passive leg raise will predict her fluid responsiveness.
    D. A low pulmonary artery occlusion pressure will best predict her fluid responsiveness.

22. In which of the following patients would use of a conventional pulse contour monitoring device measuring stroke volume variability and cardiac output provide the most reliable data?
    A. Cirrhotic patient with severe sepsis who is tachypneic
    B. Septic intubated patient with severe acute respiratory distress syndrome receiving lung protective strategy with tidal volume of 5 mL/kg
    C. Patient under general anesthesia in sinus rhythm undergoing major intra-abdominal surgery with prolonged cavity exposure and expected to lose a moderate volume of blood
    D. Patient status post large acute anterior myocardial infarction on pressors with an intra-aortic balloon pump
    E. Patient with a large pulmonary embolus who is tachycardic with multifocal atrial tachycardia

23. A patient in septic shock with acute respiratory failure who is receiving mechanical ventilation in pressure control mode has a pulmonary artery catheter in place to assist in management of fluids and pressor therapy.

    Convention regarding the recording of pulmonary arterial pressure is that measurements be taken at which of the following times?

    A. At peak of inhalation and just before the QRS
    B. At end of exhalation and during the QRS
    C. At peak of inhalation and just after the QRS
    D. At end of exhalation and just after the QRS

24. A 24-year-old man is involved in a motor vehicle collision. He is following commands. Head and cervical spine CT is negative, chest radiograph is normal, focused assessment with sonography in trauma (FAST) and extended FAST examinations are normal. Hemoglobin is 9.1 g/dL, base deficit is -8 mmol/L, and lactic acid level is 4.5 mmol/L. He is transferred to the ICU, where his mean arterial pressure is 51 mm Hg. On focused echocardiography, his inferior vena cava is 1.4 cm with greater than 50% collapsibility and left ventricular walls are touching on parasternal long-axis view.

    Which of the following is the most likely cause of shock?

    A. Heart failure
    B. Infection
    C. Hypovolemia
    D. Spinal cord injury

25. Which of the following is correct regarding the hemodynamic measurements afforded by a central venous catheter?
    A. Central venous pressure (CVP) is not affected by cardiac function.
    B. Isolated right ventricular dysfunction will not affect CVP.
    C. Central venous oxygen saturation parallels true mixed venous oxygen saturation.
    D. There is little value in CVP waveform analysis.

26. A 25-year-old woman is admitted to the ICU after a motor vehicle collision. On ICU day four, she has diffuse body rash and shock. A retained tampon is found on tertiary survey. After receiving broad-spectrum antibiotics and three liters of crystalloid IV fluids, she remains hypotensive. She is started on vasopressors for refractory shock and intubated for respiratory distress.

    Regarding the use of pulse pressure variation to help determine if she is volume responsive, which of the following is correct?

    A. It is accurate if the patient is taking spontaneous breaths while on mechanical ventilation.
    B. It is accurate if the patient is in atrial fibrillation.
    C. It is accurate in patients with left ventricular and right ventricular dysfunction or valvular disorders.
    D. A pulse pressure variation greater than 13% accurately predicts that the patient will be volume responsive.

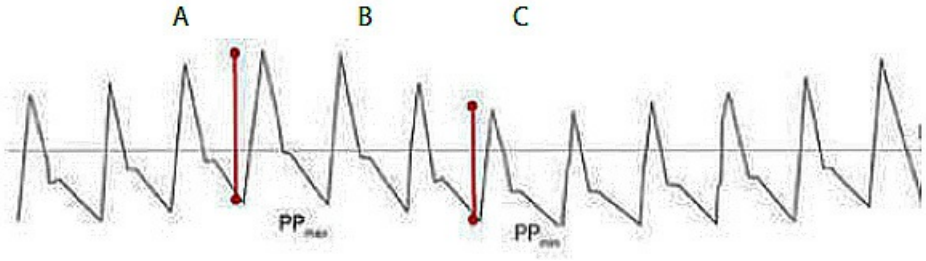
27. Two days ago, a man underwent cardiac bypass surgery with revascularization of three vessels and placement of a bioprosthetic aortic valve. His postoperative course was complicated by cardiogenic shock requiring inotropic support. He required transfusion of blood products postoperatively. He was extubated and transitioned to supplemental oxygen via nasal cannula. His inotropic support was

weaned off. He experiences an acute hypoxic event and is in acute respiratory distress and is then intubated. In the peri-intubation period, he has a cardiac arrest. As part of the procedure, a continuous capnogram is placed in line with the endotracheal tube.

Regarding end-tidal carbon dioxide ($ETCO_2$), which of the following statements is true?

A. An esophageal intubation is always manifested with a flat $ETCO_2$.
B. A decrease in $ETCO_2$ can be caused by fever, hypoventilation, partial airway obstruction, and the use of sodium bicarbonate.
C. An increase in $ETCO_2$ can be caused by hypothermia and hypovolemia.
D. An $ETCO_2$ value of greater than 20 mm Hg is a reflection of poor-quality chest compressions.
E. A sudden increase in $ETCO_2$ during chest compressions can be a sign of return of spontaneous circulation.

28. The arterial line tracing shown below is from a patient on positive pressure mechanical ventilation. Which letter best corresponds to the inspiratory phase of a positive pressure breath

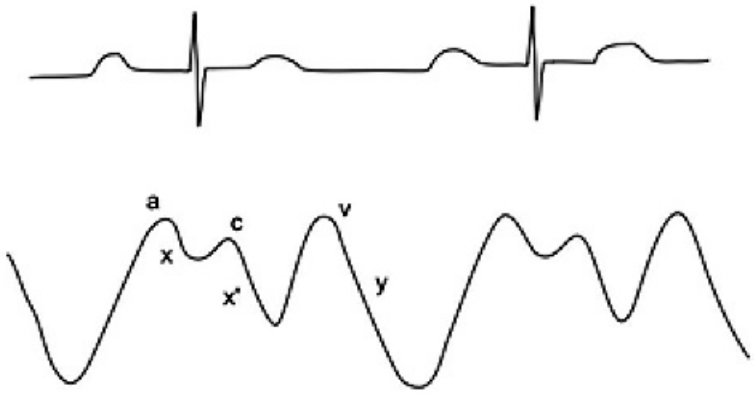


A. A
B. B
C. C
D. Cannot tell from the information provided

29. Which of the following best characterizes the relationship of cardiac output and stroke volume during positive pressure ventilation while pulse pressure variation is observed on an arterial line tracing?
A. Right ventricular (RV) stroke volume increases and is highest during inspiration.
B. RV stroke volume decreases during expiration.
C. Left ventricular stoke volume is highest during expiration.
D. Systolic blood pressure decreases during the inspiratory phase.
E. RV stroke volume and cardiac output increase during the expiratory phase.

30. Which of the following will most likely interfere with obtaining an accurate assessment of pulse pressure variation for predicting fluid responsiveness?
    A. Ventilation with tidal volume set at 10 mL/kg of ideal body weight
    B. Ventilation with tidal volume set at 6 mL/kg of ideal body weight
    C. Muscle relaxation with vecuronium
    D. Continuous renal replacement therapy running at –50 mL/hr

31. An 83-year-old, 41-kg (90.4-lb) woman with aortic stenosis (aortic valve area 0.9 cm^2) and syncopal episodes presents for an aortic valve replacement. Her preoperative echocardiogram demonstrates an ejection fraction of 60%, moderate aortic stenosis, moderate aortic insufficiency, and mild pulmonic insufficiency with mild pulmonary hypertension and evidence of diastolic relaxation abnormality. She also is found to have a 70% stenosis of her right coronary artery (RCA). She is admitted to the ICU after an uneventful coronary artery bypass graft to her and an aortic valve replacement. Over the course of the evening, her central venous pressure (CVP) increases from 10 to 15 mm Hg and phenylephrine is started because her blood pressure begins to decrease and is unresponsive to the administration of two liters crystalloid. Pulmonary arterial pressures increase from 20/15 mm Hg to 40/20 mm Hg, and her urine output begins to decrease, with an elevated lactate level. Arterial blood gas analysis reveals pH 7.21, partial arterial oxygen pressure 167 mm Hg (30% fraction of inspired oxygen), partial arterial carbon dioxide pressure 33 mm Hg. Chest tube output remains serosanguinous 20 mL/hour. Cardiac enzymes are within normal limits. CVP tracing is shown below.



Which of the following is the most likely cause of the patient's clinical picture?

    A. Cardiac tamponade
    B. Pulmonary embolus
    C. Tricuspid regurgitation
    D. Kinking of RCA graft causing right ventricular ischemia

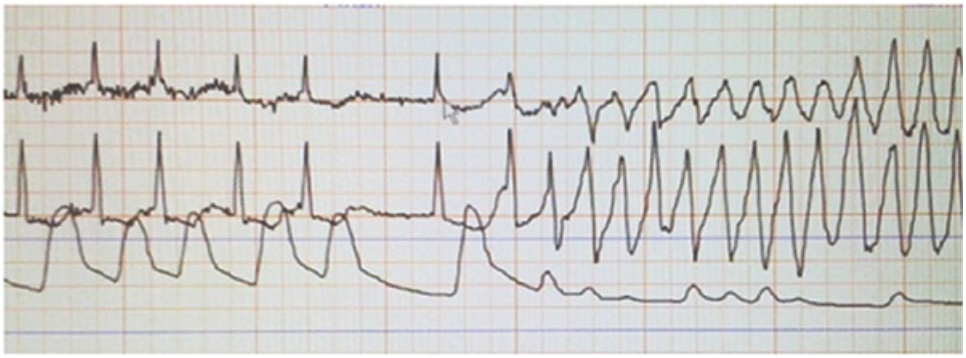
32. A 78-year-old woman admitted to the ICU for chest trauma develops a

supraventricular arrhythmia with rapid ventricular response. Her blood pressure is 80/50 mm Hg, so the decision is made to perform synchronized cardioversion with 200 joules. Before synchronized cardioversion, she becomes unresponsive and pulseless as the rhythm changes to that shown in the figure below. The shock button on the defibrillator is pressed but it fails to deliver a shock.

Which of the following is the most likely reason for this failure?

A. The defibrillator battery failed.
B. The device is unable to sync.
C. Ventricular fibrillation cannot be shocked in sync mode.
D. A lead has lost contact, causing the irregular rhythm.

33. A patient in the ICU being treated with ciprofloxacin for colitis suddenly develops the rhythm and arterial line tracing shown below.



Which of the following is the most important next step in resuscitation for this patient?

A. IV magnesium, 2 g
B. IV vasopressin, 40-unit bolus
C. Overdrive pacing
D. Chest compressions at a rate of 100 per minute

34. A 65-year-old man collapsed on the street and a bystander performed cardiopulmonary resuscitation (CPR). Emergency medical personnel arrive nine minutes later and find the patient in asystole. CPR is continued and return of spontaneous circulation is obtained 20 minutes post arrest. The initial ECG suggests an anterior ST elevation myocardial infarction. The patient is transferred to a local hospital and undergoes emergency coronary angiography, which

reveals a proximal left anterior descending artery occlusion, treated with percutaneous stenting. At 90 minutes post arrest, he is admitted to the ICU, where therapeutic hypothermia is immediately initiated. Three days later he is warmed, and neurologic examination is performed.

Which of the following is the most reliable indicator of a poor neurologic outcome?

A. Presence of myoclonus
B. Absence of pupillary reflex
C. Absence of corneal reflex
D. Absence of motor movements

35. A 27-year-old man falls off a fishing boat and is rescued by prehospital providers after being submerged for 25 minutes in 3°C (37.4˚F) water. He is pulseless and, after defibrillation with an automated external defibrillator, there is a transient return of spontaneous circulation (ROSC) and cardiopulmonary resuscitation is continued. At hospital admission, his core temperature is 18.2°C (64.8°F), pupils are fixed and dilated, and ventricular fibrillation is identified. Multiple defibrillation attempts, along with the administration of advanced cardiac life support protocol drugs are unsuccessful at establishing ROSC. Laboratory results are: arterial blood gases, pH 6.71, partial arterial carbon dioxide pressure 75, partial arterial oxygen pressure 70, base excess -22.1 mmol/L; sodium 142 mEq/L, potassium 5.9 mEq/L, chloride 108 mEq/L, bicarbonate 10 mEq/L, lactate 18 mmol/L.

Which of the following is the most appropriate next step in management?

A. Administer procainamide before making a defibrillation attempt.
B. Initiate rewarming with forced air, lavage of warm saline in the stomach, and infusion of warm saline IV.
C. Initiate venoarterial extracorporeal membrane oxygenation support.
D. Obtain brain CT to identify irreversable changes secondary to hypoxia.

36. A 53-year-old woman collapses on the street, witnessed by bystanders, who initiate cardiopulmonary resuscitation and call emergency medical services (EMS). When EMS arrive, they find her to be in ventricular fibrillation and resuscitate her with chest compressions, epinephrine, and defibrillation. On arrival in the emergency department, she is intubated for airway protection, given her depressed mental status, and remains hemodynamically stable. Her ECG shows diffuse ST depressions.

Which of the following interventions is most likely to improve her neurologic outcome?

A. Amiodarone, 150 mg bolus, followed by 1 mg/min for 8 hours, then 0.5 mg/min for 16 hours
B. Active temperature control to a target temperature of 33-36°C (91.4-96.8°F) for at least 24 hours

C. Lung-protective ventilation strategy (including tidal volume 4-8 mL/kg of ideal body weight)
D. Immediate cardiac catheterization for revascularization

37. A 58-year-old man with a history of chronic low back pain, hyperlipidemia, and moderate chronic obstructive pulmonary disease (COPD) is evaluated in the emergency department for progressively worsening dyspnea. He is admitted to the hospital for COPD exacerbation. He is treated with albuterol nebulizer, prednisone, and noninvasive ventilation. His symptoms improve and he is discharged on hospital day five. One week later, he collapses at the airport while traveling. He is unresponsive and pulseless.

Which of the following is the most appropriate immediate course of action?

A. Administer IM naloxone, 0.4 mg.
B. Check airway patency.
C. Put automated external defibrillator pads in place.
D. Start chest compressions.

38. A 45-year-old homeless man is admitted to the psychiatric ward for acute psychosis. His vital signs have been stable and he is eating well. On hospital day 3, he complains of shortness of breath. His blood pressure is 80/35 mm Hg, heart rate 165 beats/min respiratory rate 20 breaths/min and oxygen saturation 94% on 4 L/min nasal cannula. ECG reveals supraventricular tachycardia.

Which of the following is the most appropriate intervention at this time?

A. Metoprolol, 5 mg IV
B. Naloxone, 0.4 mg IV
C. Synchronized cardioversion
D. Verapamil, 2.5 mg IV

39. A 71-year-old, 87-kg (192 lbs) man was admitted to the hospital nine days ago for worsening dyspnea and orthopnea. He is now transferred from the ward to the ICU for acute-onset fever of 38.8°C (101.8°F), tachycardia, and hypotension. He has a history of severe mitral stenosis. A transthoracic echocardiogram obtained on admission demonstrates a mean transvalvular gradient of 17 mm Hg and a valve area of 0.88 cm^2.

Which of the following is the most appropriate initial management of this patient?

A. Bumetanide, 4 mg IV bolus
B. Esmolol, 100 mg IV bolus followed by IV esmolol infusion
C. Epinephrine, 0.1 µg/kg/min IV infusion
D. Ringer lactated solution, 250 mL IV bolus

40. A 68-year-old woman with a long history of smoking and hypertension presents with moderate back pain. A CT angiogram identifies an enlarged thoracic aorta (5.6 cm in diameter), with a pedunculated outpouching near the takeoff of the left subclavian artery. An esmolol infusion is started overnight for blood pressure and heart rate control. The next morning, she undergoes an endovascular repair of the aneurysm and is then admitted to the cardiovascular ICU. Several hours later, the patient has decreased lower extremity movement on neurologic examination.

    Which of the following is the most appropriate course of action?

    A. Clamp the spinal drain.
    B. Increase the blood pressure.
    C. Transfuse red blood cells.
    D. Obtain an emergent CT myelogram.

41. A 35-year-old, previously healthy man is evaluted in the emergency department for worsening dyspnea. He says that his shortness of breath started during the past week and is getting worse. He denies chest pain or leg swelling but reports subjective fevers and chills. He is admitted to the medical floor for presumed pneumonia and started on antibiotics based on his low-grade fever, tachycardia, oxygen requirement, and chest radiograph showing diffuse interstitial disease and mild pulmonary edema. During the next 12 hours his symptoms worsen, and he is transferred to the ICU for agitation, worsening dyspnea, and hypotension unresponsive to IV fluids. Vitals signs are: temperature 39°C (102.2°F), heart rate 128 beats/min, blood pressure 85/60 mm Hg, respiratory rate 24 breaths/min, oxygen saturation 93% on nonrebreather mask. Physical examination is notable for faint diastolic murmur, bilateral lung crackles, and track marks on the left forearm. Laboratory analysis is notable for white blood cell count of 23,000/μL, creatinine 1.8 mmol/L, lactate 4 mmol/L, and troponin of 1.04 ng/ml. ECG shows sinus tachycardia. Blood cultures are positive for methicillin-resistant Staphylococcus aureus.

    Which of the following is the best next step in management?

    A. Broaden antibiotics and give 2 liters IV normal saline for hypotension and lactic acidosis.
    B. Broaden antibiotics, obtain immediate echocardiography, consult cardiac surgery, and institute appropriate medical management.
    C. Call cardiology for catheterization laboratory activation and placement of intra-aortic balloon pump.
    D. Broaden antibiotics, obtain immediate echocardiography, institute appropriate medical management, and consult cardiac surgery when blood cultures clear.

42. An 83-year-old man with severe aortic stenosis, chronic obstructive pulmonary disease, and coronary artery disease, who is status post coronary artery bypass graft, hypertension, and hyperlipidemia, is admitted to the ICU hemodynamically

stable and comfortable after a transcatheter aortic valve replacement via a transfemoral approach using a balloon expandable valve. Sixty minutes after ICU admission, his vital signs have acutely changed: temperature is 37.9°C (100.2°F), blood pressure 82/50 mm Hg, heart rate 145 beats/min, oxygen saturation 90% on nonrebreather face mask. He is awake and denies chest pain. Physical examination demonstrates clear lungs bilaterally, regular tachycardia, low-pitched early diastolic murmur, and a soft S1 sound. His jugular venous pulsation is visible 5 cm above the sternal notch and refills slowly after occlusion. His extremities are cold, and he has thready pulses at the radial, dorsalis pedis, and posterior tibial arteries.

Which of the following is the most likely etiology for his change in physiology?

A. Pericardial tamponade
B. Acute mitral insufficiency
C. Acute aortic insufficiency
D. Aortic dissection

43. A 60-year-old man was admitted to the oncology floor for a urinary tract infection associated with mild confusion. His medical history is significant for metastatic non-small cell lung cancer, status post chemo- and radiation therapy, hypertension, and a deep venous thrombosis, for which he takes enoxaparin. Throughout the night, he is noted to have more shortness of breath and new-onset hypotension, and is urgently transferred to the ICU, where his vital signs are: temperature 38°C (100.4°F), heart rate 140 beats/min, respiratory rate 35 breaths/min, blood pressure 70/50 mm Hg, oxygen saturation 99% on a nonrebreather mask. Physical examination is notable for equal and reactive pupils, distended neck veins with supple neck, clear lungs, distant heart sounds, soft abdomen, cool extremities without edema, and confusion. Chest radiograph shows clear lungs and cardiomegaly. ECG shows sinus tachycardia with low voltage. Laboratory results are pending.

Which of the following is the most appropriate next step in management?

A. Intubate, then administer 2 L IV crystalloid fluid bolus and broad-spectrum antibiotics, and obtain pan-cultures.
B. Initiate crystalloid resuscitation while performing bedside cardiac ultrasound.
C. Initiate bilevel positive airway pressure; IV morphine, 2 mg, for dyspnea; IV furosemide, 40 mg; and consult cardiology for new-onset congestive heart failure.
D. Initiate massive blood transfusion protocol and give protamine for enoxaparin reversal.
E. Give IV tissue plasminogen activator for massive pulmonary embolism.

44. A 30-year-old man with a history of seizures, for which he takes phenytoin, is evaluated in the emergency department for shortness of breath and fatigue. He says that his symptoms have progressed during the past few weeks despite an

antibiotic prescribed by his primary care provider. Vitals signs on arrival are: temperature 38.5°C (101.3°F), heart rate 110 beats/min, respiratory rate 26 breaths/min, blood pressure 100/70 mm Hg, oxygen saturation 93% on 8-L/min nasal cannula. Physical examination is notable for normal mentation, supple neck, elevated jugular venous distension, tachycardia with an S3 gallop, crackles in the lung bases, soft abdomen, warm extremities with 1+ bilateral lower extremity pitting edema, and a faint but diffuse macular rash on his trunk and legs. ECG shows nonspecific T wave inversions. Chest radiograph shows mild pulmonary edema. Laboratory assessment is notable for a troponin 3.0 ng/ml, B-type natriuretic peptide 3,000 pg/ml , creatinine 1.70 mg/dL, sodium 130 mEq/L, potassium 4.4 mEq/L, white blood cell count 13,000/µL, hemoglobin 12 g/dL, platelets 265,000/µL, eosinophils 1,100/µL, aspartate aminotransferase 280 U/L, alanine aminotransferase 250 U/L, alkaline phosphatase 60 U/L, bilirubin 1.0 mg/dL. Echocardiography shows biventricular systolic dysfunction with ejection fraction of 20%.

Which of the following diagnostic tests is most important in determining treatment and prognosis?

A. Skin punch biopsy
B. Right upper quadrant ultrasound
C. Right heart catheterization
D. Endomyocardial biopsy
E. Blood cultures

Part 2 Answers:
Cardiovascular Critical Care

1. Rationale

Answer: C

All patients with stress-induced cardiomyopathy who develop shock need urgent echocardiography to evaluate for left ventricular outflow tract obstruction, occuring in 13% to 18% of patients. Shock in patients with left ventricular outflow tract obstruction should not be treated with inotropic agents, which can worsen the obstruction. Beta-blockers may resolve the obstruction and improve hemodynamics. Alpha-agonists may also improve hemodynamics by increasing afterload and reducing the gradient. However, the use of alpha-agonists requires close observation for vasoconstrictive effects that may be dangerous in patients at risk for coronary vasospasm. Patients who do not respond to initial medical therapy may respond to an intra-aortic balloon pump despite the small risk that afterload reduction will exacerbate the obstruction.

References:

1. Bybee KA, Kara T, Prasad A, et al. Systematic review: transient left ventricular apical ballooning: a syndrome that mimics ST-segment elevation myocardial infarction. *Ann Intern Med.* 2004 Dec 7;141(11):858-865.
2. Sharkey SW, Lesser JR, Zenovich AG, et al. Acute and reversible cardiomyopathy provoked by stress in women from the United States. *Circulation.* 2005 Feb 1;111(4):472-479.
3. Villareal RP, Achari A, Wilansky S, Wilson JM. Anteroapical stunning and left ventricular outflow tract obstruction. *Mayo Clin Proc.* 2001 Jan;76(1):79-83.
4. Madhavan M, Rihal CS, Lerman A, Prasad A. Acute heart failure in apical ballooning syndrome (Tako Tsubo/stress cardiomyopathy): clinical correlates and Mayo Clinic risk score. *J Am Coll Cardiol.* 2011 Mar 22;57(12):1400-1401.

2. Rationale

Answer: A

Prolongation of the QT interval can be congenital or acquired by drug administration. This may be the result of the drug itself or the inhibition of metabolic pathways that will increase the effective dose of the drug. A QTc greater than 500 ms is a prolonged QT that may result in torsades de pointes (TdP) and possibly sudden death.

Repletion of magnesium is useful for the prevention and treatment of TdP, and removal of any agent that may prolong the QTc is optimal. Amiodarone would be harmful because it could actually lower the heart rate and increase the QT interval. Bicarbonate has no role in QTc prolongation. Methadone could lead to prolonged QT syndrome and should be discontinued.

References:

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3. Rationale

Answer: B

This patient has evidence of cardiogenic shock secondary to Takotsubo cardiomyopathy from intense emotional stress. This is a rapidly reversible heart failure syndrome that often mimics acute coronary syndrome and is essentially a diagnosis of exclusion. Patients often have ST elevation on ECG and elevated troponin levels and either no coronary artery disease or very minimal amounts on catheterization. Classic findings on echocardiography are apical ballooning due to hypokinesis of the apex and a hyperdynamic basal segment. The pathophysiology of the disease is thought to be excessive catecholamine stress on the heart.

Treatment for patients with Takotsubo cardiomyopathy is generally supportive but a minority of patients will develop hemodynamic compromise requiring further action. Although no guidelines exist, it is generally recommended to avoid giving additional catecholamines, such as dobutamine or norepinephrine, since this may worsen the condition and stress on the heart. If left ventricular outflow tract (LVOT) obstruction is present, tachycardia should be avoided, since it will reduce diastolic filling time. Increased inotropic stimulation can also worsen LVOT obstruction. Phenylephrine is the vasopressor of choice, combined with beta blockade in this scenario. An intra-aortic balloon pump is an option for patients in cardiogenic shock without LVOT obstruction, as well as aggressive diuresis.

References:

1. Merchant EE, Johnson SW, Nguyen P, Kang C, Mallon WK. Takotsubo cardiomyopathy: a case series and review of the literature. *West J Emerg Med*. 2008 May;9(2):104-111.
2. Gianni M, Dentali F, Grandi AM, Sumner G, Hiralal R, Lonn E. Apical ballooning syndrome or Takotsubo cardiomyopathy: a systematic review. *Eur Heart J.* 2006

Jul;27(13):1523-1529.

4. Rationale

Answer: B

Patients with advanced heart failure have improved survival rates and quality of life when treated with implantable left ventricular assist devices (LVADs) compared to medical therapy. LVADs are now placed as a bridge to cardiac transplantation and as end-destination therapy. With the higher prevalence of these devices in the community, it is important for the intensivist to have an understanding of their basics. The inflow cannula (blood to device) is inserted into the apex of the left ventricle. The outflow cannula (blood to patient) is inserted into the ascending or descending aorta. The pump speed with the programmable variable is titrated in the operating room and ICU. In the immediate postoperative period, complications include bleeding, hypovolemia, arrhythmia, thrombosis, in-flow cannula “suck-down” events, device malposition, and right-sided heart failure. Later complications include infection, thrombosis, and drive line/machine issues. Troubleshooting these early complications in the ICU requires a thorough review of the available hemodynamic parameters, review of the right-side heart physiology, and close evaluation of echocardiographic findings. In this case, the bedside echocardiogram clearly shows right ventricular compression and physiologic parameters consistent with tamponade.

References:

1. Pratt AK; Shah NS; Boyce SW. Left ventricular assist device management in the ICU. *Crit Care Med.* 2014 Jan;42(1):158-168.
2. Slaughter MS, Rogers JG, Milano CA et al; HeartMate II Investigators. Advanced heart failure treated with continuous-flow left ventricular assist device. *N Engl J Med.* 2009 Dec 3;361(23):2241-2251.

5. Rationale

Answer: A

Cerebral hyperperfusion syndrome following a carotid endarterectomy classically occurs two to three hours postoperatively. Signs and symptoms can include ipsilateral headache, eye pain, somnolence, agitation, confusion, and seizures. It is thought to be a result of impaired autoregulation distal to the stenosis, resulting in excessive blood flow after removal of the stenosis. Systemic hypertension can exacerbate the resulting cerebral edema, so pharmacologic reduction in cerebral perfusion pressure with drugs such as labetalol is appropriate. The syndrome usually resolves within 24 hours after surgery. Treating symptoms with additional narcotics would be beneficial only if the blood pressure elevation is the result of surgical pain, which does not appear to be the case. Radiographic and Doppler imaging in the absence of lateral neurologic deficits are not warranted.

References:

1. Herrick IA, Higashida RT, Gelb AW. Occlusive cerebrovascular disease: anesthetic considerations. In: Cottrell JE, Young WL. *Cottrell and Young's Neuroanesthesia.* 5th ed. Philadelphia, PA: Elsevier Mosby; 2010:290-291.
2. Smaka TJ, Miller TE, Hutchens MP, et al. Anesthesia for vascular surgery. In: Barash PG, Cullen BF, Stoelting RK, Cahalan M, Stock MC, Ortega R. *Clinical Anesthesia.* 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013: 1127.
3. Karapanayiotides T, Meuli R, Devuyst G, et al. Postcarotid endarterectomy hyperperfusion or reperfusion syndrome. *Stroke.* 2005 Jan;36(1):21-26.

6. Rationale

Answer: D

Qualitative capnometry is a simple and rapid confirmatory test for appropriate endotracheal tube placement. The device is attached in-line between the endotracheal tube and the delivery system. The chemical indicator in the device will change color depending on the CO_2 concentration detected. The higher the CO_2 level, the more color change will be seen from purple to yellow.

In patients with profoundly low cardiac output, end-tidal CO_2 levels may be significantly lowered due to diminished lung perfusion. Ventilation is directly correlated to pulmonary perfusion. A profoundly low cardiac output could cause the clinical scenario in this case. Possible additional factors are ineffective chest compressions, massive pulmonary emboli, tension pneumothorax, or some other cause of inadequate cardiac output during cardiopulmonary resuscitation. Often there will be a significant increase in end-tidal CO_2 levels once return of spontaneous circulation has been achieved. Severe acidosis would not be associated with a lower level of end-tidal CO_2.

Venous hyperoxia has been documented in post-cardiac arrest patients after the return of spontaneous circulation. It is presumed to be secondary to bioenergetics failure and defects in oxygen utilization after a prolonged pulseless time. This does not have any impact on end-tidal CO_2 detection.

It would be extremely unlikely that low-level color change is due to hypoventilation after endotracheal intubation. It would be even more unlikely that the low-level color change persisted after the delivery of multiple breaths.

References:

1. Jin X, Weil MH, Tang W, et al. End-tidal carbon dioxide as a non-invasive indicator of cardiac index during circulatory shock. *Crit Care Med.* 2000 Jul;28(7):2415-2419.
2. Rivers EP, Rady MY, Martin GB, et al. Venous hyperoxia after cardiac arrest. Characterization of a defect in systemic oxygen utilization. *Chest.* 1992 Dec;102(6):1787-1793.
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Emerg Med. 1991 Mar;20(3):267-270.

4. Brown LH, Gough JE, Seim RH. Can quantitative capnometry differentiate between cardiac and obstructive causes of respiratory distress? *Chest.* 1998 Feb;113(2):323-326.

7. Rationale

Answer: C

A potential complication of peripheral venoarterial extracorporeal membrane oxygenation (ECMO) is differential hypoxia, also known as north-south syndrome. If there is adequate native cardiac function with concomitant respiratory failure, the mixing point of retrograde blood flow from the femoral artery can be more distal, leading to upper body hypoxemia. This can be monitored by comparing arterial blood gas analysis results from the patient's right radial artery to those from the left, as well as comparing to post-oxygenator blood gas values. Solutions to this problem can be to change the central cannulation, increase ECMO flows, or consider a change to venovenous ECMO if cardiac function is adequate.

Based on the post-oxygenator blood gas values, the oxygenator is working effectively and does not need to be changed, nor does an additional one need to be added. Increasing the fraction of inspired oxygen, which is already at 60%, would be suboptimal for a patient with acute respiratory distress syndrome, and could lead to oxygen free radical toxicity.

References:

1. Cove ME. Disrupting differential hypoxia in peripheral veno-arterial extracorporeal membrane oxygenation. *Crit Care.* 2015;19(1):280.
2. Chung M, Shiloh AL, Carlese A. Monitoring of the adult patient on venoarterial extracorporeal membrane oxygenation. *Scientific World Journal.* 2014;2014. Article ID 393258.

8. Rationale

Answer: D

The patient presents with acute pericarditis probably related to his pneumonia. The prototypical features of acute pericarditis are acute chest pain with radiation to the trapezius ridge, that is improved with sitting forward, pericardial friction rub, and an ECG tracing with diffuse ST elevation with concave upstrokes and reciprocal ST depression in leads VR and V1. Transthoracic echocardiography should be obtained to evaluate for the presence of pericardial effusions that can lead to pericardial tamponade. In 80% to 90% of acute pericarditis cases, the etiology is idiopathic. Up to 90% of acute idiopathic pericarditis cases are self-limiting. Recommended initial treatment is nonsteroidal anti-inflammatory drugs. Combination therapy with colchicine can also be used. A recent study showed that combination therapy has been shown to reduce the rate of persistent and recurrent pericarditis.

References:

1. LeWinter MM. Acute pericarditis. *N Engl J Med.* 2014 Dec 18;371(25):2410-2416.
2. Imazio M, Brucato A, Cemin R, et al; ICAP Investigators. A randomized trial of colchine for acute pericarditis. *N Engl J Med.* 2013 Oct 17;369(16):1522-1528.
3. Spodick DH. Acute pericarditis: current concepts and practice. *JAMA.* 2003 Mar 5:289(9):1150-1153.

9. Rationale

Answer: B

This patient has an inferior ST elevation myocardial infarction (STEMI) with cardiogenic shock. Even though he recently had surgery, aspirin is indicated. The 2015 American Heart Association (AHA) guidelines recommend doses of 162-325 mg. Nitroglycerin is appropriate in STEMI to relieve chest pain; however, both hypotension with a systolic blood pressure less than 90 mm Hg and a suspected right ventricular infarct, such as in this case, are contraindications to nitroglycerin. Similarly, morphine can be considered for chest pain but is not the most important next step. Diltiazem is contraindicated in STEMI with evidence of cardiogenic shock. Currently, the administration of supplemental oxygen to normoxic patients with acute coronary syndrome is not well supported by data. The 2015 AHA guidelines state that withholding oxygen in normoxic patients can be considered. Therefore, with the patient's oxygen saturation of 98%, providing 100% oxygen is unlikely to be the most important next step.

References:

1. O'Connor RE, Al Ali AS, Brady WJ, et al. Part 9: Acute coronary syndromes: 2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation.* 2015 Nov 3;132(18 Suppl 2):S483-S500

10. Rationale

Answer: B

Several studies have demonstrated the superior sensitivity of precordial leads compared to limb leads for the detection of perioperative myocardial ischemia. London et al demonstrated that precordial leads V4 and V5 had the highest sensitivity individually. Combining leads II, V4, and V5 had a sensitivity of 96%, which increased to 100% with the addition of V2 and V3. This stresses the importance of appropriate lead placement as well as review of all leads when there is clinical concern.

References:

1. Mark JB. Multimodal detection of perioperative myocardial ischemia. *Tex Heart Inst J*. 2005;32(4):461-466.

2. London MJ, Hollenberg M, Wong MG, et al. Intraoperative myocardial ischemia: localization by continuous 12-lead electrocardiography. *Anesthesiology.* 1988 Aug;69(2):232-241.
3. Landesberg G, Mosseri M, Wolf Y, Vesselov Y, Weissman C. Perioperative myocardial ischemia and infarction: identification by continuous 12-lead electrocardiogram with online ST-segment monitoring. *Anesthesiology.* 2002 Feb;96(2):264-70.
4. Kaplan JA, King SB 3rd. The precordial electrocardiographic lead (V5) in patients who have coronary-artery disease. *Anesthesiology.* 1976 Nov;45(5):570-574.

11. Rationale

Answer: A

This patient has Wolff-Parkinson-White (WPW) syndrome, as evidenced by the short PR interval and presence of a delta wave on the ECG. WPW is one of the pre-excitation syndromes, which cause early depolarization of the ventricle through an abnormal connection between atria and ventricles called the accessory pathway. WPW syndrome is very rare, existing in only 0.1-3 per 1000, and is usually asymptomatic. Some patients, however, may experience syncope and palpitations. They are at greater risk for atrial fibrillation, which can lead to ventricular fibrillation. Patients are also at risk for circus reentrant tachycardias leading to paroxysmal supraventricular tachycardia or ventricular tachycardia and also for sudden cardiac death. Treatment options for people with arrhythmias and WPW syndrome include nonpharmacologic therapies (ie, catheter ablation of the accessory pathway) and pharmacologic therapy (to slow ventricular heart rates or to prevent arrhythmias).

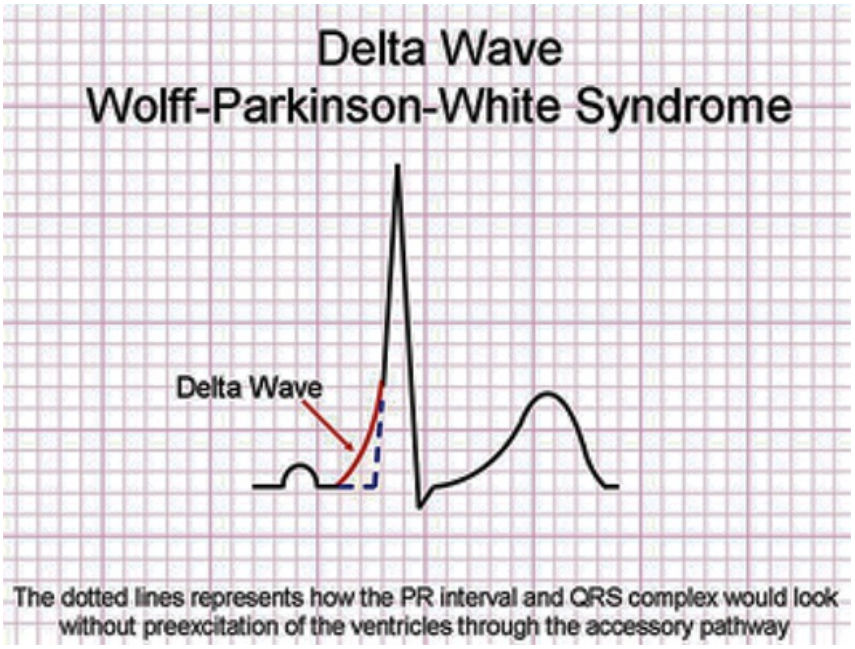
In patients with WPW, a sinus beat originates from the sinoatrial (SA) node and goes through the accessory pathway and also through the atrioventricular (AV) node. Since the ECG is a summation of vectors seen by each lead, the result is a shorter PR interval and wider QRS than normal; we also see the characteristic delta wave. ST-T wave changes are also possible. In general, the AV node has a longer refractory time than the accessory pathway; therefore, an impulse transmitted through the accessory pathway will activate the ventricles earlier than if it had traveled through the AV node. Impulses can be transmitted in a retrograde or anterograde fashion through the accessory pathway, thus allowing for the development of circus reentrant tachycardias.

Sympathetic stimulation (anxiety, hypovolemia, hypoxemia and acidosis, light planes of anesthesia) as well as drugs (pancuronium, meperidine, ketamine, ephedrine, digoxin, verapamil) and electrolyte abnormalities (potassium and calcium) can induce tachyarrythmias by increasing conduction through the accessory pathway.

When atrial contraction becomes chaotic, as in atrial fibrillation (atria can produce 300 to 500 contractions per minute), the AV node will produce a narrow complex beat (irregularly irregular narrow-complex tachycardia) and the accessory pathway will produce a wide complex beat (irregularly irregular wide-complex tachycardia). P waves will not be present. WPW atrial fibrillation is the only arrhythmia in which there is irregularly irregular wide- and narrow-complex tachycardia.

The combination of atrial fibrillation and WPW can be fatal because of rapid conduction of the atrial activity through the accessory pathway, resulting in rapid ventricular rates and leading to ventricular fibrillation. AV nodal blocking agents (metoprolol, diltiazem, digoxin, sotalol) should be avoided in this setting because they paradoxically increase ventricular rates since more atrial activity will pass through the fast-conducting accessory pathway and fewer through the AV node itself. Procainamide has been the traditional recommended therapy for unstable WPW. It is a class Ia antiarrythmic, which increases the refractory period and decreases conduction through the accessory pathway.

Procainamide is typically infused intravenously at 20 to 50 mg/min, given while monitoring blood pressure closely every 5 to 10 minutes until the arrhythmia terminates, hypotension ensues, the QRS is prolonged by more than 50%, or a total of 17 mg/kg (1.2 g for a 70-kg (154.3-lb) patient) has been given. Even if it does not result in tachycardia termination, IV procainamide will usually slow the tachycardia rate and improve the hemodynamic state. Of course, synchronized cardioversion should be performed in patients who are hemodynamically unstable.



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2. Fengler BT, Brady WJ, Plautz CU. Atrial fibrillation in the Wolff-Parkinson-White syndrome: ECG recognition and treatment in the ED. *Am J Emerg Med.* 2007 Jun;25(5):576-583.
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5. Wolff L, Parkinson J, White PD. Bundle-branch block with short P-R interval in healthy young people prone to paroxysmal tachycardia. *Am Heart J.* 1930 Aug;5(6):685-704.

12. Rationale

Answer: C

In the management of aortic stenosis, maintenance of sinus rhythm is beneficial, to allow appropriate diastolic filling needed to maintain adequate cardiac output. Cannon a waves are created when blood pushes against stenotic mitral or tricuspid valves and when there is a loss of atrioventricular (AV) synchrony. The a wave produced by the simultaneous contraction of the atria and ventricles occurs later in the cardiac cycle at the timing of the normal v wave. The combination of the a and v waves creates the cannon wave. Cannon waves will also appear if there are premature ventricular contractions, or reentrant ventricular tachycardia.

References:

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2. Shah MR, Hasselblad V, Stevenson LW. Impact of the pulmonary artery catheter in critically ill patients: meta-analysis of randomized clinical trials. *JAMA.* 2005 Oct 5;294(13):1664-1670.
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4. http://www.modernmedicine.com/modern-medicine/content/pa-catheters-what-waveforms-reveal.

13. Rationale

Answer: B

This patient has a toxic level of digoxin, which commonly occurs in older patients who develop acute kidney injury. Digoxin is associated with a number of cardiac dysrrhythmias, including supraventricular tachycardia, sinus bradycardia, atrioventricular blocks, and ventricular tachycardia. Calcium chloride is theoretically contraindicated in digoxin overdose because it may potentiate digoxin's mechanism of action. Digoxin immune Fab is the best treatment for digoxin overdose. In acute ingestions, activated charcoal could be considered, but her symptoms have been present for more than a day. Potassium repletion is not indicated in digoxin toxicity. At this time, given her blood pressure, there is no role for epinephrine. Dialysis has, at best, minimal effects on digoxin clearance.

References:

1. Chan BS, Buckley NA. Digoxin-specific antibody fragments in the treatment of digoxin toxicity. *Clin Toxicol (Phila).* 2014 Sep-Oct;52(8):824-836.
2. Yang EH, Shah S, Criley JM. Digitalis toxicity: a fading but crucial complication to recognize. *Am J Med.* 2012 Apr;125(4):337-343.

14. Rationale

Answer: B

Atrial fibrillation (AF) that occurs during critical illness presents challenges for management. Recent evidence suggests that patients in whom AF develops during acute illness (eg, sepsis) have high long-term risks for AF-associated complications, such as stroke, heart failure, and death. Therefore, all patients with AF lasting longer than 48 hours should be evaluated for anticoagulation. Decisions about appropriate thromboprophylaxis require individual assessment of stroke risk and bleeding risk on such therapy. Validated risk scoring tools have been developed for clinical use to assess the risks of bleeding and thrombosis.

The CHADS2 score is a simple and popular tool to assess thrombosis risk in patients with AF. However, recent data suggests that this score fails to account for risk in several common subpopulations, including patients with peripheral vascular disease, women, and those for whom variations in thrombotic risk occur with age. To account for these limitations, the CHA2DS2-VASc score was developed and is currently recommended for use in AF risk assessment. In general, for patients who have had prior stroke, transient ischemic attack, or CHA2DS2-VASc score of 2 or higher, oral anticoagulants are recommended, such as warfarin or a direct thrombin inhibitor. The decision to anticoagulate a patient must be weighed against the risk of bleeding. The HAS-BLED score was recently developed and is recommended to assist in bleeding risk assessment. Patients with a HAS-BLED score of 3 or greater are considered to be at high risk for bleeding while undergoing anticoagulation.

This patient illustrates the implications of using risk stratification tools. Her HAS-BLED score is 1 (age greater than 65 years), indicating that her risk of bleeding on anticoagulation is low. If her stroke risk were assessed with the CHADS2, her score would be 0 and she would therefore be prescribed either aspirin or no antithrombotic therapy. In contrast, on the CHA2DS2-VASc, she would score 3 (female, age 70 years, and previous myocardial infarction: 1 point each), placing her at high risk of stroke and therefore making her a candidate for oral anticoagulation therapy.

References:

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3. Lip GY, Frison L, Halperin JL, Lane DA. Comparative validation of a novel risk score for predicting bleeding risk in anticoagulated patients with atrial fibrillation:

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4. Tracy C, Boushahri A. Managing arrhythmias in the intensive care unit. *Crit Care Clin.* 2014 Jul;30(3):365-390.
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15. Rationale

Answer: B

The intra-aortic balloon pump (IABP) is a mechanical circulatory device that has been used to support patients in cardiogenic shock from myocardial infarction, intractable ventricular arrhythmias, and acute decompensated heart failure. The timing of inflation and deflation of the IABP is crucial in facilitating hemodynamic support by increasing coronary perfusion and reducing afterload. Electrocardiography and systemic aortic pressure waveforms can be used to trigger the IABP. In a patient with sinus rhythm, the IABP is set to inflate mid-T wave and deflate at the peak of the R wave on ECG, which corresponds to the start of diastole and systole, respectively. In the aortic pressure waveform trigger mode, the balloon inflates with the dicrotic notch, which corresponds to aortic valve closure, and deflates before the systolic arterial upstroke that represents aortic valve opening.

The pressure waveform depicted shows diastolic augmentation and an absence of a dicrotic notch. This indicates that the balloon is inflating early. Early balloon inflation impairs systolic function by increasing afterload and myocardial oxygen demand.

References:

1. Trost JC, Hillis LD. Intra-aortic balloon counterpulsation. *Am J Cardiol.* 2006 May 1; 97(9):1391-1398.
2. Maccioli GA, Lucas WJ, Norfleet EA. The intra-aortic balloon pump: a review. *J Cardiothorac Anesth.* 1988 Jun;2(3); 365-373.

16. Rationale

Answer: C

Resistance to loop diuretics is a common complication of chronic therapy in congestive heart failure. Furosemide effectively blunts the reabsorption of sodium and water in the thick ascending limb of the loop of Henle, but this delivers a greater luminal sodium concentration to the distal convoluted tubule (DCT). Cells in the DCT hypertrophy in response to this increased sodium concentration, and absorb more sodium and water, which decreases the effectiveness of furosemide.

Loop diuretics act at targets on the luminal side of the thick ascending limb of the loop of Henle. To get to its target, furosemide must be filtered at the glomerulus and then secreted into the tubular lumen by the organic ion transporter. Blood urea nitrogen

and other organic acids compete for binding sites on that transporter and make furosemide secretion less efficient.

The reduction in plasma volume caused by effective diuresis results in activation of the renal-angiotensin-aldosterone system and the sympathetic nervous system. This reduces glomerular filtration rate, leads to decreased tubular flow, and increased reabsorption of sodium and water.

Furosemide binding to plasma proteins increases the effectiveness of the drug because plasma binding is required for secretion into the tubular lumen. Hypoalbuminemia is common in heart failure and enhances conversion of furosemide to its inactive form. Increased plasma protein binding increases, not decreases, the effectiveness of furosemide as a loop diuretic, which is why co-administration of furosemide with albumin has been demonstrated to improve the response to diuretics in patients with cirrhosis and nephrotic syndrome.

References:

1. Ter Maaten JM, Valente MA, Damman K, Hillege HL, Navis G, Voors AA. Diuretic response in acute heart failure—pathophysiology, evaluation, and therapy. *Nat Rev Cardiol.* 2015 Mar;12(3):184-192.
2. Wargo KA, Banta WM. A comprehensive review of the loop diuretics: should furosemide be first line? *Ann Pharmacother.* 2009 Nov;43(11):1836-1847.

17. Rationale

Answer: C

This patient's device has an increase in power required to drive the impeller at an unchanged speed and a reduced pulsatility index. The pulsatility index is an ongoing measure of the contribution of the patient's native left ventricular (LV) contraction to flow through the device. Impeller thrombosis obstructs optimal impeller function and increases the power required to achieve the set speed. In addition, the degree to which native LV contraction can contribute to increases in flow through the impeller is blunted by the presence of a thrombus in the blood flow path. This leads to a decrease in the pulsatility index. Increased serum lactate dehydrogenase (LDH) and total bilirubin are consistent with red cell hemolysis, which is a hallmark of pump thrombosis. Because the impeller is less effective at generating flow, total cardiac output can decrease, which might lead to a decrease in mixed venous oxygen saturation ($SmvO_2$). Popliteal vein thrombosis might increase LDH and total bilirubin, but it should not change the power requirement or decrease the patient's mixed venous oxygen saturation. Right ventricular failure might decrease $SmvO_2$ and increase total bilirubin, but would not decrease pump power or increase LDH. Similarly, acute mitral regurgitation might reduce the $SmvO_2$ and increase total bilirubin, but would not cause a change in pump power or increase LDH. The option most consistent with these findings is impeller thrombosis.

Reference:

1. Bartoli, CR, Ailawadi G, Kern JA. Diagnosis, nonsurgical management, and prevention of LVAD thrombosis. *J Card Surg.* 2014 Jan;29(1):83-94.

18. Rationale

Answer: C

This patient has a rapidly failing heart and requires immediate stabilization until she can either undergo definitive operative management or otherwise be hemodynamically stabilized. Other possible interventions include the placement of alternative cardiac assist devices. All other proposed interventions might be expected to lead to immediate cardiovascular collapse. In particular, initiating a phenylephrine infusion, which might be a feasible intervention after the insertion of a cardiac assist device, would, as a primary intervention in this acute setting, increase afterload and further decrease cardiac index. The patient is already in fulminate congestive heart failure and giving more fluids would exacerbate her already tenuous hemodynamic condition. Low-dose esmolol might be cautiously used in other similar situations but here would undoubtedly contribute to the patient's hypotension.

References:

1. Thiele H, Zeymer U, Neumann FJ, et al; IABP-SHOCK II Trial Investigators. Intraaortic balloon support for myocardial infarction with cardiogenic shock. *N Engl J Med.* 2012 Oct 4;367(14):1287-96.
2. O'Neill WW, Kleiman NS, Moses J, et al. A prospective, randomized clinical trial of hemodynamic support with Impella 2.5 versus intra-aortic balloon pump in patients undergoing high-risk percutaneous coronary intervention: the PROTECT II study. *Circulation.* 2012 Oct 2;126(14):1717-1727.

19. Rationale

Answer: D

This patient has an elevated lactate dehydrogenase, with low pulsatility index, and high pump power, which indicates pump thrombosis. With the thrombosis in his device, there is increased resistance in the LVAD, which reduces its ability to offload the heart. The left ventricle must now expel most of the blood through the aortic valve instead of through the device, which explains the normal blood pressure. Thrombolytic therapy has been attempted to remove clot burden in the LVAD with nominal success but is associated with higher risk of bleeding complications. In the context of pump thrombosis, increasing the LVAD speed will hemolzye blood more. The patient's INR is appropriate; increasing the goal therapy will increase risk of bleeding. The best course of action is to exchange the device.

References:

1. Starling RC, Moazami N, Silvestry SC, et al. Unexpected abrupt increase in left ventricular assist device thrombosis. *N Engl J Med.* 2014 Jan 2;370(1):33-40.
2. Najjar SS, Slaughter MS, Pagani FD, et al; HVAD Bridge to Transplant AVDANCE

Trial Investigators. An analysis of pump thrombosis events in patients in the HeartWare ADVANCE bridge to transplant and continued access protocol trial. *J Heart Lung Transplant.* 2014 Jan;33(1):23-34.

3. Zalewski CM, Cohen JE, Hill CE, et al. Early identification of impending LVAD thrombosis utilizing an ultra-high predictive serum marker in lactate dehydrogenase. *J Heart Lung Transplant.* 2014 Apr;33(4 Suppl):S242.

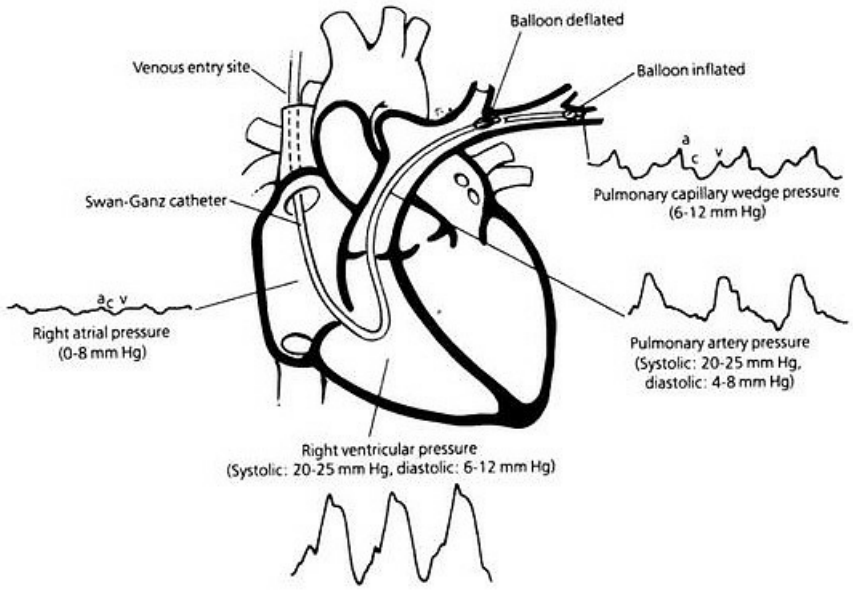
20. Rationale

Answer: C

The first description of a pulmonary arterial catheter (PAC) inserted without the use of fluoroscopy appeared in 1970. It has multiple ports to allow for measurement of intracardiac pressures and thermodilution cardiac output, infusion of medications, and atrial or ventricular pacing. The catheter can be placed at bedside in the ICU without fluoroscopy through a large-bore central venous introducer. The PAC's position can be identified using the characteristic waveforms as the catheter traverses through the superior vena cava, right atrium, and right ventricle into the pulmonary artery. The figure below shows the waveforms seen as the PAC traverses cardiac structures.

The correlation between the right atrial, ventricular, pulmonary arterial, or pulmonary arterial occlusion pressure (also called pulmonary capillary wedge pressure) and left ventricular pressure is poor and, as such, these measurements can at best be considered surrogates. Fluctuations in intrathoracic and pericardial pressures negatively impact the utility of wedge pressure measurement as well, since left ventricular filling pressure is truly a measurement of the transmural pressure across the ventricular wall. PACs still have an important role in the managemet of pulmonary hypertension, including diagnosis and monitoring response to therapy.

The Berlin criteria for acute respiratory distress syndrome no longer include PAC findings due to poor interobserver reliability in the diagnosis of noncardiogenic extravascular fluid. The use of PACs in the routine management of septic shock and traumatic brain injury is not supported by clinical trials.



References:

1. Swan HJ, Ganz W, Forrester J, 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 Aug 27;283(9):447-451.
2. Gidwani UK, Mohanty B, Chatterjee K. The pulmonary artery catheter: a critical reappraisal. *Cardiol Clin.* 2013 Nov;31(4):545-565.
3. Chatterjee K, De Marco T, and Alpert JS. Pulmonary hypertension: Hemodynamic diagnosis and management. *Arch Intern Med.* 2002 Sep 23;162(17):1925-1933.
4. Binanay C, Califf RM, Hasselblad V, et al; ESCAPE Investigators and ESCAPE Study Coordinators. Evaluation study of congestive heart failure and pulmonary artery catheterization effectiveness: the ESCAPE trial. *JAMA.* 2005 Oct 5;294(13):1625-1633.

21. Rationale

Answer: C

Increased evidence has shown that static markers, such as central venous pressure (CVP) and pulmonary artery occlusion pressure (PAOP), of preload responsiveness are inaccurate. A growing body of literature supports the use of dynamic markers as better indicators. These include pulse pressure variation (PPV), stroke volume variation, and passive leg raise. The passive leg-raising technique involves lowering a patient's thorax into a horizontal position and raising the legs 45 degrees in the air for 30 to 90 seconds. Passive leg raise is equivalent to a 150- to 300-mL IV bolus. Venous blood from the legs flows into the thorax, leading to an increase in preload and a subsequent increase in stroke volume, if the patient is volume responsive. This method of assessing volume responsiveness is accurate in patients who are spontaneously breathing, mechanically ventilated, and who have cardiac arrhythmia, provided they are monitored with a cardiac output monitoring device to assess stroke volume. Devices that have been used are pulse contour continuous cardiac output,

Vigileo/FloTrac, esophageal Doppler, and echocardiography.

PPV would be inaccurate in this patient because she is spontaneously breathing over the ventilator and her tidal volume is less than 8 mL/kg of IBW. PPV relies on heart and lung interactions, which are not constant in this patient. CVP due to the changes in venous tone, intrathoracic pressures, and heart compliance leads to a poor relationship between CVP and right ventricular end-diastolic volume in the critically ill patient. Numerous studies have demonstrated a poor relationship between CVP and the change in CVP in demonstrating fluid responsiveness. Similar results have been shown for PAOP.

References:

1. Marik PE, Cavallazzi R, Vasu T, Hirani A. Dynamic changes in arterial waveform derived variables and fluid responsiveness in mechanically ventilated patients: a systematic review of the literature. *Crit Care Med.* 2009 Sep;37(9):2642-2647.
2. Cavallaro F, Sandroni C, La Torre G, et al. Diagnostic accuracy of passive leg raising for prediction of fluid responsiveness in adults: systematic review and meta-analysis of clinical studies. *Intensive Care Med.* 2010 Sep;36(9):1475-1483.
3. Marik PE, Baram M, Vahid B. Does central venous pressure predict fluid responsiveness? A systematic review of the literature and the tale of seven mares. *Chest.* 2008 Jul;134(1):172-178.
4. Monnet X, Rienzo M, Osman D, et al. Passive leg raising predicts fluid responsiveness in the critically ill. *Crit Care Med.* 2006 May;34(5)1402-1407.
5. Boulain T, Achard JM, Teboul JL, Richard C, Perrotin D, Ginies G. Changes in BP induced by passive leg raising predict response to fluid loading in critically ill patients. *Chest.* 2002 Apr;121(4):1245-1252.

22. Rationale

Answer: C

Conventional monitors of stroke volume variation and cardiac output measurement are highly dependent on the aortic pulse contour for their measurements. Arrhythmias that alter beat-to-beat cardiac loading conditions will affect the reliability of measurements, as will use of an intra-aortic balloon pump by altering the diastolic waveform. Conditions associated with low vascular resistance also are problematic for these devices. Cyclic variations in respiratory waveform, as would be expected in a spontaneously breathing patient or in a patient with acute pulmonary disease manifesting with severe pulmonary noncompliance, also affect the reliability of the measurements. The monitors are generally recommended when patients are on a respirator with tidal volumes of at least 8 mL/kg. Hence the intraoperative patient without an arrhythmia receiving controlled ventilation while under anesthesia presents the most ideal conditions for this type of monitoring device.

References:

1. Argueta E, Berdine G, Pena C, Nugent KM. FloTrac® monitoring system: what are its uses in critically ill medical patients? *Am J Med Sci.* 2015 Apr;349(4):352-356.
2. Marik PE. Noninvasive cardiac output monitors: a state-of the-art review. *J Cardiothorac Vasc Anesth.* 2013 Feb;27(1):121-134.
3. Marik PE, Cavallazzi R, Vasu T, Hirani A. Dynamic changes in arterial waveform derived variables and fluid responsiveness in mechanically ventilated patients: a systematic review of the literature. *Crit Care Med.* 2009 Sep;37(9):2642-2647.

23. Rationale

Answer: D

For both ventilated and nonvenilated patients, hemodynamic parameters are measured when the chest comes to rest at the end of the exhalatory phase of the respiratory cycle. The point in the cardiac cycle where central venous pressure and pulmonary artery occlusion pressure (PAOP) readings are taken is the end of diastole, which coincides with the point at which the C wave occurs. The C wave is often not visible; however, in the case of the PAOP, the timing of the C wave coincides with the end of the QRS.

References:

1. Leatherman JW, Marini JJ. Clinical use of the pulmonary artery catheter. In: Hall JB, Schmidt GA, Wood LDH, eds. *Principles of Critical Care. 2nd ed.* Boston, MA: McGraw-Hill; 1998:155-176.
2. Brierre SP, Summer W, Happel KI, Taylor DW. Interpretation of pulmonary artery catheter tracings. *Clin Pulm Med.* 2002;9(6):335-341.

24. Rationale

Answer: C

In recent years ultrasonography, particularly echocardiography, has become much more popular among intensivist for its portability, noninvasiveness, and ability to be repeated as many times as necessary. Disadvantages include operator dependency and the need for significant training, since under- or overestimation of findings can lead to erroneous therapy.

In this patient, the echocardiographic findings speak against heart failure in that he has preserved contractility. Infection is unlikely, given the clinical scenario. His hemodynamic picture and echocardiographic findings suggest hypovolemia. Possible sources of bleeding, given the normal focused assessment with sonography in trauma examination and chest radiograph, include retroperitoneal hematoma or blood loss from long bone fracture.

References:

1. Murthi SB, Markandaya M, Fang R, et al. Focused comprehensive, quantitative,

functionally based echocardiographic evaluation in the critical care unit is feasible and impacts care. *Mil Med.* 2015 Mar;180(3 Suppl):74-79.
2. Porter TR, Shillcutt SK, Adams MS, et al. Guidelines for the use of echocardiography as a monitor for therapeutic intervention in adults: a report from the American Society of Echocardiography. *J Am Soc Echocardiogr.* 2015 Jan;28(1):40-56.

25. Rationale

Answer: C

Central venous pressure (CVP) is an accurate reflection of right atrial pressure, which is the back pressure for venous return. Right atrial pressure is typically kept low, so venous return is unimpeded. As such, cardiac dysfunction is typically reflected by an elevation in CVP. CVP is a reflection of right-sided filling pressures; therefore, processes that affect right-sided cardiac function can elevate this hemodynamic parameter. These include pulmonary hypertension, right ventricular dysfunction, and tricuspid regurgitation. The absolute values of central venous oxygen saturation are not identical to true mixed venous oxygen saturation and are typically higher during shock states. However, as hemodynamics change, the trend in these two parameters follow the same pattern. Analysis of CVP waveforms can provide useful insight into hemodynamics. For example, a large v wave indicates tricuspid regurgitation, and a large y descent indicates restrictive cardiac dysfunction. However, there is currently significant debate as to the utility of CVP monitoring, especially with respect to fluid status.

References:

1. Mark JB. *Atlas of Cardiovascular Monitoring.* London: Churchill Livingstone; 1997.
2. Sondergaard S, Parkin G, Aneman A. Central venous pressure: we need to bring clinical use into physiological context. *Acta Anaesthesiol Scand.* 2015 May;59(5):552-560.

26. Rationale

Answer: D

Determining volume responsiveness is a critical step in resuscitation care. Using dynamic markers of preload responsiveness is increasing, given the physiologic superiority of this approach and the poor sensitivity and specificity of static markers, such as central venous pressure. Dynamic measurements such as pulse pressure variation, stroke volume variation, and ultrasound assessment, provide more accurate determinations of the patient's place on the Frank-Starling curve. Pulse pressure variation is often cited in the literature as one of the most precise measurements for determining volume status, but it is important to note that particular conditions apply. Positive pressure ventilation induces cyclic changes in preload and afterload on the right and left ventricle that are more pronounced when the patient is on the steep portion of the Frank-Starling curve. A pulse pressure variation of greater than 13%

has been verified in the literature to indicate that the patient will likely be volume responsive. However, in order for this to be accurate, the patient must be in sinus rhythm, must not be taking spontaneous breaths, ideally should not be ventilated with very low tidal volumes, and should not have significant left ventricular or right ventricular dysfunction. This case also demonstrates the importance of performing a teritary survey on all trauma patients.

References:

1. Marik PE, Monnet X, Teboul JL. Hemodynamic parameters to guide fluid therapy. *Ann Intensive Care.* 2011 Mar 21;1(1):1.
2. Michard F, Richards G, Biais M. Lopes M, Auler JO. Using pulse pressure variation or stroke volume variation to diagnose right ventricular failure? *Crit Care.* 2010;14(6):451.

27. Rationale

Answer: E

Quantitative capnography should be considered for all mechanically ventilated patients because it provides a direct measurement of pulmonary ventilation. A normal $ETCO_2$ value in a healthy adult should be 35 to 45 mm Hg. Capnography indirectly provides measurements on metabolism and cardiac output. Physiologic states that decrease whole body metabolism, hypothermia, and poor circulating volume will be reflected numerically as a decrease in $ETCO_2$. In contrast, physiologic states that increase whole body metabolism, such as fever, will be reflected as an increase in $ETCO_2$. Physiologic states that decrease cardiac output, such as a pulmonary embolism, will be reflected as a decrease in $ETCO_2$. Pharmacologic interventions, such as giving a load of sodium bicarbonate, will be reflected almost immediately with an increase in $ETCO_2$ as the lungs compensate for the increased carbon dioxide load. Quantitative capnography can provide confirmatory information with endotracheal intubation. An esophageal intubation may initially have an $ETCO_2$ waveform due to intragastric CO_2 that rapidly disappears. Two practical uses of quantitative capnography during cardiopulmonary resuscitation are: 1) evaluating the effectiveness of chest compressions, and 2) identifying return of spontaneous circulation (ROSC). High-quality chest compressions are reflected by $ETCO_2$ values between 10 and 20 mm Hg in the intubated patient. ROSC is reflected as a spontaneous significant increase in $ETCO_2$ (toward the physiologic normal range of 35 mm Hg) as the heart improves cardiac output by regaining a rhythm and circulates CO_2 into the lungs.

References:

1. Blanch L, Romero PV, Lucangelo U. Volumetric capnography in the mechanically ventilated patient. *Minerva Anestesiol.* 2006 Jun;72(6):577-585.
2. Kodali BS. Capnography outside the operating rooms. *Anesthesiology.* 2013 Jan;118(1):192-201.

3. Thompson JE, Jaffe MB. Capnographic waveforms in the mechanically ventilated patient. *Respir Care.* 2005 Jan; 50(1):100-108.

28. Rationale

Answer: A

The variation of the pulse pressure on an arterial line tracing during positive pressure mechanical ventilation reflects the effects of increasing and decreasing intrathoracic pressure in an alternating fashion, on stroke volume. This is sometimes best thought of by looking at the effects on the right and left heart separately.

Focusing on the right side of the heart, during inspiration on a positive pressure breath, there is an increase in intrathoracic pressure as air is forced into the lungs and alveoli from the ventilator. The increased lung volume and pressure in the lungs and alveoli increases pulmonary vascular resistance, which increases right ventricular (RV) afterload. At the same time, the increase in intrathoracic pressure impedes venous return into the chest through the vena cava, which causes a decrease in preload. The combined effect of a decrease in preload and increase in afterload cause a decrease in stroke volume and cardiac output from the right heart into the pulmonary vasculature during inspiration.

During the positive pressure breath, the vena cava begins to back up (venous return is impeded) until the expiratory phase begins and the patient exhales. During exhalation, the intrathoracic pressure drops and the there is a rush of blood into the right side of the heart, and RV preload increases. At the same time, with air now leaving the lung, the decrease in pulmonary vascular resistance and RV afterload favors an increase in stroke volume from the right ventricle. The net result is an increase in stroke volume and cardiac output during the expiratory phase of mechanical ventilation for the right side of the heart.

On the left side of the heart we see the opposite effects, in part due to a time lag between the cardiac output during the preceding few beats, which is now arriving to the left. The primary mechanism affecting stroke volume in the left heart during inspiration is an increase in venous return, as the blood that was in the pulmonary vascular system is being pushed out as the lungs expand. In addition, although the cardiac output from the right side of the heart is diminished during the inspiratory phase, the blood returning to the left atrium from the lungs is the blood that was pumped from the right ventricle to the pulmonary vasculature during the expiratory phase immediately beforehand, which had a high stroke volume and high cardiac output. These two effects lead to an increase in venous return for the left ventricle and an increase in stroke volume throughout the inspiratory phase. This manifests as a progressive increase in the systolic pressure on the arterial waveform, as well as an increase in the pulse pressure throughout the inspiratory phase of a positive pressure mechanical breath (option A).

Again, the opposite occurs on the left side of the heart during the expiratory phase. There is less venous return to the left ventricle because the cardiac output from the right was reduced during the preceding few beats. This results in a decrease in stroke volume, and decrease in systolic pressure on the arterial waveform (options B and C).

These alterations in increasing and decreasing stroke volume with changes in intrathoracic pressure are exacerbated when a patient is on the ascending limb of the Frank-Starling curve. When end-diastolic volume is already adequate and the patient is on the plateau of the curve, the effects of positive pressure ventilation are diminished.

The arterial line and ventilator tracings show the pulse pressure variations during mechanical ventilation. The systolic blood pressure and pulse pressure are maximal during inspiration and decline in expiration.

References:

1. Marino PL. Principles of mechanical ventilation. In: *The ICU Book.* 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007: ch. 24.
2. De Backer D, Heenen S, Piagnerelli M, Koch M, Vincent JL. Pulse pressure variations to predict fluid responsiveness: influence of tidal volume. *Intensive Care Med.* 2005 Apr;31(4):517-523.

29. Rationale

Answer: E

Focusing on the right side of the heart, during inspiration on a positive pressure breath, there is an increase in intrathoracic pressure as air is forced into the lungs and alveoli from the ventilator. The increased lung volume and pressure in the lungs and alveoli increases pulmonary vascular resistance, which increases right ventricular (RV) afterload. At the same time, the increase in intrathoracic pressure impedes venous return into the chest through the vena cava, which causes a decrease in preload. The combined effect of a decrease in preload and increase in afterload results in a decrease in stroke volume and cardiac output from the right heart into the pulmonary vasculature during inspiration.

During the positive pressure breath, the vena cava begins to back up (venous return is impeded) until the expiratory phase begins and the patient exhales. During exhalation, the intrathoracic pressure drops and the there is a rush of blood into the right side of the heart, and right ventricular preload increases. At the same time, with the air now leaving the lung, the decrease in pulmonary vascular resistance and RV afterload favors an increase in stroke volume from the right ventricle. The net result is an increase in stroke volume and cardiac output during the expiratory phase of mechanical ventilation for the right side of the heart.

The primary mechanism affecting stroke volume in the left heart during inspiration is an increase in venous return, as the blood that was in the pulmonary vascular system is being pushed out as the lungs expand. This leads to an increase in venous return for the left ventricle and an increase in stroke volume throughout the inspiratory phase. This manifests as a progressive increase in the systolic pressure on the arterial waveform, as well as an increase in the pulse pressure throughout the inspiratory phase of a positive pressure mechanical breath.

Reference:

1. De Backer D, Heenen S, Piagnerelli M, Koch M, Vincent JL. Pulse pressure variations to predict fluid responsiveness: influence of tidal volume. *Intensive Care Med.* 2005 Apr;31(4):517-523.

30. Rationale

Answer: B

The changes in pulse pressure variation (PPV) on an arterial line tracing are a manifestation of the change in intrathoracic pressure. Increasing the tidal volume will result in a greater change in intrathoracic pressure and have a greater effect on right ventricular (RV) venous return. Likewise, decreasing tidal volumes will mute this effect and diminish the variability. For optimal detection of PPV, tidal volumes of 8 to 10 mL/kg or greater have been recommended.

Muscle relaxation with vecuronium (option C) will not interfere with accurate PPV measurements. Ventilator dyssynchrony will interrupt the rhythmic change in positive pressure in the chest and may interfere with accurately interpreting PPV. Muscle relaxation would therefore assist in obtaining accurate readings.

Continuous renal replacement therapy running at net –50 mL/hr (option D) would not have an effect on the accuracy of PPV. It may make PPV more pronounced over time because volume is taken off but it will not change the ability to accurately assess PPV.

Atrial fibrillation, premature ventricular contractions, premature atrial contractions, third-degree heart block, supraventricular tachycardia, ventricular tachycardia, and ventricular fibrillation will all interfere with the regular rhythmic heart rate needed to reliably determine PPV. Other variables that may decrease the effects of positive pressure ventilation on PPV include high respiratory rates, decreased lung compliance, decreased chest wall compliance, and RV failure.

Reference:

1. Lakhal K, Ehrmann S, Benzekri-Lefèvre D, et al. Respiratory pulse pressure variation fails to predict fluid responsiveness in acute respiratory distress syndrome. *Crit Care.* 2011;15(2):R85.

31. Rationale

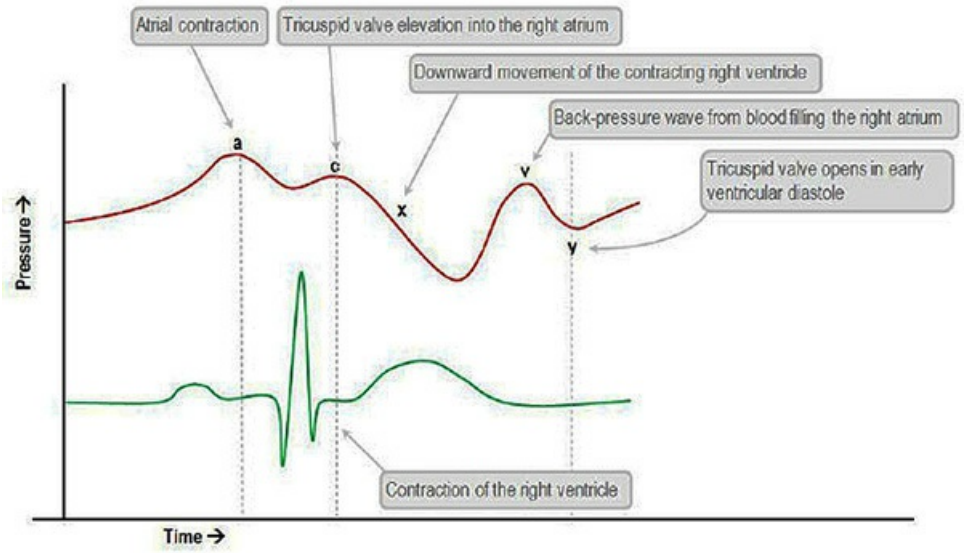
Answer: C

This patient has clearly developed right heart failure as evidenced by her rising CVP, elevated pulmonary artery pressures, declining blood pressure, and renal failure. In cardiac tamponade, atrial and ventricular pressures equalize; therefore, when the tricuspid valve opens, there is not a prominent y descent. The x descent appears steep with an attenuated y descent.

A pulmonary embolus (PE) would cause right ventricular (RV) strain and elevated CVP. A PE large enough to cause RV failure would also cause hypoxemia and tachypnea, leading to respiratory alkalosis.

This patient demonstrates RV failure leading to elevated CVP, low mean arterial pressure due to severe tricuspid regurgitation, and volume overload. In a patient this size, the two liters of fluid given are likely to cause acute dilation of the right ventricle, stretching of the tricuspid annulus and acute tricuspid regurgitation that may lead to hepatic congestion, liver failure, and renal failure. Medical management includes inotropes and elevated heart rate to decrease diastolic filling time. The CVP waveform depicts an exaggerated v wave indicative of elevated RA pressure from backflow from the right ventricle into the RA through the patent tricuspid valve during ventricular systole when blood is supposed to be ejecting through the pulmonic valve.

RV ischemia due to graft dysfunction is not likely to cause severe tricuspid regurgitation without any other right ventricular wall motion abnormalities. A list of various CVP waveforms and their associated pathology is found below:



Abnormal cvp waveforms

Condition	characteristics
➢Atrial fibrillation	▪ Loss of a wave ▪ Prominent c wave
➢Atrioventricular dissociation	▪ Cannon a wave
➢Tricuspid regurgitation	▪ Tall systolic c-v wave ▪ Loss of x decent
➢Tricuspid stenosis	▪ Tall a wave ▪ Attenuation of y decent
➢Right ventricular ischemia	▪ Tall a & v waves ▪ Steep x & y decent
➢Pericardial constriction	▪ Tall a & v waves ▪ Steep x & y decent
➢Cardiac tamponade	▪ Dominant x decent ▪ Attenuated y decent

References:

1. Rogers JH, Bolling SF. The tricuspid valve: current perspective and evolving management of tricuspid regurgitation. *Circulation.* 2009 May 26;119(20):2718-2725.
2. Lancellotti P, Moura L, Pierard LA, et al; European Association of Echocardiography. European Association of Echocardiography recommendations for the assessment of valvular regurgitation. Part 2: mitral and tricuspid regurgitation (native valve disease). *Eur J Echocardiogr.* 2010 May;11(4):307-332.
3. Pinsky MR, Payen D. *Functional hemodynamic monitoring.* Crit Care. 2005;9(6):566-72.

32. Rationale

Answer: C

When using a non-automated defibrillator, clinicians should monitor for rhythm changes before delivery of synchronized cardioversion or defibrillation. A battery failure is a rare event, and is prevented further by regular system checks and maintenance to guarantee that the device is fully charged. Sudden arrhythmias are always dynamic scenarios in which a loose lead could be responsible for the observed rhythm.

Clearly this patient had a supraventricular arrhythmia with hemodynamic instability, so the decision was made to cardiovert, and the defibrillator was placed in synch mode. However, the rhythm evolved into ventricular fibrillation, which will not be shocked when the sync button remains on.

References:

1. Link MS, Atkins DL, Passman RS, et al. Part 6: electrical therapies: automated external defibrillators, defibrillation, cardioversion, and pacing: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation.* 2010 Nov 2;122(18 Suppl 3):S706-S719.
2. Anter E, Callans DJ, Wyse DG.Pharmacological and electrical conversion of atrial fibrillation to sinus rhythm is worth the effort. *Circulation.* 2009 Oct 6;120(14):1436-1443.
3. Berg R, Hilwig R, Kern KB, Sanders AB, Xavier LC, Ewy GA. Automated external defibrillation versus manual defibrillation for prolonged ventricular fibrillation: lethal delays of chest compressions before and after countershocks. *Ann Emerg Med.* 2003 Oct;42(4):458-467.

33. Rationale

Answer: D

The rhythm shown is a polymorphic ventricular tachycardia, also known as torsades de pointes (TdP), which may be associated with medications that prolong the QT

interval, such as ciprofloxacin. While magnesium is an appropriate treatment for this condition, this patient has clearly lost cardiac output, as indicated by the flattening of the arterial line tracing. To maintain cerebral perfusion, cardiopulmonary resuscitation should be started immediately while magnesium is being obtained. Vasopressin is no longer indicated in cardiac arrest per the 2015 American Heart Association advanced cardiac life support algorithms. Isoproterenol may be used, rarely, in some cases of bradycardia-associated TdP, but this is not the first intervention indicated. Synchronized cardioversion is not appropriate because the patient is clearly not stable, given this tracing.

Reference:

1. Link MS, Berkow LC, Kudenchuk PJ, et al. Part 7: Adult Advanced Cardiovascular Life Support: 2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation.* 2015 Nov 3;132(18 Suppl 2):S444-S4464.

34. Rationale

Answer: B

The prognosis of patients who are admitted in an unconscious state after successful cardiopulmonary resuscitation has significantly improved during the past decade, in large part because of aggressive post-resuscitation care, including the use of therapeutic targeted temperature management (TTM). In the early phase of post-resuscitative care, assessment of neurologic outcome remains a challenge.

In patients not treated with TTM, a lack of motor response or extensor response to pain and the absence of brainstem reflexes (including pupillary, corneal, and oculocephalic reactivity) at 72 hours post cardiac arrest are regarded as reliable signs of poor neurologic outcome. However, hypothermia reduces clearance of the sedative and analgesic agents commonly used during TTM. In addition, some patients may have altered renal and hepatic function after cardiac arrest, which may further delay drug clearance. The combined effects of TTM and controlled sedation alters portions of the neurologic examination, making it insufficiently accurate to predict prognosis in the early phase of unconsciousness post cardiac arrest. A recent meta-analysis of studies in patients treated with TTM post cardiac arrest found that a score of 1 to 2 on the motor portion of the Glascow Coma Scale at 72 hours had a high average false-positive rate of 21%. Brainstem responses had better accuracy, but absent corneal reflexes yielded an average false-positive rate of 2%, while bilaterally absent pupillary reflexes had the lowest false-positive rate (0.4%) to predict poor neurologic outcome. The presence of myoclonus, (distinct from status myoclonus) also has a high false-positive rate (5%) and should not be used to predict poor neurologic outcomes. A multimodal approach, including full neurologic examination, electrophysiologic testing (EEG and somatosensory evoked potentials), neuroimaging, and chemical biomarkers, provides the most reliable information for prognostication of unconscious cardiac arrest survivors.

References:

1. Ben-Hamouda N, Taccone FS, Rossetti AO, Oddo M. Contemporary approach to neurologic prognostication of coma after cardiac arrest. *Chest.* 2014 Nov;146(5):1375-1386.
2. Callaway CW, Soar J, Aibiki M, et al; Advanced Life Support Chapter Collaborators. Part 4: Advanced Life Support: 2015 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations. *Circulation.* 2015 Oct 20;132(16 Suppl 1):S84-S145.
3. Dragancea I, Horn J, Kuiper M, et al; TTM Trial Investigators. Neurological prognostication after cardiac arrest and targeted temperature management 33°C versus 36°C: results from a randomised controlled clinical trial. *Resuscitation.* 2015 Aug;93:164-170.
4. Kamps MJ, Horn J, Oddo M, et al. Prognostication of neurologic outcome in cardiac arrest patients after mild therapeutic hypothermia: a meta-analysis of the current literature. *Intensive Care Med.* 2013 Oct;39(10):1671-1682.
5. Taccone F, Cronberg T, Friberg H, et al. How to assess prognosis after cardiac arrest and therapeutic hypothermia. *Crit Care.* 2014 Jan 14;18(1):202.

35. Rationale

Answer: C

After submersion in water, victims initially hold their breath, which is then typically followed by laryngospasm, hypoxia and hypercarbia that then cause relaxation of the larynx and allow the aspiration of water. With decreases in body temperature, normal sinus rhythm transforms into sinus bradycardia, which is followed by atrial fibrillation, ventricular fibrillation, and asystole. Ongoing severe acidosis and hypoxemia contribute to instability of myocardial membranes and prevent restoration of normal sinus rhythm.

In this case, venoarterial extracorporeal membrane oxygenation (V-A ECMO) will help to rewarm, provide hemodynamic support in the settings of malignant ventricular arrhythmia and severe acidosis, and oxygenate. In the settings of non-hypothermia-induced out-of-hospital and in-hosptial cardiac arrest V-A ECMO is associated with survival rates of 10% to 30%. Rewarming with forced air, IV fluids, warm humidified gases, and gastric and bladder lavage are only effective in hypothermic patients with stable circulation.

Ongoing attempts at defibrillation are unlikely to succeed until the patient is adequately rewarmed (greater than 30°C [86°F]). At 18°C (64.4°F), the brain can tolerate periods of circulatory arrest ten times longer than at 37°C. Dilated pupils can be caused by a variety of insults and must not be regarded as a sign of death. Good neurologic recovery has been reported after cardiac arrest and a core temperature of 13.7°C (56.66°F) after immersion in cold water with prolonged CPR. Therefore, patients should not be considered dead until rewarming efforts have failed.

References:

1. Lavonas EJ, Drennan IR, Gabrielli A, et al. Part 10: Special Circumstances of

Resuscitation: American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation.* 2015 Nov 3;132(18 Suppl 2):S501-S518.
2. Layon AJ, Modell JH. Drowning: Update 2009. *Anesthesiology.* 2009 Jun;110(6):1390-1401.
3. Walpoth BH, Locher T, Leupi F, Schüpbach P, Mühlemann W, Althaus U. Accidental deep hypothermia with cardiopulmonary arrest: extracorporeal blood rewarming in 11 patients. *Eur J Cardiothorac Surg.* 1990;4(7):390-393.
4. Wanscher M, Agersnap L, Ravn J, et al. Outcome of accidental hypothermia with or without circulatory arrest: experience from the Danish Præstø Fjord boating accident. *Resuscitation.* 2012 Sep;83(9):1078-1084.

36. Rationale

Answer: B

Amiodarone may be used to treat or prevent ventricular dysrhythmias associated with cardiac arrest, but it has not been shown to improve neurologically intact survival after cardiac arrest.

Targeted temperature management has been shown to provide a significant neurologically intact survival benefit over no temperature control in two randomized trials. A subsequent trial did not demonstrate a difference between active management at 33°C (91.4°F) versus 36°C (96.8°F), and it remains unclear whether some patients benefit from different specific targets.

While lung-protective strategy is generally considered good practice, and post-cardiac arrest patients are at increased risk for lung injury, there has not been an established benefit regarding neurologically intact survival.

While immediate cardiac catheterization is supported by a literature base for patients with primary ventricular dysrhythmias, the established benefit for neurologically intact survival is not as well established as that for targeted temperature management.

References:

1. Camuglia AC, Randhawa VK, Lavi S, Walters DL. Cardiac catheterization is associated with superior outcomes for survivors of out of hospital cardiac arrest: review and meta-analysis. *Resuscitation.* 2014 Nov;85(11):1533-1540.
2. Mentzelopoulos SD, Malachias S, Chamos C, et al. Vasopressin, steroids, and epinephrine and neurologically favorable survival after in-hospital cardiac arrest: a randomized clinical trial. *JAMA.* 2013 Jul 17;310(3):270-279.
3. Bernard SA, Gray TW, Buist MD, et al. Treatment of comatose survivors of out-of-hospital cardiac arrest with induced hypothermia. *N Engl J Med.* 2002 Feb 21;346(8):557-563.
4. Nielsen N, Wetterslev J, Cronberg T, et al; TTM Trial Investigators. Targeted temperature management at 33°C versus 36°C after cardiac arrest. *N Engl J Med.* 2013 Dec 5;369(23):2197-2206.

37. Rationale

Answer: D

The American Heart Association guidelines for cardiac life support recommend the immediate initiation of chest compressions, rather than airway management, in out-of-hospital cardiac arrest. While airway management and use of an automated external defibrillator are important for resuscitation, chest compressions are the initial step in the algorithm. Early initiation of chest compressions has been shown to improve neurologic outcomes in out-of-hospital cardiac arrest. Nalaxone administration may be beneficial in a patient who is suspected of being unresponsive due to an opioid overdose. If opioid overdose is expected in a pulseless patient, the initial step is still chest compressions.

References:

1. SOS-KANTO study group. Cardiopulmonary resuscitation by bystanders with chest compression only (SOS-KANTO): an observational study. *Lancet.* 2007 Mar 17;369(9565):920-926.
2. Bobrow BJ, Spaite DW, Berg RA, et al. Chest compression-only CPR by lay rescuers and survival from out-of-hospital cardiac arrest. *JAMA.* 2010 Oct 6;304(13):1447-1454.
3. Callaway CW, Soar J, Aibiki M, et al; Advanced Life Support Chapter Collaborators. Part 4: Advanced Life Support: 2015 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations. *Circulation.* 2015 Oct 20;132(16 Suppl 1):S84-S145.

38. Rationale

Answer: C

Synchronized cardioversion is appropriate at this time since he is symptomatic, is hypotensive, and has an organized rhythm. Metoprolol and verapamil administration will worsen his hypotension. There is no suggestion of a narcotic overdose that would be treated with naloxone.

References:

1. Helton MR. Diagnosis and management of common types of supraventricular tachycardia. *Am Fam Physician.* 2015 Nov 1;92(9):793-800.
2. Trappe HJ. Treating critical supraventricular and ventricular arrhythmias. *J Emerg Trauma Shock.* 2010.

39. Rationale

Answer: D

This patient has severe mitral stenosis complicated by acute fever, tachycardia, and hypotension. With a valve area of 0.88 cm^2, coupled with his known transvalvular

gradient, the necessary time for adequate ventricular filling in diastole is longer than if the mitral stenosis were not present. Consequently, tachycardia and loss of atrial contraction can be poorly tolerated. At the time of ICU transfer the cause of his hypotension is not known. Diuretics and beta-adrenergic antagonists may be appropriate for decompensated severe mitral stenosis and evidence of pulmonary congestion, but in the setting of hypotension of unknown etiology, these drugs are not warranted. IV epinephrine is not the best first choice when the cause of hypotension and the patient's underlying hemodynamic state is unknown. The best initial management of this patient's hypotension is a judicious fluid bolus while additional imaging and monitoring is obtained to determine more definitive therapy.

References:

1. Wunderlich NC, Beigel R, Siegel RJ. Management of mitral stenosis using 2D and 3D echo-Doppler imaging. *JACC: Cardiovasc Imaging.* 2013 Nov;6(11):1191-1205.
2. Aronow WS. Management of mitral stenosis *J Cardiovasc Dis Diagn.* 2013 1:e104.

40. Rationale

Answer: B

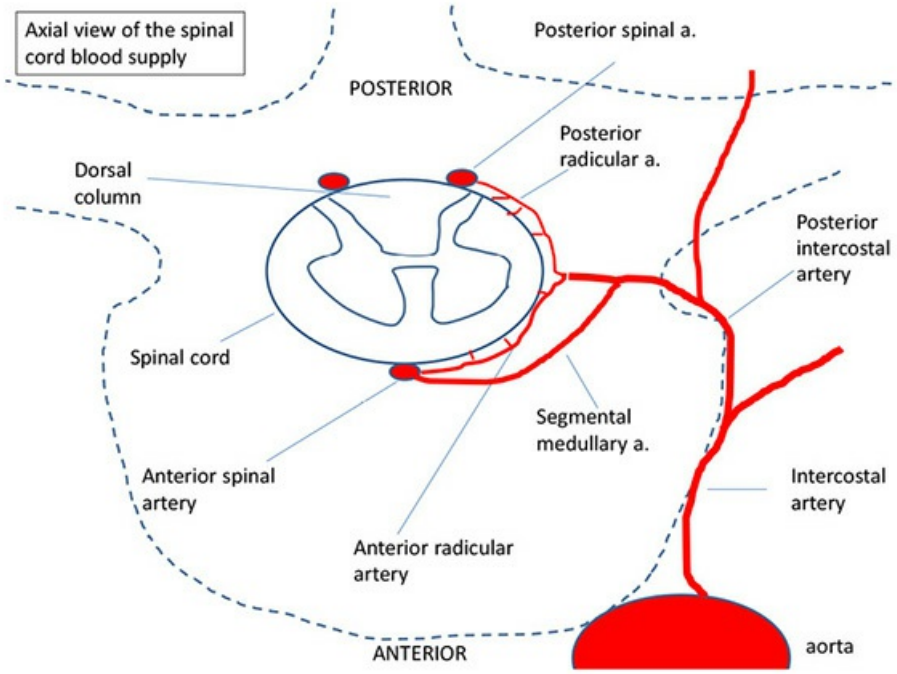
Blood supply to the thoracic spinal cord is largely dependent on a single anterior spinal artery and two posterolateral spinal arteries traveling cephalad to caudad. These arteries are largely dependent on blood supply from the anterior and posterior radicular arteries and the segmental medullary arteries. These originate from the segmental (intercostal) arteries, which arise from the thoracic aorta (see figure shown below). The largest of the segmental medullary arteries is the artery of Adamkiewicz, originating from the lower thoracic aorta (T8-L1) in most people.

Interruption of blood flow through the intercostal arteries can occur as a result of endovascular graft deployment in the aorta. Patients at higher risk for spinal cord ischemia postoperatively include those with: 1) decrease/disruption of collateral circulation due to prior abdominal aortic aneurysm repair, severe atherosclerosis of the thoracic aorta resulting in decreased collateral circulation, or more extensive graft coverage of thoracic aorta, 2) hypotension resulting in decreased spinal cord perfusion pressure, or 3) increased spinal fluid pressure or central venous pressure.

Spinal cord perfusion pressure is calculated as mean arterial pressure minus cerebrospinal fluid pressure (or central venous pressure). Spinal drains are often placed before thoracic endograft procedures to reduce the resistance to blood flow, thereby encouraging spinal cord perfusion.

Maintaining spinal cord perfusion is especially critical in the early postoperative period, when the spinal cord may be recovering from intraoperative ischemic insult. Decreased neurologic function after aortic repair is a neurologic emergency; taking action to improve spinal cord perfusion is essential to minimize long-term squealae. The spinal drain can be opened or repositioned to increase drainage of cerebrospinal fluid to improve spinal cord perfusion. Increasing blood pressure will also increase

spinal cord perfusion.



References:

1. Cheung AT, Pochettino A, McGarvey ML, et al. Strategies to manage paraplegia risk after endovascular stent repair of descending thoracic aortic aneurysms. *Ann Thorac Surg.* 2005 Oct;80(4):1280-1288.
2. Griepp RB, Griepp EB. Spinal cord perfusion and protection during descending thoracic and thoracoabdominal aortic surgery: the collateral network concept. *Ann Thorac Surg.* 2007 Feb;83(2):S865-S869; discussion S890-S892.
3. Ullery BW, Cheung AT, Fairman RM, et al. Risk factors, outcomes, and clinical manifestations of spinal cord ischemia following thoracic endovascular aortic repair. *J Vasc Surg.* 2011 Sep;54(3):677-684.

41. Rationale

Answer: B

Acute aortic insufficiency is a medical emergency requiring prompt surgical intervention. However, the diagnosis is often challenging to make, leading to delays in management. As is the case here, presentations mimicking pneumonia or nonvalvular heart failure may complicate the picture, delaying definitive therapy. Given the diastolic murmur, evidence of mixed cardiogenic and septic shock, needle track marks, and blood cultures positive for methicillin-resistant Staphylococcus aureus (MRSA), the most likely diagnosis is infective endocarditis causing acute aortic regurgitation.

Treatment should be directed at broadening antibiotic coverage to include MRSA, obtaining an immediate echocardiography to confirm the diagnosis, and involving

cardiac surgery for definitive management. Instituting appropriate medical therapy, including vasopressors, inotropes, and intubation, is necessary, but is not a substitute for surgical therapy in such a critically ill state. Providing additional IV fluid boluses is unlikely to improve hypotension, and may worsen oxygenation given evidence of cardiogenic shock. Placing an intra-aortic balloon pump is contraindicated here due to aortic insufficiency and worsening of the regurgitation when the balloon inflates during diastole. Delaying surgical repair for days until blood cultures return negative is not optimal management in this setting.

References:

1. Stout KK, Verrier ED. Acute valvular regurgitation. *Circulation.* 2009 Jun 30;119(25):3232-3241.
2. Kang DH, Kim YJ, Kim SH, et al. Early surgery versus conventional treatment for infective endocarditis. *N Engl J Med.* 2012 Jun 28;366(26):2466-2473.

42. Rationale

Answer: C

Acute aortic insufficiency, either perivalvular or central, is a known complication of transcatheter aortic valve replacement (TAVR), with an incidence reported as high as 70%. Acute aortic regurgitation results in sudden volume overload to the left ventricle (LV) during systole. As a result of this, LV end-systolic volume is higher than normal and the pressure gradient between the left atrium and the LV decreases earlier in subsequent diastole. This results in early mitral valve closure, which is audible as a soft S1 sound. Early systolic and even diastolic mitral regurgitation have been observed due to changes in ventriculo-arterial gradient in the LV. This leads to a reduction in LV stroke volume and a reflex tachycardia. As a result, patients often have thready pulses and cold extremities.

Pericardial tamponade has been observed after TAVR, but is rare. In addition, the patient's jugular venous pulsation is reported to be 5 cm above the sternal angle with slow refill, which is inconsistent with tamponade. Sepsis is associated with tachycardia and hypotension, but usually not with cold extremities and a normal temperature. Acute third-degree heart block has been reported after TAVR, but is not usually associated with a rapid heart rate. Complete loss of atrioventricular conduction can cause decreased cardiac output and hypotension, but usually the cause of diminished cardiac output is bradycardia, not decreased stroke volume. In addition a diastolic murmur is usually not observed. Ascending aortic dissection is a rare but known complication, certainly rarer than aortic insufficiency. However, this should be accompanied by coronary ischemia. A typical murmur associated with acute mitral regurgitation is a high-pitched, blowing holosystolic murmur.

References:

1. Hamirani YS, Dietl CA, Voyles W, Peralta M, Begay D, Raizada V. Acute aortic regurgitation. *Circulation.* 2012 Aug 28;126(9):1121-1126.
2. Agarwal S, Tuzcu, EM, Krishnaswamy A, et. al. Transcatheter aortic valve

replacement: current perspectives and future implications. *Heart.* 2015 Feb;101(3):169-177.

43. Rationale

Answer: B

This patient has a malignant pericardial effusion that has led to tamponade physiology and obstructive shock. The most prudent course of action when first examining him would be to perform a rapid ultrasound assessment for shock and hypotension (RUSH) examination and provide an IV fluid bolus once the effusion is seen. At that point, a decision would need to be made to drain the effusion at the bedside or in the catheterization laboratory, depending on his clinical status. Bedside ultrasound for acute dyspnea and shock is a critical tool for intensivists. This will help rapidly narrow the differential diagnosis and improve decision making.

Intubating the patient may eventually be necessary but, given his mental status, adequate oxygenation, and profound hypotension, this may not be the first action to take. Septic shock certainly remains in the differential diagnosis, and providing antibiotics and obtaining cultures may still be advisable even with tamponade findings on ultrasound. Based on history and examination, it is less likely that this presentation is acute heart failure or pulmonary embolism, and bedside cardiac ultrasound will also help to prove this. A significant retroperitoneal bleed may be the cause of his hypotension, but history and examination are relatively inconsistent with this, and protamine is not a pure reversal agent for enoxaparin, but it may help.

References:

1. Spodick D. Acute cardiac tamponade. *N Engl J Med.* 2003 Aug 14;349(7): 684-690.
2. Perera, P, Mailhot T, Riley D, Mandavia D. The RUSH exam: Rapid Ultrasound in Shock in the evaluation of the critically ill. *Emerg Med Clin North Am.* 2010 Feb;28(1):29-56.

44. Rationale

Answer: D

Although a rare and challenging diagnosis to make, this patient has hypersensitivity eosinophilic myocarditis and is in fulminant heart failure. The offending agent in this case is phenytoin, which the patient has taken for seizures for many years. Although not always present, peripheral eosinophilia can be a clue, in addition to the faint rash noted on the trunk. Due to the high mortality associated with this disease, early diagnosis is key, and an endomyocardial biopsy is the test of choice. Once the diagnosis is confirmed, in addition to withdrawal of the offending drug, immunosuppressive therapy can commence, often with dramatic results.

A right upper quadrant ultrasound would be prudent, given the elevated liver function tests, but this is most likely due to congestive hepatopathy, and would not yield a diagnosis. Similarly, a skin punch biopsy and blood cultures would probably be

performed on this patient to look for autoimmune and infectious causes, but an endomyocardial biopsy would still be needed. A chest CT would be a low-yield test, and may even cause harm, given his acute kidney injury.

References:

1. Al Ali AM, Straatman LP, Allard MF, Ignaszewski AP. Eosinophilic myocarditis: case series and review of literature. *Can J Cardiol.* 2006 Dec;22(14):1233-1237.
2. Ginsberg F, Parrillo JE. Eosinophilic myocarditis. *Heart Fail Clin.* 2005 Oct;1(3):419-429.

Part 3:

Pulmonary Critical Care

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Pulmonary Critical Care

Instructions: For each question, select the most correct answer.

1. A 23-year-old man with recent community-acquired pneumonia is admitted to the hospital for worsening respiratory status. He continues to deteriorate rapidly,

requiring emergent intubation due to decreasing oxygen saturation. Chest radiograph is shown below. Despite maximal ventilatory support, oxygenation continues to decrease to below 50 mm Hg, and venovenous extracorporeal membrane oxygenation (ECMO) is implemented shortly thereafter. After initiation of flow through the ECMO circuit, arterial blood gas results show: pH 7.19, partial arterial carbon dioxide pressure 67 mm Hg, and partial arterial oxygen pressure 72 mm Hg.

The most effective method of increasing carbon dioxide elimination is to increase which of the following parameters?

A. Blood flow rate
B. Sweep gas flow
C. Blood pressure
D. Cannula size
E. Ventilatory respiratory rate

2. A 48-year-old man with recently diagnosed myasthenia gravis treated with pyridostigmine is started on prednisone. A few days later, he has fever of 39.4°C (102.92°F), flu-like symptoms, blurred vision, dysphagia, generalized weakness, and shortness of breath. Because of persistent shortness of breath and increasing secretions, he is brought to the emergency department and admitted to the ICU. His oxygen saturation is 92% on 5 L/min of oxygen. Chest radiograph is clear. Vital capacity is 15 mL/kg, maximal inspiratory pressure is –20 cm H_2O, and maximal expiratory pressure is 35 cm H_2O. Arterial blood gas analysis shows: pH 7.26, partial arterial carbon dioxide pressure 70 mm Hg, carbon dioxide 30 mEq/L, partial arterial oxygen pressure 68 mm Hg, and arterial oxygen

saturation 92%.

Which of the following is the most appropriate next step in the management of his respiratory distress?

A. Endotracheal intubation
B. Increasing pyridostigmine dose
C. IV immunoglobulin
D. Noninvasive ventilation with bilevel positive airway pressure
E. Chest physiotherapy vest with heliox

3. A 52-year-old woman with a past history of chronic obstructive pulmonary disease and hypertension is postoperative single left lung transplant. On postoperative day two, her oxygenation status has deteriorated. Arterial blood gas analysis obtained on assist-control ventilation, with a rate of 20/min, tidal volume of 350 mL, FIO_2 of 0.7, and positive end-expiratory pressure of 10 cm H_2O, show: pH 7.37, partial arterial carbon dioxide pressure 38 mm Hg, and partial arterial oxygen pressure 69 mm Hg. Chest radiography identifies extensive infiltrate in the lung allograft. Temperature is 36.7°C (98.1°F), heart rate 94/min, blood pressure 138/74 mm Hg, and respiratory rate 20 breaths/min.

   Which of the following strategies should be implemented first to improve survival?

   A. Emergency bronchoscopy
   B. Dual-lung ventilation
   C. Lung-protective ventilation
   D. Pulse steroids

4. A 63-year-old man with a past history of hypertension and diabetes mellitus presents with community-acquired pneumonia that progresses to acute respiratory distress syndrome. On hospital day two, mechanical ventilation is initiated. Continuous enteral nutrition is initiated via a 14-French nasogastric tube targeted to deliver 25 kcal/kg/d.

   Which of the following strategies should be implemented to reduce ventilator-associated pneumonia during mechanical ventilation?

   A. Monitor residual gastric volume.
   B. Elevate head of bed.
   C. Administer H2 blockers.
   D. Administer proton pump inhibitors.
   E. Administer postpyloric feeding.

5. A 75-year-old man presents with a several-week history of productive cough, occasionally blood-streaked sputum, night sweats, and pleuritic chest pain. Chest CT is pending.

Which of the following is the most common radiologic manifestation of nocardiosis in nonendemic areas?

A. Cavitatory nodule
B. Centrilobular micronodules
C. Ground-glass opacity
D. Pleural effusion

6. A 52-year-old woman with a past medical history of morbid obesity presents to the emergency department (ED) with subacute-on-chronic dyspnea, hypoxemia, and increased lower extremity edema. Four weeks ago, as an outpatient, she had chronic hypoxemia. Arterial blood gas analysis in the outpatient setting demonstrated chronic hypoxemia and hypercapnia with pH 7.38, partial arterial carbon dioxide pressure ($PaCO_2$) 60 mm Hg, and partial arterial oxygen pressure (PaO_2) 60 mm Hg on ambient air. In the ED, arterial blood gas analysis show: pH 7.28, $PaCO_2$ 82 mm Hg, and PaO_2 52 mm Hg with 40% oxygen via face mask. Chest radiograph, limited due to body habitus, identifies no appreciable infiltrates. Temperature is 36.7°C (98.1°F), heart rate 82 beats/min, blood pressure 152/84 mm Hg, and respiratory rate 14 breaths/min. She is drowsy but easily arousable. She is admitted to the medical ICU based on the arterial blood gas values.

   Which of the following strategies should be implemented first to improve her ventilatory status?

   A. Diuresis
   B. Noninvasive ventilation
   C. Nebulizer treatment
   D. Invasive mechanical ventilation
   E. Steroids

7. A 69-year-old man with diabetes is mechanically ventilated for severe sepsis and acute respiratory distress syndrome due to community-acquired pneumonia. On day one, he receives assist-control ventilation with fraction of inspired oxygen (FIO_2) of 0.7 and positive end-expiratory pressure (PEEP) of 12 cm H_2O; by day three, FIO_2 is 0.45 and PEEP is 6 cm H_2O. He is on a propofol infusion and has received intermittent fentanyl, but now appears to be in no pain. His Richmond Agitation-Sedation Scale score is -4, indicating that he responds to physical, and not to verbal, stimulation.

   Which of the following is the best course of action regarding weaning him from sedation and ventilation?

   A. Change propofol infusion to intermittent bolus sedation and change to pressure support ventilation.
   B. Stop sedation and, once awake, start a spontaneous breathing trial.
   C. Switch from propofol to fentanyl and reduce PEEP to 5 cm H_2O.

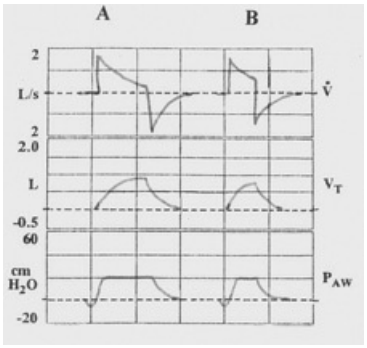
D. Gradually reduce both the sedation dosage and the ventilatory support.

8. A 50-year-old woman sustained severe facial trauma in a motor vehicle accident. She is obtunded, with a respiratory rate of 40 breaths/min. Arterial blood gas analysis shows: pH 7.20, partial arterial carbon dioxide pressure 65 mm Hg, and partial arterial oxygen pressure 60 mm Hg on high-flow face mask oxygen. The decision is made to intubate her for airway protection and mechanical ventilation.

   Which of the following is the best method to secure her airway?

   A. Fiberoptic nasal intubation
   B. Oral intubation with in-line cervical spine stabilization
   C. Cricothyrotomy
   D. Blind nasotracheal intubation

9. In the figure shown below, two pressure support breaths in the same patient are depicted.



   What has occurred between breath A and breath B?

   A. The inspiratory time setting has lengthened.
   B. The patient's compliance has worsened.
   C. The volume backup setting has increased.
   D. The flow cycle percentage criteria have been increased.
   E. The mandatory breath rate has increased.

10. A morbidly obese man with a body mass index of 50 is in the medical ICU with respiratory failure due to pneumonia. He is on the Acute Respiratory Distress Syndrome Network (ARDSNet) protocol, and the end-inspiratory pressure (Pplat), is 35 cm H_2O. Chest radiography indicates significant bibasilar atelectasia.

    Which of the following best characterizes the status of the Pplat as an indicator of end-inspiratory transpulmonary pressure?

    A. Reasonable estimate
    B. Underestimate

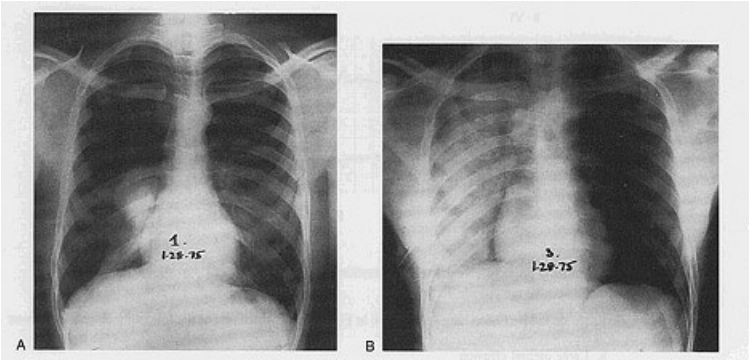
C. Overestimate
D. Unrelated

11. A patient with chronic obstructive pulmonary disease underwent a single-lung transplant. Pneumonia has developed in the transplanted left lung, requiring mechanical ventilatory support. A double-lumen tube is inserted to ventilate each lung separately.

    Which of the following is the most important strategy for setting up the two ventilators?

    A. Tidal volume settings should be 6 mL/kg ideal body weight in each lung.
    B. Positive end-expiratory pressure should be equal in both lungs.
    C. Respiratory rate should be synchronized in the two lungs.
    D. A plateau pressure of 30 cm H_2O should be maintained in both lungs.

12. Shown below are radiographs before and after a thoracostomy tube insertion for a large pneumothorax in a hemodynamically stable patient.



    Which of the following clinical conditions is most likely present in this patient?

    A. Tension pneumothorax on the left side
    B. Near-total right lung atelectasis
    C. Long-standing pneumothorax
    D. Pneumopericardium

13. A 38-year-old pregnant woman with a history of asthma and hypertension is evaluated in the emergency department for severe respiratory distress. She is treated with nebulized albuterol, ipratropium, and IV corticosteroids. Her potassium level is increased, with normal creatinine level, and the plan is to hold her angiotensin-converting enzyme inhibitor. After one hour of therapy, she is not improving significantly. Respiratory rate is 28 breaths/min, and she has continued respiratory distress. Oxygen saturation is 90%, with high-flow oxygen through the nebulizer and additional supplemental oxygen through a nasal cannula. The respiratory therapist suggests heliox therapy.

Which of the following is the reason that heliox cannot be used in this patient?

A. Pregnancy
B. Degree of hypoxemia
C. Hyperkalemia
D. Concomitant steroid administration

14. A 64-year-old woman with chronic, severe back pain has been mechanically ventilated for five days secondary to hypoxemic respiratory failure. She is receiving appropriate antibiotics for *Staphylococcus aureus* pneumonia. Her past medical history is significant for anxiety and hypertension. She has been positive on the Confusion Assessment Method for the ICU for the past three days. At times she appears to have hyperactive agitation and has remained in upper-extremity restraints for her own safety. Her current sedation regimen is a continuous infusion of propofol, 0.05 mg/kg/min, that is being titrated to a Richmond Agitation-Sedation Scale goal of -1.

    Which of the following should be the next step in sedation management?

    A. Start continuous infusion of fentanyl.
    B. Start continuous infusion of midazolam.
    C. Start continuous infusion of haloperidol.
    D. Start continuous infusion of dexmedetomidine.
    E. Increase continuous infusion dose of propofol.

15. A 24-year-old woman is in the ICU with status asthmaticus. She has received corticosteroids, anticholinergic medications, multiple rounds of bronchodilators, and parenteral magnesium, with little clinical improvement. Her most recent arterial blood gas analysis shows evidence of hypercapnia, and she is intubated without difficulty. A continuous ketamine infusion is ordered for sedation.

    Which of the following is a pulmonary effect of ketamine?

    A. Decreased dynamic compliance
    B. Increased minute ventilation
    C. Decreased functional residual capacity
    D. Bronchodilitation
    E. Decreased pharyngeal secretions

16. A 27-year-old man with viral pneumonia is significantly short of breath, with negative sputum and blood cultures. He is hemodynamically stable, but is having difficulty bringing up his secretions. Arterial blood gas analysis on 6-liter nasal cannula shows pH 7.35, partial arterial carbon dioxide pressure 39 mm Hg, partial arterial oxygen pressure 51 mm Hg, with oxygen saturation of 87%.

    Which of the following is the most appropriate next step in management?

A. Intubate for hypoxic respiratory failure.
B. Start noninvasive ventilation for hypoxic respiratory failure.
C. Start 3% saline nebulizations to loosen his secretions.
D. Start nasal high-flow oxygen therapy.
E. Start broad-spectrum antibiotics.

17. A 39-year-old woman with acute respiratory distress syndrome secondary to aspiration has a partial arterial oxygen pressure-to-fraction of inspired oxygen (F_{IO_2}) ratio of 86. Her plateau pressure was 33 cm H_2O before paralysis and now is 29 cm H_2O. She requires 8 µg/min of norepinephrine to keep her mean arterial pressure above 65 mm Hg. She is being ventilated with 6 mL/kg predicted body weight. Her ventilator settings are: F_{IO_2}70%, respiratory rate 28 breaths/min, tidal volume 360 mL, positive end-expiratory pressure 16 cm H_2O, arterial blood gases: pH 7.25, partial arterial carbon dioxide pressure 41 mm Hg, partial arterial oxygen pressure 60 mm Hg, peak pressure 32 cm H_2O, plateau pressure 29 cm H_2O.

Which of the following is the most appropriate next step in management?

A. Initiate an inhaled pulmonary vasodilator.
B. Prone the patient.
C. Perform a recruitment maneuver.
D. Initiate statin drug therapy.
E. Initiate venovenous extracorpeal membranous oxygenation.

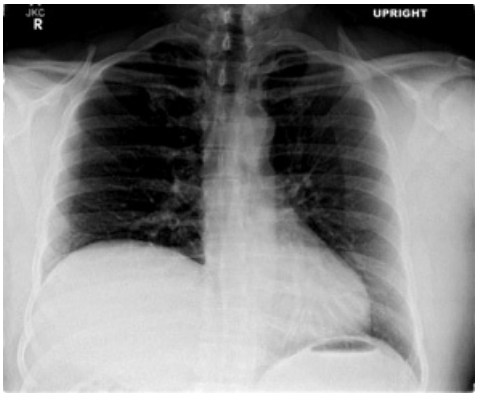
18. A 45-year-old man is admitted to the ICU after a 30-foot fall from a telephone pole while he was working. He sustained a traumatic subarachnoid hemorrhage, pulmonary contusions, grade II liver and kidney lacerations, and a broken right femur and acetabulum. He is intubated in the emergency department with a Glasgow Coma Scale (GCS) score of 12 and moderate hypoxia, with oxygen saturations of 88% on a nonrebreather mask. During the next two days his oxygenation worsens. Acute respiratory distress syndrome is suspected from the trauma and blossoming pulmonary contusions. He is heavily sedated, paralyzed with cisatracurium, and requires no intracranial pressure monitoring. Ventilator settings are: assist control/pressure control, respiratory rate 35 breaths/min, F_{IO_2} 100%, positive end-expiratory pressure (PEEP) 22 cm H_2O, peak airway pressure 35 cm H_2O. Tidal volumes are at 6 mL/kg predicted body weight. Most recent arterial blood gas analysis shows: pH 7.24, partial arterial carbon dioxide pressure 60 mm Hg, partial arterial oxygen pressure 50 mm Hg.

Which of the following is the most appropriate next step in management?

A. Start inhaled nitric oxide.
B. Increase respiratory rate to compensate for respiratory acidosis.
C. Increase PEEP to improve oxygenation.

D. Place the patient in prone position.
E. Change the ventilator mode to assist control/volume control and maintain FIO_2 and PEEP.

19. A 43-year-old woman with end-stage idiopathic pulmonary fibrosis underwent a right lung transplant. A right thoracotomy incision was made to implant the lung, and the operation was completed without any complications. She was brought to the ICU and ventilated, with plans to extubate the following morning. On postoperative day one, a spontaneous breathing trial (SBT) is aborted within five minutes after she becomes tachypneic at a respiratory rate of 44 breaths/min and desaturates to 89% on FIO_2 0.4. After a week of failed SBT, a tracheostomy tube is placed and she is able to ambulate. Bronchoscopy shows well-healing bronchial anastomosis without debris in the airways. Breath sounds are clear. She is able to participate in physical rehabilitation, but attempts to wean her from the ventilator are met with hypercapnia and tachypnea. The chest radiograph shown below has been unchanged since postoperative day two.



Further work-up should include which of the following tests?

A. Edrophonium test
B. Chest fluoroscopy (sniff test)
C. Flexible fiberoptic bronchoscopy
D. Tacrolimus trough levels

20. Which of the following patients is most likely to derive benefit from systemic thrombolytic therapy for pulmonary embolism?
A. 42-year-old woman, body mass index (BMI) 45, with remote bariatric surgery and a normal ECG, elevated troponin and B-type natriuretic peptide, with echocardiogram showing D-shaped right ventricle
B. 67-year-old man, BMI 28, with history of smoking and chronic obstructive pulmonary disease, elevated troponin, T-wave inversion, who takes norepinephrine for systolic blood pressure (SBP) less than 90 mm Hg
C. 75-year-old woman, BMI 32, with diabetes, hypertension, knee replacement two weeks ago, elevated troponin, and T-wave inversion
D. 58-year-old man, BMI 25, with hypertension, previous intracranial

hemorrhage, elevated troponin, T-wave inversion, and on norepinephrine for SBP less than 90 mm Hg

21. A 56-year-old man is admitted to the ICU with septic shock from multifocal pneumonia complicated by acute respiratory failure. On ICU day two, he remains on mechanical ventilation and has been weaned off vasopressors. He quickly becomes agitated and his oxygen saturation drops to 82% on the following ventilator settings: mode volume assist control, respiratory rate 22 breaths/min, tidal volume 450 mL, positive end-expiratory pressure (PEEP) 5 cm H_2O, F_{IO_2} 60%.

    Which of the following is the most appropriate course of action?

    A. Ensure adequate sedation and then paralyze him with cisatracurium.
    B. Obtain chest radiograph.
    C. Increase PEEP and fraction of inspired oxygen (F_{IO_2}) according to the Acute Respiratory Distress Syndrome Network (ARDSNet) table to maintain oxygen saturation above 92%.
    D. Ensure airway patency and appropriate functioning patient-mechanical ventilator circuit.
    E. Perform bilateral needle decompression to rule out pneumothorax.

22. A 60-year-old woman is admitted to the hospital with chronic obstructive pulmonary disease exacerbation. She is intubated in the emergency department, and a subclavian triple-lumen catheter is placed for increased IV access due to hypotension. Vasopressors and IV fluids are initiated, but her hypotension persists. A resident uses an ultrasound to examine her lungs for a pneumothorax.

    Which of the following ultrasound principles is most applicable to the diagnosis of pneumothorax?

    A. The absence of lung sliding is more specific than sensitive for pneumothorax.
    B. The absence of lung sliding confirms the presence of pneumothorax.
    C. In a supine patient, lung sliding is less sensitive than portable chest radiography in detecting pneumothoraces in trauma patients.
    D. The presence of A line artifacts rules out a pneumothorax.
    E. The presence of B line artifacts rules out a pneumothorax.

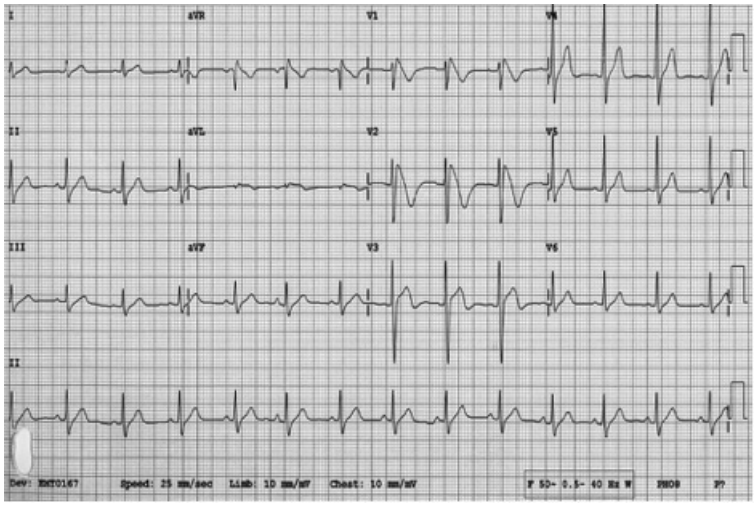
23. A 55-year-old man with a history of severe chronic obstructive pulmonary disease (COPD) requiring intubation is admitted to the ICU for a COPD exacerbation due to seasonal influenza. He becomes more fatigued throughout the evening and is intubated for severe respiratory distress despite optimal medical management and noninvasive positive pressure ventilation. Post-intubation, the first arterial blood gas analysis reveals: pH 7.20, partial arterial carbon dioxide pressure 65 mm Hg, partial arterial oxygen pressure 150 mm Hg on ventilator settings of assist control/volume control, rate 16 breaths/min, tidal volume 450 mL, positive

end-expiratory pressure 5 cm H_2O, fraction of inspired oxygen 40%. Respiratory rate is increased to 24 breaths/min to address the respiratory acidosis. One hour later, he has a pulseless electrical activity arrest. The respiratory therapist is having difficulty using the bag valve mask, and end-tidal carbon dioxide is less than 10 mm Hg with adequate chest compressions. There are no breath sounds over either lung field.

Which of the following is the most appropriate next step in management?

A. IV epinephrine, 1 mg
B. Bilateral needle thoracostomy
C. Venoarterial extracorporeal membrane oxygenation
D. Reintubation due to endotracheal tube dislodgement
E. Disconnection of the bag valve mask from the endotracheal tube

24. A 41-year-old man with a history of schizophrenia had a sudden cardiac arrest while touring a local fire department. The initial rhythm noted by emergency medical personnel was ventricular fibrillation. Three rounds of cardiopulmonary resuscitation were administered, with three defibrillations. The patient had return of spontaneous circulation and was transported to the hospital, where he was admitted to the critical care unit. Family members report that he has no known coronary artery disease risk factors and exercises regularly without chest pain. He does not take any medications for his schizophrenia, and family members do not believe that he uses any illicit substances. Physical examination is unremarkable. His first set of cardiac enzymes reveal a creatinine kinase level of 500 U/L, creatinine kinase MB 19 U/L, and troponin I 1.8 µg/mL. His ECG on arrival is shown below.

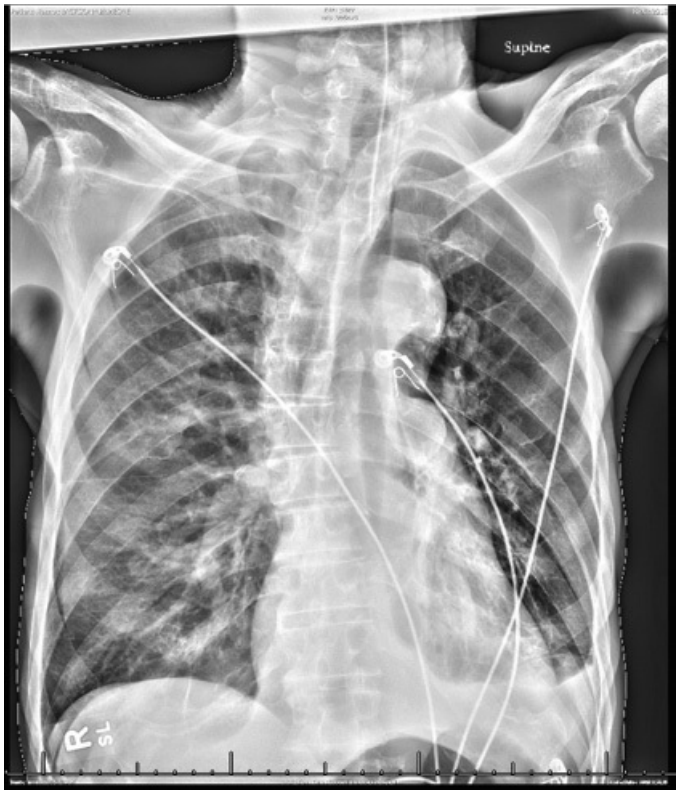


Which of the following is the most appropriate next step in management?

A. Implantable automatic defibrillator
B. Thrombolysis
C. Procainamide
D. Beta-blocker

E. Amiodarone

25. An 86-year-old African-American man with a history of diabetes is evaluted in the emergency department after being found unresponsive. Point-of-care blood sugar on arrival is 45 mg/dL. He is given 1 ampule of dextrose 50% with improvement in blood sugar, but Glasgow Coma Scale (GCS) score remains 8. He is preoxygenated with bag-mask ventilation and intubated with positive color on end-tidal carbon dioxide capnometer. Post-intubation chest radiograph is shown below. He is placed on pressure-regulated volume control, with tidal volume 450 mL, respiratory rate 12 breaths/min, positive end-expiratory pressure 5 cm H_2O and fraction of inspired oxygen 40%. After intubation, peak inspiratory pressures were high at 55, cm H_2O with expiratory tidal volume between 180 and 200 mL. Arterial blood gas analysis shows: pH 7.11, partial pressure of carbon dioxide 130 mm Hg, partial pressure of oxygen 69 mm Hg. Current blood pressure is 80/40 mm Hg, heart rate 120 beats/min, respiratory rate 25 breaths/min, and saturation on pulse oximetry 85%.



Which of the following is the most appropriate next step in management?

A. Change ventilator setting to pressure control in order to avoid barotrauma caused by high peak pressure.
B. Repeat chest radiograph to assess for pneumothorax.
C. Assess endotracheal tube placement.
D. Start norepinephrine for hypotension and shock and bicarbonate infusion for life-threatening acidosis.

26. A third-year resident is unable to place an infraclavicular subclavian triple-lumen catheter using landmark techniques after two attempts and decides to use an ultrasound to guide his third attempt.

    Which of the following concepts is most applicable to this situation?

    A. A prospective randomized controlled trial has shown that subclavian venous catherization with ultrasound guidance takes less time than the landmark technique.
    B. One of the most commons mistakes learners make when trying landmark infraclavicular subclavian venous access is using too steep of an angle.
    C. Ultrasound-guided infraclavicular subclavian venous catherization can lead to the catherization of the axillary rather than the subclavian vein.
    D. Trainees are more successful placing left-sided subclavian access rather than right-sided access.
    E. Subclavian lines have the same pneumothorax incidence as internal jugular lines.

27. A 73-year-old man with a history of colon cancer who had a right open colectomy with ileo-transverse anastomosis is intubated on mechanical ventilation. On postoperative day one he develops sinus tachycardia and mild decrease in oxygen saturation and hypotension with mean arterial pressure of 55 mm Hg. Chest radiograph is unchanged, with some interstitial infiltrates and small right pleural effusion. B-type natriuretic peptide is mildly elevated and troponins are normal. ECG shows only sinus tachycardia. A chest CT with IV contrast and pulmonary embolism (PE) protocol shows a moderate-sized PE in the right main pulmonary artery, and immediate anticoagulation via heparin infusion is initiated.

    Which of the following echocardiographic findings is/are expected in this patient?

    A. Left ventricular hypokinesis
    B. Moderate pericardial effusion
    C. Significant left atrial dilation and normal left ventricle
    D. Right ventricular dilation and left hyperdynamic left ventricle
    E. Normal findings

28. A 48-year-old woman has been in the ICU for the past nine days with urosepsis. Her condition has improved greatly with antibiotics and fluid resuscitation, but her course has been complicated by sick sinus syndrome, requiring placement of a dual-chamber permanent pacemaker. Before the procedure, she was awake, hemodynamically stable, and saturating 98% on 3-liter nasal cannula. Recent chest radiograph suggests moderate pulmonary edema, and she has been responding well to diuretic therapy. She returns to the ICU from the catheterization laboratory under conscious sedation with midazolam and fentanyl. The pacemaker is set at DDD with a backup rate of 70 beats per minute (bpm). Ten minutes later, she is noted to be agitated, dyspneic, tachycardic, and hypotensive. ECG reveals sinus tachycardia, with no apparent pacemaker

activity. She is somnolent and confused. Vital signs are: temperature 36.8°C (98.2°F), blood pressure 79/63 mm Hg, heart rate 128 beats/min, respiratory rate 34 breaths/min, and oxygen saturation 89% on 10-liter face mask. The incision site over her right chest is clean and dry. Physical examination reveals equal and reactive but small pupils bilaterally, greatly diminished breath sounds on the right, weak but palpable radial pulses, and elevated jugular venous distention.

Which of the following is the most appropriate intervention?

A. Endotracheal intubation
B. Reversal of sedation with IV naloxone and flumazenil
C. Needle thoracostomy of the right chest
D. Immediate CT angiogram of the chest

29. A 27-year-old woman is in the trauma resuscitation bay in unstable condition and in need of resusciation after a high-speed motor vehicle collision. She has an altered mental status and agonal respirations with gurgling noises from her airway but equal breath sounds. She is cold and diaphoretic, with blood pressure 87/40 mm Hg and heart rate 140 beats/min. Her airway is secured and peripheral IV access (14 g and 16 g) to begin crystalloid and blood product resuscitation is obtained. Portable chest radiograph **(Figure 1),** pelvis radiograph **(Figure 2),** and bedside ultrasound **(Figure 3)** are shown below. After initial fluid resuscitation, there is no change in vital signs.

Figure 1

Figure 2

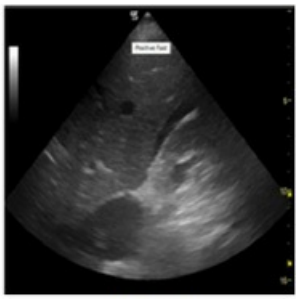


Figure 3

Which of the following is the most appropriate next course of action?

A. Placement of subclavian triple-lumen catheter for central venous access and blood transfusion
B. Diagnostic peritoneal lavage in trauma bay
C. Placement of intracranial pressure monitor
D. CT to rule out life-threatening injuries
E. Immediate exploratory laparotomy

30. A 58-year-old man who is postoperative day one after a Whipple procedure develops increased shortness of breath. Oxygen saturation is 86% on 2-liter nasal cannula, respiratory rate is 32 breaths/min, and he is using accessory

respiratory muscles. He is hemodynamically stable, alert, and oriented.

Which of the following interventions is most appropriate at this time?

A. Increase supplemental oxygen to keep oxygen saturation above 94%.
B. Start aggressive chest physical therapy.
C. Start noninvasive ventilation.
D. Start high-flow oxygen via nasal cannula.

31. A gravida 3, para 2 woman at 33 weeks' gestation is evaluated in the emergency department in acute hypoxic respiratory failure. She reports subjective fevers and chills and a productive cough. Physical examination shows her to be in acute distress with tachypnea and accessory muscle use. Vital signs include blood pressure of 197/92 mm Hg and oxyhemoglobin saturation of 86% on a nonrebreather face mask. Auscultation of her lung fields elicits shallow breaths, bilateral crackles, and focal rhonchi throughout the right middle and upper lobes. As part of the preparation for intubation, she is placed on high-flow nasal cannula oxygenation throughout the intubation procedure to allow for apneic oxygenation.

Which of the following is a relevant concept regarding the use of apneic oxygenation?

A. It is contraindicated in pregnancy.
B. It decreases the incidence of hypercapnia.
C. It delays time to desaturation throughout the intubation.
D. It decreases the incidence of anoxic brain injury in the fetus.

32. A 32-year-old man with 55% total body surface area non-circumferential burns remains mechanically ventilated in the ICU four days after injury. Overnight his oxygen requirements increased due to hypoxemia; pulse oximetry is currently 88%. His mechanical ventilator is set on assist control/volume control with tidal volume 420 mL, respiratory rate 20 breaths/min, positive end-expiratory pressure (PEEP) 12.5 cm H_2O, and fraction of inspired oxygen (FIO_2) 80%. Arterial blood gas analysis shows partial arterial oxygen pressure of 52 mm Hg. On an inspiratory pause maneuver, plateau airway pressure is 29 cm H_2O. Chest radiograph shows bilateral pulmonary opacities. He has no known history of heart disease, and his predicted body weight is 70 kg (154.3 lb). The clinician is concerned about his refractory hypoxemia.

Which of the following is the most appropriate next step in management?

A. Start inhaled nitric oxide at a concentration of 20 ppm; wean the FIO_2 as tolerated.
B. Increase the set PEEP to 15 cm H_2O.
C. Initiate venovenous extracorporeal membrane oxygenation
D. Initiate high-frequency oscillatory ventilation at an initial set mean airway

pressure of 35 cm H_2O; wean the FIO_2 as tolerated.

E. Prone the patient with a goal of 16 hours of prone time regardless of facial edema.

33. A 58-year-old man is in the ICU three days after being involved in a motor vehicle accident. His injuries include bilateral pulmonary contusions, rib fractures, splenic laceration, femur fracture, and multiple superficial lacerations. He has been weaned off vasoactive medications, and is on a continuous infusion of fentanyl for analgesia. Chest radiograph shows bilateral airspace opacities. Echocardiogram obtained yesterday shows no obvious abnormality and an estimated ejection fracture greater than 55%. He remains on mechanical ventilation for support of his hypoxemic respiratory failure. He is spontaneously breathing, with a respiratory rate of 18 breaths/min. His current mode of ventilation is airway pressure release ventilation on the following settings: positive end-expiratory pressure (PEEP)-high 25 cm H_2O, PEEP-low 0 cm H_2O, time (T)-high 6.75, T-low 0.75 sec., fraction of inspired oxygen 0.5.

    Which of the following is a current criteria for the diagnosis of ARDS?

    A. Timing of onset greater than one week
    B. PEEP greater than 10 cm H_2O
    C. Absence of left ventricular dysfunction on echocardiography
    D. Treatment not impacted by degree of hypoxemia

34. A 36-year-old man was injured in a high-speed motor vehicle accident. He was unbelted and, as a result, was ejected from the vehicle. On arrival in the trauma bay, his Glasgow Coma Scale (GCS) score is 7, and he is emergently intubated. Injuries include a moderate subdural hematoma and subarachnoid hemorrhage, as well as diffuse axonal injury, multiple bilateral nondisplaced rib fractures, bilateral pulmonary contusions, grade 3 splenic injury managed nonoperatively, and left femur fracture managed with an intramedullary rod on post-trauma day six. On post-trauma day nine, his GCS score is 11T, and he qualifies for extubation.

    Which of the following criteria for extubation is best supported by literature?

    A. Negative inspiratory force
    B. Vital capacity
    C. Successful 30-minute spontaneous breathing trial
    D. Cuff leak
    E. Muscle strength

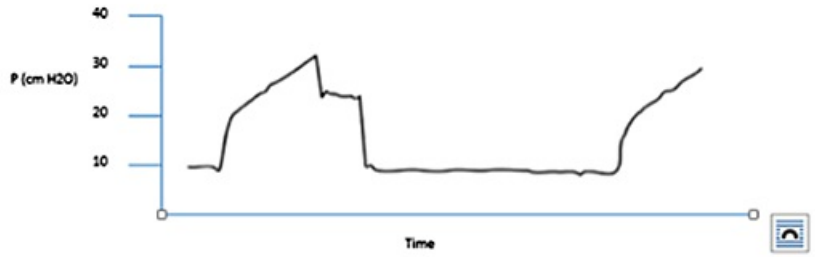
35. The following data are obtained from a 45-year-old man receiving mechanical ventilation in the ICU: exhaled tidal volume 500 mL/breath, peak inspiratory pressure 40 cm H_2O, plateau pressure 35 cm H_2O, positive end-expiratory

pressure 10 cm H_2O.

Which of the following is the static compliance (mL/cm H_2O)?

A. 30.5
B. 25
C. 20
D. 16.7

36. A 65-year-old man is admitted to the ICU with pneumonia and respiratory failure. He is mechanically ventialated, sedated with propofol and fentanyl (Richmond Agitation-Sedation Scale - 4). His settings are assist control/volume control with respiratory rate 18 breaths/min, tidal volume 450 mL, positive end-expiratory pressure (PEEP) 10 cm H_2O, and fraction of inspired oxygen (FIO_2) 50%, with oxygen saturation as measured by pulse oximetry (SpO_2) 97%. Peak inspiratory pressure (PIP) is 23 cm H_2O and plateau pressures are 20 cm H_2O. After cleaning the patient, his SpO_2 suddenly drops to 90%. The FIO_2 is increased to 100%, and now the SpO_2 has increased to 95%. The waveform shown below is seen on the ventilator.



[Diagram showing pressure-time ventilator waveform with PEEP of 10, PIP of 34, and Plateau pressure of 21 cm H2O.]

What of the following is the most likely diagnosis?

A. Tension pneumothorax
B. Pulmonary embolism
C. Mucous plug
D. Migration of the tube (mainstem intubation)
E. Air trapping (breath stacking)

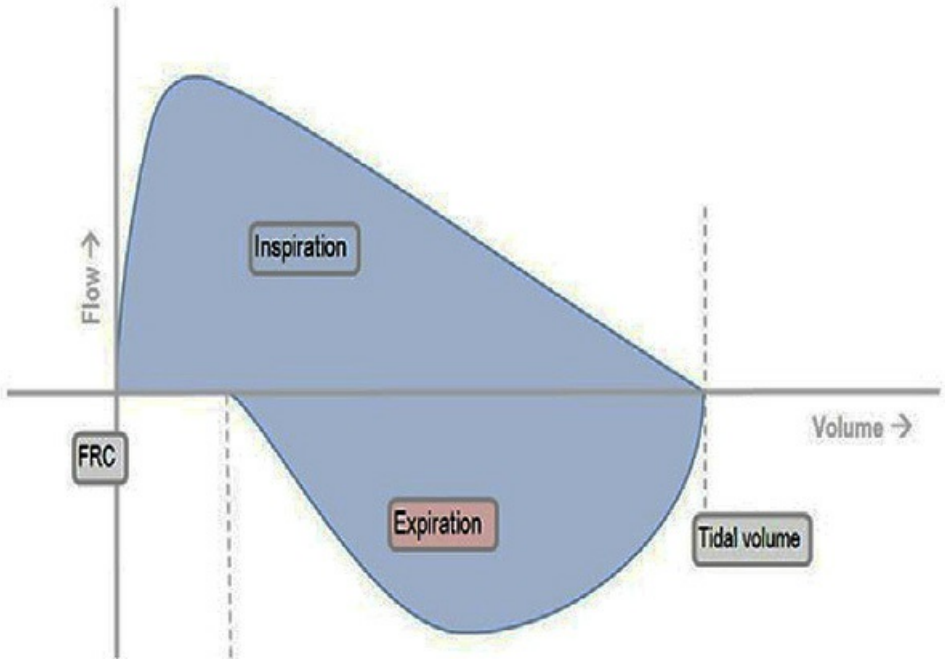
37. A 65-year-old woman with a history of chronic obstrutive pulmonary disease is intubated for respiratory failure after several days of increasing symptoms. After initial stabilization on the ventilator, her oxygen saturation suddenly decreases to 80% despite a fraction of inspired oxygen of 100%. With the help of an inspiratory hold maneuver, the clinician is able to ascertain the following

parameters: peak inspiratory pressure 45 cm H_2O, plateau pressure 20 cm H_2O, positive end-expiratory pressure 5 cm H_2O.

Which of the following is the most likely reason for her sudden hypoxia?

A. Decreased dynamic lung compliance, suggesting pneumothorax
B. Decreased static lung compliance, suggesting bronchospasm
C. Increased dynamic lung compliance, suggesting pneumothorax
D. Increased static lung compliance, suggesting pneumothorax
E. Decreased dynamic lung compliance, suggesting bronchospasm

38. A 67-year-old woman is intubated and mechanically ventilated through a size 6.5 cuffed endotracheal tube after a thoraco-abdominal aneurysm repair. During the course of approximately 20 minutes, her oxygen saturation as measured by pulse oximetry begins to decrease from 97% to 91%, and her end-tidal carbon dioxide increases from 36 mm Hg to 52 mm Hg. A flow-volume loop displayed on the ventilator is shown below.



Which of the following is the most appropriate next step in management?

A. Decrease the tidal volume delivered by the ventilator.
B. Administer inhaled bronchodilators.
C. Suction the endotracheal tube.
D. Reintubate the patient.
E. Check whether the endotracheal tube balloon is inflated.

39. A 31-year-old woman has progressive dyspnea. She is short of breath with minimal exertion and at rest. She cannot walk across the room, has dizziness and

near-syncope when she stands, and has 2+ lower extremity edema. An echocardiogram shows a pulmonary artery systolic pressure of 72 mm Hg, right atrial enlargement, right ventricular enlargement, and bowing of the interventricular septum during systole and diastole consistent with right ventricular pressure and volume overload. Workup for secondary causes of pulmonary artery hypertension is negative. A right heart catheter is placed and shows right atrial pressure 18 mm Hg, pulmonary artery pressure 93/30 mm Hg with mean pulmonary artery pressure 51 mm Hg and pulmonary capillary wedge pressure 9 mm Hg. Cardiac output, by Fick method, is 2.5 L/min, and cardiac index 1.3 L/min/m^2, with a pulmonary vascular resistance of 16.8 Wood units. The patient is admitted to the ICU with right heart failure.

Which of the following is the most appropriate first-line treatment for this patient?

A. IV epoprostenol
B. Inhaled epoprostenol
C. IV treprostinil
D. Oral ambrisentan and oral tadalafil
E. Oral and IV sildenafil

40. A 43-year-old woman with pulmonary arterial hypertension (PAH) due to scleroderma, diagnosed four years ago, currently stable on IV epoprostenol, oral sildenafil, and warfarin, presents with right upper quadrant pain. When her PAH was first diagnosed, she was New York Heart Association (NYHA) functional class (FC) IV. On therapy she has improved to NYHA FC II. She has been experiencing intermittent right upper quadrant (RUQ) pain that is exacerbated by eating a fatty meal. It worsened after she ate yesterday. Workup shows gallstones, with biliary ductal dilation and pericholecystic fluid on RUQ ultrasound. Laboratory data is notable for white blood cell count 14,200/μL, total bilirubin 3.2 mg/dL, alkaline phosphatase 425 U/L, and INR 2.8. She is diagnosed with acute cholecystitis and is scheduled to undergo surgery later today.

    Which of the following is the proper perioperative management of her PAH therapy?

    A. Continue all her current treatments without change.
    B. Reverse the warfarin and continue the epoprostenol and sildenafil.
    C. Reverse the warfarin, hold the epoprostenol due to its platelet-inhibitory effect, and continue the sildenafil.
    D. Reverse the warfarin, hold the epoprostenol due to its platelet-inhibitory effect, and hold the sildenafil due to risk of systemic hypotension.

41. A 57-year-old man with a history of colon cancer on active chemotherapy, hypertension, hyperlipidemia, and coronary artery disease presents with sudden-onset shortness of breath. He was shaving at home when he suddenly developed acute dyspnea. In the emergency department, he is saturating 82% on 6 L/min nasal cannula, with respiratory rate 32 breaths/min, heart rate 124 beats/min,

blood pressure 110/76 mm Hg. He is afebrile. He is started on high-flow nasal cannula oxygen at 20 L/min, with 60% fraction of inspired oxygen to keep his saturation above 92%. He says he feels better once high-flow oxygen is started, and his tachypnea resolves significantly. Chemistry is within normal limits, with bicarbonate of 21 mEq/L. Arterial blood gas analysis shows: pH 7.54, partial pressure of carbon dioxide 22 mm Hg, and partial pressure of oxygen 54 mm Hg. An emergent CT shows a central clot. An emergent echocardiogram shows a dilated and hypokinetic right ventricle. Laboratory results show: troponin I 1.2 ng/mL, creatinine 1.0 mg/dL, lactate 1.0 mmol/L.

Which of the following is the most appropriate next step?

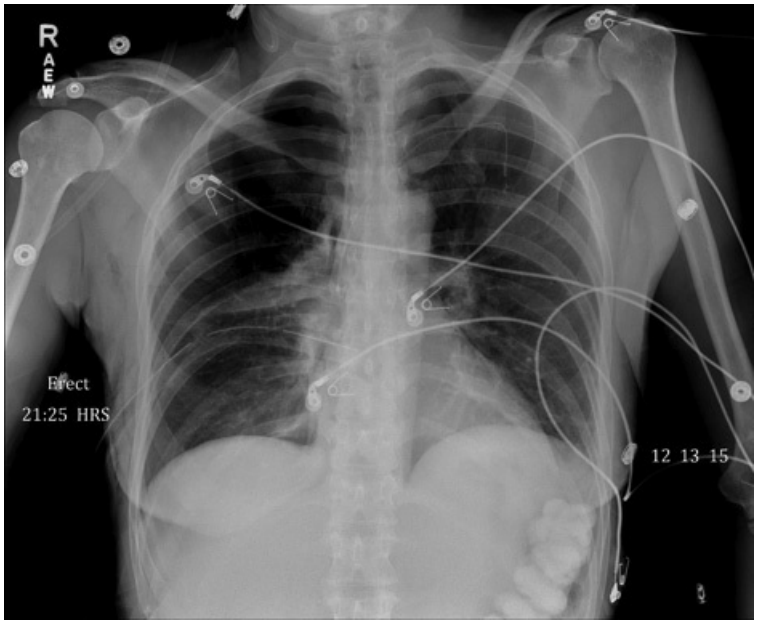
A. IV thrombolytics
B. Therapeutic low-molecular-weight heparin
C. Intubation and mechanical ventilation
D. Inferior vena cava filter
E. Duplex ultrasound of lower extremities

42. A 35-year-old woman with no significant medical history is evaluated in the emergency department after collapsing while shopping. Shortly after initial assessment, she loses pulses and requires cardiopulmonary resuscitation (CPR). CPR is continued and, after 1 mg epinephrine and endotracheal intubation, she has return of spontaneous circulation. She is stable for 5 minutes and then has another cardiac arrest, responding again to CPR and 1 mg of epinephrine. Her vital signs are: blood pressure 88/52 mm Hg, heart rate 115 beats/min, temperature 37.3°C (99.1°F), and respiratory rate 14 breaths/min. Emergency medical personnel report that, while on the scene, the patient's friend said that they had just returned from a trip to South America and had partaken of illicit drug use there. The clinician performs a quick bedside echocardiogram, which shows moderate right ventricular hypokinesis and dilation with end-diastolic diameter 32 mm in parasternal view.

Which of the following is the most appropriate next step in management?

A. Emergent chemistry panel with creatinine level
B. Emergent chest CT with angiography
C. Heparin weight-based bolus followed by continuous infusion
D. Alteplase, 10 mg IV bolus, followed by 90 mg over 2 hours
E. Emergent ventilation/perfusion scan

43. An 18-year-old man is transferred from an outside facility for management of a pneumothorax. A 14-French pigtail catheter was placed at the outside facility, but the pneumothorax did not resolve, so a second opinion is sought. A trainee places a surgical chest tube (see radiograph below), but the pneumothorax does not resolve. The patient reports pain at the insertion site, spikes a low-grade fever and becomes tachycardic. He is hemodynamically stable and has serosanguinous fluid draining from the pleurovac, with a continuous air leak.



Which of the following is the most appropriate next step?

A. Noncontrast chest CT to evaluate location of surgical chest tube
B. Removal of surgical chest tube and placing another pigtail catheter
C. Thoracic surgery consultation for loculated pneumothorax
D. Antibiotics for pneumonia
E. Emergent complete blood count to evaluate for bleeding

44. A 77-year-old man is transferred to the ICU for tachypnea, hypoxemia, and hemoptysis. He has a past history of laryngeal mass, which was resected six days ago and was complicated by a non-ST elevation myocardial infarction three days ago. At that time, he underwent cardiac catheterization and stent insertion in the left anterior descending, circumflex coronary, and posterior descending arteries. Since going to the catherization laboratory, he has been on a continuous heparin infusion. On examination, he is sitting upright and is actively suctioning bright red blood via a Yankauer catheter. His vital signs are: blood pressure 97/54 mm Hg, heart rate 131 beats/min, respiratory rate 38 breaths/min, oxygen saturation as measured by pulse oximetry 90% on 10-liter nasal cannula. He reports that his breathing is becoming more difficult.

Which of the following is the most appropriate next step in management?

A. Left lateral decubitis position
B. Noninvasive ventilation
C. Venovenous extracorporeal membrane oxygenation
D. Direct laryngoscopy
E. Cricothyroidectomy

Part 3 Answers:
Pulmonary Critical Care

1. Rationale

Answer: B

The only significant parameter of which an increase would improve carbon dioxide elimination is sweep gas flow. Increasing the ventilatory respiratory rate may help, but will probably be ineffective because of significant lung injury. Increasing the other parameters will aid with oxygenation, but not with carbon dioxide exchange.

References:

1. Brodie D, Bacchetta M. Extracorporeal membrane oxygenation for ARDS in adults. *N Engl J Med.* 2011 Nov 17;365(20):1905-1914.
2. Allen S, Holena D, McCunn M, Kohl B, Sarani B. A review of the fundamental principles and evidence base in the use of extracorporeal membrane oxygenation (ECMO) in critically ill adult patients. *J Intensive Care Med.* 2011 Jan-Feb;26(1):13-26.
3. Del Sorbo L, Cypel M, Fan E. Extracorporeal life support for adults with severe acute respiratory failure. *Lancet Respir Med.* 2014 Feb;2(2):154-164.

2. Rationale

Answer: A

In patients with myasthenic crisis, subjective assessment is combined with pulmonary function testing to guide the decision about ventilator support. General warning signs include increasing generalized weakness, dysphagia, dysphonia, and dyspnea on exertion and at rest. Signs on subjective assessment include tachycardia, weak cough, staccato speech, accessory muscle use, rapid shallow breathing, abdominal paradox, orthopnea, and weakness of trapezius and neck muscles. Objective assessment should follow the 20/30/40 rule: vital capacity less than 20 mL/kg (normal 40-70 mL/kg), maximal inspiratory pressure less than or equal to 30 cm H_2O (normal greater than or equal to 100 cm H_2O), and maximal expiratory pressure less than 40 cm H_2O (normal greater than 200 cm H_2O) should prompt airway protection with endotracheal intubation.

Noninvasive bilevel positive airway pressure (BiPAP) can be effective for treating acute respiratory failure in patients with myasthenia gravis. A BiPAP trial before the

development of hypercapnia (greater than 50 mm Hg) can prevent intubation and prolonged ventilation, reducing pulmonary complications and lengths of ICU and hospital stays. However, this patient has significant hypercapnia and increased secretions and might not benefit from BiPAP. There is no role for heliox in the management of myasthenic crisis. IV immunoglobulin or plasma exchange is considered the standard of care for patients with myasthenic crisis. However, this patient needs airway protection before definitive treatment. With regard to intubation, nondepolarizing agents (eg, vecuronium) have increased potency, and reduced doses are required for paralysis. Propofol and fentanyl can be used safely for intubation without using neuromuscular blockers. This patient needs ventilator support. Increasing the pyridostigmine dose will not prevent the need for intubation. Pyridostigmine can be stopped during mechanical ventilation and gradually restarted. Excess of pyridostigmine can cause cholinergic crisis. Steroids can also exaggerate myasthenia. However, steroids are considered for myasthenic crisis if there is no improvement after five days of plasma exchange.

References:

1. Seneviratne J, Mandrekar J, Wijdicks EF, Rabinstein AA. Noninvasive ventilation in myasthenic crisis. *Arch Neurol.* 2008 Jan;65(1):54-58.
2. Wendell LC, Levine JM. Myasthenia crisis. *Neurohospitalist.* 2011 Jan;1(1):16-22.
3. Baraka A. Anaesthesia and myasthenia gravis. *Can J Anaesth.* 1992 May;39(5 Pt 1):476-486.
4. Koenig SJ, Lakticova V, Narasimhan M, Doelken P, Mayo PH. Safety of propofol as an induction agent for urgent endotracheal intubation in the medical intensive care unit. *J Intensive Care Med.* 2015 Dec;30(8):499-504.
5. Wijdicks EFM. Myasthenia gravis. In: Wijdicks EFM. *The Practice of Emergency and Critical Care Neurology.* London: Oxford University Press; 2010:608-628.

3. Rationale

Answer: C

This patient has primary graft dysfunction (PGD), a common postoperative complication and leading cause of early morbidity and mortality after lung transplantation. A form of lung injury characterized by hypoxemia, PGD is the result of complex interplay between inflammation and immunologic responses to ischemia-reperfusion in the lung allograft after transplantation. In the absence of an effective pharmacologic therapy, the best approach is to use lung-protective ventilation in accord with the management of acute respiratory distress syndrome. Diuresis may improve hypoxemia, but there is no evidence that it will improve survival in lung injury. Extracorporeal life support is a reasonable option, as is rescue therapy, but is not the first-line approach to the PGD. Without evidence of venous thromboembolism, there is no indication for systemic anticoagulation.

References:

1. Lee JC, Christie JD. Primary graft dysfunction. *Proc Am Thorac Soc.* 2009 Jan 15;6(1):39-46.
2. Suzuki Y, Cantu E, Christie JD. Primary graft dysfunction. *Semin Respir Crit Care Med.* 2013 Jun;34(3):305-319.
3. Fischer S, Bohn D, Rycus P, et al. Extracorporeal membrane oxygenation for primary graft dysfunction after lung transplantation: analysis of the Extracorporeal Life Support Organization (ELSO) registry. *J Heart Lung Transplant.* 2007 May;26(5):472-477.
4. Diamond JM, Lee JC, Kawut SM, et al; Lung Transplant Outcomes Group. Clinical risk factors for primary graft dysfunction after lung transplantation. *Am J Respir Crit Care Med.* 2013 Mar 1;187(5):527-534.

4. Rationale

Answer: B

ICU-acquired infection surveillance is an important component of quality critical care. Ventilator-associated pneumonia (VAP) is estimated to occur in 15% to 20% of mechanically ventilated patients. A recent trial found that the tradition of routine monitoring of residual gastric volume was not associated with a significantly decreased risk of VAP compared to a strategy in which volumes were not monitored (16.7% in the nonmonitored group and 15.8% in the monitored group). The supine position, in contrast to the semirecumbent position (greater than 45° head of bed), is a risk factor for VAP; therefore it is recommended to elevate the head of the bed in mechanically ventilated patients to decrease the risk of VAP. H2-blockers, proton pump inhibitors, and postpyloric feeding have not been shown to reduce the risk of VAP. In fact, proton pump inhibitors may increase the risk.

References:

1. Reignier J, Mercier E, Le Gouge A, et al; Clinical Research in Intensive Care and Sepsis (CRICS) Group. Effect of not monitoring residual gastric volume on risk of ventilator-associated pneumonia in adults receiving mechanical ventilation and early enteral feeding: a randomized controlled trial. *JAMA.* 2013 Jan 16;309(3):249-256.
2. American Thoracic Society; Infectious Diseases Society of America. Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. *Am J Respir Crit Care Med.* 2005 Feb 15;171(4):388-416.
3. Drakulovic MB, Torres A, Bauer TT, Nicolas JM, Nogué S, Ferrer M. Supine body position as a risk factor for nosocomial pneumonia in mechanically ventilated patients: a randomised trial. *Lancet.* 1999 Nov 27;354(9193):1851-1858.

5. Rationale

Answer: A

The most frequent radiologic manifestations of nocardiosis are airspace consolidation

(52.8%), usually homogenous, but occasionally patchy, and nodules (82.3%), single or multiple, that can be confused with metastatic carcinoma. Pleural involvement with empyema is present in approximately one-third of cases. The most common radiographic manifestation is cavitation, which is found in both consolidation and nodules. Centrilobular micronodules are characteristic of hypersensitivity pneumonitis.

References:

1. Chen J, Zhou H, Xu P, Zhang P, Ma S, Zhou J. Clinical and radiographic characteristics of pulmonary nocardiosis: clues to earlier diagnosis. *PLoS One.* 2014 Mar 3;9(3):e90724.
2. Martinez R, Reyes S, Menéndez R. Pulmonary nocardoisis: risk factors, clinical features, diagnosis, and prognosis. *Curr Opin Pulm Med.* 2008 May;14(3):219-227.
3. Yildiz O, Doganay M. Actinomycoses and Nocardia pulmonary infections. *Curr Opin Pulm Med.* 2006 May;12(3):228-234.

6. Rationale

Answer: B

This presentation is classic for obstructive sleep apnea complicated by obesity hypoventilation syndrome. The patient's ability to tolerate the observed degree of respiratory acidosis reflects the chronicity of the disease and the gradual progression if untreated. The initial management decision is whether to institute invasive or noninvasive management. Given the morbidity and mortality associated with the use of mechanical ventilation, and the nonurgent presentation, the best approach is to initiate noninvasive ventilation and assess for responsiveness. In the outpatient setting, continuous positive airway pressure is initiated and transitioned to bilevel support if hypoxemia cannot be corrected. In this urgent scenario, initiation of bilevel support is reasonable. If the patient's symptoms are refractory to escalating levels of noninvasive ventilation, or if her condition worsens, invasive mechanical ventilation would be required.

The presence of lower extremity edema suggests cor pulmonale and/or pulmonary hypertension. Over time, diuresis may prove to be an effective strategy, but is less useful in the acute setting than the initiation of ventilator support given her lethargy and arterial blood gas values. An echocardiogram would be useful to examine the left and right ventricular size and function, and to assess for pulmonary hypertension. Neither nebulizer treatment nor steroids would have a role in obesity hypoventilation syndrome.

References:

1. Piper AJ, Grunstein RR. Obesity hypoventilation syndrome: mechanisms and management. *Am J Respir Crit Care Med.* 2011 Feb 1;183(3):292-298.
2. Kessler R, Chaouat A, Schinkewitch P, et al. The obesity-hypoventilation syndrome revisited: a prospective study of 34 consecutive cases. *Chest.* 2001 Aug;120(2):369-376.

3. Piper AJ, Wang D, Yee BJ, Barnes DJ, Grunstein RR. Randomised trial of CPAP vs bilevel support in the treatment of obesity hypoventilation syndrome without severe nocturnal desaturation. *Thorax.* 2008 May;63(5):395-401.

7. Rationale

Answer: B

When Girard et al put together spontaneous awakening and spontaneous breathing in the Awakening and Breathing Controlled Trial, the result was a reduction of four days in both ICU and hospital stays. Patients had a 14% absolute risk reduction for survival at one year, one of the largest survival advantages ever shown in a critical care randomized trial. Patients did have higher self-extubation rates, but not higher rates of reintubations, indicating that they were ready for extubation but that the team was too slow. A reduction in coma, but not delirium, was also observed. In only the sepsis subgroup, who made up about half of the study population, was there a reduction in both coma and delirium duration. For mechanically ventilated adults already managed with protocolized sedation, the addition of daily sedation interruption may not have an additional benefit of reducing the duration of mechanical ventilation or ICU stay.

References:

1. Girard TD, Kress JP, Fuchs BD, et al. Efficacy and safety of a paired sedation and ventilator weaning protocol for mechanically ventilated patients in intensive care (Awakening and Breathing Controlled trial) a randomised controlled trial. *Lancet.* 2008 Jan 12;371(9607):126-134.
2. Hooper MH, Girard TD. Sedation and weaning from mechanical ventilation: linking spontaneous awakening trials and spontaneous breathing trials to improve patient outcomes. *Crit Care Clin.* 2009 Jul;25(3):515-525.
3. Luetz A, Goldmann A, Weber-Carstens S, Spies C. Weaning from mechanical ventilation and sedation. *Curr Opin Anaesthesiol.* 2012 Apr;25(2):164-169.
4. Mehta S, Burry L, Cook D, et al; SLEAP Investigators; Canadian Critical Care Trials Group. Daily sedation interruption in mechanically ventilated critically ill patients cared for with a sedation protocol: a randomized controlled trial. *JAMA.* 2012 Nov 21;308(19):1985-1992.

8. Rationale

Answer: B

The patient's altered mental status may be a result of the deteriorating gas exchange or a possible head injury. A high index of suspicion for cervical spine and head injuries should be present. Because the extent of her facial injuries is unknown, all forms of nasal intubation are relatively contraindicated. Her facial injuries may be associated with a fracture of the cribriform plate, which predisposes the endotracheal tube to be passed into the cranium. Oral intubation with direct laryngoscopy and manual in-line axial traction is a good option. Oral fiberoptic intubation is also a viable alternative. Cricothyrotomy would be indicated only if the patient's respiratory status suddenly

deteriorates and orotracheal intubation is not possible.

Reference:

1. Marshall SA, Ling GSF. Critical care management of traumatic brain injury. In: Society of Critical Care Medicine. *Comprehensive Critical Care: Adult.* Mt. Prospect, IL: Society of Critical Care Medicine; 2012:74.

9. Rationale

Answer: D

Pressure support (PS) is a patient-triggered, pressure-targeted, flow-cycled form of mechanical ventilatory support. Clinicians can select the breath-triggering sensitivity and the pressure target. Until recently, however, the flow-cycling (flow termination) criteria were fixed by the ventilator manufacturer as some percentage of the peak inspiratory flow. To improve patient ventilator synchrony and/or reduce the potential for excessive inspiratory time (a problem in patients with obstructive lung disease), newer ventilators allow the clinician to adjust the flow-cycling criteria; this is what has happened in this patient. Option D is correct. In breath A, the peak inspiratory flow is 75 L/min, and the breath is cycling (flow terminated) when flow falls to 20% of this flow, or 15 L/min. In breath B, the clinician has increased the flow cycling criteria to 50% of the peak inspiratory flow, or 38 L/min. Stopping flow when it is still high relative to peak flow has shortened the inspiratory time and reduced the delivered volume.

An alternative approach to controlling inspiratory time using a patient-triggered, pressure-targeted breath is to use a pressure assist breath (pressure assist-control ventilation [PACV] with the set rate below the spontaneous rate) where the clinician directly sets the inspiratory time. The mode here, however, is stated as PS, not PACV. A reduced compliance with PS will reduce both the peak inspiratory flow and delivered volume, but breath timing changes are occurring here. The PS mode does not have a volume setting, although some ventilators do provide a feedback pressure setting based on delivered volume, which is known as the volume support mode. There is no rate setting in pressure support.

References:

1. Dekel, B., Segal, E. and Perel, A., 1996. Pressure support ventilation. *Archives of Internal Medicine,* 156(4), pp.369-373.
2. MacIntyre, N.R. and Ho, L.I., 1991. Effects of initial flow rate and breath termination criteria on pressure support ventilation. *CHEST Journal,* 99(1), pp.134-138.

10. Rationale

Answer: C

Current mechanical ventilation strategies are designed to provide enough inspiratory and expiratory pressure to recruit and ventilate the lungs while avoiding excessive

end-inspiratory stretching of lung units. In general, the goal is to limit end-inspiratory transpulmonary pressure to less than 30 to 35 cm H_2O, the transpulmonary stretching pressure of the normal human lung at total lung capacity. However, transpulmonary pressure (alveolar pressure minus surrounding intrapleural pressure) is difficult to measure clinically. Because of this, a common practice is to simply assume that thoracic cage compliance is very high, intrapleural pressure is consequently very low, and thus the measured airway pressure under no-flow conditions (plateau pressure [Pplat]) is a reasonable reflection of the transpulmonary pressure.

Morbid obesity (body mass index greater than 40) produces a marked reduction in thoracic cage compliance. Studies looking at mechanical ventilation in such patients have generally shown very high intrapleural pressures with the application of a positive pressure breath. The simple Pplat measurement thus will reflect not only transpulmonary pressure across the alveolus but also the intrapleural pressure required to push out the stiff thoracic cage. Pplat alone will grossly overestimate the transpulmonary pressure and put an inappropriate limit on the airway pressures that could be used to support morbidly obese patients. Esophageal pressure monitoring would give a more accurate measure of the transpulmonary pressures.

References:

1. Pelosi P, Croci M, Ravagnan I, Vicardi P, Gattinoni L. Total respiratory system, lung, and chest wall mechanics in sedated-paralyzed postoperative morbidly obese patients. *Chest.* 1996 Jan;109(1):144-151.
2. Pelosi P, Croci M, Ravagnan I, et al. The effects of body mass on lung volumes, respiratory mechanics, and gas exchange during general anesthesia. *Anesth Analg.* 1998 Sep;87(3):654-660.

11. Rationale

Answer: D

Managing a patient with markedly different lung mechanics in each lung poses significant problems, as in this patient with a single left lung transplant producing a markedly stiff lung on the left and a high-compliance lung with narrow airways on the right. When managed with a single ventilatory support strategy, undesirable gas distribution and ventilation-perfusion relationships may result. Positive end-expiratory pressure (PEEP) application can be problematic, in that PEEP would be desirable in the edematous stiff lung but clearly undesirable in an obstructive lung that is already overdistended.

To address this, double-lumen tubes allow independent ventilatory parameters to be set in each lung. In setting up these ventilators, the ventilatory pattern and PEEP in each lung can then be titrated to the specific clinical goal. Since a primary goal of any ventilatory strategy is to prevent overdistension and ventilator-induced lung injury. Limiting the end-inspiratory (maximal) stretching pressure (plateau pressure) in the lungs to less than 30 to 35 cm H_2O reduces this risk.

A 6 mL/kg ideal body weight tidal volume in each lung would be a total tidal volume of

12 mL/kg ideal body weight, clearly excessive and likely to produce ventilator-induced lung injury in healthier regions of either lung. The differential PEEP is one of the goals of independent lung ventilation. PEEP is needed in the edematous lung, not the emphysematous lung. The respiratory rate settings in the two lungs do not need to be synchronized.

References:

1. Anantham D, Jagadesan R, Tiew PE. Clinical review: independent lung ventilation in critical care. *Crit Care.* 2005;9(6):594-600.
2. Gravazzeni V, Iapichino G, Mascheroni D, et al. Prolonged intependent lung respiratory treatment after single lung transplantation in pulmonary emphysema. *Chest.* 1993 Jan;103(1):96-100.
3. Powner DJ. Differential lung ventilation during adult donor care. *Prog Transplant.* 2010 Sep;20(3):262-267.
4. [No authors listed]. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. The Acute Respiratory Distress Syndrome Network. *N Engl J Med.* 2000 May 4;342(18):1301-1308.

12. Rationale

Answer: C

Unilateral reexpansion pulmonary edema is seen in the images; it is recognized as a complication that can occur during management of pneumothorax. Reexpansion pulmonary edema tends to occur with greater frequency in patients aged 20 to 39 years, when there is complete collapse of the lung, and when the pneumothorax has remained untreated for more than 72 hours. It is also more likely to occur when negative pressure is applied after insertion of a thoracostomy tube. Older age seems to afford some protection. Pathogenesis is unknown. Various factors, such as bronchial obstruction, decreased surfactant, and increased capillary permeability, have been implicated. Long-standing pleural effusions may be associated with it, as well as rapid withdrawal of amounts of more than 1 or 2 liters of pleural fluid.

Reference:

1. Perricone G, Mazzarelli C. Images in clinical medicine. Reexpansion pulmonary edema after thoracentesis. *N Engl J Med.* 2014 Mar 20;370(12):e19.

13. Rationale

Answer: B

In this scenario, heliox is contraindicated because of the degree to which the patient requires oxygen. A helium-to-oxygen admixture is typically 70:30 (30% oxygen). Therefore, anyone requiring more than 30% oxygen should not receive heliox therapy because of the risk of hypoxia. Because helium is less dense than air, it will decrease resistance in the large airways. Heliox improves airflow limitation in large airways by

decreasing turbulent flow. This improves ventilation and carbon dioxide elimination. Heliox may also improve intrinsic positive end-expiratory pressure, decrease pulsus paradoxus, and improve peak expiratory flow rate. In short, it may improve ventilation until bronchodilators and corticosteroids can improve the degree of bronchospasm. However, there have been no large controlled trials to demonstrate any impact on outcome.

The patient's pregnancy should not alter her therapy. In general, the risk of inadequate therapy for asthma outweighs the risks associated with the use of asthma medications. Conventional therapy for asthma (bronchodilators and corticosteroids) should be administered to all pregnant patients with acute asthma exacerbation, but epinephrine therapy is not recommended in pregnancy.

Reference:

1. LaRosa JA, Dellinger RP. ICU management of obstructive airway disease. In: Society of Critical Care Medicine. *Comprehensive Critical Care: Adult.* Mt. Prospect, IL: Society of Critical Care Medicine; 2012:331.

14. Rationale

Answer: A

Recent Society of Critical Care Medicine guidelines have examined appropriate continuous infusion strategies for patients requiring indwelling devices and mechanical ventilation. These recommendations are based on the pain, agitation, and delirum guidelines. Once an appropriate sedation strategy goal is identified (eg, a Richmond Agitation-Sedation Scale goal based on patient characteristics, disease state, critical illness, etc.), appropriate medications can be selected. The first goal for continuous infusion should be to adequately control pain by using a short-acting narcotic agent such as fentanyl. Once pain has been adequately addressed, providing sedation is the next step. Ideally, intermittent doses of sedatives should be used first. If that fails to control agitation, then a continuous sedative infusion should be initiated. Studies have shown an increased association between delirium and continuous benzodiazepine infusions. At this time, continuous benzodiazepine infusions would be considered a second-line sedative agent. Potential first-line agents include dexmedetomidine and propofol. Neither of these agents has shown a superior effect profile for reducing delirium. Antipsychotics, including haloperidol, have also been studied as potential agents to limit ICU delirium. Studies have shown haloperidol to have a favorable affect on acute agitation, but no significant decrease on overall delirium. Once pain and agitation have been controlled, the clinician should continue to screen for delirium with tools such as the Confusion Assessment Method for the ICU, since morbidity and mortality have been linked to unrecognized delirium.

References:

1. Barr J, Fraser GL, Puntillo K, et al; American College of Critical Care Medicine. Clinical practice guidelines for the management of pain, agitation, and delirium in adult patients in the intensive care unit. *Crit Care Med.* 2013 Jan;41(1):263-306.

2. Page VJ, Ely EW, Gates S, et al. Effect of intravenous haloperidol on the duration of delirium and coma in critically ill patients (Hope-ICU): a randomised, double-blind, placebo-controlled trial. *Lancet Respir Med.* 2013 Sept;1(7):515-523.

15. Rationale

Answer: D

Ketamine is a dissociative agent with some analgesic properties, and can be ideal for patients with expiratory flow limitation. Effects of ketamine include vagolysis and direct smooth muscle relaxation, therefore helping with bronchospasm refractory to bronchodilators. This will lead to a decrease in peak inspiratory pressures and an increase in dynamic compliance. Ketamine causes minimal respiratory depression since it does not inhibit the central carbon dioxide reflex. Ketamine will preserve functional residual capacity, minute ventilation, and tidal volume, unlike other sedatives that are used for induction. In fact, some studies show a small increase in respiratory rate and corresponding improved oxygenation and improved ventilation. Finally, variation exists with ketamine dosing. Ketamine increases oropharyngeal secretions and does not affect pulmonary secretions.

References:

1. Lazarus, SC. Clinical practice. Emergency treatment of asthma. *N Engl J Med.* 2010 Aug 19;363(8):755-764.
2. Miller AC; Jamin CT; Elamin EM. Review: continuous intravenous infusion of ketamine for maintenance sedation. *Minerva Anestesiol.* 2011 Aug;77(8):812-820.
3. Higgins, JC. The 'crashing asthmatic.' *Am Fam Physician.* 2003 Mar 1;67(5):997-1004.

16. Rationale

Answer: D

This patient has hypoxic respiratory failure, and limited interventions have proven useful in decreasing mortality from this common condition. High-flow nasal oxygen therapy, which is heated and humidified oxygen delivered through a nasal cannula, was shown in a randomized controlled trial to decrease 90-day mortality in patients with hypoxic respiratory failure compared to noninvasive ventilation. High-flow oxygen therapy creates a positive pressure effect on the upper airway and is tolerated better than other forms of ventilation. If the patient required mechanical ventilation to support him through his viral pneumonia, then that would be the correct choice, but a trial of noninvasive ventilation before mechanical ventilation with its concomitant morbidities is reasonable. The literature is mixed on whether noninvasive ventilation decreases mortality in patients with hypoxic respiratory failure. In the previously referenced trial, high-flow oxygen therapy was superior to noninvasive ventilation. Neither nebulizations to loosen secretions nor broad-spectrum antibiotics have been shown to decrease mortality in viral pneumonia.

References:

1. Frat JP, Thille AW, Mercat A, et al; FLORALI Study Group; REVA Network. High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure. *New Engl J Med.* 2015 Jun 4;372(23):2185-2196.
2. Carrillo A, Gonzalez-Diaz G, Ferrer M, et al. Non-invasive ventilation in community-acquired pneumonia and severe acute respiratory failure. *Intensive Care Med.* 2012 Mar;38(3):458-466.
3. Nishimura M. High-flow nasal cannula oxygen therapy in adults. *J Intensive Care.* 2015 Mar 31;3(1):15.

17. Rationale

Answer: B

The patient has severe acute respiratory distress syndrome (ARDS), according to the Berlin Criteria, which are: mild hypoxemia (200 mm Hg < partial arterial oxygen pressure [PaO_2]/fraction of inspired oxygen [FIO_2] ≤ 300 mm Hg); moderate hypoxemia (100 mm Hg < PaO_2/FIO_2 ≤ 200 mm Hg); or severe hypoxemia (PaO_2/FIO_2 ≤ 100 mm Hg).

The mortality for severe ARDS by Berlin criteria is 45%, with few interventions showing clinical benefit. Low tidal volume ventilation (<6 mL/kg/predicted body weight [PBW] with goal plateau pressures less than 30 cm H_2O) decreased mortality by 8.8% in a randomized controlled trial. Inhaled pulmonary vasodilators, by selective vasodilatation to ventilated alveoli, improve oxygenation in patients with ARDS, but they do not improve mortality. A meta-analysis of inhaled nitric oxide use showed that it is associated with an increased incidence of acute kidney injury. In a randomized controlled trial examining optimal positive end-expiratory pressure (PEEP) settings, the open-lung approach combining low tidal volume, lung recruitment maneuvers, and high PEEP did not decrease mortality in patient with ARDS. It did decrease death from refractory hypoxemia and did not lead to significantly more barotrauma. In a randomized controlled trial, statins decreased neither ventilator-free days nor mortality in patients with ARDS. Venovenous extracorpeal membranous oxygenation (VV ECMO) continues to be used more frequently for severe ARDS. The CESAR trial showed that referral to an ECMO-capable center reduced mortality in severe ARDS, but the control arm received significantly less lung-protective ventilation than the ECMO-referred cohort, which is a criticism of the trial. VV ECMO can improve oxygenation and provide near total lung rest to decrease ventilator-associated lung injury, and should be offered on a case-by-case basis after conventional therapies and adjunctive ARDS management strategies have been exhausted.

Prone positioning was associated with a 16% absolute risk reduction for mortality when done for early, severe ARDS, and proning was maintained for prolonged periods. Patients in this study were proned for at least 16 hours and ventilated with low-tidal volume (6 mL/kg/PBW).

References:

1. Guerin C, Baboi L, Richard JC. Mechanisms of the effects of prone positioning in acute respiratory distress syndrome. *Intensive Care Med.* 2014 Nov;40(11):1634-1642.
2. Meade MO, Cook DJ, Guyatt GH, et al; Lung Open Ventilation Study Investigators. Ventilation strategy using low tidal volumes, recruitment maneuvers, and high positive end-expiratory pressure for acute lung injury and acute respiratory distress syndrome: a randomized controlled trial. *JAMA.* 2008 Feb 13;299(6):637-645.
3. Peek GJ, Clemens F, Elbourne D, et al. CESAR: conventional ventilatory support vs extracorporeal membrane oxygenation for severe adult respiratory failure. *BMC Health Serv Res.* 2006 Dec 23;6:163.

18. Rationale

Answer: D

There has been tremendous growth in the field of severe acute respiratory distress syndrome (ARDS) during the past 15 years. Most importantly, lung-protective ventilation with tidal volumes near 6 mL/kg predicted body weight has significantly decreased patient mortality. Beyond that, there has been much debate over other adjuncts that may also improve mortality. These include paralytics, optimal positive end-expiratory pressure (PEEP) levels, inhaled pulmonary vasodilators (nitric oxide, epoprostenol), high-frequency oscillatory ventilation, and prone positioning.

This patient has severe ARDS after significant trauma and, despite optimal ventilator management, is still hypoxic with a partial arterial oxygen pressure of 50 mm Hg. At this point, further supportive measures are required to improve oxygenation. PEEP at 22 cm H_2O is near maximum and, on pressure control ventilation with a peak airway pressure of 35 cm H_2O, further titration upwards may subject the lungs to unwanted ventilator-associated lung injury. Permissive hypercapnea in ARDS management is well tolerated, and with a pH of 7.24 and a respiratory rate of 35 breaths/min, no further adjustments should be made. No single mode of ventilation has been proven to be superior to another; therefore, changing the mode to assist control/volume control is unlikely to help. Inhaled pulmonary vasodilators such as epoprostenol and nitric oxide are often used, but no study has shown a decrease in mortality with their use. Furthermore, nitric oxide may be linked to acute kidney injury and is very expensive. Prone ventilation in severe ARDS has been shown to decrease mortality if done early and for long enough periods of time. The patient's subarachnoid hemorrhage with no intracranial pressure issues is not a contraindication to prone ventilation.

References:

1. Guérin C, Reignier J, Richard JC, et al; PROSEVA Study Group. Prone positioning in severe acute respiratory distress syndrome. *N Engl J Med.* 2013 Jun 6;368(23):2159-2168.
2. Ruan SY, Huang TM, Wu HY, Wu HD, Yu CJ, Lai MS. Inhaled nitric oxide therapy and risk of renal dysfunction: a systematic review and meta-analysis of randomized trials. *Crit Care.* 2015 Apr 3;19:137.

3. [No authors listed]. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. The Acute Respiratory Distress Syndrome Network. *N Engl J Med.* 2000 May 4;342(18):1301-1308.

19. Rationale

Answer: B

This patient has a right hemidiaphragm dysfunction, which is probably a complication of her operation. During thoracic surgery, the phrenic nerve can be stretched, crushed, or inadvertently transected. A noninvasive method of measuring diaphragmatic excursion is the fluoroscopic sniff test, in which the patient is instructed to breathe deeply and then sniff in the upright position and again in the lateral position. The lack of caudal movement of the affected diaphragm during deep inspiration and paradoxic movement with sniffing is a positive finding. The test has a false-positive rate of approximately 6% in unilateral diaphragmatic dysfunction and is not helpful in bilateral hemidiaphragmatic dysfunction. Potential treatments include temporary ventilator support, diaphragm plication, and phrenic nerve pacing. Intraoperative nondepolorizing neuromuscular blockade has a half-life of hours, not days. While mucous plugs can contribute to atelectasis and lobar collapse, the last fiberoptic examination was clean in the presence of the raised diaphragm and breath sounds are clear. Tacrolimus toxicity is not associated with diaphragm weakness.

References:

1. McCool FD, Tzelepis GE. Dysfunction of the diaphgram. *N Engl J Med.* 2012 Mar 8;366(10):932-942.
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20. Rationale

Answer: B

Systemic thrombolysis for the treatment of pulmonary embolism is recommended in the presence of hypotension, systolic blood pressure <90 mm Hg, (massive pulmonary embolism [PE]) and low bleeding risk. Patients with signs of right ventricular dysfunction (biomarkers, echocardiographic changes) are less likely to derive direct benefit than those with hemodynamic instability. Evaluation for bleeding includes review of relative and absolute contraindications as well as factors contributing to bleeding (ie, age, gender, race). Both patients B and D have massive PE but patient D has an absolute contraindication for thrombolysis.

References:

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21. Rationale

Answer: D

This patient is having a ventilator crisis, which can be caused by a number of different scenarios. It is important to quickly make the diagnosis while minimizing morbidity and exposure to unhelpful and potentially harmful therapies. A helpful mnemonic is DOPE, which stands for displacement, obstruction, pneumothorax, and equipment failure.

The first thing that should be accomplished is to ensure that the endotracheal tube is still secure and in the correct location and the patient-ventilator circuit is intact and functioning. This should follow a stepwise approach and proceed from the patient to the ventilator. Look, listen and feel at the airway. The endotracheal tube (ETT) should not be pushed out or at a shallower depth than previously recorded. Direct inspection of the airway with a laryngoscope may be required to ensure that the ETT is not above the vocal cords. There should be no audible air leaks, and the pilot balloon should not be deflated or easy to fully compress. A pilot balloon that does not retain pressure probably signals a leak somewhere in the system. If the tube is dislodged or malfunctioning, it should be replaced immediately because this is an emergency. An exhaled tidal volume that is significantly less than prescribed tidal volume strongly suggests tube displacement or cuff leak. A quick inspection of the ventilator tubing will reveal any dislodgment. Next, obstruction is ruled out by placing a suction catheter down the tube.

The P in DOPE classically stands for pneumothorax. Other P's should also be considered: plugging of mucus and too much (auto)-PEEP. Pneumothorax should be evaluated by multiple means. The first is to listen for decreased breath sounds and look for asymmetric chest rise and tracheal deviation. However, clinical examination can be inaccurate. A decrease in compliance, as evidenced by increased ventilator pressures, can often be seen. Empiric treatment of pneumothorax is sometimes required, but this is not the most appropriate next step. A chest radiograph can be helpful but, again, this is not the most appropriate next step because it can take a significant amount of time to obtain, leading to a delay in diagnosis. Provider-initiated point-of-care ultrasound can be used to quickly rule out pneumothorax. Ultrasound and chest radiograph can also diagnose mucus plugging. Examination of ventilator waveforms and performance of an expiratory pause pressure can determine auto-PEEP. In some scenarios, such as a crashing patient with an obstructive lung disease such as asthma or chronic obstructive pulmonary disease, it may be appropriate to disconnect the patient from the ventilator, allow a full exhale and then manually breath for the patient with a bag valve mask (BVM). If the patient is easy to oxygenate and ventilate with a BVM, this suggests ventilator equipment failure. It is only after these maneuvers are tried should other treatment strategies for hypoxemia be initiated.

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2. Mosier JM, Hypes C, Joshi R, Whitmore S, Parthasarathy S, Cairns CB. Ventilator strategies and rescue therapies for management of acute respiratory failure in the emergency department*. Ann Emerg Med.* 2015 Nov;66(5):529-541.

22. Rationale

Answer: E

Pneumothoraces occur commonly in ICU patients, with an estimated frequency of 6%. Lung sliding is a useful tool to detect them. The absence of lung sliding is highly sensitive (95.3%) to detect pneumothoraces, but less specific (91.1%). It can be absent in patients with acute respiratory distress syndrome, emphysematous blebs, pleurodesis, and a multitude of other conditions. Lung ultrasound is more sensitive than anteroposterior films in supine patients after blunt trauma for detecting pneumothoraces, but radiographs have higher specificity. A line artifacts do not rule out pneumothorax, but B line artifacts do. A lines are multiple reflections of the pleural interface. B lines are vertical lines that project from the visceral-parietal pleura interface due to repetitive reflections of the ultrasound waves within the lung parenchyma because of a higher concentration of fluid.

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23. Rationale

Answer: E

Managing the mechanical ventilator for a severe chronic obstructive pulmonary disease (COPD) exacerbation can be a fine balance between ensuring adequate ventilation to prevent life-threatening acidosis and mitigating dangerous levels of intrinsic positive end-expiratory pressure that can develop. Permissive hypercapnea is typically tolerated quite well. In this case, increasing the respiratory rate in order to normalize the blood gas resulted in a reduction in exhalation time. In a patient with severe COPD and expiratory flow limitation, the resultant auto-PEEP resulted in cardiovascular collapse. Disconnecting the patient from the ventilator and allowing him

to exhale may result in return of spontaneous circulation.

Performing bilateral needle thoracostomies may be considered in this case, given the higher likelihood of pneumothoraces in a patient with COPD but this is less likely in this scenario. Similarly, epinephrine is standard for advanced cardiac life support, but that will not solve the problem causing this patient's cardiac arrest. Venoarterial extracorporeal membrane oxygenation could be considered, but attempting other maneuvers first is more prudent. Finally, given the low but still present end-tidal carbon dioxide, it is unlikely that the endotracheal tube has become dislodged.

References:

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24. Rationale

Answer: A

This patient's clinical history and ECG findings are typical of Brugada syndrome. The most common presentation of patients with Brugada syndrome is syncope, ventricular fibrillation-induced cardiac arrest, and cardiac death. ECG findings follow a Brugada pattern, which consists of a pseudo-right bundle branch block and persistent ST segment elevation in leads V1-V3. There have been isolated cases of similar findings involving the inferior ECG leads. Previously, there were three different patterns of ST elevation described and used in practice; subsequent consensus is that there are two distinct patterns: In type 1, the elevated ST segments that are greater than 2 mm descend with an upward convexity to an inverted T wave. This is referred to as the coved-type Brugada pattern. In type 2, the ST segment has a "saddleback" ST-T wave configuration in which the elevated ST segment descends toward the baseline, then rises again to an upright or biphasic T wave.

This patient's ECG illustrates a type 1 Brugada pattern. The average age at diagnosis is 41 and, for unknown reasons, patients with schizophrenia are more likely than the general population to have Brugada-pattern ECGs. There does not seem to be a significant impact of schizophrenia medications, and the Brugada pattern and clinical significance of this association is undetermined. The syndrome is autosomal dominant due to a mutation in a cardiac sodium channel. A mutation in the alpha-subunit gene, SCN5A, has been identified in 15% to 30% of patients.

An implantable defibrillator should be considered to prevent recurrent ventricular fibrillation and sudden death. Thrombolysis is not applicable for patients with Brugada syndrome. Patients treated with type 1a antiarrhythmics, such as procainamide, after cardiac arrest who have normal ECGs at baseline may elicit ECG findings similar to Brugada pattern. Beta-blockers and amiodarone are not helpful in this syndrome and should be avoided.

References:

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2. Wilde AA, Antzelevitch C, Borggrefe M, et al; Study Group on the Molecular Basis of Arrhythmias of the European Society of Cardiology. Proposed diagnostic criteria for the Brugada syndrome. *Eur Heart J.* 2002 Nov;23(21):1648-1654.
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25. Rationale

Answer: C

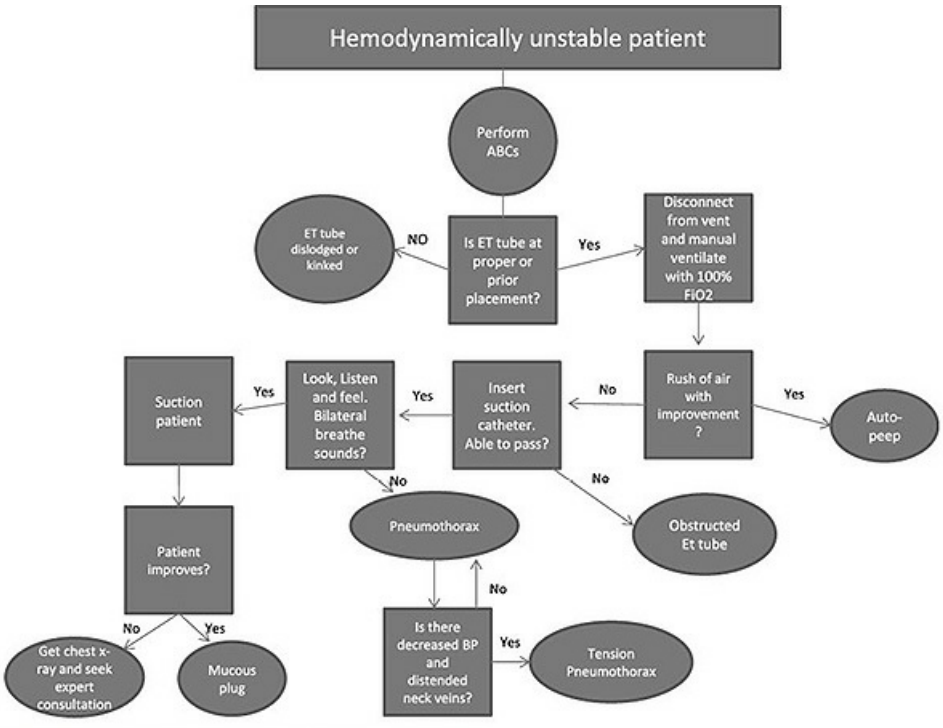
The high peak airway pressure (HPAP) alarm is one of the most common alarms for patients receiving mechanical ventilation. In patients, such as this one, who are hemodynamically unstable, differential diagnosis of HPAP includes auto-PEEP, tension pneumothorax, a kinked or dislodged endotracheal tube (ETT) and a large mucus plug. The diagnostic algorithm for a hemodynamically unstable patient is shown below.

The first step in a hemodynamically unstable patient with HPAP, is to disconnect the patient from the ventilator while assessing whether the ETT is dislodged. If the ETT is properly placed and a rush of air is heard when disconnecting the patient from the ventilator with improvement in hemodynamics within a few seconds, the most likely cause is auto-PEEP. If the problem is not corrected after the patient is disconnected from the ventilator, the next step is to hand-ventilate and assess ease of squeezing and the amount of chest wall rise. If resistance is met and asymmetric chest wall rise is appreciated, the next step is to assess for breath sounds. In the absence of breath sounds, tension pneumothorax should be suspected and needle decompression performed. Lastly, if breath sounds are present, a suctioning catheter should be inserted. If suctioning catheter cannot be passed, a kinked ETT should be suspected. If suctioning catheter passes with ease, the patient should be suctioned. If there is improvement, then mucus plug is the most likely diagnosis.

The high peak inspiratory pressures and low expiratory tidal volume immediately after intubation suggest an airway related problem. In this clinical scenario, an esophageal intubation is of great concern; other clues to ETT misplacement are inability to ventilate and oxygenate with severe respiratory acidosis and hypoxemia in conjunction with HPAP. Changing the ventilator setting to pressure control will decrease the pressure in the airway, but will not correct the underlying problem of a misplaced ETT. This is a life-threatening situation and should be corrected as soon as possible.

Of note, this patient's chest radiograph and end-tidal carbon dioxide (CO_2) suggest

proper ETT placement. While chest radiographs are useful for detecting endobronchial placement of ETT, detecting esophageal intubation may be difficult because the esophagus lies posterior to the trachea. It should never be relied upon to detect esophageal intubation since dealth may result if ETT misplacement is not detected until a radiograph is obtained. The measurement of CO_2 in the exhaled gas has become one of the standard methods of verifying ETT location. CO_2 detection relies on the presence of pulmonary circulation (ie, it might not be detected in patients with inadequate cardiopulmonary resuscitation) and, also, severe airway obstruction may prevent sufficient CO_2 exhalation to be detected by capnometers. Small concentrations of CO_2 may be detected after an esophageal intubation, especially if bag-and-mask ventilation has insufflated exhaled air into the stomach. Repeating chest radiograph to assess for a pneumothorax in a hemodynamically unstable patient will lead to an unnecessary delay in treatment. Tension pneumothorax is a life-threatening condition and, if clinically suspected, needle decompression should be performed without confirmatory test. In this case, the HPAP started right after intubation and chest radiograph performed post-intubation did not show a pneumothorax, making tension pneumothorax less likely. Starting vasopressors would not correct the underlying problem and might delay appropriate treatment. There is no role for bicarbonate infusion since the patient is in severe respiratory acidosis due to a ventilation problem.



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26. Rationale

Answer: C

The optimal technique for central line insertion is constantly being refined. A randomized controlled trial showed that experienced operators can safely place subclavian venous access in critically ill patients using ultrasound guidance. Experienced clinicians benefitted from the use of real-time ultrasound guidance and had lower incidences of mechanical complications, including pneumothoraces and arterial punctures. The ultrasound group also took statistically less time to place venous access, had fewer numbers of attempts and achieved placement 100% of the time compared to the landmark group. In contrast, catheter misplacement was the same in both groups.

Learners who perform the anatomic-based placement technique make six common technical errors: 1) failure to palpate two bony landmarks, 2) failure to insert the needle at the recommended distance of 1 cm inferior and lateral to the medial third of the clavicle, 3) insertion of the needle through the clavicular periosteum, 4) too shallow of a trajectory of the needle, 5) aiming the needle too cephelad, and 6) failure to keep the needle in place for wire passage. Learners are more successful in placing right-sided subclavians rather than left-sided ones, probably due to hand dominance. The use of ultrasound guidance for the subclavian approach is hindered by shadowing from the clavicle, and what is cannulated is the axillary vein, which then joins the subclavian vein. Complication rates from central venous access increase with the number of attempts and the choice of site, as noted in the three-site trial where patients with subclavian lines had 1.5% penumothorax rate versus those with internal jugular lines who had a 0.5% pneumothorax rate.

References:

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27. Rationale

Answer: D

Pulmonary embolism (PE) is associated with variable degrees of pulmonary arterial obstruction, if the clot burden is large, that leads to an acute increase in pulmonary artery pressure. In response to this increased afterload, the right ventricular wall tension increases abruptly, leading to ventricular dilation; the left ventricle under these circumstances can remain normal or even become hyperdynamic. The true sensitivity and specificity of transthoracic echocardiography in the diagnosis of PE is difficult to assess and is related to preexisting conditions such as chronic obstructive pulmonary disease and the size and hemodynamic compromise of the clot burden, but sensitivity ranges from 60% to 90% and specificity ranges from 80% to 95%. Other useful indicators are increase of tricuspid regurgitant peak gradient calculated on a four-chamber view plus central venous pressure that translates into high pulmonary pressure. PE in mechanically ventilated patients is more common than expected; some of these events happen despite adequate thromboprophylactic regimens (52%). The other options are incorrect because none of these echocardiographic changes occur in patients with PE.

References:

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28. Rationale

Answer: C

The rate of pneumothorax complicating permanent pacemaker implantation via the subclavian approach is anywhere from less than 1% to 2.6%. Despite this, routine post-procedural chest radiograph is not always performed in uncomplicated cases. In this patient, the most likely diagnosis, given the constellation of clinical findings of greatly diminished breath sounds on the right side, elevated jugular venous distension,

tachycardia, hypotension with narrowed pulse pressure, tachypnea, and hypoxemia, is tension pneumothorax. The most critical immediate intervention is to perform a needle or tube thoracostomy to relieve the tension and re-expand the lung before the onset of complete hemodynamic collapse. Endotracheal intubation will probably be unnecessary if urgent decompressive thoracostomy is performed, and the likelihood of tolerating anesthetic induction in the presence of a tension pneumothorax is doubtful. Although pulmonary embolism is also a possibility, the absence of breath sounds immediately after this procedure should increase the likelihood of tension pneumothorax. A chest CT angiogram would help to differentiate between these two potential diagnoses, but would only delay the urgent treatment necessary to restore hemodynamic stability. Furthermore, compromising this patient's situation by sending her for a CT in her currently unstable state is not recommended.

References:

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29. Rationale

Answer: E

This multisystem trauma patient is in acute circulatory shock. Trauma patients should receive an organized and rapid team-based resuscitation that follows Advanced Trauma Life Support (ATLS) or Anaesthesia Trauma And Critical Care (ATACC) guidelines. Both of these courses focus on rapid assessment and immediate stabilization of airway, breathing, and circulation. This patient has been successfully intubated, and resuscitation with crystalloids and ideally blood products has begun. Clinical assessment, radiograph, and ultrasound can be used to rapidly diagnosis the cause of acute circulatory shock. Hypovolemic shock from acute blood loss is the most common cause, but obstructive (tension pneumothorax, cardiac tamponade), cardiogenic (blunt cardiac injury), and distributive shock (neurogenic) can also occur.

Extended focuses assessment with sonography in trauma (eFAST) examination can help the clinician rapidly diagnosis tension pneumothorax, pericardial tamponade, and intraperitoneal free fluid, which, in this clinical situation, probably means intra-abdominal bleeding. The patient is hypotensive after initial resuscitation. Chest radiograph does not reveal pneumothorax, and pelvic radiograph reveals no fracture. The view of the right upper quadrant on the eFAST examination reveals fluid in the Morrison pouch between the liver and kidney. In this clinical scenario, these findings cause concern for intra-abdominal hemorrhage. The patient should immediately undergo exploratory laparotomy and damage control surgery focusing on rapid control

of life-threatening hemorrhage and control of contamination (as opposed to a definitive and complete operation).

The placement of IV access is critically important in the unstable trauma patient. The ability to provide rapid fluid resuscitation is required because hypovolemic shock from acute blood loss is the most likely cause of acute circulatory shock in this patient. If adequate peripheral access is obtained, obtaining central access should not delay surgical control of bleeding. If central venous access is needed, it is necessary to understand the differences and strengths of different types of central venous access. Standard triple-lumen catheters are useful for administering multiple different medications at once as well as vasopressors. Their length and relatively narrow internal diameters do not facilitate rapid flow. In fact, the distal brown lumen of a triple-lumen catheter has a slower maximum flow rate (52 mL/min) than a 20-gauge peripheral IV (60 mL/min). If central access is required, a cordis or introducer should be used. A pressure bag or rapid infuser will greatly increase flow.

Diagnostic peritoneal lavage (DPL) is unnecessary in the setting of a positive eFAST examination in this hemodynamically unstable blunt trauma patient. DPL is an alternative to eFAST for the detection of massive hemorrhage in an unstable trauma patient, although it can require more time, and is invasive and prone to more complications in inexperienced hands. The presence of a positive eFAST examination makes DPL unnecessary and the time wasted delaying surgery could be harmful.

Blunt trauma patients often have injuries of multiple different organ systems. A major concern is delayed treatment of other life-threatening injuries. It may be tempting to obtain a CT to rule out intracranial injuries. However, delaying control of life-threatening bleeding can prove fatal. Management of neurotrauma focuses on preserving cerebral perfusion pressure, which is equal to mean arterial pressure minus intracranial pressure. Hemorrhage and hypotension should be managed before diagnosis of potential intracranial injuries. Empiric placement of an intracranial monitor is controversial at best in an under-resuscitated patient. Either way it should not delay damage control surgery.

References:

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2. Greene N, Bhananker S, Ramaiah R. Vascular access, fluid resuscitation, and blood transfusion in pediatric trauma. *Int J Crit Illn Inj Sci.* 2012 Sep;2(3):135-142.

30. Rationale

Answer: C

After abdominal surgery, this patient is at risk for reintubation. He is hemodynamically stable and conscious. A multicenter prospective trial evaluated patients after abdominal surgery at risk of reintubation. Patients with high risk of reintubation were randomized to either noninvasive ventilation or supplemental oxygen. The noninvasive

ventilation group had significantly fewer patients who required reintubation (33% vs. 45%). In patients with low risk of reintubation, use of high-flow nasal cannula reduced the risk of reintubation (4.9% vs. 12.3%). The benefit of high-flow nasal cannula in high-risk patients compared to noninvasive ventilation has not been studied. However, it is important to not delay reintubation if noninvasive ventilation does not improve the respiratory failure or if the patient develops other indications for intubation, such as inability to control the airway or hemodynamic instability. Delaying intubation in these situations increases mortality.

References:

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2. Jaber S, Lescot T, Futier E, et al; NIVAS Study Group. Effect of noninvasive ventilation on tracheal reintubation among patients with hypoxemic respiratory failure following abdominal surgery: a randomized clinical trial. *JAMA.* 2016 Apr 5;315(13):1345-1353.

31. Rationale

Answer: C

Adequate fetal oxygenation requires a maternal arterial oxygen tension (PaO_2) greater than 70 mm Hg, which corresponds to an oxygen saturation as measured by pulse oximetry of 95%. Hypoxemia in the pregnant patient has dual impact on the mother and fetus and should be immediately reversed with supplemental oxygen. Pregnancy induces anatomic changes that include an elevated diaphragm and an increase in diameter of the chest cavity. Pregnancy leads to decreased functional residual capacity and increased minute ventilation. Hypoxemia during airway management has the potential to be a severe cause of morbidity and mortality, even more so in the hypoxic pregnant patient with limited reserve. Even with preoxygenation, patients with little reserve can have rapid desaturation events during airway manipulation. Nasal prongs are ubiquitous in most healthcare settings. A simple intervention is to start high-flow oxygenation at 10-15 L/min with any planned airway manipulation. Even with induction and/or paralysis, oxygen will still move down-gradient into the alveoli and diffuse into the passing oxygen-poor bloodstream. Apneic oxygenation has been shown to delay time to desaturation and maintain a higher PaO_2 throughout the intubation procedure. In fact, this technique is often used during brain death examinations to prevent hypoxemia. Carbon dioxide continues to diffuse from the bloodstream into the alveoli but does not travel further (leading to less diffusion and increased buildup in the circulating blood). Apneic oxygenation does not protect against hypercapnia or respiratory acidosis, similar to what is induced with the brain death examination. No data exist to show that apneic oxygenation decreases the incidence of anoxic brain injury in the fetus.

References:

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32. Rationale

Answer: E

This patient has severe acute respiratory distress syndrome (ARDS) based on a partial arterial oxygen pressure-to-fraction of inspired oxygen ratio of less than 100. Various interventions for refractory hypoxemia have been covered in the literature, such as 1) alveolar recruitment with dedicated ventilator recruitment maneuvers, 2) following positive end-expiratory pressure (PEEP) tables to increase mean airway pressure, 3) open-lung ventilation strategies such as airway pressure release ventilation, 4) inhaled pulmonary vasodilators to help with ventilation/perfusion mismatch, 5) paralytic infusions, and 6) prone positioning. Recently, Guerin et al showed that prone positioning applied early in severe ARDS led to an absolute risk reduction in mortality of approximately 16%. Their strategy was to apply prone positioning early, after a stabilization period, and for at least 16 hours a day. Their data showed no difference in the incidence of complications, including extubations, between the study groups. The OSCILLATE trial investigators showed an increase in mortality in moderate to severe ARDS with early application of high-flow oscillator ventilation. This patient already has a plateau pressure of 29 mm H_2O. Increasing the PEEP to 15 cm H_2O will have the effect of pushing his pleateau pressure above 30 cm H_2O, unless compliance improves with increased PEEP, and prior ARDS data has shown increased mortality with maintained plateau pressure over 30 cm H_2O. Referral to a center capable of providing venovenous extracorporeal membrane oxygenation (ECMO) was shown to reduce mortality in severe ARDS, but there are several potential therapies before initiating ECMO. Inhaled nitric oxide has been shown to improve oxygenation, but does not improve outcome, and is associated with kidney injury.

References:

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33. Rationale

Answer: C

Risk stratification of acute respiratory distress syndrome (ARDS) into mild, moderate, and severe allows clinicians to label hypoxic patients and offer evidence-based treatment strategies. As an intensivist, basic understating of this severity scale will help with acute management. The Berlin definition of 2011 states, “ARDS is an acute diffuse, inflammatory lung injury, leading to increased pulmonary vascular permeability, increased lung weight, and loss of aerated lung tissue… [with] hypoxemia and bilateral radiographic opacities, associated with increased venous admixture, increased physiological dead space and decreased lung compliance.” Timing of onset must be within one week of a known clinical insult or new or worsening respiratory symptoms. Oxygenation definitions were based on a partial arterial oxygen pressure (PaO_2)-to-fraction of inspired oxygen (FIO_2) ratio with the patient receiving a minimum of 5 cm H_2O positive end-expiratory pressure (PEEP): mild (200 mm Hg < PaO_2:FIO_2 ≤ 300 mm Hg), moderate (100 mm Hg < PaO_2:FIO_2 ≤ 200 mm Hg), severe (≤100 mm Hg). To diagnose ARDS, cardiogenic pulmonary edema must be ruled out. The treatment algorithm differs depending on both the degree of hypoxemia and the severity of ARDS, including PEEP titration.

References:

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34. Rationale

Answer: C

The option with the most literature support is a successful spontaneous breathing trial (SBT). In the United States, about 800,000 patients need mechanical ventilation every year for acute respiratory failure of different etiologies. Once all the inflammatory, metabolic, traumatic, or infectious conditions that led to intubation are resolved, the patient should be transitioned to SBT before extubation. It has been shown that ICU protocol-driven extubation shortens ventilation days. For an SBT to be successful, the patient must breath spontaneously with little or no ventilator support for at least 30 minutes without tachypnea (respiratory rate greater than 35 breaths/min), no oxygen desaturation below 90%, heart rate below 140 beats/min, no systolic blood pressure fluctuations of more than 180 or less than 90 mm Hg, no anxiety, and no diaphoresis. If this is successful, the patient should be able to protect the airway without too many secretions. All the other options, although useful, are not supported by literature in and of themselves.

Reference:

1. McConville JF, Kress JP. Weaning patients from the ventilator. *N Engl J Med.*

2012 Dec 6;367(23):2233-2239.

35. Rationale

Answer: C

Compliance is defined as a change in volume for any given pressure change. It has two different measurements: static compliance (Cstat) and dynamic compliance (Cdyn). Cstat reflects pulmonary compliance in periods without gas flow. The plateau pressure is the pressure at end inspiration when gas flow ceases. This will account for both chest wall and lung compliance.

Cdyn is measured while gas continues to flow. This also reflects the contribution of lung and airway resistance. Cdyn = VT/(peak airway pressure - PEEP). Cstat is the ratio of tidal volume to the difference between plateau pressure and PEEP. Cstat = VT/(plateau airway pressure [Pplat] - PEEP) = 500/(35-10) = 20.

References:

1. Lu, Q, Rouby, JJ. Measurement of pressure-volume curves in patients on mechanical ventilation. Methods and significance. *Crit Care.* 2000;4(2):91-100.
2. Grinnan DC, Truwit JD. Clinical review: respiratory mechanics in spontaneous and assisted ventilation. *Crit Care.* 2005 Oct 5;9(5):472-484.

36. Rationale

Answer: C

Increases in peak inspiratory pressure (PIP) without significantly increasing the plateau pressure, suggest that the increase in pressure from baseline is due to an increase in airway resistance, not a decrease in lung compliance. Since air is not moving when the plateau pressure is measured (during an inspiratory pause maneuver), the plateau pressure is not altered by changes in airflow resistance through the airways. This patient has pneumonia and is probably producing a lot of mucus and secretions that he is unable to cough up because of his deep level of sedation causing airway obstruction and mucus plugging after being turned. Tension pneumothorax, migration of the tube (mainstem intubation), and air trapping (breath stacking) all have an increase in plateau pressure as well as an increase in PIP. A pulmonary embolism would not be expected to have any effect on airway pressures.

Reference:

1. Marino PL. Principles of mechanical ventilation. In: *The ICU Book.* 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007: ch. 24.

37. Rationale

Answer: E

Static lung compliance is defined as the change in volume for a given applied

pressure: Static compliance (Cstat) = tidal volume/(plateau pressure [PPlat] - positive end-expiratory pressure [PEEP]). Common causes of decreased static lung compliance ("stiff lungs") include restrictive lung diseases, pneumothorax, pleural effusion, and acute respiratory distress syndrome.

Dynamic lung compliance is the compliance of the lungs during movement of air: Dynamic compliance (Cdyn) = tidal volume/(peak inspiratory pressure [PIP] - PEEP). It is more directly affected by obstructive physiology, such as endotracheal tube occlusion, bronchial secretions, or bronchospasm.

This patient has decreased dynamic lung compliance, demonstrated by the increase in PIP, but static lung compliance is unchanged. This suggests an obstructive process such as bronchospasm.

Reference:

1. Marino PL. Principles of mechanical ventilation. In: *The ICU Book.* 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007: ch. 24.

38. Rationale

Answer: E

The flow volume loop demonstrates a leak in the ventilator circuit. Inspired volume is greater than exhaled volume. This can be at any level in the circuit but commonly a ruptured balloon can cause a leak. In the setting of a circuit leak, decreasing the tidal volume would decrease minute volume and increase end-tidal carbon dioxide, and might worsen oxygenation by permitting alveolar collapse. Inhaled bronchodilators are not appropriate since there is no evidence of acute obstructive lung disease. Suctioning the endotracheal tube is not likely to be effective since there is no evidence of intrathoracic obstruction. Reintubating the patient might be necessary but this would not be the next step since the cuff might require simple reinstillation of air.

References:

1. Main E, Castle R, Stocks J, James I, Hatch D. The influence of endotracheal tube leak on the assessment of respiratory function in ventilated children. *Intensive Care Med*. 2001 Nov;27(11):1788-1797.
2. Guntupalli KK, Bandi V, Sirgi C, Pope C, Rios A, Eshenbacher W. Usefulness of flow volume loops in emergency center and ICU settings. *Chest.* 1997 Feb;111(2):481-488.

39. Rationale

Answer: A

This patient has pulmonary arterial hypertension (PAH), and right heart failure. She has New York Heart Association (NYHA) functional class (FC) IV symptoms (dyspnea at rest/right heart failure). The hemodynamics are consistent with severe PAH with depressed cardiac output and cardiac index and a severely elevated pulmonary

vascular resistance. The elevated right atrial pressure and low cardiac index are poor prognostic indicators.

For a patient with NYHA FC IV symptoms, the treatment of choice is IV epoprostenol. It is the only medication with a class I indication for NYHA FC IV PAH, based on the 2013 National Institute for Health Care Excellence guidelines and the 2015 European Society of Cardiology (ESC)/European Respiratory Society (ERS) guidelines, level of evidence grade A. In a clinical trial by Barst et al, epoprostenol was shown to increase six-minute walk distance, and there was a survival benefit seen in patients on therapy (no deaths in the treatment group, but there were 8 deaths out of 40 patients in the placebo group). Epoprostenol is administered as a continuous IV infusion. It has a short half-life (3 to 5 minutes) and requires a pump to ensure delivery. The infusion cannot be interrupted because stopping it can lead to severe rebound pulmonary hypertension, which can be fatal.

Inhaled epoprostenol has been proposed as an alternative to inhaled nitric oxide in the ICU. There is no data on the use of inhaled epoprostenol in right heart failure. Treprostinil was initially approved for subcutaneous administration for patients with idiopathic PAH and PAH associated with connective tissue disease. It is also a continuous infusion, but has a longer half-life than epoprostenol. IV treprostinil has been shown to have bioequivalence, but there is no data in NYHA FC IV patients. The 2015 ESC/ERS guidelines give it a Class 2b recommendation, with a level of evidence of C for NYHA FC IV PAH.

Ambrisentan and tadalafil are both oral medications approved for treatment of PAH. In the AMBITION study, these agents were shown to have less “clinical worsening events” in NYHA FC II and III patients when started in combination at the time of diagnosis compared to starting either of the medications alone. The combination has not been studied in NYHA FC IV patients. Oral sildenafil has been shown to improve exercise capacity in NYHA FC II and III PAH. It has not been studied in NYHA FC IV PAH. In the 2015 ESC/ERS guidelines, oral sildenafil is given a level 2b recommendation in FC IV PAH, level of evidence C. The IV form was approved in 2009 for continuation of treatment in patients who cannot continue their oral therapy. There is no data on the combination of oral sildenafil and IV sildenafil.

References:

1. Galiè N, Corris PA, Frost A, et al. Updated treatment algorithm of pulmonary arterial hypertension. *J Am Coll Cardiol.* 2013 Dec 24;62(25 Suppl):D60-D72.
2. Galiè N, Humbert M, Vachiery J, et al. 2015 ESC/ERS guidelines for the diagnosis and treatment of pulmonary hypertension: The Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS): Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC), the International Society for Heart and Lung Transplatation (ISHLT). *Eur Heart J.* 2016 Jan 1;37(1):67-119.
3. Barst RJ, Rubin LJ, Long WA, et al; Primary Pulmonary Hypertension Study Group. A comparison of continuous intravenous epoprostenol (prostacyclin) with conventional therapy for primary pulmonary hypertension. *N Engl J Med.* 1996

Feb 1;334(5):296-302.
4. Galiè N, Barberà JA, Frost A, et al; AMBITION Investigators. Initial use of ambrisentan plus tadalafil in pulmonary arterial hypertension. *New Engl J Med.* 2015 Aug 27;373(9):834-844.

40. Rationale

Answer: B

The right heart does not tolerate the changes that come with surgery and intubation due to the effects on cardiac output (CO) and pulmonary vascular resistance (PVR). The right heart is susceptible to increases in PVR. During surgery, hypoxemia, hypercarbia, and acidosis should all be avoided because they can lead to PVR increases. Maintaining the CO and avoiding myocardial depressants is also important. Despite the issues that PAH patients have with surgery, surgery may still be necessary.

Managing medications through the perioperative period can be challenging. Some of the effects of prostacyclins are pulmonary vascular vasodilatation, inhibition of platelet aggregation, and antiproliferative effects in the pulmonary circulation. Three prostacyclins are currently approved in the United States, each with different routes of administration: epoprostenol (IV), treprostinil (subcutaneous, inhaled, and oral) and iloprost (inhaled).

Epoprostenol is a synthetic prostacyclin and was the first medication approved for treating PAH. It has a very short half-life of 3 to 5 minutes and therefore must be administered by continuous infusion. It is not stable at room temperature and must be kept chilled. A newer version uses a buffer at a different pH that allows better stability at room temperature and therefore chilling is not needed. Because of its short half-life, abrupt discontinuation can lead to severe rebound pulmonary hypertension, which can be fatal. Although prostacyclins have platelet inhibitory effects, they should not be stopped for procedures because of the risk of rebound pulmonary hypertension.

Treprostinil is a prostacyclin analog that initially was approved for subcutaneous administration. It has a longer half-life of 4 to 5 hours. IV, inhaled, and oral versions have since been approved. Iloprost is a prostacyclin analog with a short half-life that is administered via nebulization every 2.5 to 3 hours.

Sildenafil, a phosphodiesterase type-5 inhibitor (PDE5-I), is approved for treating PAH. It works via the nitric oxide pathway. By blocking PDE5, the breakdown of cyclic GMP is inhibited, leading to vasodilation. In clinical trials sildenafil has been shown to increase exercise capacity and improve hemodynamics in patients with PAH. In the PACES study, the combination of epoprostenol and high-dose sildenafil was shown to provide additional benefit compared to epoprostenol alone. An IV version has been approved and can be substituted in patients who are unable to take oral medications. The sildenafil dose is halved when administered intravenously.

There is retrospective data to show that warfarin may provide a survival benefit in patients with PAH. The use of warfarin in these patients is recommended. Holding warfarin in this patient is necessary for surgery and can be done safely. Because the

surgery is planned for today, the INR will need to be reversed. Postoperatively, a heparin-based therapy can be used until it is safe to restart the warfarin.

References:

1. Ortega R, Connor C. Intraoperative management of patients with pulmonary hypertension. *Adv Pulm Hypertens.* 2013 Spring;12(1):18-23.
2. Dezube R, Housten T, Mathai S. Post-operative care of the patient with pulmonary hypertension. *Adv Pulm Hypertens.* 2013 Spring;12(1):24-30.
3. Galiè N, Corris PA, Frost A, et al. Updated treatment algorithm of pulmonary arterial hypertension. *J Am Coll Cardiol*. 2013 Dec 24;62(25 Suppl):D60-D72.
4. Simonneau G, Rubin LJ, Galiè N, et al; PACES Study Group. Addition of sildenafil to long-term intravenous epoprostenol therapy in patients with pulmonary arterial hypertension: a randomized trial. *Ann Intern Med.* 2008 Oct 21;149(8):521-530.

41. Rationale

Answer: B

This patient has a submassive pulmonary embolism (PE), causing significant symptoms and evidence of right ventricular (RV) failure, but without hemodynamic instability. The only clear indication for thrombolytics is massive PE with hemodynamic instability. Thrombolytics may be considered in submassive PE with worsening RV failure, worsening dyspnea, or worsening hemodynamics on a case-by-case basis. The PEITHO study showed that, while there is a modest improvement in mortality/prevention of hemodynamic instability with thrombolytics, there is a significant increase in extracranial, cranial, and major bleeding. This was confirmed by a subsequent meta-analysis, but it is also known that patients with RV dysfunction and submassive PE have mortality twice that of those without it. Intubation is not indicated here because the patient has improved significantly on high-flow nasal cannula. Duplex ultrasound of the legs would be indicated later on but is not the most appropriate next step. There is no indication for an inferior vena cava filter at this point.

References:

1. Cho JH, Kutti Sridharan G, Kim SH, et al. Right ventricular dysfunction as an echocardiographic prognostic factor in hemodynamically stable patients with acute pulmonary embolism: a meta-analysis. *BMC Cardiovasc Disord.* 2014 May 6;14:64.
2. Meyer G, Vicaut E, Danays T, et al; PEITHO Investigators. Fibrinolysis for patients with intermediate-risk pulmonary embolism. *N Engl J Med.* 2014 Apr 10;370(15):1402-1411.
3. Riera-Mestre A, Becattini C, Giustozzi M, Agnelli G. Thrombolysis in hemodynamically stable patients with acute pulmonary embolism: a meta-analysis. *Thromb Res.* 2014 Dec;134(6):1265-1271.
4. Konstantinides SV. 2014 ESC guidelines on the diagnosis and management of acute pulmonary embolism. *Eur Heart J.* 2014 Dec;35(45):3145-3146.

42. Rationale

Answer: D

This presentation is most consistent with massive pulmonary embolism (PE). Patients presenting with PE have a wide spectrum of clinical severity. While some patients have frank hemodynamic collapse and cardiac arrest, others have an asymptomatic PE that is discovered incidentally during workup of another condition. When a patient presents with suspected acute PE, initial resuscitative therapy should focus on oxygenation and stabilizion. There are multiple degrees of therapy; the treatment plan should be tailored to the patient relative to the presentation. Resuscitative therapy ranges from supplemental oxygen to ventilator support, hemodynamic support, anticoagulation, and/or fibrinolysis.

The use of fibrinolytics in acute PE remains a controversial topic. Most agree that cardiac arrest and haemodynamic instability with systolic blood pressure less than 90 mm Hg is an indication for thrombolysis. With the increased use of bedside ultrasonography, there is now an aid to diagnosis that may also determine treatment. If a patient is hemodynamically unstable with echocardiographic evidence of right heart dilation and dysfunction, then the next step should be thrombolytic therapy once absolute contraindications have been ruled out. Controversy still exists on appropriate treatment for stable patients with right ventricular dysfunction on echocardiography.

This patient has already had two cardiac arrests and is too unstable for confirmatory CT; therefore the initiation of thrombolytics is warranted.

References:

1. Fengler BT, Brady WJ. Fibrinolytic therapy in pulmonary embolism: an evidence-based algorithm. *Am J Emerg Med.* 2009 Jan;27(1):84-95.
2. Roy PM, Colombet I, Durieux P, Chatellier G, Sors H, Meyer G. Systematic review and meta-analysis of strategies for the diagnosis of suspected pulmonary embolism. *BMJ.* 2005 Jul 30;331(7511):259.
3. Goldhaber SZ. Echocardiography in the management of pulmonary embolism. *Ann Intern Med.* 2002 May 7;136(9):691-700.
4. Kenny JF, Zhong X, Brown C, Das D, Royall B, Kapoor M. Bedside echocardiography for undifferentiated hypotension: diagnosis of a right heart thrombus. *West J Emerg Med.* 2015 Jan;16(1):178-180.

43. Rationale

Answer: A

The British Thoracic Society (BTS), because of serious harm (12 deaths and 15 cases of serious harm) caused by the placement of chest tubes between 2005 and 2008, developed a set of guidelines for chest tube insertion. The guidelines recommend a standardized training program before performing the procedure, using ultrasound when possible and small-bore chest tube placement first except to drain hemothoraces. The BTS guidelines also recommended needle drainage of pneumothoraces and only placement of a chest tube, if needle drainage fails. These

recommendations are not supported by a significant amount of evidence, but in this patient the placement of a surgical chest tube by a trainee is questionable. The radiograph causes concern for the surgical chest tube entering the mediastinum. The patient's fever and tachycardia cause concern for mediastinitis. A CT to locate the chest tube is indicated, and consultation with a thoracic surgeon will possibly be needed. The initial pneumothorax did not resolve because the small-bore chest tube was clogged. This occurs more frequently with small-bore catheters than with large-bore chest tubes, but flushing small-bore chest catheters often relieves this problem.

References:

1. Kulvatunyou N, Vijayasekaran A, Hansen A, et al. Two-year experience of using pigtail catheters to treat traumatic pneumothorax: a changing trend. *J Trauma.* 2011 Nov;71(5):1104-1107.
2. Havelock T, Teoh R, Laws D, Gleeson F; BTS Pleural Disease Guideline Group. Pleural procedures and thoracic ultrasound: British Thoracic Society Pleural Disease Guideline 2010. *Thorax.* 2010 Aug;65(Suppl 2):ii61-ii76.
3. Tsai WK, Chen W, Lee JC, et al. Pigtail catheters vs large-bore chest tubes for management of secondary spontaneous pneumothoraces in adults. *Am J Emerg Med.* 2006 Nov;24(7):795-800.
4. Contou D, Razazi K, Katsahian S, et al. Small-bore catheter versus chest tube drainage for pneumothorax. *Am J Emerg Med.* 2012 Oct;30(8):1407-1413.
5. Liman ST, Elicora A, Akgul AG, et al. Is a small-bore catheter efficient for most pleural pathologies? *Surg Today*. 2014 May;44(5):834-838.

44. Rationale

Answer: D

This patient has symptomatic massive airway hemorrhage and requires airway management to prevent complete obstruction and hypoxia. Video laryngoscopy might be more difficult than direct laryngoscopy because the camera view is obstructed by blood. Even though he has supraglottic obstruction, bilevel positive airway pressure might drive blood and thrombi deeper into his trachea and make his own clearance mechanisms less effective. Cannulation for venovenous extracorporeal membrane oxygenation would not be the fastest way to restore oxygenation and would require some anticoagulation, which could worsen bleeding. Awake cricothyroidotomy might be necessary, but would not be the first step unless traditional direct laryngoscopy were deemed impossible. For hemoptysis localized to an individual lung, positioning the patient with the bleeding lung down might help prevent aspiration-induced hypoxemia in the nonbleeding lung.

References:

1. Johnson JL. Manifestations of hemoptysis. How to manage minor, moderate, and massive bleeding. *Postgrad Med.* 2002 Oct;112(4):101-113.
2. Jean-Baptiste E. Clinical assessment and management of massive hemoptysis. *Crit Care Med.* 2000 May;28(5)1642-1647.

Part 4:

Critical Care Infectious Diseases

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Critical Care Infectious Diseases

Instructions: For each question, select the most correct answer.

1. A 66-year-old man with a past medical history of diabetes mellitus, hypertension, depression, and anaphylaxis due to cephalosporins and vancomycin is admitted

to the ICU after a motor vehicle collision. After two weeks in the hospital, his temperature is 39.1°C (102.4°F). He is taking citalopram, trazodone, tramadol, and fentanyl as needed for pain. Complete blood cell count shows hemoglobin level of 7.4 g/dL, white blood cell count 2,000/μL, and platelet count 60,000/μL. Cultures from peripheral blood and central venous catheters rapidly grow gram-positive cocci in clusters. Other cultures are negative. Chest radiograph shows a tracheostomy and a right internal jugular central line in place. No significant lung infiltrates are noted. Direct molecular assay identifies the organism in the blood as methicillin-resistant *Staphylococcus aureus.* Conventional (nonmolecular) testing of sensitivities is pending.

After removing the central line, which of the following drugs is the best choice for this patient?

A. Linezolid
B. Piperacillin/tazobactam
C. Meropenem
D. Daptomycin
E. Vancomycin

2. A 70-year-old man with a past medical history of chronic kidney disease and chronic obstructive pulmonary disease is admitted from a nursing facility with healthcare-associated pneumonia and respiratory failure necessitating intubation. He is started on an empiric antimicrobial regimen of cefepime and vancomycin. On day three of treatment, the regimen is consolidated to vancomycin alone based on bronchoalveolar lavage analysis, which shows abundant polymorphonuclear cells, many gram-positive cocci, and abundant methicillin-resistant *Staphylococcus aureus* (MRSA) on culture with a vancomycin minimum inhibitory concentration of 2 μg/mL. On day five, he continues to require full respiratory support and has intermittent fever. The vancomycin trough level was 16.7 μg/mL on day two and is 15.2 μg/mL on day five.

   Which of the following is the most appropriate antimicrobial therapy for treatment of this patient's MRSA?

   A. Daptomycin, 6 mg/kg IV every 24 hours
   B. Increasing vancomycin dose to achieve trough level closer to 20 μg/mL
   C. Linezolid, 600 mg IV every 12 hours
   D. Tigecycline, 100 mg IV once, then 50 mg every 12 hours

3. A 19-year-old woman who is 29 weeks pregnant and lives on a dairy farm is admitted to the ICU with acute meningitis and shock. Cerebrospinal fluid analysis shows white blood cell count of 9,500/hpf, red blood cell count 200/hpf, protein level 242 mg/dL, and glucose level 19 mg/dL. Initial Gram stain is pending.

   Which of the following is the best empiric antibiotic regimen for this patient?

   A. Vancomycin and ceftriaxone

B. Meropenem, trimethoprim/sulfamethoxazole, and vancomycin
C. Vancomycin, cefotaxime, and ampicillin
D. Vancomycin and chloramphenicol

4. A 48-year-old man is diagnosed with septic shock due to a urinary tract infection. His past medical history is significant for poorly controlled diabetes and hypertension. After 24 hours of treatment with ciprofloxacin, he remains febrile and in shock. An abdominal/pelvic CT shows a dilated right renal pelvis and gas in the right kidney extending beyond the Gerota fascia. No ureteral stones are present.

   Which of the following is the best next step in this patient's care?

   A. Broadened antibiotic coverage to cover gas-forming organisms with gentamicin and meropenem
   B. Broadened antibiotic coverage, goal-directed resuscitation per the Surviving Sepsis Guidelines, and an insulin infusion to maintain strict glycemic control
   C. Emergency surgical consultation for nephrectomy
   D. Placement of a right nephrostomy tube in preparation for surgery

5. A young adult is found unresponsive at a party with dried gastric contents around his mouth. His teeth are in good repair. He is intubated without difficulty for poor airway protection and empirically given clindamycin and ampicillin/sulbactam for community-acquired aspiration pneumonia. He is extubated on day two. He reports a sore throat and productive cough of clear phlegm. Oxygen saturation is 95% on 2 L/min nasal cannula. Maximal temperature is 38°C (100.4°F). Laboratory results are normal except for white blood cell count of 12,000/μL and procalcitonin level of 1.2 μg/L. Blood culture results are negative. Chest radiography reveals improved pulmonary infiltrates. He wants to sign out against medical advice.

   Which of the following are the most likely diagnosis and the best recommendation regarding antibiotics?

   A. Aspiration pneumonia, no antibiotics
   B. Aspiration pneumonia, oral antibiotics
   C. Aspiration pneumonia, parenteral antibiotics
   D. Chemical (aspiration) pneumonitis, no antibiotics
   E. Chemical (aspiration) pneumonitis, oral antibiotics

6. A 68-year-old man sustains an acute subdural hematoma and grossly contaminated open skull fracture in a fall. He has diabetes mellitus and hypertension. He is admitted requiring surgical evacuation.

   Which of the following is the best recommendation regarding antibiotic prophylaxis in this patient?

A. No antibiotic prophylaxis is required.
B. Antibiotic prophylaxis is required only if the patient is febrile.
C. Anaerobic coverage with metronidazole is required.
D. A combination of vancomycin and ceftazidime is required.
E. Antifungal coverage with fluconazole is required.

7. A 64-year-old man with septic shock is admitted to the ICU. The Centers for Medicare and Medicaid Services core measures for the management of septic shock require that the patient's volume status be reassessed within six hours.

   Which of the following assessments qualify for full reassessment?

   A. Passive leg raise
   B. Cardiovascular ultrasound
   C. Mixed venous blood gas analysis
   D. Comprehensive physical examination
   E. Central venous pressure

8. A 29-year-old man with no significant medical history is admitted to the medical ICU with acute liver failure. He was healthy until he started having nausea about 10 days ago and noted throughout the week that his eyes were turning yellow and his urine was very dark. He also reports fever, headache, and general malaise. He denies IV drug abuse and has one tattoo from five years ago. He says that he drinks socially and often has one beer nightly after a day of work cleaning sewers. He denies any toxic ingestion, does not take medications, and has no family history of liver disease. On examination, he is alert and oriented with stable vital signs and is afebrile. His entire body is jaundiced, and his abdomen is soft without ascites. Laboratory assessment shows: white blood cell count 24,400/μL, hematocrit 35 g/dL, platelets 122,000/μL, sodium 140 mEq/L, potassium 4.0 mEq/L, bicarbonate 26 mEq/L, blood urea nitrogen 101 mg/dL, creatinine 4.05 mg/dL, total bilirubin 45 mg/dL, direct bilirubin 34 mg/dL, aspartate aminotransferase 192 U/L, alanine aminotransferase 227 U/L, alkaline phosphatase 73 U/L, and acetaminophen level negative.

   Which of the following is/are the most appropriate next step(s) in management?

   A. Obtain hepatitis panel and start IV lamivudine.
   B. Consult a nephrologist for urgent dialysis.
   C. Obtain ethanol level and urine drug screen and start prednisone for probable alcoholic hepatitis.
   D. Start IV penicillamine and notify transplant surgery.
   E. Start IV doxycycline and continue supportive care.

9. A 73-year-old man with a history of hypertension, diabetes, chronic obstructive pulmonary disease, and benign prostatic hyperplasia is postoperative day three

after hip fracture surgery complicated by significant blood loss. He was extubated yesterday and weaned off vasopressors this morning. He is afebrile. This morning, the nurse notes that the urine in the indwelling catheter collection bag is cloudy. Urinalysis demonstrates budding yeasts, and urine culture demonstrates *Candida* species.

Which of the following is the most appropriate next step?

A. Start fluconazole.
B. Obtain blood cultures.
C. Obtain an ophthalmologic examination.
D. Replace the indwelling urinary catheter.

10. A young woman is admitted to the hospital for cellulitis after she abraded her hand on a metal gate. A few hours later, she develops fever, rigors, and an increasingly swollen, erythematous hand, shown below. Palpation of the hand reveals crepitus.

Which of the following is the most important intervention?

A. Obtain surgical consultation.
B. Broaden antibiotics to cover anaerobes.
C. Begin resuscitation with 2-liter normal saline bolus.
D. Elevate the hand to reduce swelling.

11. A 54-year-old man is admitted to the ICU for hypotension. One month ago, he was discharged from the hospital after a two-week course of vancomycin and

cefepime for healthcare-associated pneumonia. Three days ago, he underwent a transrectal ultrasound-guided prostate biopsy, after which he visited the emergency department for fever and chills and was sent home with oral ciprofloxacin. He returned to the emergency department this morning with worsening fatigue, fever, chills, and hypotension, and was admitted to the ICU. He was started on IV piperacillin/tazobactam. Forty-eight hours later, he has a blood pressure of 80/50 mm Hg and tachycardia. Preliminary blood cultures are pending. He is receiving fluid resuscitation and vasopressor support.

Which of the following is the most appropriate next course of treatment for this patient?

A. Add a fourth-generation cephalosporin.
B. Add vancomycin for gram-positive coverage.
C. Switch his antibiotic to a carbapenem.
D. Add colistin.
E. Continue piperacillin/tazobactam.

12. A 37-year-old man is admitted to the hospital for alcoholic-induced pancreatitis and has been in the ICU for 52 days. He has undergone pancreatic necrosectomy and multiple subsequent debridement surgeries. He has had several transcutaneous drains placed by interventional radiology into multiple intra-abdominal abscesses. He is febrile with leukocytosis. His most recent culture results show that he has polymicrobial growth, including gram-negative bacilli, anaerobic; gram-negative bacilli, aerobic, lactose fermenter, oxidase-negative, indole-positive; gram-positive cocci in chains, aerobic, no hemolysis. The attending physician selects the appropriate broad-spectrum antimicrobial therapy while awaiting formal speciation and sensitivities.

    The patient's bacteria growth profile will most likely show which of the following organisms?

    A. *Fusobacterium* species, *Klebsiella pneumonia, Streptococcus pyogenes*
    B. *Enterococcus faecalis, Staphylococcus epidermidis, Bacillus cereus*
    C. *Bacteroides fragilis, Enterobacter cloacae, Enterococcus faecium*
    D. *Serratia* species, *Proteus mirabilis, Haemophilus* species
    E. *Gardnerella* species, *Clostridium difficile, Enterococcus* species

13. An elderly patient is admitted to the ICU for septic shock. Urine culture is significant for *Proteus* species. The antibiogram is shown below.

		Aminoglycosides			B-Lactams			Cephalosporins				Quinolones		Others
Gram negative	# of patients	Amikacin	Gentamicin	Tobramycin	Ampicillin	Imipenem	Piperacillinp Tazobactam	Cefzolin	Cefoxitin	Ceftriaxone	Ceftazidime	Ciprofloxacin	Nitrofurantion	TMP/SMX
Echerichia coli	4	100	100	100		100	100				100	75		
Klebsiella sp	13	100	84.6	92.3	38.5	100	92.3	84.6	100	100	100	38.5	92.3	38.5
Proteus sp	7	71.4	57.1	71.4		85.7	85.7			57.1	57.1		28.6	71.4
Pseudomonas aeruginosa	13	100	83.3	92.3	91.7		100		81.8	100	100	30.8		69.2

	Penicillins				Cephalosporins		Quinolones		Others						
Gram positive	# of patients	Penicillins	Ampicillin	Oxacillin	Nafcillin	Cephalothin	Ceftriaxone	Ciprofloxacin	Moxifloxacin	Gentamacin	Linezoid	Rifampin	Tetracydine	TMP/SMX	Vancomycin	Nitrofurantion
Staph aureus (all)	8	0		0	0			0	0	87.5	100	100	100	100	100	100
Methicillin Resistant (MRSA)	8	0		0	0				0	87.5	100	100	100	100	100	100
Methicillin Susceptible (MRSA)	0															
Enterococcus sp	4	100	100					50		75			25		100	100

Which of the following is the best empiric antibiotic for this patient?

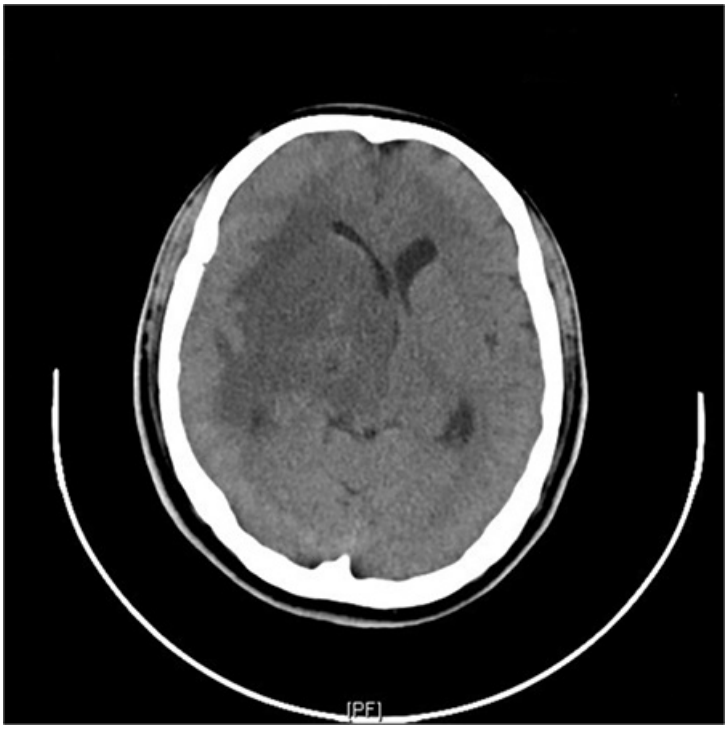
A. Amikacin
B. Gentamicin
C. Piperacillin/tazobactam
D. Trimethoprim/sulfamethoxazole

14. A 59-year-old woman is admitted to the ICU after having fever and chills for three days. Two blood cultures are positive for vancomycin-resistant *Enterococcus faecium.* Transthoracic echocardiogram reveals vegetation on the mitral valve. She is started on IV daptomycin, 10 mg/kg every 24 hours, and IV gentamicin, 1 mg/kg every 8 hours.

    Which of the following laboratory parameters should be monitored for daptomycin toxicity?

    A. Creatinine kinase
    B. Uric acid
    C. Activated partial thromboplastin time
    D. Platelets
    E. Amylase

15. A 35-year-old man with a seven-day history of confusion, fever, chills, and cough is admitted to the hospital for evaluation. His blood pressure is 140/82 mm Hg, heart rate 108 beats/min, respiratory rate 28 breaths/min, temperature 37.9°C (100.2°F), and oxygen saturation 95% on room air. On clinical examination, he is in distress and can move the right upper and lower extremities but is hemiparetic on the left. The right pupil is dilated at 4 mm but reactive, and the left pupil is 2 mm and reactive. CT is shown below. He is intubated and started on IV ceftriaxone and vancomycin. His head is placed at 45 degrees, and a bolus of mannitol is administered.



Which of the following is the most appropriate next step in this patient's treatment?

A. Add IV ampicillin to the antibiotic regimen.
B. Perform lumbar puncture to obtain cerebrospinal fluid for chemical analysis and culture.
C. Institute hypothermia with a core temperature goal of 33°C (91.4˚F).
D. Administer IV dexamethasone.

16. Which of the following patients is most likely to benefit from IV dexamethasone to reduce neurologic sequelae caused by meningitis?
    A. 32-year-old man admitted to the neurosurgical ICU three weeks ago who develops a *Pseudomonas*-related meningitis from his ventriculoperitoneal shunt
    B. 56-year-old woman admitted with presumed *Streptococcus pneumoniae* meningitis who has not received her first dose of antibiotics
    C. 75-year-old woman admitted to the ICU for herpes simplex encephalitis
    D. 65-year-old man admitted for *Streptococcus pneumoniae* meningitis who has received appropriate antimicrobial therapy for three days
    E. 38-year old paraplegic woman in the ICU being treated for an epidural abscess due to *Staphylococcus aureus* bacteremia

17. A 68-year-old man with a recent sinus infection presents to the emergency department minimally responsive. Per report, he has had headache and nausea and was vomiting all day. Temperature is 37°C (98.6°F), heart rate 90 beats/min, blood pressure 145/90 mm Hg, respiratory rate 12 breaths/min. On examination,

pupils are equal, round, and reactive. He mumbles to verbal stimulation, localizes to noxious stimulation in the right upper and lower extremities, and withdraws to noxious stimulation in the left upper and lower extremities. Head CT reveals an irregular area of low density in the right frontoparietal region with minimal mass effect. Brain MRI with gadolinium shows a similar hyperintense lesion on T2 and diffuse ring enhancement; the lesion is hyperintense on diffusion-weighted imaging. Neurosurgery is consulted, and he is admitted to the neurology ICU.

Which of the following is the most appropriate treatment while awaiting neurosurgery evaluation?

A. Dexamethasone
B. Ceftriaxone and vancomycin
C. Metronidazole and vancomycin
D. Ceftriaxone and metronidazole

18. A 22-year-old woman is evaluated in the emergency department (ED) for fever, pleuritic chest pain, dyspnea, and hypotension. She was in her usual state of good health until four days ago when she developed a sore throat, nausea, and myalgia. Physical examination is remarkable for an injected pharynx without any neck tenderness or swelling. Chest radiograph reveals bilateral patchy and irregular parenchymal opacities. She is diagnosed with pneumonia and admitted to the ICU where blood cultures are obtained. Empiric treatment with piperacillin/tazobactam and azithromycin is initiated, and she is resuscitated with IV fluids. Chest CT demonstrates right-sided pleural effusion and multiple cavitary and nodular opacities consistent with septic emboli. The next day, her blood cultures grow *Fusobacterium necrophorum,* and antibiotic therapy is narrowed down to piperacillin/tazobactam.

Which of the following diagnostic tests is most appropriate for this patient?

A. Transthoracic echocardiogram
B. Transesophageal echocardiogram
C. Carotid ultrasound
D. Neck CT

19. A 65-year-old woman who had an aortic valve replacement seven months ago is three weeks status post a pacemaker placement for sick sinus syndrome. She is now admitted to the ICU with a temperature of 39.6°C (103.3°F), blood pressure of 110/55 mm Hg, and heart rate of 66 beats/min. Chest radiograph is consistent with pulmonary edema without focal infiltrative process. Urinalysis is negative for signs of urinary tract infection. Transesophageal echocardiography shows vegetation on the aortic valve, as well as aortic insufficiency. Three sets of blood cultures are pending, and a cardiac surgery has been consulted.

Which of the following antibiotics are indicated at this time?

A. Vancomycin and gentamicin

B. Vancomycin, gentamicin, and rifampin
C. Vancomycin, gentamicin, and ciprofloxacin
D. Ampicillin/sulbactam and gentamicin
E. Ceftriaxone and gentamicin

20. A 54-year-old man with a history of hypertension and gastroesophageal reflux disorder presents to the emergency department (ED) with right upper quadrant abdominal pain and lightheadedness. On admission, blood pressure is 87/46 mm Hg, heart rate 124 beats/min, respiratory rate is 22 breaths/min, oxygen saturation 94%, temperature 39°C (102.2°F). On examination, he is confused, and his skin is jaundiced. White blood cell count is 21,000/μL. Hypotension persists after receiving crystalloid, 2,000 mL. Bedside abdominal ultrasound performed in the ED reveals stones in the gallbladder and biliary dilation. Fluid resuscitation is continued. Vasopressors are administered to achieve a mean arterial pressure of greater than 65 mm Hg. Broad-spectrum antibiotics and analgesia are also administered.

    Which of the following is the most appropriate next step in management?

    A. Magnetic resonance cholangiopancreatography
    B. Gastrointestinal consultation for emergent endoscopic retrograde cholangiopancreatography
    C. Abdominal CT
    D. Surgical consultation for urgent cholecystectomy

21. A 65-year-old man who has had a prolonged and complicated ICU stay after coronary artery bypass graft of three vessels six days ago has been treated with broad-spectrum antibiotics for presumed aspiration pneumonia. He is now extubated but has frequent watery stools and abdominal distention. Temperature is 38.9°C (102°F), and white blood cell count is 39,000 cells/mm^3. Stool is positive for *Clostridium difficile* toxins A and B. He requires a low-dose norepinephrine infusion to keep his mean blood pressure above 65 mm Hg.

    Which of the following is the most appropriate next intervention?

    A. IV vancomycin
    B. Oral vancomycin
    C. Oral vancomycin and IV metronidazole combination
    D. Gastrointestinal consultation for colonoscopy
    E. Exploratory laparotomy

22. A 65-year-old woman with hypertension, congestive heart failure (CHF), and dementia was recently hospitalized with CHF and subsequently discharged to an assisted care facility, where she now resides. For severe reflux, she had been started on omeprazole. She is readmitted to the hospital one week later in CHF. On readmission, she is in respiratory distress, so she is intubated and presently

mechanically ventilated. Her inpatient medications now include lisinopril, furosemide, omeprazole, sliding-scale insulin coverage, propofol infusion, and fentanyl infusion. White blood cell count is 30,000/μL, hemoglobin 8.5 g/dL, sodium 145 mEq/L, chloride 95 mEq/L, potassium 5.5 mEq/L. She becomes hypotensive and is subsequently also placed on a norepinephrine infusion to maintain adequate blood pressure. The lisinopril is held, and an orogastric tube is placed for evacuation of the stomach and eventual feeding. She also has copious diarrhea, for which IV hydration is instituted to maintain adequate fluid balance. *Clostridium difficile* colitis has been diagnosed.

Which of the following medications may have contributed to this clinical picture?

A. Furosemide
B. Omeprazole
C. Fentanyl
D. Lisinopril
E. Propofol

23. A 68-year-old man undergoes exploratory laparotomy and bowel resection for colon cancer. On postoperative day six, he develops fever, tachycardia, and leukocytosis, and undergoes abdominal CT, which reveals a peritoneal abscess. He undergoes percutaneous drainage of the abscess and is started on IV vancomycin and IV piperacillin/tazobactam. On postoperative day 12, he develops diarrhea, recurrent fever to 38.8°C (101.8°F), and increased white blood cell count to 18,000/μL. Other laboratory findings include hemoglobin 9.7 g/dL, serum creatinine 1.8 mg/dL, and serum albumin 2.4 g/dL.

    In addition to full-contact precautions, which of the following additional precautions is most appropriate for this patient?

    A. Alcohol-based hand sanitizer before and after patient encounter
    B. Soap hand washing before and after patient encounter
    C. Chlorhexidine bath for patient
    D. Reverse isolation room

24. A 34-year-old woman with a history of diabetes and placement of a ventriculoperitoneal (VP) shunt three weeks ago for hydrocephalus presents with new-onset headache, vomiting, and altered mental status. She is admitted to the ICU for further assessment and care.

    Which of the following is the most common pathogen infecting VP shunts?

    A. Herpes virus
    B. *Pseudomonas* species
    C. *Cryptococcus* species
    D. Skin flora
    E. Streptococci

25. Which of the following statements is true regarding carbapenem-resistant organisms?
    A. Genes encoding carbapenemase-producing enzymes cannot be transmitted from one bacterial species to another.
    B. Only one type of carbapenemase-producing enzyme exists.
    C. Carbapenem resistance has been reported in *Enterobacteriaceae* such as *Klebsiella* species and *Escherichia coli*, but not *Pseudomonas* species.
    D. Carbapenemase-producing bacteria may carry genes that confer high levels of resistance to many other antimicrobials.

26. A patient with severe sepsis due to *Escherichia coli* has been on meropenem, but culture sensitivity results demonstrate that the organism is resistant to carbapenems.

    Which antibiotic is most likely to be effective in treating this organism?

    A. Piperacillin/tazobactam
    B. Ciprofloxacin
    C. Linezolid
    D. Colistin

27. A 49-year-old woman who has metastatic breast cancer is evaluated in the emergency department for shortness of breath, fever, and chills. She is undergoing chemotherapy through a tunneled central venous catheter; her last cycle was five days ago. Blood cultures are drawn and she is started empirically on cefepime. Vital signs are: temperature 39.4°C (102.9°F); heart rate 121 beats/min, blood pressure 78/42 mm Hg, and respiratory rate 30 breaths/min. Chest radiography reveals pulmonary infiltrates. White blood cell count is 600/μL, bands 55%, segmented cells 10%. On further examination, it is noted that the area around her intravascular catheter site demonstrates redness and some swelling.

    Which of the following is the most appropriate change to her antimicrobial regimen?

    A. Switch cefepime to linezolid.
    B. Switch cefepime to piperacillin/tazobactam.
    C. Add vancomycin.
    D. Add oxacillin.
    E. Switch cefepime to ceftriaxone and azithromycin.

28. A notice from the Department of Public Health and Homeland Security states that someone has claimed to have released a toxin into a nearby subway station. Within the hour, dozens of patients begin to arrive at the hospital for evaluation. Initially, they are asymptomatic. However, while being monitored over the next two hours, they begin to report double vision, slurred speech, and difficulty

speaking. Some patients begin to have trouble lifting their arms, and some are noted to be gasping for air using accessory muscles.

Which of the following are the most likely cause of the symptoms and the most appropriate treatment?

A. Botulism, mechanical ventilation
B. Organophosphate poisoning, pralidoxime
C. Sarin gas poisoning, atropine
D. Cyanide poisoning, hydroxocobalamin
E. Anthrax, ciprofloxacin

Part 4 Answers:
Critical Care Infectious Diseases

1. Rationale

Answer: D

The U.S. Food and Drug Administration (FDA) has approved new rapid tests that can be used on blood cultures to identify methicillin-resistant *Staphylococcus aureus* (MRSA), so that the organism may be identified before conventional susceptibility results are obtained.

Linezolid is not FDA-approved for *S aureus* bacteremia. There are no significant data supporting its use for MRSA bacteremia. Patients can develop worsening pancytopenia/thrombocytopenia secondary to linezolid. Linezolid can also interact with selective serotonin reuptake inhibitors (SSRIs) and other drugs that may increase the serotonin level to cause serotonin syndrome. This patient is taking SSRIs and medications that can increase the serotonin level and predispose the patient to a higher risk of serotonin syndrome if linezolid is used.

If a strain of *Staphylococcus* is resistant to oxacillin or methicillin, it is resistant to all ß-lactam antibiotics, including penicillins, cephalosporins, and carbapenems. Thus, meropenem, cefepime, and ceftazidime are not active. This resistance is mediated by a change in the bacterial penicillin-binding protein, so ß-lactamase inhibitors such as sulbactam, clavulanic acid, and tazobactam have no effect. So piperacillin/tazobactam or ampicillin/sulbactam have no activity. Also, with the patient's history of anaphylaxis secondary to cephalosporins, caution must be taken when administering penicillins or carbapenems.

Daptomycin and vancomycin are good options for MRSA bacteremia. However, with the patient's history of anaphylaxis to vancomycin, daptomycin is preferred.

References:

1. Marlowe EM, Bankowski MJ. Conventional and molecular methods for the detection of methicillin-resistant Staphylococcus aureus. *J Clin Microbiol.* 2011 Sep;49(9 Suppl):S53-S56.
2. U.S. Food and Drug Administration. Information for Healthcare Professionals: Linezolid (marketed as Zyvox). 2007. http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatien
3. Thwaites GE, Edgeworth JD, Gkrania-Klotsas E, et al. Clinical management of Staphylococcus aureus bacteraemia. *Lancet Infect Dis.* 2011 Mar;11(3):208-222.

4. Woytowish MR, Maynor LM. Clinical relevance of linezolid-associated serotonin toxicity. *Ann Pharmacother.* 2013 Mar;47(3):388-397.
5. Kelkar PS, Li JT. Cephalosporin allergy. *N Engl J Med.* 2001 Sep 13;345(11):804-809.

2. Rationale

Answer: C

Linezolid is effective for treating methicillin-resistant *Staphylococcus aureus* (MRSA) pneumonia and is an appropriate alternative therapy. This patient did not respond to treatment despite the vancomycin trough being maintained within the goal range of 15-20 µg/mL. Increasing the vancomycin dose to achieve a vancomycin trough closer to 20 µg/mL would not achieve pharmacokinetic goals because of the high minimum inhibitory concentration of 2 µg/mL, and it would increase the risk of nephrotoxicity. Daptomycin cannot be used to treat pneumonia because it is bound by surfactant and cannot achieve sufficient concentrations in the respiratory tract. Tigecycline is not generally indicated for ICU patients because of an increased risk of all-cause mortality versus comparator agents in clinical trials.

References:

1. Liu C, Bayer A, Cosgrove SE, et al; Infectious Diseases Society of America. Clinical practice guidelines by the Infectious Diseases Society of America for the treatment of methicillin-resistant Staphylococcus aureus infections in adults and children. *Clin Infect Dis.* 2011 Feb 1;52(3):e18-e55.
2. Segarra-Newnham M, Church TJ. Pharmacotherapy for methicillin-resistant Staphylococcus aureus nosocomial pneumonia. *Ann Pharmacother.* 2012 Dec;46(12):1678-1687.
3. Tygacil package insert. Revised October 2013. http://labeling.pfizer.com/showlabeling.aspx?id=491&pagename=tygacil_fly&cbn=1-8765237%3A1-8765544. Accessed April 22, 2014.

3. Rationale

Answer: C

The most common causative agent of bacterial meningitis in patients aged 16 to 50 is *Streptococcus pneumoniae,* followed by *Neisseria meningitidis.* Empiric coverage of these pathogens with vancomycin and a third-generation cephalosporin is adequate. In pregnancy, however, there is also a risk of *Listeria monocytogenes* meningitis. Listeria is a facultative anaerobic gram-positive bacillus that is often transmitted via soft cheeses and smoked meats. Suppressed T cell immunity in pregnancy, especially in the third trimester, puts these patients at risk. Importantly, *L monocytogenes* is not susceptible to cephalosporins or vancomycin. Adding ampicillin or penicillin G is necessary for adequate empiric antibiotic coverage.

References:

1. Allerberger F, Wagner M. Listeriosis: a resurgent foodborne infection. *Clin Microbiol Infect.* 2010 Jan;16(1):16-23.
2. Van de Beek D, de Gans J, Tunkel AR, Wijdicks EF. Community-acquired bacterial meningitis in adults. *N Engl J Med.* 2006 Jan 5;354(1):44-53.

4. Rationale

Answer: C

Emphysematous pyelonephritis is a surgical emergency. It is most common in patients with diabetes mellitus. Coliform gram-negative rods such as *Escherichia coli* account for most cases. Treatment in most cases is nephrectomy. In cases where there is limited gas or a nontoxic clinical appearance, there may be a role for conservative therapy; however, the threshold for surgical intervention should be low. Placement of a nephrostomy tube would be indicated for pyelonephritis with hydronephrosis but would not be sufficient treatment for emphysematous pyelonephritis. Appropriate antibiotic coverage and aggressive resuscitation are also essential, but are not a substitute for surgical source control.

References:

1. Tang HJ, Li CM, Yen MY, et al. Clinical characteristics of emphysematous pyelonephritis. *J Microbiol Immunol Infect.* 2001 Jun;34(2):125-130.
2. Huang JJ, Tseng CC. Emphysematous pyelonephritis: clinicoradiological classification, management, prognosis, and pathogenesis. *Arch Intern Med.* 2000 Mar 27;160(6):797-805.
3. Ubee SS, McGlynn L, Fordham M. Emphysematous pyelonephritis. *BJU Int.* 2011 May;107(9):1474-1478.

5. Rationale

Answer: D

A young, healthy person with no medical history becomes unresponsive at a party with signs of aspiration. He is given empiric antibiotic therapy for aspiration and has rapid clinical improvement, including extubation, minimal oxygen requirement, and slowly improving infiltrates. Although he has leukocytosis and a low-grade fever, he is considered to have aspiration pneumonitis rather than aspiration pneumonia based on current clinical findings. Unfortunately, there is currently no gold standard in differentiating between these two diagnoses. Many clinicians treat aspiration empirically with antibiotics, but if the patient has aspiration pneumonitis, this is not a recommended practice. Currently, the Syndrome and Aspiration Pneumonia in Intensive Care (SPIRE) study is examining the frequency of bacterial pneumonia in patients admitted to the ICU requiring mechanical ventilation with coma. The elevated procalcitonin level signals that the patient does have a bacterial infection, but it does not have good diagnostic value in differentiating between bacterial aspiration

pneumonia and aspiration pneumonitis.

References:

1. Lanspa MJ, Jones BE, Brown SM, Dean NC. Mortality, morbidity, and disease severity of patients with aspiration pneumonia. *J Hosp Med.* 2013 Feb;8(2):83-90.
2. Marik PE. Pulmonary aspiration syndromes. *Curr Opin Pulm Med.* 2011 May;17(3):148-154.
3. El-Solh AA, Vora H, Knight PR 3rd, Porhomayon J. Diagnostic utility of serum procalcitonin levels in pulmonary aspiration syndromes. *Crit Care Med.* 2011 Jun;39(6):1251-1256.

6. Rationale

Answer: D

Antibiotic prophylaxis is required under certain circumstances to prevent postoperative infection. In a prospective randomized trial, there was a significant reduction of postoperative infection in patients treated with perioperative prophylactic antibiotics. Most of the pathogens are gram-positive bacteria; first-generation cephalosporins should be sufficient. A combination of vancomycin and ceftazidime may be used in grossly contaminated wounds.

References:

1. Young RF, Lawner PM. Perioperative antibiotic prophylaxis for prevention of postoperative neurosurgical infections. A randomized clinical trial. *J Neurosurg.* 1987 May;66(5):701-705.
2. Dempsey R, Rapp RP, Young B, Johnston S, Tibbs P. Prophylactic parenteral antibiotics in clean neurosurgical procedures: a review. *J Neurosurg.* 1988 Jul;69(1):52-57.
3. Cacciola F, Cioffi F, Anichini P, Di Lorenzo N. Antibiotic prophylaxis in clean neurosurgery. *J Chemother.* 2001 Nov;13 Spec No 1(1):119-122.

7. Rationale

Answer: D

The Centers for Medicare and Medicaid Services core measures require either a comprehensive physical examination or two other measures of volume status. The comprehensive physical examination must include either: focused examination documented by provider that includes vital signs (including blood pressure, pulse, respiratory rate, and temperature), cardiopulmonary examination (heart and lung), capillary refill evaluation, peripheral pulse evaluation, and skin examination; or two of the following: central venous pressure measurement, central venous oxygen measurement, bedside cardiovascular ultrasound, passive leg raise or fluid challenge.

References:

1. ProCESS Investigators, Yealy DM, Kellum JA, et al. A randomized trial of protocol-based care for early septic shock. *N Engl J Med.* 2014 May 1;370(18):1683-1693.
2. ARISE Investigators; ANZICS Clinical Trials Group, Peake SL, et al. Goal-directed resuscitation for patients with early septic shock. *N Engl J Med.* 2014 Oct 16;371(16):1496-1506.
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4. Levy MM, Rhodes A, Phillips GS, et al. Surviving Sepsis Campaign: association between performance metrics and outcomes in a 7.5-year study. *Intensive Care Med.* 2014 Nov;40(11):1623-1633.
5. Dellinger RP, Levy MM, Rhodes A, et al; Surviving Sepsis Campaign Guidelines Committee including the Pediatric Subgroup. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock: 2012. *Crit Care Med.* 2013 Feb;41(2):580-637.
6. Surviving Sepsis Campaign. Updated Bundles in Response to New Evidence. http://www.survivingsepsis.org/SiteCollectionDocuments/SSC_Bundle.pdf. Accessed June 6, 2016.

8. Rationale

Answer: E

This patient has leptospirosis. Initial symptoms can be protean in nature, resembling the flu. In its most severe form, Weil disease, it can lead to kidney failure, liver failure, pulmonary hemorrhage, meningitis, and death. It is most commonly spread through rodent urine coming into contact with breaks in the skin barrier. The patient works in sewers, so he probably contacted it this way. Antibiotics such as doxycycline are recommended although clear mortality benefit is uncertain. Supportive care in addition to antibiotics is the mainstay of treatment.

It is possible that this patient could have been infected with hepatitis A/E given his profession, but treatment is generally supportive. Also, his transaminases are not as high as expected with acute hepatitis. Lamivudine can be considered in acute hepatitis B infection but is not standard of care. Wilson disease is unlikely given the acute nature of his symptoms; thus penicillamine and transplant are incorrect. He may require dialysis in the future but does not need it urgently given his electrolytes and normal mental status despite elevated urea nitrogen. His history and clinical and laboratory findings are less supportive of acute alcoholic hepatitis. Prednisone, which is of questionable benefit anyway in alcoholic hepatitis, may be detrimental to his condition.

References:

1. Maroun E, Kushawaha A, El-Charabaty E, Mobarakai N, El-Sayegh S. Fulminant leptospirosis (Weil's disease) in an urban setting as an overlooked cause of multiorgan failure: a case report. *J Med Case Rep.* 2011 Jan 14;5:7.
2. Thursz MR, Richardson P, Allison M, et al; STOPAH Trial. Prenisolone or

pentoxifylline for alcoholic hepatitis. *N Engl J Med.* 2015 Apr 23;372(17):1619-1628.
3. Reshef R, Sbeit W, Tur-Kaspa R. Lamivudine in the treatment of acute hepatitis B. *N Engl J Med.* 2000 Oct 12;343(15):1123-1124.

9. Rationale

Answer: D

Funguria is common in patients in the hospital and the ICU, and is usually benign. The most common pathogen is *Candida* species. Risk factors for funguria include immunosuppression, diabetes, use of broad-spectrum antibacterial agents, use of central venous catheters, malignancy, receipt of parenteral nutrition, urinary tract abnormalities and obstruction, recent urologic procedure, and presence of urinary tract devices.

In most cases, patients are asymptomatic, and the candiduria represents contamination or colonization. Usually observation without treatment is all that is required if no predisposing factor is identified. If there is a predisposing factor, then managing that factor, such as removing or replacing the urinary catheter, may be sufficient to eliminate the candiduria, without antifungal therapy. Therefore, antifungal treatment in asymptomatic patients is typically reserved for high-risk patients such as neonates with low birth weight, severely immunocompromised patients, or patients undergoing urinary tract procedures.

Colonization is difficult to differentiate from infection based on urinalysis and culture alone, and the patient's clinical history must be considered. Patients who are symptomatic or who have concerning systemic signs or symptoms (flank pain, hypotension, etc.) should be treated with an antifungal and evaluated for disseminated infection with blood cultures. Because the kidney is the most common organ involved in systemic *Candida* infections, persistent candiduria should be further evaluated with renal ultrasound or CT to identify localized infection. Furthermore, the skin should be examined for sources such as fungal lesions and evidence of infected vascular access devices.

Patients with candidemia should have an ophthalmological examination, regardless of ocular symptoms, to evaluate for endophthalmitis and chorioretinitis. Early ophthalmological examination can aid in the management and reduction of long-term visual deficit.

References:

1. Kauffman CA. Diagnosis and management of fungal urinary tract infection. *Infect Dis Clin North Am.* 2014 Mar;28(1):61-74.
2. Kauffman CA, Fisher JF, Sobel JD, Newman CA. Candida urinary tract infections—diagnosis. *Clin Infect Dis.* 2011 May;52 Suppl 6:S452-S456.
3. Pappas PG, Kauffman CA, Andes D, et al; Infectious Diseases Society of America. Clinical practice guidelines for the management of candidiasis: 2009 update by the Infectious Diseases Society of America. *Clin Infect Dis.* 2009 Mar

1;48(5):503-535.
4. Au L, Guduru K, Lipscomb G, Kelly SP. Candida endophthalmitis: a critical diagnosis in the critically ill. *Clin Ophthalmol.* 2007 Dec;1(4):551-554.

10. Rationale

Answer: A

This presentation is concerning for necrotizing fasciitis. Prompt surgical intervention is the most important intervention. While evidence-based sepsis care with fluid resuscitation is indicated, and broad-spectrum antibiotics are important, surgical intervention is required for necrotizing fasciitis. Once the patient's presentation is so concerning for necrotizing fasciitis, especially with palpable crepitus, delaying surgical consultation to obtain a plain film is unlikely to change the management.

References:

1. Hakkarainen TW, Kopari NM, Pham TN, Evans HL. Necrotizing soft tissue infections: review and current concepts in treatment, systems of care, and outcomes. *Curr Probl Surg.* 2014 Aug;51(8):344-362.
2. Sarani B, Strong M, Pascual J, Schwab CW. Necrotizing fasciitis: current concepts and review of the literature. *J Am Coll Surg.* 2009 Feb;208(2):279-288.

11. Rationale

Answer: C

Given this patient's recent procedural history, combined with his recent antibiotic exposure, he is at risk for infection with extended-spectrum ß-lactamase-producing gram-negative pathogens. The current treatment of choice for this is the carbapenem family (imipenem, meropenem, doripenem, and ertapenem). He already had a two-week treatment with a fourth-generation cephalosporin and is now probably resistant. Vancomycin could be considered but, given his procedure, it is unlikely that he has a gram-positive infection. Colistin should be used only for extreme drug-resistant organisms. Given his ongoing shock, continuing his current antibiotic regimen is inappropriate.

References:

1. Kandemir Ö, Bozlu M, Efesoy O, Güntekin O, Tek M, Akbay E. The incidence and risk factors of resistant E. coli infections after prostate biopsy under fluoroquinolone prophylaxis: a single-centre experience with 2215 patients. *J Chemother.* 2015 Jan 28: 1973947815Y0000000001. [Epub ahead of print].
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3. Biehl LM, Schmidt-Hieber M, Liss B, Cornely OA, Vehreschild MJ. Colonization

and infection with extended spectrum beta-lactamase producing Enterobacteriaceae in high-risk patients—review of the literature from a clinical perspective. *Crit Rev Microbiol.* 2016 Feb;42(1):1-16.

12. Rationale

Answer: C

Understanding Gram stain results can help guide and tailor appropriate antimicrobial therapy in a timely fashion. Microorganism flow sheets can be used based on the Gram stain results to help delineate exact potential organisms. Subsequent institution-specific antibiograms can guide antimicrobial titration. Based on the Gram stain data, the only appropriate combination of organisms is selected. *Klebsiella pneumonia* is oxidase negative and indole negative, *Staphylococcus epidermidis* is a gram-positive cocci in clusters. *Serratia* species, *Proteus mirabilis, Haemophilus* species are all gram-negative organisms. *Gardnerella* species, *Clostridium difficile, Enterococcus* species are all gram-positive organisms.

References:

1. Sogaard M, Norgaard M, Schonhyder H. First notification of positive blood cultures: high accuracy of the Gram stain report. 2007; *J Clin Microbiol* 45:1113-1117.
2. Randhawa V, Sanwar S, Walker S, et al. Weighted-incidence syndromic combination antibiograms to guide empiric treatment of critical care infections: a retrospective cohort study. *Crit Care* 2014;18:R112

13. Rationale

Answer: C

The antibiogram is an important tool in the selection of empiric therapy for bacterial infection. It is specific to each hospital; the culture data are derived from patients at the facility who contracted the bacteria. The bacterial isolates are subjected to antimicrobial susceptibility testing and reporting.

In this facility, seven patients had cultured *Proteus* species when the antibiogram was developed. The susceptibility to amikacin was 71.4%, or five out of seven patients with *Proteus* species, 57.1% susceptibility to gentamicin, 85.7% susceptibility to piperacillin/tazobactam, and 71.4% susceptibility to trimethoprim/sulfamethoxazole. Piperacillin/tazobactam had the highest percentage of susceptibility and should be used as an empiric agent.

References:

1. Agency for Healthcare Research and Quality. *Concise Antibiogram Toolkit.* June 2014. http://www.ahrq.gov/professionals/quality-patient-safety/patient-safety-resources/resources/nh-aspguide/module2/toolkit1/cat_sources.html. Accessed February 18, 2016.

2. Horvat RT. Review of antibiogram preparation and susceptibility testing systems. *Hosp Pharm.* 2010 Nov;45(Suppl 1):S6-S9.

14. Rationale

Answer: A

In the early 1990s, clinical trials for daptomycin used a 12-hour dosing interval. After observing a signal of an adverse skeletal muscle effect at a dose of 4 mg/kg administered every 12 hours, the trials were voluntarily suspended. Further studies in dogs also revealed decreased skeletal muscle activity and increases in creatinine kinase levels. The U.S. Food and Drug Administration ultimately approved daptomycin, 4- to 6-mg/kg every 24 hours, in patients with a creatinine clearance greater than 30mL/min. The Infectious Diseases Society of America has endorsed higher doses for bacteremia and endocarditis. Therefore, it is recommended to monitor creatinine kinase levels once weekly while on therapy. Option A is correct.

References:

1. Bhavnani SM, Rubino CM, Ambrose PG, Drusano GL. Daptomycin exposure and the probability of elevations in the creatine phosphokinase level: data from a randomized trial of patients with bacteremia and endocarditis. *Clin Infect Dis.* 2010 Jun 15;50(12):1568-1574.
2. Arbeit RD, Maki D, Tally FP, Campanaro E, Eisenstein BI; Daptomycin 98-01 and 99-01 Investigators. The safety and efficacy of daptomycin for the treatment of complicated skin and skin-structure infections. *Clin Infect Dis.* 2004 Jun 15;38:1673-1681.
3. Liu C, Bayer A, Cosgrove SE, et al; Infectious Diseases Society of America. Clinical practice guidelines by the Infectious Diseases Society of America for the treatment of methicillin-resistant Staphylococcus aureus infections in adults and children. *Clin Infect Dis.* 2011 Feb 1;52(3):e18-e55.

15. Rationale

Answer: D

This is a young patient with progressive neurologic deterioration secondary to a right basal ganglia mass. His clinical picture suggests impending herniation. The CT suggests vasogenic cerebral edema, and the clinical examination with asymmetric pupils suggest that a lumbar puncture may be too risky because it would facilitate further downward transtentorial herniation. The main indication for steroids is vasogenic edema associated with brain tumors or accompanying brain irradiation and surgical manipulation. Although the precise mechanism of the beneficial effects of steroids in this paradigm are unknown, steroids decrease tight-junction permeability and in turn stabilize the disrupted blood-brain barrier. Evidence suggests that therapeutic hypothermia may be considered as an alternative for managing intracranial hypertension in stroke and cardiac arrest, but its use in infectious encephalitis may be harmful. Addition of ampicillin could be considered; however, it will not have any impact on the ensuing transtentorial herniation. *Listeria*

monocytogenes, although an uncommon cause of illness in the general population, is an important pathogen in pregnant women, neonates, elderly people, and immunocompromised people.

References:

1. Raslan A, Bhardwaj A. Medical management of cerebral edema. *Neurosurg Focus.* 2007 May 15;22(5):E12.
2. Rabinstein AA. Treatment of brain edema. *Neurologist.* 2006 Mar;12(2):59-73.
3. Mourvillier B, Tubach F, van de Beek D, et al. Induced hypothermia in severe bacterial meningitis: a randomized clinical trial. *JAMA.* 2013 Nov 27;310(20):2174-2183.
4. Rincon F, Badjatia N. Central nervous system infections in the neurointensive care unit. *Curr Treat Options Neurol.* 2006 Mar;8(2):135-144.

16. Rationale

Answer: B

Unfavorable neurologic outcomes are not necessarily the result of inadequate treatment with antimicrobial agents. Cerebrospinal fluid cultures are often sterile 24 to 48 hours after the start of antibiotic therapy. Studies in animals have shown that bacterial lysis, induced by treatment with antibiotics, leads to inflammation in the subarachnoid space, which may contribute to an unfavorable outcome. These studies also show that adjuvant treatment with antiinflammatory agents, such as dexamethasone, reduces both cerebrospinal fluid inflammation and neurologic sequelae but not overall mortality. Dexamethasone should be administered before or with the first dose of antibiotics to achieve maximal benefit. The recommended dose in adults is 10 mg every six hours, IV, for four days.

References:

1. De Gans J, van de Beek D; European Dexamethasone in Adulthood Bacterial Meningitis Study Investigators. Dexamethasone in adults with bacterial meningitis. *N Engl J Med.* 2002 Nov 14;347(20):1549-1556.
2. Brouwer MC, McIntyre P, Prasad K, van de Beek D Corticosteroids for acute bacterial meningitis. *Cochrane Database Syst Rev.* 2015 Sep 12;(9):CD004405.
3. Tunkel AR, Hartman BJ, Kaplan SL, et al. Practice guidelines for the management of bacterial meningitis. *Clin Infect Dis.* 2004 Nov 1;39(9):1267-1284.

17. Rationale

Answer: D

This patient has a brain abscess probably secondary to direct spread from his sinus infection. Often patients with brain abscess do not have fever. The MRI imaging characteristic that distinguishes an abscess from a neoplasm is hyperintensity on

diffusion-weighted imaging. Dexamethasone would be the correct treatment for a neoplasm but is indicated for a brain abscess only with substantial mass effect given the disadvantages of slowing capsule formation, increasing risk of ventricular rupture, and decreasing penetration of antibiotics into the abscess. The best antibiotic regimen for a patient with a brain abscess from sinus extension is ceftriaxone and metronidazole, which will cover aerobic streptococci, anaerobic streptococci, *Haemophilus* species, non-*fragilis Bacteroides* species, and *Fusobacterium* species. Ceftriaxone and vancomycin, or metronidazole and vancomycin would not provide sufficient coverage.

References:

1. Canale DJ. William Macewen and the treatment of brain abscesses: revisited after one hundred years. *J Neurosurg.* 1996 Jan;84(1):133-142.
2. Gortvai P, De Louvois J, Hurley R. The bacteriology and chemotherapy of acute pyogenic brain abscess. *Br J Neurosurg.* 1987;1(2):189-203.
3. Brouwer MC, Tunkel AR, McKhann GM 2nd, van de Beek D. Brain abscess. *N Engl J Med.* 2014 Jul 31;371(5):447-456.

18. Rationale

Answer: D

Lemierre syndrome is a potentially fatal form of septic thrombophlebitis of the internal jugular vein (IJV), which frequently affects young, immunocompetent people. It was once rare, but its increasing incidence during the past 20 years is attributed to antibiotic resistance and changes in antibiotic prescription patterns. It typically starts in the palatine tonsils or peritonsillar tissue and spreads into the IJV-containing lateral pharyngeal space, causing septic thrombophlebitis, which is usually followed by distal septic embolization, resulting in multiorgan involvement, with the lung being the most commonly affected site. Other commonly involved sites are joints, muscle, soft tissue, meninges, spleen, and liver. Lemierre syndrome is usually caused by *Fusobacterium necrophorum,* although a wide variety of bacteria have been reported as causative organisms.

Initial clinical presentation can be subtle; sometimes persistent fever is the only prominent symptom. The syndrome is frequently not suspected until microbiologic data is available; hence, a high level of clinical suspicion is needed for timely diagnosis. Physical examination might reveal an exudative tonsillitis or milder form of pharyngitis; however, these oropharyngeal signs might not be evident because the septic thrombophlebitis or metastatic complication usually occurs one to three weeks after the primary infection. Typical signs of IJV thrombophlebitis are pain and swelling along the sternocleidomastoid muscle, but these are found in only approximately half of affected patients.

Lemierre syndrome is diagnosed based on the presence of a thrombus in the IJV and positive blood culture. Neck CT with contrast is the diagnostic modality of choice to demonstrate the thrombus. Doppler ultrasonography is an alternative, being less invasive, though also less sensitive, particularly for thrombi located in the area deep to

clavicle and mandible, and can miss newly formed thrombus with low echogenicity. A prolonged course of IV antibiotics covering *F necrophorum* and oral streptococci is the cornerstone of treatment. ß-lactamase-producing strains of *F necrophorum* have been reported; therefore, a ß-lactam alone is not recommended. The role of anticoagulation is unclear, but it is generally not indicated unless there is evidence of thrombus expansion. Surgical ligation or excision of the IJV may be necessary in the case of uncontrolled sepsis or septic emboli despite adequate antibiotic treatment.

References:

1. Dorfman A, Shokoohi H, Taheri MR. Lemierre's syndrome and rapidly deteriorating respiratory failure in the emergency department. *Am J Emerg Med.* 2012 Oct;30(8):1658.e5-e7.
2. Karkos PD, Asrani S, Karkos CD, et al. Lemierre's syndrome: a systematic review. *Laryngoscope.* 2009 Aug;119(8):1552-1559.
3. Kuppalli K, Livorsi D, Talati NJ, Osborn M. Lemierre's syndrome due to Fusobacterium necrophorum. *Lancet Infect Dis.* 2012 Oct;12(10):808-815.
4. Reynolds SC, Chow AW. Severe soft tissue infections of the head and neck: a primer for critical care physicians. *Lung.* 2009 Sep-Oct;187(5):271-279.
5. Wright WF, Shiner CN, Ribes JA. Lemierre syndrome. *South Med J.* 2012 May;105(5):283-288.

19. Rationale

Answer: B

Prosthetic valve endocarditis (PVE) occurs in 1% to 6% of patients with valve prosthesis and carries a mortality risk between 20% and 80%. This patient also has a permanent pacemaker that is likely colonized with the pathogen. Her blood pressure and heart rate are stable at this time. For patients who present with prosthetic devices early antibiotic therapy is recommended. Empiric regimens are based on risk factors that include the patient's prior antibiotic history as well as the presence and age of a prosthetics. In the case of a relatively fresh prosthetic valve (less than 12 months), the European Society of Cardiology recommends a regimen of vancomycin and gentamicin, as well as rifampin. Rifampin is a suggested addition because it is thought to sterilize artificial surfaces infected with *Staphylococcus aureus.* Patients with a surgical indication for removal of infected prosthetic valves have lower six-month mortality rates than those treated with only antibiotics. In a prospective study, the most common reason for not undergoing surgery was poor prognosis regardless of treatment, hemodynamic instability, stroke, and sepsis.

References:

1. Habib G, Lancellotti P, Antunes MJ, et al. 2015 ESC Guidelines for the management of infective endocarditis: The Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC). Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM). *Eur Heart J.* 2015 Nov 21;36(44):3075-

3128.
2. Alestig K, Hogevik H, Olaison L. Infective endocarditis: a diagnostic and therapeutic challenge for the new millennium. *Scand J Infect Dis.* 2000;32(4):343-356.
3. Habib G, Tribouilloy C, Thuny F, et al. Prosthetic valve endocarditis: who needs surgery? A multicentre study of 104 cases. *Heart.* 2005 Jul;91(7):954-959.
4. Chu H, Park LP, Athan E, et al; International Collaboration on Endocarditis (ICE) Investigators. Association between surgical indications, operative risk and clinical outcome in infective endocarditis: a prospective study from the International Collaboration on Endocarditis. *Circulation.* 2015 Jan 13;121(2):131-140.
5. Chirouze C, Alla F, Fowler VG Jr, et al; ICE Prospective Investigators. Impact of early valve surgery on outcome of Staphylococcus aureus prosthetic valve infective endocarditis: analysis in the International Collaboration of Endocarditis-Prospective Cohort Study. *Clin Infect Dis.* 2015 Mar 1;60(5):741-749.

20. Rationale

Answer: B

This patient has septic shock from acute cholangitis and requires urgent biliary decompression. The treatment of choice is endoscopic retrograde cholangiopancreatography (ERCP). Percutaneous trans-hepatic biliary drainage is another possible nonsurgical method, and may be preferred to ERCP in some situations. In this case, definitive treatment should not be delayed to obtain more imaging; therefore, options A and C are incorrect.

Acute cholangitis is a result of bacterial infection superimposed on obstruction of the biliary tree. It is believed that bacteria gain access to the biliary tree by retrograde ascent from the duodenum or from portal venous blood. As a result, infection ascends into the hepatic ducts, causing serious infection. Increased biliary pressure pushes the infection into the biliary canaliculi, hepatic veins, and perihepatic lymphatics, sometimes leading to bacteremia. High biliary pressures caused by obstruction may impair the biliary secretion of antibiotics, so treatment may require decompression and drainage of the biliary system.

The most common cause of cholangitis in the United States is choledocholithiasis secondary to cholelithiasis. Less common causes of cholangitis include malignant obstruction, benign strictures, post-procedural cholangitis, and primary sclerosing cholangitis. Rare causes of cholangitis include obstruction from hemobilia, parasites, and hereditary abnormalities of the biliary tree. Of the common complications of gallstones, cholangitis is the most rapidly lethal entity, making accurate diagnosis and early treatment imperative. Mortality rates for patients who fail conservative therapy and do not have appropriate drainage approach 100%.

Clinical presentation varies, with 50% to 70% of patients having the classic Charcot triad of fever, abdominal pain, and jaundice. A presentation that also includes altered mental status and hypotension is known as the Reynolds pentad. Diagnosis of ascending cholangitis is usually clinical, although laboratory data and imaging can help distinguish it from other conditions. Typically, laboratory data reveal leukocytosis,

hyperbilirubinemia, elevated alkaline phosphatase, and mildly elevated transaminases.

Serum amylase may be elevated in up to 30% of patients. Ultrasonography or CT are the most commonly used first-line imaging modalities. Ultrasound is highly sensitive for cholelithiasis but less sensitive (approximately 50%) for choledocholithiasis. Choledocholithiasis may, however, be inferred if there is associated biliary dilation in the presence of cholelithiasis. A normal ultrasound does not rule out cholangitis. MRI and magnetic resonance cholangiopancreatography are accurate for detecting choledocholithiasis and determining biliary anatomy, but these tests are probably of limited value in acute cholangitis. Initial management of ascending cholangitis consists of fluid resuscitation, correction of electrolyte abnormalities, analgesia, and empiric antibiotics. Blood cultures should be obtained before antibiotic administration, and patients' status should be nothing-by-mouth. For patients with severe cholangitis, endoscopic drainage has replaced emergency surgical common bile duct exploration and T-tube drainage as standard treatment. This patient will probably need cholecystectomy, but it should be performed after endoscopic treatment of the choledocholithiasis and after resolution of the cholangitis episode.

References:

1. Yusoff IF, Barkun JS, Barkun AN. Diagnosis and management of cholecystitis and cholangitis. *Gastroenterol Clin North Am.* 2003 Dec;32(4):1145-1168.
2. Lai E, Mok FP, Tan ES, et al. Endoscopic biliary drainage for severe acute cholangitis. *N Engl J Med.* 1992 Jun 11;326(24):1582-1586.
3. Kiriyama S, Takada T, Strasberg SM, et al; Tokyo Guidelines Revision Committee. New diagnostic criteria and severity assessment of acute cholangitis in revised Tokyo guidelines. *J Hepatobiliary Pancreat Sci.* 2012 Sep;19(5):548-556.

21. Rationale

Answer: C

Patients who have severe and complicated *Clostridium difficile* infection (CDI) should be treated with vancomycin, 500 mg orally four times a day, and metronidazole, 500 mg IV every eight hours. This is defined by one or more of the following criteria being attributable to CDI: admission to ICU for CDI, hypotension with or without required use of vasopressors, fever ≥38.5°C, ileus or significant abdominal distention, mental status changes, white blood cell count ≥35,000 cells/mm^3 or < 2,000 cells/mm^3, serum lactate level >2.2 mmol/L, end-organ failure.

The clinician should consider the addition of vancomycin per rectum (500 mg in 500 mL saline as enema) four times a day for patients in whom oral antibiotics cannot reach a segment of the colon, such as with Hartman pouch, ileostomy, or colon. Diversion and can be considered in all cases of severe or complicated CDI. In the absence of ileus or significant abdominal distention, oral or enteral feeding should be continued. Supportive care should be provided, including IV fluid resuscitation, electrolyte replacement, and venous thromboembolism prophylaxis. Presumably, the broad-spectrum antibiotics used to treat this patient's pneumonia have contributed to

his CDI, so discontinuing the offending agents or narrowing the antibiotics should also be considered, if possible. Abdominal and pelvic CT can be used as adjuncts to determine the severity and extent of disease and can detect colon wall thickening, ascites, toxic megacolon, ileus, or perforation. Surgical consultation should be considered here as well, since patients who have toxic megacolon or who become clinically unstable due to CDI benefit from urgent total colectomy. This patient is not clinically unstable at this time, and therefore does not have an indication for exploratory laparotomy.

Colonoscopy is not indicated in this case because the diagnosis was made based on stool assay, and colonoscopy may put the patient at risk for bowel perforation. For patients with mild to moderate disease (defined as diarrhea plus any additional signs or symptoms not meeting severe or complicated criteria), the treatment is metronidazole, 500 mg orally three times a day for 10 days. If the patient cannot tolerate metronidazole, vancomycin 125 mg orally four times a day for 10 days is indicated. If there is no improvement in five to seven days, switching to vancomycin, 125 mg orally four times a day for 10 days, should be considered. IV vancomycin is not indicated for CDI.

References:

1. Cohen SH, Gerding DN, Johnson S, et al; Society for Healthcare Epidemiology of America; Infectious Diseases Society of America. Clinical practice guidelines for Clostridium difficile infection in adults: 2010 update by the Society for Healthcare Epidemiology of America (SHEA) and the Infectious Diseases Society of America (IDSA.) *Infect Control Hosp Epidemiol.* 2010 May;31(5):431-455.
2. Surawicz CM, Brandt LJ, Binion DG, et al. Guidelines for diagnosis, treatment, and prevention of Clostridium difficile infections. *Am J Gastroenterol.* 2013 Apr;108(4):478-498.

22. Rationale

Answer: B

Clostridium difficile colitis is commonly associated with previous exposure to antibiotics. Almost all antibiotics can contribute to the development of *C diff* colitis. Even though oral vancomycin is a treatment for *C diff* colitis, it may still contribute to it. Proton pump inhibitors, such as omeprazole, appear to increase the risk of *C diff* colitis. None of the other options are known to be associated with *C diff* colitis. Treatment in critically ill patients consists of enteral and parenteral rectal vancomycin as well as IV metronidazole. Stool transplant has been successful in more severe cases. In the setting of toxic megacolon, preferred management consists of surgical consult and colectomy.

References:

1. Kwok CS, Arthur AK, Anibueze CI, Singh S, Cavallazzi R, Loke YK. Risk of Clostridium difficile infection with acid suppressing drugs and antibiotics: meta-analysis. *Am J Gastroenterol.* 2012 Jul;107(7):1011-1019.

2. Larentis DZ, Rosa RG, Dos Santos RP, Goldani LZ. Outcomes and risk factors associated with Clostridium difficile diarrhea in hospitalized adult patients. *Gastroenterol Res Pract.* 2015;2015:346341.
3. Deshpande A, Pasupuleti V, Thota P, et al. Community-associated Clostridium difficile infection and antibiotics: a meta-analysis. *J Antimicrob Chemother.* 2013 Sep;68(9):1951-1961.
4. Slimings C, Riley TV. Antibiotics and hospital-acquired Clostridium difficile infection: update of systematic review and meta-analysis. *J Antimicrob Chemother.* 2014 Apr;69(4):881-891.

23. Rationale

Answer: A

This patient most likely has *Clostridium difficile* infection (CDI). In addition to confirmatory testing and initiation of treatment, it is important to establish appropriate measures to prevent dissemination of CDI to other patients in the same patient care unit. The Centers for Disease Control and Prevention (CDC) recommends that all patients with confirmed and suspected CDI be placed on contact isolation precautions that include individual patient room, gowns and gloves for all patient contact, and personalized patient care items and equipment. Furthermore, the CDC emphasizes meticulous hand hygiene for all healthcare providers before patient contact and after removing gloves, with soap and water. It is important to note than in some cases, hand washing with soap and water is recommended over alcohol-based products because of the inability of alcohol-based products to kill *Clostridium* spores. Chlorhexidine baths have no clear role in CDI.

References:

1. Sartelli M, Malangoni MA, Abu-Zidan FM, et al. WSES guidelines for management of Clostridium difficile infection in surgical patients. *World J Emerg Surg.* 2015 Aug 20;10:38.
2. Surawicz CM, Brandt LJ, Binion DG, et al. Guidelines for diagnosis, treatment, and prevention of Clostridium difficile infections. *Am J Gastroenterol.* 2013 Apr;108(4):478-498.
3. Centers for Disease Control and Prevention. Healthcare-associated infections (HAIs). Last updated: September 23, 2015. http://www.cdc.gov/hai/organisms/cdiff/Cdiff_clinicians.html. Accessed June 6, 2016.
4. Dubberke ER, Carling P, Carrico R, et al. Strategies to prevent Clostridium difficile infections in acute care hospitals: 2014 update. *Infect Control Hosp Epidemiol.* 2014 Jun;35(6):628-645.

24. Rationale

Answer: D

Ventriculoperitoneal (VP) shunts are used to treat hydrocephalus, diverting

cerebrospinal fluid to another part of the body for reabsorption. The proximal portion of the shunt catheter is most commonly placed in one of the cerebral ventricles; the distal portion of the shunt can be internalized or externalized. Internalized shunts most commonly drain into the peritoneum of the abdomen.

The overall infection rate for VP shunts has been reported to be as high as 10%. The highest infection rates have been observed during the first month after initial placement or in patients requiring shunt revisions. This is important because up to 50% of patients will require shunt revision within two years.

Early shunt infections most frequently develop via colonization of the shunt with skin flora, presumably related to the recent surgical procedure; staphylococci are the predominant pathogens. Late VP shunt infections (several months after insertion and revision) are usually caused by *Streptococcus* species and gram-negative pathogens such as *Pseudomonas aeruginosa,* and occur more commonly as a result of bowel perforation or peritonitis.

References:

1. Korinek AM, Fulla-Oller L, Boch AL, Golmard JL, Hadiji B, Puybasset L. Morbidity of ventricular cerebrospinal fluid shunt surgery in adults: an 8-year study. *Neurosurgery.* 2011 Apr;68(4):985-995.
2. Ragel BT, Browd SR, Schmidt RH. Surgical shunt infection: significant reduction when using intraventricular and systemic antibiotic agents. *J Neurosurg.* 2006 Aug;105(2):242-247.
3. Steinbok P, Milner R, Agrawal D, et al. A multicenter multinational registry for assessing ventriculoperitoneal shunt infections for hydrocephalus. *Neurosurgery.* 2010 Nov;67(5):1303-1310.
4. Wells DL, Allen JM. Ventriculoperitoneal shunt infections in adult patients. *AACN Adv Crit Care.* 2013 Jan-Mar;24(1):6-12.

25. Rationale

Answer: D

Carbapenem antibiotics play an important role in critical care because they retain activity against gram-negative pathogens that contain cephalosporinases and extended-spectrum ß-lactamases. However, the emergence of carbapenemase-producing bacteria has become a serious threat to public health. Depending on the enzyme, carbapenemase activity may be encoded on chromosomes or plasmids of certain bacteria.

Carbapenemase-producing *Enterobacteriaceae*, most commonly producing *Klebsiella pneumoniae* carbapenemase (KPC), have become more prevalent in the United States since the early 2000s. The KPC enzyme confers resistance to all ß-lactams and, because it resides on transmissible plasmids, it can be transferred from *Klebsiella* to other bacteria. Carbapenem resistance has also been reported in other gram-negative bacteria such as *Pseudomonas aeruginosa* and *Acinetobacter baumannii.*

In addition, several different metallo-ß-lactamase-producing strains leading to carbapenem resistance have been identified, including New Delhi metallo-ß-lactamase, Verona integron-encoded metallo-ß-lactamase, and imipenemase metallo-ß-lactamase. Although more commonly found abroad, these strains have been identified in the United States in patients who have lived or traveled abroad. Contaminated devices may also harbor them. A highly publicized case in 2013 identified transmission of New Delhi metallo-ß-lactamase-producing *Escherichia* coli to many patients after exposure to a single contaminated duodenoscope.

Prior use of broad-spectrum cephalosporins or carbapenems is an important risk factor because of the ability for negative strains to acquire genes from other bacteria and become resistant to carbapenems. Additional risk factors include ICU stay, immunosuppression (such as organ transplantation, diabetes, and malignancy), mechanical ventilation, and indwelling catheters.

Detection of carbapenemase-producing *Enterobacteriaceae* can be challenging because some isolates have minimum inhibitory concentrations (MICs) that fall slightly below the traditional breakpoints for susceptibility and may not be recognized as carbapenemase producers by the clinical laboratory. In addition to ß-lactam/carbapenem resistance, these bacteria often carry genes that confer high levels of resistance to many other antimicrobials, often leaving very limited therapeutic options When culture results identify resistance to any carbapenem or a high MIC, it is prudent to consult an infectious disease specialist for further guidance.

References:

1. Epstein L, Hunter JC, Arwady MA, et al. New Delhi metallo-ß-lactamase-producing carbapenem-resistant Escherichia coli associated with exposure to duodenoscopes. *JAMA.* 2014 Oct 8;312(14):1447-1455.
2. Gupta N, Limbago BM, Patel JB, Kallen AJ. Carbapenem-resistant Enterobacteriaceae: epidemiology and prevention. *Clin Infect Dis.* 2011 Jul 1;53(1):60-67.
3. Patel G, Huprikar S, Factor SH, Jenkins SG, Calfee DP. Outcomes of carbapenem-resistant Klebsiella pneumoniae infection and the impact of antimicrobial and adjunctive therapies. *Infect Control Hosp Epidemiol.* 2008 Dec;29(12):1099-1106.
4. Schwaber MJ, Klarfeld-Lidji S, Navon-Venezia S, Schwartz D, Leavitt A, Carmeli Y. Predictors of carbapenem-resistant Klebsiella pneumoniae acquisition among hospitalized adults and effect of acquisition on mortality. *Antimicrob Agents Chemother* 2008 Mar;52(3):1028-1033.

26. Rationale

Answer: D

The emergence of carbapenem-resistant *Enterobacteriaceae* (CRE) is quickly becoming a worldwide problem, especially in hospitalized patients treated with broad-spectrum antibiotics, which is a risk factor for it. The Centers for Disease Control and Prevention estimates that the two most common types of CRE infections, those

related to *Klebsiella* and *Escherichia* species, cause more than 9,000 healthcare-associated infections per year in the United States. Resistance occurs via the presence of a carbapenem-hydrolyzing ß-lactamase (carbapenemase), which is often present on bacterial plasmids or transposons, thereby allowing transmission between bacterial genera. Possession of a carbapenemase typically confers resistance to all ß-lactam antibiotics, including those with ß-lactamase inhibitors. Also, very high resistance to fluoroquinolones is seen. The mortality rate from CRE infections is extremely high (up to 48%), and treatment is most commonly undertaken with combination therapy, which has been demonstrated to decrease mortality and result in fewer treatment failures compared to monotherapy. The most commonly susceptible antimicrobials are the polymyxins (colistin or polymyxin B), which, depending on in vitro susceptibility testing, are usually combined with fosfomycin, aminoglycosides, tigecycline, or rifampin. Ceftazidime/avibactam, a newer agent recently approved for the treatment of complicated intra-abdominal and urinary tract infections, combines a third-generation cephalosporin with a ß-lactamase inhibitor that, unlike the others, has been shown to possess activity against certain classes of carbapenemases. While promising, experience with this drug in treating CRE is still limited. Although these organisms can cause serious infection, asymptomatic intestinal colonization with carbapenemase-producing strains is common and does not necessarily warrant treatment in the absence of clinical infection.

References:

1. Perez F, El Chakhtour NG, Papp-Wallace KM, Wilson BM, Bonomo RA. Treatment options for infections caused by carbapenem-resistant Enterbacteriaceae: Can we apply “precision medicine” to antimicrobial chemotherapy? *Expert Opin Pharmacother.* 2016 Apr;17(6):761-781.
2. Morrill HJ, Pogue JM, Kaye KS, LaPlante KL. Treatment options for carbapenem-resistant Enterobacteriaceae infections. *Open Forum Infect Dis.* 2015 May 5;2(2):ofv050.

27. Rationale

Answer: C

Vancomycin (or any other agent active against aerobic gram-positive cocci) is not recommended as a standard part of the initial antibiotic regimen for fever and neutropenia. These agents should be considered for specific clinical indications, including suspected catheter-related infection, skin or soft tissue infection, pneumonia, or hemodynamic instability.

The addition of an agent against methicillin-resistant *Staphylococcus aureus* is warranted. Gram-negative coverage is still warranted in febrile neutropenic patients, so switching to only linezolid would be inappropriate. There is no reason to suspect failure of cefepime, so switching to piperacillin/tazobactam is unnecessary. Oxacillin is inappropriate for empiric coverage of potential multidrug-resistant gram-positive organisms. There is no suspicion for community-acquired pneumonia, and ceftriaxone and azithromycin are not recommended as empiric therapy.

References:

1. Freifeld AG, Bow EJ, Sepkowitz KA, et al; Infectious Diseases Society of America. Clinical practice guideline for the use of agents in neutropenic patients with cancer: 2010 update by the Infectious Diseases Society of America. *Clin Infect Dis.* 2011 Feb 15;52(4):e56-e93.
2. De Naurois J, Novitzky-Basso I, Gill MJ, Marti FM, Cullen MH, Roila F; ESMO Guidelines Working Group. Management of febrile neutropenia: ESMO Clinical Practice Guidelines. *Ann Oncol.* 2010 May;21 Suppl 5:v252-v256.

28. Rationale

Answer: A

Botulism is caused by contact with toxins from *Clostridium botulinum*; it can occur with ingestion or inhalation, as well as wound infection. Botulism symptoms are descending paralysis with cranial nerve dysfunction, eventually progressing to ventilatory failure, without fever or changes in mentation. The diagnosis of botulism is largely clinical but can be confirmed with bioassays or detection of the toxin in the blood. Initial treatment may involve supportive care with mechanical ventilation, and the administration of the equine-derived heptavalent (A-G) antitoxin, available from the Centers for Disease Control and Prevention. Intensivists should be aware not only of the effects of botulism, but also of local and regional resources and planning in the case of bioterrorism attack. Both organophosphate poisoning and sarin poisoning present with the classic SLUDGEM syndrome: salivation, lacrimation, urination, diaphoresis, gastrointestinal upset, emesis, miosis. Both can also be treated with either atropine or pralidoxime. Cyanide poisoning presents with generalized weakness, associated with neurologic symptoms such as headache, confusion, and seizures, and cardiac symptoms such as arrhythmias and hypotension. High concentrations of cyanide are rapidly fatal. Initial signs and symptoms of inhalation anthrax are sore throat, shortness of breath, mild fever, fatigue, and muscle aches. Treatment involves ciprofloxacin.

References:

1. Adalja AA, Toner E, Inglesby TV. Clinical management of potential bioterrorism-related conditions. *N Engl J Med.* 2015 Mar 5;372(10):954-962.
2. Centers for Disease Control and Prevention. Emergency Preparedness. http://emergency.cdc.gov/. Accessed June 6, 2016.

Part 5:

Gastrointestinal Disorders

Part 5:
Gastrointestinal Disorders

Instructions: For each question, select the most correct answer.

1. A 60-year-old man is evaluated in the emergency department for a 12-hour history of severe gastric pain. He has a past history of diabetes mellitus,

hypertension, and hyperlipidemia. Vital signs are: temperature 39°C (102.2°F), heart rate 120 beats/min, blood pressure 110/50 mm Hg, respiratory rate 25 breaths/min, oxygen saturation 98% on room air. Formal abdominal ultrasonography reveals gallbladder stones, a common bile duct diameter of 9 mm and evidence of intraductal stones. Laboratory results include: white blood cell count 20,000/mm^3, hematocrit 40%, platelets 500,000/mm^3, lipase 10,000 U/L, calcium 7.0 mg/dL, potassium 4.5 mEq/L, blood urea nitrogen 70 mg/dL, creatinine 2.30 mg/dL, aspartate aminotransferase 400 U/L, alanine aminotransferase 250 U/L, alkaline phosphatase 300 U/L, bilirubin 5.0 mg/dL, lactate 3.0 mg/dL. He is admitted to the ICU with suspected gallstone pancreatitis. After 12 hours in the ICU, despite IV fluid resuscitation and broad-spectrum antibiotics, his condition deteriorates, with worsening pain, increasing lactate level to 5.0 mg/dL, and hypotension.

Which of the following is the most appropriate next step in management?

A. Give more IV fluids and switch antibiotic from piperacillin/tazobactam to meropenem.
B. Consult gastroenterology for urgent endoscopic retrograde cholangiopancreatography (ERCP).
C. Continue conservative management because the pancreatitis could worsen with ERCP.
D. Consult surgery for placement of a percutaneous trans-hepatic cholangiography tube.
E. Consult nephrology for dialysis because of his worsening clinical status.

2. A 35-year-old woman is evaluated in the emergency department for fever, severe epigastric abdominal pain, and nausea that have worsened during the course of 12 hours. She denies any medical history; her father has a history of gallstones. Vital signs are: temperature 38.4°C (101.1°F), heart rate 115 beats/min, blood pressure 90/60 mm Hg, respiratory rate 19 breaths/min, oxygen saturation 93% on 2-L nasal cannula. After blood is drawn for laboratory testing, she is given 4 liters of lactated Ringer solution over four hours. She is also given IV hydromorphone, 1 mg, for pain, and vancomycin, 1 g, and cefepime, 2 g, for fever. An abdominal ultrasound is equivocal for gallbladder wall thickening, but shows pericholecystic fluid and a dilated pancreatic duct. The pancreas appears inflamed, but no necrosis or cyst is noted. Critical care service is consulted for severe pancreatitis. Vital signs after 4 liters of crystalloid are: temperature 38.9°C (102°F), heart rate 109 beats/min, blood pressure 110/75 mm Hg, respiratory rate 22 breaths/min, oxygen saturation 91% on 2-L nasal cannula. Laboratory testing reveals: blood urea nitrogen 45 mg/dL, creatinine 1.0 mg/dL, aspartate aminotransferase 235 U/L, alanine aminotransferase 129 U/L, amylase 2,023 U/L, bilirubin 2.9 mg/dL, lipase 4,320 U/L, white blood cell count 14,000/mm^3, hemoglobin 15.5 g/dL, hematocrit 47%, platelets 450,000/mm^3, lactate 2.1 mg/dL.

Which of the following principles applies to this patient's management?

A. Immediate CT with contrast will provide the most prognostic information.
B. Empiric antibiotics should be continued, because they will decrease her risk of death.
C. Initially, she should be given bowel rest because enteral feeding may worsen prognosis.
D. Chest radiography may be helpful in determining her disease predicted mortality at 30 days.
E. Further IV fluids will decrease her risk of death.

3. A 32-year-old man is evaluated in the emergency department for severe epigastric abdominal pain. History and lipase elevation are diagnostic of acute pancreatitis. Review of systems and other diagnostic workup are negative. Because of persistent fluid requirements to maintain an adequate mean arterial pressure, he is admitted to the ICU.

   Which of the following is the best approach regarding antimicrobial therapy for this patient?

   A. He should be started empirically on broad-spectrum antibiotics to prevent infection of necrotic pancreatitis.
   B. He should be started empirically on antibiotics aimed only at anaerobes.
   C. He should be given perioperative antibiotics only, before surgery.
   D. Without another source of infection present, he should not be given any antibiotics.

4. Which of the following is the most appropriate approach to nutritional support in a 45-year-old woman with pancreatitis?
   A. Total parenteral nutrition should be given early, and total bowel rest favored.
   B. Total parenteral nutrition is the preferred nutrition source, but only after seven days of bowel rest and inability to take anything by mouth.
   C. Enteral nutrition is the preferred source of nutrition, but only after seven days of bowel rest and inability to take anything by mouth.
   D. Enteral nutrition should be instituted as early as possible.

5. A 55-year-old man with a history of hepatitis C and alcoholic cirrhosis is admitted to the ICU from the emergency department (ED) with suspected upper gastrointestinal bleeding. He has a history of esophageal varices requiring banding in the past year. He was started on a proton pump inhibitor and octreotide in the ED, and gastroenterology was consulted. Soon after arrival to the ICU, he decompensates with copious hematemesis and becomes hypotensive. An upper endoscopy for source control is not available for at least one hour.

   In addition to continued resuscitation while awaiting gastroenterology, which of the following is the most appropriate management for this patient?

A. Place a nasogastric tube, start antibiotics for spontaneous bacterial peritonitis (SBP) prophylaxis, and start a low-dose beta-blocker to decrease portal venous pressure.
B. Intubate for airway protection, and place a Blakemore tube for hemorrhage control.
C. Place a Blakemore tube for hemorrhage control, and start antibiotics for SBP prophylaxis.
D. Intubate for airway protection, place a Blakemore tube for hemorrhage control, and start antibiotics for SBP prophylaxis.

6. A 24-year-old woman with a history of depression is brought to the emergency department by emergency medical services (EMS) for lethargy and confusion. The patient was last seen by family about eight hours ago. Emergency medical service personnel had found an empty bottle of acetaminophen at the scene. The patient has a Glasgow Coma Scale score of 10, but is hypotensive. She requires a 2-liter bolus of IV fluid to stabilize her blood pressure. Laboratory findings are: aspartate aminotransferase 54 U/L, alanine aminotransferase 32 U/L, alkaline phosphate 110 U/L, albumin 3.8 g/dL, INR 1.2, lactate 1.0 mg/dL. Arterial blood gas analysis reveals: pH 7.35, partial pressure of carbon dioxide 35 mm Hg, partial pressure of oxygen 95 mm Hg. Acetaminophen level is 400 mg/dL. ECG shows normal sinus rhythm.

   Which of the following is the most appropriate next step in this patient's management?

   A. Naloxone
   B. Vasopressors
   C. Intubation
   D. Observation
   E. *N*-acetylcysteine

7. A 63-year-old man with a history of liver cirrhosis secondary to hepatitis C and alcohol abuse is admitted to the ICU with profound hypotension. He had been evaluated in the emergency department after having worsening abdominal pain and fever for the past three days. He is in severe respiratory distress and is intubated. Blood pressure is 80/40 mm Hg despite adequate fluid resuscitation. He is started on vasopressors after placement of a central venous Line. Spontaneous bacterial peritonitis (SBP) is suspected, and a diagnostic paracentesis is performed and peritoneal fluid sent for analysis.

   Which of the following statements is true?

   A. Renal failure is not an independent predictor of mortality in patients with SBP.
   B. The most common SBP organisms are *Escherichia coli* and *Streptococcus pneumoniae*.

C. A diagnosis of SBP can be confirmed by a white blood cell count of 400/μL, polymorphonuclear leukocytes of 80% and red blood cell count of 2,000 μL.
D. Blood cultures are not needed in a patient with SBP.
E. Fresh frozen plasma should be given for an INR of 1.7, to avoid hemorrhagic complications of a diagnostic paracentesis.

8. A 64-year-old man who has a history of coronary artery disease and who underwent coronary artery bypass grafting two weeks ago is evaluated in the emergency department for fatigue and melena. He is started on pantoprazole infusion. Esophagoduodenoscopy (EGD) reveals a duodenal ulcer with two large vessels visible; these are clipped and injected with epinephrine. Eight hours later, he has two large maroon-colored bowel movements with clots. He undergoes urgent transcatheter arterial embolization (TAE) of the gastroduodenal artery. Hemoglobin remains stable at 8.3 g. Twenty-four hours later, he has further episodes of melena. Complete blood count reveals hemoglobin level of 5.9 g.

   Which of the following is the most appropriate next step in management?

   A. Restart proton pump inhibitor.
   B. Repeat EGD.
   C. Repeat TAE.
   D. Consult surgery for duodenectomy.
   E. Perform bleeding scan.

9. A 38-year-old woman at 34 weeks' gestation is admitted to the ICU with altered mental status and jaundice. Right upper quadrant ultrasound reveals a fatty liver.

   Which of the following is the most appropriate therapeutic intervention?

   A. Ursodeoxycholic acid
   B. Cholestyramine
   C. Magnesium sulfate
   D. Delivery of the fetus

10. A 38-year-old man, previously in good health, presents with hematemesis. He has no history to suggest liver disease with gastric or esophageal varices. Bright red blood is aspirated after placement of a nasogastric tube and is not cleared with 500 mL lavage.

    Which of the following is the best first step in management, pending diagnostic endoscopy?

    A. Continuous infusion of vasopressin
    B. Continuous infusion of H2 blockers
    C. Continuous infusion of proton pump inhibitors
    D. Administration of sucralfate and H2 blockers in sequence

E. Administration of fresh frozen plasma

11. A 42-year-old woman has a two-week history of nausea and vomiting. She had bariatric surgery two months ago. She reports generalized weakness, fatigue, confusion, weakness of the lower extremities associated with numbness in both hands and feet, and blurry vision. Physical examination shows sinus tachycardia, horizontal nystagmus, and peripheral neuropathy with muscle weakness and decreased reflexes.

    The most appropriate next step is IV administration of

    A. systemic steroids
    B. antibiotics
    C. thiamine
    D. immunoglobulin

Part 5 Answers:
Gastrointestinal Disorders

1. Rationale

Answer: B

This patient has gallstone pancreatitis with associated cholangitis and rapid deterioration, requiring urgent source control. The exact role and timing of endoscopic retrograde cholangiopancreatography (ERCP) in gallstone pancreatitis has been a topic of debate for years, with many studies finding conservative management equivalent to ERCP intervention in the first 24 to 72 hours after onset. However, this is in the absence of cholangitis and biliary obstruction, for which urgent ERCP is indicated, especially with rapid clinical deterioration.

Providing additional IV fluids for severe sepsis secondary to cholangitis is appropriate. However, switching antibiotics, which should provide adequate coverage, less than 24 hours after initiation and not obtaining source control will not improve his condition. Worsening pancreatitis is a known complication of ERCP, but the benefit outweighs the risk in this case, with biliary obstruction and severe sepsis from cholangitis. Guideline recommendations are in favor of ERCP for definitive management compared to placement of a percutaneous trans-hepatic cholangiography tube. This may be considered in a patient who is unable to tolerate ERCP or if ERCP is unavailable. Dialysis may be needed if his clinical condition worsens with associated renal failure, but this is likely to improve once source control is obtained. There is no acute indication for dialysis at this time.

References:

1. Fogel EL, Sherman S. ERCP for gallstone pancreatitis. *N Engl J Med.* 2014;370(2):150-157.
2. Tse F, Yuan Y. Early routine endoscopic retrograde cholangiopancreatography strategy versus early conservative management strategy in acute gallstone pancreatitis. *Cochrane Database Syst Rev.* 2012 May 16;(5):CD009779.

2. Rationale

Answer: D

The most widely used scoring system for acute pancreatitis is the Acute Physiologic and Chronic Health Evaluation (APACHE) II, but it is cumbersome. The Bedside Index for Severity in Acute Pancreatitis (BISAP) scoring system is validated and easier to

calculate. The BISAP score consists of blood urea nitrogen greater than 25, impaired mental status, systemic inflammatory response syndrome, age >60, and pleural effusion. A score of 3 or more shows a significant increase in mortality in patients with acute pancreatitis. The presence of pleural effusion in this patient takes her score from 2 to 3, which increases her 30-day mortality. A chest radiograph also can show presence of pneumonia and acute respiratory distress syndrome (ARDS); it completes the clinical picture. An abdominal CT aids in prognosis and risk stratification regarding necrotizing pancreatitis, but an abdominal ultrasound has already been done. There is no immediate need for an abdominal CT.

This patient population has significant inflammatory response, which can mimic septic shock, but they do not routinely need empiric antibiotics. Pancreatitis can be sterile, necrotizing, or infected; these often resemble each other as to clinical picture. In the absence of other confounding factors, the position of both the American College of Gastroenterology and the American Gastroenterology Association is to hold off antibiotics until infection is proven.

Multiple studies suggest that early feeding may improve outcome in severe acute pancreatitis; the recommendation is to optimize nutrition because of their catabolic state. This patient has been given an appropriate fluid bolus before the critical care consultation, with a mild improvement in vital signs. She may require further volume loading, but there is no obvious indication for continued large-volume resuscitation with crystalloids. She has not had a chest radiograph, and she may already have the beginnings of ARDS.

References:

1. Papachristou GI, Muddana V, Yadav D, et al. Comparison of BISAP, Ranson's, APACHE-II, and CTSI scores in predicting organ failure, complications, and mortality in acute pancreatitis. *Am J Gastroenterol.* 2010 Feb;105(2):435-441.
2. Singh VK, Wu BU, Bollen TL, et al. A prospective evaluation of the bedside index for severity in acute pancreatitis score in assessing mortality and intermediate markers of severity in acute pancreatitis. *Am J Gastroenterol*. 2009 Apr;104(4):966-971.
3. Cho YS, Kim HK, Jang EC, et al. Usefulness of the bedside index for severity in acute pancreatitis in the early prediction of severity and mortality in acute pancreatitis. *Pancreas.* 2013 Apr;42(3):483-487.
4. Dellinger EP, Tellado JM, Soto NE, et al. Early antibiotic treatment for severe acute necrotizing pancreatitis: a randomized, double-blind, placebo-controlled study. *Ann Surg.* 2007 May;245(5):674-683.
5. Tenner S, Baillie J, DeWitt J, Vege SS, American College of Gastroenterology. American College of Gastroenterology guideline: management of acute pancreatitis. *Am J Gastroenterol.* 2013 Sep;108(9):1400-1415.

3. Rationale

Answer: D

Infection in the setting of severe acute pancreatitis worsens outcome. Unfortunately,

administering antibiotics to prevent this complication is ineffective. Early antibiotic prophylaxis in this setting is controversial, but there is no data that supports this practice. In the setting of infected pancreatitis, antibiotics typically aimed at gastrointestinal tract microbes should be given. The most studied class of antibiotics in this situation are carbapenems, which are typically given. There is no role for emergent surgery in this patient.

References:

1. Janisch N, Gardner T. Recent advances in managing acute pancreatitis. *F1000Res*. 2015 Dec 18;4.
2. Whitcomb DC. Acute pancreatitis. *N Engl J Med.* 2006 May 18;354(20):2142-2150.

4. Rationale

Answer: D

There is a lack of evidence to support the historic practice of strict nothing-by-mouth status in the setting of acute pancreatitis. In the absence of contraindications to enteral feeding, a patient with pancreatitis should be approached no differently than other critically ill patients. In the setting of pancreatitis, early enteral nutrition is associated with fewer infectious and inflammatory complications, reduced need for operative interventions, decreased organ failure, and reduced risk of death.

Reference:

1. Lodewijkx PJ, Besselink MG, Witteman BJ, et al; On Behalf of the Dutch Pancreatitis Study Group. Nutrition in acute pancreatitis: a critical review. *Expert Rev Gastroenterol Hepatol*. 2016 May;10(5):571-580.

5. Rationale

Answer: D

Cirrhotic patients with esophageal varices can decompensate very quickly and require skilled resuscitation to maximize their chances for survival. This patient had a sentinel bleed before ICU arrival and was started on appropriate therapy while in the emergency department. On arrival to the ICU, his condition worsened; with significant upper gastrointestinal bleeding, airway management is critical. Intubation is necessary for any gastrointestinal procedure as is placing a Blakemore tube in the esophagus to avoid exsanguination while awaiting gastroenterology. Often overlooked, but critical to improved outcomes, is antibiotic prophylaxis to prevent spontaneous bacterial peritonitis in cirrhotic patients with variceal hemorrhage. Starting a third-generation IV cephalosporin has been shown to reduce all-cause mortality, infection-related mortality, rebleeding events and hospitalization lengths of stay. Inserting a nasogastric tube is not incorrect because it has never been shown to worsen variceal bleeding, but starting a beta-blocker in the acute setting of hypotension is incorrect because it may worsen hemodynamics.

References:

1. Chavez-Tapia NC, Barrientos-Gutierrez T, Tellez-Avila FI, Soares-Weiser K, Uribe M. Antibiotic prophylaxis for cirrhotic patients with upper gastrointestinal bleeding. *Cochrane Database Syst Rev.* 2010 Sep Sep 8;(9):CD002907.
2. Osman D, Djibré M, Da Silva D, Goulenok C. Management by the intensivist of gastrointestinal bleeding in adults and children. *Ann Intensive Care.* 2012 Nov 9;2(1):46.

6. Rationale

Answer: E

Acetaminophen toxicity is among the most common drug toxicities seen in the emergency department (50.2/1000 visits), given its widespread over-the-counter availability. There are four clinical phases of acetaminophen toxicity: phase 1 (0-24 hours): asymptomatic, mild increase in transaminases; phase 2 (18-72 hours): right upper quadrant pain, hypotension; phase 3 (72-96 hours): jaundice, hypoglycemia, coagulopathy; phase 4 (4 days - 3 weeks): recovery. This patient is in phase 1 and there is no indication for intubation or vasopressors because she is still responsive to IV fluids.

Naloxone has no role in acetaminophen overdose because patients who take acetaminophen use up their glutathione stores, leading to *N*-acety- *p*-benzoquinonimine (NAPQI) excess. Excess NAPQI is further propagated in the hepatic cells, leading to hepatic necrosis. *N*-acetylcysteine (NAC) replenishes depleted glutathione reserves in the liver and enhances nontoxic metabolism of acetaminophen. Patients with acetaminophen overdose are stratified according to the Rumack-Matthew nomogram; all high-risk patients should be started on NAC therapy, preferably before elevation of aspartate aminotransferase (AST), and continued as long as AST does not rise or serum acetaminophen levels are undetectable. If the patient shows signs of hepatic dysfunction or has a massive dose of acetaminophen (>30 g) or serum acetaminophen level greater than 500mg/L, then the patient should be transferred to a liver transplant center for urgent evaluation of possible impending liver failure.

References:

1. Underhill TJ, Greene MK, Dove AF. A comparison of the efficacy of gastric lavage, ipecacuanha and activated charcoal in the emergency management of paracetamol overdose. *Arch Emerg Med*. 1990 Sep;7(3):148-154.
2. Spiller HA, Krenzelok EP, Grande GA, Safir EF, Diamond JJ. A prospective evaluation of the effect of activated charcoal before oral N-acetylcysteine in acetaminophen overdose. *Ann Emerg Med*. 1994 Mar;23(3):519-S523.
3. Smilkstein MJ, Knapp GL, Kulig KW, Rumack BH. Efficacy of oral N-acetylcysteine in the treatment of acetaminophen overdose. Analysis of the national multicenter study (1976 to 1985). *N Engl J Med*. 1988 Dec 15;319(24):1557-1562.

4. Bailey B, Amre DK, Gaudreault P. Fulminant hepatic failure secondary to acetaminophen poisoning: a systematic review and meta-analysis of prognostic criteria determining the need for liver transplantation. *Crit Care Med.* 2003 Jan;31(1):299-305.
5. Ibrahim T, Agnihotri S, Agnihotri AK. Paracetamol toxicity—an overview. *Emergency Med.* 2013;3:158.

7. Rationale

Answer: C

Bacterial translocation is the key mechanism in SBP. The diagnosis of spontaneous bacterial peritonitis is made by the presence of more than 250 polymorphonuclear leukocytes (PMNs) per mm^3 of ascitic fluid. This count, however, must be corrected for the presence of red blood cells (RBCs), the level of which is commonly elevated if the patient has a traumatic paracentesis. The correction factor is a decrease of 1 PMN for every 250 RBCs per mm^3 of blood. The most common organisms implicated are *Escherichia coli* and *Klebsiella* species. Ascitic and blood cultures should be performed because 50% of SBP cases are associated with bacteremia. Broad-spectrum antibiotics are warranted until sensitivities can be obtained. Cefotaxime has the highest rate of resolving infections and minimal side effects. Paracentesis in the critically ill may need to be performed; the use of ultrasound and an experienced operator decreases risk to the patient. A prospective study of 1100 patients showed that an INR of 1.7 should not require correction to safely perform paracentesis. Renal failure remains an independent predictor of mortality in patients with SBP.

References:

1. Such J, Runyon BA. Spontaneous bacterial peritonitis. *Clin Infect Dis*. 1998 Oct;27(4):669-697.
2. Riggio O, Angeloni S. Ascitic fluid analysis for diagnosis and monitoring of spontaneous bacterial peritonitis. *World J Gastroenterol*. 2009 Aug 21;15(31):3845-3850.
3. Chavez-Tapia NC, Soares-Weiser K, Brezis M, Leibovici L. Antibiotics for spontaneous bacterial peritonitis in cirrhotic patients. *Cochrane Database Syst Rev*. 2009 Jan 21;(1):CD002232.
4. Felisart J, Rimola A, Arroyo V, et al. Cefotaxime is more effective than is ampicillin-tobramycin in cirrhotics with severe infections. *Hepatology*. 1985 May-Jun;5(3):457-462.
5. Garcia-Tsao G. Spontaneous bacterial peritonitis: a historical perspective. *J Hepatol*. 2004 Oct;41(4):522-527.

8. Rationale

Answer: C

Multiple studies have demonstrated transcatheter arterial embolization (TAE) to be an appropriate intervention after initial endoscopy failed to control bleeding. In instances

of peptic or duodenal ulcer rebleeding after initial TAE, a subsequent embolization may be performed in patients who fail initial TAE (option C). In 2004, Ripoll et al performed a retrospective analysis of 70 patients who underwent surgery versus TAE for management of refractory upper gastrointestinal bleeding. The study group found no significant difference in rebleeding rate, need for subsequent procedures, or mortality. Additionally, a 2014 meta-analysis of studies comparing TAE to emergency surgery showed increased rebleeding rate among patients who underwent TAE; however, the morbidity rate was equivocal. There is little utility in performing a repeat esophagoduodenoscopy in a patient who failed clipping, epinephrine injections, and initial TAE. A surgical consult should be obtained, but surgery should not be definitive therapy until a second TAE does not control bleeding. Conservative management with transfusion alone is not appropriate because the patient has evidence of severe rebleeding of a known duodenal ulcer, which requires source control. A bleeding scan would not be useful because the source of the bleeding is known.

References:

1. Ljungdahl M, Eriksson LG, Nyman R, Gustavsson S. Arterial embolisation in management of massive bleeding from gastric and duodenal ulcers. *Eur J Surg.* 2002;168(7):384-390.
2. Wong TC, Wong KT, Chiu PW, et al. A comparison of angiographic embolization with surgery after failed endoscopic hemostasis to bleeding peptic ulcers. *Gastrointest Endosc.* 2011 May;73(5):
900-908.
3. Eriksson LG, Ljungdahl M, Sundbom M, Nyman R. Transcatheter arterial embolization versus surgery in the treatment of upper gastrointestinal bleeding after therapeutic endoscopy failure. *J Vasc Interv Radiol.* 2008 Oct;19(10):1413-1418.
4. Beggs AD, Dilworth MP, Powell SL, Atherton H, Griffiths EA. A systematic review of transarterial embolization versus emergency surgery in treatment of major nonvariceal upper gastrointestinal bleeding. *Clin Exp Gastroenterol.* 2014 Apr 16;7:93-104.
5. Ripoll C, Bañares R, Beceiro I, et al. Comparison of transcatheter arterial embolization and surgery for treatment of bleeding peptic ulcer after endoscopic treatment failure. *J Vasc Interv Radiol.* 2004 May;15(5):447-450.

9. Rationale

Answer: D

Acute fatty liver of pregnancy is a life-threatening condition occurring in the last trimester. Differentiation from HELLP syndrome (hemolysis, elevated liver function, low platelet count) and severe preeclampsia may require a liver biopsy. Acute fatty liver is associated with hepatic dysfunction, including synthetic function. Ammonia and transaminase levels are higher, hypoglycemia is more frequent, and disseminated intravascular coagulation is common. The treatment of choice is delivery of the fetus and supportive care. Ursodeoxycholic acid is appropriate treatment for intrahepatic cholestasis of pregnancy.

References:

1. Rahman TM, Wendon J. Severe hepatic dysfunction in pregnancy. *QJM.* 2002 Jun;95(6):343-357.
2. Ibda JA. Acute fatty liver of pregnancy: an update on pathogenesis and clinical implications. *World J Gastroenterol.* 2006;12:7397-7404.
3. Chen H, Yuan L, Tan J, Liu Y, Zhang J. Severe liver disease in pregnancy. *Int J Gynaecol Obstet.* 2008 Jun;101(3):277-280.

10. Rationale

Answer: C

Peptic ulcer is the most frequent cause of acute upper gastrointestinal tract bleeding resulting in hospitalization (more than 50% of cases). Proton pump inhibitors (PPIs) are frequently used as part of initial management. Compared with either placebo or H2 blockers, PPI treatment significantly reduces rates of ulcer rebleeding and surgical intervention. A meta-analysis of randomized controlled trials of PPI treatment for ulcer bleeding found no significant effect on 30-day all-cause mortality, which was the predetermined primary end point for the clinical trials. Initiation of treatment before endoscopy decreases the stigmata of bleeding seen on endoscopy but has no effect on bleeding, transfusion requirement, need for surgery, or mortality.

Although some have recommended pre-endoscopic PPI therapy to downstage the endoscopic lesion, this approach should not delay endoscopy. Endoscopy is a diagnostic and therapeutic intervention and should be done in a time sensitive manner. Pre endoscopic PPI therapy may be most beneficial in instances of delayed early endoscopic treatment or when available endoscopic expertise is limited or suboptimal. Finally, all patients with bleeding peptic ulcers should be tested for *H pylori* and treated when present with proper follow up to confirm eradication.

Reference:

1. Kumar R, Mills AM. Gastrointestinal bleeding. *Emerg Med Clin N Am*. 2011 May;29(2):239-252.

11. Rationale

Answer: C

Thiamin deficiency is rare and mostly caused by depletion of vitamin B_1 stores. People may become deficient in thiamin by not ingesting enough vitamin B_1 in the diet or through the body's excess use; the latter may result from hyperthyroidism, pregnancy, lactation, or fever. Thiamin deficiency can occur after bariatric surgery. With nervous system involvement, it is called dry beriberi. Neurologic findings can be peripheral neuropathy characterized by symmetrical impairment of sensory, motor, and reflex functions of the extremities, especially in the distal lower limbs. The peripheral neuropathy in thiamin deficiency may also present with a subacute motor axonal neuropathy, mimicking Guillain-Barré syndrome. Another presentation of

neurologic involvement is Wernicke encephalopathy, in which an orderly sequence of symptoms occurs, including vomiting, horizontal nystagmus, palsies of the eye movements, fever, ataxia, and progressive mental impairment, leading to Korsakoff syndrome. Prognosis is good since the condition mostly responds to thiamin replacement.

References:

1. Isselbacher KJ. *Harrison's Principles of Internal Medicine*. 13th ed. New York: McGraw-Hill; 1994:474-475.
2. Spinazzi M, Angelini C, Patrini C. Subacute sensory ataxia and optic neuropathy with thiamine deficiency. *Nat Rev Neurol.* 2010 May;6(5):288-293.
3. Matrana MR, Davis WE. Vitamin deficiency after gastric bypass surgery: a review. *South Med J.* 2009 Oct;102(10):1025-1031.
4. Karuppagounder SS, Xu H, Pechman D, Chen LH, DeGiorgio LA, Gibson GE. Translocation of amyloid precursor protein C-terminal fragment(s) to the nucleus precedes neuronal death due to thiamine deficiency-induced mild impairment of oxidative metabolism. *Neurochem Res.* 2008 Jul;33(7):1365-1372

Part 6:

Neurological Disorders

Part 6:
Neurological Disorders

Instructions: For each question, select the most correct answer.

1. A 77-year-old man anticoagulated with warfarin for atrial fibrillation has a subdural hematoma and intracerebral hemorrhage following a fall. He undergoes

emergent decompressive craniectomy with evacuation of the hematoma and placement of an external ventricular drain (EVD). His neurologic status continues to improve but on postoperative day seven he has altered mental status, temperature of 38.9°C (102°F), and leukocytosis (21 x 10^9/L). Head CT shows stable postoperative changes. Cerebrospinal fluid (CSF) sample reveals: white blood cell count 120/cm^3, red blood cell count 1,800/cm^3, glucose 22 mg/dL, protein 55 mg/dL. Blood, sputum, urine, and CSF cultures are sent for analysis.

Which of the following is the most appropriate next step in this patient's management?

A. Remove the EVD, and start IV vancomycin and IV gentamicin.
B. Replace the EVD, and start intraventricular vancomycin.
C. Replace the EVD, and start IV vancomycin.
D. Remove the EVD, and start IV vancomycin and IV cefepime.

2. A 50-year-old man is brought to the emergency department encephalopathic, with a Glasgow Coma Scale score of 6. History is limited but includes psychiatric illness with antipsychotic medication nonadherence. He is intubated to secure his airway and admitted to the ICU. Initial laboratory data reveal: sodium 161 mEq/L, white blood cells 11,500/µL, blood urea nitrogen 127 mg/dL, hemoglobin 17.1 g/dL, creatinine 2.8 mg/dL. Toxicology screen is negative. Head CT reveals no acute pathology. During the course of the following week, he is hydrated; his acute renal failure and hypernatremia resolve, but he remains neurologically impaired. His eyes open but there is no visual pursuit. He is adynamic in bed, and extremities are flaccid. Further neurologic testing is performed. An EEG shows a nonspecific pattern of electrical activity, with no epileptic activity. Lumbar puncture shows white blood cells 0, glucose 80 mg/dL, protein 42 g/L. Repeat head CT shows no acute pathology. Brain MRI shows extensive periventricular white matter changes and no brainstem abnormalities.

   The patient's encephalopathy is most consistent with which of the following disorders?

   A. Anti-NMDA receptor encephalitis
   B. Drug-related encephalopathy
   C. Infectious meningoencephalitis
   D. Malignant catatonia
   E. Osmotic demyelination syndrome

3. A 21-year-old woman with a long history of recreational drug abuse is admitted to the ICU with severe agitation. Toxicology screen reveals only cannabis metabolites. Attempts are made to use opiates and benzodiazepines empirically to treat for a withdrawal syndrome, but to no avail. She continues to manifest frequent bursts of purposeless activity, does not follow verbal commands, and exhibits perifacial dystonic movements. EEG reveals a pattern consistent with nonspecific encephalopathy. Head CT is nonrevealing. Lumber puncture reveals

clear fluid with cerebrospinal fluid (CSF) pleocytosis and CSF protein of 100 mg/dL. CSF cultures are negative, as is herpes polymerase chain reaction. CSF assay for anti-NMDA receptor antibodies is positive. During the following weeks, she is treated with high-dose steroids, IV immunoglobulin, and plasmapheresis without improvement.

Which of the following is the most appropriate next step in this patient's management?

A. Antipsychotic agents
B. Cyproheptadine
C. Antithymocyte globulin
D. Electroconvulsive therapy
E. Clonidine

4. A 48-year-old woman presents to the emergency department (ED) obtunded after the worst headache of her life. Head CT reveals subarachnoid hemorrhage. While in the ED, her mental status worsens and she is intubated for airway protection. Repeat head CT reveals an increase in ventricular size but no increase in bleeding.

   Which of the following is the most definitive course of action?

   A. Administer mannitol.
   B. Place intraparenchymal intracranial pressure monitor.
   C. Begin continuous EEG.
   D. Place external ventricular drain and remove cerebrospinal fluid.
   E. Hyperventilate.

5. A 60-year-old woman is evaluated in the emergency department for the worst headache of her life. She now has a bilateral occipital headache and nausea. Neurologic examination is otherwise unremarkable. Noncontrast head CT is shown below.

Which of the following is the best initial management?

A. Treat the blood pressure if systolic blood pressure is greater than 180 mm Hg.
B. Perform a CT angiogram to assess the source of bleeding.
C. Perform a lumbar puncture to assess for xanthochromia.
D. Perform a diagnostic cerebral angiogram to assess the source of bleeding.

6. A 41-year-old man with a mechanical aortic valve who is on warfarin therapy is brought to the emergency department by emergency medical services after the acute onset of right-sided weakness. One hour ago, he had no symptoms. His temperature is 36.9°C (98.4°F), heart rate 90 beats/min, blood pressure 183/95 mm Hg, and respiratory rate 18 breaths/min. On examination, he has a left gaze preference, right homonymous hemianopia, right facial droop, right arm plegia, and right leg paresis. He is mute. Noncontrast head CT is normal. INR is 1.3.

   Which of the following treatments should the patient receive as early as possible, and for what reason?

   A. Endovascular therapy with a stent retriever because his clinical syndrome is consistent with a large vessel occlusion
   B. Endovascular therapy with a stent retriever because he is on warfarin and therefore IV recombinant tissue plasminogen activator (rtPA) is contraindicated
   C. Endovascular therapy with a stent retriever because his systolic blood pressure is 183 mm Hg and therefore IV rtPA is contraindicated
   D. IV rtPA because there is no contraindication to it

7. A young man is involved in a high-speed motor vehicle collision while intoxicated. He is intubated in the emergency department with etomidate and succinylcholine. Head CT is notable for diffuse axonal injury, with scattered punctate hemorrhages. He is admitted to the ICU, where he is given midazolam and fentanyl infusions overnight. The next morning, while his sedation is held for an hour, his pupils are 5 mm and unreactive, and he has no cough or gag reflexes.

   Which of the following is the best course of action?

   A. Explain to his family that he has no brainstem reflexes, and he is therefore brain dead.
   B. Perform apnea testing to confirm brain death.
   C. Obtain neurovascular imaging to confirm brain death.
   D. Continue to hold all sedation and follow his neurologic examination.
   E. Administer flumazenil and naloxone in an attempt to wake him.

8. A 29-year-old man hanged himself and is resuscitated at the site by emergency medical services for pulseless electrical activity arrest lasting 19 minutes. On arrival in the emergency department, he is comatose. Temperature-targeted therapy is initiated on ICU admission. He remains comatose. Two days after completion of hypothermia, his pupils become widely dilated without reaction to light and, as the day progresses, he is declared dead by neurologic criteria. Other than depression, he had had no major medical illness before his hanging. His family has given consent for organ donation. Therapy has now been directed toward optimization of organ function before procurement.

   Which of the following hormone replacement strategies should be taken into account?

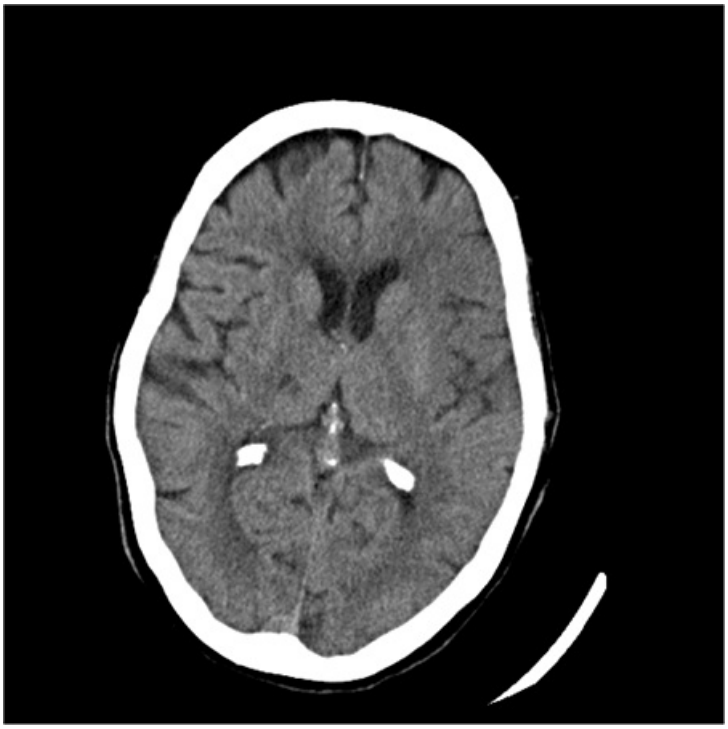
   A. Thyroid supplementation should be initiated with thyroxine rather than triiodothyronine.
   B. A vasopressin infusion should be considered for hypotension refractory to fluids.
   C. High-dose corticosteroids serve no utility and should not be administered.
   D. Hyperglycemia should be managed aggressively to achieve normoglycemia.

9. Which of the following is the correct approach to fluid management of the potential multiorgan donor after brain death?
   A. Maintenance of mean arterial pressure ≥60 mm Hg
   B. Aggressive fluid administration titrated to elevated filling pressures
   C. Urine output ≥2 mL/kg/hr
   D. Colloids preferred over crystalloids

10. In the United States, except when there are mitigating circumstances, which of the following is the recommended method for brain death determination?
   A. EEG

B. Clinical examination
C. Cerebral angiography
D. Cerebral nuclear perfusion scan
E. Transcranial Doppler

11. A 75-year-old woman with a medical history of atrial fibrillation and hypertension is brought to the emergency department by her husband for sudden onset of aphasia, left hemiparesis, and dysarthria two hours ago. She takes warfarin for stroke prevention. Vital signs are: blood pressure 208/108 mm Hg, heart rate 108 beats/min, respiratory rate 16 breaths/min, oxygen saturation 96%, and temperature 36.8°C (98.2°F). On examination, she has aphasia, is unable to name or repeat objects, and appears confused. She has no withdrawal of the right upper and lower extremity, and her gaze does not pass the midline. White blood cell count is 14,500/µL, INR is 1.6, partial thromboplastin time is 28 sec, and platelet count is 190,000/µL. CT is shown below.



Which of the following is the most appropriate intervention?

A. Administer IV recombinant tissue plasminogen activator (rtPA) and delay treatment of blood pressure until repeat CT is obtained.
B. Treat blood pressure immediately to a goal systolic blood pressure <185 mm Hg and administer IV rtPA.
C. Administer fresh frozen plasma.
D. Administer IV phosphenytoin for seizure prophylaxis.

12. A 59-year-old, active man with a medical history of atrial fibrillation, diabetes mellitus, systolic heart failure, and hypertension is brought to the emergency

department by his wife for sudden onset of aphasia, left hemiparesis, and dysarthria eight hours ago. He takes aspirin and pravastatin for stroke prevention. Vital signs are: blood pressure 188/98 mm Hg, heart rate 108 beats/min, respiratory rate 26 breaths/min, oxygen saturation 86%, and temperature 38.2°C (100.8°F). On examination, he is hard to arouse, has a left-sided gaze palsy with symmetric and reactive pupils, and a dense right-sided hemiplegia. Glasgow Coma Scale score is 7; National Institutes of Health Stroke Scale score is 23. He is intubated for mechanical ventilation, an infusion of 25% mannitol is started, his head is elevated at a 30° angle, and he is transferred to the ICU. White blood cell count is 12,500/µL, INR 1.4, partial thromboplastin time is 28 sec, and platelets are 150,000/µL. CT is shown below.

Which of the following is the best next intervention?

A. Adjust the ventilator to immediately hyperventilate.
B. Administer IV tissue plasminogen activator (tPA).
C. Request emergent consult for endovascular intra-arterial tPA.
D. Request emergent neurosurgical consult for decompressive hemicraniectomy.

13. A 34-year-old woman with a medical history significant for tobacco and cocaine abuse is brought to the emergency department (ED) by a family member after a witnessed seizure. She is currently unarousable. Vital signs are: blood pressure 198/100 mm Hg, heart rate 62 beats/min, respiratory rate 8 breaths/min. Glasgow Coma Scale score is 6. She is immediately intubated and elicits bilateral extensor motor responses with bilateral dilated pupils at 5 mm. The ED physician decides to mechanically ventilate to hyperventilate her, and administers a dose of IV mannitol 25%. CT is shown below.

Besides controlling her blood pressure, which of the following therapies is most appropriate?

A. IV tissue plasminogen activator
B. Phosphenytoin bolus
C. Dexamethasone bolus
D. Placement of an external ventricular drain

14. A 44-year-old woman with a history of prior stroke and atrial fibrillation, and who takes dabigatran for anticoagulation, is admitted to the hospital for management of a large intracerebral hemorrhage, shown below. She is intubated for lethargy and admitted to the ICU. Vital signs are: blood pressure 175/98 mm Hg, heart rate 108 beats/min, respiratory rate 22 breaths/min, and temperature 36.7°C (98°F). Her Glasgow Coma Scale score is 7.

Which of the following treatments is most appropriate?

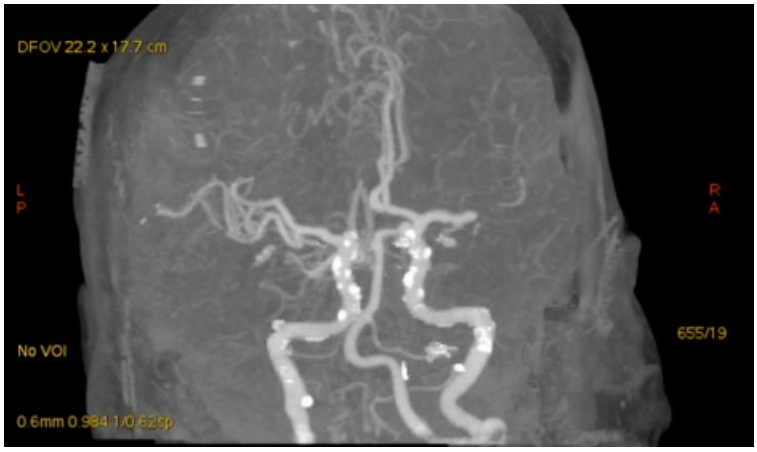
A. Idarucizumab
B. Prothrombin complex concentrate
C. Vitamin K
D. Factor VII
E. Fresh frozen plasma

15. A 54-year-old man with a history of hypertension is admitted to the ICU for evaluation of a left basal ganglia intracerebral hemorrhage measuring 45 mL and intraventricular hemorrhage. There is evidence of early onset of obstructive hydrocephalus. On admission, his Glasgow Coma Scale score is 6, and he is intubated for mechanical ventilation. He also has a right hemiplegia with extensor posturing. Blood pressure is 198/109 mm Hg, heart rate 109 beats/min, and respiratory rate 24 breaths/min. He has mild obesity.

    Which of the following interventions could potentially improve his chance of survival?

    A. Intraventricular tissue plasminogen activator
    B. Lowering systolic blood pressure to less than 140 mm Hg
    C. Hypothermia (core temperature 35°C [95°F])
    D. Antiseizure medication for seven days
    E. Insertion of an external ventricular drain

16. Which of the following pairs of physical examination findings most likely corresponds to the head CT angiogram shown below?



A. Left facial droop and right-sided hemiparesis
B. Right facial droop and left-sided hemiparesis
C. Right facial droop and right-sided hemiparesis
D. Left facial droop and left-sided hemiparesis

17. A 65-year-old woman with hypertension, paroxysmal atrial fibrillation, and hyperlipidemia, who is not on anticoagulation, is evaluated in the emergency department of a large tertiary referral center with left-sided weakness that began two hours ago. On examination, she has a right gaze preference, left facial droop, left arm plegia, left leg paresis, dysarthria, dysphagia, and extinction to double simultaneous stimulation on the left. National Institutes of Health Stroke Scale score is 17. Temperature is 37°C (98.6°F), heart rate 110 beats/min, blood pressure 173/90 mm Hg, and respiratory rate 20 breaths/min. Noncontrast head CT is normal. She is given IV recombinant tissue plasminogen activator (rtPA). Head CT angiogram reveals a right M1 middle cerebral artery occlusion.

    Which of the following is the best next step?

    A. Once IV rtPA infusion is complete, recheck examination; if not improved, perform endovascular therapy with stent retriever.
    B. Wait 20 minutes, recheck examination; if not improved, perform endovascular therapy with stent retriever.
    C. Wait 30 minutes, recheck examination; if not improved, perform endovascular therapy with stent retriever.
    D. Order a CT perfusion to evaluate for salvageable penumbra before deciding on endovascular therapy.
    E. Immediately perform endovascular therapy with stent retriever.

18. An otherwise healthy 45-year-old man is involved in a high-speed motor vehicle collision. Head CT is negative. During the ongoing evaluation, he develops a left hemiparesis.

    To find the cause of this change, he should undergo which of the following studies?

A. Noncontrast head CT
B. CT angiography of head and neck
C. Arterial Doppler of carotid arteries
D. Noncontrast brain MRI

19. A 38-year-old man with a history of hypertension and traumatic brain injury is evaluated for three generalized tonic-clonic seizures that he had at home. En route to the hospital via ambulance, he had one additional seizure with worsening mental status, and was treated with oxygen; normal saline, 1,000 mL; IV thiamine; and glucose, 25 g. On arrival at the emergency department he is stuporous and hypoxic, so he is immediately intubated using rocuronium. Vital signs are: blood pressure 158/100 mm Hg, heart rate 108 beats/min, respiratory rate 16/min (per ventilator), temperature 37.2°C (99°F), and oxygen saturation 99%. Neurologic examination shows bilateral 3-mm reactive pupils and normal fundus. The rest of the examination is unobtainable since he has residual chemical paralysis.

    Which of the following is the most appropriate course of action at this point?

    A. Mannitol, 1 g/kg IV
    B. Lorazepam, 0.1 mg/kg IV
    C. Brain MRI with and without contrast
    D. Fosphenytoin, 20 mg/kg IV

20. An 18-year-old man with no significant past medical history is admitted to the hospital for a two-day history of headache, nausea, and vomiting. In the emergency department he is confused and agitated. One generalized tonic-clonic seizure lasting one minute is noted, followed by stupor and lack of arousability for at least five minutes. Vital signs are: blood pressure 158/105 mm Hg, heart rate 128 beats/min, respiratory rate 28 beats/min, and pulse oximetry 88%.

    Which of the following is the best intervention for this patient beyond assessing and maintaining patency of the airway?

    A. EEG
    B. Head CT
    C. Lorazepam
    D. Fosphenytoin
    E. Levetiracetam

21. A 60-year-old, 80-kg man is evaluated in the emergency department with status epilepticus. He has a history of intracranial tumor. Emergency medical personnel gave him midazolam, 8 mg, IV bolus, in the ambulance, and lorazepam, 4 mg, IV bolus, in the emergency department. He remains unresponsive with left gaze deviation, and is subsequently intubated.

Which of the following is/are the best next step(s) in management?

A. Propofol infusion
B. Additional lorazepam
C. Diagnostic EEG and neurology consult
D. Loading dose of fosphenytoin
E. Levetiracetam

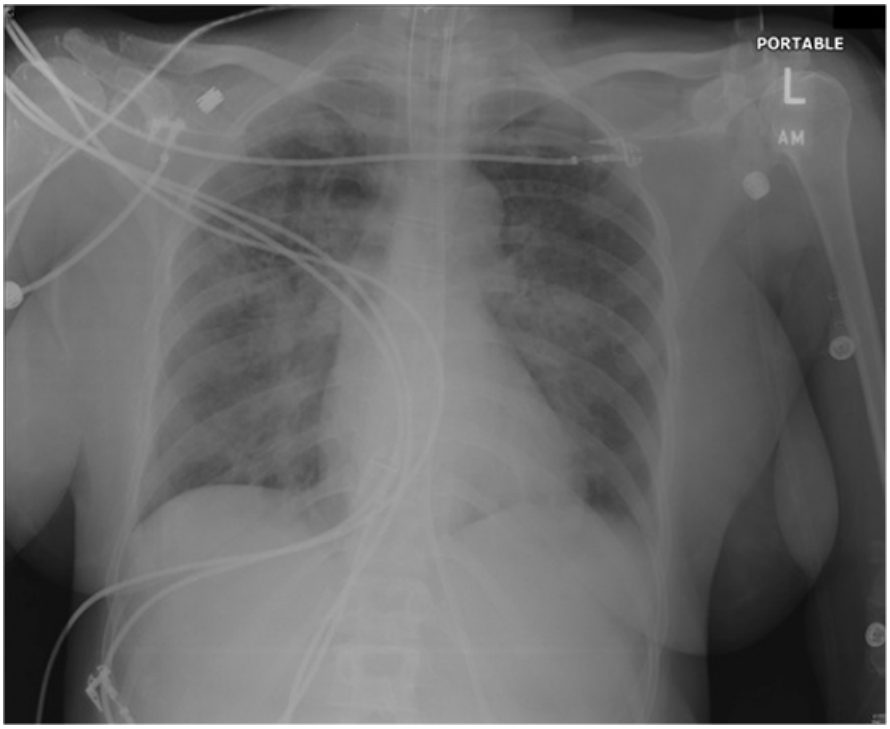
22. A 48-year-old woman with a history of severe traumatic brain injury one year ago presents to the emergency department (ED) unresponsive after a witnessed episode of three minutes of generalized shaking, for which she is given lorazepam, 4 mg. While en route to have a head CT, she begins to have generalized tonic-clonic movements. She is given lorazepam, 4 mg, and the movements resolve. Head CT reveals bifrontal encephalomalacia. Her temperature is 37°C (98.6°F), heart rate 105 beats/min, blood pressure 163/90 mm Hg, respiratory rate 16 breaths/min, and weight 60 kg (132 lbs). On examination, her eyes are closed and she is not responsive to verbal stimuli; pupils are equal, round and reactive; corneal reflexes are present bilaterally; cough and gag reflexes are present; and she flexes to noxious stimuli in all four extremities. There is concern for airway compromise, and the ED team is intubating her.

    Which of the following is the most appropriate next treatment for the patient's presenting symptoms?

    A. Propofol infusion
    B. IV levetiracetam load
    C. Lorazepam, 2 mg intravenous push
    D. Midazolam infusion

23. A 58-year-old woman with a past medical history of hypertension is admitted to the ICU for evaluation of the worst headache of her life and a syncopal event at home. Initial head CT reveals diffuse subarachnoid hemorrhage. Her Glasgow Coma Scale score is 7, blood pressure 178/100 mm Hg, heart rate 108 beats/min, respiratory rate 42 beats/min, pulse oximetry 88% on 4-liter nasal cannula. She is intubated with FiO_2 1.0. Chest radiograph is shown below.

    Arterial blood gas analysis reveals: pH 7.20, pCO_2 30 mm Hg, pO_2 88 mm Hg, and hemoglobin oxygen saturation 97%. Initial echocardiography shows a hyperdynamic state with no regional wall motion abnormalities. Right ventricular function appears to be within normal limits. The inferior vena cava collapsibility index is 50%.



Which of the following is the most likely explanation for her hypoxic respiratory failure?

A. Neurogenic pulmonary edema
B. Congestive heart failure secondary to diastolic dysfunction
C. Pulmonary embolism with acute cor pulmonale
D. Pneumothorax
E. Aspiration pneumonia

24. A 64-year-old, 70-kg man with a medical history significant for hypertension, diabetes mellitus, and coronary artery disease is admitted to the hospital for progressive shortness of breath, retrosternal chest pain during the past 48 hours, and weakness and paresthesia starting in the lower extremities and now in the upper extremities. Vital signs are: heart rate 120 beats/min, respiratory rate 32 breaths/min, blood pressure 90/48 mm Hg, and oxygen saturation 92%. Arterial blood gas analysis reveals: pH 7.48, pCO_2 30 mm Hg, pO_2 66 mm Hg. A bedside pulmonary function testing reveals a negative inspiratory force -10 cm H_2O and a vital capacity of 0.4 L. On examination, his mental status is normal, without signs of aphasia or neglect, cranial nerves are normal, motor examination reveals asymmetric weakness with 2/4 in lower extremities and 3/5 in the upper extremities. There is areflexia with proprioceptive loss in the lower extremities. White blood cells are 7,800/µL, blood urea nitrogen 28 mg/dL, creatinine 1.0 mg/dL, sodium 140 mEq/L. Cerebrospinal fluid analysis reveals glucose of 78 mg/dL, protein 78 mg/dL and cell count of 2 lymphocytes.

Which of the following is/are the best immediate intervention(s) for this patient?

A. IV ceftriaxone and vancomycin

B. Intubation and mechanical ventilation
C. IV gammaglobulin
D. Plasma exchange

25. A 38-year-old man with hypertension is evaluated in the emergency department for a five-day history of progressive weakness. He first noticed low back pain about a week ago and then weakness in both legs. Yesterday, he noted weakness in his arms. On examination, he has difficulty speaking more than a few words without becoming short of breath. Mental status and cranial nerves are intact. He has 2/5 strength in both lower extremities and 3/5 strength in both upper extremities. He notes paresthesia in his hands and feet, but sensory examination is unremarkable. Reflexes are absent. Pulmonary function tests reveal a forced vital capacity of 800 mL and negative inspiratory force of -20 cm H_2O. He is intubated. Results from a lumbar function are pending.

    Which of the following treatments is most appropriate at this time?

    A. Plasma exchange only
    B. Plasma exchange in combination with IV immunoglobulin
    C. IV methylprednisolone
    D. IV rituximab

26. A 28-year-old man is admitted to the neurologic ICU for management of severe traumatic brain injury sustained in a motorcycle accident in which he was not wearing a helmet. On admission, vital signs are: blood pressure 158/98 mm Hg, heart rate 128 beats/min, respiratory rate 22/min (overbreathing the ventilator), temperature 37.8°C (100.4°F). Glasgow Coma Scale score is 6. An external ventricular drain (EVD) is placed for intracranial pressure (ICP) monitoring. ICP is 28 mm Hg and remains elevated for 30 minutes. The patient's head is elevated, and he receives IV fentanyl and propofol for analgosedation.

    Which of the following is the next step in this patient's management?

    A. Immediate pentobarbital coma
    B. Immediate hypothermia to 33°C
    C. Neurosurgical evaluation for bifrontal hemicraniectomies
    D. Draining cerebrospinal fluid via EVD
    E. No further intervention

27. A 35-year-old man is evaluated in the emergency department after a motorcycle accident. He is obtunded. He does not open his eyes to voice or painful stimuli. He is mumbling sounds and withdrawing to painful stimuli. Vital signs are: blood pressure 85/50 mm Hg, heart rate 144 beats/min, respiratory rate 22 breaths/min, oxygen saturation 92% on nonrebreather face mask. He is intubated for airway protection. After intubation, he remains hypotensive despite 2-liter normal saline crystalloid resuscitation. Focused assessment with sonography in

trauma (FAST) examination reveals free fluid in the Morison pouch. He undergoes damage control laparotomy. After laparotomy and abdominal packing for a splenic laceration, head CT reveals small areas of frontal contusion/hemorrhage, but no midline shift or mass effect. Neurologic examination is unchanged. He is transferred to the ICU and intubated.

According to the most recent guidelines, which of the following is the most appropriate recommendation regarding neuromonitoring?

A. Clinical examination with hourly neuroexamination
B. Clinical examination with hourly neuroexamination and serial head CT
C. Clinical examination with hourly neuroexamination, repeat head CT in 12-24 hours, and intracranial pressure monitoring
D. Clinical examination with hourly neuroexamination, repeat head CT in 12-24 hours, and continuous EEG monitor
E. Brain tissue oxygenation probe

28. A 57-year-old woman is evaluated in the emergency department after sustaining blunt trauma to the right temporal area. Blood pressure is 77/48 mm Hg. Glasgow Coma Scale score is 8. Heart rate is 99 beats/min. Oxygen saturation as measured by pulse oximetry (SpO_2) is 88%. Arterial blood gas analysis reveals: $PaCO_2$ 55 mm Hg, PaO_2 58 mm Hg. Head CT shows no abnormalities.

Which of the following findings would warrant placement of an intracranial pressure monitor?

A. PaO_2 of less than 60 mm Hg
B. SpO_2 of less than 90%
C. Systolic blood pressure of 77 mm Hg
D. $PaCO_2$ of 55 mm Hg
E. Positive otoscopic examination showing bulging of right tympanum

29. A 37-year-old man sustains a traumatic brain injury with subarachnoid hemorrhage and subdural hematoma in a motorcycle crash. He undergoes evacuation of the hematoma, after which he is extubated and transferred to the ICU with a Glasgow Coma Scale score of 15. He is started on levetiracetam for seizure prophylaxis. On postoperative day two, he becomes acutely agitated and is tremulous. Temperature is 38.8°C (101.8°F), blood pressure 180/110 mm Hg, heart rate 136/min, and respiratory rate 34 breaths/min. On examination, he is moaning, trying to get out of bed, and diaphoretic. Pupils are equal and reactive; lungs are clear to auscultation bilaterally.

Which of the following is the most appropriate next step in management?

A. Immediate repeat head CT
B. Hypertonic saline bolus

C. Rapid-sequence intubation for airway protection
D. Lorazepam 2 mg IV

30. A 65-year-old man with a medical history of Parkinson disease is admitted to the hospital for evaluation of renal failure in the setting of dehydration. He is admitted to the general medical ward, where an infusion of normal saline is started. During the night, he is found to be lethargic and confused, and falls in the bathroom. Vital signs are: heart rate 42 beats/min, respiratory rate 18 breaths/min and shallow, blood pressure 90/58 mm Hg, temperature 37.1°C (98.8°F), and oxygen saturation 92%. Neurologic examination reveals a Glasgow Coma Scale score of 11. He is lethargic and not following commands, has weakness in the upper extremities, and cannot move his lower extremities. He is intubated and transferred to the ICU, where a cervical spine CT is performed (shown below).

Based on this evaluation, which of the following is the most appropriate next therapy for this patient?

A. IV ceftriaxone, 2g, immediately
B. IV dexamethasone, 10 mg bolus
C. Immobilization of cervical spine with stiff collar
D. Assessment of cranial nerves, including oculocephalic nerves

31. An 18-year-old man crashes while snowboarding. He is helicoptered to a level 1 trauma center. En route, he receives 2 liters normal saline. At the trauma center's emergency department, he is found to have a C5 comminuted fracture with spinal cord injury at the same level. Vital signs are: heart rate 80 beats/min, blood pressure 90/50 mmHg, respiratory rate 16 breaths/min, and oxygen saturation

96% on two liters. On neurologic examination, he follows commands, and there is no aphasia or neglect. Glasgow Coma Scale score is 15. Cranial nerves are normal. Motor examination reveals motor-related cortical potentials 0/5 upper extremities and lower extremities, and no reflexes. Rectal sphincter tone is decreased, and sensation is lost in perineal area and up to the C5 dermatome.

In the ensuing hours, he is most likely to lose which of the following functions?

A. Urinary output
B. Respiratory drive
C. Temperature regulation
D. Sacral sparing
E. Consciousness

32. During a domestic dispute, a 22-year-old man is hit multiple times in the neck with a baseball bat. Now, he is not able to move. On examination, he is unable to feel pain or temperature but has vibration sense and proprioception.

Which of the following syndromes best describes his injury?

A. Central spinal cord syndrome
B. Posterior spinal cord syndrome
C. Anterior spinal cord syndrome
D. Posterior spinal artery syndrome
E. Central spinal artery syndrome

33. A 22-year-old man is admitted to the ICU for severe dehydration due to polydipsia. Vital signs are: heart rate 110 beats/min, blood pressure 92/48 mm Hg, respiratory rate 28 breaths/min, oxygen saturation 98% on 2 L. He is lethargic but follows commands. Initial chemistry panel results are: sodium 128 mEq/dL, potassium 4.7 mEq/dL, chloride 94 mEq/dL, bicarbonate 16 mEq/L, blood urea nitrogen 34 mg/dL, creatinine 1.2 mg/dL, glucose 436 mg/dL. He is volume resuscitated with 0.9% normal saline and started on appropriate medical therapy. His hemodynamic profile improves. Repeat electrolytes after four hours of treatment are: sodium 131 mEq/dL, potassium 4.0 mEq/dL, chloride 100 mEq/dL, bicarbonate 20 mEq/L, blood urea nitrogen 28 mg/dL, creatinine 1.1 mg/dL, glucose 202 mg/dL. His mentation initially improves with treatment, but then he becomes obtunded and unresponsive, and requires intubation for airway protection.

Which of the following is the most likely cause of this clinical picture?

A. Central pontine myelinolysis from rapid sodium correction
B. Cerebral edema from rehydration and rapid correction of glucose
C. Symptomatic hyponatremia
D. Hypoactive delirium
E. Left hemispheric infarct

34. A 70-year-old man is admitted to the ICU, intubated after undergoing thoracoabdominal aneurysm repair. His past medical history includes coronary artery disease, chronic kidney disease, and alcoholic cirrhosis. Vital signs include: temperature 34.8°C (94.6°F), heart rate 101 beats/min, systolic blood pressure 130 mm Hg. On physical examination, he is unresponsive and does not move his legs to noxious stimuli. In the operating room he receives a total IV anesthetic with propofol and remifentanil infusions to facilitate somatosensory and motor evoked potential monitoring. When evoked potential monitoring is completed (approximately one hour before ICU admission), he is given a dose of hydromorphone for analgesia and a dose of cisatracurium to facilitate exchange from a double-lumen to a single-lumen tube. Train-of-four stimulation is subsequently performed, which reveals 0 out of 4 twitches.

    Administration of which of the following drugs is most appropriate to facilitate rapid evaluation of his neurologic examination?

    A. Neostigmine/glycopyrrolate
    B. Sugammadex
    C. Naloxone
    D. Flumazenil

Part 6 Answers:
Neurological Disorders

1. Rationale

Answer: D

Signs of external ventricular drain (EVD) infection are manifested with changes in mental status, fever, leukocytosis, and cerebrospinal fluid (CSF) alterations. The incidence of central nervous system (CNS) infection secondary to EVDs ranges from 0 to 20% depending on the definition of infection and the study population. Several large studies and meta-analyses estimated incidence of ventriculomeningitis related to EVDs to be between 6% and 8%. Patients with subarachnoid hemorrhages have the highest risk of CNS infection. Duration of EVD catheterization has been implicated in the increased risk of infection, with the majority of infections occurring within the first 10 days after placement. Reinsertion of the EVD, CSF leak from ventriculostomy site, frequent CSF sampling, and neurosurgery are associated with higher risk of CNS infection. Diagnosis of ventriculomeningitis secondary to EVD is based on a combination of clinical signs (fever, headache, meningeal and cranial nerves signs), CSF changes (increased white blood cells and protein, decreased glucose) and bacteriologic findings from CSF. In the settings of traumatic brain injury or neurosurgery, diagnostic criteria are not specific.

Early administration of antibiotics is crucial. Most commonly identified pathogens in the cultures from EVD contain skin flora, but recent studies identified increased incidence of infections secondary to gram-negative rods, including *Pseudomonas* and *Acinetobacter.* Therefore, initial empiric treatment should be directed to cover methicillin-resistant *Staphylococcus aureus* and gram-negative rods, including *Pseudomonas*. Gentamicin does not penetrate the blood-brain barrier effectively. Intraventricular antibiotics is a controversial approach and typically reserved for severe or recurrent ventriculomeningitis. The combination of IV vancomycin and cefepime is the optimal choice.

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2. Lozier AP, Sciacca RR, Romagnoli MF, Connolly ES Jr. Ventriculostomy-related infections: a critical review of the literature. *Neurosurgery.* 2002 Jul;51(1):170-181.
3. Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of health

care-associated infection and criteria for specific types of infections in the acute care setting. *Am J Infect Control.* 2008 Jun;36(5):309-332.

2. Rationale

Answer: E

Osmotic demyelination involving the pons has long been recognized as a complication of the management of hyponatremia manifesting as coma and spastic quadriparesis in its most severe form. However, more recently it has been recognized that other osmotic disorders, such as hypernatremia, hyperglycemia, and hypoglycemia may predispose a patient to myelinolysis in the course of treatment. Furthermore, it has been recognized that the spectrum of injury is broadly manifested as either pontine myelinolysis or extra-pontine myelinolysis. The disorder has therefore been renamed osmotic demyelination syndrome in order to recognize the full spectrum of disease.

The patient's toxicology screen is nonrevealing, and history indicates that he was nonadherent with his medications, making a drug-related toxic encephalopathy less likely. Cerebrospinal fluid revealed no evidence of inflammation, making infectious meningoencephalitis unlikely and, similarly, anti-NMDA receptor encephalitis (an autoimmune disorder to cerebral NMDA receptors) unlikely. Malignant catatonia, which is common in psychotic patients, is associated with toxicity in the form of autonomic dysregulation and muscular rigidity not seen in this patient.

References:

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3. Rationale

Answer: D

This patient has anti-NDMA receptor encephalitis, which is an autoimmune disorder treated initially with antiinflammatory agents and escalating to IV immunoglobulin or plasmapheresis if unresponsive. Her clinical presentation is that of excitatory catatonia. Given her lack of response to benzodiazepines, the next step is electroconvulsive therapy. Antithymocyte globulin is a potent immune-suppressive agent used in solid organ transplant and certain bone marrow disorders. Cyproheptadine is used to treat central serotonin syndrome. Clonidine historically has been useful in the management of various withdrawal syndromes but has not been

used to treat catatonia. Neither antithymocyte globulin, cyproheptadine, nor clonidine have a central role in the management of catatonic disorders. Antipsychotic agents bear the potential risk of worsening the clinical manifestations of severe catatonic disorders; their use is discouraged.

References:

1. Chapman MR, Vause HE. Anti-NMDA receptor encephalitis: diagnosis, psychiatric presentation, and treatment. *Am J Psychiatry.* 2011 Mar;168(3):245-251.
2. Guidelines and Evidence-Based Medicine Subcommittee of the Academy of Psychosomatic Medicine; European Association of Psychosomatic Medicine. *Clinical Monograph: Catatonia in Medically Ill Patients: An Evidence-based Medicine (EBM) Monograph for Psychosomatic Medicine Practice.* 2015.
3. Taylor MA, Fink M. Catatonia in psychiatric classification: a home of its own. *Am J Psychiatry.* 2003 Jul; 160(7):1233-1241.

4. Rationale

Answer: D

This patient has a subarachnoid hemorrhage (SAH), with early evidence of hydrocephalus. SAH is associated with high morbidity and mortality. There are multiple associated complications that are highly dependent on timing from aneurysm rupture. During the first three days, and before the aneurysm is secured, three major complications should be evaluated: rebleeding, acute hydrocephalus, and seizures or nonconvulsive status epilepticus. The head CT did not show increased hemorrhage but did show an increase in the size of the temporal horns of the ventricular system. This is concerning for hydrocephalus. Along with the decreased mental status, these findings are concerning for elevated intracranial pressure (ICP), so a monitor should be placed to control ICP and maintain adequate cerebral perfusion pressure.

There are two ways to measure ICP. One is an intraparenchymal monitor, sometimes colloquially referred to as a “bolt,” that will measure ICP but will not allow cerebrospinal fluid (CSF) removal, so it is less than ideal. Following the Monro-Kellie hypothesis, increased CSF and blood volume will increase ICP when all compensatory mechanisms are exhausted. The other and most appropriate treatment to manage elevated ICP in this patient is to remove CSF in a controlled fashion, then divert further CSF with a temporary drain. This is best accomplished by an external ventricular drain inserted into a lateral ventricle, which can remove CSF and treat the hydrocephalus. CSF should be removed slowly and in a controlled fashion because of the theoretical concern about aneurysm re-rupture when the external forces compressing the artery are removed. Seizures are an important source of morbidity, but in this patient with acute hydrocephalus, ICP should be managed first.

Reference:

1. Edlow JA, Samuels O, Smith WS, Weingart SD. Emergency neurological life support: subarachnoid hemorrhage. *Neurocrit Care.* 2012 Sep;17 Suppl 1:S47-S53.

5. Rationale

Answer: B

The head CT depicts a subarachnoid hemorrhage. Without a history of trauma, the clinician must assume the cause to be aneurysmal rupture. The guidelines advocate for treating systolic blood pressure when it is greater than 160 mm Hg. Lumbar puncture is indicated only when the history is followed by a head CT negative for bleeding. Although cerebral angiography is the gold standard, CT angiography and magnetic resonance angiography are adequately sensitive to show the presence of an aneurysm.

Reference:

1. Connolly ES, Rabinstein AA, Carhuapoma JR, et al; American Heart Association Stroke Council; Council on Cardiovascular Radiology and Intervention; Council on Cardiovascular Nursing; Council on Cardiovascular Surgery and Anesthesia; Council on Clinical Cardiology. Guidelines for the management of aneurysmal subarachnoid hemorrhage: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke.* 2012 Jun;43(6):1711-1737.

6. Rationale

Answer: D

The most recently published American Heart Association guidelines state that patients eligible for IV recombinant tissue plasminogen activator (rtPA) should receive it even if endovascular treatments are being considered (class I, level of evidence A). Patients with large-vessel occlusions may be eligible for endovascular therapy in addition to IV rtPA but IV rtPA should not be withheld. The patient's INR is only 1.3. An INR greater than 1.7 is a contraindication for IV rtPA, as is systolic blood pressure greater than 185 mm Hg.

References:

1. Powers WJ, Derdeyn CP, Biller J, et al; American Heart Association Stroke Council. 2015 American Heart Association/American Stroke Association focused update of the 2013 guidelines for the early management of patients with acute ischemic stroke regarding endovascular treatment: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke.* 2015 Oct;46(10):3020-3035.
2. Demaerschalk BM, Kleindorfer DO, Adeoye OM, et al; American Heart Association Stroke Council and Council on Epidemiology and Prevention. Scientific rationale for the inclusion and exclusion criteria for intravenous alteplase in acute ischemic stroke: a statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke.* 2016 Feb;47(2):581-641.

7. Rationale

Answer: D

This patient was intoxicated at the time of the motor vehicle collision, and he has been given continuous infusions of sedatives overnight. Any consideration of brain death testing is premature, before the ICU team is certain that all confounding factors, such as sedation or intoxication, have been excluded. Additionally, patients should be normothermic and without electrolyte or metabolic derangements, such as hypernatremia or hypercarbia, which may impact neurologic status. Only after all potential confounders have been eliminated should brain death testing proceed. While nonconvulsive status epilepticus is a reasonable concern in a patient with traumatic brain injury, holding sedation to follow the examination is appropriate. An EEG should be obtained if nonconvulsive status epilepticus is suspected. Flumazenil and naloxone are both contraindicated in this situation because the patient may be seizing; the prudent option is to wait for the benzodiazepines and narcotics to clear.

References:

1. Wijdicks EF. Determining brain death. *Continuum (Minneap Minn).* 2015 Oct;21(5 Neurocritical Care):1411-1424.
2. Busl KM, Greer DM. Pitfalls in the diagnosis of brain death. *Neurocrit Care.* 2009;11(2):276-287.

8. Rationale

Answer: B

Endocrine deficiencies are common after brain death because the hypothalamus and pituitary gland are susceptible to hypoxic injury in the face of elevated intracranial pressure leading to the absence of blood flow to the brain. Not only is vasopressin of value in managing diabetes insipidus, which is common with brain death, but it also serves as a first-line agent in the management of hypotension due to vasodilation.

High-dose corticosteroids are believed to reduce the injurious effects of systemic inflammation activated in the course of brain death, and therapy has been associated with improved organ function post-transplant. Thyroid replacement is particularly useful in managing donors who are hemodynamically unstable or who have cardiac dysfunction that demonstrates a left ventricular ejection fraction less than 45%. While triiodothyronine has a more rapid onset of activity, the use of either has demonstrated equivalent effectiveness. Hyperglycemia is common in brain-dead donors with the same inherent metabolic consequences as in typical ICU patients. While there are no specific studies involving glycemic control in this population, there is evidence that hyperglycemia impacts the function of donated organs. The literature guiding glycemic control in typical critically ill patients has therefore been extrapolated to the care of potential organ donors. Therefore, management should comply with local ICU hyperglycemia guidelines and protocols.

Reference:

1. Kotloff RM, Blosser S, Fulda GJ, et al; Society of Critical Care Medicine/American College of Chest Physicians/Association of Organ Procurement Organizations Donor Management Task Force. Management of the potential organ donor in the ICU: Society of Critical Care Medicine/American College of Chest Physicians/Association of Organ Procurement Organizations consensus statement. *Crit Care Med.* 2015 Jun;43(6):1291-1325.

9. Rationale

Answer: A

Management of the potential multiorgan donor involves different time horizons than management of the critically ill ICU patient. Decisions regarding hemodynamic support reflect the attempt to balance the effects of interventions to achieve the maximal ability to procure all possible organs. The brain-dead donor is frequently hypovolemic due to vasodilation with relative hypovolemia and fluid losses from injury with blood loss and polyuria from diabetes insipidus as well as capillary leak from systemic inflammation. Fluid therapy should be administered with the guidance of hemodynamic parameters to achieve euvolemia. The lungs are particularly sensitive to fluid fluxes.

Fluids, which can be administered as crystalloids or colloids or combinations of both, should be given to achieve reasonable organ perfusion pressure and a urine flow of ≥1 mL/kg/hr. Of crystalloids, normal saline and lactated Ringer solution are generally preferred. It is recommended that routine use of dextrose-containing fluids be avoided. Colloids (except for hetastarch, which has come under scrutiny because of its association with renal injury in critically ill ICU patients) are as acceptable as crystalloids.

Reference:

1. Kotloff RM, Blosser S, Fulda GJ, et al; Society of Critical Care Medicine/American College of Chest Physicians/Association of Organ Procurement Organizations Donor Management Task Force. Management of the potential organ donor in the ICU: Society of Critical Care Medicine/American College of Chest Physicians/Association of Organ Procurement Organizations consensus statement. *Crit Care Med.* 2015 Jun;43(6):1291-1325.

10. Rationale

Answer: B

The American Academy of Neurology Practice Parameter delineates the medical standards for the determination of brain death. The parameter emphasizes the three clinical findings necessary to confirm irreversible cessation of all functions of the entire brain, including the brainstem: coma (with a known cause), absence of brainstem reflexes, and apnea. In the case of confounders, ancillary testing is recommended but, in general, the clinical examination should be sufficient.

Reference:

1. Wijdicks EFM, Varelas PN, Gronseth GS, Greer DM; American Academy of Neurology. Evidence-based guideline update: determining brain death in adults: report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology.* 2010 Jun;74(23):1911-1918.

11. Rationale

Answer: B

This patient is experiencing an acute ischemic stroke; she is within the three-hour window for revascularization with IV recombinant tissue plasminogen activator (rtPA); however, her blood pressure should be gently corrected because IV rtPA may be contraindicated in patients with very high blood pressure. She does not appear to be experiencing an ictal event such as a seizure. Seizures could be considered part of the differential diagnosis but should not delay the administration of IV rtPA. Evidence suggests that a seizure at symptom onset should not be considered an absolute contraindication to IV rtPA for patients with acute ischemic stroke. She does not require fresh frozen plasma because rtPA can safely be given if INR less than 1.7 and the hyperintensities seen on the CT are calcifications in the arachnoid processes of the lateral ventricles. The CT shows a subtle lack of left-sided gray-white-matter differentiation at the opercular and insular ribbon, which is considered an early sign of hemispheric infarction.

References:

1. Jauch EC, Saver JL, Adams HP Jr, et al; American Heart Association Stroke Council; Council on Cardiovascular Nursing; Council on Peripheral Vascular Disease; Council on Clinical Cardiology. Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke.* 2013 Mar;44(3):870-947.
2. Selim M, Kumar S, Fink J, Schlaug G, Caplan LR, Linfante I. Seizure at stroke onset: should it be an absolute contraindication to thrombolysis? *Cerebrovasc Dis.* 2002;14(1):54-57.
3. [No authors listed]. Tissue plasminogen activator for acute ischemic stroke. The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. *N Engl J Med.* 1995 Dec 14;333(24):1581-1587.

12. Rationale

Answer: D

This patient has a large left-hemispheric infarction (LHI), as seen on CT. He is not a candidate for IV or intra-arterial tissue plasminogen activator (tPA) because more than four-and-a-half and six hours, respectively, have passed since symptom onset. Both revascularization alternatives (IV and intra-arterial) are contingent on administration within a reasonable window. He does not appear to be herniating so in this setting hyperventilation is contraindicated because it can reduce the already impaired cerebral blood flow. Heparin does not have an immediate role in his

management. Evidence suggests that the use of heparin in the setting of atrial fibrillation-related embolic stroke offers no benefit for stroke recurrence and may in fact increase the risk of hemorrhage in LHI. Decompressive hemicraniectomy has been associated with improved mortality and functional outcome after LHI in patients younger than 60. The decision to proceed with DHC depends on patient and family preferences.

References:

1. Torbey MT, Bösel J, Rhoney DH, et al. Evidence-based guidelines for the management of large hemispheric infarction: a statement for health care professionals from the Neurocritical Care Society and the German Society for Neuro-intensive Care and Emergency Medicine. *Neurocritic Care.* 2015 Feb;22(1):146-164.
2. Powers WJ, Derdeyn CP, Biller J, et al; American Heart Association Stroke Council. 2015 American Heart Association/American Stroke Association focused update of the 2013 guidelines for the early management of patients with acute ischemic stroke regarding endovascular treatment: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke.* 2015 Oct;46(10):3020-3035.
3. Berge E, Abdelnoor M, Nakstad PH, Sandset PM. Low molecular-weight heparin versus aspirin in patients with acute ischaemic stroke and atrial fibrillation: a double-blind randomised study. HAEST Study Group. Heparin in Acute Embolic Stroke Trial. *Lancet.* 2000 Apr 8;355(9211):1205-1210.
4. Prabhakaran S, Ruff I, Bernstein RA. Acute stroke intervention: a systematic review. *JAMA.* 2015 Apr 14;313(14):1451-1462.>

13. Rationale

Answer: E

This patient has acute obstructive hydrocephalus with intraventricular hemorrhage involving the fourth ventricle, possibly related to her cocaine abuse. She will benefit from emergency cerebrospinal fluid drainage via an external ventricular drain. The role of antiseizure medications has been studied in retrospective observational studies of intracerebral hemorrhage, and in this case may not save her life. Finally, steroids and IV tissue plasminogen activator have no role in the management of acute hydrocephalus secondary to intracerebral or intraventricular hemorrhage.

References:

1. Hemphill JC 3rd, Greenberg SM, Anderson CS, et al; American Heart Association Stroke Council; Council on Cardiovascular and Stroke Nursing; Council on Clinical Cardiology. Guidelines for the management of spontaneous intracerebral hemorrhage: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke.* 2015 Jul;46(7):2032-2060.
2. Liliang PC, Liang CL, Lu CH, et al. Hypertensive caudate hemorrhage prognostic

predictor, outcome, and role of external ventricular drainage. *Stroke.* 2001 May;32(5):1195-1200.
3. Rincon F, Mayer SA. (2008). Clinical review: critical care management of spontaneous intracerebral hemorrhage. *Critical Care.* 2008;12(6):237.

14. Rationale

Answer: A

This patient has an intracerebral hemorrhage in the setting of anticoagulation with a direct thrombin inhibitor (dabigatran). In this setting, reversal of anticoagulation is indicated. Evidence suggests that idarucizumab is the agent of choice to reverse the effects of dabigatran-induced coagulopathy. Prothrombin complex concentrate is indicated for reversal of life-threatening bleeding related to warfarin, rivaroxaban, and apixaban. Vitamin K and fresh frozen plasma are indicated for reversal of coagulopathy related to warfarin. In the case of severe intracranial hemorrhages related to warfarin, prothrombin complex concentrate is preferred over vitamin K and fresh frozen plasma. Factor VII is indicated for hemophilia in the setting of inhibitors but has not been shown to reduce mortality. It is important to recognize that these reversal agents can be associated with adverse effects such as thrombosis, anaphylactic reactions, and volume overload.

References:

1. Frontera JA, Lewin JJ 3rd, Rabinstein AA, et al. Guideline for reversal of antithrombotics in intracranial hemorrhage: a statement for healthcare professionals from the Neurocritical Care Society and Society of Critical Care Medicine. *Neurocrit Care.* 2016 Feb;24(1):6-46.
2. Pollack CV Jr, Reilly PA, Eikelboom J, et al. Idarucizumab for dabigatran reversal. *N Engl J Med.* 2015 Aug 6;373(6):511-520.

15. Rationale

Answer: E

Intracerebral hemorrhage (ICH) is by far the most destructive form of stroke. Apart from management in a specialized stroke or neurologic ICU, no specific medical therapies have been shown to consistently improve outcome after ICH. Ventilatory support, blood pressure control, reversal of any preexisting coagulopathy, intracranial pressure monitoring, osmotherapy, fever control, seizure prophylaxis, treatment of hyperglycemia, and nutritional supplementation are the cornerstones of supportive care in the ICU. Ventricular drainage should be performed urgently in all stuporous or comatose patients with intraventricular blood and acute hydrocephalus. Early placement of a ventricular drain in this case may save the patient's life.

References:

1. Liliang PC, Liang CL, Lu CH, et al. Hypertensive caudate hemorrhage prognostic predictor, outcome, and role of external ventricular drainage. *Stroke.* 2001

May;32(5):1195-1200.
2. Rincon F, Mayer SA. (2008). Clinical review: critical care management of spontaneous intracerebral hemorrhage. *Critical Care.* 2008;12(6):237.

16. Rationale

Answer: D

Middle cerebral artery occlusion causes contralateral hemiparesis (worse in the arm and face than in the leg), dysarthria, contralateral homonymous hemianopia, aphasia (if dominant hemisphere is affected), or apraxia and sensory neglect (if non-dominant hemisphere is affected). The angiogram depicts bilateral calcified carotid arteries with a cutoff beyond the right middle cerebral artery M1 division.

Reference:

1. Hwang DY, Matouk CC, Sheth KN. Management of the malignant middle cerebral artery syndrome. *Semin Neurol.* 2013 Nov;33(5):448-455.

17. Rationale

Answer: E

According to the most recent recently published American Heart Association guidelines, patients should receive endovascular therapy with a stent retriever if they meet all the following criteria (class I, level of evidence A): Prestroke modified Rankin scale score of 0 to 1 (minimal or no previous neurologic deficit), acute ischemic stroke receiving IV recombinant tissue plasminogen activator (rtPA) within four-and-a-half hours of onset according to guidelines from professional medical societies, causative occlusion of the internal carotid or proximal middle cerebral artery (MCA) (M1), age ≥18 years, National Institutes of Health Stroke Scale score ≥6, Alberta Stroke Program Early CT Score (ASPECTS) ≥6 (score to assess early ischemic changes on noncontrast head CT, 10 is normal, 0 is ischemic/hypodense changes in the entire MCA territory), and treatment can be initiated (groin puncture) within six hours of symptom onset.

Observing patients after IV rtPA to assess for clinical response before pursuing endovascular therapy is not required to achieve beneficial outcomes, and is not recommended. CT perfusion to evaluate for an ischemic penumbra is not necessary because the patient is within the six-hour endovascular window and has a normal noncontrast head CT (or ASPECTS score of 10); it will also delay endovascular therapy, which should be performed as early as possible.

Reference:

1. Powers WJ, Derdeyn CP, Biller J, et al; American Heart Association Stroke Council. 2015 American Heart Association/American Stroke Association focused update of the 2013 guidelines for the early management of patients with acute ischemic stroke regarding endovascular treatment: a guideline for healthcare professionals from the American Heart Association/American Stroke Association.

Stroke. 2015 Oct;46(10):3020-3035.

18. Rationale

Answer: D

Classically, per the Eastern Association for the Surgery of Trauma 2010 guidelines, cerebral angiography of the head was the standard to diagnose and treat blunt cerebrovascular injury. Currently, however, CT angiography has largely replaced conventional angiography for the diagnosis of blunt cerebrovascular injury. Neither noncontrast head CT nor brain MRI would identify carotid dissection, unless sufficient time has elapsed for a stroke to be visible on imaging. The development of an intracranial hemorrhage causing neurologic deficit is unlikely, given the initially normal head CT. Carotid dissection should be highly suspected, given the mechanism of injury and the neurologic findings. Arterial Doppler is insufficiently sensitive or specific to detect the injury.

Reference:

1. Bromberg WJ, Collier BC, Diebel LN, et al. Blunt cerebrovascular injury practice management guidelines: the Eastern Association for the Surgery of Trauma. *J Trauma.* 2010 Feb;68(2):471-477.

19. Rationale

Answer: B

This patient has had several seizures without return to his neurologic baseline. He meets criteria for status epilepticus (SE): five minutes of ongoing seizure activity or consecutive seizures without recovery of consciousness. Just because he is chemically paralyzed does not mean he is not actively seizing. Evidence suggests that the best first-line intervention for SE is IV lorazepam, 0.1mg/kg. The best second-line intervention is fosphenytoin or valproic acid. There is no indication that he has transtentorial herniation. MRI may play an important role, but not for acute management of SE.

References:

1. Brophy GM, Bell R, Claassen J, et al; Neurocritical Care Society Status Epilepticus Guideline Writing Committee. Guidelines for the evaluation and management of status epilepticus. *Neurocrit Care.* 2012 Aug;17(1):3-23.
2. Treiman DM, Meyers PD, Walton NY, et al. A comparison of four treatments for generalized convulsive status epilepticus. Veterans Affairs Status Epilepticus Cooperative Study Group. *N Engl J Med.* 1998 Sep 17;339(12):792-798.

20. Rationale

Answer: C

This patient should be considered to be in nonconvulsive status epilepticus (NCSE)

until proven otherwise. NCSE is defined as five minutes or more of 1) continuous clinical and/or electrographic seizure activity or 2) recurrent seizure activity without recovery (returning to baseline) between seizures. Both CT and EEG are important tools for the workup of this patient with new-onset seizure disorder but this should not delay starting antiseizure therapies. The goal of management for a patient in potential SE is to abort the seizures. The recommendation for first-line medication in suspected SE is a benzodiazepine such as lorazepam. Phenytoin and fosphenytoin are considered second-line agents with good antiseizure profiles. In a landmark randomized clinical trial, lorazepam was superior to phenytoin in controlling seizures. Levetiracetam should not be considered a first- or second-line agent when NCSE is suspected.

References:

1. Brophy GM, Bell R, Claassen J, et al; Neurocritical Care Society Status Epilepticus Guideline Writing Committee. Guidelines for the evaluation and management of status epilepticus. *Neurocrit Care.* 2012 Aug;17(1):3-23.
2. Treiman DM, Meyers PD, Walton NY, et al. A comparison of four treatments for generalized convulsive status epilepticus. Veterans Affairs Status Epilepticus Cooperative Study Group. *N Engl J Med.* 1998 Sep 17;339(12):792-798.

21. Rationale

Answer: D

This patient has status epilepticus that is refractory to benzodiazepines. The best next step is to load him with fosphenytoin. Propofol infusion is not incorrect, but must be done once the patient has failed at least two initial standard therapies. Although clinically, levetiracetam is used, there is not sufficient data to use it in status epilepticus as a first-line agent. The patient is still seizing, and an EEG is a diagnostic modality, not a treatment option.

Reference:

1. Brophy GM, Bell R, Claassen J, et al; Neurocritical Care Society Status Epilepticus Guideline Writing Committee. Guidelines for the evaluation and management of status epilepticus. *Neurocrit Care.* 2012 Aug;17(1):3-23.

22. Rationale

Answer: B

The concern is that the patient is in status epilepticus (SE), defined as five minutes or more of continuous clinical (and/or electrographic) seizure activity or recurrent seizure activity without recovery between seizures. SE is treated with benzodiazepines as emergent initial therapy. According to the most recent Neurocritical Care Society guidelines, treatment with benzodiazepines should be followed by urgent-control antiseizure drug therapy including IV fosphenytoin/phenytoin, valproate, or levetiracetam. C is incorrect because the patient has already received 8 mg of

lorazepam (max does 0.1 mg/kg). A and D are incorrect because these are treatments for refractory SE. The Neurocritical Care Society Guidelines define refractory SE as that not responding to standard treatment regimens, such as an initial benzodiazepine followed by another antiseizure drug. This patient will also need continuous EEG to rule out nonconvulsive seizure activity.

References:

1. Brophy GM, Bell R, Claassen J, et al; Neurocritical Care Society Status Epilepticus Guideline Writing Committee. Guidelines for the evaluation and management of status epilepticus. *Neurocrit Care.* 2012 Aug;17(1):3-23.

23. Rationale

Answer: A

Neurogenic pulmonary edema (NPE) is an under-recognized and under-diagnosed form of pulmonary compromise that complicates acute neurologic illness and is not explained by cardiovascular or pulmonary pathology. According to the 2012 Berlin definition of acute respiratory distress syndrome (ARDS), NPE should be considered a form of ARDS, with the caveat that it has different pathophysiology. The echocardiogram suggests a hyperdynamic state in the setting of mild volume depletion, so acute diastolic congestive heart failure is unlikely. Though comatose patients can develop aspiration pneumonia or pneumonitis, the x-ray patter and onset is unlikely to be explained by an infection process. The chest radiograph does not reveal a pneumothorax. A normal right ventricular function on echocardiography eliminates a significant pulmonary embolism with hemodynamic or respiratory compromise.

References:

1. Busl KM, Bleck TP. Neurogenic pulmonary edema. *Crit Care Med.* 2015 Aug;43(8):1710-1715.
2. ARDS Definition Task Force, Ranieri VM, Rubenfeld GD, et al. Acute respiratory distress syndrome: the Berlin definition. *JAMA.* 2012 Jun 20;307(23):2526-2533.

24. Rationale

Answer: B

The patient describes the onset of ascending paresthesia and weakness complicated by areflexia and proprioceptive loss. This picture is characteristic of acute inflammatory demyelinating polyradiculoneuropathy (AIDP). On examination he demonstrates signs of cardiac and respiratory instability. Tachycardia, hypotension, chest pain, and mild hypoxemia suggest that he requires immediate intubation for mechanical ventilation. The bedside pulmonary function tests indicate poor inspiratory effort, and the arterial blood gases demonstrate the preliminary phase of imminent respiratory failure. Although the treatment for AIDP may well be IV immunoglobulin (IV Ig) or plasma exchange, the first step in this patient's management is to protect his

airway and assist his ventilation. Steroids have not shown to provide any benefit in the management of AIDP.

The American Academy of Neurology guidelines note that: 1) treatment with plasma exchange or IV Ig hastens recovery from AIDP, 2) the beneficial effects of plasma exchange and IV Ig are equivalent, 3) combining the two treatments is not beneficial, and 4) glucocorticoid treatment is not recommended. Finally, antibiotics are not indicated because the cerebrospinal fluid studies show no evidence of meningitis.

References:

1. Yuki N, Hartung HP. Guillain-Barré syndrome. *N Engl J Med.* 2012 Jun 14;366(24):2294-2304.
2. Hughes RA, Swan AV, van Doorn PA. Intravenous immunoglobulin for Guillain-Barré syndrome. *Cochrane Database Syst Rev.* 2014 Sep 19;(9):CD002063.
3. Raphaël JC, Chevret S, Hughes RA, Annane D. Plasma exchange for Guillain-Barré syndrome. *Cochrane Database Syst Rev*. 2012 Jul 11;(7):CD001798.
4. Hughes RA, Wijdicks EF, Barohn R, et al; Quality Standards Subcommittee of the American Academy of Neurology. Practice parameter: immunotherapy for Guillain-Barré syndrome: report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology.* 2003 Sep;61(6):736-740.

25. Rationale

Answer: A

This patient has Guillain-Barré syndrome (GBS). The lumbar puncture typically shows elevated cerebrospinal fluid protein with a cell count of less than 10/mm^3 (albuminocytologic dissociation). The most recent American Academy of Neurology guidelines recommend treatment with plasma exchange or IV immunoglobulin (IV Ig) to hasten recovery. These two treatments are equally effective in patients with advanced GBS symptoms. Plasma exchange requires placement of a dialysis catheter, with the inherent risk associated with the procedure. IV Ig can be associated with anaphylactic reactions, aseptic meningitis, fluid overload, and acute renal failure. Combining the two treatments is not recommended and steroid treatment is not beneficial. There is no role for rituximab in treating GBS.

Reference:

1. Hughes RA, Wijdicks EF, Barohn R, et al; Quality Standards Subcommittee of the American Academy of Neurology. Practice parameter: immunotherapy for Guillain-Barré syndrome: report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology.* 2003 Sep;61(6):736-740. Current guideline. Reaffirmed on October 15, 2005, August 2, 2008, and July 13, 2013.

26. Rationale

Answer: D

The Brain Trauma Foundation guidelines encourage intracranial pressure (ICP) monitoring via external ventricular drain (EVD), which facilitate cerebrospinal fluid drainage for ICP control. The roles of hypothermia, hemicraniectomy, and ICP monitoring in traumatic brain injury (TBI) were recently challenged by three prospective randomized controlled trials. In the EuroTHERM study, patients received IV pentobarbital versus a regimen of hypothermia for refractory intracranial hypertension. The hypothermic group had worse long-term outcomes overall. The study was criticized because hypothermic patients did not receive hyperosmolar or hypertonic saline before randomization, amounting to a degree of selection bias. In the DECRA study, patients with severe TBI were randomized to medical therapy versus bifrontal hemicraniectomies. The surgical group had worse long-term outcomes. The study was criticized because patients in the surgical group may have had transtensorial herniation before randomization (abnormal cranial nerves or pupillary reflexes). Finally, in the BEST-TRIP study, patients with severe TBI in South America were randomized to ICP monitoring versus a regimen of clinical monitoring. There was no difference in outcomes between groups. The study was criticized because of differences in population and healthcare systems, which make it difficult to generalize results to more advanced healthcare systems in which pre- and post-hospital care may be more aggressive.

References:

1. Chestnut RM, Temkin N, Carney N, et al; Global Neurotrauma Research Group. A trial of intracranial-pressure monitoring in traumatic brain injury. *N Engl J Med.* 2012 Dec;367(26):2471-2481.
2. Cooper DJ, Rosenfeld JV, Murray L, et al; DECRA Trial Investigators; Australian and New Zealand Intensive Care Society Clinical Trials Group. Decompressive craniectomy in diffuse traumatic brain injury. *N Engl J Med.* 2011 Apr 21;364(16):1493-1502.
3. Andrews PJ, Sinclair HL, Rodriguez A, et al; Eurotherm3235 Trial Collaborators. Hypothermia for intracranial hypertension after traumatic brain injury. *N Engl J Med.* 2015 Dec 17;373(25):2403-2412.
4. Brain Trauma Foundation; American Association of Neurological Surgeons; Congress of Neurological Surgeons; Joint Section on Neurotrauma and Critical Care, AANS/CNS, et al. Guidelines for the management of severe traumatic brain injury. VIII. Intracranial pressure thresholds. *J Neurotrauma.* 2007;24 Suppl 1:S55-S58.

27. Rationale

Answer: C

This patient has severe traumatic brain injury (TBI), as defined by his clinical examination and neuroimaging. His physical examination reveals an initial Glasgow Coma Scale (GCS) score of 7: no eye opening (E1), incomprehensible sounds (V2), flexion/withdrawal from pain (M4). In the ICU, his GCS would be described as 6T: no eye opening (E1), intubated (V1T), flexion/withdrawal from pain (M4). The most recent Brain Trauma Foundation (BTF) guidelines from 2007 recommend intracranial

pressure (ICP) monitoring after TBI for the following patients: 1) GCS 3-8 with abnormal CT (hematoma, contusion, swelling, herniation, or compressed basal cistern), 2) GCS 3-8 with normal CT if greater than or equal to 2 of the following are present: age greater than 40 years, unilateral or bilateral motor posturing, and SBP less than 90.

In the recent BEST-TRIP study by Chestnut et al, the role of ICP monitoring in patients with severe TBI was evaluated against a protocol of imaging and clinical examination (ICE). This multicenter randomized trial showed that the use of the previously unstudied ICE in a hospital with limited economic resources that lacks ICP monitoring may lead to non-inferior clinical outcomes, compared to the BTF guidelines-driven control of ICP using ICP monitoring. General consensus and the BTF guidelines still recommend the use of ICP monitoring after severe TBI.

Continuous EEG monitoring currently is not indicated for routine TBI management, but should be used when seizures are suspected (i.e., obvious clinical seizures, encephalopathy, coma/stupor, or when clinical examination is worse than head CT findings). However, seizures in comatose patients may be more common than previously thought. Claassen et al detected seizures in 19% of critically ill patients on continuous EEG. In their subgroup of 51 patients with TBI, 9 (18%) had nonconvulsive status epilepticus.

Low brain tissue oxygenation levels have been associated with worse outcomes after TBI; however, its role in management remains experimental at this time.

References:

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3. Swadron SP, LeRoux P, Smith WS, Weingart SD. Emergency neurological life support: traumatic brain injury. *Neurocrit Care.* 2012 Sep;17 Suppl 1:S112-S121.
4. Claassen J, Mayer SA, Kowalski RG, Emerson RG, Hirsch LJ. Detection of electrographic seizures with continuous EEG monitoring in critically ill patients. *Neurology.* 2004 May 25;62(10):1743-1748.
5. Chestnut RM, Bleck TP, Citerio G, et al. A consensus-based interpretation of the benchmark evidence from South American trials: treatment of intracranial pressure trial. *J Neurotrauma.* 2015 Nov 15;32(22):1722-1724.
6. Brain Tissue Oxygen Monitoring in Traumatic Brain Injury (TBI) (BOOST 2). https://clinicaltrials.gov/ct2/show/NCT00974259

28. Rationale

Answer: C

According to The Brain Trauma Foundation, in a patient with severe head injury (Glasgow Coma Scale score 3-8) and a normal head CT, indications for intracranial pressure monitoring include two or more of the following indications: age older than 40 years, systolic blood pressure less than 90 mm Hg, posturing unilaterally or bilaterally.

References:

1. Tang A, Pandit V, Fennell V, et al. Intracranial pressure monitor in patients with traumatic brain injury. *J Surg Res.* 2015 Apr;194(2):565-570.
2. Talving P, Karamanos E, Teixeira PG, et al. Intracranial pressure monitoring in severe head injury: compliance with the Brain Trauma Foundation guidelines and effect on outcomes: a prospective study. *J Neurosurg.* 2013 Nov;119(5):1248-1254.

29. Rationale

Answer: D

There are multiple possible etiologies for this patient's acute change in mental status. Differential diagnosis includes recurrent intracranial bleeding, cerebral edema, electrolyte abnormalities, alcohol withdrawal, and infection. While a repeat CT should be performed to rule out worsening cerebral edema or recurrent bleeding, it would be reasonable to control his agitation and evaluate his electrolytes first. If there is evidence of hyponatremia and/or cerebral edema, a bolus of hypertonic saline may be indicated, but unless there are acute signs of cerebral herniation (dilated pupil, Cushing reflex), it would be best to check the electrolytes first. Alcohol withdrawal syndrome (AWS) is characterized by tachycardia, hypertension, fever, agitation, diaphoresis, tremor, and delirium. These signs and symptoms usually manifest within 48-96 hours after the patient's last drink, and can progress to delirium tremens and seizures if not treated promptly. The mainstay of treatment for acute signs of AWS is a benzodiazepine, such as lorazepam. Any patient in whom AWS is suspected should also be given thiamine and folate. After the acute symptoms are controlled, a thorough workup, including complete blood count, chemistries, blood cultures, and imaging, should be performed to rule out other etiologies.

Reference:

1. Sarff M, Gold JA. Alcohol withdrawal syndromes in the intensive care unit. *Crit Care Med.* 2010 Sep;38(9 Suppl):S494-S501.

30. Rationale

Answer: C

This patient fell in the hospital and sustained possible trauma above the clavicles, including the head and cervical spine. The clinical examination is compatible with an acute high spinal cord injury. He was appropriately intubated. He should be

immediately immobilized because he has a C1 odontoid fracture, which should be considered unstable until treated. The role of blood pressure optimization is debatable, but observational studies have shown that, in acute spinal cord injury, mean arterial pressure levels above 80 mm Hg may be associated with improved outcomes. The use of steroids in acute spinal cord injury is also debatable on the basis of the most recent NASCIS III study, which showed no outcome effect.

In 2013, based on the available evidence, the American Association of Neurological Surgeons and Congress of Neurological Surgeons stated that the use of glucocorticoids in acute spinal cord injury is not recommended. Position statements from the Canadian Association of Emergency Physicians, and endorsed by the American Academy of Emergency Medicine, concur that treatment with glucocorticoids is a treatment option and not a treatment standard. It appears that the patient does not require IV antibiotics at this time.

References:

1. Hurlbert RJ, Hadley MN, Walters BC, et al. Pharmacological therapy for acute spinal cord injury. *Neurosurgery.* 2013 Mar;72 Suppl 2:93-105.
2. Canadian Association of Emergency Physicians. *Steroids in Acute Spinal Cord Injury.* Position statement. www.caep.ca.
3. Hugenholtz H, Cass DE, Dvorak MF, et al. High-dose methylprednisolone for acute closed spinal cord injury—only a treatment option. *Can J Neurol Sci.* 2002 Aug;29(3):227-235.
4. American Academy of Emergency Medicine. *Steroids in Acute Spinal Cord Injury.* Position statement. www.aaem.org/positionstatements.
5. Bracken MB, Shepard MJ, Holford TR, et al. Administration of methylprednisolone for 24 or 48 hours or tirilazad mesylate for 48 hours in the treatment of acute spinal cord injury. Results of the Third National Acute Spinal Cord Injury Randomized Controlled Trial. National Acute Spinal Cord Injury Study. *JAMA.* 1997 May 28;227(20):1597-1604.

31. Rationale

Answer: B

This patient has a C5 spinal cord injury with evidence of spinal shock. With an isolated spinal cord injury at the C5 level, he still has C4 capability (phrenic nerve). He is most likely to lose his respiratory drive on the basis of spreading spinal cord edema, so he must be monitored for respiratory decompensation. Although he appears hemodynamically stable, typical features of spinal shock in the ensuing hours are areflexia, hypotension, and bradycardia. Without head injury, he is not at risk of losing consciousness or temperature regulation on the basis of brain injury. Due to the high spinal cord injury level, he does not have sacral sparing on the basis of neurologic examination.

References:

1. Section on Disorders of the Spine and Peripheral Nerves of the American Association of Neurological Surgeons and the Congress of Neurological Surgeons. *Guidelines for the Management of Acute Cervical Spine and Spinal Cord Injuries.* http://www.aans.org/Education%20and%20Meetings/~/media/Files/Education%2(
2. Como JJ, Sutton ER, McCunn M, et al. Characterizing the need for mechanical ventilation following cervical spinal cord injury with neurologic deficit. *J Trauma.* 2005 Oct;59(4):912-6; discussion 916.

32. Rationale

Answer: C

Anterior spinal cord syndrome or anterior spinal artery syndrome is caused by ischemia of the anterior spinal artery leading to motor loss below the level of injury, and loss of pain and temperature sensation. There is intact vibration sense and proprioception. Central cord syndrome consists of loss of motor and sensation in arms and legs, usually associated with arthritis in the neck and age older than 50 years. Posterior cord syndrome is very rare and is caused by a hyperextension injury, with a loss of proprioception and vibration sense. Anterior spinal artery syndrome is the same as anterior spinal cord syndrome.

References:

1. Foo D, Rossier AB. Anterior spinal artery syndrome and its natural history. *Paraplegia.* 1983 Feb;21(1):1-10.
2. Cheshire WP, Santos CC, Massey EW, Howard JF Jr. Spinal cord infarction: etiology and outcome. *Neurology.* 1996 Aug;47(2):321-330.
3. Belen GJ, Weingarden SI. Posterior central cord syndrome following a hyperextension injury: case report. *Paraplegia.* 1988 Jun;26(3):209-211.

33. Rationale

Answer: B

This patient has diabetic ketoacidosis (DKA). The mainstay treatment is resuscitation with isotonic solutions, electrolyte replacements, particularly potassium, and insulin. Central pontine myelinolysis is described as a noninflammatory osmotic demyelination of the central basis pontis. It is thought to occur more frequently in severe hyponatremia of 120 mEq/L or less, which is not the case for this patient. He has hyponatremia; however, when accounting for hyperglycemia, his corrected sodium is 133-136 mEq/dL, depending on the correction formula used. Hypoactive delirium is characterized as decreased alertness with slow movements, lethargy, sparse speech, and apathy. He has cerebral edema from rapid correction of glucose and rehydration, which is common after treatment for DKA. His symptoms have degenerated from stupor to coma.

The mechanism remains unclear but may be explained on the basis of neuronal adaptation to hyperosmolar states and rapid correction of the blood osmolarity. In this

case, neurons would lose interstitial free water to equalize the osmolarity across membranes. With rapid correction, water moves from the cerebrospinal fluid and blood into the brain (thereby increasing the interstitial volume) and to the uptake of solutes by the cells (thereby pulling water into the cells and restoring the cell volume). Treatment ranges from supportive care for mild symptoms to hypertonic solutions and loop diuretics.

References:

1. Stagno D, Gibson C, Breitbart W. The delirium subtypes: a review of prevalence, phenomenology, pathophysiology, and treatment response. *Palliat Support Care.* 2004 Jun;2(2):171-179.
2. Sterns RH, Riggs JE, Schochet SS Jr. Osmotic demyelination syndrome following correction of hyponatremia. *N Engl J Med.* 1986 Jun 12;314(24):1535-1542.
3. Vincent JL, Abraham E, Moore FA, Kochanek PM, Moore FA, Fink MP. *Textbook of Critical Care.* 6th ed. Philadelphia, PA: Elsevier; 2011:1207.
4. Strange K. Regulation of solute and water balance and cell volume in the central nervous system. *J Am Soc Nephrol.* 1992 Jul;3(1):12-27.

34. Rationale

Answer: A

Neuromuscular blocking agents are used in the operating room to facilitate intubation and to optimize surgical conditions. An undesirable sequelae of these agents is residual neuromuscular blockade, which is due to incomplete metabolism and excretion of the drugs at the end of surgery, which can be influenced by a number of factors, including fluid and electrolyte imbalances, hepatic and renal dysfunction, hypothermia, drug interactions, and preexisting neurologic disease.

Train-of-four (TOF) peripheral nerve stimulation is the primary qualitative method used for assessment of neuromuscular blockade; it involves administering four supramaximal electrical impulses every 0.5 seconds to the ulnar, facial, or posterior tibial nerve. In the absence of neuromuscular blockade, TOF stimulation produces four muscle twitches from the associated muscles that are innervated by the stimulated nerve. Fade of the twitch response occurs with increasing neuromuscular blockade and can be evaluated by comparing the strength (TOF ratio) of the fourth twitch to that of the first twitch. TOF testing in this patient is consistent with deep pharmacologic paralysis due to rocuronium. Reversal of the deep neuromuscular blockade is therefore necessary to assess his neurologic examination.

Neostigmine is an acetylcholinesterase inhibitor commonly used to reverse nondepolarizing neuromuscular blockade at the end of surgery. Glycoprryolate is also administered to blunt the muscarinic effects of neostigmine. Neostigmine will reverse all nondepolarizing neuromuscular blockers. Sugammadex will reverse rocuronium and vecuronium, but is ineffective at reversing cisatricurium.

Sugammadex is the first of a new class of drugs effective for reversing the aminosteroid neuromuscular blocking agents (NMBAs) (rocuronium, vecuronium and

pancuronium) but it does not reverse cisatracurium. Reversal of the neuromuscular blockade by sugammadex consists of two phases. First, sugammadex encapsulates, and thereby inactivates, the NMBA molecules in the plasma, resulting in the rapid reduction of free molecules. The subsequent drop in plasma NMBA concentration produces a concentration gradient that allows for more NMBA to move from the neuromuscular junction into plasma. The sugammadex-NMBA complex is eliminated via the kidneys. It is important to note that reversal by sugammadex is independent of the degree of neuromuscular blockade. In practice, this allows even deep neuromuscular blockade to be predictably and reliably reversed.

References:

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2. Greenberg SB, Vender J. The use of neuromuscular blocking agents in the ICU: where are we now? *Crit Care Med.* 2013 May;41(5):1332-1344.
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4. Ledowski T. Sugammadex: what do we know and what do we still need to know? A review of the recent (2013 to 2014) literature. *Anaesth Intensive Care.* 2015 Jan;43(1):14-22.

Part 7:

Hematologic and Oncologic Disorders

Part 7:
Hematologic and Oncologic Disorders

Instructions: For each question, select the most correct answer.

1. A 45-year-old man is admitted to the ICU with respiratory failure 10 days after undergoing hematopoietic stem cell transplantation for lymphoma. Medical history

includes hypertension and stage 2 chronic kidney disease. His post-transplant course was uncomplicated until three days before ICU admission when he developed dyspnea, nonproductive cough, high fever, and severe mucositis. Chest radiograph at that time showed bilateral interstitial and alveolar infiltrates most concentrated in perihilar areas. Pan-culture is ordered, and empiric broad-spectrum antibiotics are administered. High-resolution chest CT shows bilateral ground glass infiltrates. Bronchoalveolar lavage (BAL) is performed, which reveals progressively bloodier fluid return with each lobe examined. BAL is negative for bacteria, and there are no hemosiderin-laden macrophages.

Which of the following pulmonary syndromes is the most likely diagnosis for this patient?

A. Engraftment syndrome
B. Acute graft-versus-host disease
C. Diffuse alveolar hemorrhage
D. Bronchiolitis obliterans

2. A 50-year-old man with no significant past medical history is status post Hartmann procedure for a perforated diverticulum with purulent peritonitis. Postoperative hemoglobin level dropped significantly, so he was given a transfusion of 2 units of packed red blood cells; there were “coffee grounds” in the nasogastric aspirate. No further bleeding has been noted and no additional investigations were undertaken. On postoperative day (POD) seven, he remains intubated because of severe alcohol withdrawal. He has been consistently febrile, although he was successfully weaned off vasopressors 72 hours ago. Renal and hepatic function are within normal limits. This morning his platelet count is 45,000 x $10^3/mm^3$. Platelet counts have shown the following trend: baseline, 350 x $10^3/mm^3$; POD 1, 254 x $10^3/mm^3$; POD 2, 214 x $10^3/mm^3$; POD 3, 185 x $10^3/mm^3$; POD 4, 132 x $10^3/mm^3$; POD 5, 109 x $10^3/mm^3$; POD 6, 72 x $10^3/mm^3$. Medications include ventilator-associated pneumonia prophylaxis with chlorhexidene, pantoprazole, piperacillin/tazobactam, enoxaparin, vancomycin, fentanyl, lorazepam, midazolam, haloperidol, parenteral nutrition. Doppler ultrasound of the lower extremities is negative.

   In addition to discontinuing enoxaparin, which of the following is the most appropriate treatment to address his thrombocytopenia?

   A. Argatroban
   B. Aspirin
   C. Fondaparinux
   D. Mechanical prophylaxis

3. A 65-year-old man is status post three-vessel coronary artery bypass graft two weeks ago with prolonged respiratory failure. He is currently being treated for a right proximal deep vein thrombosis secondary to heparin-induced thrombocytopenia with an argatroban infusion at 0.8 µg/kg/min. Forty-eight hours

ago, his platelet count recovered to baseline, and warfarin was initiated. He is currently hemodynamically stable with a low but stable hemoglobin. Laboratory findings are: prothrombin time 48 sec, INR 4.5, partial thromboplastin time 75 sec.

Which of the following are the most appropriate next steps?

A. Stop argatroban, and hold warfarin.
B. Stop argatroban, hold warfarin, and administer vitamin K.
C. Continue argatroban, and hold warfarin for tonight.
D. Continue argatroban and warfarin.

4. A 47-year-old man sustained hemorrhagic shock, pelvic and hip fractures, lung contusions, and a left pneumothorax in a motor vehicle collision. He underwent emergent angiography with embolization of the right pudendal artery. During resuscitation, he received 12 units of packed red blood cells (RBCs), 10 units of fresh frozen plasma, 1 unit of platelets and 10 packed units of cryoprecipitate. On completion, hemoglobin was 10.2 g/dL but decreased 12 hours later to 8.2 g/dL. Repeat angiography was negative for active bleeding. An additional 2 units of RBCs were transfused with an appropriate response (10.3 g/dL). However, three days later, his hemoglobin concentration has decreased to 7.1 g/dL. CT angiography of abdomen, chest, and pelvis is negative for active bleeding.

   Which of the following is the most likely explanation for his decreased hemoglobin concentration?

   A. Impaired iron metabolism
   B. Intravascular hemolysis
   C. Impaired erythropoietin metabolism
   D. Decreased native RBC production

5. A 34-year-old woman with a penicillin allergy is recovering from an open hemicolectomy in the ICU. Her pain is well controlled with an epidural. She receives piperacillin/tazobactam antibiotic by mistake and subsequently develops severe systemic patchy erythema, wheezing, and hypotension. She is immediately treated with epinephrine, and clinically improves. Twelve hours later, she develops wheezing and hypotension.

   Which of the following is the most likely cause of her new symptoms?

   A. Administration of penicillin antibiotic
   B. Migration of epidural catheter into the intrathecal space
   C. Anastomotic leak
   D. Relapse of anaphylaxis

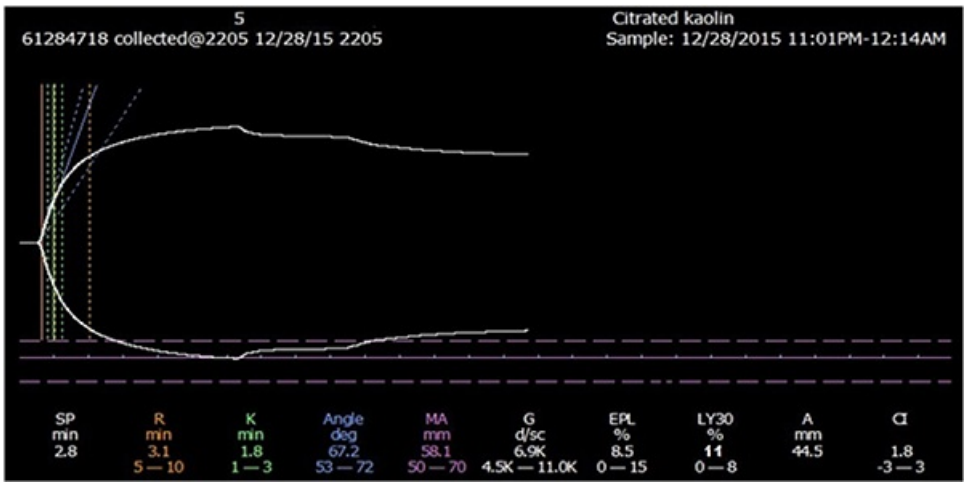
6. A 56-year-old man underwent coronary artery bypass grafting. On postoperative day six, he develops right upper extremity edema. A Doppler ultrasound shows

thrombosis of the right subclavian vein. Laboratory tests reveal: white blood cell count 11,400/μL, hemoglobin 8.8 g/dL, platelet count 64,000/μL, sodium 147 mEq/L, potassium 4.0 mEq/L, chloride 109 mEq/L, bicarbonate 24 mEq/L, blood urea nitrogen 32 mg/dL, creatinine 1.0 mg/dL.

Which of the following is the best treatment strategy?

A. Start heparin infusion with goal activated partial thromboplastin time (aPTT) 1.5-3 times baseline.
B. Start subcutaneous low-molecular-weight-heparin (enoxaparin), 1 mg/kg.
C. Start argatroban infusion with goal aPTT 1.5-3 times baseline.
D. Start warfarin and titrate dosing to goal INR of 2.

7. A 37-year-old man is admitted to the ICU after repair of a thoracic aortic tear caused by blunt trauma to the chest. During the next four hours, he has consistent chest tube output of approximately 100-150 mL/hour of sanguineous fluid. Current vital signs are: temperature 37.1°C (98.8°F), blood pressure 96/64 mm Hg, heart rate 102 beats/min, respiratory rate 14 breaths/min (mechanically ventilated), and oxygen saturation measured by pulse oximetry 100% on fraction of inspired oxygen 40%. Laboratory findings include: hemoglobin 9.1 gm/dL, platelets 121,000/mm^3, prothrombin time 10.1 sec, partial thromboplastin time 26.3 sec. There are no morphologic changes on ECG, complete metabolic panel is normal, and he has been making approximately 0.7-1.0 mL/kg/hr of urine. Kaolin thromboelastography results are shown below.



Which of the following interventions is most appropriate?

A. Packed red blood cells
B. Tranexamic acid
C. Fresh frozen plasma
D. Desmopressin

8. A 43-year-old man undergoes an exploratory laparotomy for appendiceal carcinoma as a possible curative intervention. He loses a significant amount of

blood that requires transfusion of six units of packed red blood cells (PRBCs), two units of fresh frozen plasma (FFP), and a six-pack of platelets. The post-transfusion complete blood count results are: white blood cell count 12,300/μL, hemoglobin 12.2 g/dL, hematocrit 36.5, platelets 122/mm^3. INR is 1.2. Partial thromboplastin time is within normal limits. The patient continues to ooze in the post-anesthesia care unit. Thromboelastography (TEG) is ordered because coagulopathy is suspected. TEG results are: reaction time, 4.5 min; kinetics, 2.3 min; alpha, 55 degrees; maximum amplitude, 65 mm; amplitude at 30 minutes, 3.5%; and coagulation index, -2.1. He does not take any anticoagulants at home, and he was not given any during surgery.

Based on this information, which of the following is the most appropriate next step in treatment?

A. PRBCs
B. FFP
C. Tranexamic acid
D. Platelets
E. 0.9% normal saline

9. A 67-year-old woman is evaluated in the emergency department for a three-day history of dysuria and generalized fatigue. Temperature is 36.7°C (98.1°F), heart rate 115 beats/min, blood pressure 80/50 mm Hg, and oxygen saturation 93% on room air. She receives 2 liters of crystalloid but remains hypotensive. She is admitted to the ICU with septic shock and gram-negative bacteremia requiring vasopressors. Her mentation improves, but repeat laboratory testing shows new anemia and thrombocytopenia. Laboratory findings are: hemoglobin 10.5 g/dL, platelet count 70,000/mm^3, INR 2.2, prothrombin time greater than 3 sec, elevated fibrin degradation products, partial thromboplastin time 50 sec, fibrinogen 190 mg/dL. A blood smear shows multiple schistocytes. She has no signs of overt bleeding or oozing from any vascular sites.

   In addition to treating her sepsis, which of the following treatments is indicated?

   A. Fresh frozen plasma
   B. Platelets
   C. Plasma exchange
   D. Treatment of the underlying condition
   E. Factor VII

10. A 55-year-old man with a history of cirrhosis secondary to chronic alcohol abuse is admitted to the ICU for septic shock due to spontaneous bacterial peritonitis. He has a paracentesis with removal of 6 liters, which is found to have 500 neutrophils. He is started on ceftriaxone and transfused appropriately with albumin. However, he is found to have coagulopathy and thrombocytopenia. He has no signs of active bleeding at this time. Pertinent laboratory findings are: hemoglobin 11.5 g/dL, platelets 50,000/mm^3, INR 3.1.

Which of the following tests is most likely to be helpful in differentiating coagulopathy of chronic liver disease from disseminated intravascular coagulation?

A. Fibrinogen
B. Factor V
C. Factor VIII
D. Bleeding time
E. Partial thromboplastin time

11. A 41-year-old woman with history of systemic lupus erythematosus, controlled on disease-modifying therapy, is evaluated in the emergency department for a three-day history of headache, nausea, and vomiting. Vital signs are: temperature 36.7°C (98.1°F), heart rate 90 beats/min, blood pressure 120/76 mm Hg, oxygen saturation 98% on room air. On physical examination, she is alert, awake, and oriented to person and place. She has mild scleral icterus and mild diffuse abdominal tenderness. She also has an erythematous non-blanching rash on the bilateral lower extremities. The rest of her physical examination is unremarkable. Pertinent laboratory findings are: creatine 1.1 mg/dL, hemoglobin 9.2 g/L, hematocrit 30%, platelets 70,000/mm^3, INR 1.0, total bilirubin 3.2 mg/dL, direct bilirubin 0.4 mg/dL. CTs of the head and abdomen are unremarkable. After her CT, three hours after arrival, she has a generalized tonic-clonic seizure, and is intubated for airway protection. Vital signs are unchanged. However, repeat bloodwork shows worsening thrombocytopenia, with a platelet count of 20,000/mm^3. A peripheral blood smear shows fragmented red blood cells. She is admitted to the ICU with a presumptive diagnosis of thrombotic thrombocytopenic purpura.

    After obtaining central venous access, which of the following steps should be performed until platelet count is greater than or equal to 150,000/mm^3 for at least 48 hours?

    A. Initiate plasmapheresis.
    B. Transfuse platelets to achieve platelet count of 50,000/mm^3 and initiate plasma exchange.
    C. Initiate plasma exchange.
    D. Administer glucocorticoids and initiate plasma exchange.
    E. Administer glucocorticoids and initiate plasmapheresis.

12. A 65-year-old woman with a history of hypertension and peptic ulcer disease presents with three episodes of melena at home, occasional hematochezia, lightheadedness, and fatigue. Vital signs are: temperature 37.2°C (99°F), heart rate 130 beats/min, blood pressure 100/60 mm Hg, and oxygen saturation 93% on 2-L nasal cannula. After large-bore access is obtained, she is given 2 liters of crystalloid. Hemoglobin is 5.6 g/dL (one week ago it was 11.2 g/dL). She undergoes emergent endoscopy, which shows an actively bleeding ulcer with

erosion of the gastroduodenal artery. The ulcer is cauterized and hemostasis is achieved. She is transferred to the ICU for closer hemodynamic monitoring. During the first six hours after admission, she received about 5 units of packed red blood cells (PRBCs) for resuscitation. Hemoglobin has remained stable at 7.5 g/dL after the endoscopic procedure.

Which of the following statements regarding coagulopathy related to repeated PRBC transfusions in hemorrhagic shock best reflects consensus guidelines?

A. One unit of fresh frozen plasma (FFP) should be transfused for every unit of PRBCs.
B. One unit of FFP should be transfused for every two units of PRBCs.
C. There are no consensus guidelines regarding the optimal ratio of FFP to PRBCs for transfusion.
D. Cryoprecipitate should be administered to any patient who receives more than 2 units of PRBCs.

13. A 24-year-old man is admitted for pulmonary embolism with right ventricular strain. He has a past medical history of multiple deep venous thrombosis. Coagulation workup is negative for protein C/S deficiency, factor V Leiden, prothrombin G20210, and antiphospholipid syndrome. His prothrombin time is normal; however, his prolonged activated partial thrombin time is greater than two times the upper limit of normal in the absence of heparin administration.

A deficiency of which of the following factors is the cause of his hypercoagulable state?

A. Factor VII
B. Factor VIII
C. Factor XI
D. Factor XII

14. A 45-year-old man is admitted to the ICU after a motor vehicle collision and is found to have a continuing transfusion requirement. Injuries include a grade III laceration of the spleen, multiple rib fractures, and bilateral femoral fractures. In the operating room he receives 15 units of packed red blood cells, and 10 units of fresh frozen plasma.

Which of the following is most likely to cause coagulopathy as a result of the transfusion of blood products in this patient?

A. Decreased serum fibrinogen concentration
B. Decreased serum ionized calcium concentration
C. Dilutional thrombocytopenia
D. Disseminated intravascular coagulation

Part 7 Answers:
Hematologic and Oncologic Disorders

1. Rationale

Answer: C

Acute respiratory failure is the most common reason for ICU admission following hematopoietic stem cell transplantation (HSCT). As the incidence of infectious complications of HSCT has diminished as a result of effective antimicrobial prophylaxis, noninfectious pulmonary insults have emerged as a major cause of morbidity and mortality. Several acute lung injury syndromes (idiopathic pneumonia syndrome, engraftment syndrome, diffuse alveolar hemorrhage) are now well characterized. Although they have somewhat similar clinical features, distinguishing between them is important for initiating appropriate treatment and for prognosticating outcome.

Diffuse alveolar hemorrhage (DAH) usually presents within the first month after HSCT. Risk factors for DAH are intensive chemotherapy before HSCT, total body irradiation, older age, white blood cell count recovery, severe mucositis, and renal insufficiency. Patients typically present with dyspnea, nonproductive cough, fever, and diffuse pulmonary infiltrates. Hemoptysis is rare. Chest radiograph shows bilateral interstitial and alveolar infiltrates that tend to be perihilar and in the lower lobes. These radiologic findings may precede the clinical presentation by an average of three days. High-resolution chest CT shows bilateral ground glass infiltrates. Demonstration of progressively bloodier return from bronchoalveolar lavage (BAL) in the absence of an identifiable respiratory tract infection is considered a key diagnostic feature. However, in one study, more than half of patients with autopsy-proven DAH had non-bloody BAL fluid. The presence of more than 20% hemosiderin-laden macrophages in BAL fluid is an alternative diagnostic criterion, but because it may take 48 to 72 hours for this to appear, the absence of hemosiderin does not exclude a fresh bleeding episode. Treatment consists of high-dose systemic corticosteroids, although there are no prospective randomized studies to confirm the benefit of this treatment in HSCT recipients. Although thrombocytopenia is common in HSCT patients, platelet transfusion does not result in improvement in respiratory status. Death is usually a result of sepsis or multisystem organ failure rather than respiratory failure from refractory hemorrhage.

Bronchiolitis obliterans is an inflammatory disease of the small airways that develops late in the course of HSCT. It leads to progressive obstructive airway disease without parenchymal involvement. Bronchiolitis obliterans gradually progresses over months to years, and patients eventually die of respiratory failure. Systemic corticosteroids are

not typically beneficial. Chronic therapy with macrolides may slow its progression.

Engraftment syndrome is characterized by fever, erythrodermatous rash, and noncardiogenic pulmonary edema that occurs during the neutrophil recovery phase of HSCT. Although the syndrome's etiology is poorly understood, the release of proinflammatory cytokines during engraftment is thought to play a primary role. The administration of granulocyte-colony stimulating factor may increase the incidence and severity of engraftment syndrome. Discontinuation of this agent is recommended for patients who develop this complication. For patients with significant pulmonary involvement, corticosteroid administration has been recommended, although mortality is high among those who progress to respiratory failure.

Acute graft-versus-host disease (GVHD) is a common complication of HSCT that is an exaggerated but otherwise normal response of donor immune cells to host antigens. Clinically GVHD manifests as injury to the skin, gastrointestinal mucosa, and liver that occurs in two general scenarios: classic, occurring within the first 100 days after HSCT; or late onset, occurring after 100 days. The diagnosis of acute GVHD is based on a combination of clinical and biopsy findings. Glucocorticoids are the gold standard for GVHD treatment. Other treatments include immunosuppressants such as cyclosporine or mycophenolate mofetil, IV immunoglobulin, and occasionally extracorporeal phototherapy. Gastrointestinal involvement may necessitate parenteral nutrition to rest the gut. Octreotide may be useful for severe diarrhea. Mortality is usually secondary to sepsis rather than a direct result of GVHD.

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2. Lara AR, Schwarz MI. Diffuse alveolar hemorrhage. *Chest.* 2010 May;137(5):1164-1171.
3. Soubani AO, Pandya CM. The spectrum of noninfectious pulmonary complications following hematopoietic stem cell transplantation. *Hematol Oncol Stem Cell Ther.* 2010;3(3):143-157.
4. Soubani AO. Critical care considerations of hematopoietic stem cell transplantation. *Crit Care Med.* 2006 Sep;34(9 Suppl):S251-S267.

2. Rationale

Answer: D

Argatroban is incorrect. Application of pretest probability assessment using the 4Ts scoring system reveals that timing is not consistent with heparin-induced thrombocytopenia (HIT) since the onset was after a trending of platelet fall observed before initiation of low-molecular-weight heparin four days before (0 points). Although the degree of platelet fall (greater than 50%) assigns 2 points, there are other definite reasons for thrombocytopenia (piperacillin/tazobactam, smoldering infection) (0 points) and no evidence of a new thrombosis (0 points). Therefore, the total 4Ts score is 2, which denotes low probability and is driven solely by the degree of platelet fall. Although this scoring system may not be completely reliable in identifying risk in

critically ill patients, the disparity is caused by lack of knowledge regarding previous heparin exposure as well as alternative causes of HIT. The patient has no prior heparin exposure, and has other possible reasons for thrombocytopenia. Because of this (initiation of alternate anticoagulation is recommended with moderate to high pretest probability) along with a platelet count below 50 x 103/mm^3 (major bleeding risk factor) and previous bleeding, therapeutic anticoagulation with argatroban would bring more risk than benefit.

Aspirin is incorrect because the current platelet level puts him at a high risk of bleeding. Fondaparinux is incorrect because it is contraindicated for a platelet count below 50 x 103/mm^3. Mechanical prophylaxis is correct. His low platelet count, below 50 x 103/mm^3 (major bleeding risk factor) and previous bleeding substantiates stopping pharmacologic prophylaxis and initiating mechanical methods until platelet count improves.

References:

1. Kahn SR, Lim W, Dunn AS et al; American College of Chest Physicians. Prevention of VTE in nonsurgical patients: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest.* 2012 Feb;141(2 Suppl):e195S–e226S.
2. Linkins LA, Dans AL, Moores LK, et al; American College of Chest Physicians. Treatment and prevention of heparin-induced thrombocytopenia: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest.* 2012 Feb;141(2 Suppl):e495S-e530S.
3. Crowther M, Cook D, Guyatt G, et al; PROTECT collaborators; Canadian Critical Care Trials Group; Australian and New Zealand Intensive Care Society Clinical Trials Group. Heparin-induced thrombocytopenia in the critically ill: Interpreting the 4Ts test in a randomized trial. *J Crit Care.* 2014 Jun;29(3):470.e7-e15.

3. Rationale

Answer: D

Argatroban falsely elevates the INR, and it should not be interpreted as an indicator of the effect of warfarin without interruption of the argatroban infusion. Additionally, the period of overlap is insufficient to expect a complete therapeutic effect from warfarin. A minimum of five days of overlap is necessary to allow for inhibition of prothrombin. Finally, since the INR is primarily artifact, and the patient is not bleeding, administration of vitamin K is inappropriate.

References:

1. Linkins LA, Dans AL, Moores LK, et al; American College of Chest Physicians. Treatment and prevention of heparin-induced thrombocytopenia: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest.* 2012 Feb;141(2 Suppl):e495S-e530S.

2. Argatroban [package insert]. Research Triangle Park, NC: GlaxoSmithKline; 2016.

4. Rationale

Answer: B

Multiple units of blood products were given as part of resuscitation. The typical life span of a red blood cell (RBC) is approximately 120 days, but stored RBCs have significantly shorter life spans due to oxidative damage to RBC membranes; this leads to decreased plasticity and deformability with subsequent hemolysis. More than 20% of packed RBCs are destroyed within 24 hours after transfusion, with the average life span of transfused packed RBCs being only 90 days. In addition, the patient has upregulation of inflammatory cytokines (interleukin[IL]-1 and tumor necrosis factor alpha [TNF-α]) as result of the trauma, which leads to increased vulnerability to oxidative stress and decrease in deformability. One mechanism is probably related to the direct damaging effects of reactive oxygen species from activated phagocytes on RBC membrane proteins. Increased concentrations of nitric oxide and increased intracellular concentration of calcium decrease the deformability of RBCs and might predispose to intravascular hemolysis.

Most of the iron in the body recirculates as old RBCs die, heme is metabolized, and iron is reused for erythropoiesis. Hepcidin plays a key role in iron metabolism, regulating the movement of iron into plasma. Expression of hepcidin leads to intracellular retention of iron. Hepcidin transcription is repressed by iron deficiency and hypoxia. Release of proinflammatory cytokines, including IL-6, leads to activation of hepcidin synthesis and suppression of iron metabolism. In this patient, the proinflammatory state is likely to affect iron metabolism; however, the acute drop in hemoglobin concentration is probably not secondary to impaired erythropoiesis.

Critical illness and trauma affect erythropoietin metabolism in several ways. First, concentration of erythropoietin in the blood of patients with critical illness or trauma is disproportionally low compared to the level of anemia. It produces suppressive effects of IL-1b and TNF-α on erythropoietin. In addition, inflammatory cytokines produce direct suppressive effects on erythroid colony formation. Administration of recombinant erythropoietin in critical illness has produced conflicting results in terms of amount of transfused packed RBCs, while increasing the survival in the subgroup of trauma patients. In this patient, the acute drop in hemoglobin concentration is unlikely due to decreased erythropoiesis.

References:

1. Singh S, Gudzenko V, Fink MP. Pathophysiology of perioperative anaemia. *Best Pract Res Clin Anaesthesiol.* 2012 Dec;26(4):431-439.
2. Luten M, Roerdinkholder-Stoelwinder B, Schaap NP, de Grip WJ, Bos HJ, Bosman GJ. Survival of red blood cells after transfusion: a comparison between red cells concentrates of different storage periods. *Transfusion.* 2008 Jul;48(7):1478-1485.
3. Zaets SB, Berezina TL, Morgan C, et al. Effect of trauma-hemorrhagic shock on

red blood cell deformability and shape. *Shock.* 2003 Mar;19(3):268-273.
4. Corwin HL, Gettinger A, Fabian TC, et al; EPO Critical Care Trials Group. Efficacy and safety of epoetin alfa in critically ill patients. *N Engl J Med.* 2007 Sep 6; 357(10):965-976.

5. Rationale

Answer: D

Anaphylaxis can occur as a result of an immune-mediated reaction or direct non-immune-mediated reaction. Immunologic anaphylaxis occurs following an initial sensitization. A second exposure generates an immune-mediated (most commonly IgE-mediated) reaction resulting in the release of inflammatory mediators from mast cells and basophils. Common perioperative medications/exposures causing immunologic anaphylaxis include neuromuscular blocking drugs (NMBDs), antibiotics, and latex.

Non-immunologic anaphylaxis occurs after the direct activation of mast cells and basophils, without immunologic involvement. This may occur on first exposure rather than requiring a prerequisite exposure for sensitization. Common examples include vancomycin, morphine, and cold temperature exposure. Any agent that can generate a non-immunologic reaction also has the potential to generate an immune-mediated reaction.

Relapse of anaphylaxis may occur up to 72 hours (median 11 hours) after the initial event, and has been reported in 1-20% of patients. The mechanism is not clearly understood, but may be caused by decreased plasma concentrations of anaphylaxis medications or a true immunologic phenomenon. After a severe hypersensitivity reaction, close observation for up to 72 hours in an ICU is strongly recommended.

References:

1. Lee S, Bellolio MF, Hess EP, Erwin P, Murad MH, Campbell RL. Time of onset and predictors of biphasic anaphylactic reactions: a systematic review and meta-analysis. *J Allergy Clin Immunol Pract.* 2015 May-Jun;3(3):408-416.
2. Mertes PM, Tajima K, Regnier-kimmoun MA, et al. Perioperative anaphylaxis. *Med Clin North Am.* 2010 Jul;94(4):761-789.
3. Kemp SF. The post-anaphylaxis dilemma: how long is long enough to observe a patient after resolution of symptoms? *Curr Allergy Asthma Rep.* 2008 Mar;8(1):45-48.

6. Rationale

Answer: C

This patient has diagnostic criteria consistent with heparin-induced thrombocytopenia (HIT), including evidence of thrombosis and thrombocytopenia on day six after heparin administration. It can be assumed that he received heparin during his coronary artery bypass grafting surgery. HIT is characterized by a decrease in platelet count of more

than 50% from the highest platelet count after heparin is started, an onset of five to 10 days after heparin is started, hypercoagulability, and the presence of heparin-dependent, platelet-activating IgG antibodies. The next step in confirming the diagnosis is to test the blood for platelet factor 4-heparin antibodies. Although enzyme immunoassays to detect these antibodies have a high negative predictive value, they have a low positive predictive value and thus should only be performed if clinical suspicion for HIT is high, as it is for this patient. Platelet factor 4-heparin antibodies activate platelets to increase thrombin generation; therefore, patients with HIT are at increased risk for thrombosis and should be anticoagulated. However, anticoagulation with heparin, low-molecular-weight heparin, or warfarin are all contraindicated. The most appropriate treatment is direct thrombin inhibition with an argatroban infusion. Warfarin is contraindicated in acute HIT because it may lead to venous limb gangrene.

Reference:

1. Linkins LA, Dans AL, Moores LK, et al; American College of Chest Physicians. Treatment and prevention of heparin-induced thrombocytopenia: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest.* 2012 Feb;141(2 Suppl):e495S-e530S.

7. Rationale

Answer: B

The concern here is the cause of the patient's high sanguineous chest tube output. He has an acceptable blood pressure with appropriate urine output and no evidence of end-organ dysfunction, making the transfusion of packed red blood cells inappropriate at this time. By conventional coagulation tests and thromboelastography (TEG), he is normal to slightly hypercoagulable, making the transfusion of fresh frozen plasma unnecessary. The maximum amplitude, which is a reflection of platelet function, is normal, suggesting that desmopressin would not be helpful in reducing chest tube output. The abnormality, as diagnosed by TEG, is fibrinolysis as measured by the amplitude at 30 minutes. The patient is able to form a clot; however, due to increased plasmin activity, he is unable to maintain the structure. The appropriate treatment is tranexamic acid, which inhibits fibrinolysis by reversibly binding to the lysine receptor sites on plasmin.

References:

1. CRASH-2 trial collaborators, Shakur H, Roberts I, et al. Effects on tranexamic acid on death, vascular occlusive vents, and blood transfusion in trauma patients with significant hemorrhage (CRASH-2): a randomised, placebo-controlled trial. *Lancet.* 2010 Jul 3;376(9734):23-32.
2. Longstaff C. Studies on the mechanisms of action of aprotinin and tranexamic acid as plasmin inhibitors and antifibrinolytic agents. *Blood Coagul Fibrinolysis.* 1994 Aug;5(4):537-542.
3. Trapani L. Thromboelastography: current applications, future directions. *Open J Anesthesiol.* 2013;3:23-27.

8. Rationale

Answer: C

This probably represents surgical bleeding, which might benefit from tranexamic acid administration or, if serious enough, surgical exploration. Thromboelastography (TEG) is frequently used to pinpoint the defects responsible for abnormal clotting. The benefits have been established, especially for cardiac surgery. Hematologic and TEG values are all within normal limits; there is no rationale for giving additional blood products. Giving normal saline would be counterproductive because it would dilute existing clotting factors.

References:

1. Clevenger B, Mallett SV, Klein AA, Richards T. Patient blood management to reduce surgical risk. *Br J Surg.* 2015 Oct;102(11):1325-1337; discussion 1324.
2. Ak K, Isbir CS, Tetik S, et al. Thromboelastography-based transfusion algorithm reduces blood product use after elective CABG: a prospective randomized study. *J Card Surg.* 2009 Jul-Aug;24(4):404-410.

9. Rationale

Answer: D

This patient has septic shock from a urinary source, and she has developed disseminated intravascular coagulation (DIC), as evidenced by elevation in coagulation factors, microangiopathic hemolytic anemia with schistocytes, and thrombocytopenia. DIC causes dysfunction in the blood coagulation system, resulting in the abnormal deposition of fibrin, causing microvascular thrombi and contributing to multiorgan failure. Patients have thrombosis or severe bleeding. DIC in the setting of purpura fulminans has a mortality rate of 18%; the presence of DIC is an independent predictor of mortality in patients with sepsis. Sepsis is the most frequent cause of DIC in the ICU. Common organisms implicated in its pathogenesis include *Staphylococcus aureus* and *Escherichia coli.* Even though this patient's blood smear has schistocytes, she does not have any other clinical manifestations of thrombotic thrombocytopenic purpura (TTP), including altered mental status or renal failure. Although all five classical findings of TTP are not found in a majority of patients, TTP patients do not have abnormal coagulation tests. IV immunoglobulin has no role in this patient's management.

According to the International Society on Thrombosis and Haemostasis, patients can have overt or non-overt DIC, based on this scoring system and management algorithm: 1) Platelet count. 50,000-100,000 per mm^3 (1 point), less than 50,000 per mm^3 (2 points); 2) Elevated d-dimer, fibrin degradation products. No increase (0 points), moderate increase (2 points), strong increase (3 points); 3) Prolonged prothrombin time. Less than 3 sec (0 points), 3-6 sec (1 point), greater than or equal to 6 sec (2 points); 4) Fibrinogen. Greater than or equal to 1g/L (0 points), less than or equal to 1g/L (1 point). Total score of greater than 5 points means overt DIC, for

which coagulation studies should be repeated at least daily. Total score of less than 5 points means non-overt DIC, for which coagulation studies and scoring should be repeated within 1 to 2 days. Current guidelines do not recommend the replacement of blood products in patients who are not actively bleeding. Therefore, the correct management in this patient is observation with repeat coagulation studies in 1 to 2 days.

References:

1. Levi M, Toh CH, Thachil J, Watson HG. Guidelines for the diagnosis and management of disseminated intravascular coagulation. British Committee for Standards in Haematology. *Br J Haematol.* 2009 Apr;145(1):24-33.
2. Toh CH, Hoots WK; SSC on Disseminated Intravascular Coagulation of the ISTH. The scoring system of the Scientific and Standardisation Committee on Disseminated Intravascular Coagulation of the International Society on Thrombosis and Haemostasis: a 5-year overview. *J Thromb Haemost.* 2007 Mar;5(3):604-606.
3. Hunt BJ. Bleeding and coagulopathies in critical care. N Engl J Med. 2014 Feb 27;370(9):847-859.
4. Levi M, Ten Cate H. Disseminated intravascular coagulation. *N Engl J Med.* 1999 Aug 19;341(8):586-592.

10. Rationale

Answer: C

Liver disease can lead to derangements in coagulation and platelet function. The liver is the main site for synthesis of fibrinogen and factors II, V, VII, IX, X, XI, and XII. It is also the site of vitamin K-dependent gamma-carboxylation of factors II, VII, IX and X. In some instances, it may be difficult to differentiate coagulopathy of chronic liver disease from disseminated intravascular coagulation (DIC), especially in the setting of septic shock. In this case, a factor VIII level would be helpful. Factor VIII is synthesized primarily in the endothelium and is usually normal or increased in acute or chronic liver failure. However, factor VIII levels are significantly decreased in DIC. Fibrinogen and factor V would be decreased in both DIC and chronic liver disease with coagulopathy. Similarly, bleeding time and partial thromboplastin time would be elevated, hence less helpful in distinguishing between the two disorders. Thrombocytopenia can be present in chronic liver disease as a result of portal hypertension and sequestration of platelets into the spleen.

While patients may have laboratory abnormalities that would raise concern for increased risk of bleeding, patients with cirrhosis also have an equivalent decrease in anticoagulant factors, including protein C, protein S, and plasminogen. These patients are not auto-anticoagulated. In fact, portal vein thrombosis can complicate chronic liver disease in as many as 15% of cases. The administration of blood products is therefore reserved for patients with coagulopathy and active bleeding. Empiric administration of blood, fresh frozen plasma, or platelets can increase portal venous pressures and may increase risk of variceal hemorrhage or thrombosis. Therefore,

the correct management in this patient is observation.

References:

1. Hunt BJ. Bleeding and coagulopathies in critical care. *N Engl J Med.* 2014 Feb 27;370(9):847-859.
2. Senzolo M, Burra P, Cholongitas E, Burroughs AK. New Insights into the coagulopathy of liver disease and liver transplantation. *World J Gastroenterol.* 2006 Dec 28;12(48):7725-7736.

11. Rationale

Answer: D

This case illustrates important concepts about the variability in presentation of thrombotic thrombocytopenic purpura (TTP). TTP is an acquired hematologic disorder in which there is qualitative or quantitative deficit in ADAMTS13 (a metalloprotease responsible for cleaving von Willebrand factor), leading to widespread thrombus formation, microangiopathic hemolytic anemia and platelet consumption. TTP carries almost 100% mortality if untreated. It is most frequently seen in young adults; patients can present with nonspecific symptoms including headache, confusion, abdominal pain, and nausea. Furthermore, it is important to recognize that patients may not be critically ill on presentation. In addition, although TTP is classically associated with a pentad of renal failure, high fever, altered mental status, thrombocytopenia, and hemolytic anemia, these clinical manifestations are seldom all seen together. In fact, acute kidney injury and renal failure is less common in TTP than nonspecific gastrointestinal symptoms and mild to moderate central nervous system disturbances. TTP is ultimately a clinical diagnosis; prompt treatment (within four to eight hours of presentation) should be administered when there is clinical suspicion.

The mainstay in TTP treatment is plasma exchange. This is often combined with either corticosteroids (usually pulse dose methylprednisolone, 1 mg/kg/day IV for three days) or rituximab, which has been known to decrease the duration of plasma exchange. Plasma exchange should be continued until the platelet count reaches greater than or equal to 50,000/mm^3 for at least 48 hours, while continuing corticosteroids. If there is no sign of relapse and platelet count remains greater than or equal to 150,000/mm^3, central venous catheters can be removed and corticosteroids tapered.

Platelet transfusion in TTP is contraindicated because it can worsen thrombotic microangiopathy. Furthermore, these patients are generally at higher risk of thrombotic complications versus bleeding. Plasmapheresis has no role in the management of TTP, since it is not thought to be antibody mediated.

References:

1. Scully M, Hunt BJ, Benjamin S, et al; British Committee for Standards in Haematology. Guidelines on the diagnosis and management of thrombotic thrombocytopenic purpura and other thrombotic microangiopathies. *Br J Haematol.* 2012 Aug; 158(3):323-335.

2. Rock GA, Shumak KH, Buskard NA, et al. Comparison of plasma exchange with plasma infusion in the treatment of thrombotic thrombocytopenic purpura. Canadian Apheresis Study Group. *N Engl J Med.* 1991 Aug 8;325(6):393-397.
3. Bell WR, Braine HG, Ness PM, Kickler TS. Improved survival in thrombotic thrombocytopenic purpura-hemolytic uremic syndrome. Clinical experience in 108 patients. *N Engl J Med.* 1991 Aug 8;325(6):398-403.
4. George JN. How I treat patients with thrombotic thrombocytopenic purpura: 2010. *Blood.* 2010 Nov 18;116(20):4060-4069.

12. Rationale

Answer: C

The concept of acquired coagulopathies after packed red blood cell (PRBC) transfusion in hemorrhagic shock is controversial. Many clinicians have adopted a transfusion ratio of fresh frozen plasma (FFP) to PRBCs of 1:1 or 1:2, based on retrospective studies of military and civilian casualties. Massive transfusion strategies have been associated with less organ dysfunction, more ventilator-free days, and less abdominal compartment syndrome. The use of FFP is not without risk; there is a documented increased risk of transfusion-associated acute lung injury, acute respiratory distress syndrome (ARDS), and multiple organ dysfunction. There is currently no consensus guideline on the use of FFP after repeated red cell transfusions. The North American Pragmatic, Randomized Optimal Platelets and Plasma Ratios (PROPPR) trial, a phase III randomized controlled trial, is currently investigating the effects of transfusion ratios of different blood products in patients receiving massive red cell transfusions. Their primary end points are 24-hour and 30-day mortality.

References:

1. Hunt BJ. Bleeding and coagulopathies in critical care. *N Engl J Med.* 2014 Feb 27;370(9):847-859.
2. Borgman MA, Spinella PC, Perkins JG, et al. The ratio of blood products transfused affects mortality in patients receiving massive transfusions at a combat support hospital. *J Trauma.* 2007 Oct;63(4):805-813.
3. Malone DL, Hess JR, Fingerhut A. Massive transfusion practices around the globe and a suggestion for a common massive transfusion protocol. *J Trauma.* 2006 Jun;60(6 Suppl):S91-S96.
4. Cotton BA, Au BK, Nunez TC, Gunter OL, Robertson AM, Young PP. Predefined massive transfusion protocols are associated with a reduction in organ failure and postinjury complications. *J Trauma.* 2009 Jan;66(1):41-48.

13. Rationale

Answer: D

Factor VII is important in the initial coagulation process by interacting with tissue factor at the site of injury to generate thrombin. Factor VII deficiency is an autosomal

recessive disease that occurs in 1 in 300,000 to 1 in 500,000 and is associated with increased bleeding. Factor VII deficiency would result in a prolonged prothrombin time but not activated partial thrombin time (aPTT). Factor VIII deficiency, an X-linked recessive trait, results in a prolonged aPTT. Depending on the severity, patients can present with severe internal and external bleeding. Factor XI deficiency is responsible for hemophilia C, which can affect both sexes and occurs predominantly in Ashkenazi Jews. Spontaneous hemorrhage is atypical, and excessive bleeding occurs in the setting of trauma or surgery. Its deficiency results in a prolonged aPTT.

In vitro, factor XII initiates the intrinsic coagulation pathway through contact activation with negatively charged surfaces. Its activity is one of the factors measured by aPTT. Factor XII's role in vivo is the promotion of fibrinolysis by activation of plasminogen activator. Factor XII deficiency results in a prolonged aPTT, but instead of being associated with increased bleeding, it has been implicated in major thromboembolic events and retinal vein occlusions.

References:

1. Perry DJ. Factor VII deficiency. *Br J Haematol.* 2002 Sep;118(3):689-700.
2. Wight J, Paisley S. The epidemiology of inhibitors in haemophilia A: a systematic review. *Haemophilia.* 2003 Jul;9(4):418-435.
3. Kuhli C, Scharrer I, Koch F, Ohrloff C, Hattenbach LO. Factor XII deficiency: a thrombophilic risk factor for retinal vein occlusion. *Am J Ophthalmol.* 2004 Mar;137(3):459-464.
4. Renné T, Schmaier AH, Nickel KF, Blombäck M, Maas C. In vivo roles of factor XII. *Blood.* 2012 Nov 22;120(22): 4296-4303.

14. Rationale

Answer: C

Bleeding following massive transfusion can be caused by hypothermia, dilutional coagulopathy, platelet dysfunction, fibrinolysis, or hypofibrinogenemia. Transfusion of large number of blood products (> 10-15 units) such as packed red blood cells (PRBC) and fresh frozen plasma (FFP) is most likely to produce dilution thrombocytopenia and this can lead to acquired coagulopathy. In this case the transfusion of 15 units of PRCS + 10 units of FFP will cause significant dilutional thrombocytopenia. In order to prevent this phenomenon massive transfusion protocols endorsed by the American College of Surgeons recommend the administration of platelets of one single donor apheresis or random donor platelet pool for each six units of PRBCs.

References:

1. Levy JH. Massive transfusion coagulopathy. *Semin Hematol.* 2006 Jan;43(1 Suppl 1):S59-63.
2. Hardy JF, De Moerloose P, Samama M, Groupe d'intérêt en Hémostase Péeiopératoire. Massive transfusion and coagulopathy: pathophysiology and

implications for clinical management. *Can J Anaesth.* 2004 Apr;51(4):293-310.

3. Bollinger D, Görlinger K, Tanaka KA. Pathophysiology and treatment of coagulopathy in massive hemorrhage and hemodilution. *Anesthesiology.* 2010 Nov;113(5):1205-1219.

Part 8:

Surgery, Trauma, and Transplantation

Part 8:
Surgery, Trauma, and Transplantation

Instructions: For each question, select the most correct answer.

1. A 22-year-old man with a gunshot wound is found to be hypotensive, with multiple small bowel and colonic injuries. Primary suture repair is performed. Blood loss

during surgery is significant; four units of packed red blood cells are administered. The patient is hemodynamically stable on arrival to the ICU.

Which of the following is the most appropriate duration of perioperative antibiotic coverage?

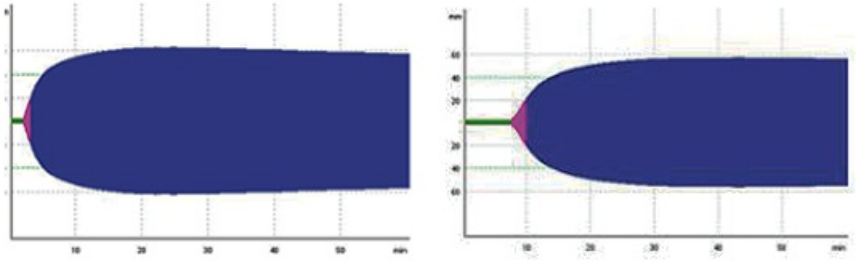
A. No antibiotics indicated
B. 24 hours
C. 48 hours
D. 7 days
E. 10 days

2. A 22-year-old man crashed into a tree at 60 miles per hour. He was ejected from the car and was found by emergency medical services unresponsive with agonal respirations, was intubated for a Glasgow Coma Scale (GCS) score of 3 and transported to the closest level 1 trauma center, 45 minutes away. On arrival, his GCS score remains 3, he is intubated, with equal breath sounds bilaterally, a firm abdomen, and no evidence of active external hemorrhage. Temperature is 34°C (93.2°F), heart rate 140 beats/min, blood pressure 80/40 mm Hg, oxygen saturation 93% on 100% fraction of inspired oxygen. Chest radiograph shows right lower lobe aspiration, pulmonary contusions and the endotracheal tube in the correct position. Pelvis radiograph shows an open-book pelvic fracture. Focused assessment with sonography in trauma (FAST) examination shows anechoic fluid in Morison pouch.

   In addition to placing a pelvic binder, which of the following are the most appropriate next steps in management?

   A. Give bolus of 3 liters IV crystalloid, and transfer patient directly to operating room.
   B. Transfer patient directly to operating room, without giving any IV fluids, and practice permissive hypotension.
   C. Start uncrossed blood product resuscitation, and consult with interventional radiology for patient's unstable pelvic bleeding.
   D. Start uncrossed blood product resuscitation, transfer patient directly to operating room, and consider tranexamic acid.

3. A 70-year-old man was involved in a head-on motor vehicle collision in which he was the restrained driver traveling 40 miles per hour. He is brought by emergency medical services to the emergency department, where he is combative, with a Glasgow Coma Scale (GCS) score of 8, and intubated for airway protection and further imaging. Vital signs are stable. CTs of the head, cervical spine, chest, abdomen, and pelvis reveal a right subdural hematoma without midline shift and a grade II spleen laceration. His family cannot remember any of his medications. Trauma laboratory results are pending. Thromboelastography (TEG) is shown below.



Reference Patient

Based on the TEG results and the patient's injuries, which of the following products is most appropriate?

A. Platelets
B. Tranexamic acid
C. Fresh frozen plasma or prothrombin complex concentrate
D. Cryoprecipitate

4. A 34-year-old woman recently arrived in the ICU after sustaining multiple orthopedic injuries as an unrestrained passenger in a motor vehicle accident. She is hypotensive, but fluid responsive. Her lungs are evaluated via ultrasonography as part of an extended focused assessment with sonography in trauma (eFAST) examination.

   Which of the following findings on ultrasonography is most indicative of pneumothorax?

   A. Lung sliding
   B. B lines
   C. Lung point
   D. A lines
   E. Free air

5. A 19-year-old, 90-kg (198-lb) man sustains a grade IV splenic laceration in a motor vehicle collision. Because of hemodynamic instability, he undergoes damage control laparotomy. He is transferred to the ICU for ongoing resuscitation. Vital signs on arrival include blood pressure 80/40 mm Hg and heart rate 125 beats/min. Urine output is 15 mL/hour. After resuscitation with crystalloid and blood products, blood pressure is 117/75 mm Hg, heart rate 99 beats/min, and urine output 100 mL/hour. Lactate level is 5.2 mmol/L, and base deficit is -9 mmol/L.

   Which of the following is the most appropriate course of action at this time?

   A. Further aggressive resuscitation should be withheld.

B. His base deficit should be corrected with the administration of sodium bicarbonate.
C. Aggressive fluid resuscitation should be continued.
D. A pulmonary artery catheter should be placed to better define his hemodynamics and titrate his resuscitation.

6. A 25-year-old man sustains a stab wound to the upper abdomen, with omentum visible on examination. He arrives in the emergency department with a systolic blood pressure of 86 mm Hg and answers questions appropriately.

   Which of the following should be done for this patient?

   A. Given his normal mental status, a chest and abdominal CT should be obtained to better define his injury and for operative planning.
   B. Large-bore IV access should be obtained, and crystalloid and packed red blood cell transfusion should immediately be undertaken until blood pressure is normalized.
   C. Emergent local wound exploration should be performed to assess the need for operation.
   D. Large-bore IV access should be obtained, and he should be allowed to be hypotensive with no resuscitative efforts until reaching the operating room.

7. A 31-year-old man is brought to the ICU after emergent laparotomy for blunt trauma. In the operating room, he had been found to have liver, bowel, and splenic injuries, requiring bowel resection and reanastamosis and splenectomy. He received 25 units of packed red blood cells, 15 units of fresh frozen plasma, 6 units of platelets, and 4 units of crystalloid. In the ICU, he requires ongoing resuscitation for reversal of tissue hypoperfusion. Two hours later, his abdomen is distended and his bladder pressure is elevated.

   Which of the following signs would be most congruent with abdominal compartment syndrome?

   A. Central venous pressure (CVP) 25 mm Hg, elevated peak and plateau airway pressures, oliguria, bladder pressure 25 mm Hg
   B. CVP 25 mm Hg, elevated peak and plateau airway pressures, oliguria, bladder pressure 6 mm Hg
   C. CVP 5 mm Hg, elevated peak pressure, normal plateau airway pressure, normal urine output, bladder pressure 15 mm Hg
   D. Bladder pressure greater than 30 mm Hg

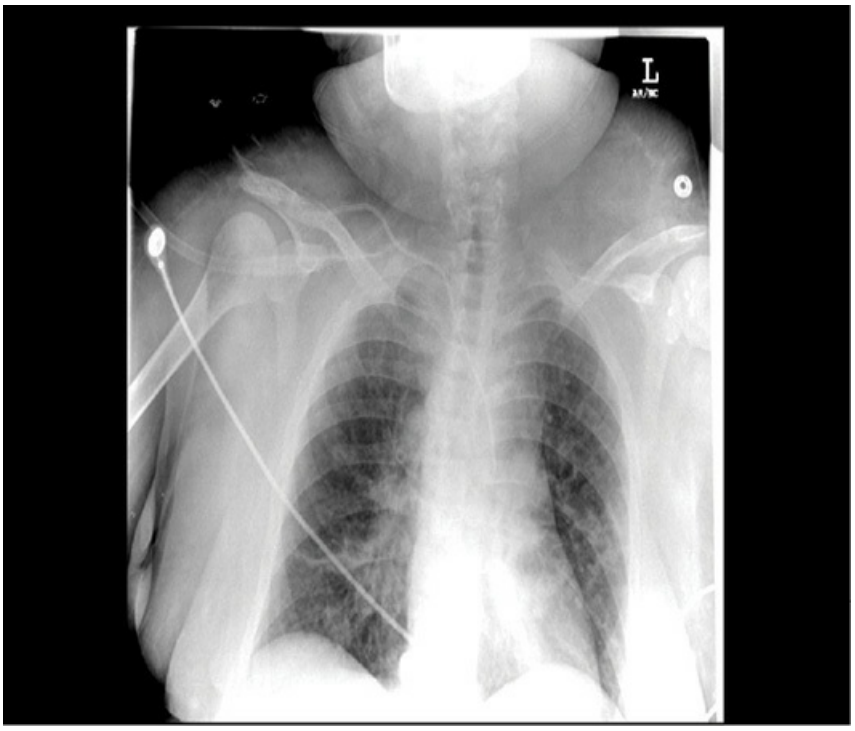
8. A 35-year-old man has been admitted for severe pancreatitis. He received an aggressive fluid resuscitation of more than 6 liters of normal saline. Because he was having trouble breathing, he was intubated, and a nasogastric tube and Foley catheter were inserted. His abdominal pressure is now 35 cm H_2O. Head of bed is 30 degrees. Peak airway pressures are rising, and his urine output has

decreased to less than 30 mL/hour.

Which of the following is the most appropriate next step in this patient's management?

A. Call surgery to transfer him to the operating room.
B. Chemically paralyze him with appropriate sedation.
C. Place him in reverse Trendelenburg position.
D. Try to perform paracentesis with an indwelling catheter.
E. Start a furosemide infusion with albumin or mannitol.

9. A patient with persistent, severe ileus, who is unable to tolerate enteral feeding for more than a week in the setting of necrotizing pancreatitis has a central line placed for initiation of total parenteral nutrition (TPN). Chest radiograph is shown below.



Which of the following steps should be performed before starting TPN in this patient?

A. Advance the central line by 2 cm.
B. Pull back the central line by 2 cm.
C. Insert a chest tube on the right.
D. Consult a vascular surgeon.

10. A 72-year-old man is postoperative day two (hospitalization day four) after a three-vessel, on-pump coronary artery bypass graft. His medical history includes coronary artery disease, hypertension, hyperlipidemia, and asthma. His platelet

count has decreased from a preoperative value of 130 x 10^9/L to 78 x 10^9/L this morning. His hemoglobin remains the same, and white blood cell count is 14.2 x 10^9/L, up from a preoperative value of 8.6 x 10^9/L. Vital signs remain stable, and he is without complaints. On physical examination, there are no signs of bleeding, rash, or extremity swelling.

Which of the following is the most appropriate next step in management?

A. Continue heparin, but discontinue aspirin
B. Continue both aspirin and subcutaneous heparin.
C. Continue aspirin, but switch heparin to argatroban.
D. Discontinue both aspirin and heparin until platelet count normalizes.
E. Transfuse platelets.

11. A 72-year-old man is admitted to the ICU following evaluation in the emergency department for a three-hour history of pressure-like substernal chest pain with dyspnea. ECG reveals new T-wave inversions in the inferior leads. Troponin-I levels are 0.04 ng/ml and then 0.06 ng/ml (normal range <0.01 ng/ml). Cardiac catheterization reveals 90% occlusion of the proximal left anterior descending artery, proximal OM1, and mid-right coronary artery. He undergoes urgent six-vessel coronary artery bypass graft without complication.

    Which of the following is the most appropriate management of his antiplatelet therapy on arrival to the ICU?

    A. Start aspirin and clopidogrel.
    B. Start aspirin only.
    C. Start clopidogrel only.
    D. There is no indication for antiplatelet therapy at this time.

12. A 32-year-old woman who is gravida 2, para 1, at 29 weeks' gestation loses consciousness during a routine obstetric examination at the hospital. When the maternal cardiopulmonary arrest team arrives, her Glasgow Coma Scale score is 3, and her pupils are dilated and sluggish. She has no pulse or respiration. Advanced cardiac life support protocol is initiated immediately. Despite four minutes of resuscitative measures, including chest compressions, defibrillation, and administration of IV epinephrine, the rhythm shown below persists.

Which of the following is the most appropriate next intervention?

A. Direct cardiac massage via thoracotomy
B. Emergency cesarean section
C. Cardiopulmonary bypass
D. Overdrive transcutaneous pacing

13. A 27-year-old woman with morbid obesity who is at 37 weeks' gestation is undergoing induction of labor for preeclampsia. At the patient's request, an epidural anesthetic is administered for pain relief. As the loading dose of bupivacaine is given, the obstetrician arrives to rupture the patient's membranes. Several minutes later, the patient experiences shortness of breath and becomes panicked and thrashes about in bed. She becomes cyanotic, loses consciousness, and becomes hypotensive.

    Which of the following is the most appropriate intervention?

    A. Transfusion of blood for a uterine rupture
    B. Placement on venoarterial extracorporeal membrane oxygenation (VA-ECMO) for amniotic fluid embolus
    C. Placement on venoarterial extracorporeal membrane oxygenation (VA-ECMO) for pulmonary embolus
    D. Administration of an intralipid for the inadvertent intravascular injection of local anesthetic

14. A 19-year-old college football player presents from football practice with a core body temperature of 41°C (105.8°F) and stupor. He is tachycardic with a heart rate of 130 beats/min, blood pressure 125/45 mm Hg, respiratory rate 28 breaths/min, and oxygen saturation 97% on room air.

    Which of the following is the most appropriate course of action?

    A. Initiate mechanical ventilation to decrease work of breathing.
    B. Resuscitate with cold IV saline.
    C. Fan with cool misting spray.
    D. Administer dantrolene.
    E. Administer IV acetaminophen.

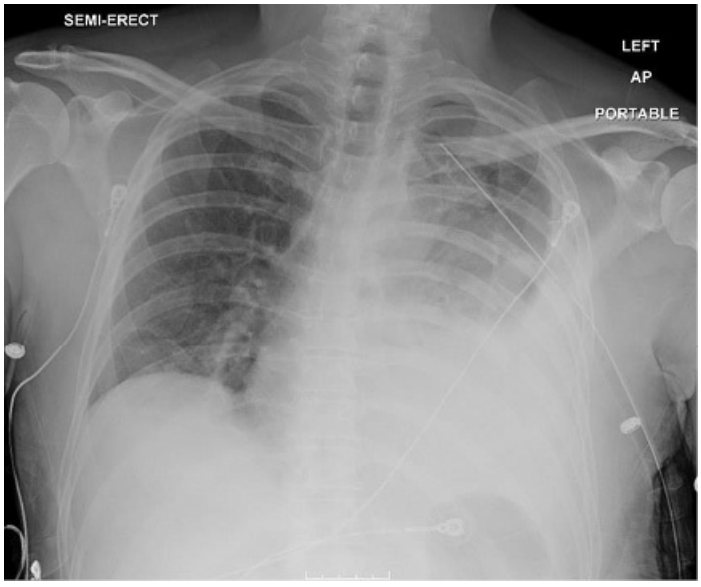
15. A 57-year-old woman sustained an unwitnessed fall at home. She underwent a craniotomy for subdural hematoma, and is now admitted to the ICU on mechanical ventilation. On postoperative day three, she develops acute respiratory distress syndrome, with a fever and worsening leukocytosis of 23,000/mm^3. She is intolerant to tube feeding, with abdominal distention. She is on pressure-regulated volume control (PRVC) ventilation with fraction of inspired oxygen 80%, positive end-expiratory pressure 12 cm H_2O, respiratory rate 18 breaths/min, tidal volume 490 mL (7 mL/kg). Arterial blood gas results: pH 7.32,

partial pressure of carbon dioxide 48 mm Hg, partial pressure of oxygen 62 mm Hg, oxygen saturation 90%.

Which of the following is the most appropriate next step in this patient's management?

A. After a pulmonary recruitment maneuver, change the ventilation from PRVC to airway pressure release ventilation.
B. Start broad-spectrum antibiotics for presumed ventilator-associated pneumonia (VAP).
C. Start broad-spectrum antibiotics, after obtaining a bronchoalveolar lavage specimen for bacteriology, for presumed VAP.
D. Obtain abdominal and pelvic CT.
E. Obtain CT angiography of the chest.

16. A 27-year-old man is admitted to ICU after an emergency craniotomy, splenectomy, and femoral fracture fixation. He also underwent left chest tube insertion for hemothorax. On hospital day three, the chest radiograph, shown below, still shows no improvement of the left chest opacification.



Which of the following is the most effective management for this patient?

A. Video-assisted thorascopic surgery and evacuation of hemathorax
B. Insertion of a second chest tube
C. Intrapleural fibrinolysis with streptokinase
D. Increase the preexisting chest suction from -20 cm H_2O to -40 cm H_2O
E. Observation without changing the current treatment

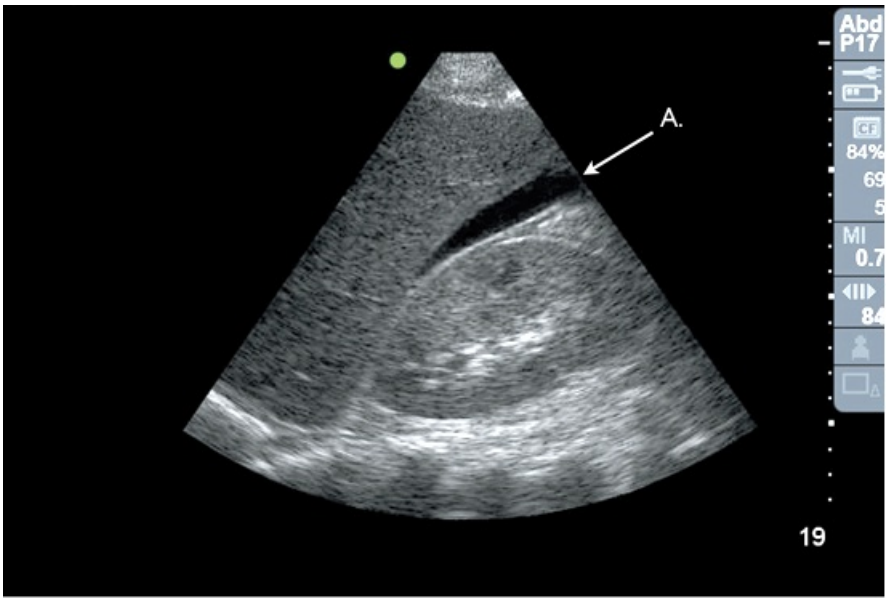
17. A 55-year-old man with a history of cirrhosis presents with hepatic encephalopathy. He is intubated on a mechanical ventilator. Physical examination is remarkable for tense ascites and 3+ lower extremity edema that developed

over a one-week period. He exhibits significant hypotensive episodes requiring significant pressor support to maintain a mean arterial pressure above 70 mm Hg. Central venous pressure is 15 mm Hg, with urine output of 10 mL/hour. Bladder pressures have increased from 15 mm Hg to 25 mm Hg. Serum laboratory values one week after presentation are: sodium 126 mEq/L, potassium 5.2 mEq/L, chloride 93 mEq/L, carbon dioxide 13 mEq/L, blood urea nitrogen 25 mg/dL, creatinine 1.9 mg/dL. Urine laboratory values one week after presentation are: creatinine 68 mg/dL, sodium 11 mEq/L.

Which of the following is the most appropriate next step in this patient's management?

A. Abdominal CT with contrast
B. Decompressive laparotomy
C. Foley catheter placement and assessment of post-void residual
D. IV bolus with isotonic crystalloid fluids
E. Large-volume paracentesis

18. An unstable, 27-year-old woman who was involved in a high-speed motor vehicle collision has just been brought to the trauma resuscitation bay and is being resuscitated. She has altered mental status, agonal respirations with gurgling noises from her airway, but equal breath sounds. She is cold and diaphoretic, with a blood pressure of 87/40 mm Hg and heart rate of 140 beats/min. Her airway has been secured, and peripheral IV access (14 g and 16 g) has been obtained to begin crystalloid and blood product resuscitation. Chest and pelvic radiographs are normal. A bedside ultrasound reveals the image shown below. After initial fluid resuscitation, there is no change in vital signs.



Which of the following should be the next course of action?

A. Placement of a central line
B. Diagnostic peritoneal lavage

C. Placement of an intracranial pressure monitor
D. Abdominal and pelvic CTs
E. Immediate exploratory laparotomy

19. A 75-year-old man sustained a subdural hematoma, grade II splenic injury, and pelvic fracture in a motor vehicle collision. His Glasgow Coma Scale (GCS) score is 8, and he is intubated in the emergency department. His past medical history includes hypertension, diabetes, atrial fibrillation, and chronic renal insufficiency. Vital signs are: blood pressure 110/86 mm Hg, heart rate 105 beats/min. His wife says that he took apixaban four hours before the accident. His hemoglobin is 8.9 g/dL, and serum creatinine is 1.5 mg/dL. He is admitted to ICU for resuscitation. He will undergo emergency craniotomy after the coagulopathy is corrected.

    Which of the following is the best way to treat this patient's coagulopathy?

    A. Prothrombin complex concentrate
    B. Fresh frozen plasma
    C. Recombinant factor VIIa
    D. Tranexamic acid
    E. Emergency hemodialysis

20. A 75-year-old woman is evaluated in the emergency department after falling from a barstool while decorating her Christmas tree. Imaging reveals right rib fractures from 1 to 12, with a segment of flail chest, in addition to pulmonary contusion. She is admitted to the ICU for respiratory monitoring.

    Which of the following is the best option to improve this patient's pulmonary status?

    A. Epidural analgesia
    B. Morphine, as patient-controlled analgesia
    C. Surgical fixation of rib fractures
    D. Morphine, as needed, and IV acetaminophen
    E. Analgesia with intrapleural catheter

21. A 58-year-old man with hepatitis C and hepatocellular carcinoma undergoes an orthotopic liver transplantation. He receives 14 units of packed red blood cells, 10 units of fresh frozen plasma, and 2 units of platelets intraoperatively. On arrival in the ICU, he is intubated, sedated, and hypotensive, requiring vasopressor support.

    Which of the following signs is most associated with poor allograft function?

    A. Elevated transaminases
    B. Metabolic alkalosis
    C. Ongoing coagulopathy

D. Hypercalcemia
E. Hypoalbuminemia

Part 8 Answers:
Surgery, Trauma, and Transplantation

1. Rationale

Answer: B

The administration of antibiotics that provide coverage of aerobic and anaerobic bacteria results in the smallest number of postoperative infections. Prophylactic antibiotic administration has a potential therapeutic role. What must be determined is the time period during which contamination of the abdominal cavity becomes an established infection. At exploration, the intestinal wound is closed, eliminating further contamination and soiling of the peritoneal cavity. Additional antibiotic administration should not be necessary. A meta-analysis reviewed 17 studies assessing the effectiveness of single-agent versus combination therapy containing aminoglycosides for penetrating wounds. It was determined that single ß-lactam agents were as effective as combination therapy. Prophylactic antibiotics are required for only 24 hours in the presence of injury to any hollow viscus.

Delgado et al compared the duration of antibiotics after penetrating abdominal wounds associated with a bowel injury and rates of infections. Although retrospective, the authors concluded that there was no reduction in infection rates when antibiotics were administered for longer than 24 hours (18 of 76 vs. 3 of 21; $p = 0.278$).

Patients with risk factors for postoperative complications were defined as those who had two or more units of blood transfused, penetrating abdominal trauma score greater than or equal to 12, or operative time exceeding two hours. Furthermore, patients were stratified according to high and low risk for infection. In the 78 low-risk patients, there was no difference in infection rates when antimicrobials were stopped after 24 hours.

References:

1. Fabian TC, Croce MN, Payne LW, Minard G, Pritchard FE, Kudsk KA. Duration of antibiotic therapy for penetrating abdominal trauma: a prospective trial. *Surgery*. 1992 Oct;112(4):788-795.
2. Fabian TC, Hoefling SJ, Strom PR, Stone HH. Use of antibiotic prophylaxis in penetrating abdominal trauma. *Clin Ther*. 1982;5 Suppl A:38-47.
3. Delgado G Jr, Barletta JF, Kanji S, Tyburski JG, Wilson RF, Devlin JW. Characteristics of prophylactic antibiotic strategies after penetrating abdominal trauma at a level I urban trauma center: a comparison with the EAST guidelines. *J Trauma.* 2002 Oct;53(4):673-678.

4. Goldberg ST, Anand RJ, Como JJ, et al; Eastern Association for the Surgery of Trauma. Prophylactic antibiotic use in penetrating abdominal trauma: an Eastern Association for the Surgery of Trauma practice management guideline. *J Trauma Acute Care Surg.* 2012 Nov;73(5 Suppl 4):S321-S325.

2. Rationale

Answer: D

This patient is hypotensive and probably bleeding from an intra-abdominal source and/or an unstable pelvic fracture. He should have a pelvic binder placed to attempt to stabilize the pelvic fracture and tamponade any bleeding while being urgently transferred to the operating room, given a positive focused assessment with sonography in trauma (FAST) examination and hemodynamic instability. Current updates of the Advanced Trauma Life Support (ATLS) guidelines place a heavier emphasis on early blood product resuscitation (with less crystalloids) and the consideration of permissive hypotension in select patients. It must be suspected that this patient, who was intubated on the scene for a Glasgow Coma Scale (GCS) score of 3, has a traumatic brain injury until proven otherwise, and would not be a good candidate for permissive hypotension. Interventional radiology may be required at some point in his care, given the unstable pelvic fracture and suspected bleeding, but not before going to the operating room, given the positive FAST examination and hypotension.

Consideration of tranexamic acid is warranted, given the severity of the injury and the early arrival to the trauma center after the accident. This is based on the prospective CRASH-2 trial, which showed a reduction in all-cause mortality if tranexamic acid is given to patients in severe shock within three hours of injury. This is not part of the ATLS guidelines yet; further research to confirm tranexamic acid's utility is underway.

References:

1. American College of Surgeons. *Advanced Trauma Life Support.* 9th ed. American College of Surgeons; 2012.
2. Dutton RP, Mackenzie CF, Scalea TM. Hypotensive resuscitation during active hemorrhage: impact on in-hospital mortality. *J Trauma.* 2002 Jun;52(6):1141-1146.
3. CRASH-2 trial collaborators, Shakur H, Roberts I, et al. Effects on tranexamic acid on death, vascular occlusive vents, and blood transfusion in trauma patients with significant hemorrhage (CRASH-2): a randomised, placebo-controlled trial. *Lancet.* 2010 Jul 3;376(9734):23-32.

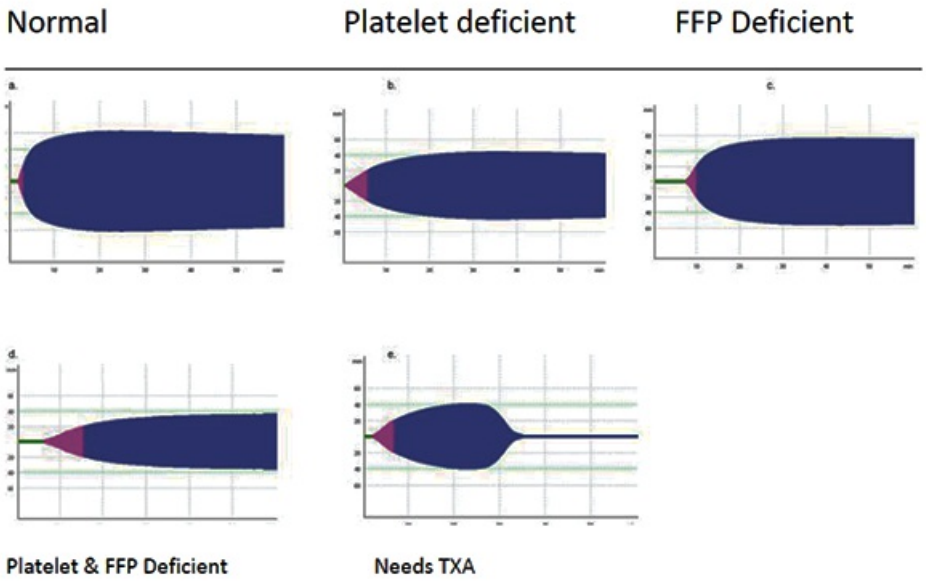
3. Rationale

Answer: C

Thromboelastography (TEG) has become increasingly common in the management of trauma patients. Compared to static laboratory measurements of clotting factors (prothrombin time, partial thromboplastin time, INR, platelet count), TEG provides a

more rapid and dynamic assessment of whole blood coagulation. This allows for a global assessment of hemostatic function and can facilitate timely intervention. Although no formal trials have demonstrated statistical benefits of TEG in trauma patients, many trauma centers have nonetheless adopted its use.

Many patients sustaining trauma take some type of blood-thinning medication for various reasons. This information is often not known to medical providers. In this patient, with a subdural hematoma and Glasgow Coma Scale score of 8, rapid reversal of the anticoagulant is necessary to achieve the best possible outcome. Compared to the reference, the R time is prolonged, meaning that he is deficient in clotting factors. Fresh frozen plasma or prothrombin complex concentrate may help to reverse this, keeping in mind that some novel anticoagulants may still not respond to these treatments. The alpha angle and maximum amplitude are within normal limits, so he should not need cryoprecipitate or platelets. Finally, there is no evidence of fibrinolysis requiring the use of tranexamic acid.



Reference:

1. Thakur M, Ahmed AB. A review of thromboelastography. *Int J Periop Ultrasound Appl Technol.* 2012;1(1):25-29.

4. Rationale

Answer: C

Normal lungs demonstrate a back-and-forth movement of the pleural line (movement of the visceral pleura along the parietal pleura) between the rib spaces. In a pneumothorax, air separates the visceral and parietal pleura. This prevents visualization of the parietal pleural because air has high acoustic impedance and, as a result, lung sliding is absent. Using M-mode sonography, the normal seashore appearance is lost and depicts a barcode appearance. See **Figure 1**, shown below. Panel A shows the granular seashore appearance of normal lung sliding. Panel B

shows the horizontal barcode appearance that occurs with loss of lung sliding.

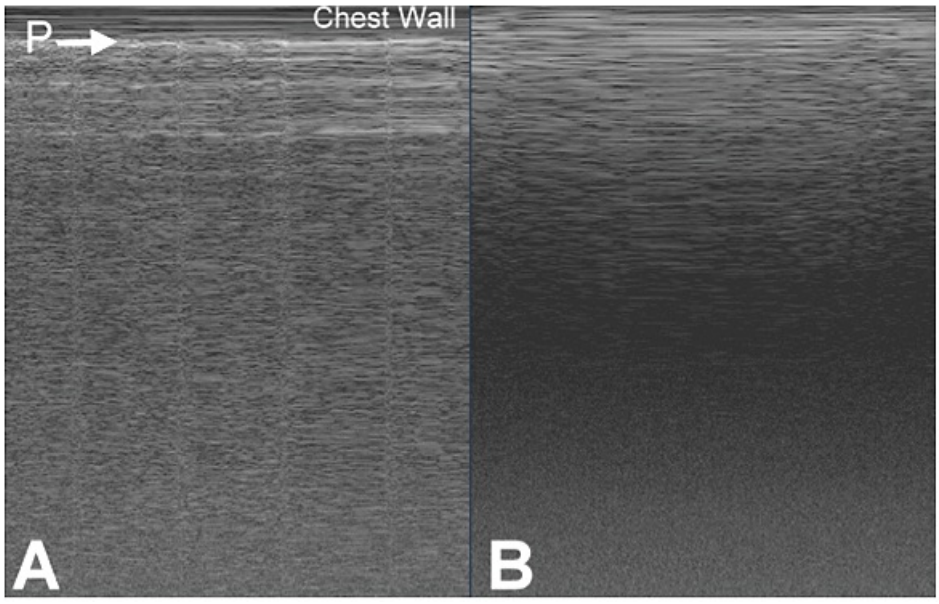
B lines, also called comet tail artifacts, are normal reverberation artifacts that appear as hyperechoic vertical lines extending from the pleura to the bottom of the display screen image. See **Figure 2**, shown below. These artifacts move with lung sliding and are expected in normal aerated lungs; their presence suggests that a pneumothorax is unlikely.

A lines are normal reverberation artifacts that occur from sound waves reflecting off the lung pleura. See **Figure 3**, shown below. They appear as equally spaced repetitive horizontal lines throughout the lung image. Normally, B lines extend from the pleural line and erase A lines, because they emanate out to the edge of the image. In a pneumothorax, air in the pleural space results in a high acoustic impedance, preventing the passage of ultrasound waves, although A lines continue to be present, but B lines are lost.

Lung point describes the location at which the interface between the lung visceral and parietal pleura is disrupted due to the presence of air. This is appreciated in a pneumothorax when moving the ultrasound probe in a medial-to-lateral direction, from the anterior to lateral chest wall, and observing lung sliding in one area and loss of lung sliding in another.

Free air is not a sign of pneumothorax because air is difficult to see in ultrasound and causes difficult ultrasonographic windows.

Figure 1. Lung sliding on M-mode sonography



P = pleura.

Figure 2. B lines

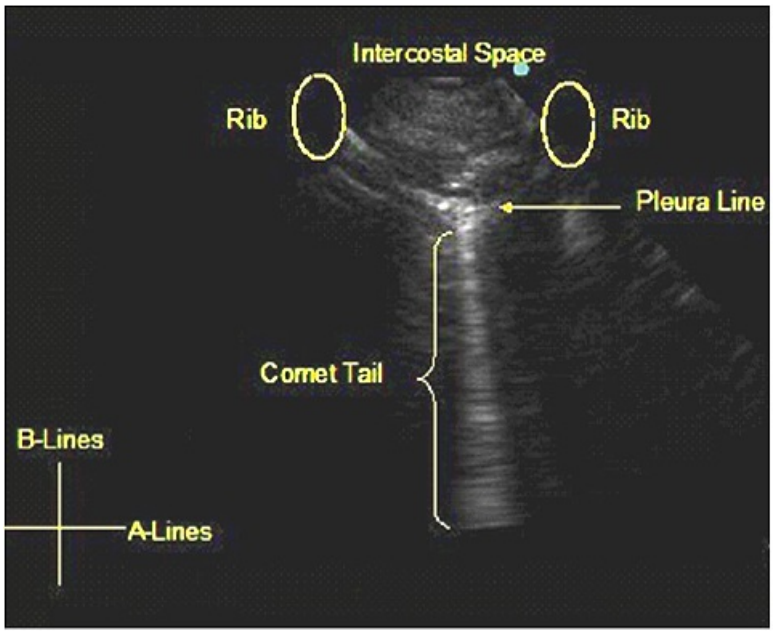
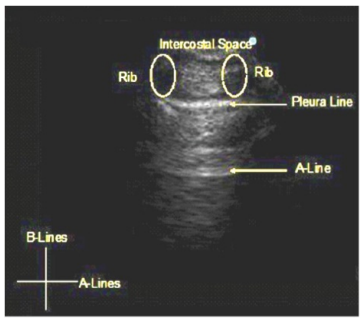


Figure 3. A lines



References:

1. Husain LF, Hagopian L, Wayman D, Baker WE, Carmody KA. Sonographic diagnosis of pneumothorax. *J Emerg Trauma Shock.* 2012 Jan;5(1):76-81.
2. Volpicelli G. Sonographic diagnosis of pneumothorax. *Intensive Care Med.* 2011 Feb;37(2):224-232.
3. Bouhemad B, Zhang M, Lu Q, Rouby JJ. Clinical review: bedside lung ultrasound in critical care practice. *Crit Care.* 2007;11(1):205.
4. Lichtenstein DA, Mezière G, Lascols N, et al. Ultrasound diagnosis of occult pneumothorax. *Crit Care Med.* 2005 Jun;33(6):1231-1238.
5. Kirkpatrick AW, Sirois M, Laupland KB, et al. Hand-held thoracic sonography for detecting post-traumatic pneumothoraces: the extended focused assessment with sonography for trauma (EFAST). *J Trauma.* 2004 Aug;57(2):288-295.

5. Rationale

Answer: C

The optimal end point for trauma resuscitation is not known. It is a good sign that urine output and vital signs are normalized, but what is known is that if resuscitation

stops there, a significant percentage of patients will be left under-resuscitated (cryptic shock) and at risk for multiorgan failure and death. The most prudent strategy is to combine the entire clinical picture with multiple markers of hypoperfusion, to include vital signs, physical examination, urine output, lactate, base deficit, mixed venous oxygen saturation, etc., while weighing the risk-to-benefit analysis of ongoing fluid and product administration (eg, potential for worsening oxygenation or abdominal compartment syndrome). Base deficit has been studied in the trauma population, with a correlation to outcome. However, this data is not robust, and no specific threshold level or correction time frame can be reported with any confidence. Furthermore, base deficit is a crude marker of hypoperfusion that can be highly influenced by treatment, such as chloride administration. There is no clear role for a pulmonary artery catheter in this patient.

References:

1. Hoste EA, Maitland K, Brudney CS, et al; ADQI XII Investigators Group. Four phases of intravenous fluid therapy: a conceptual model. *Br J Anaesth.* 2014 Nov;113(5):740-747.
2. Régnier MA, Raux M, Le Manach Y, et al. Prognostic significance of blood lactate and lactate clearance in trauma patients. *Anesthesiology.* 2012 Dec;117(6):1276-1288.

6. Rationale

Answer: D

The concept of permissive hypotension and delayed resuscitation for penetrating trauma has gained increased traction since a landmark study published in the 1990s showed that this strategy reduced mortality. By increasing blood pressure with initial resuscitative efforts, there is a concern that the initial friable clot will dislodge, and lead to increased re-bleeding. Therefore, unless this patient's blood pressure falls further, or his mental status is lost, he should be transferred immediately to the operating room, and resuscitation should commence. There is no role for CT or local wound exploration in this patient, because it is obvious that his injury violates the peritoneum.

Reference:

1. Bickell WH, Wall MJ Jr, Pepe PE, et al. Immediate versus delayed fluid resuscitation for hypotensive patients with penetrating torso injuries. *N Engl J Med.* 1994 Oct 27;331(17):1105-1109.

7. Rationale

Answer: A

This patient's presentation is classic for abdominal compartment syndrome: blunt trauma to the abdomen requiring massive resuscitation. Normal intra-abdominal pressure is 5 to 7 mm Hg and should be measured at end-expiration, in the supine

position, absent of abdominal muscle contraction, with a zeroed transducer at the level of the mid-axillary line. Intra-abdominal hypertension can exist without abdominal compartment syndrome, in such conditions as morbid obesity and ascites. Abdominal compartment syndrome is the presence of intra-abdominal hypertension (>20 mm Hg) associated with new or worsening organ dysfunction. Abdominal compartment syndrome can affect most all organ systems. This patient has some of the classic findings. Central venous pressure will be elevated. Due to a reduction in compliance, both peak and plateau airway pressures will increase, and ventilation will become increasingly difficult. Of note, an elevated peak airway pressure and normal plateau pressure would indicate a resistance problem, such as endotracheal tube occlusion or bronchoconstriction. Due to a reduction in perfusion pressure to the kidney, oliguria will occur. When bladder pressure is normal, other causes for deterioration should be sought, such as acute respiratory distress syndrome with concomitant acute cor pulmonale.

References:

1. Kirkpatrick AW, Roberts DJ, De Waele J, et al; Pediatric Guidelines Sub-Committee for the World Society of the Abdominal Compartment Syndrome. Intra-abdominal hypertension and the abdominal compartment syndrome: updated consensus definitions and clinical practice guidelines from the World Society of the Abdominal Compartment Syndrome. *Intensive Care Med.* 2013 Jul;39(7):1190-1206.
2. Hunt L, Frost SA, Hillman K, Newton PJ, Davidson PM. Management of intra-abdominal hypertension and abdominal compartment syndrome: a review. *J Trauma Manag Outcomes.* 2014 Feb 5;8(1):2.

8. Rationale

Answer: B

The management of intra-abdominal hypertension should progress from least invasive to most invasive. Also, maneuvers should be performed to prevent an invasive maneuver. For this patient, the most appropriate next step is to chemically paralyze him. With the head of bed at 30 degrees, he still has intra-abdominal hypertension, so a reverse Trendelenburg position would not be helpful. Since the venous return is compromised, the furosemide infusion would not be helpful even with albumin or mannitol, and may worsen renal function.

Reference:

1. Kirkpatrick AW, Roberts DJ, De Waele J, et al; Pediatric Guidelines Sub-Committee for the World Society of the Abdominal Compartment Syndrome. Intra-abdominal hypertension and the abdominal compartment syndrome: updated consensus definitions and clinical practice guidelines from the World Society of the Abdominal Compartment Syndrome. *Intensive Care Med.* 2013 Jul;39(7):1190-1206.

9. Rationale

Answer: D

This central line was inserted into an artery. Although advances in ultrasound guidance have reduced the risk of inadvertent arterial cannulation, complications such as arterial cannulation and pneumothoraces still occur. Therefore, close evaluation of the post-procedure chest radiograph is imperative. A case series demonstrated that simply pulling inadvertently placed arterial lines and applying pressure, without surgical evaluation, can lead to increased complications. Therefore, prompt surgical consultation for consideration of surgical exploration or endovascular repairs is appropriate. This chest radiograph does not show any pathology requiring chest tube placement.

References:

1. Guilbert MC, Elkouri S, Bracco D, et al. Arterial trauma during central venous catheter insertion: case series, review and proposed algorithm. *J Vasc Surg.* 2008 Oct;48(4):918-925.
2. Idialisoa R, Jouffroy R, Saint Martin LC, et al. Transient neurological deficit due to a misplacement of central venous catheter despite ultrasound guidance and ultrasound assistance. *Anaesth Crit Care Pain Med.* 2015 Oct;34(5):301-302.

10. Rationale

Answer: B

The primary cause of heparin-induced thrombocytopenia (HIT) type II is the development of antibodies to heparin-platelet factor 4. Patients undergoing cardiopulmonary bypass (CPB) are exposed to a large heparin bolus during surgery, but less than 3% of patients undergoing CPB develop HIT. Thrombocytopenia after cardiac surgery is primarily due to mechanical destruction of platelets on the bypass circuit, as well as the hemodilution that occurs while on bypass. The platelet nadir after CPB is two to three days postoperatively, which is where this patient is. The platelet count typically drops by 30% in patients who underwent CPB. The most likely cause of his platelet count drop is CPB, based on the timing and degree of decrease. HIT must be considered, but it is unlikely because his platelet count drop is not 50% or greater. In HIT patients, the decrease in platelet count typically begins five to 14 days after starting heparin. Furthermore, there is no sign of thrombosis. Discontinuing aspirin is not necessary because there are no clinical signs of bleeding. There is no indication for transfusing platelets in this patient.

The diagnosis of HIT is difficult in patients who undergo CPB; efforts have been made to identify simple criteria for HIT diagnosis. A score was developed to aid in diagnosis, which was derived from a retrospective review of 84 patients undergoing CPB. The elements of the score were the pattern of thrombocytopenia (biphasic versus linear drop in platelet count), the length of time of CPB greater than or equal to 118 min, and an interval of greater than or equal to five days. The score had a 97% negative predictive value for excluding an HIT diagnosis. HIT is important to diagnose in cardiac surgery patients because it has been associated with a 50% increase in

mortality and a significant increase in morbidity.

References:

1. Seigerman M, Cavallaro P, Itagaki S, Chung I, Chikwe J. Incidence and outcomes of heparin-induced thrombocytopenia in patients undergoing cardiac surgery in North America: an analysis of the nationwide inpatient sample. *J Cardiothorac Vasc Anesth.* 2014 Feb;28(1):98-102.
2. Matthai WH Jr. Thrombocytopenia in cardiovascular patients: diagnosis and management. *Chest.* 2005 Feb;127(2 Suppl):46S-52S.
3. Selleng K, Warkentin ET, Greinacher A. Heparin-induced thrombocytopenia intensive care patients. *Crit Care Med.* 2007 Apr;35(4):1165-1176.
4. Louet-Le Louët A, Boutouyrie P, Alhenc-Gelas M, et al. Diagnostic score for heparin-induced thrombocytopenia after cardiopulmonary bypass. *J Thromb Haemost.* 2004 Nov;2(11):1882-1888.
5. Warkentin TE, Greinacher A. Heparin-induced thrombocytopenia and cardiac surgery. *Ann Thorac Surg*. 2003 Aug;76(2):638-648.

11. Rationale

Answer: B

The American Heart Association/American College of Cardiology guidelines recommend starting aspirin within six hours after surgery. Clopidogrel may be used alone in patients who are allergic to aspirin. Dual-antiplatelet therapy with aspirin and clopidogrel has not shown to have a greater benefit than aspirin alone. Antiplatelet therapy is needed to prevent graft occlusion.

References:

1. Mangano DT; Multicenter Study of Perioperative Ischemia Research Group. Aspirin and mortality from coronary bypass surgery. *N Engl J Med.* 2002 Oct 24;347(17):1309-1317.
2. Berger JS, Frye CB, Harshaw Q, Edwards FH, Steinhubl SR, Becker RC. Impact of clopidogrel in patients with acute coronary syndromes requiring coronary artery bypass surgery: a multicenter analysis. *J Am Coll Cardiol.* 2008 Nov 18;52(21):1693-1701.

12. Rationale

Answer: B

This parturient had a witnessed ventricular fibrillation (VF) arrest. Similar to any cardiac arrest, it is important to consider the etiology. Possible etiologies of VF arrest include coronary artery disease, ischemic and non-ischemic cardiomyopathies, valvular lesions, pulmonary embolus, aortic dissection, and electrophysiologic abnormalities. Additional etiologies relevant to pregnancy should also be considered.

Normal physiologic changes of pregnancy must be considered when resuscitating a

pregnant patient. These include possible difficult airway due to pharyngeal edema and enlarged breast tissue; increased risk of aspiration due to relaxation of the lower esophageal sphincter; decreased chest wall compliance due to enlarged breasts; decreased functional residual capacity due to upward displacement of the diaphragm by the gravid uterus; increased oxygen consumption due to the developing fetus; upward displacement of the heart due to the gravid uterus; sequestration of up to 30% of circulating blood volume in the second half of pregnancy due to compression of the inferior vena cava, iliac vessels, and abdominal aorta by the gravid uterus; decreased effect of chest compressions due to decreased venous return leading to supine hypotension; and obstruction of forward blood flow by the gravid uterus.

In general, resuscitative algorithms are the same for pregnant as for non-pregnant patients, with one exception: rather than placing the patient in the left lateral position (at least 15° tilt), manually displacing the uterus to the left of the abdomen to relieve aortocaval compression is better for venous return to the heart. If she has been receiving a magnesium infusion, it should be stopped, and calcium administered. Additionally, a maternal cardiopulmonary arrest team should be in place, consisting of the usual adult resuscitation team, an obstetrician, obstetric anesthesiologist, obstetric nurse, and the neonatology team.

If there is no return of spontaneous circulation after four minutes of resuscitative efforts in a patient with an obviously gravid uterus, emergency cesarean section should be considered, with the aim of delivering the fetus within five minutes of cardiac arrest onset. An obviously gravid uterus is one that is deemed to be sufficiently large to cause aortocaval compression. Delivery of the fetus and placenta improves venous return and cardiac output, facilitating closed chest compressions, reducing oxygen consumption, and making ventilation easier; it can also allow internal cardiac massage by heart compression (with the diaphragm still intact) against the anterior chest wall.

After 15 minutes of unsuccessful closed chest cardiopulmonary resuscitation (CPR), direct cardiac massage via thoracotomy or through the diaphragm (if the abdomen is open) can be implemented. This would not be done before an emergency cesarean section in this case. Direct cardiac massage results in near-normal systemic perfusion throughout the compression cycle and with higher cranial and myocardial flow than that achieved with external chest compressions of conventional CPR.

Successful use of cardiopulmonary bypass in maternal resuscitation has been described in case reports of women with circulatory collapse due to amniotic fluid embolism and pulmonary embolism. However, use of this technology requires a specialized team and preparation time; cesarean delivery should not be delayed in this case.

Overdrive pacing is not indicated for VF, even when the rhythm has deteriorated to asystole, because the hypoxic human heart will not respond to pacing with mechanical contractions. Although the use of pacing for patients with asystole lacks evidence, it may be useful when the asystole is caused by a primary conduction system problem and ventricular standstill is noted quickly on the monitor, when standstill is drug induced, in cases of reflex vagal standstill, and when asystole follows defibrillation.

References:

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3. Stanten RD, Iverson LI, Daugharty TM, Lovett SM, Terry C, Blumenstock E. Amniotic fluid embolism causing catastrophic pulmonary vasoconstriction: diagnosis by transesophageal echocardiogram and treatment by cardiopulmonary bypass. *Obstet Gynecol*. 2003 Sep;102(3):496-498.
4. Jeejeebhoy FM, Zekio CM, Lipman S, et al. Cardiac arrest in pregnancy. A scientific statement from the American Heart Association. *Circulation.* 2015;132:1747-1773

13. Rationale

Answer: B

This patient most likely has had an amniotic fluid embolus (AFE). AFE typically occurs during labor and delivery or in the immediate postpartum period, although it can occur as late as 48 hours postpartum. About 70% of cases occur before delivery. AFE has also been reported following induced abortion, feticide, intrapartum amnioinfusion, transabdominal amniocentesis, blunt abdominal trauma, surgical trauma, cerclage removal, and manual removal of placenta. Exposure of the maternal circulation to amniotic fluid or fetal antigens is a prerequisite for AFE. It can occur via one of three routes: uterine trauma sites, endocervical veins, or placental attachment site. Risk factors include maternal age 35 years or older, cesarean delivery, forceps-assisted and vacuum-assisted vaginal deliveries, placenta previa, abruption placenta, eclampsia, and fetal distress.

The classic presentation of AFE is characterized by sudden cardiovascular collapse, with profound systemic hypotension, cardiac dysrhythmia, cyanosis, dyspnea or respiratory arrest, pulmonary edema or adult respiratory distress syndrome, altered mental status, and hemorrhage from disseminated intravascular coagulation (DIC). Seizures are also possible. Many patients progress to multiorgan failure. The hemodynamic response to AFE seems to be biphasic, based on transesophageal echocardiography studies, with initial pulmonary hypertension and right ventricular failure, followed later by left ventricular failure, most likely caused by the dilated right ventricle (RV) interfering with left-sided filling, but also possibly caused by direct myocardial depression by amniotic fluid or other immune modulators, or by ischemic injury to myocardium. Hypoxemia results from ventilation/perfusion mismatching caused by severe pulmonary vasoconstriction.

There is no consensus as to the exact pathophysiology of the syndrome, nor are there strict diagnostic criteria. AFE is thought to result from an immune-mediated mechanism, given its similarity to septic shock or anaphylactic shock. It may result from an abnormal immunologic response of the mother following exposure to fetal antigens, leading to the release of various proinflammatory mediators.

AFE remains a diagnosis of exclusion. Management is largely supportive. The presentation of AFE may mimic pulmonary embolus, sepsis, hemorrhage and DIC from other causes, or anaphylaxis. Cornerstones of management include securing the airway and providing mechanical ventilation, as well as supporting circulation with pressors and inotropes. Full laboratory evaluation should be undertaken, including arterial blood gases, chemistry, complete blood count, and coagulation studies. Transesophageal echocardiography, arterial blood pressure monitoring, and pulmonary artery catheters may be useful. Blood product administration is usually necessary. Specific therapies targeted at pulmonary hypertension and RV failure have proved helpful; these include inodilators such as milrinone and dobutamine, as well as selective pulmonary vasodilators such as nitric oxide. Intra-aortic balloon pump and extracorporeal membrane oxygenation have also been used. Emergent cesarean section should also be considered to improve resuscitative efforts in the mother.

Uterine rupture usually presents with decline in fetal heart rate, abdominal pain and vaginal bleeding, loss of fetal station on vaginal examination and, later, hypovolemic shock. A patient with intravascular injection of local anesthetic would have signs of central nervous system toxicity (lightheadedness, visual or auditory disturbances, muscle twitching, seizure, and coma) and, at very high concentrations, cardiovascular collapse. If she had progressed to eclampsia, she would have presented with seizure.

References:

1. Conde-Agudelo A, Romero R. Amniotic fluid embolism: an evidence-based review. *Am J Obstet Gynecol.* 2009 Nov;201(5):445.e1-445.e13.
2. McDonnell NJ, Chan BO, Frengley RW. Rapid reversal of critical haemodynamic compromise with nitric oxide in a parturient with amniotic fluid embolism. *Int J Obstet Anesth*. 2007 Jul;16(3):269-273.
3. Sadera G, Vasudevan B. Amniotic fluid embolism. *J Obstet Anaesth Crit Care.* 2015;5(1):3-8.

14. Rationale

Answer: C

This patient has heat stroke. Heat stroke is divided into two categories: exertional, occurring most often in young people or athletes, and non-exertional, more common in older patients with comorbidities. The diagnosis requires an elevated core body temperature greater than or equal to 40°C (104°F), altered mental status, and central nervous system dysfunction, including coma and seizures. Patients also develop systemic inflammatory response syndrome, often leading to widespread organ dysfunction or failure. A cooling mist is the preferred treatment for exertional heat stroke. If not available, the patient should be diffusely covered with ice packs. He may require intubation, but bringing down his temperature is the lifesaving maneuver at this time. Dantrolene would be an appropriate intervention if there were a history concerning for malignant hyperthermia. Although IV acetaminophen may be used, water vapor cooling is the mainstay of therapy.

References:

1. Gaudio FG, Grissom CK. Cooling methods in heat stroke. *J Emerg Med.* 2016 Apr;50(4):607-616.
2. Newport M, Grayson A. Towards evidence-based emergency medicine: best BETs from the Manchester Royal Infirmary. BET 3: In patients with heatstroke is whole-body ice-water immersion the best cooling method? *Emerg Med J.* 2012 Oct;29(10):855-856.
3. Bouchama A, Knochel JP. Heat stroke. *N Engl J Med.* 2002 Jun 20;346(25):1978-1988.

15. Rationale

Answer: D

Sepsis is the most common cause of acute respiratory distress syndrome (ARDS). It should be the first etiology considered whenever ARDS develops in a patient who is predisposed to serious infection or in association with a new fever or hypotension. This patient could have had a preexisting community-acquired pneumonia, or an early ventilator-associated pneumonia. However, severe ARDS (partial arterial oxygen pressure/fraction of inspired oxygen ratio of 62/0.8 = 78) with gastrointestinal manifestation raises a severe concern of missed intra-abdominal catastrophe, which could be the cause of the patient's fall. Ventilation management is important, but is not the priority. Pulmonary embolism could be included in the differential diagnosis, but would not explain the feeding intolerance and leukocytosis.

References:

1. Pepe PE, Potkin RT, Reus DH, Hudson LD, Carrico CJ. Clinical predictors of the adult respiratory distress syndrome. *Am J Surg*. 1982 Jul;144(1):124-130.
2. Hudson LD, Milberg JA, Anardi D, Maunder RJ. Clinical risks for development of the acute respiratory distress syndrome. *Am J Respir Crit Care Med*. 1995 Feb;151(2 Pt 1):293-301.

16. Rationale

Answer: A

In patients with suspected retained hemothorax, a CT is needed if there is persistent radiographic abnormalities. The preferred method of evacuation of retained hemothorax is video-assisted thoracosopic surgery (VATS) over a second chest tube. VATS should be performed as early as possible with the first five days after the thoracic trauma.

References:

1. DuBose J, Inaba K, Demetriades D, et al; AAST Retained Hemothorax Study Group. Management of post-traumatic retained hemothorax: a prospective, observational, multicenter AAST study. *J Trauma Acute Care Surg.* 2012 Jan;72(1):11-22.

2. Mowery NT, Gunter OL, Collier BR, et al. Practice management guidelines for management of hemothorax and occult pneumothorax. *J Trauma.* 2011 Feb;70(2):510-518.

17. Rationale

Answer: E

The diagnosis is based on the increase in intra-abdominal pressure contributing to acute renal failure. The increase in intra-abdominal pressures by bladder manometry by more than 20 mm Hg suggests abdominal compartment syndrome. If removal of ascitic fluid does not resolve acute kidney injury, emergent surgical decompression may be warranted. Abdominal CT would delay management and the use of IV contrast would not be recommended in the setting of kidney injury. Low urine sodium does not suggest a post-obstructive process. Although low urine sodium suggests prerenal etiology, there is no evidence that this is secondary to volume depletion. Therefore, there is no indication for volume resuscitation.

References:

1. Doty JM, Saggi BH, Blocher CR, et al. Effects of increased renal parenchymal pressure on renal function. *J Trauma.* 2000 May;48(5):874-877.
2. Doty JM, Saggi BH, Sugerman HJ, et al. Effect of increased renal venous pressure on renal function. *J Trauma.* 1999 Dec;47(6):1000-1003.

18. Rationale

Answer: E

This multisystem trauma patient is in acute circulatory shock. Trauma patients should receive an organized and rapid team-based resuscitation that follows Advanced Trauma Life Support (ATLS) or Anesthesia Trauma and Critical Care (ATACC) guidelines. Both of these focus on rapid assessment and immediate stabilization of airway, breathing, and circulation. The patient has been successfully intubated, and resuscitation with crystalloids and, ideally, blood products has begun. Clinical assessment, radiography, and ultrasound can be used to rapidly diagnosis the cause of acute circulatory shock. Hypovolemic shock from acute blood loss is the most common cause, but obstructive (tension pneumothorax, cardiac tamponade), cardiogenic (blunt cardiac injury), and distributive shock (neurogenic) can also occur.

An extended focused assessment with sonography in trauma (eFAST) examination can help the clinician rapidly diagnosis tension pneumothorax, pericardial tamponade, and intraperitoneal free fluid, which probably means intra-abdominal bleeding in this clinical situation. The patient is hypotensive after initial resuscitation. She has a positive FAST examination and is hypotensive; therefore, she needs to undergo an exploratory laparotomy.

Standard triple-lumen catheters are useful for administering multiple different medications at once as well as vasopressors. Their length and relatively narrow internal diameter do not facilitate rapid flow.

A diagnostic peritoneal lavage is unnecessary in the setting of a positive FAST examination in this hemodynamically unstable blunt trauma patient. A major concern is delayed treatment of other life-threatening injuries. Although the diagnostic utility of CT is important, it should not delay definitive treatment. Delaying control of life-threatening bleeding can prove fatal. Management of neurotrauma focuses on preserving cerebral perfusion pressure, which equals mean arterial pressure minus intracranial pressure. Hemorrhage and hypotension should be managed before diagnosis of potential intracranial injuries. Empiric placement of an intracranial monitor is controversial at best in an under-resuscitated patient. Either way it should not delay laparotomy.

References:

1. Emergency Medicine Updates. Flow rates of various vascular catheters. November 25, 2009. http://emupdates.com/2009/11/25/flow-rates-of-various-vascular-catheters/. Accessed June 13, 2016.

19. Rationale

Answer: A

Current recommendations for the management of direct factor Xa inhibitors are to use activated charcoal within four hours of ingestion and four-factor prothrombin complex concentrate (PCC) or activated PCC (FEIBA).

Emergency Management of the Coagulopathic Patient

Scenario	Agent	Dose	Level of Evidence[a]
Warfarin	Fresh frozen plasma or PCC (3- or 4-factor) and Vitamin K	10-15 mL/kg 15-30 U/kg 10 mg IV	II II II
Direct thrombin inhibitor	<u>Dabigatran</u> Activated charcoal within 2 hrs of ingestion, and idarucizumab and consider hemodialysis or idarucizumab redosing for refractory bleeding after initial administration <u>Other DTIs</u> Activated PCC (FEIBA) or 4-factor PCC	50 g 5 g IV (in two 2.5 g/50 mL vials) 50 units/kg IV 50 units/kg IV	I II
Direct factor Xa inhibitors	Activated charcoal (50 g) within 2 hrs of	50 g	III

(apixaban, edoxaban, rivaroxaban)	ingestion and activated PCC (FEIBA) or 4-factor PCC	 50 units/kg IV 50 units/kg IV	

Abbreviations: DTI, direct thrombin inhibitor; PCC, prothrombin complex concentrae.
[a]Class I = based on one or more high-quality randomized controlled trials. Class II = based on two or more high-quality prospective or retrospective cohort studies. Class III = based on case reports and series or expert opinion.

References:

1. Frontera JA, Lewin JJ III, Rabinstein AA, et al. Guideline for reversal of antithrombotics in intracranial hemorrhage: a statement for healthcare professionals from the Neurocritical Care Society and Society of Critical Care Medicine. *Neurocritical Care.* 2016 Feb;24(1):6-46.
2. Moorman ML, Nash JE, Stabi KL. Emergency surgery and trauma in patients treated with the new oral anticoagulants: dabigatran, rivaroxaban, and apixaban. *J Trauma Acute Care Surg.* 2014 Sep;77(3):486-494.
3. Faraoni D, Levy JH, Albaladejo P, Samama CM; Groupe d'intérêt en Hémostase Péeiopératoire. Updates in the perioperative and emergency management of non-vitamin K antagonist oral anticoagulants. *Crit Care.* 2015 Apr 29;19:203.

20. Rationale

Answer: A

The management of pulmonary contusion from rib fractures is primarily concerned with treatment of the pulmonary contusion. The principle factor is pain control, optimally achieved by epidural analgesia, intercostal nerve blocks, or paravertebral block. Chest physiotherapy is also essential. Surgical fixation has been increasingly popular in recent years for patients with thoracic injury and flail chest, and has shown benefits of improved mechanics, rapid liberation from mechanical ventilation, and rapid return to work. However, these are all small, single-limb observational studies. This modality may be considered in cases of severe flail chest failing to wean from the ventilator. The patient subgroup that would benefit from early prophylactic fracture fixation has not been identified.

References:

1. Simon B, Ebert J, Bokhari F, et al; Eastern Association for the Surgery of Trauma. Management of pulmonary contusion and flail chest: an Eastern Association for the Surgery of Trauma practice management guideline. *J Trauma Acute Care Surg.* 2012 Nov;73(5 Suppl 4):S351-S361.
2. Parry NG, Moffat B, Vogt K. Blunt thoracic trauma: recent advances and outstanding questions. *Curr Opin Crit Care.* 2015 Dec;21(6):544-548.

21. Rationale

Answer: C

After orthotopic liver transplant, there are encouraging indicators of satisfactory allograft function, including good mental status, hemodynamic stability, good urine output, bile production (seen intraoperatively), correction of coagulopathy, improvement in electrolytes, and improvement of metabolic acidosis as the new liver is able to clear lactate and metabolize citrate. Signs that the new liver may not be functioning well include persistent metabolic acidosis, ongoing coagulopathy, hemodynamic instability, hypocalcemia due to citrate toxicity (especially in the setting of massive transfusion of blood products), hypoglycemia, hyperkalemia, increasing encephalopathy, and poor renal function, although none of these signs are specific. Transaminases obtained immediately after surgery will be increased, and often peak within 24 hours of transplant, then should begin to decrease if the new liver is functioning.

Reference:

1. Razonable RR, Findlay JY, O'Riordan A, et al. Critical care issues in patients after liver transplantation. *Liver Transpl.* 2011 May;17(5):511-527.

Part 9:

Pharmacology and Toxicology

Part 9:
Pharmacology and Toxicology

Instructions: For each question, select the most correct answer.

1. A 63-year-old man with type 1 diabetes mellitus, renal insufficiency, and a seizure disorder is admitted to the ICU after an exploratory laparotomy for a lacerated

liver and perforated colon caused by trauma. He is empirically treated with imipenem/cilastatin. On postoperative day two, he has septic physiology with sequelae of acute respiratory distress syndrome and renal failure, requiring continuous renal replacement therapy (CRRT). A cisatracurium infusion is started to facilitate ventilation. Sedation and analgesia are provided with propofol and hydromorphone infusions.

Which of the following is the most accurate assessment of the patient's medication regimen?

A. The metabolites of cisatracurium will accumulate in renal failure and lower the seizure threshold.
B. Hydromorphone is needed because propofol has no analgesic properties.
C. Imipenem/cilastatin will be cleared with CRRT and does not require dose adjustment.
D. The metabolites of hydromorphone will accumulate in renal failure and increase sedation.

2. A 65-year-old man presents to the emergency department with pleuritic chest pain and a productive cough. He has a medical history of hypertension, diabetes, end-stage renal disease, for which he undergoes hemodialysis. He was recently discharged after being hospitalized for pneumonia. Laboratory data includes: white blood cell count 15,000/mm^3 with 91% polymorphonuclear leukocytes, hemoglobin 10.4 g/dL, blood urea nitrogen 55 g/L, creatinine 6.9 mg/dL. Chest radiograph shows right upper and middle lobe infiltrates and mild pulmonary edema. Vancomycin, cefepime and azithromycin are started empirically for pneumonia, and he is admitted to the ICU for observation. Gram stain of sputum shows abundant gram-negative rods that are subsequently reported to be *Pseudomonas aeruginosa* sensitive to cefepime. On ICU day four, he is lethargic and confused. Myoclonic jerks are noted in the extremities and occasionally the trunk. He is treated with lorazepam for suspected alcohol withdrawal. During the next 12 hours, his level of consciousness continues to deteriorate, and he is responsive only to painful stimulation. Neurologic examination at this time does not reveal neck rigidity or any focal neurologic deficit. Temperature, vital signs, and the rest of the physical examination are normal. Brain CT and spinal fluid analysis are unrevealing. Glucose and ammonia are within normal range. Serum electrolytes and renal function show no difference from previous profile. Liver and thyroid function tests are within normal limits. An EEG shows generalized background slowing and multiphasic sharp waves.

Which of the following is the most appropriate next step in treatment?

A. Restart vancomycin.
B. Switch cefepime to meropenem.
C. Discontinue cefepime.
D. Discontinue azithromycin and start levofloxacin.

3. A 27-year-old woman with a history of depression and chronic pain is found unresponsive after an apparent suicide attempt. Multiple empty pill bottles, including fluoxetine, amitriptyline, and oxycodone, are found at her bedside. She is intubated in the field and brought to the emergency department, where a critical care consultation is performed. Urine drug screen is positive for opiates and tetrahydrocannabinol. A noncontrast head CT is unremarkable. Vital signs are: heart rate 120 beats/min, blood pressure 90/50 mm Hg, respiration rate 24 breaths/min, temperature 37.2°C (98.9°F), and oxygen saturation 100% on fraction of inspired oxygen of 1.0. ECG reveals the following intervals: PR 140 msec, corrected QT 500 msec, and QRS 180 msec.

   Which of the following interventions is most indicated for this patient?

   A. Naloxone
   B. Flumazenil
   C. Sodium bicarbonate
   D. Cyproheptadine
   E. Supportive therapy

4. Which of the following glycopeptide antibiotics affects the accurate measurement of anticoagulation effects?
   A. Dalbavancin
   B. Vancomycin
   C. Oritavancin
   D. Teicoplanin

5. A 54-year-old man presents with septic shock due to left lower extremity cellulitis with methicillin- resistant *Staphylococcus aureus* bacteremia. He develops respiratory failure that requires intubation, and is placed on mechanical ventilation. The ICU team starts a fentanyl infusion at 250 µg/hour and a lorazepam infusion at 10 mg/hour for analgosedation. Four days later, he develops metabolic acidosis, new-onset renal failure, and an osmolar gap.

   Which of the following substances is the most likely explanation for the new metabolic derangements?

   A. Ethylene glycol
   B. Isopropyl alcohol
   C. Cyanide
   D. Methanol
   E. Propylene glycol

6. A 19-year-old woman is brought to the emergency department (ED) by her friends for altered mental status while at a party. At one point during the evening, her friends noticed that she was not responding. When she did not wake up a

few hours later, they brought her to the ED. They report that she was fine before they left for the party, and she had not been ill. They admit that there was alcohol at the party, but become evasive when asked about illicit substances. On examination, she is well-developed and well-nourished. She is not in respiratory distress and is unarousable to stimuli. On sternal rub, she groans but does not wake up. Heart rate is 94 beats/min, respiratory rate 18 breaths/min, blood pressure 142/70 mm Hg, and temperature 38.1°C (100.6°F). Pupils are dilated and reactive. Oral membranes are dry. Jaw is clenched. Neck is supple. Cardiac, pulmonary and abdominal examinations are unrevealing. No peripheral edema is present. She has normal reflexes. Her skin is warm and dry; no needle marks are noted. During the examination, she has a tonic-clonic seizure that responds to IV lorazepam. Laboratory blood results are: sodium 110 mEq/L, potassium 3.0 mEq, BUN 11 mg/dL, creatinine 0.5 mg/dL, lactate 1.1 mg/dL. Hepatic panel is within normal limits. White blood cell count 59 $10^3/mm^3$, normal differential, hemoglobin 14.2 g/dL, platelet count 223 $10^3/mm^3$, INR 1.0. Chest radiograph is unrevealing. ECG shows normal sinus rhythm with a rate of 94 beats/min and no ST-T wave abnormalities. Urine toxicology screen is negative for benzodiazepines, opiates, cocaine metabolites, and cannabinoids. Blood toxicology shows alcohol level of 22 mg/dL (mildly increased), and negative for salicylates and acetaminophen. Head CT shows no acute infarct, bleeding, or mass.

Which of the following is the most likely cause of her altered mental status?

A. 3,4-methylenedioxymethamphetamine (MDMA)
B. Heroin overdose
C. Alcohol poisoning
D. Acute bacterial meningitis

7. A 38-year-old man sustains a cerebral hemorrhage in a motor vehicle accident. He requires emergent intubation with subsequent mechanical ventilation. Medications required during ventilator support include propofol for sedation control, fentanyl for pain control, and rocuronium for neuromuscular blockade. For elevated intracranial pressure, IV hypertonic saline and mannitol infusion are initiated by the critical care team. To maintain cerebral perfusion pressure, norepinephrine is given. On ICU day four, he develops acute kidney injury, along with severe metabolic acidosis, hemodynamic instability, elevated troponin, and ST depressions in the anterolateral leads. Urinalysis reveals the presence of blood with no red blood cells. Creatinine phosphokinase is 45,489 U/L.

   Which of the following medications is most likely attributed to the acute kidney injury?

   A. Propofol
   B. Rocuronium
   C. Norepinephrine
   D. Fentanyl
   E. Midazolam

8. A 40-year-old woman with obesity is admitted to an outpatient surgery center for a hysterectomy secondary to painful intrauterine fibroids. Medical history is significant for diabetes mellitus complicated by intermittent nausea and gastroparesis, for which she takes metoclopramide (last dose two days ago); depression, for which she takes amitriptyline; and a recent upper respiratory tract infection, for which she has been taking scheduled over-the-counter cough medicine for the past week including the morning of surgery. She also reports an allergic-type reaction to penicillin as a child, with hives and shortness of breath. She is induced with fentanyl, lidocaine, propofol, and succinylcholine. An endotracheal tube is easily inserted and the case proceeds without difficulty. Vancomycin, 1 g, is given as antibiotic prophylaxis because of her allergy to penicillin. Methylene blue, 100 mg, is given toward the end of the case to confirm that no violation of the upper urinary tract system took place. She is successfully extubated and transferred to the post-anesthesia care unit. Approximately 30 minutes later, she is found to be agitated, tachypneic, and nonresponsive to commands, with dilated pupils, lower extremity rigidity, tachycardia to 119 beats/min and temperature of 40°C (104°F). She is emergently intubated. Blood gas analysis post-intubation results are: pH 7.35, partial arterial carbon dioxide pressure 45 mm Hg, partial arterial oxygen pressure 240 mm Hg on 100% fraction of inspired oxygen, bicarbonate 23 mEq/L.

   Which of the following diagnoses is most likely?

   A. Neuroleptic malignant syndrome
   B. Tricyclic antidepressant overdose
   C. Malignant hyperthermia
   D. Serotonin toxicity (formerly called serotonin syndrome)

9. A 50-year-old man with abdominal sepsis for perforated appendicitis develops a fever of 40°C (104°F), and is treated with IV acetaminophen.

   Which of the following side effects is most likely to be associated with IV acetaminophen in this patient?

   A. Hypotension
   B. Acute kidney injury
   C. Thrombosis
   D. Increased opioid requirements

10. A 29-year-old man is evaluated in the emergency department after intentional ingestion of 50 verapamil pills (40-mg tablets) and 50 atenolol pills (100-mg tablets). Calcium gluconate and glucagon are administered without improvement. Vasopressors are started to support his blood pressure.

    Which of the following is the most appropriate next step in treatment?

    A. Insulin and dextrose 10% infusion
    B. Venoarterial extracorporeal membrane oxygenation

C. More calcium gluconate
D. Emergent dialysis
E. Epinephrine infusion

11. A 26-year-old man is found in his basement obtunded and very tachypneic. He is brought to the emergency department, where the most significant physical examination findings are depressed mental status and high respiratory rate. Laboratory studies reveal a pure anion gap acidosis, with an anion gap of 38, an osmolar gap of 6 mOsm/kg, a creatinine of 2.2 mg/dL, and a pH of 6.95.

    Which of the following is a principle that should guide this patient's management?

    A. The lack of an osmolar gap rules out toxic alcohol ingestion.
    B. Antidotal treatment with ethanol or fomepizole is the definitive treatment of choice.
    C. There is no role for sodium bicarbonate administration.
    D. Emergent hemodialysis is the most appropriate therapy.

12. A 28-year-old man sustained severe brain injury from hypoxia-ischemia after cardiac arrest due to hypoxic respiratory failure in the setting of a heroin overdose. He undergoes a trial of targeted temperature management (TTM) to hypothermia (core temperature of 33°C [91.4°F]) in the ICU; shivering is managed with infusions of fentanyl, meperidine, midazolam, and cisatracurium. After 24 hours, he is re-warmed to a core temperature of 37°C (98.6°F). His renal and liver functions are deteriorating. On day two, the family requests a formal evaluation for prognosis and determination of neurologic function. His vital signs are: blood pressure 148/98 mm Hg, heart rate 78 beats/min, respiratory rate 16 breaths/min per ventilator and oxygen saturation 98% (fraction of inspired oxygen 0.5, positive end-expiratory pressure 8 cmH_20). On examination, he is comatose, with a Glasgow Coma Scale score of 3. No motor responses are seen. Corneal, pupillary, oculocephalic, cold caloric, gag, and cough reflexes are absent. Sodium is 148mEq/L, blood urea nitrogen 108 mg/dL, creatinine is 4.2 mg/dL, bicarbonate is 18 mEq/L, aspartate aminotransferase is 2818 IU, and alanine aminotransferase is 3245 IU. Neuron-specific enolase is 44 µg/L.

    Which of the following is the best approach to determine brain death in this patient, on the basis of neurologic criteria?

    A. Begin renal replacement therapy to clear the cisatracurium.
    B. Obtain an EEG.
    C. Await clearance of sedatives and reevaluate after 72 hours after TTM.
    D. Obtain an immediate cerebral blood flow scan.

Part 9 Answers:
Pharmacology and Toxicology

1. Rationale

Answer: B

Propofol is commonly used for sedation in the ICU. It is a hypnotic agent without analgesic properties. Imipenem/cilastatin requires reduction in dosing with renal insufficiency and during continuous renal replacement therapy. Hydromorphone is metabolized in the liver to hydromorphone-6-glucuronide, which is cleared by the kidney. Unlike the metabolite of morphine, morphine-6-glucuronide, hydromorphone-6-glucuronide has no analgesic properties. Cisatracurium is a nondepolarizing neuromuscular blocking agent that is commonly used in ICUs. It is degraded by Hofmann elimination, which depends on pH and temperature but not organ function. Therefore, the cisatracurium dose does not require adjustment for patients with renal or liver insufficiency. Cisatracurium has no metabolites. Some studies suggest that early administration of neuromuscular blocking agents in severe acute respiratory distress syndrome is associated with improved 90-day survival and increased time off the ventilator without increased muscle weakness.

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1. Felden L, Walter C, Harder S, et al. Comparative clinical effects of hydromorphone and morphine: a meta-analysis. *Brit J Anaesth.* 2011 Sep;107(3):319-328.
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4. Warr J, Thiboutot Z, Rose L, Mehta S, Burry LD. Current therapeutic uses, pharmacology, and clinical considerations of neuromuscular blocking agents for critically ill adults. *Ann Pharmacother.* 2011 Sep;45(9):1116-1126.

2. Rationale

Answer: B

In a case of encephalopathy without a readily apparent cause, assessment for potential medication toxicity may prove explanatory. A number of antibiotics have been associated with neurologic symptoms, including penicillins, cephalosporins, fluoroquinolones, tetracyclines, sulfonamides, and metronidazole. Risk factors for antibiotic-associated neurotoxicity include older age, critical illness, renal dysfunction, and prior neurologic disease. For this patient, cefepime toxicity is the most likely etiology of his neurologic deterioration.

Cefepime is a fourth-generation cephalosporin bactericidal for a broad spectrum of organisms, including *Pseudomonas aeruginosa*. Cefepime is predominantly renally excreted (85% unchanged) and, in patients with renal failure, it can accumulate in both blood and cerebrospinal fluid, and can reach toxic concentrations. This most commonly occurs when standard dose adjustments of cefepime for renal function are not made, but can also occur despite dose adjustment. The latency between the start of cefepime treatment and the development of neurologic manifestations has been reported to occur in as little as one day.

A wide variety of manifestations have been reported from cefepime-induced neurotoxicity, including confusion, hallucinations, agitation, myoclonic jerks, seizures, delirium, and coma. It has also been reported to cause nonconvulsive status epilepticus, a disorder characterized by alteration of consciousness without convulsions. On EEG, periodic sharp waves and triphasic waves are characteristic. If cefepime-induced neurotoxicity is suspected, cefepime should be discontinued in favor of an alternative antibiotic. Cefepime is dialyzable, and up to 70% of a dose may be removed by a three-hour hemodialysis session. Benzodiazepines or other anti-seizure medications should be used to treat seizure activity. Neurologic symptoms typically regress within two to seven days after stopping cefepime.

The pathogenesis of cefepime neurotoxicity has not been fully elucidated. Penicillins and cephalosporins are believed to exert an inhibitory effect on gamma-aminobutyric acid (GABA) transmission via their ß-lactam ring structure, which shares similar structural features to those of GABA neurotransmitters. In renally impaired patients, neurotoxicity appears to be mediated by a rise in serum cefepime concentrations and increased permeability of the blood-brain barrier secondary to uremia.

References:

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2. Gangireddy VG, Mitchell LC, Coleman T. Cefepime neurotoxicity despite renal adjusted dosing. *Scand J Infect Dis.* 2011 Oct;43(10):827-829.
3. Grill MF, Maganti R. Cephalosporin-induced neurotoxicity: clinical manifestations, potential pathogenic mechanisms, and the role of electroencephalographic monitoring. *Ann Pharmacother.* 2008 Dec;42(12):1843-1850.
4. Grill MF, Maganti RK. Neurotoxic effects associated with antibiotic use: management considerations. *Br J Clin Pharmacol.* 2011 Sep;72(3):381-393.
5. Thabet F, Al Maghrabi M, Al Barraq A, Tabarki B. Cefepime-induced

nonconvulsive status epilepticus: case report and review. *Neurocrit Care.* 2009;10(3):347-351.

3. Rationale

Answer: C

In a patient with a polysubstance overdose, identifying the specific agent responsible for toxicity is crucial because specific therapies may be indicated. All patients with known or suspected overdose should have an ECG on admission. Tricyclic antidepressants generally cause prolongation of several intervals, including the corrected QT (QTc) and the QRS; these effects are largely secondary to blocking effects on cardiac sodium channels. Left untreated, these abnormalities can progress to fatal ventricular dysrhythmias. Hypotension results from a combination of reduced myocardial contractility and decreased systemic vascular resistance due to alpha-adrenergic blockage. Sodium bicarbonate is indicated in this situation; repeat boluses should be administered until normalization of the QRS interval is observed. Naloxone is used to reverse opiate toxicity, which generally does not cause ECG abnormalities. Flumazenil is contraindicated because patients with any sodium channel blocking agent, including tricyclic antidepressants, is at high risk for seizures. Cyproheptadine may be administered to patients with serotonin syndrome, which generally presents with fever, and is probably not part of this clinical scenario. Lipid emulsion has been reported to be successful in case reports, but would not be first-line therapy for this patient.

References:

1. Thanacoody HK, Thomas SH. Tricyclic antidepressant poisoning: cardiovascular toxicity. *Toxicol Rev*. 2005;24(3):205-214.
2. Bradberry SM, Thanacoody HK, Watt BE, Thomas SH, Vale JA. Management of the cardiovascular complications of tricyclic antidepressant poisoning: role of sodium bicarbonate. *Toxicol Rev.* 2005;24(3):195-204.
3. Varney SM, Bebarta VS, Vargas TE, Boudreau S, Castaneda M. Intravenous lipid emulsion therapy does not improve hypotension compared to sodium bicarbonate for tricyclic antidepressant toxicity: a randomized, controlled pilot study in a Swine model. *Acad Emerg Med.* 2014 Nov;21(11): 1212-1219.
4. Blaber MS, Khan JN, Brebner JA, McColm R. “Lipid rescue” for tricyclic antidepressant cardiotoxicity. *J Emerg Med.* 2012 Sep;43(3):465-467.

4. Rationale

Answer: C

Glycopeptide antibiotics all demonstrate great efficacy against ß-lactam-resistant gram-positive organisms. The more recently approved lipoglycopeptide antibiotics, dalbavancin and oritavancin, also demonstrate in vitro activity to vancomycin-intermediate *Staphylococcus aureus* and vancomycin-resistant *Staphylococcus*

aureus. Oritavancin, as opposed to dalbavancin, falsely elevates the activated partial thromboplastin time for 48 hours and the prothrombin time/INR for 24 hours, thus making titration of heparin and warfarin dosing unreliable. It does this by binding and activating the phospholipid reagents used in these assays. Also, oritavancin results in enhanced exposure to warfarin when dosed in overlap. As such, it is recommended that treatment with heparin be avoided in the initial 48 hours after dosing with oritavancin, and that treatment with oritavancin be very carefully weighed in patients on warfarin.

References:

1. Laessig KA. U.S. Food and Drug Administration. Center for Drug Evaluation and Research. Deputy Division Director Summary Memo. Application number: 206-334Orig1s000 Summary Review. Silver Spring MD: U.S. Food and Drug Administration; August 6, 2014.
2. Orbactiv (oritavancin) for injection [package insert]. Parsipanny, NJ: The Medicines Company;
   August 2014.
3. Making a Difference in Infectious Diseases Newsletter. 2014 Winter;4(4). Mt. Pleasant, SC: Making a Difference in Infectious Diseases.

5. Rationale

Answer: E

Due to its insolubility, injectable lorazepam is diluted in propylene glycol. Propylene glycol toxicity can occur with lorazepam infusions for more than 48 hours, particularly at doses of 6 to 8 mg/hour or greater; presence of an osmolar gap, metabolic acidosis, unexplained new-onset renal failure, and respiratory failure should prompt concern for propylene glycol toxicity, and lorazepam should be discontinued.

References:

1. Arroliga AC, Shehab N, McCarthy K, Gonzales JP. Relationship of continuous infusion lorazepam to serum propylene glycol concentration in critically ill adults. *Crit Care Med.* 2004 Aug;32(8):
   1709-1714.
2. Horinek EL, Kiser TH, Fish DN, MacLaren R. Propylene glycol accumulation in critically ill patients receiving continuous intravenous lorazepam infusions. *Ann Pharmacother.* 2009 Dec;43(12):
   1964-1971.
3. Barr J, Fraser GL, Puntillo K, et al; American College of Critical Care Medicine. Clinical practice guidelines for the management of pain, agitation, and delirium in adult patients in the intensive care unit. *Crit Care Med.* 2013 Jan;41(1):263-306.

6. Rationale

Answer: A

3, 4-methylenedioxymethamphetamine (MDMA) is an amphetamine derivative that has been said to cause euphoria and decrease inhibitions. Side effects include dry mouth, bruxism, jaw clenching, anxiety, panic attacks, tachycardia, hypertension, hyperthermia, and excessive thirst. More severe side effects include serotonin syndrome, rhabdomyolysis, subarachnoid hemorrhage, fulminant hepatic failure, coma, and severe hyponatremia, which can be associated with seizures. The risk of death from first use of MDMA has been estimated between 1 in 20,000 and 1 in 50,000.

The cause of hyponatremia from MDMA is thought to be due to a combination of syndrome of inappropriate antidiuretic hormone with excessive water intake. The increased antidiuretic hormone leads to increased free water reabsorption, lowering the serum sodium level. This is then compounded by the increased water intake from the sensation of excess thirst that MDMA causes, dropping the sodium level further. There is also salt loss from excessive sweating caused by increased physical activity. The acute hyponatremia leads to cerebral edema and can cause seizures, as in this patient.

Heroin, also known as diacetylmorphine, is a narcotic with a very high addictive potential. Signs of heroin overdose include altered mental status, respiratory depression, and miotic pupils. Heroin overdose is most commonly associated with IV route of administration. Respiratory depression can lead to cardiorespiratory arrest and death. Naloxone is used to reverse the effects of heroin. In this patient with altered mental status, the normal respiratory rate, dilated pupils, lack of injection marks, and negative urine toxicology screen argue against heroin overdose. (Of note, many IV drug users use inconspicuous sites, so not finding injections sites does not exclude injection use.) Hyponatremia is not typically associated with heroin overdose.

Potomania is ethanol poisoning from massive intakes of alcohol. It can lead to hyponatremia. This patient's alcohol level is elevated, indicating alcohol consumption, but not to a high enough level to cause this degree of hyponatremia.

Acute bacterial meningitis can cause altered mental status in a patient with fever. The lack of a history of illness and the time course of her illness make the diagnosis less likely. On examination, the clinician would look for photophobia and neck stiffness. Pupillary response can range from sluggish to dilated, and is nonspecific. While hyponatremia can occur, it is usually not this severe. The normal white blood cell count also argues against infection. In this patient, it would not have been unreasonable to perform a lumbar puncture to exclude acute bacterial meningitis, but the lack of other findings suggestive of meningitis makes it a less likely diagnosis.

References:

1. White MC. How MDMA's pharmacology and pharmacokinetics drive desired effects and harms.
   J Clin Pharmacol. 2014 Mar;54(3):245-252.
2. Hall AP, Henry JA. Acute toxic effects of 'Ecstasy' (MDMA) and related compounds: overview of pathophysiology and clinical management. *Br J Anaesth.* 2006 Jun;96(6):678-685.

3. Sporer KA. Acute heroin overdose. *Ann Intern Med.* 1999 Apr 6;130(7):584-590.

7. Rationale

Answer: A

Case series studies have demonstrated that the presenting symptoms of acute kidney injury, rhabdomyolysis, and cardiac dysfunction are associated with propofol infusion syndrome. In this setting, rhabdomyolysis occurs from prolonged and high doses of propofol, which eventually can contribute to acute kidney injury. Risk factors for propofol infusion syndrome includes prolonged administration with high doses of propofol and concurrent administration of catecholamines and corticosteroids. In addition to acute renal failure, propofol infusion syndrome has been associated with severe metabolic acidosis, bradycardia, and cardiovascular instability. None of the other options are known to be associated with this clinical presentation.

References:

1. Wong JM. Propofol infusion syndrome. *Am J Ther.* 2010 Sep-Oct;17(5):487-491.
2. Diedrich DA, Brown DR. Analytic reviews: propofol infusion syndrome in the ICU. *J Intensive Care Med.* 2011 Mar-Apr;26(2):59-72.

8. Rationale

Answer: D

Methylene blue is a known monoamine oxidase inhibitor (MAOI). It is a potent reversible inhibitor of MAO A and, at concentrations reported in the literature after IV administration, MAO B would be partially inhibited but MAO A would be completely inhibited. This inhibition of MAO A can lead to disturbances in 5-hydroxytryptamine (5-HT) (serotonin) metabolism, leading to serotonin toxicity (formerly called serotonin syndrome). The patient reported taking scheduled dextromethorphan for a week before surgery. The dextromethorphan-MAOI interaction appears to be due to 5-HT potentiation. In cat studies, dextromethorphan has been shown to markedly enhance the response of noradrenaline and 5-HT but to antagonize the effects of tyramine. This suggests that it blocks the uptake of these amines in the adrenergic nerve endings. Serotonin toxicity is characterized by increased heart rate, shivering, sweating, dilated pupils, myoclonus (usually more prominent in the lower extremities), hyperreflexia, hyperthermia, hypertension, and agitation. Hyperthermia can lead to rhabdomyolysis and renal failure.

Neuroleptic malignant syndrome usually involves muscle cramps and tremors (not myoclonus), fevers and symptoms of autonomic nervous system instability such as unstable blood pressure, as well as altered mental status. These symptoms are most likely caused by blockade of the dopamine receptor D2, leading to abnormal function of the basal ganglia similar to Parkinson disease. Symptoms generally come on quickly after the initiation of dopamine antagonists and peak at around three days. This patient was taking metoclopramide (a dopamine D2 antagonist) intermittently for nausea and gastroparesis, but had not taken any the morning of surgery. The half-life

of metoclopramide is five to six hours; therefore, this is a much less likely cause of her symptoms.

She takes amitriptyline for depression. Amitriptyline is a tricyclic antidepressant, which can cause vasodilation, dry mouth, urinary retention, tachycardia, hypotension, and altered mental status, symptoms likely due to the anticholinergic effects of tricyclic antidepressants. The treatment is physostigmine. She had been taking amitriptyline before surgery. There is no reason to believe that she had recently overdosed on it.

Malignant hyperthermia (MH) is induced by succinylcholine, but is an autosomal dominant disease process characterized by a mutation in the ryanodine receptor on the sarcoplasmic reticulum in skeletal muscle cells, which release calcium in response to increased levels of intracellular calcium, leading to muscle contraction. In MH, there is an excessive release of sarcoplasmic reticular calcium leading to prolonged muscle contraction. Symptoms of MH include high temperature, increased heart rate, tachypnea, increased carbon dioxide production, increased oxygen consumption, mixed acidosis, rigid muscles, and rhabdomyolysis. The first evidence of MH is usually a rise in end-tidal carbon dioxide. In this patient, a pure respiratory acidosis is present.

References:

1. Ramsay RR, Dunford C, Gillman PK. Methylene blue and serotonin toxicity: inhibition of monoamine oxidase A (MAO A) confirms a theoretical prediction. *Br J Pharmacol.* 2007 Nov;152(6):
   946-951.
2. Sinclair JG. Dextromethorphan-monoamine oxidase inhibitor interaction in rabbits. *J Pharm Pharmacol.* 1973 Oct;25(10):803-808.
3. Boyer EW, Shannon M. The serotonin syndrome. *N Engl J Med.* 2005 Mar 17;352 (11):1112-1120.
4. Strawn JR, Keck PE Jr, Caroff, SN. Neuroleptic malignant syndrome. *Am J Psychiatry.* 2007 Jun;164(6):870-876.

9. Rationale

Answer: A

Acetaminophen (also called paracetamol) is the most widely used analgesic and antipyretic worldwide. Its side effects are generally mild with recommended doses; its use has steadily increased because of its safety profile compared to nonsteroidal antiinflammatory drugs. The IV preparation of acetaminophen offers the ability to achieve therapeutic blood concentrations more readily and more reliably, which may be particularly beneficial for use in critically ill patients.

However, emerging clinical data suggest that IV paracetamol has a propensity to cause hypotension in critically ill patients. One of the first studies, by de Maat et al, specifically examined the hemodynamic effects of the new ready-to-use formulation of IV paracetamol. It found a decrease in systolic blood pressure of at least 10 mm Hg within 30 minutes of IV administration in one-third of patients. Postulated mechanisms

for the hypotension include paracetamol-induced increases in skin blood flow (consistent with its antipyretic action) and the effects of mannitol, which is used as a stabilizing agent in the IV formulation.

Other adverse effects with therapeutic acetaminophen use are rare. It can cause transient abnormalities of liver function. Very rarely, blood disorders, including drug-induced immune thrombocytopenia, have been reported. Pyroglutamic acidosis is a rare adverse effect associated with therapeutic acetaminophen use, most frequently identified in malnourished female patients who have renal insufficiency or failure. Acute allergic reactions to acetaminophen are very rarely described.

Meta-analyses have demonstrated that the addition of acetaminophen to morphine reduces morphine requirements in postsurgical patients by about 20%. As a result, acetaminophen is commonly administered along with opioids as part of a strategy of multimodal analgesia.

References:

1. Boyle M, Nicholson L, O'Brien M, et al. Paracetamol induced skin blood flow and blood pressure changes in febrile intensive care patients: an observational study. *Aust Crit Care.* 2010 Nov;23(4):208-214.
2. Chiam E, Weinberg L, Bellomo R. Paracetamol: a review with specific focus on the haemodynamic effects of intravenous administration. *Heart Lung Vessel.* 2015;7(2):121-132.
3. Chiam E, Weinberg L, Bailey M, McNicol L, Bellomo R. The haemodynamic effects of intravenous paracetamol (acetaminophen) in healthy volunteers: a double-blind, randomized, triple crossover trial. *Br J Clin Pharmacol.* 2016 Apr;81(4):605-612.
4. de Maat MM, Tijssen TA, Brüggemann RJ, Ponssen HH. Paracetamol for intravenous use in medium—and intensive care patients: pharmacokinetics and tolerance. *Eur J Clin Pharmacol.* 2010 Jul;66(7):713-719.
5. Jefferies S, Saxena M, Young P. Paracetamol in critical illness: a review. *Crit Care Resusc.* 2012 Mar;14(1):74-80.

10. Rationale

Answer: A

This patient is currently in profound cardiogenic and distributive shock from poisoning with both calcium channel blockade and beta-adrenergic blockade. Appropriate first-line therapy remains glucagon and calcium, but in extreme circumstances, high-dose insulin has been shown to be effective. However, in the setting of prolonged hypotension, vasopressor support is indicated, with seeming equipoise between epinephrine, norepinephrine, and dopamine. Vasopressin also appears to show some benefit, and sometimes multiple vasopressors are required. Because of primary distributive shock, venoarterial extracorporeal membrane oxygenation has limited utility.

Insulin is acting as a chronotrope and inotrope, and is therefore giving him vital

hemodynamic support. While atenolol primarily does not bind protein in the body, verapamil does exist in the body as a protein-bound drug (about 75%). This makes dialysis a poor management choice for this mixed toxidrome.

References:

1. St-Onge M, Dubé PA, Gosselin S, et al. Treatment for calcium channel blocker poisoning: a systematic review. *Clin Toxicol (Phila).* 2014 Nov;52(9):926-944.
2. Levine M, Curry SC, Padilla-Jones A, Ruha AM. Critical care management of verapamil and diltiazem overdose with a focus on vasopressors: a 25-year experience at a single center. *Ann Emerg Med.* 2013 Sep;62(3):252-258.

11. Rationale

Answer: D

In a patient with a presentation such as this, with no hard findings of a toxidrome other than depressed mental status, and a very high anion gap, toxic alcohol ingestion must be suspected. In this case, the patient drank antifreeze, leading to an ethylene glycol overdose. Ethylene glycol is metabolized by alcohol dehydrogenase to glycolic and oxalic acid; methanol is metabolized to formic acid. The osmolar gap is useful in diagnosing these ingestions, but not foolproof. As the alcohol is metabolized, the osmolar gap narrows and the anion gap increases. In this patient, with an anion gap of 38 and a pH of 6.95, significant metabolism has occurred, which accounts for his critically ill state and lack of osmolar gap. Also, treatment with ethanol or fomepizole (a competitive inhibitor of alcohol dehydrogenase) will not remove the toxic metabolites, but will aid in the prevention of further accumulation/metabolism of more metabolites. This patient needs emergent hemodialysis to correct his life-threatening acidosis, and remove toxic metabolites. In addition, adjunctive therapy would include fomepizole until ethylene glycol levels are undetectable, sodium bicarbonate (before dialysis is initiated at least) to enhance formate and oxalate elimination by ion trapping, as well as thiamine and pyridoxine supplementation.

Another toxic alcohol to consider is isopropyl alcohol, which is found in rubbing alcohol. This is metabolized to acetone, which is eliminated in the urine. In contrast to ethylene glycol and methanol, isopropyl alcohol will not cause a metabolic acidosis, but has been known to cause nausea, vomiting, and gastrointestinal bleeding, in addition to severe intoxication.

Reference:

1. Kraut JA, Kurtz I. Toxic alcohol ingestions: clinical features, diagnosis, and management. *Clin J Am Soc Nephrol*. 2008 Jan;3(1):208-225.

12. Rationale

Answer: C

The clinical examination in brain death is the most unequivocal in neurology. It should be performed with care and accuracy. In the era of hypothermia, evidence suggests

that the best approach before providing prognostic information is to wait for a period of 72 hours after rewarming. This is particularly important if the patient has been exposed to sedatives and paralytics in the setting of organ dysfunction, which could confound the clinical examination. The American Academy of Neurology practice parameter recommends excluding the presence of a central nervous system (CNS)-depressant drug effect by history, drug screen, calculation of clearance using five times the drug's half-life (assuming normal hepatic and renal function) or, if available, drug plasma levels below the therapeutic range. Prior use of hypothermia (after cardiopulmonary resuscitation for cardiac arrest) may also delay drug metabolism. If these two circumstances are present, then longer periods of observation may be needed. EEG could be misleading in patients with lingering effects of CNS depressants. Neuron-specific enolase is not diagnostic for brain death but could provide prognostic information when used with other variables such as the clinical examination. A flow scan would help in the determination of brain death if the physician cannot accurately assess neurologic function after a reasonable period of observation, but it may be premature in this case.

References:

1. Webb AC, Samuels OB. Reversible brain death after cardiopulmonary arrest and induced hypothermia. *Crit Care Med.* 2011 Jun;39(6):1538-1542.
2. Nielsen N, Wetterslev J, Cronberg T, et al; TTM Trial Investigators. Targeted temperature management at 33°C versus 36°C after cardiac arrest. *N Engl J Med.* 2013 Dec 5;369(23):2197-2206.
3. Wijdicks EF, Varelas PN, Gronseth GS, Greer DM; American Academy of Neurology. Evidence-based guideline update: determining brain death in adults: report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology.* 2010 Jun 8;74(23):1911-1918.

Part 10:

Research, Ethics, and Administration

Part 10:
Research, Ethics, and Administration

Instructions: For each question, select the most correct answer.

1. Hospital administration has decided to reorganize the provision of critical care services, transitioning to a closed model with interdisciplinary rounds, in an effort

to improve care coordination and outcomes.

Guiding principles for team interactions would benefit from which of the following techniques?

A. Rapid cycle process
B. Root cause analysis
C. Crew resource management
D. Six Sigma principles

2. An investigator proposes to perform a study to determine the effect of new-onset fever on long-term functional outcome. The investigator hypothesizes that fever is associated with poor outcome. In order to test the hypothesis, the investigator proposes following the outcomes of febrile patients in the ICU and comparing them to the outcomes of a group of patients without fever during a six-month period.

   The design of this study is best described as which type of study?

   A. Experimental clinical trial
   B. Case-control study
   C. Prospective cohort study
   D. Retrospective cohort study
   E. Ecological study

3. Which of the following practices for decreasing central line-associated bloodstream infections is best supported by evidence?
   A. Cleaning the skin with chlorhexidine before a procedure
   B. Changing central lines every seven days
   C. Multidisciplinary rounds
   D. Preferential placement of internal jugular lines over other sites
   E. Daily blood cultures

4. Which of the following circumstances is most associated with pressure ulcers?
   A. Intermittent hemodialysis
   B. Noninvasive ventilation
   C. Continuous renal replacement therapy
   D. Surgery lasting longer than two hours

5. A 25-year-old man with obesity is admitted to the ICU with sepsis secondary to community-acquired pneumonia. Blood pressure is 80/40 mm Hg, heart rate 108 beats/min, respiratory rate 24 breaths/min, pulse oxymetry 90% on 4-liter nasal canula, and lactic acid level 5.6 mmol/L. The ICU team requests the patient's permission to insert a central line through an internal jugular approach to begin

pressors. After being informed about the indications, risks and benefits, the patient refuses to authorize it and requests that all of the necessary drugs be administered through a peripheral intravenous line. The intensivist refuses to administers the pressors through the peripheral IV because of the risk of infiltration with the potential loss of limb.

The intensivist is exercising which of the following ethical priciples?

A. Non-abandonment versus nonmaleficence
B. Bioethics versus legal obligation
C. Autonomy versus nonmaleficence
D. Autonomy versus beneficence

6. A 65-year-old woman is evaluated in the emergency department for sudden onset of right hemiparesis and aphasia. Blood pressure is 178/106 mm Hg, heart rate 98 beats/min, respiratory rate 24 breaths/min, pulse oxymetry 98% on 2-liter nasal cannula, and National Institutes of Health Stroke Scale score is 16. The on-call neurologist recommends IV recombinant plasminogen activator (rtPA). However, there are no family members with which to discuss potential risks, benefits, or alternatives.

   On the basis of which of the following principles is a physician allowed to administer IV rtPA to this patient?

   A. Autonomy
   B. Nonmaleficence
   C. Implied consent
   D. Utilitarianism

7. A recently published study that followed 30,000 patients during a 20-year period demonstrated that the development of systolic hypertension above 140 mm Hg was associated with doubling of the risk of stroke or transient ischemic attack.

   This study design corresponds to which of the following study types?

   A. Case-control
   B. Cohort
   C. Clinical trial
   D. Cross-sectional
   E. Ecological

Part 10 Answers:
Research, Ethics, and Administration

1. Rationale

Answer: C

Efforts to improve care in the medical community have taken a systems approach, recognizing the multidimensional and comprehensive care provided by many individuals to a single patient. Crew resource management techniques, long used in the aviation industry to enhance communication skills, decision making, problem solving, and teamwork, along with empowering a greater body of personnel, have served as a model for the collaborative care model of a multidisciplinary ICU team. Rapid cycle process and Six Sigma principles are quality management tools used to improve aspects of care and decrease variability in the provision of care and outcomes. Root cause analysis is a process used to investigate the central causes of an error in care or a near miss commonly used by hospital risk management departments.

References:

1. Marshall D. *Crew Resource Management: From Patient Safety to High Reliability*. Centennial, CO: Safer Healthcare; 2010.
2. Haerkens M, Jenkins DH, van der Hoeven JG. Crew resource management in the ICU: the need for culture change. *Ann Intensive Care.* 2012 Aug;2:39-44.
3. Dunn EJ, Mills PD, Neily J, Crittendon MD, Carmack AL, Bagian JP. Medical team training: applying crew resource management in the Veterans Health Administration. *Jt Comm J Qual Patient Saf.* 2007 Jun;33(6):317-325.

2. Rationale

Answer: C

A cohort study is a form of longitudinal or observational study designed to look at the association between an exposure and an outcome. When the cohort study is begun before the outcome occurs, it is a prospective cohort study. If the outcome has already occured, investigators can explore the association by ascertaining the exposure back in time. In this case, it is a retrospective cohort study.

A case-control study is a type of observational study in which two existing groups differing in outcome are identified and compared on the basis of some supposed causal attribute or exposure. Controls are selected independent of exposure. When

the selection occurs on the basis of one characteristic, it is considered a matched study.

An ecological study is an observational study in which at least one variable is measured at the group level.

A randomized controlled clinical trial is superior methodology in the hierarchy of evidence in therapy, because it limits the potential for any biases by randomly assigning one patient pool to an intervention and another patient pool to non-intervention or placebo.

Reference:

1. Porta M, ed. *A Dictionary of Epidemiology*. 5th ed. New York, NY: Oxford University Press; 2008.

3. Rationale

Answer: A

Central line-associated bloodstream infections (CLABSIs) are associated with 28,000 deaths in the United States annually and cost 2.3 billion dollars. Pronovost et al participated in a project to reduce CLABSIs in the state of Michigan between 2004 and 2005 and demonstrated a reduction in CLABSIs by 66%. This project comprised 85% of Michigan's ICU beds. A follow-up analysis at three years demonstrated a sustained improvement. A central line bundle incorporated five Centers for Disease Control and Prevention recommendations: hand washing, using full-barrier precautions during the insertion of central venous catheters, cleaning the skin with chlorhexidine, avoiding the femoral site if possible, and removing unnecessary catheters. A large randomized trial showed that subclavian placement decreased the rate of infection, but is associated with more pneumothoraces. No data supports the changing of central lines every seven days or daily blood cultures. Multidisciplinary rounds are important in the ICU, but rounding without addressing the need for central lines has not proven to decrease CLABSIs.

References:

1. Pronovost P, Needham D, Berenholtz S, et al. An intervention to decrease catheter-related bloodstream infections in the ICU. *N Engl J Med.* 2006 Dec 28;355(26):2725-2732.
2. Lipitz-Snyderman A, Needham DM, Colantuoni, et al. The ability of intensive care units to maintain zero central line-associated bloodstream infections. *Arch Int Med.* 2011 May 9;171(9):856-858.
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4. Parienti JJ, Mongardon N, Mégarbane B, et al; 3SITES Study Group. Intravascular complications of central venous catheterization by insertion site. *N Engl J Med.* 2015 Sep 24;373(13):1220-1229.

5. Albrecht RM. Patient safety: the what, how, and when. *Am J Surg.* 2015 Dec;210(6):978-982.

4. Rationale

Answer: B

In 2008, the Centers for Medicare & Medicaid Services created incentives for hospitals to prevent pressure ulcers; however, they remain frequent events in ICUs. The exact incidence is unclear because of a lack of identification of ulcers on patient admission to the ICU and variations in data reporting. The incidence has been reported to vary between 3% and 20%. Mechanical ventilation has been associated with an increased incidence of pressure ulcers, secondary to patients being sedentary, and noninvasive ventilation has also been implicated. Both intermittent and continuous dialysis have been associated with an increased incidence of pressure ulcers, but surgery lasting longer than two hours has not been associated with it. Surgery lasting longer than four hours has been associated with it.

It is important to identify patients at risk and to develop strategies to prevent pressure ulcers in critically ill patients. The Critical Care Pressure Ulcer Assessment Tool Made Easy (CALCULATE) score was developed through literature review and refined through clinical implementation. The score consists of risk factors identified through the medical literature for pressure ulcers, including: too unstable to turn, low protein, dialysis, fecal incontenience, mechanical ventilation, long surgery/cardiac arrest during admission, and impaired circulation. The score was used over a four-month period, and impaired mobility was added as another risk factor. The two most commonly used scales in the United States are the Braden Scale and the Norton Scale.

Preventing pressure ulcers is important because they increase mortality, morbidity, pain, and hospital costs. A multitude of preventive measures exist, but a focused program that ensures excellent communication between leadership and staff seems most vital in decreasing pressure ulcers.

References:

1. VanGilder C, Amlung S, Harrison P, Meyer S. Results of the 2008-2009 International Pressure Ulcer Prevalence Survey and a 3-year, acute care, unit-specific analysis. *Ostomy Wound Manage.* 2009 Nov 1;55(11):39-45.
2. Richardson A, Barrow I. Part 1: Pressure ulcer assessment—the development of Critical Care Pressure Ulcer Assessment Tool made Easy (CALCULATE). *Nurs Crit Care.* 2015 Nov;20(6):308-314.
3. Girard R, Baboi L, Ayzac L, Richard JC, Guérin C; Proseva trial group. The impact of patient positioning on pressure ulcers in patients with severe ARDS: results from a multicentre randomised controlled trial on prone positioning. *Intensive Care Med.* 2014 Mar;40(3):397-403.
4. Richardson A, Straughan C. Part 2: Pressure ulcer assessment: implementation and revision of CALCULATE. *Nurs Crit Care.* 2015 Nov;20(6):315-321.
5. Cooper KL. Evidence-based prevention of pressure ulcers in the intensive care

unit. *Crit Care Nurse.* 2013 Dec;33(6):57-66.

5. Rationale

Answer: C

Ethical principles classically associated with the ethical decision-making process are autonomy, beneficence, nonmaleficence, and legal obligation. Autonomy usually takes preference over other factors even though other treatment options are necessary (beneficence) and are explained (legal obligation). Nonmaleficence is the right of the physician to refuse to agree to treatment that would be harmful to the patient. The physician cannot abandon a patient who does not agree to treatment until another physician agrees to assume care. For this patient, respect of the patient's wishes (autonomy) and the desire of the physician to not provide an intervention that would be harmful (nonmaleficence) are present.

References:

1. U.S. Department of Health & Human Services. Office for Human Research Protections. Department of Health, Education, and Welfare. *The Belmont Report. Office of the Secretary. Ethical Principles and Guidelines for the Protection of Human Subjects of Research. The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research.*Washington, DC: U.S. Department of Health & Human Services; April 18, 1979. http://www.hhs.gov/ohrp/regulations-and-policy/belmont-report/. Accessed June 22, 2016.
2. Fisher M. Ethical issues in the intensive care unit. *Curr Opin Crit Care.* 2004;10:292.

6. Rationale

Answer: C

In emergency or life-threatening and time-critical situations, physicians have the duty to preserve life. In very few life-threatening conditions, such as sepsis or myocardial infarction, patients can be involved in the consent process. However, physicians often use an implied consent principle to perform life-saving interventions in patients who lack decision-making capacity or surrogates. The emergency doctrine of implied consent allows providers to deliver certain interventions that, if not performed in a timely manner, could potentially lead to increased morbidity and mortality. If the following conditions are met, the physician can use the implied consent doctrine: the treatment in question represents the usual and customary standard of care for the condition being treated, it would clearly be harmful to the patient to delay treatment while awaiting explicit consent, and the patient ordinarily would be expected to consent to the treatment in question if he/she had the capacity to do so.

Reference:

1. Bernat JL. *Ethical Issues in Neurology*. 3rd. ed. Philadelphia: Lippincontt

Williams & Wilkins; 2008.

7. Rationale

Answer: B

This study design is a cohort study, in which a population is followed until the development of an outcome. The exposure of interest in this case is systolic hypertension. Case-control studies are smaller epidemiologic studies in which exposures are actually identified after the onset of an outcome. A clinical trial is a study with an experimental design in which two groups are exposed to different interventions, usually a placebo and an experimental drug or procedure. Ecological research involves studies of risk-modifying factors on health or other outcomes based on populations defined either geographically or temporally. Both risk-modifying factors and outcomes are averaged for the populations in each geographical or temporal unit and then compared using standard statistical methods.

Reference:

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