

FLUIDS, ELECTROLYTES, AND NUTRITION

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Learning Objectives

1. Recommend an appropriate intravenous fluid regimen and monitoring parameters given a patient clinical scenario.
2. Discuss the appropriate roles and risks of hypertonic and hypotonic saline, recommend treatment regimens, and discuss appropriate monitoring parameters to ensure safe and effective use of these intravenous fluids.
3. Assess electrolyte abnormalities and recommend an appropriate pharmacologic treatment plan based on individual patient signs and symptoms.
4. Recommend a patient-specific enteral nutrition (EN) or parenteral nutrition (PN) formula, infusion rate, and monitoring parameters based on nutritional needs, comorbidities, and clinical condition.

Abbreviations in This Chapter

AA	amino acid
ADH	antidiuretic hormone
ASPEN	American Society for Parenteral and Enteral Nutrition
BEE	basal energy expenditure
BUN	blood urea nitrogen
D ₅ W	5% dextrose
EC	extracellular
ECG	electrocardiogram
EN	enteral nutrition
GI	gastrointestinal
IBW	ideal body weight
IC	intracellular
ICU	intensive care unit
IS	interstitial
LBW	lean body weight
MW	molecular weight
NG	nasogastric
PN	parenteral nutrition
SCr	serum creatinine
SIADH	syndrome of inappropriate secretion of antidiuretic hormone
TBF	total body fluid
WBC	white blood cell count

Self-Assessment Questions

Answers and explanations to these questions can be

found at the end of this chapter.

1. A 74-year-old woman (weight 72 kg) arrives in the emergency department with a 3-day history of cough, body temperature of 102°F (38.9°C), and lethargy. She has the following vital signs and laboratory values: blood pressure 72/40 mm Hg, heart rate 115 beats/minute, urine output 10 mL/hour, white blood cell count (WBC) 18×10^3 cells/mm³, hemoglobin 12.5 g/dL, and blood urea nitrogen (BUN)/serum creatinine (SCr) ratio of 28:1.7 mg/dL (baseline SCr 1.2 mg/dL), and blood glucose 82 mg/dL. After a 500-mL fluid bolus of 0.9% sodium chloride, her blood pressure is 80/46 mm Hg and her heart rate is 113 beats/minute. Her chest radiograph is consistent with pneumonia. Her medical history includes coronary artery disease and arthritis. Which is the most appropriate treatment at this time?
 - A. Furosemide 40 mg intravenously.
 - B. 5% albumin 500 mL infused over 4 hours plus norepinephrine titrated to maintain a systolic blood pressure of 90 mm Hg or higher.
 - C. 1000-mL fluid bolus with 5% dextrose (D₅W) and 0.9% sodium chloride.
 - D. 1000-mL fluid bolus with 0.9% sodium chloride.
2. An order has been received for 2% sodium chloride. Assume no commercially available product is available. Using 0.9% sodium chloride and 23.4% sodium chloride, first determine how much of each is necessary to prepare 1 L of 2% sodium chloride. Second, calculate the osmolarity of 2% sodium chloride. Finally, determine whether the resultant solution should be administered through a central or peripheral intravenous infusion (molecular weight [MW] of sodium chloride is 58.5, osmotic coefficient is 0.93).
 - A. Mix 951 mL of 0.9% sodium chloride plus 49 mL of 23.4% sodium chloride; osmolarity = 635 mOsm/L; peripheral intravenous infusion.
 - B. Mix 951 mL of 0.9% sodium chloride plus 49 mL of 23.4% sodium chloride; osmolarity = 954 mOsm/L; central intravenous infusion.
 - C. Mix 850 mL of 0.9% sodium chloride plus 150 mL of 23.4% sodium chloride; osmolarity = 954 mOsm/L; central intravenous infusion.

- D. Mix 850 mL of 0.9% sodium chloride plus 150 mL of 23.4% sodium chloride; osmolarity = 513 mOsm/L; peripheral intravenous infusion.
3. A 68-year-old man is admitted to the hospital for worsening shortness of breath during the past 2 weeks caused by heart failure. His serum sodium concentration on admission was 123 mEq/L. Other abnormal laboratory values include brain natriuretic peptide of 850 pg/mL and SCr of 1.7 mg/dL. Chest radiography is consistent with pulmonary edema. The patient weighs 85 kg on admission, which is up 3 kg from his baseline weight. The patient is not experiencing nausea, headache, or mental status changes. The physician orders 3% sodium chloride to treat the hyponatremia. Which recommendation is best?
 - A. 3% sodium chloride is an appropriate choice because the hyponatremia is probably acute.
 - B. A 250-mL bolus of 3% sodium chloride is appropriate if used in combination with furosemide to prevent volume overload.
 - C. 3% sodium chloride is appropriate if the serum sodium does not increase more than 10 mEq/L in 24 hours.
 - D. The risks of 3% sodium chloride outweigh the potential benefit for this patient.
 4. A 55-year-old man with diabetes and kidney disease has hyperkalemia. His laboratory values include potassium (K^+) 7.2 mEq/L, calcium (Ca^{2+}) 9 mg/dL, albumin 3.5 g/dL, and blood glucose 302 mg/dL. His electrocardiogram (ECG) is abnormal, with peaked T waves. What is the best recommendation for initial treatment?
 - A. Regular insulin 10 units intravenously plus 50 g of dextrose intravenously.
 - B. 10% calcium gluconate 10 mL intravenously.
 - C. Sodium polystyrene sulfonate (Kayexalate) 15 g orally.
 - D. Sodium bicarbonate 50 mEq intravenously over 5 minutes.
 5. A 68-year-old woman (weight 60 kg) is admitted to the hospital after a cardioembolic stroke. Her medical history is significant for atrial fibrillation, acute myocardial infarction, and diabetes. She has been unconscious for 48 hours. The medical team decides to start providing nutrition. All of her laboratory values, including glucose concentrations, are normal. Although she currently has no enteral access, she does have a peripheral intravenous catheter. Which nutritional regimen is best for this patient?
 - A. Insert a central intravenous catheter and initiate parenteral nutrition (PN) containing 60 g of amino acids (AAs), 250 mL of 20% lipid emulsion, 300 g of dextrose, standard electrolytes, multivitamins, and trace elements in a volume of 2000 mL administered over 24 hours.
 - B. Insert a central intravenous catheter and initiate PN containing 40 g of AAs, 250 mL of 20% lipid emulsion, 200 g of dextrose, standard electrolytes, multivitamins, and trace elements in a total volume of 2000 mL administered over 24 hours.
 - C. Insert a nasogastric (NG) or nasoduodenal feeding tube and infuse an isotonic formula (1 kcal/mL) starting at 25 mL/hour and advance to a goal rate of 65 mL/hour.
 - D. Insert a percutaneous endoscopic gastrostomy feeding tube and infuse an isotonic formula (1 kcal/mL) starting at 25 mL/hour and advance to a goal rate of 100 mL/hour.
 6. A 70-year-old man is admitted to the hospital with peritonitis caused by severe inflammatory bowel disease. The patient has received adequate fluid resuscitation, and he is prescribed appropriate antibiotics. After several days of the patient being unable to tolerate oral or enteral nutrition, the physician consults the pharmacist to recommend a PN formula to be administered through a central line. The patient is hemodynamically stable, with normal electrolyte concentrations. Weight is 55 kg, BUN/SCr is 20/1.1 mg/dL, and WBC is 17×10^3 cells/mm³. Assuming that appropriate electrolytes, multivitamins, and trace elements are included, which PN formula, when administered over 24 hours, will best provide this patient adequate calories, AAs, and lipids?
 - A. AAs 10% 700 mL, dextrose 30% 325 mL,

- lipid 20% 500 mL.
- B. AAs 10% 450 mL, dextrose 70% 400 mL, lipid 20% 250 mL.
- C. AAs 10% 800 mL, dextrose 70% 350 mL, lipid 20% 250 mL.
- D. AAs 15% 900 mL, dextrose 50% 500 mL, lipid 20% 250 mL.
7. A 59-year-old man has been admitted to the hospital after several days of vomiting and diarrhea. In the emergency department, he had several runs of nonsustained ventricular tachycardia. His plasma potassium on admission is 2.8 mEq/L. After 100 mEq of potassium chloride is infused over 24 hours, his repeated K^+ is 3.2 mEq/L, and he continues to have runs of ventricular tachycardia. Other laboratory values include Na^+ 143 mEq/L, magnesium 1.4 mg/dL, phosphorus 3 mg/dL, Ca^{2+} 9 mg/dL, and ionized Ca^{2+} 1.1 mmol/L. Which treatment would be best to give next?
- A. Administer potassium chloride 20 mEq intravenously over 1 hour each for 4 doses and recheck K^+ .
- B. Administer magnesium sulfate as a 2 g slow intravenous infusion over 2 hours.
- C. Administer potassium phosphate 15 mmol intravenously over 4 hours.
- D. Administer calcium gluconate 2 g intravenously over 5 minutes.
8. Which nutritional strategy can best prevent gut mucosal atrophy and subsequent bacterial translocation?
- A. PN enriched with glutamine.
- B. PN enriched with branched-chain AAs.
- C. Enteral nutrition (EN).
- D. Zinc supplementation.
9. A female patient (weight 80 kg) in the intensive care unit has developed acute kidney injury caused by sepsis, and she requires intermittent hemodialysis daily to maintain her BUN/SCr ratio at 49:2.5 mg/dL. Currently, she is receiving appropriate antibiotics and is hemodynamically stable. She has also been receiving PN providing 72 g of AAs per day. What is the best recommendation for this patient's protein intake?
- A. Reduce AAs to 40 g/day.
- B. Reduce AAs to 64 g/day.
- C. Increase AAs to 96 g/day.
- D. Increase AAs to 160 g/day.

BPS Pharmacotherapy Specialty Examination Content.

This chapter covers the following sections of the Pharmacotherapy Specialty Examination Content Outline

1. Domain 1: Patient-Centered Pharmacotherapy
 - a. Task 1, Knowledge statements a-c, e, f, h, j-m, p, q
 - b. Task 2, Knowledge statements a, b, d
 - c. Task 3, Knowledge statements a-e
 - d. Task 4, Knowledge statements a
2. Domain 2: Application of Evidence to Practice and Education. Task 1, Knowledge statements g
3. Domain 3: Healthcare Systems and Population Health
 - a. Task 1, Knowledge statements e
 - b. Task 2, Knowledge statements a

I. FLUID MANAGEMENT

A. Distribution of total body fluid (TBF) (Figure 1)

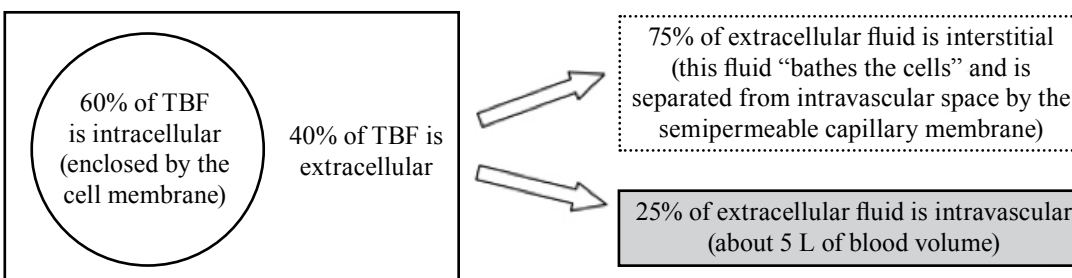


Figure 1. Distribution of total body fluid.

TBF = total body fluid.

1. Estimated as 60% of lean body weight (LBW) in men and 50% in women; a healthy adult (weight 70 kg) has about 42 L of fluid
2. Total body water is further divided into intracellular (IC) space and extracellular (EC) space.
 - a. About 60% of TBF is IC, and 40% is EC; the IC and EC fluid compartments are separated by cell membranes, which are highly permeable to water.
 - b. The EC compartment is also divided into the interstitial (IS) space and the intravascular space; the IS and intravascular fluid compartments are separated by the capillary membrane, which is permeable to almost all solutes except proteins.
 - i. 75% of the EC fluid is in the IS space.
 - ii. 25% of the EC fluid is in the intravascular space; the EC fluid in the intravascular space is known as *plasma*, and it measures about 3 L; if you also consider about 2 L of fluid found in red blood cells (thus, IC fluid), the total blood volume is about 5 L.
3. The approximate distribution of TBF into the IC and EC compartments with further distribution of the EC fluid into the IS and intravascular compartments is important to remember for determining the distribution of intravenous fluid.

B. Distribution of intravenous fluid (Table 1)

Table 1. Distribution of Intravenous Fluid

Intravenous Fluid	Infused Volume (mL)	Equivalent Intravascular Volume Expansion (mL)
Normal saline	1000	250
Lactated Ringer solution	1000	250
Normosol-R and Plasma-Lyte	1000	250
5% Dextrose	1000	100
Albumin 5%	500	500
Albumin 25%	100	500
Hydroxyethyl starch 6%	500	500

1. Crystalloids are intravenous fluids that can contain water, sodium (Na^+), chloride (Cl^-), and other electrolytes. Lactated Ringer solution is a crystalloid that contains mostly Na^+ and Cl^- , but also lactate, potassium (K^+), and calcium (Ca^{2+}). Normosol-R and Plasma-Lyte are crystalloids that contain mostly Na^+ and Cl^- but also acetate, K^+ , and magnesium (Mg^{2+}). D_5W is also a crystalloid, but it should not be used for fluid resuscitation because of the smaller amount of fluid that remains in the intravascular compartment.
 - a. Na and Cl^- do not freely cross into cells, but they will distribute evenly in the EC space.
 - b. For 0.9% sodium chloride or lactated Ringer solution, only 25% remains in the intravascular space, and 75% distributes in the IS space; therefore, when 1 L of 0.9% sodium chloride or lactated Ringer solution is administered, about 250 mL of fluid remains in the intravascular compartment.
 2. D_5W is isosmotic and, because of rapid metabolism, it has the net effect of administering “free” water.
 - a. D_5W is metabolized to water and carbon dioxide.
 - b. Water can cross any membrane in the body; therefore, it is evenly distributed in TBF (“free” because it is free to cross any membrane).
 - i. Many experts avoid administering D_5W whenever possible in patients with neurologic injury and elevated intracranial pressure (ICP) because it can cross into cerebral cells, causing further elevation in ICP.
 - ii. Some practitioners avoid the use of D_5W because of the risk of hyperglycemia, although D_5W contains only 5 g of dextrose/100 mL, which is equivalent to 17 kcal/100 mL.
 - c. For D_5W , 60% distributes to the IC space and 40% distributes to the EC space. Of the 40% distributed to the EC space, 25% remains in the intravascular space, and 75% distributes to the IS space. Therefore, when 1 L of D_5W is administered intravenously, about 100 mL of fluid remains in the intravascular compartment.
 3. Colloids include packed red blood cells, pooled human plasma (5% albumin, 25% albumin, and 5% plasma protein fraction), semisynthetic glucose polymers (dextran), and semisynthetic hydroxyethyl starch (hetastarch).
 - a. Colloids are too large to cross the capillary membrane; therefore, they remain primarily in the intravascular space (although a small portion “leaks” into the IS space).
 - b. Except for 25% albumin, administering 500 mL of colloid results in a 500-mL intravascular volume expansion.
 - c. Because 25% albumin has an oncotic pressure about 5-fold that of normal plasma, it causes a fluid shift from the IS space into the intravascular space. For this reason, 100 mL of 25% albumin results in around 500 mL of intravascular volume expansion. This hyperoncotic solution should generally be avoided in patients requiring fluid resuscitation, because although the intravascular space expands, fluid shifts out of the IS space, potentially causing dehydration. It may be useful in patients who do not require fluid resuscitation but who could benefit from a redistribution of fluid (e.g., ascites, pleural effusions).
 - d. Hydroxyethyl starch and dextran products have been associated with coagulopathy and kidney impairment. In addition to acute kidney injury, hydroxyethyl starch is associated with increased mortality in critically ill patients (JAMA 2013;309:678-88; N Engl J Med 2012;367:124-34).
- C. Fluid Resuscitation
1. Intravascular fluid depletion can occur because of shock (hypovolemic or septic shock), and it is associated with reduced cardiac function and organ hypoperfusion.
 2. Signs or symptoms (Box 1) usually occur when about 15% (750 mL) of blood volume is lost (e.g., hemorrhage) or shifts out of the intravascular space (e.g., septic shock).

Box 1. Signs and Symptoms of Intravascular Volume Depletion

Tachycardia (HR > 100 beats/minute)
 Hypotension (SBP < 80 mm Hg)
 Orthostatic changes in HR or BP
 Increased BUN/SCr ratio > 20:1
 Dry mucous membranes
 Decreased skin turgor
 Reduced urine output
 Dizziness
 Improvement in HR and BP after a 500- to 1000-mL fluid bolus

BP = blood pressure; BUN = blood urea nitrogen; HR = heart rate; SBP = systolic blood pressure; SCr = serum creatinine.

3. Fluid resuscitation is indicated for patients with signs or symptoms of intravascular volume depletion.
4. The goal of fluid resuscitation is to restore intravascular volume and to prevent organ hypoperfusion.
5. Because intravascular volume depletion can cause organ dysfunction and death, prompt resuscitation is necessary.
 - a. Intravenous fluids are infused rapidly, preferably through a large-bore catheter.
 - b. Intravenous fluids are administered as a 500- to 1000-mL bolus, (~30 mL/kg in septic patients) after which the patient is reevaluated; this process is continued as long as signs and symptoms of intravascular volume depletion are improving (Box 1).

Table 2. Content of Common Crystalloid Solutions

	Contents (mEq/L)	Osmolarity (mOsmol/L)
Sodium chloride 0.9% (NS)	Na 154 Cl 154	308
Lactated Ringer (LR)	Na 130 Cl 109 K 4 Ca 3 Lactate 28	273
Normosol-R	Na 140 Cl 98 K 5 Mg 3 Acetate 27/Gluconate 23	295

Ca = calcium; Cl = chloride; K = potassium; Mg = magnesium; Na = sodium.

6. Crystalloids (0.9% sodium chloride or lactated Ringer solution) are recommended for fluid resuscitation in hypovolemia (Table 2).
 - a. Lactated Ringer solution is historically preferred in surgery and trauma patients, but no evidence suggests superiority over normal saline for fluid resuscitation in these settings.
 - b. The lactate in lactated Ringer solution is metabolized to bicarbonate, and it can theoretically be useful for metabolic acidosis; however, lactate metabolism is impaired during shock. Thus, lactated Ringer solution may be an ineffective source of bicarbonate.

- c. Lactated Ringer solution has been considered to provide a more physiologic amount of Cl (109 mmol/L) than 0.9% sodium chloride (154 mmol/L). A balanced fluid regimen (e.g., lactated Ringer solution, Plasma-Lyte 148) was associated with a reduction in the incidence of acute kidney injury compared with a standard regimen (e.g., 0.9% sodium chloride, colloids containing Cl 120–130 mmol/L) (JAMA 2012;308:1566). In a multicenter, retrospective cohort study, a balanced solution (lactated Ringer) was compared with isotonic fluid (0.9% sodium chloride) in patients with sepsis. In these patients with vasopressor-dependent sepsis, those receiving balanced fluid had a lower risk of in-hospital mortality (Crit Care Med 2014;42:1585-91). More recent studies have shown that, compared with 0.9% sodium chloride, balanced crystalloids result in a lower rate of a composite outcome of any cause of death, new renal replacement therapy, and persistent renal dysfunction in intensive care unit (ICU) patients. There was no difference found in hospital-free days in non-ICU patients (N Engl J Med 2018; 378:819-39).
 7. There is no difference between crystalloids and colloids in the time to achieve fluid resuscitation or in patient outcomes. Colloids have not been shown to be superior to crystalloids, and they are associated with higher cost and some adverse effects. The following are examples of other, although controversial, uses of colloids:
 - a. Colloids can be considered after fluid resuscitation with crystalloid (usually 4–6 L) has failed to achieve hemodynamic goals or after clinically significant edema limits the further administration of crystalloid.
 - b. Albumin can be considered in patients with a low albumin concentration who have required a large volume of resuscitation fluids.
 - c. Albumin (theoretically, 25% is preferred) can be considered in conjunction with diuretics for patients with clinically significant edema (e.g., pulmonary edema causing respiratory failure) and a low albumin concentration, when appropriately dosed diuretics are ineffective.
- D. Maintenance intravenous fluids
1. Maintenance intravenous fluids are indicated in patients who are unable to tolerate oral fluids.
 2. The goal of maintenance intravenous fluids is to prevent dehydration and to maintain a normal fluid and electrolyte balance.
 3. Maintenance intravenous fluids are typically administered as a continuous infusion through a peripheral or central intravenous catheter.
 4. Common methods of estimating the daily volume in children and adults:
 - a. Administer 100 mL/kg for first 10 kg, followed by 50 mL/kg for the next 10–20 kg (i.e., 1500 mL for the first 20 kg) plus 20 mL/kg for every kilogram greater than 20 kg *or*
 - b. Administer 20–40 mL/kg/day (for adults only).
 - c. Adjust fluids according to the individual patient's input, output, and estimated insensible loss.
 5. A typical maintenance intravenous fluid is D₅W with 0.45% sodium chloride plus 20–40 mEq of potassium chloride per liter. The potassium chloride content can be adjusted for the individual patient.
 6. If 150 mEq of sodium bicarbonate is added to 850 mL of 0.9% sodium chloride, the resultant solution is equivalent to about 1.6% sodium chloride. When an infusion of 150 mEq of sodium bicarbonate per liter is indicated, it is recommended to add sodium bicarbonate to D₅W or sterile water for injection instead of 0.9% sodium chloride.

Patient Case

Questions 1 and 2 pertain to the following case.

A 65-year-old man (weight 80 kg) with a 3-day history of a body temperature of 102°F (38.9°C), lethargy, and productive cough is hospitalized for community-acquired pneumonia. His medical history includes uncontrolled hypertension and coronary artery disease. His vital signs include heart rate 104 beats/minute, blood pressure 112/68 mm Hg, and body temperature 101.4°F (38.6°C). His urine output is 10 mL/hour, K 4 mEq/L, BUN is 46 mg/dL, SCr is 1.7 mg/dL, and WBC is 10.4×10^3 cells/mm³. Other laboratory values are normal.

1. Which is most appropriate at this time?
 - A. Furosemide 40 mg intravenously.
 - B. Albumin 25% 100 mL intravenously over 60 minutes.
 - C. Lactated Ringer solution 1000 mL intravenously over 60 minutes.
 - D. D₅W/0.45% sodium chloride plus potassium chloride 20 mEq/L to infuse at 110 mL/hour.
2. After 2 days of appropriate antibiotic treatment, the patient has a WBC of 9×10^3 cells/mm³, and he is afebrile. His blood pressure is 135/85 mm Hg, and his urine output is 45 mL/hour. His albumin is 3.2 g/dL, BUN is 14 mg/dL, and SCr is 1.4 mg/dL. All other laboratory values are normal. His appetite is still poor, and he is not taking adequate fluids. He has peripheral intravenous access. Which option is most appropriate to initiate?
 - A. Peripheral PN to infuse at 110 mL/hour.
 - B. Albumin 5% 500 mL intravenously over 60 minutes.
 - C. D₅W/0.45% sodium chloride plus potassium chloride 20 mEq/L to infuse at 110 mL/hour.
 - D. Lactated Ringer solution to infuse at 75 mL/hour.

II. OSMOLALITY

- A. Plasma osmolality is normally 275–290 mOsm/kg.
 1. Terminology
 - a. Osmolality is a measure of the osmoles of solute per kilogram of solvent (Osm/kg), whereas osmolarity is a measure of osmoles of solute per liter of solution (Osm/L).
 - b. Plasma osmolarity (mOsm/L) can be calculated as $\text{osmolality} \times 0.995$, showing that there is no clinically significant difference between them (i.e., plasma osmolarity is about 1% lower than plasma osmolality).
 2. Plasma osmolality is maintained within a normal range by thirst and secretion of arginine vasopressin (i.e., antidiuretic hormone [ADH]) from the posterior pituitary.
 3. Sodium salts are the primary determinant of plasma osmolality, and they regulate fluid shifts between the IC and EC fluid compartments.
 4. Plasma osmolality (mOsm/kg) can be estimated: $(2 \times \text{Na}^+ \text{ mEq/L}) + (\text{glucose mg/dL}/18) + [(\text{BUN mg/dL}) \div 2.8]$.
 5. Increases in plasma osmolality cause an osmotic shift of fluid into the plasma, resulting in cellular dehydration and shrinkage.
 6. Decreases in plasma osmolality cause an osmotic shift of fluid into cells, resulting in cellular overhydration and swelling.

- B. Intravenous fluids can be classified by their osmolarity relative to plasma.
1. Isotonic fluid does not result in a fluid shift between fluid compartments because the osmolarity is similar to plasma.
 2. Hypertonic fluid, such as NaCl 3%, can cause fluid to shift from the IC to the EC compartment, with subsequent cellular dehydration and shrinkage.
 3. Hypotonic fluid, such as NaCl 0.225%, with an osmolarity less than 150 mOsm/L can cause fluid to shift from the EC to the IC compartment, with subsequent cellular overhydration and swelling.
 - a. Red blood cell swelling can cause cell rupture (i.e., hemolysis).
 - b. Brain cells can swell, causing cerebral edema and herniation; this is most likely to occur with acute hyponatremia (occurring in less than 2 days).
- C. Definitions
1. Equivalent weight = Molecular weight (MW) divided by valence.
 - a. A milliequivalent (mEq) = 1/1000 of an equivalent.
 - b. Examples of equivalent weight are shown in Table 3.
 - c. 1 mol = equivalent weight

Table 3. Electrolyte MW, Valence, and Equivalent Weight

Electrolyte	MW	Valence	Equivalent Weight (g)
Sodium	23	1	23
Potassium	39	1	39
Chloride	35.5	1	35.5
Magnesium	24	2	12

MW = molecular weight.

2. Osmoles = number of particles in a solution (assuming complete dissociation).
 - a. A milliosmole = 1/1000 of an osmole.
 - b. Examples of osmoles are shown in Table 4.

Table 4. Osmoles

Salt	Osmoles
NaCl	2
KCl	2
CaCl ₂	3

CaCl₂ = calcium chloride; KCl = potassium chloride; NaCl = sodium chloride.

3. Converting MW to milliequivalents (Box 2)

Box 2. Converting MW to Milliequivalents

Convert 23.4% NaCl (concentrated NaCl) to mEq/mL
MW of NaCl = 23 + 35.5 = 58.5 (add MW of Na + Cl)
$\frac{23.4 \text{ g}}{100 \text{ mL}} \times \frac{1 \text{ equiv}}{58.5 \text{ g}} \times \frac{1000 \text{ mEq}}{1 \text{ equiv}} = 4 \text{ mEq/mL}$

MW = molecular weight; NaCl = sodium chloride.

D. Calculating the osmolarity of intravenous fluids in milliosmoles per liter

1. The osmotic coefficient can be used to calculate the osmolarity of intravenous fluids because salt forms do not completely dissociate in solution. However, commercially available products often have different reported osmolarities than if the osmolarity is calculated using the osmotic coefficient.
 - a. With sodium chloride, for example, there is some ionic attraction between Na^+ and Cl^- , and they do not completely dissociate; rather, they are about 93% dissociated in solution (thus, the osmotic coefficient is 0.93).
 - b. In clinical practice and in commercially available products, most do not consider the osmotic coefficient when calculating the osmolarity of sodium chloride or other electrolytes. In reality, the osmotic coefficient is probably not clinically relevant (but it is used in the following examples for completeness).
2. Normal saline (0.9% sodium chloride) (Table 5)

Table 5. Calculation for Normal Saline Using the Osmotic Coefficient

Molecular Weight	Osmoles	Osmotic Coefficient
58.5 g/mol	2	0.93
$\frac{0.9 \text{ g}}{100 \text{ mL}} \times \frac{1 \text{ mol}}{58.5 \text{ g}} \times \frac{2 \text{ Osm}}{1 \text{ mol}} \times \frac{1000 \text{ mOsm}}{1 \text{ Osm}} \times \frac{1000 \text{ mL}}{1 \text{ L}} \times 0.93 = 287 \text{ mOsm/L}$		

3. D₅W (MW 198 g/mol) (Box 3)

Box 3. Calculation for D₅W

$$\frac{5 \text{ g}}{100 \text{ mL}} \times \frac{1 \text{ mol}}{198 \text{ g}} \times \frac{1000 \text{ mOsm}}{1 \text{ mol}} \times \frac{1000 \text{ mL}}{1 \text{ L}} = 252.5 \text{ mOsm/L}$$

4. Osmolarity of D₅W/normal saline using the osmotic coefficient = 252.5 mOsm/L + 287 mOsm/L = 539.5 mOsm/L.
5. Osmolarity of normal saline + potassium chloride 20 mEq/L (Box 4)

Box 4. Calculation for NS plus KCl Using the Osmotic Coefficient**Step 1: Convert mEq to weight (g)**

$$20 \text{ mEq} \times \frac{1 \text{ equiv}}{1000 \text{ mEq}} \times \frac{74.5 \text{ g}}{1 \text{ equiv}} = 1.49 \text{ g of KCl}$$

Step 2: Calculate mOsm/L

$$\frac{1.49 \text{ g}}{\text{L}} \times \frac{1 \text{ mol}}{74.5 \text{ g}} \times \frac{2 \text{ Osm}}{1 \text{ mol}} \times \frac{1000 \text{ mOsm}}{1 \text{ Osm}} = 40 \text{ mOsm/L}$$

Step 3: Add osmolarity of NS + KCl = 287 mOsm/L + 40 mOsm/L = 327 mOsm/L

NS = normal saline; KCl = potassium chloride.

III. HYPERTONIC SALINE

- A. Concentration: Typically use 3% (954 mOsm/L), 7.5% (2393 mOsm/L), or 23.4% (7462 mOsm/L). Sodium chloride 3% and 23.4% are available commercially, whereas other concentrations must be extemporaneously prepared.
- B. Common uses of hypertonic saline
 - 1. Hypertonic saline is used in traumatic brain injury to reduce an elevated ICP and thereby increase cerebral perfusion pressure. It is typically used if sustained ICP is greater than 20 mm Hg as measured with an ICP monitor.
 - 2. Hypertonic saline is used for symptomatic hyponatremia (symptoms described later in the Hyponatremia section).
 - a. Symptoms generally do not occur unless serum sodium is 120 mEq/L or less, and they increase in severity as Na^+ decreases.
 - b. Symptoms of severe hyponatremia include coma and seizures.
 - c. In an effort to prevent severe symptoms from occurring, some practitioners treat asymptomatic or moderately symptomatic (e.g., lethargy, confusion) hyponatremia before serum sodium concentrations reach 120 mEq/L or less because of the increased risk of severe symptoms below this concentration.
- C. Inappropriate use of hypertonic saline
 - 1. Chronic asymptomatic hyponatremia
 - a. Asymptomatic syndrome of inappropriate secretion of antidiuretic hormone (SIADH) is usually treated with fluid restriction of less than 1000 mL of fluid per day.
 - b. Hyponatremia is generally a water problem (i.e., an excess of free water) rather than a deficiency of Na^+ ; thus, hypertonic saline makes little sense in the absence of symptoms (see Hyponatremia section).
 - 2. Hyponatremia associated with severe hyperglycemia (pseudohyponatremia; i.e., diabetic ketoacidosis)
 - a. Typically, serum sodium decreases in a nonlinear fashion in response to hyperglycemia (i.e., Na^+ decreases by about 1.6 mEq/L for every 100-mg/dL elevation in glucose of 100–400 mg/dL; however, another version of the formula shows that Na^+ decreases by about 2.4 mEq/L for every 100-mg/dL elevation in glucose above 100 mg/dL). $\text{Corrected Na}^+ = \text{serum Na}^+ + [1.6 (\text{glucose} - 100)/100]$
 - b. As hyperglycemia is corrected with insulin, the serum sodium will normalize.
 - 3. Hyponatremia associated with hypervolemia (i.e., heart failure leads to tissue hypoperfusion, which triggers ADH secretion, causing reabsorption of water from the kidneys and leading to hyponatremia)
 - a. In general, this situation is treated with fluid restriction or diuresis.
 - b. Symptomatic hyponatremia is uncommon in patients with heart failure.
 - c. Hypertonic saline could be considered in symptomatic patients; however, they may also need diuresis to prevent worsening volume overload.

- D. Preparation of hypertonic saline (Commercially available products should be used whenever possible to minimize the risk of error) (Figure 2)

Steps	Example
Choose base solutions	For this example, use concentrated NaCl available as 23.4% vials and sterile water to make 1000 mL of 7.5% HS
Set up alligation	<p>Diagram: 23.4% and 0 are connected by arrows to 7.5%.</p>
Add and subtract	<p>Diagram: 23.4% and 0 are connected by arrows to 7.5%. From 7.5%, arrows point to 7.5 parts (from 23.4% NaCl) and 15.9 parts (from sterile water). A line is drawn under 15.9 parts, and 23.4 parts total is written below it.</p>
Divide	$7.5 \text{ parts} / 23.4 \text{ parts} = x / 1000 \text{ mL}; x = 320.5 \text{ mL of } 23.4\% \text{ NaCl}$ $15.9 \text{ parts} / 23.4 \text{ parts} = x / 1000 \text{ mL}; x = 679.5 \text{ mL of sterile water}$

Figure 2. Calculations to prepare hypertonic saline.

HS = hypertonic saline; NaCl = sodium chloride.

E. Hypertonic saline dose

1. Dose options for traumatic brain injury and other neurological injuries
 - a. 3% hypertonic saline 250 mL or 2–4 mL/kg intravenously over 1–15 minutes administered for elevated ICP
 - b. 23.4% hypertonic saline 30 mL over 20–30 minutes administered for elevated ICP
 - i. Standing orders such as 30 mL every 4–6 hours are sometimes used or may be used as needed for a sustained ICP greater than 20 mm Hg.
 - ii. If hypertonic saline is needed for prolonged reduction in ICP, a 3% hypertonic saline continuous infusion may be recommended.
2. Dose options for patients with symptomatic hyponatremia
 - a. Treatment of patients with symptomatic hyponatremia involves a small but quick increase in serum sodium by 0.75–1 mEq/L/hour to a concentration of 120 mEq/L, though not more than 10–12 mEq in 24 hours. Next, the infusion can be reduced so that Na^+ increases by 0.5 mEq/L/hour. For severe symptoms, it is reasonable to increase serum sodium by up to 2 mEq/L/hour for a short time, as long as the maximum change of 10–12 mEq in 24 hours is not exceeded. If hypertonic saline is used for mild symptoms, a slower change in serum sodium of 0.5 mEq/L/hour would be appropriate, although some would avoid hypertonic saline altogether. Some protocols are more conservative, recommending a maximum change of 8 mEq in 24 hours. If the maximum rate is exceeded in 24 hours or the rate in sodium rise is increasing too rapidly, some practitioners recommend counteracting the quick rise with desmopressin or dextrose 5% in water (more info in hypernatremia section).
 - b. Estimate an infusion rate of 3% hypertonic saline by multiplying ideal body weight (IBW) by desired rate of serum sodium increase per hour. (Note: IBW is used to avoid overdosing patients with obesity.)
 - i. For example, $70 \text{ kg} \times 1 \text{ mEq/L/hour} = 70 \text{ mL/hour}$ to increase serum sodium by 1 mEq/L in 1 hour. The infusion can be adjusted to achieve goal changes in serum sodium.
 - ii. Infusion rate of 3% hypertonic saline is generally 1–2 mL/kg/hour.
 - iii. In general, 3% hypertonic saline is not recommended in asymptomatic patients; if used in an asymptomatic patient, the administration rate should generally not exceed 0.5–1 mL/kg/hour.

- c. Alternatively, some practitioners recommend a 250-mL bolus of 2%–3% hypertonic saline over 30 minutes or 50 mL of 3% hypertonic saline administered as a bolus every 30 minutes for two doses.
- F. Administration of hypertonic saline
 1. Use central intravenous access because the osmolarity is greater than 900 mOsm/L.
 2. If no central line is available, consider using 2% hypertonic saline.
 3. Some practitioners use 3% hypertonic saline through a peripheral intravenous access site in an emergency, because the osmolarity is close to the cutoff range for peripheral administration. Recent literature suggests that 3% sodium chloride can safely be administered through a peripheral line (J Neurosci Nurs 2017;49:191-5). If a peripheral site is used, use a large vein and monitor for phlebitis.
- G. Clinical goals and monitoring for administering hypertonic saline in patients with symptomatic hyponatremia
 1. Goals
 - a. Decrease symptoms (described later).
 - b. Safe serum sodium achieved usually in the range of 120–125 mEq/L to avoid adverse neurologic outcomes. Note that the immediate goal for patients with symptomatic hyponatremia is not necessarily a normal serum sodium.
 - c. Reached maximum safe amount of change in serum sodium
 - i. Maximum safe amount of change is generally regarded as 10–12 mEq/L in 24 hours.
 - ii. Some practitioners suggest a maximum change of 8 mEq/L in 24 hours.
 2. Monitoring of serum sodium every 1–4 hours depending on severity of symptoms
- H. Complications of hypertonic saline
 1. Osmotic demyelination syndrome (includes central pontine and extrapontine myelinolysis) can occur with rapid correction of hyponatremia.
 - a. It is characterized initially by lethargy and affect changes, followed by permanent neurologic damage, including paraparesis, quadriparesis, dysarthria, dysphagia, and coma.
 - b. It is more likely to occur with rapid correction of chronic hyponatremia than with acute hyponatremia. This partly explains why it is advisable not to administer hypertonic saline in patients with chronic asymptomatic hyponatremia.
 - c. Prevent this complication by avoiding changes in serum sodium of more than 10–12 mEq/L in 24 hours or more than 18 mEq/L in 48 hours.
 2. Hypokalemia can occur with large volumes of hypertonic saline.
 3. Hyperchloremic acidosis can result from the administration of chloride salts (i.e., sodium chloride). It can be prevented by administering hypertonic saline in a 1:1 or 2:1 ratio of sodium chloride and sodium acetate or using fluid with less chloride content.
 4. Hypernatremia
 5. Phlebitis if administered in a peripheral vein
 6. Heart failure
 - a. Fluid overload can result from initial volume expansion.
 - b. Over time, hypertonic saline can have a diuretic effect, leading to intravascular volume depletion.
 7. Coagulopathy caused by platelet dysfunction
 8. Hypotension if hypertonic saline is administered rapidly
- I. Other considerations when using hypertonic saline.
 - a. Because hypokalemia can cause hyponatremia, remember to correct K^+ depletion if present. As K^+ is replaced, serum sodium will increase.

IV. HYPOTONIC INTRAVENOUS FLUIDS

- A. Hypotonic fluids administered intravenously can cause cell hemolysis and patient death.
 - 1. Albumin 25% diluted with sterile water to make albumin 5% has an osmolarity of about 60 mOsm/L, which can cause hemolysis.
 - 2. “Quarter normal saline,” or 0.225% sodium chloride, has an osmolarity of 77 mOsm/L and can cause hemolysis.
- B. Avoid using intravenous fluid with an osmolarity less than 150 mOsm/L.
 - 1. Sterile water alone should *never* be administered intravenously.
 - 2. Some prescribers use hypotonic saline for a patient with hypernatremia.
 - a. In reality, a patient with mild hypernatremia generally needs water, not additional Na⁺.
 - b. Therefore, for patients with hypernatremia, enteral administration of water is preferable.
 - c. If the enteral route is unavailable, recommend D₅W administered intravenously.
- C. Prevent a potentially fatal error by recommending one of the following alternatives to 0.225% sodium chloride:
 - 1. Recommend changing 0.225% sodium chloride to D₅W alone or a combination of D₅W and 0.225% sodium chloride.
 - 2. Alternatively, if there are concerns related to hyperglycemia with using D₅W (50 g of dextrose or 170 kcal/L), recommend using 2.5% dextrose and 0.225% sodium chloride.
 - 3. Alternatively, potassium chloride can be added to increase osmolarity.
 - 4. Recommend administering water enterally (by mouth or feeding tube).
 - 5. If 0.225% sodium chloride is used, recommend use by central venous line.

V. HYPONATREMIA AND HYPO-OSMOLALITY STATES

- A. Sodium salts are the primary determinants of plasma osmolality (and subsequent fluid shifts between the IC and EC compartments).
 - 1. A reduction in serum sodium to less than 136 mEq/L usually correlates with a reduction in plasma osmolality.
 - 2. Hyponatremia with subsequent hypo-osmolality causes fluid to shift into cells (cellular overhydration). Hypotonic hyponatremia can be divided into three types according to volume status (Table 6).

Table 6. Classification of Hyponatremia

	Hypovolemic Hyponatremia	Euvolemic Hyponatremia	Hypervolemic Hyponatremia
Description	Deficit of both Na ⁺ and fluid, but total Na ⁺ is decreased more than total body water	Normal total body Na ⁺ with excess fluid volume (i.e., dilutional)	Excess Na ⁺ and fluid, but fluid excess predominates
Example	Fluid loss (e.g., emesis, diarrhea, fever), third spacing, renal loss (diuretics), cerebral salt wasting	SIADH, medications	Heart failure, cirrhosis, nephrotic syndrome
Diagnosis	Urine Na ⁺ < 25 mEq/L indicates nonrenal loss of Na ⁺ (e.g., emesis, diarrhea); urine Na ⁺ > 40 mEq/L indicates renal loss of Na ⁺ ^a	Urine osmolality > 100 mOsm/kg (indicates impaired water excretion in presence of plasma osmolality < 275 mOsm/kg); urine sodium > 40 mEq/L ^a	Urine Na ⁺ < 25 mEq/L indicates edematous disorders (i.e., heart failure, cirrhosis, nephrotic syndrome); urine Na ⁺ > 25 mEq/L indicates acute or chronic renal failure ^a
Treatment	Fluid resuscitation (see above); in patients with cerebral salt wasting because of a neurologic injury, hyponatremia can be prevented in patients with neurologic injuries with sodium chloride tablets or fludrocortisone	If drug-induced SIADH, remove offending agent; fluid restriction; demeclocycline; vasopressin receptor antagonists (e.g., conivaptan, tolvaptan), some institutions use urea	Sodium and water restriction; treat underlying cause; vasopressin receptor antagonists (e.g., conivaptan, tolvaptan), diuretics

Na⁺ = sodium; SIADH = syndrome of inappropriate secretion of antidiuretic hormone.

^aUrine Na⁺ measurement may be inaccurate if a patient is receiving diuresis.

3. In select cases, hyponatremia is associated with either a normal or an elevated plasma osmolality.
 - a. This is known as *pseudohyponatremia* because Na⁺ content in the body is not actually reduced. Instead, Na⁺ shifts from the EC compartment into the cells in an attempt to maintain plasma osmolality in a normal range. Another adaptation to increased plasma osmolality is the shift of water from inside cells to the EC compartment, which further dilutes the Na⁺ concentration.
 - i. Severe hyperlipidemia can be associated with a normal or elevated plasma osmolality.
 - ii. Severe hyperglycemia (i.e., during diabetic ketoacidosis) is associated with an elevated plasma osmolality.
 - b. Once the underlying condition is corrected, Na⁺ will shift out of the cells, and hyponatremia will resolve.

B. Causes of hyponatremia

1. Replacement of lost solute with water
 - a. Loss of solute (e.g., vomiting, diarrhea) usually involves the loss of isotonic fluid; therefore, alone, it will not cause hyponatremia.
 - b. After the loss of isotonic fluid, hyponatremia can develop when the lost fluid is replaced with water.
 - c. A common cause of hyponatremia in hospitals is the postoperative administration of hypotonic fluid.
2. Volume depletion and organ hypoperfusion stimulate ADH secretion to increase water reabsorption in the collecting tubules, potentially causing hyponatremia.
3. SIADH and cortisol deficiency are both related to the excessive release of ADH.

4. Medications, including thiazide diuretics, antiepileptic drugs (e.g., carbamazepine, oxcarbazepine), and antidepressants (especially selective serotonin reuptake inhibitors, but also tricyclic antidepressants), can cause hyponatremia. Drug-induced hyponatremia is more likely to occur in older adults and in those who drink large volumes of water.
5. Renal failure impairs the ability to excrete dilute urine, predisposing to hyponatremia.

C. Symptoms of hyponatremia (Table 7)

Table 7. Symptoms of Hyponatremia

Serum Sodium (mEq/L)	Clinical Manifestations
120–125	Nausea, malaise
115–120	Headache, lethargy, obtundation, unsteadiness, confusion
< 115	Delirium, seizure, coma, respiratory arrest, death

1. Symptoms are generally attributable to hypo-osmolality, with subsequent water movement into brain cells causing cerebral edema.
2. If hyponatremia occurs chronically, cerebral cell swelling is prevented by osmotic adaptation.
 - a. Solutes move out of brain cells to prevent the osmotic shift of water into brain cells.
 - b. For this reason, patients with chronic hyponatremia may show less severe or no symptoms.
3. Neurologic symptoms are related to the rate of change in the serum sodium and to the degree of change in serum sodium.
4. Acute hyponatremia occurs over 1–3 days.

D. Treatment of hyponatremia

1. Treat underlying cause.
2. Raise serum sodium at a safe rate, defined as a change no greater than 10–12 mEq/L in 24 hours.
3. Treatment depends on volume status, the presence and severity of symptoms, and the onset of hyponatremia.
 - a. If the patient is euvolemic or edematous, there are typically two treatment options:
 - i. Fluid restriction (to less than 1000 mL/day) is the typical first-line recommendation for asymptomatic patients. Note that sodium administration is not recommended for asymptomatic patients because it can worsen edema.
 - ii. Vasopressin antagonists (e.g., intravenous conivaptan, oral tolvaptan) can be used in euvolemic (i.e., SIADH) or hypervolemic (i.e., heart failure) patients to promote aquaresis, increase serum sodium, alleviate symptoms, and reduce weight; however, this approach is costly and has not been shown to improve clinical outcomes (i.e., fall prevention, hospitalization, hospital length of stay, quality of life, mortality) in prospective randomized controlled trials. Vasopressin antagonists are substrates and inhibitors of cytochrome P450 3A4 isoenzymes. Monitor for drug interactions with other 3A4 inhibitors that could increase effect and lead to a rapid increase in serum sodium. Fluid restriction in combination with a vasopressin antagonist during the first 24 hours can also increase the risk of overly rapid correction of serum sodium. If needed, fluid restriction can be used after 24 hours. Tolvaptan should not be administered for more than 30 days to minimize risk of liver injury. Monitor for recurrence of hyponatremia once treatment is discontinued. In hypervolemic hyponatremia, diuretics can also be used cautiously.

- b. If the patient has intravascular volume depletion, volume must be replaced first with intravenous crystalloids (e.g., 0.9% sodium chloride).
 - i. Until intravascular volume is restored, the patient will continue to secrete ADH, causing water reabsorption and subsequent hyponatremia.
 - ii. Once intravascular volume is restored, ADH secretion will decrease, causing water to be excreted. This can lead to a rapid correction of serum sodium; careful monitoring is necessary to prevent overly rapid correction.
 - iii. Volume status can be assessed by skin turgor, jugular venous pressure, and urine sodium.
 - c. Once intravascular volume is restored, patients who experienced volume depletion, diuretic-induced hyponatremia, or adrenal insufficiency may still need Na^+ .
 - i. The amount of Na^+ (in milliequivalents) needed to raise the serum sodium to a safe concentration of about 120 mEq/L (if the serum sodium is less than this) is estimated using LBW as follows: $0.5 (\text{LBW}) \times (120 - \text{Na}^+)$ for women (multiply LBW by 0.6 for men). LBW has been estimated using weight in kilograms and height in centimeters for men as $\text{LBW} = [(0.3)(\text{kg}) + (0.3)(\text{cm}) - 29]$ or for women as $\text{LBW} = [(0.3)(\text{kg}) + (0.4)(\text{cm}) - 43]$; formula published in 1966 (J Clin Pathol 1966;19:389).
 - ii. Alternatively, this equation can be modified to estimate the Na^+ deficit in the following manner: $0.5 (\text{LBW}) \times (140 - \text{Na}^+)$ for women (multiply LBW by 0.6 for men). If calculating the Na^+ deficit, it is recommended to administer 25%–50% of the deficit during the first 24 hours to prevent the overly rapid correction of serum sodium.
 - iii. Regardless of the method used to estimate Na^+ replacement, the amount of Na^+ administered should be guided by serial serum sodium concentrations (e.g., every 4 hours).
 - d. Patients with symptomatic hyponatremia should be treated with hypertonic saline (see Hypertonic Saline section).
4. Correct hypokalemia, if present, with hyponatremia.
- a. Hypokalemia will cause a reduction in serum sodium because Na^+ enters cells to account for the reduction in IC K^+ to maintain cellular electroneutrality.
 - b. Administration of K^+ will help correct hyponatremia.
 - c. Use caution when giving K^+ to prevent overly rapid correction of serum sodium.

Patient Case

Questions 3–5 pertain to the following case.

A 72-year-old woman (weight 60 kg) with a history of hypertension has developed hyponatremia after starting hydrochlorothiazide 3 weeks earlier. She experiences dizziness, fatigue, and nausea. Her serum sodium is 116 mEq/L. Her blood pressure is 86/50 mm Hg, and heart rate is 122 beats/minute.

3. In addition to discontinuing hydrochlorothiazide, which initial treatment regimen is best?
- A. Administer 0.9% sodium chloride infused at 100 mL/hour.
 - B. Administer 0.9% sodium chloride 500-mL bolus.
 - C. Administer 3% sodium chloride infused at 60 mL/hour.
 - D. Administer 23.4% sodium chloride 30-mL bolus as needed.

Patient Case (Cont'd)

4. Which is the best treatment goal for the first 24 hours in correcting the patient's serum sodium from her initial value of 116 mEq/L?
- A. Increase Na⁺ concentration to 140 mEq/L.
 - B. Increase Na⁺ concentration to 132 mEq/L.
 - C. Increase Na⁺ concentration to 126 mEq/L.
 - D. Maintain serum sodium of 116–120 mEq/L.
5. One day later, the patient has somewhat improved. Her blood pressure is 122/80 mm Hg, and heart rate is 80 beats/minute. Her serum sodium is 120 mEq/L, and K⁺ is 3.2 mEq/L; she still feels tired. She is eating a regular diet. Her ECG is normal. Which is the best recommendation?
- A. D₅W/0.9% sodium chloride plus potassium chloride 40 mEq/L to infuse at 100 mL/hour.
 - B. 0.9% sodium chloride infused at 100 mL/hour.
 - C. 3% sodium chloride infused at 60 mL/hour.
 - D. Potassium chloride 20 mEq by mouth every 6 hours for 4 doses.

VI. HYPERNATREMIA AND HYPEROSMOLAL STATES

- A. Hyperosmolality with serum sodium greater than 145 mEq/L
 - 1. The osmotic gradient associated with hypernatremia causes water movement out of cells and into the EC space.
 - 2. Symptoms are related primarily to the dehydration of brain cells.
- B. Causes of hypernatremia
 - 1. Loss of water because of fever, burns, infection, renal loss (e.g., diabetes insipidus), gastrointestinal (GI) loss
 - 2. Retention of Na⁺ because of the administration of hypertonic saline or any form of Na⁺
 - 3. Certain neurologic injuries receive hypertonic saline to target a higher sodium goal
- C. Prevention of hypernatremia through osmoregulation
 - 1. Plasma osmolality is maintained at 275–290 mOsm/kg, despite changes in water and Na⁺ intake.
 - 2. Hypernatremia is prevented first by the release of ADH, causing water reabsorption.
 - 3. Hypernatremia is also prevented by thirst.
 - a. Hypernatremia occurs primarily in adults with altered mental status who have an impaired thirst response or do not have access to or the ability to ask for water.
 - b. Hypernatremia can also occur in infants.
- D. Cerebral osmotic adaptation
 - 1. Similar to patients with hyponatremia, patients with chronic hypernatremia can have cerebral osmotic adaptation.
 - a. Brain cells take up solutes, Na⁺, and K⁺, thus limiting the osmotic gradient between the IC and EC fluid compartments.
 - b. This prevents cellular dehydration, and it will increase the brain volume toward a normal value, despite hypernatremia.
 - 2. Because of osmotic adaptation, patients with chronic hypernatremia may be asymptomatic.

- E. Symptoms of hypernatremia are primarily neurologic.
1. Similar to hyponatremia, the symptoms of hypernatremia are related to the rate of increase in plasma osmolality and the degree of increase in plasma osmolality.
 2. Earlier symptoms include lethargy, weakness, and irritability.
 3. Symptoms can progress to twitching, seizures, coma, and death if serum sodium is greater than 158 mEq/L. However, some neurologic injuries may have higher serum sodium targets.
 4. Cerebral dehydration can cause cerebral vein rupture with subsequent intracerebral or subarachnoid hemorrhage.
- F. Treatment of hypernatremia
1. Rapid correction of chronic hypernatremia can result in cerebral edema, seizure, permanent neurologic damage, and death.
 - a. With osmotic adaptation, the brain volume is raised toward normal despite an elevated serum osmolality.
 - b. Osmotic adaptation combined with a rapid reduction in plasma osmolality can cause an osmotic gradient, causing water to move into brain cells with subsequent cerebral edema.
 2. In patients with symptomatic hypernatremia, serum sodium should be reduced slowly by no more than 0.5 mEq/L/hour or 12 mEq/L/day.
 3. Treat hypernatremia by replacing water deficit slowly over several days to prevent overly rapid correction of serum sodium.
 - a. Using LBW, the estimated water deficit (in liters) is $(0.4 \times \text{LBW}) \times [(\text{Serum sodium}/140) - 1]$ in women (multiply LBW by 0.5 in men).
 - b. Note that in women and men, total body water is typically about 50% and 60%, respectively, of LBW. Thus, some sources recommend a variation on the earlier equation as follows: Water deficit = $(0.5 \times \text{LBW}) \times [(\text{Serum sodium}/140) - 1]$ in women (multiply LBW by 0.6 in men). However, patients with hypernatremia are generally water depleted; thus, the equation using the lower values above (i.e., 40% or 0.4 and 50% or 0.5) is reasonable.
 4. Administer free water orally or intravenously as D₅W.
 5. If concurrent Na⁺ and water depletion occur (e.g., vomiting, diarrhea, diuretic-induced depletion), use a combination of D₅W and 0.225% sodium chloride.
 6. If the patient is hypotensive because of volume depletion, first restore intravascular volume with 0.9% sodium chloride to restore tissue perfusion. Normal saline is the preferred crystalloid for fluid resuscitation, and it is still relatively hypotonic in the patient with hypernatremia.
 7. Patients with severe central diabetes insipidus may require desmopressin (DDAVP) (a synthetic analog of ADH) to replace insufficient or absent endogenous ADH. Diabetes insipidus is marked by increased urine output and decreased urine specific gravity.

Patient Case

6. A 74-year-old woman (weight 50 kg) has been receiving isotonic tube feedings at 60 mL/hour for the past 8 days through her gastrostomy feeding tube. She recently had an ischemic stroke; she is responsive but is not able to communicate. Her serum sodium was 142 mg/dL on the day the isotonic formula was initiated, and it has risen steadily to 149, 156, and 159 mg/dL on days 3, 4, and 8, respectively, after the start of the tube feedings. What is the best treatment for her hypernatremia?
- A. Administer sterile water intravenously at 80 mL/hour.
 - B. Administer D₅W intravenously at 80 mL/hour.
 - C. Administer D₅W/0.225% sodium chloride intravenously at 80 mL/hour.
 - D. Administer water by enteral feeding tube 200 mL every 6 hours.

VII. DISORDERS OF K⁺

- A. Normal plasma potassium concentrations are 3.5–5 mEq/L.
- B. K⁺ is the primary IC cation (maintains electroneutrality with Na, the primary EC cation).
- C. K⁺ balance is maintained between the IC and EC compartments by several factors, including the following:
 - 1. β₂-Adrenergic stimulation (caused by epinephrine) promotes cellular uptake of K⁺.
 - 2. Insulin promotes cellular uptake of K⁺.
 - 3. Plasma potassium concentration directly correlates with movement of K⁺ in and out of cells because of passive shifts based on the concentration gradient across the cell membrane. (A normal response to diarrhea-induced hypokalemia is for K⁺ to shift out of the cells passively, minimizing the reduction in plasma potassium concentration.)
- D. Normal plasma concentrations of K⁺ are maintained by renal excretion.
- E. Hypokalemia (K⁺ concentration less than 3.5 mEq/L)
 - 1. Causes of hypokalemia
 - a. Reduced intake seldom causes hypokalemia because renal excretion is minimized because of increased renal tubular absorption.
 - b. Increased shift of K⁺ into cells can occur with the following:
 - i. Alkalosis
 - ii. Insulin or a carbohydrate load
 - iii. β₂-Receptor stimulation caused by stress-induced epinephrine release or administration of a β-agonist (e.g., albuterol, dobutamine)
 - iv. Hypothermia
 - c. Increased GI losses of K⁺ can occur with vomiting, diarrhea, intestinal fistula, or enteral tube drainage, and chronic laxative abuse.
 - d. Increased urinary losses can occur with mineralocorticoid excess (e.g., aldosterone) and diuretic use (e.g., loops and thiazides).
 - e. Hypomagnesemia is commonly associated with hypokalemia caused by increased renal loss of K⁺; correction of plasma potassium requires simultaneous correction of serum magnesium.
 - 2. Symptoms of hypokalemia generally occur when plasma potassium is less than 3 mEq/L and can include the following:
 - a. Muscle weakness occurs most commonly in the lower extremities, but it can progress to the trunk, upper extremities, and respiratory muscles. Muscle weakness in the GI tract can manifest as paralytic ileus, abdominal distention, nausea, vomiting, and constipation.
 - b. ECG changes (flattened T waves or elevated U wave) occur.
 - c. Cardiac arrhythmias (bradycardia, heart block, ventricular tachycardia, ventricular fibrillation) occur.
 - d. Digoxin toxicity can occur despite normal serum digoxin concentrations in the presence of hypokalemia.
 - e. Rhabdomyolysis can occur because hypokalemia can cause reduced blood flow to skeletal muscle.
 - 3. Treatment of hypokalemia
 - a. K⁺ deficit can be estimated as 200–400 mEq of K⁺ for every 1 mEq/L reduction in plasma potassium (assuming a normal distribution of K⁺ between EC and IC compartments).
 - b. Although the K⁺ deficit can be estimated, K⁺ replacement is guided by K⁺ concentrations; recheck every 2–4 hours if K⁺ is less than 3 mEq/L.

- c. Potassium chloride is the preferred salt in patients with concurrent metabolic alkalosis because these patients typically lose Cl^- through diuretics or GI loss. This is the most common presentation of hypokalemia.
- d. Potassium acetate can be administered intravenously, or potassium bicarbonate can be administered orally for patients with a metabolic acidosis that requires frequent K^+ supplementation.
- e. Guidelines for administering K^+ (Table 8)

Table 8. K^+ Replacement

Plasma K^+ (mEq/L)	Treatment ^a	Comments
3–3.5	Oral KCl 40–80 mEq/day if no signs or symptoms (doses > 60 mEq should be divided to avoid GI adverse effects)	Recheck K^+ daily
2.5–3	Oral KCl 120 mEq/day (in divided doses) or IV 60–80 mEq administered at 10–20 mEq/hr if signs or symptoms	Monitor K^+ closely (i.e., 2 hr after infusion)
2–2.5	IV KCl 10–20 mEq/hr until normalized	Consider continuous ECG monitoring
< 2	IV KCl 20–40 mEq/hr until normalized	Requires continuous ECG monitoring

^aTreatment doses are for patients with normal kidney function and should be reduced for patients with kidney dysfunction or older adults.

ECG = electrocardiogram; GI = gastrointestinal; IV = intravenous; KCl = potassium chloride; K^+ = potassium.

- i. Patients without ECG changes or symptoms of hypokalemia can be treated with oral supplementation.
- ii. Avoid mixing K^+ in dextrose, which can cause insulin release with a subsequent IC shift of K^+ .
- iii. To avoid irritation, no more than about 60–80 mEq/L should be administered through a peripheral vein.
- iv. Recommended infusion rate is 10–20 mEq/hour to a maximum of 40 mEq/hour.
- v. Patients who receive K^+ at rates faster than 10–20 mEq/hour should be monitored using a continuous ECG.

F. Hyperkalemia

1. Causes of hyperkalemia

- a. Increased intake
- b. Shift of K^+ from the IC to the EC compartment causes hyperkalemia and can occur with the following:
 - i. Acidosis
 - ii. Insulin deficiency
 - iii. β -Adrenergic blockade
 - iv. Digoxin overdose
 - v. Rewarming after hypothermia (e.g., after cardiac surgery)
 - vi. Succinylcholine
- c. Reduced urinary excretion can occur with:
 - i. Kidney dysfunction
 - ii. Intravascular volume depletion
 - iii. Hypoaldosteronism
 - iv. K^+ -sparing diuretics
 - v. Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers
 - vi. Trimethoprim

2. Symptoms of hyperkalemia
 - a. Muscle weakness or paralysis is caused by changes in neuromuscular conduction; it typically occurs when plasma potassium exceeds 8 mEq/L.
 - b. Abnormal cardiac conduction can first manifest as peaked, narrowed T waves (typically, when plasma potassium exceeds 6 mEq/L) and widening of the QRS, and it can progress to ventricular fibrillation and asystole.
 - c. Not all patients will experience ECG changes, and the initial manifestation of hyperkalemia can be ventricular fibrillation; thus, consider emergency treatment even in patients with no ECG changes if plasma potassium exceeds 6.5 mEq/L.
 - d. Conduction disturbances are increased by hypocalcemia, hyponatremia, acidosis, and rapid elevation in the plasma potassium concentration.
3. Pseudohyperkalemia should be considered if there is no apparent cause or symptoms of hyperkalemia.
 - a. Can occur if K^+ is released from cells while or after obtaining the blood specimen, usually because of trauma during venipuncture (hemolysis)
 - b. Can result from measurement of the serum rather than the plasma potassium concentration; caused by K^+ release during coagulation
 - c. Contamination of blood specimen with potassium-containing intravenous fluids or parenteral nutrition
4. Treatment of hyperkalemia
 - a. Patients with an asymptomatic elevation in the plasma potassium who do not have signs or symptoms can be treated with a cation exchange resin (e.g., sodium polystyrene sulfonate) alone.
 - b. Urgent and immediate treatment is required for patients with the following signs or symptoms:
 - i. Plasma potassium greater than 6.5 mEq/L
 - ii. Severe muscle weakness
 - iii. ECG changes
 - c. Calcium should be administered intravenously to patients with symptomatic hyperkalemia to prevent hyperkalemia-induced arrhythmias, even if patients demonstrate normocalcemia.
 - i. Calcium gluconate can be administered peripherally, and it is preferred to calcium chloride because of a reduced risk of tissue necrosis; dose is 10 mL (equivalent to 1 g, 90 mg elemental, or 4.65 mEq) of 10% calcium gluconate administered over 2–10 minutes. It can be repeated in 5 minutes if no improvement in ECG. Calcium chloride can be used if central intravenous access is available; however, the dose should be adjusted because 10 mL (1 g, 270 mg elemental, or 13.6 mEq) provides 3-fold the amount of elemental Ca as calcium gluconate.
 - ii. Onset is within minutes, but duration is short (30–60 minutes).
 - iii. It does not reduce plasma potassium, but it antagonizes the effect of K^+ in cardiac conduction cells
 - iv. Use in urgent circumstances while waiting for other measures (e.g., insulin and glucose) to lower plasma potassium.
 - v. Use caution in patients receiving digoxin because hypercalcemia can precipitate digoxin toxicity, and there are reports of sudden death.
 - d. The following treatment options are transient, causing a temporary shift of K^+ from the EC fluid into the cells, and should be used for symptomatic hyperkalemia.
 - i. Insulin and glucose
 - (a) Dose is regular insulin 10 units intravenously plus 25–50 g of dextrose administered as a 50% dextrose intravenous push to prevent hypoglycemia.
 - (b) Typically lowers plasma potassium by 0.5–1.5 mEq/L within 1 hour and may last for several hours
 - (c) If patients have hyperglycemia, insulin alone can be administered.

- (d) More predictable than sodium bicarbonate or β_2 -adrenergic agonists in patients with kidney failure
- (e) Caution with increased risk of insulin errors when used in emergencies (e.g., incorrectly preparing insulin infusions). Errors involving calculations (100 units/mL) and use of 5- or 10-mL syringes instead of an insulin syringe are possible.
- (f) Monitor for signs and symptoms of hypoglycemia even if dextrose is given
- ii. Sodium bicarbonate
 - (a) Dose is 50 mEq of intravenous sodium bicarbonate infused slowly over 5 minutes; it can be repeated after 30 minutes if needed.
 - (b) It can lower plasma potassium within 30–60 minutes and persist for several hours.
 - (c) The efficacy of bicarbonate is disputed, and it seems least effective in patients with advanced kidney disease; it may be effective in patients with underlying metabolic acidosis. Sodium bicarbonate use has recently been limited by shortages. Its use should be reserved for other conditions during shortages.
- iii. β_2 -Adrenergic agonists (e.g., albuterol)
 - (a) Dose is albuterol 10–20 mg nebulized over 10 minutes or 0.5 mg intravenously (not available in the United States).
 - (b) The dose will lower plasma potassium by 0.5–1.5 mEq/L.
 - (c) Onset is within 30 minutes with inhalation.
 - (d) Avoid use in patients with coronary ischemia because of the risk of tachycardia.
 - (e) Up to 40% of patients do not respond to inhaled albuterol (especially patients taking β -blockers); therefore, it is not recommended as a single agent for urgent treatment of hyperkalemia. Consider use in combination with insulin.
- e. The previous treatment options should be followed by one of the following agents to remove excess K^+ from the body.
 - i. Diuretics
 - (a) Loop or thiazide-type diuretics increase K^+ renal excretion.
 - (b) Ineffective in patients with advanced kidney disease
 - ii. Cation exchange resins
 - (a) Sodium polystyrene sulfonate exchanges Na^+ for K^+ , resulting in GI excretion of K^+ . Exercise caution in patients with kidney disease or heart failure caused by Na^+ (and subsequent fluid) retention.
 - (b) Because of its slow onset (2 hours) and unpredictable efficacy, sodium polystyrene sulfonate is not indicated for emergency treatment of hyperkalemia.
 - (c) It was approved by the U.S. Food and Drug Administration in 1958, before demonstrated efficacy was required. No controlled trials show efficacy.
 - (d) Oral dose of sodium polystyrene sulfonate is 15 g repeated every 6 hours as needed. This can be mixed in 20–100 mL of water or syrup, but it is no longer recommended to mix in 70% sorbitol because of the risk of intestinal necrosis (there are also reports with the premixed 33% sorbitol suspension, but 70% sorbitol appears to have a stronger correlation with intestinal necrosis). Bowel injury is linked to the deposition of drug crystals in the GI tract. Oral sorbitol can prevent constipation associated with the resin; however, the highest risk of intestinal necrosis occurs when administered to patients within 1 week of surgery (occurs in about 1.8% of patients).
 - (e) Although the oral route is more effective, 30–50 g can also be given as a retention enema mixed in 100–200 mL of an aqueous vehicle (e.g., water, 10% dextrose) that has been warmed to body temperature and kept in the colon for 30–60 minutes, or up to 3 hours. Irrigate the colon afterward. Sorbitol is not recommended as a vehicle for rectal use because of the risk of intestinal necrosis and other serious GI adverse events.

- (f) A systematic review found that GI injury is also associated with sodium polystyrene preparations without sorbitol (Am J Med 2013;126:264).
 - (g) Two potassium binders have recently been approved for use in hyperkalemia. As opposed to sodium polystyrene sulfonate, patiomer exchanges Ca^{2+} for K^+ , resulting in GI excretion of K^+ . As with other binders, caution should be used if patiomer is administered with other medications because it may reduce their absorption. Like sodium polystyrene sulfonate, patiomer should not be used for life-threatening hyperkalemia, because it has a slower onset of action. The other potassium-binding agent, sodium zirconium cyclosilicate, works by exchanging potassium for hydrogen and sodium.
- iii. Dialysis
- (a) It is used when other measures are ineffective or when severe hyperkalemia is present.
 - (b) Plasma potassium falls by more than 1 mEq/L in the first hour of dialysis and by about 2 mEq/L after 3 hours of dialysis.
 - (c) Hemodialysis removes K^+ faster than peritoneal dialysis.
 - (d) Monitor for rebound increase in K^+ after dialysis.
 - (e) It is used in patients with advanced kidney disease

Patient Case

7. A 61-year-old man comes to the emergency department with shortness of breath and bilateral lower leg edema. Pertinent vital signs and laboratory values include heart rate 30 beats/minute, blood pressure 102/57 mm Hg, K^+ 7.9 mEq/L, Na^+ 139 mEq/L, glucose 278 mg/dL, Ca^{2+} 8.8 mg/dL, digoxin 2.2 ng/mL, BUN 49 mg/dL, and SCr 2.4 mg/dL. His ECG shows wide QRS and peaked T waves. His medical history includes heart failure, atrial fibrillation, coronary artery disease, peripheral arterial disease, and diabetes. The patient has peripheral intravenous access and an external pacemaker. Which treatment is most appropriate?
- A. Calcium gluconate 10 mL intravenously over 2 minutes.
 - B. Insulin 10 units intravenously.
 - C. Sodium bicarbonate 50 mEq intravenously over 10 minutes.
 - D. Albuterol 10 mg nebulized over 10 minutes.

VIII. DISORDERS OF MAGNESIUM HOMEOSTASIS

- A. Normal serum magnesium concentration is 1.7–2.3 mg/dL (1.4–1.8 mEq/L or 0.85–1.15 mmol/L).
- B. Hypomagnesemia (serum magnesium concentration less than 1.7 mg/dL)
 - 1. Usually associated with impaired intestinal absorption (e.g., ulcerative colitis, diarrhea, pancreatitis, chronic laxative abuse), inadequate intake, hypokalemia, or increased renal excretion (e.g., diuretic use)
 - a. Common in hospitalized patients
 - b. Often associated with alcoholism and delirium tremens
 - 2. Often occurs concurrently with hypokalemia and hypocalcemia
 - 3. Signs and symptoms
 - a. Neuromuscular symptoms include tetany, twitching, and seizures.
 - b. Cardiovascular symptoms include arrhythmias, sudden cardiac death, and hypertension.
 - 4. Treatment
 - a. Oral supplements (e.g., magnesium oxide, magnesium-containing antacids, or laxatives) can be used for asymptomatic patients; however, treatment is limited by the high frequency of diarrhea.

- b. Symptomatic patients should initially be treated with 1–4 g (8–32 mEq) of magnesium sulfate by slow intravenous infusion (about 1 g/hour to avoid hypotension or increased renal excretion because of rapid administration). Initial boluses can be followed by about 0.5 mEq/kg/day added to intravenous fluid and administered as a continuous infusion. For emergency treatment (e.g., torsades), magnesium can be administered by intravenous push. Asymptomatic patients with mild to moderate hypomagnesemia should also be treated with 1–4 g of magnesium sulfate by slow intravenous infusion.
 - c. Reduce the dose by half in patients with kidney insufficiency.
 - d. About half of administered magnesium is excreted in the urine; therefore, magnesium replacement can occur over 3–5 days.
 - e. Intravenous magnesium has also been affected by shortages. Reserve use for symptomatic patients.
- C. Hypermagnesemia (serum magnesium greater than 2.3 mg/dL)
- 1. Rarely occurs and is generally associated with chronic kidney disease
 - 2. Signs and symptoms include nausea, vomiting, bradycardia, hypotension, heart block, asystole, respiratory failure, and death; signs and symptoms rarely occur unless magnesium concentration is greater than 4–5 mg/dL.
 - 3. Treatment
 - a. Discontinue all magnesium-containing medications.
 - b. Asymptomatic patients with normal kidney function can be treated with 0.9% sodium chloride and loop diuretics.
 - c. Symptomatic patients should be treated with 100–200 mg of elemental Ca^{2+} administered intravenously over 5–10 minutes for cardiac stability.
 - d. Hemodialysis may be needed for patients with kidney disease.

IX. DISORDERS OF PHOSPHORUS HOMEOSTASIS

- A. Normal serum phosphorus concentration is 2.5–4.5 mg/dL.
- B. Hypophosphatemia (serum phosphorus concentration less than 2.5 mg/dL)
- 1. Causes of hypophosphatemia
 - a. Increased renal elimination (e.g., diuretics, glucocorticoids, sodium bicarbonate)
 - b. Rapidly feeding patients with chronic malnutrition (see “refeeding syndrome” in Parenteral Nutrition section)
 - c. Respiratory alkalosis
 - d. Treatment of diabetic ketoacidosis; phosphorus shifts into the IC compartment as diabetic ketoacidosis is corrected
 - 2. Signs and symptoms
 - a. Tissue hypoxia can occur because of a decrease in oxygen release to peripheral tissues.
 - b. Neurologic manifestations include confusion, delirium, seizures, and coma.
 - c. Pulmonary and cardiac symptoms can include respiratory failure, difficulty weaning from mechanical ventilation, heart failure, and arrhythmias.
 - d. Other organ systems affected include muscle, hematologic, bone, and kidney.
 - 3. Prevention and treatment
 - a. Prevent hypophosphatemia by supplementing intravenous fluid with 10–30 mmol/L intravenous phosphorus in patients at risk of hypophosphatemia (e.g., malnourished, alcoholism, diabetic ketoacidosis).

- b. Oral phosphorus products (e.g., K-Phos Neutral; also contain K^+ and Na) can be used for asymptomatic patients, but they are poorly absorbed.
 - c. Symptomatic patients typically receive 15–30 mmol and sometimes up to 60 mmol (or 0.5–0.75 mmol/kg of IBW) of phosphorus (sodium phosphate or potassium phosphate) administered intravenously over 3–6 hours (maximum rate is 7.5 mmol/hour). Note Na^+ content (4 mEq per 3 mmol of phosphate) and K^+ content (4.4 mEq per 3 mmol of phosphate).
- 4. Phosphate shortages
 - a. Reserve phosphate products for patients who need them most (e.g., children, neonates, diabetic ketoacidosis, refeeding syndrome, critically ill patients).
 - b. Intravenous fat emulsions contain 15 mmol/L as egg phospholipids; this may be sufficient phosphate for some patients.
- C. Hyperphosphatemia
 - 1. It typically occurs in patients with chronic kidney disease or hypoparathyroidism.
 - 2. In general, patients are asymptomatic, but they can have signs and symptoms including hypocalcemia, ECG changes, paresthesias, and vascular calcifications.
 - 3. For treatment, see Treatment of Hyperphosphatemia in the Nephrology chapter.

X. DISORDERS OF CALCIUM HOMEOSTASIS

- A. Normal serum calcium concentration is 8.5–10.5 mg/dL (total Ca^{2+} includes bound and unbound Ca^{2+}), and normal ionized calcium is 1.1–1.3 mmol/L (or 4.4–5.3 mg/dL).
- B. Distribution of Ca^{2+}
 - 1. EC fluid contains less than 1% of the total body stores of Ca^{2+} ; 99% of total body stores of Ca^{2+} are in skeletal bone.
 - a. About half of Ca^{2+} in the EC compartment is bound to plasma proteins (primarily albumin).
 - b. The active form of Ca^{2+} is the unbound or ionized Ca^{2+} .
 - 2. Ionized Ca^{2+} is regulated by parathyroid hormone, phosphorus, vitamin D, and calcitonin.
- C. Hypocalcemia
 - 1. It occurs in patients with chronic kidney disease, hypoparathyroidism, vitamin D deficiency, alcoholism, and hyperphosphatemia, and in patients receiving large amounts of blood products or patients undergoing continuous renal replacement therapy (CRRT [i.e., Ca^{2+} chelates with citrate used as anticoagulation in blood products or for plasmapheresis or CRRT.])
 - 2. Factors that cause an increase in EC Ca^{2+} binding to albumin (e.g., metabolic alkalosis) can cause a reduction in plasma ionized Ca^{2+} concentration, leading to symptomatic hypocalcemia.
 - 3. A low serum albumin will cause a falsely low total serum calcium reading; therefore, an adjustment is necessary. Subtract a patient's serum albumin from a normal serum albumin of 4 g/dL, multiply by 0.8 mg/dL, and then add to the total serum calcium concentration to correct the value. An ionized calcium level may be a more accurate measure of calcium in critically ill patients.
 - 4. Signs and symptoms include tetany, muscle spasms, hypoactive reflexes, anxiety, hallucinations, lethargy, hypotension, and seizures.
 - 5. Treatment
 - a. Asymptomatic hypocalcemia associated with hypoalbuminemia is typically associated with normal ionized Ca^{2+} concentrations and therefore does not require treatment.

- b. Asymptomatic hypocalcemia can be treated with oral Ca^{2+} supplements at a dose of 2–4 g/day of elemental Ca^{2+} in divided doses; patients may also require vitamin D supplementation.
- c. Symptomatic hypocalcemia is treated with 200–300 mg of elemental Ca^{2+} administered intravenously over 5–10 minutes; this is sometimes followed by a continuous infusion.
 - i. Equivalent to 1 g of calcium chloride (273 mg of elemental Ca^{2+}) administered through a central intravenous catheter; peripheral administration of calcium chloride can result in severe limb ischemia
 - ii. Equivalent to 2–3 g of calcium gluconate (180–270 mg of elemental Ca^{2+}); preferred for peripheral intravenous administration
 - iii. Do not infuse Ca^{2+} at a rate faster than 60 mg of elemental Ca^{2+} per minute; rapid administration, which is not recommended, is associated with hypotension, bradycardia, or asystole.
 - iv. The duration of an intravenous dose of Ca^{2+} is ideally 1–2 hours. If a continuous infusion is used, the rate should be 0.5–2 mg/kg/hour of elemental Ca^{2+} .
- 6. Calcium shortages
 - a. If there is a shortage of calcium gluconate, do not add calcium chloride to PN. Use multielectrolyte products in PN, if possible.
 - b. The safety of diluted calcium chloride administered peripherally is unknown.
- D. Hypercalcemia (serum calcium concentration greater than 10.5 mg/dL) is usually related to malignancy or hyperparathyroidism; see the chapters on Oncology Supportive Care and Nephrology.

XI. ENTERAL NUTRITION

- A. Indication and timing: EN is used in patients who are at risk of malnutrition and in whom it is anticipated that oral feedings will be inadequate for 5–7 days. Malnutrition is associated with poor wound healing and increased risk of infection. According to the American Society for Parenteral and Enteral Nutrition (ASPEN) guidelines, well-nourished adults without excessive metabolic stress can usually tolerate little to no nutrition for up to 7 days. The 2016 ASPEN and Society of Critical Care Medicine (SCCM) guidelines for critically ill patients recommend starting enteral feeding within the first 24–48 hours after intensive care unit admission.
- B. EN contraindications
 - 1. Complete intestinal obstruction
 - 2. GI fistula (if a feeding tube cannot be placed distal to the fistula or if high-output fistula, which is defined as greater than 500 mL of output per day)
 - 3. Extremely short bowel
 - 4. Severe diarrhea or vomiting
 - 5. Hemodynamic instability or intestinal ischemia
 - 6. Paralytic ileus (however, many patients can be fed through the small bowel, despite an ileus)
 - 7. Absence of bowel sounds is not a contraindication for the provision of EN (i.e., positive bowel sounds are not required for EN initiation), which promotes gut motility
- C. EN administration routes
 - 1. Large-bore orogastric and NG tubes
 - a. NG tubes are the most common tubes for short-term enteral access.
 - b. Orogastric tubes are preferred in patients with nasal or facial trauma or sinusitis, but they are uncomfortable for alert patients.

- c. These tubes can be used for stomach decompression in addition to feeding.
 - d. Prolonged use can cause sinusitis or nasal mucosal ulceration.
 - e. Patients with a gastric ileus will not tolerate NG feedings, and there is an increased risk of aspiration.
 - 2. Small-bore feeding tubes
 - a. These tubes are most commonly placed through the nose, but they can also be placed orally in patients with nasal or facial trauma or sinusitis
 - b. They can be placed with the feeding tube tip terminating in the stomach, but because they are smaller and more flexible than NG tubes, they can also be placed past the pyloric sphincter to improve tube feeding tolerance and prevent aspiration.
 - c. Nasoduodenal tubes are also smaller than NG tubes, and they can clog from crushed medications if they are not flushed appropriately. Nasojejunal tubes are advanced into the fourth portion of the duodenum or past the ligament of Treitz.
 - d. Patients with a gastric ileus or gastroparesis may tolerate feeding by the nasoduodenal or nasojejunal route.
 - 3. Percutaneous endoscopic gastrostomy tubes are placed through the abdominal wall into the stomach for patients requiring long-term feeding; jejunostomy tubes are placed through the abdominal wall into the jejunum, usually to facilitate immediate postoperative or postinjury feeding
- D. EN delivery
- 1. Gravity control refers to delivery with tubing that is fitted with a roller clamp to allow infusion into the stomach as desired.
 - 2. Continuous infusion by an enteral feeding pump is usually used in hospitals because of the lower risk of aspiration compared with bolus feedings; it must be used for duodenal or jejunal feedings.
 - 3. Cyclic feedings are administered continuously for 10–12 hours (overnight) to facilitate patient mobility during the daytime.
 - 4. Intermittent bolus feedings of 100–300 mL for 30–60 minutes every 4–6 hours can be used only for feeding tubes ending in the stomach in stable patients.
- E. Benefit of EN
- 1. EN is preferred in patients with a functional GI tract because it is associated with a lower risk of infection than PN. Early administration of EN is associated with lower rates of infection and shorter lengths of stay.
 - 2. GI mucosal atrophy occurs with an absence of EN or oral nutrition. This can increase the risk of bacterial translocation because of gut bacteria crossing the weakened intestinal barrier.
- F. EN formulations
- 1. Formulations typically contain carbohydrate, fat, protein, electrolytes, water, vitamins, and trace elements in varying amounts.
 - 2. Intact or polymeric formulas are used in patients with normal digestive processes, and they typically contain 1–1.2 kcal/mL.
 - a. These are generally inexpensive and an appropriate first choice for many patients.
 - b. Some polymeric formulas are concentrated for patients requiring fluid restriction and contain 2 kcal/mL.
 - c. Some polymeric formulas are designed for oral administration and are used to supplement the patient's diet.
 - 3. Elemental or semi-elemental formulas are easily digested by patients with impaired digestive capacity or malabsorption (e.g., short bowel, pancreatic insufficiency); they are typically more expensive than polymeric EN.

4. Some EN contains fiber for patients with constipation. Examples include Replete with Fiber and Jevity.
5. Disease-specific EN
 - a. EN formulations for patients with renal failure are typically concentrated (i.e., 2 kcal/mL to adhere to fluid restrictions) and can contain differing amounts of protein and electrolytes.
 - b. Some EN products designed for patients with respiratory failure have more calories from fat (40%–55% of total calories) and fewer from carbohydrates to reduce the production of CO₂ and facilitate ventilator weaning. However, excessive CO₂ production is caused primarily by overfeeding with total calories rather than the total amount of carbohydrates; therefore, these more expensive formulations may be unnecessary as long as the patient is not being overfed.
 - c. EN formulations for patients with diabetes have more calories from fat, fewer calories from carbohydrates, and added fiber to improve glycemic control.
 - d. EN formulations for patients with hepatic failure and hepatic encephalopathy contain more branched-chain AAs and fewer aromatic AAs, which may improve encephalopathy (controversial), but are not commonly used.
 - e. EN for highly stressed patients (e.g., trauma, burn injury, acute respiratory distress syndrome, sepsis) is enhanced with protein, arginine, glutamine, omega-3 fatty acids, nucleotides, or beta-carotene. These enteral formulations are designed to improve immune function and clinical outcomes. Immune-modulating formulas are recommended for surgical ICU patients in the postoperative setting, but are not recommended for the medical ICU population.
 - f. Specialty formulas are not recommended for routine use in a general ICU setting.
- G. EN complications
 1. Improper tube placement or displacement
 2. Clogged feeding tubes
 - a. Prevent by flushing feeding tube before, between, and after the administration of each drug. The use of liquid formulations of medications, if available, is also recommended.
 - b. Unclog feeding tubes with warm water or a pancreatic enzyme solution mixed with oral sodium bicarbonate. Avoid using cola or juice.
 3. Aspiration
 - a. Prevent by keeping the head of bed elevated at 30–45 degrees.
 - b. Prevent delays in gastric emptying using an EN formula with less fat. Gastric motility can be increased with metoclopramide (5–10 mg intravenously every 6 hours) or erythromycin (250 mg intravenously every 6–8 hours administered until tolerating EN for at least 24 hours). Metoclopramide and erythromycin can be combined, but monitor for diarrhea and tachyphylaxis. Avoid prolonged use of promotility agents because of increased risk of adverse effects.
 - c. Administering EN by a feeding tube with the tip terminating beyond the pyloric sphincter can prevent aspiration pneumonia.
 - d. Prevent also by initiating EN at a slow rate (e.g., 20 mL/hour) and advance every 4–6 hours as tolerated to goal rate.
 4. Diarrhea
 - a. It is more common with products with a higher osmolarity.
 - b. Consider other causes of diarrhea such as antibiotic use, infection, lactose intolerance, magnesium, and sorbitol in liquid medication preparations (e.g., liquid acetaminophen, liquid loperamide).
 5. Constipation can be prevented by adding fiber or bowel stimulation.
 6. Dehydration

7. Hyponatremia occurring when patients are given insufficient water while receiving EN
 - a. Patients require about 30 mL/kg/day of water.
 - b. Hyponatremia typically occurs in patients with altered mental status who may be unable to communicate thirst.
 - c. Calorie-dense (i.e., 1.5 or 2 kcal/mL) EN formulas have less water than products containing 1 kcal/mL; therefore, additional water is needed to prevent hyponatremia.
8. Nasopharyngeal erosions, epistaxis, tracheoesophageal fistula
9. Sinusitis
10. Electrolyte abnormalities most likely to occur in patients who develop refeeding syndrome (discussed later)

Patient Case

8. A 72-year-old woman (weight 65 kg) is switched from a standard enteral formula to a concentrated tube feeding designed for patients with kidney disease, because of hyperkalemia. The patient's baseline and current SCr is 1.7 mg/dL, and her urine output is about 50 mL/hour. The tube feeding is infusing at a goal rate of 35 mL/hour through an NG feeding tube providing 2 kcal/mL, Na⁺ 41 mEq/L, and 717 mL/L of water. The patient's serum sodium was 140 mEq/L when the tube feeding was initiated a few days ago, and her Na⁺ is now 145 mEq/L. What is the best approach for preventing hyponatremia in this patient?
- A. Change to an EN formula with a lower concentration of Na⁺.
 - B. Administer intravenous D₅W at 45 mL/hour.
 - C. Administer 200 mL of water through a feeding tube every 4 hours.
 - D. Reduce the tube feeding to 30 mL/hour.

- H. EN monitoring
1. Blood glucose concentration
 2. Head of bed elevation to 30–45 degrees
 3. GI tolerance
 - a. Abdominal pain or distension
 - b. Stool frequency and volume
 - c. Nausea, vomiting, and diarrhea
 - d. Checking gastric residuals is not recommended
 4. Prealbumin weekly (exception: Caution in critically ill patients because it reflects acute-phase response rather than nutritional status); see goals in the Parenteral Nutrition section.
 5. Serum sodium and other electrolytes
 6. Wound healing a sign of adequate nutritional therapy
 7. Other medications that add additional calories (e.g., propofol, clevidipine) that require EN rates to be adjusted

I. Developing an EN Regimen (Table 9)

Table 9. Developing an EN Regimen

Steps	Calculation Guide	Example
Determine caloric requirements	25–35 kcal/kg/day <i>or</i> estimate energy requirements using an equation such as the Harris-Benedict equation (see more details in Parenteral Nutrition section and Critical Care chapter)	A 60-kg patient would require about 25 kcal/kg/day \times 60 kg = 1500 kcal
Choose a formula and assess the calories per milliliter	Usually 1, 1.2, 1.5, or 2 kcal/mL	Choose a 1-kcal/mL formula
Determine infusion rate	(Volume of EN)/24 hr	1500 mL/24 hr = 62.5 mL/hr
Ensure that patient will receive sufficient protein	See product information to find protein content (see protein requirements in Parenteral Nutrition section)	Replete with Fiber provides 64 g/L of protein; therefore, 1500 mL will provide 96 g of protein, or 1.6 g/kg for a patient weighing 60 kg
Ensure that the patient will receive about 30 mL/kg/day of water	See product information to find water content	Replete with Fiber provides 832 mL/L of free water. A patient receiving 1500 mL/day would need about 250 mL of additional water, which can be administered as water flushes through the feeding tube (i.e., 60–70 mL every 6 hr); it is important to consider other fluids that the patient may be receiving

EN = enteral nutrition.

J. Drug administration using enteral access

1. Liquids are preferable, and they should be diluted with 2–3 times the medication volume with water to decrease osmolality.
2. Diarrhea can occur with medications having a high osmolality (e.g., medications mixed in sorbitol).
3. Flush with 20 mL of water before and after each drug administered.
4. Do not crush sustained-release or enteric-coated pills.
5. Mix crushed tablets or capsule contents with 10–15 mL of water and administer each drug separately.
6. It may be necessary to discontinue tube feedings before and after drug administration temporarily to prevent reduced bioavailability (e.g., fluoroquinolones, phenytoin, warfarin, bisphosphonates).
7. Consider feeding tube location and subsequent drug absorption (e.g., for efficacy, antacids need to be administered into the stomach, not the duodenum).

XII. PARENTERAL NUTRITION

- A. Parenteral nutrition (PN) is the administration of intravenous nutrition in patients with a nonfunctioning or inaccessible GI tract in which the duration of PN is anticipated to be at least 7 days (i.e., it is anticipated that the patient will be unable to be fed orally or enterally for at least 7 days). In patients who are at high nutritional risk or severely malnourished and cannot tolerate EN, PN should be initiated as soon as possible.
- B. Indications for PN
1. Severe pancreatitis in patients who cannot tolerate EN
 2. Peritonitis
 3. Severe inflammatory bowel disease (e.g., Crohn disease, ulcerative colitis)
 4. Extensive bowel resection (e.g., short bowel syndrome) causing malabsorption or maldigestion
 5. Complete bowel obstruction
 6. Severe intractable vomiting or diarrhea
 7. Inability to meet full nutritional needs by enteral route alone (can use PN as supplement to EN)
- C. Intravenous infusion of PN (Table 10)

Table 10. Estimating the Osmolarity of PN for 1 L of Solution

Nutrient	Estimated Osmolarity
Amino acids	10 mOsm/g
Dextrose	5 mOsm/g
Lipid emulsion 10%–20%	1.3–1.5 mOsm/g
Sodium chloride/acetate	2 mOsm/mEq
Potassium chloride/acetate	2 mOsm/mEq
Calcium gluconate	0.68 mOsm/mL
Magnesium sulfate	4.06 mOsm/mL

PN = parenteral nutrition.

1. PN should be administered through a central line. This includes any intravenous catheter (e.g., peripherally inserted central catheter, Hickman, Port-A-Cath) where the tip of the catheter is in the superior vena cava or adjacent to the right atrium (femoral catheters should be avoided because of higher risk of venous thrombosis and catheter-related infection).
2. Peripheral access, which also includes midline catheters, is defined as the catheter tip position outside the central vessels or inferior or superior vena cava. If a peripheral vein is used for PN administration, the osmolarity must not exceed 900 mOsm/L. Peripheral administration can be used in patients with an appropriate indication for PN (see Indications for PN above) when central intravenous access is unavailable and the need for PN is expected to be less than 2 weeks.
 - a. Final dextrose concentration should be 10% or less.
 - b. Final AA concentration should be 2.5%–4%.
 - c. Ca^{2+} concentration should be 5 mEq/L or less.
 - d. K^{+} concentration should be 40–60 mEq/L or less.

3. In hospitalized patients, PN is typically administered as a continuous infusion, which is infused over 24 hours.
4. Ambulatory patients may prefer a cyclic PN in which the PN is usually infused for 12 hours.
5. Infusions are generally better tolerated by patients if they are removed from the refrigerator and allowed to come to room temperature before infusion.

D. Types of PN admixtures (Table 11)

Table 11. 2-in-1 PN Compared with 3-in-1 PN

	Advantages	Disadvantages
2-in-1	Longer stability Visual inspection easier Filter using 0.22-micron filter (bacteria-eliminating) Lipids require 1.2-micron filter	Increased nursing time Requires two sets of tubing and infusion pumps Increased bacterial growth in lipids Maximum 12-hr hang time of separate lipids
3-in-1	Time efficient for nurses Single bag with single tube and infusion pump Decreased vein irritation Inhibited bacterial growth	Shorter stability (1–2 days) Complex compounding (without automated compounder) Visual inspection difficult Emulsion instability Must use 1.2-micron filter, not 0.22-micron Limited compatibility with medications Catheter occlusion more common

1. 2-in-1 refers to PN in which all nutrients are mixed in the same intravenous bag, except for lipids, which are administered by a separate infusion.
 - a. Lipids are infused separately, no faster than 0.1 g/kg/hour in adults, using a 1.2-micron filter
 - b. Rapid administration of lipids is associated with headache, fever, nausea, hypertriglyceridemia, dyspnea, cyanosis, flushing, sweating, and back or chest pain.
 - c. Lipid infusion time should be less than 12 hours because of the potential for microbial growth after this time (growth is reduced when lipids are mixed with dextrose and AAs, as in the 3-in-1 described below, because of reduced pH and increased osmolarity).
 - d. Administration tubing for a 2-in-1 should be changed every 24 hours; lipid tubing should be discarded after use (no longer than 12 hours).
2. 3-in-1 (also called *total nutrient admixture*) refers to PN in which all nutrients are mixed in the same intravenous bag.
 - a. The stability of a 3-in-1 depends on the pH, which is determined primarily by the final AA concentration (maintain at least 4%).
 - b. Do not add concentrated dextrose directly to a lipid emulsion when mixing (see order of mixing discussed later).
 - c. Avoid excessive amounts of Ca^{2+} and magnesium (see recommended doses).
 - d. Administration tubing for a 3-in-1 should be changed every 24 hours.
 - e. Total nutrient admixtures should have a final concentration of amino acids $\geq 4\%$, monohydrated dextrose $\geq 10\%$, and injectable lipid emulsion $\geq 2\%$.

E. Premixed PN**1. Products available in the United States**

- a. Clinimix is a two-compartment bag containing AAs in one compartment and dextrose in the other. This product is available with and without electrolytes. The seal between the two-compartment bag must be broken to mix the AAs and dextrose. Lipids can be added to the container after compartments are mixed or can be administered by Y-site.
- b. ProcalAmine is a solution containing 3% AAs, glycerin (4.3 kcal/g), and electrolytes in a single container, but it is not sufficient for most patients because of insufficient protein and calories.
- c. Kabiven, a newer solution, contains AAs, electrolytes, dextrose, and a lipid emulsion. It is available in a 3-compartment bag for central line administration only. Perikabiven is also available for use for peripheral and central administration.

2. Patient selection

- a. Evidence is insufficient to show that customized PN is superior to standardized premixed products.
- b. Consider in stable patients who require PN.
- c. Avoid in patients with fluid restriction or high protein needs.

3. Premixed products require fewer manipulations and have a lower risk of contamination and compounding errors, but they may still require additives (e.g., electrolytes, vitamins, trace elements).**F. Nutritional components of PN formulation**

1. Dextrose used for compounding PN is usually 70%, and it contains 3.4 kcal/g. Glycerol (or glycerin) is another carbohydrate source. Glycerol provides 4.3 kcal/g, and it is used in premixed parenteral products.
2. Fat emulsion is available as 10% or 20% and contains about 10 kcal/g; it is also available as a 30% formulation for compounding in 3-in-1 only. Smoflipid was recently approved as 20%; it contains soybean oil, medium chain triglycerides, olive oil, and fish oil. Omegaven 10% was also recently approved for use in the United States. Intralipid is available as a 20% solution.
3. AAs are available as 3%–20% and provide 4 kcal/g.
4. Electrolytes are added to maintain physiologic serum concentrations.
5. Multivitamins and trace elements are added based on the recommended daily amount.

G. Developing a PN regimen for administration through a central intravenous line**1. Determine caloric requirements.**

- a. For patients with a body mass index (BMI) less than 30 kg/m², administer 25–35 kcal/kg/day based on actual body weight [BMI = (Weight in kg)/(Height in meters)²].
- b. If BMI exceeds 30 kg/m², can administer 11–14 kcal/kg based on actual body weight or 22–25 kcal/kg based on IBW.
 - i. Alternatively, some practitioners advocate using adjusted body weight (ABW) rather than IBW.
 - ii. $ABW = [(actual\ weight - IBW) \times 0.25] + IBW$.
- c. Hypocaloric feeding with high protein in EN and PN involves the administration of about 80% of caloric requirements, and it can be considered in patients with obesity (except in patients with kidney failure requiring hemodialysis and patients with hepatic failure; these patients have increased protein and caloric requirements to maintain a positive nitrogen balance).

- d. One method is to estimate basal energy expenditure (BEE) using the Harris-Benedict equation:
 - i. Men: $BEE = 66 + 13.7(\text{Weight in kg}) + 5(\text{Height in cm}) - 6.8(\text{Age in years})$.
 - ii. Women: $BEE = 655 + 9.6(\text{Weight in kg}) + 1.8(\text{Height in cm}) - 4.7(\text{Age in years})$.
 - e. Energy expenditure can also be estimated through indirect calorimetry in critically ill patients (see the Critical Care chapter).
2. Determine fluid requirements.
- a. Usually 30–35 mL/kg/day or 2500–3500 mL/day (for patients without fluid restrictions) to maintain urine output in the range of 0.5–2 mL/kg/hour
 - b. Fluid requirements for patients with fluid restrictions (e.g., kidney or cardiac dysfunction) should be individualized.
 - c. Do not use PN for fluid replacement but for maintenance fluid only.
3. Determine protein (AA) requirements.
- a. For patients with a BMI less than 30 kg/m², protein is usually in the range of 0.8–2 g/kg/day based on actual body weight (may be higher in burn or trauma patients).
 - i. Maintenance 0.8–1 g/kg/day
 - ii. Moderate stress 1.3–1.5 g/kg/day
 - iii. Severe stress 1.5–2 g/kg/day
 - b. For patients with a BMI of 30–40 kg/m², can give protein 2 g/kg/day based on IBW. For patients with a BMI greater than 40 kg/m², can give 2.5 g/kg/day based on IBW.
 - c. Patients with chronic kidney dysfunction may need protein restriction to prevent uremia.
 - i. Kidney dysfunction without dialysis, 1 g/kg/day
 - ii. Kidney failure with intermittent hemodialysis, 1.2–1.5 g/kg/day (1.5–2.5 g/kg/day if continuous renal replacement)
 - d. Calories from protein (4 kcal/g) should be included in the total caloric provisions to prevent overfeeding.
 - e. For 3-in-1 formulations, the final AA concentration should be around 4% to provide adequate buffering capacity and prevent lipid emulsion destabilization.
 - f. Complete protein requirements can be provided on day 1 of PN (i.e., there is no need to slowly titrate up to recommended amount).
4. Calculate remaining nonprotein calories and administer about 20%–30% of total calories as lipid and the remainder as dextrose.
- a. Make sure dextrose rate of administration does not exceed the maximum rate of hepatic oxidation rate of 4–5 mg/kg/minute (may be lower in critically ill patients, so monitor for hyperglycemia and adjust amount of dextrose provided if needed).
 - i. Initial dextrose amounts can be in the range of 150–200 g/day.
 - ii. May need to reduce to 100–150 g/day initially in patients with diabetes or stress-induced hyperglycemia; increase gradually during first 3–4 days to goals if blood glucose values are less than 140–180 mg/dL.
 - b. A higher percentage of calories from lipid (up to 50%–60%, or 2.5 g/kg/day) can be provided for a short time in certain cases (e.g., hyperglycemia, hypercapnia).
 - c. Essential fatty acid deficiency can be prevented by supplying approximately 2%–4% of total calories as lipid (can administer lipid emulsion once every 1–2 weeks).

5. Estimate a daily maintenance amount of electrolytes, vitamins, and trace elements (Box 5).

Box 5. Central PN calculations

Example of a central 3-in-1 PN formula for a 70-kg patient hospitalized with ischemic bowel:
1. Total calories estimated as $30 \text{ kcal/kg} \times 70 \text{ kg} = 2100 \text{ kcal}$
2. Fluid requirements estimated as $1500 \text{ mL} + (20 \text{ mL/kg} \times 50 \text{ kg}) = 2500 \text{ mL/day}$
3. Estimated protein needs are $1.5 \text{ g/kg} \times 70 \text{ kg} = 105 \text{ g}$ of protein. $4 \text{ kcal/g} \times 105 \text{ g} = 420 \text{ kcal}$ from protein; using 10% AA-based solution, will need 1050 mL to equal 105 g of protein (can round to 1000 mL if this makes compounding easier)
4. Determine calories from fat and dextrose. Total calories needed is $2100 - 420 \text{ kcal from AAs} = 1680$ remaining non-protein calories needed. Administer 25%–30% of total kilocalories as lipid, or about 500 kcal from lipid. Using 20% lipid emulsion, 250 mL is needed to equal 500 kcal (about 2 kcal/mL) Total calories needed is $2100 \text{ kcal} - 420 \text{ kcal (AA)} - 500 \text{ kcal (lipid)} = 1180 \text{ kcal}$ needed from dextrose. Assuming 3.4 kcal/g, about 350 g dextrose will be needed. Using a 70% base dextrose solution, 500 mL will be needed to equal 350 g, or 1190 kcal. Calculate the rate of dextrose administration in milligrams per kilogram per minute: $[(350 \text{ g/24 hr}) \times (1000 \text{ mg/g}) \times (1 \text{ hr/60 min})]/70 \text{ kg} = 3.5 \text{ mg/kg/min}$. This is an appropriate rate of dextrose administration.
5. The final formula will contain the following: AA 10%, 1050 mL Lipid 20%, 250 mL Dextrose 70%, 500 mL Electrolytes, multivitamins, and trace elements (about 110 mL) Final volume of 1910 mL to infuse at 1910 mL over 24 hours = 80 mL/hr (Final volume assumes the patient is receiving about 600 mL of fluid from other medications to meet fluid requirements)
6. Final concentration of macronutrients in PN is: AA 105 g/1910 mL final volume = 5.5% Lipid $50 \text{ g/1910 mL} = 2.6\%$ Dextrose $350 \text{ g/1910 mL} = 18\%$
7. Final caloric value of PN is: AA $105 \text{ g} \times 4 \text{ kcal/g} = 420 \text{ kcal}$ Lipid $50 \text{ g} \times 10 \text{ kcal/g} = 500 \text{ kcal}$ Dextrose $350 \text{ g} \times 3.4 \text{ kcal/g} = 1190 \text{ kcal}$ Total calories = $420 + 500 + 1190 = 2110 \text{ kcal/70 kg} = 30 \text{ kcal/kg}$ 24% of total calories are provided as lipid

AA = amino acid; PN = parenteral nutrition.

- a. Electrolyte abnormalities should be addressed and corrected before PN is initiated. Avoid replacing electrolyte deficiencies using PN in acutely ill patients.
- b. Maintenance electrolytes (amounts will vary and should be individualized)
 - i. Sodium 60–150 mEq/day (1–2 mEq/kg/day)
 - ii. K^+ 40–80 mEq/day (1 mEq/kg/day)
 - iii. Phosphate 10–40 mmol/day (or 15 mmol/1000 kcal)
 - iv. Ca^{2+} 10–15 mEq/day (gluconate is preferred to prevent incompatibilities)
 - v. Magnesium 8–20 mEq/day (sulfate form is preferred to Cl to prevent incompatibilities)
 - vi. Cl and acetate salt forms to maintain acid-base balance.

- vii. Electrolyte adjustment
 - (a) Typically, greater amounts of magnesium, phosphorus, and K^+ will be needed during the first few days of PN because of IC shifts.
 - (b) Cl and acetate salt forms can be adjusted as needed to maintain acid-base balance (discussed under Monitoring Patients Who Are Receiving PN).
- c. Standard trace elements containing selenium, chromium, copper, manganese, and zinc (e.g., MTE-5)
 - i. Patients with high-output fistulas, diarrhea, burns, or large open wounds may require additional zinc supplementation.
 - ii. Patients with chronic diarrhea, malabsorption, or short-gut syndrome or those with critical illness may require additional selenium supplementation.
 - iii. Patients with severe cholestasis should have copper and manganese restricted to prevent accumulation and toxicity because both undergo biliary elimination.
- d. Parenteral multivitamin added daily (generally contains 150 mcg of vitamin K).
 - i. Additional thiamine (25–100 mg) can be supplemented in patients with a history of alcohol abuse.
 - ii. During shortages of parenteral vitamins, can reduce frequency of administration to three times/week or can administer individual vitamins daily (i.e., thiamine, ascorbic acid, niacin, pyridoxine, folic acid) or monthly (i.e., vitamin B₁₂)

H. Developing a PN regimen for administration through a peripheral intravenous line (Box 6)

Box 6. Peripheral PN Calculations

Example of a peripheral 3-in-1 PN formula for a 70-kg patient:
1. Total calories estimated as $30 \text{ kcal/kg} \times 70 \text{ kg} = 2100 \text{ kcal}$
2. Fluid requirements estimated as $1500 \text{ mL} + (20 \text{ mL/kg} \times 50 \text{ kg}) = 2500 \text{ mL/day}$; prescriber wants PN to contain no more than 2000 mL
3. Calculate amount of dextrose as $2000 \text{ mL} \times 10\% = 200 \text{ g}$ of maximum dextrose recommended
4. Calculate amount of AA as $2000 \text{ mL} \times 3\% = 60 \text{ g}$
5. Add about 500 kcal as lipid (can add more if patient tolerates).
6. Calculate volume so far. Using 70% dextrose, need 286 mL to equal 200 g of dextrose. Using 10% AA, will need 600 mL to equal 60 g. Using 20% lipid, will need 250 mL. Will add electrolytes, trace elements, multivitamins, and enough sterile water for a total volume of 2000 mL
7. Final formula will contain the following: AA 10% 600 mL Lipid 20% 250 mL Dextrose 70% 286 mL Electrolytes, multivitamins, and trace elements Sterile water added for 2000 mL final volume to infuse at $2000 \text{ mL}/24 \text{ hr} = 83 \text{ mL/hr}$
8. Final concentration of macronutrients in PN is: AA $60 \text{ g}/2000 \text{ mL}$ final volume = 3% Lipid $50 \text{ g}/2000 \text{ mL} = 2.5\%$ Dextrose $200 \text{ g}/2000 \text{ mL} = 10\%$
9. Final caloric value of peripheral PN is: AA $60 \text{ g} \times 4 \text{ kcal/g} = 240 \text{ kcal}$ Lipid $50 \text{ g} \times 10 \text{ kcal/g} = 500 \text{ kcal}$ Dextrose $200 \text{ g} \times 3.4 \text{ kcal/g} = 680 \text{ kcal}$ Total calories = $240 + 500 + 680 = 1420 \text{ kcal}/70 \text{ kg} = 20 \text{ kcal/kg}$ 35% of total calories are provided as lipid

AA = amino acid; PN = parenteral nutrition.

1. It will probably not meet nutritional needs based on macronutrient and micronutrient concentration restrictions (discussed earlier).
 2. For additional calories, increase the percentage of calories administered as lipid.
- I. Order of mixing (for manual compounding)
1. Add dextrose, AAs, sterile water.
 2. Add phosphate.
 3. Add other electrolytes (except Ca) and trace minerals.
 4. Mix well to ensure that phosphate is evenly distributed and to prevent precipitation with Ca.
 5. Add Ca.
 6. Observe for precipitates or contaminants.
 7. Add lipid if 3-in-1 formulation. (Note: Do not mix dextrose and lipids directly, because the low pH of dextrose can destabilize the lipid emulsion.)
 8. Add vitamins last, as close to the time of PN administration as possible in acute care settings, or just before infusion in patients receiving home PN.
- J. Factors associated with Ca^{2+} and phosphate precipitation in PN
1. Increasing pH (more basic) increases the risk of Ca^{2+} and phosphate precipitation.
 2. Increasing Ca^{2+} or phosphate concentration increases the risk of precipitation.
 - a. If Ca^{2+} concentration is 6 mEq/L or less and phosphate concentration is 30 mmol/L or less, the risk of precipitation is low.
 - b. Calcium chloride is more likely to precipitate with phosphate than calcium gluconate; calcium chloride should never be used in compounding PN formulations.
 3. The final concentration of AA should be at least 2.5% or greater to prevent Ca^{2+} and phosphate precipitation.
 - a. AAs form soluble complexes with Ca^{2+} and phosphate.
 - b. AAs provide a buffer system to maintain a lower pH of the PN in an acceptable range to prevent Ca^{2+} or phosphate precipitation.
 4. As the temperature increases, the risk of precipitation increases.
 - a. PN should be refrigerated if not administered within 24 hours of compounding.
 - b. If refrigerated, PN should be administered within 24 hours of rewarming.
 5. A 1.2-micron filter (used for a 3-in-1 PN) might not prevent the embolism of a calcium phosphate precipitate, but it should be used anyway to reduce the risk.
 6. Order of mixing additives is important to prevent precipitation (see above)
 7. The PN should be agitated often during compounding to ensure adequate mixture into solution.
- K. Medication additives in PN
1. In general, medications should not be added to PN.
 2. Examples of medication incompatibilities are ceftriaxone (precipitates with Ca), phenytoin (can change the pH of PN), medications containing propylene glycol or ethanol as diluents (e.g., furosemide, diazepam, lorazepam, digoxin, phenytoin, etoposide), and iron dextran (trivalent cations destabilize the lipid emulsion in 3-in-1 PN formulations).
 3. Incompatible drugs should be administered through a separate intravenous catheter or a separate lumen of a central venous catheter, if possible.

4. If an incompatible intravenous drug is to be administered through the same intravenous catheter as the PN, the PN should be stopped, followed by a compatible flush before and after drug administration. The volume of flush should be sufficient to clear the entire catheter of PN and of drug (typically about 10 mL if flushing the port closest to the patient); for drugs requiring longer infusion times, see below for precautions to prevent rebound hypoglycemia with prolonged interruptions of PN.
5. Only regular insulin is compatible with PN.

L. PN complications

1. Catheter-related infections are caused primarily by *Staphylococcus aureus* and *Candida albicans*.
2. Catheter insertion complications (e.g., pneumothorax, incorrect placement) are possible.
3. Peripheral venous thrombophlebitis can occur with peripheral catheter placement. Risk is increased by day 4 of catheterization; therefore, site should be rotated every 3 days.
4. Fluid imbalance can occur.
5. Acid-base imbalances are usually related to the patient's underlying condition; however, excessive chloride salts in the PN can cause a metabolic acidosis, whereas excessive acetate salts in the PN can cause a metabolic alkalosis.
6. Hyperglycemia can lead to nosocomial and wound infections.
7. Gut atrophy can occur.
8. Overfeeding can cause hepatic steatosis, hypercapnia, hyperglycemia, and azotemia.
9. Essential fatty acid deficiency can occur.
 - a. Symptoms include skin desquamation, hair loss, impaired wound healing, hepatomegaly, thrombocytopenia, fatty liver, and anemia.
 - b. It can occur within 1–3 weeks of a lipid-free PN.
10. Refeeding syndrome can occur in acutely (can include critically ill patients) or chronically malnourished patients when EN or PN is initiated.
 - a. Characterized by hypophosphatemia, hypokalemia, hypomagnesemia
 - b. Can cause cardiac dysfunction, respiratory dysfunction, and death
 - c. Prevention of refeeding syndrome:
 - i. Identify patients at risk (e.g., anorexia, alcoholism, cancer, chronically ill, poor nutritional intake for 1–2 weeks, recent unintentional weight loss, malabsorption).
 - ii. Initially, provide less than 50% of caloric requirements, and then advance over several days to desired goal.
 - iii. Supplement vitamins before initiating PN as well as K⁺, phosphate, and magnesium (if needed); monitor daily for at least 1 week; and replace electrolytes as needed (many patients will need aggressive electrolyte replacement during the first week of PN).
11. Aluminum toxicity
 - a. More likely to occur in patients receiving long-term PN or in those with renal dysfunction (aluminum is eliminated renally)
 - b. Accumulates in bone and interferes with bone Ca²⁺ uptake, causing osteopenia
 - c. Neurotoxicity and microcytic anemia
 - d. Contaminates many intravenous electrolytes and intravenous fluids
 - e. Aluminum content documented on drug labels

12. Hepatobiliary disorders (includes steatosis, cholestasis, and gallbladder sludge or stones) can occur with long-term PN administration.
 - a. Steatosis (or fatty liver) is associated with overfeeding and a transient elevation in aminotransferase concentration. Although it is usually benign, it can progress to fibrosis or cirrhosis in patients receiving long-term PN.
 - b. Cholestasis usually occurs in children, but it can also occur in adults receiving long-term PN and can progress to cirrhosis and liver failure; a conjugated bilirubin concentration greater than 2 mg/dL is the primary sign.
 - c. Gallbladder stasis is associated with the development of gallstones, sludge, and cholecystitis; it is more attributable to a lack of EN than to PN administration.
13. Osteoporosis and osteomalacia can occur in patients receiving long-term PN, and they are associated with higher protein doses (causes increased Ca^{2+} excretion) and chronic metabolic acidosis (because of insufficient acetate).

Patient Case

9. A 43-year-old male trauma patient (height 75 inches, weight 100 kg) was recently extubated and is receiving PN. His PN formula contains 35 kcal/kg, protein 1.2 g/kg, and dextrose infusing at 4.4 mg/kg/minute, and 25% of total calories as lipid. He has gradually developed symptoms of hypercapnia and has developed a respiratory acidosis. The medical team is considering strategies to correct this to avoid reintubation. Which change to the PN formula could best correct this situation?
 - A. Change PN to EN and maintain current caloric goals.
 - B. Reduce dextrose amount in PN to 3 mg/kg/minute and increase lipid to maintain current caloric goal.
 - C. Change electrolytes to the acetate salt in the PN to correct the acid-base imbalance.
 - D. Reduce the calories to 25 kcal/kg to prevent overfeeding.

M. Monitoring patients who are receiving PN

1. Monitor for infection (temperature, WBC, intravenous access site).
2. Monitor for peripheral vein thrombophlebitis or infiltration (if peripheral access); symptoms include pain, erythema, and tenderness or a palpable cord at the site of the peripheral vein; treat by removing catheter.
3. Monitor fluid status (weight, edema, vital signs, input and output, temperature).
4. Monitor nutritional status.
 - a. Prealbumin is useful for monitoring the effects of long-term nutrition support in patients who are not critically ill (see EN Monitoring earlier) because it has a shorter half-life than albumin.
 - i. Values
 - (a) Normal range, 16–40 mg/dL
 - (b) Moderate malnutrition, 11–16 mg/dL
 - (c) Severe malnutrition, less than 11 mg/dL
 - ii. Goal for malnourished patients is an increase of at least 3–5 mg/dL/week until within normal range.
 - b. Serum albumin (normal 3.5–5 g/dL) is a poor predictor of nutritional status because it has a long half-life, and concentrations fluctuate during illness.
5. Monitor for hyperglycemia and hypoglycemia.
 - a. A common blood glucose goal is 140–180 mg/dL.
 - b. Regular insulin (initially 0.05–0.2 units per gram of dextrose) can be added to the PN for patients using a consistent dosage.

- c. For patients with hyperglycemia or fluctuating insulin dosages, insulin can be supplemented separately from the PN, although this practice varies by practitioner.
 - d. Abrupt discontinuation of PN is usually tolerated in nondiabetic patients, but rebound hypoglycemia can occur in other patients; avoid by gradually tapering off PN over 1–2 hours. Check blood glucose 30 minutes to 1 hour after discontinuing PN. If PN is discontinued abruptly, rebound hypoglycemia can be avoided by administering 5% or 10% dextrose (may not be necessary if PN is administered through a peripheral catheter).
6. Monitor for electrolyte and acid-base imbalances. The chloride and acetate salts can be adjusted based on the acid-base status of the patient.
- a. For metabolic alkalosis, Na^+ and K^+ can be administered as the chloride salts.
 - b. For metabolic acidosis, Na^+ and K^+ can be administered as the acetate salts (acetate is converted to bicarbonate).
 - c. For respiratory acid-base disorders, correct the underlying cause or adjust the ventilator settings as needed.
7. Monitor triglyceride concentrations and withhold lipids in patients with a concentration greater than 400 mg/dL. When calculating lipid requirements, account for any drugs mixed in a lipid emulsion (e.g., propofol, clevidipine).
8. Monitor hepatic function.
9. Monitor for patient readiness for oral or EN support.
- a. Well-nourished, healthy patients can change immediately from PN to oral or EN.
 - b. Older adult, debilitated, or malnourished patients may need a transition period in which oral or EN feedings are gradually increased, coinciding with a reduction in PN.

Patient Cases

10. A patient (weight 70 kg) receives propofol at 45 mcg/kg/minute. Propofol is available at a concentration of 10 mg/mL and is mixed in a 10% lipid emulsion. Assuming the patient is receiving this infusion rate for 24 hours, which best approximates the total calories provided by the propofol infusion in a 24-hour period?
- A. 200 kcal.
 - B. 250 kcal.
 - C. 300 kcal.
 - D. 500 kcal.
11. A patient (weight 65 kg) is receiving PN after abdominal surgery. The PN contains about 1600 kcal, including 100 g of protein, 500 kcal as lipid, and 200 g of dextrose. The following additives are also included in a 24-hour infusion of PN: sodium chloride 50 mEq, sodium acetate 100 mEq, potassium acetate 60 mEq, sodium phosphate 30 mmol, magnesium sulfate 12 mEq, calcium gluconate 10 mEq/day, multivitamins 10 mL, and trace elements 3 mL. The patient has an NG tube in place that is suctioning 400–500 mL/day, which is being replaced with an infusion of 0.9% sodium chloride. After 48 hours of PN, the patient has the following laboratory values: Na^+ 140 mEq/L, K^+ 3.8 mEq/L, Cl^- 93 mEq/L, serum bicarbonate 35 mEq/L, pH 7.5, PCO_2 47 mm Hg, and bicarbonate 36 mEq/L. Which adjustment to the PN formula is best at this time?
- A. Increase lipids to provide 750 kcal and reduce dextrose to 130 g.
 - B. Increase sodium acetate to 150 mEq/day and discontinue sodium chloride.
 - C. Increase sodium chloride to 150 mEq/day and discontinue sodium acetate.
 - D. Add sodium bicarbonate 50 mEq to PN.

Patient Cases (Cont'd)

Questions 12 and 13 pertain to the following case.

A 75-year-old woman (weight 50 kg) is receiving PN after an extensive bowel resection. She is expected to require about 1 week of PN. She is receiving the following macronutrients in her formula: 70% dextrose 300 mL, 20% lipid 150 mL, and 10% AA 750 mL.

12. If these macronutrients are infused over 24 hours, which choice most closely approximates the total calories this patient is receiving daily?
 - A. 20 kcal/kg.
 - B. 26 kcal/kg.
 - C. 30 kcal/kg.
 - D. 35 kcal/kg.

13. The patient has received the PN formula for 3 days. Her blood glucose concentrations have ranged from 220 to 280 mg/dL. She has orders for the following sliding scale of regular insulin: blood glucose 200–250 mg/dL, give 2 units; blood glucose 251–300 mg/dL, give 4 units; and blood glucose 301–350 mg/dL, give 6 units. She has been receiving 14–16 units of insulin daily through the sliding-scale orders. Her medical history is significant for hypertension, diabetes, chronic obstructive pulmonary disease, and colon cancer. Treatment was recently initiated with methylprednisolone 60 mg intravenously every 6 hours for a chronic obstructive pulmonary disease exacerbation. Today, the dose will be reduced to 40 mg intravenously every 8 hours. What is the best recommendation for better control of this patient's blood glucose?
 - A. Add insulin glargine 10–20 units/day to PN.
 - B. Change 70% dextrose in PN to D₅W.
 - C. Increase the sliding-scale insulin to 4 units for blood glucose 200–250 mg/dL, 8 units for blood glucose 251–300 mg/dL, and 12 units for blood glucose 301–350 mg/dL.
 - D. Add neutral protamine Hagedorn insulin (NPH) 5 units subcutaneously every 12 hours.

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Nutrition

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ANSWERS AND EXPLANATIONS TO PATIENT CASES

1. Answer: C

Although this patient's blood pressure is not necessarily low, it is probably low compared with his baseline, considering his history of hypertension. In addition to his low blood pressure, his other signs and symptoms of intravascular volume depletion include an elevated BUN/SCr ratio, an elevated heart rate, and a reduced urine output. Crystalloids or colloids are appropriate fluids for resuscitation, making lactated Ringer solution (Answer C) the best option. Furosemide (Answer A) may increase his urine output, but at the cost of further depleting the intravascular volume. Albumin 25% (Answer B) should be avoided for fluid resuscitation because it causes a shift of fluid from the IS space into the intravascular space, which can potentiate his dehydration. Answer D would be appropriate for a maintenance infusion; however, D₅W/0.45% sodium chloride plus potassium chloride 20 mEq/L would not provide optimal replacement of the intravascular space, given the distribution in TBF.

2. Answer: C

This patient has no signs or symptoms of intravascular volume depletion; therefore, he does not require fluid resuscitation. Because he is not taking adequate fluids by mouth, he should be given maintenance intravenous fluid to prevent dehydration and electrolyte imbalances. This is typically accomplished by a combination of free water and 0.45% sodium chloride with K⁺ (Answer C). The infusion rate is calculated as 1500 mL + (60 kg × 20 mL/kg) = 2700 mL/24 hours, or about 110 mL/hour. Parenteral nutrition (Answer A) is inappropriate because there is no evidence that the patient's GI tract is nonfunctional. Albumin 5% (Answer B) or lactated Ringer solution (Answer D) should be reserved for fluid resuscitation in patients with signs or symptoms of intravascular volume depletion.

3. Answer: B

Although this patient has symptomatic hyponatremia, she also has signs of intravascular volume depletion. This intravascular volume depletion is a potent stimulus for ADH secretion, which will potentiate hyponatremia. In patients with hyponatremia and intravascular volume depletion, it is important to restore intravascular volume first to prevent organ hypoperfusion and

to inhibit ADH secretion. Fluid resuscitation should be accomplished with 0.9% sodium chloride as a fluid bolus, followed by a reevaluation of fluid status (Answer B). A slower infusion of 0.9% sodium chloride (Answer A) will not restore intravascular volume quickly. Once the intravascular volume is restored, ADH secretion will cease. This can be followed by a water diuresis, with a subsequent rise in the serum sodium concentration. Of importance, the patient should be monitored closely to prevent a rise in serum sodium greater than 10–12 mEq/L/day. If serum sodium rises too fast, 0.45% sodium chloride can be infused to slow the rate of rise of serum sodium concentration. Hypertonic saline (Answers C and D) would not be advisable unless the patient continues to have symptoms of hyponatremia after appropriate fluid resuscitation.

4. Answer: C

To prevent central pontine myelinolysis in patients with hyponatremia, it is recommended that the serum sodium concentration be raised by no more than 10–12 mEq/L in 24 hours (Answer C). Of note, the goal is not to achieve a normal serum sodium concentration in 24 hours. Rapid correction of chronic hyponatremia can cause permanent neurologic damage (Answers A and B), and because this patient is symptomatic, she should not be maintained at her current sodium concentration (Answer D).

5. Answer: D

This patient has hyponatremia and hypokalemia. In patients with hypokalemia, there is a reduction in IC K⁺. To maintain cellular electroneutrality, Na⁺ will shift into cells. As K⁺ is replaced, Na⁺ shifts out of cells, and the serum sodium concentration rises. Therefore, in this case, the hypokalemia should be corrected first, which will cause a subsequent improvement in the hyponatremia. Because this patient has no ECG changes related to the hypokalemia, oral supplementation with K⁺ (Answer D) is recommended over intravenous replacement (Answer A). A dose of 60–80 mEq/day should cause an increase in the K⁺ concentration by 0.6–0.8 mEq/L. Because the patient is eating a regular diet, she should no longer require intravenous fluids (Answer B). Hypertonic saline (Answer C) is incorrect because this patient has no serious symptoms of hyponatremia.

6. Answer: D

This patient has not been given enough water, and she cannot communicate (or feel) thirst. This can be prevented by administering about 1 mL of water for every calorie administered. It should also be prevented by monitoring serum sodium concentrations and adjusting water intake as needed. To correct the hypernatremia, water should be administered, preferably through the enteral feeding tube (Answer D). If this is not possible, it can be administered intravenously as D₅W (Answer B or C), but never as sterile water (Answer A). Sterile water administered intravenously can cause hemolysis and death. The patient's water deficit (in liters) can be estimated with the equation $0.4 \times \text{LBW} \times [(\text{Na}^+/140) - 1]$. Water should be replaced over several days, taking care to avoid changes in serum sodium greater than 10–12 mEq/L in 24 hours.

7. Answer: B

This patient has ECG changes consistent with hyperkalemia. Insulin (Answer B) will have the fastest onset and most predictable action of lowering serum potassium. Calcium gluconate (Answer A) should only be used with caution in this patient because it can potentiate digoxin toxicity and bradycardia. The efficacy of sodium bicarbonate (Answer C) is not well established. Albuterol (Answer D) can be efficacious when added to insulin, but it might not be effective in about 40% of patients; therefore, it is not recommended as initial therapy or as monotherapy for hyperkalemia.

8. Answer: C

This patient is receiving a calorie-dense EN formula that typically has less water than other enteral products. Therefore, although not currently hypernatremic, the patient is at risk of developing hypernatremia because of insufficient water intake. This can be prevented by administering additional water. The preferred route is enteral, if possible. The additional water needed daily can be estimated as 1 mL/kcal or around 30 mL/kg/day. Therefore, if this patient is receiving enteral feeding at 35 mL/hour \times 2 kcal/mL, she is receiving 1680 kcal/day. She is receiving only 717 mL of water per liter of enteral formula, which is 602 mL/day for the 840 mL of enteral feeding daily (35 mL/hour \times 24 hours = 840 mL/day). Because she is receiving 1680 kcal, she needs about 1680 mL of water per day. Subtracting the water from the feedings from the total needed, $1680 - 602 =$

1078 mL is needed. This can be divided and administered through the gastric feeding tube at about 180 mL/dose every 4 hours (Answer C). Of note, the patient should be monitored for fluid overload, especially given her chronic kidney disease. Given this patient's stable kidney disease and her adequate urine output, she should be able to tolerate this amount of free water. The amount of free water needed daily is an estimation that should be adjusted on the basis of specific patient parameters (e.g., serum sodium, input, output, daily weight, edema). Free water should not be administered as intravenous dextrose (Answer B) unless enteral administration is not feasible. Answer A is incorrect because reducing Na⁺ will not prevent hypernatremia; the problem is related to too little water rather than too much Na⁺. Answer D is incorrect because the caloric goals should not be sacrificed, and they would not eliminate the problem of insufficient water administered.

9. Answer: D

This patient is developing a respiratory acidosis, possibly because of overfeeding. Although dextrose is metabolized to water and CO₂, it generally will not cause a respiratory acidosis unless the patient is being overfed. Reducing the total calories to 25 kcal/kg decreases the risk of overfeeding, and reintubation can be avoided (Answer D). Answer A is incorrect because patients can be overfed with PN or EN. Answer B is incorrect because, even if the dextrose in the PN is reduced, the patient can still develop symptoms of overfeeding. Answer C is incorrect because the underlying (overfeeding) cause should be corrected, rather than adjusting the acetate to treat a respiratory acidosis.

10. Answer: D

To determine the amount of calories provided by propofol, it must first be determined how many milliliters per day are infused. For this patient receiving propofol 45 mcg/kg/minute and weighing 70 kg, 454 mL is infused daily (assuming a constant infusion rate). Next, if a 10% lipid emulsion provides about 1.1 kcal/mL, it can be calculated that 454 mL/day of propofol provides about 500 kcal/day, making Answer D correct and Answers A–C incorrect.

11. Answer: C

This patient has developed a metabolic alkalosis, probably secondary to the loss of gastric fluid through NG suctioning. The low serum chloride and elevated serum bicarbonate concentrations support this theory. In addition, the acid base is consistent with metabolic alkalosis with compensatory respiratory acidosis. The treatment in this circumstance is to replace the lost fluid with 0.9% sodium chloride, which is being done. In addition, Na^+ and K^+ can be administered as the chloride salt rather than the acetate salt (Answer C). For this case, only Na^+ is converted to chloride salt, and K^+ is left as the acetate salt initially. With daily monitoring, the ratio of Cl^- to acetate can be adjusted further if needed. Answer B is incorrect because it would probably worsen the metabolic alkalosis as the sodium acetate is converted to bicarbonate. Answer A is incorrect because hypercapnia is a compensatory response, not the primary acid-base disturbance. Answer D is incorrect for several reasons. First, it is never advisable to add sodium bicarbonate to PN because of incompatibility and the risk of calcium-phosphate precipitation. Second, sodium bicarbonate is the incorrect treatment for metabolic alkalosis because it can worsen alkalosis.

12. Answer: B

The total calories are calculated by adding the calories provided by dextrose, lipid, and AA. Dextrose provides 714 kcal ($210 \text{ g} \times 3.4 \text{ kcal/g}$), lipid provides about 300 kcal ($30 \text{ g} \times 10 \text{ kcal/g}$), and AA provides 300 kcal ($75 \text{ g} \times 4 \text{ kcal/g}$). Adding these together provides calories of 1314 kcal/50 kg = 26.3 kcal/kg, making Answer B correct and Answers A, C, and D incorrect.

13. Answer: D

This patient's hyperglycemia could be attributable to either stress or corticosteroids. Because the corticosteroid dose is being tapered, the blood glucose concentrations will probably decrease with time. For patients with a fluctuating blood glucose concentration, it can be difficult to add insulin to PN because insulin cannot be adjusted in a timely manner. Regardless, Answer A is incorrect because long-acting insulin should not be added to PN. If insulin is added to PN, it should be regular insulin. Although some experts promote "permissive underfeeding," Answer B is incorrect because it would provide insufficient calories for this patient. Sliding scales of insulin can be useful when

used in conjunction with a basal amount of insulin in patients with a fluctuating blood glucose concentration. However, a sliding scale (Answer C) should not be used as the primary intervention for blood glucose control, because it is reactive and it fails to prevent hyperglycemia. In addition, the sliding scale described recommends insulin only when the blood glucose reaches 200, which is too high. Answer D is correct because it provides a basal amount of insulin that can be adjusted in a timely manner as the blood glucose concentrations fluctuate according to the patient's status.

ANSWERS AND EXPLANATIONS TO SELF-ASSESSMENT QUESTIONS

1. Answer: D

This patient continues to have hypotension and tachycardia, both of which are signs of intravascular volume depletion. The improvement in blood pressure and tachycardia after a fluid bolus also indicates intravascular volume depletion. Fluid administration should continue until there is no further improvement in vital signs. Patients with intravascular volume depletion require a rapid bolus of crystalloid (either 0.9% sodium chloride or lactated Ringer solution) of 500–1000 mL (or about 30 mL/kg), followed by reassessment (Answer D). A rapid bolus is essential to prevent organ dysfunction caused by hypoperfusion. Although the patient has poor urine output, administering furosemide (Answer A) will worsen volume depletion. As volume is replaced, urine output will probably increase. Administering 5% albumin in combination with a vasopressor (Answer B) should not be the initial treatment as long as vital signs are improving with the administration of fluid boluses with 0.9% sodium chloride. In addition, colloids are more expensive, and there is no evidence of better outcomes for fluid resuscitation with colloids than with crystalloids. Furthermore, infusion of albumin over 4 hours is incorrect because it would not restore intravascular volume rapidly enough to prevent organ dysfunction. Intravenous fluid containing D₅W (Answer C) is not appropriate for fluid resuscitation, regardless of the blood glucose concentration.

2. Answer: A

To answer this question, an alligation must first be set up using 0.9% and 23.4% sodium chloride. If 0.9% sodium chloride contains 154 mEq/L, 2% should contain about 342 mEq/L. After completing the alligation, the correct amounts can be double-checked by verifying the amount of sodium chloride in the prepared product: 951 mL of 0.9% sodium chloride contains 146 mEq of sodium chloride, and 49 mL of 23.4% sodium chloride contains 196 mEq of sodium chloride; therefore, 146 mEq + 196 mEq = 342 mEq/L of sodium chloride in the final product. The osmolarity is calculated as $(2 \text{ g}/100 \text{ mL}) \times (1 \text{ mol}/58.5 \text{ g}) \times (2 \text{ Osm}/\text{mol}) \times (1000 \text{ mOsm}/\text{Osm}) \times (1000 \text{ mL}/\text{L}) \times 0.93 = 635 \text{ mOsm}/\text{L}$ (Answer A is correct; Answer D is incorrect). Because of the osmotic coefficient (0.93), the sodium chloride does not completely dissociate in solution. Although use of the osmotic coefficient provides a more accurate

osmolarity, it is probably not clinically relevant in calculating the osmolarity of intravenous sodium chloride. Therefore, it is safe to estimate the osmolarity of sodium chloride as either 635 or 684 mOsm/L, because there is no apparent clinical difference between these osmolarities. Because the osmolarity is less than 900 mOsm/L, the infusion can be administered through a peripheral line, (Answers B and C are incorrect).

3. Answer: D

In this case, hyponatremia is likely because of congestive heart failure and has probably developed over a prolonged period (not acute onset). Patients with chronic hyponatremia because of heart failure are typically asymptomatic. Rapid correction of chronic hyponatremia is associated with permanent neurologic damage caused by central pontine myelinolysis. Furthermore, hypertonic saline can worsen volume overload in patients with heart failure. Although hyponatremia is a sign of worsening heart failure, correction of hyponatremia in patients with heart failure does not improve outcomes (Answer D). For these reasons, the risks of correcting the serum sodium with hypertonic saline (Answers A–C) outweigh the potential benefits.

4. Answer: B

Patients with hyperkalemia and ECG changes should be treated first with Ca²⁺ for cardiac stability (Answer B). After Ca²⁺ administration, other measures can be taken to shift K⁺ from the EC compartment to the IC compartment. Insulin (Answer A) can accomplish this; however, in this patient with hyperglycemia, insulin should be administered without glucose. Sodium polystyrene sulfonate (Kayexalate; Answer C) can be administered, but it is not effective immediately and is therefore not appropriate for first-line treatment of symptomatic hyperkalemia. Sodium bicarbonate (Answer D) is incorrect because it does not treat cardiac instability.

5. Answer: C

This patient is not receiving adequate nutritional intake because of her mental status. Because her GI tract is functional, it should be used for feeding to prevent gut mucosal atrophy. An NG or nasoduodenal feeding tube is appropriate for enteral access for short-term nutritional support (Answer C). A percutaneous gastrostomy tube (Answer D), which requires a surgical procedure,

is used for long-term nutritional support. The patient should receive 25–35 kcal/kg/day. The PN formulas (Answers A and B) should not be used in a patient with a functional GI tract. Although Answer B would be an appropriate PN formula for peripheral administration, PN is associated with more complications than EN is.

6. Answer: C

This correct formula provides about 30 kcal/kg of calories, 1.5 g of protein per kilogram (AA), and 30% of total calories as lipid (Answer C). Answer A is incorrect because it provides 1000 calories as lipid, which is about 62% of the total calories provided. Answer B is incorrect because it contains only 0.8 g/kg of AA, which is an insufficient amount considering the patient's stress and apparent absence of kidney injury. Answer D is incorrect because it contains too much AA.

7. Answer: B

This patient has hypomagnesemia and hypokalemia. Correction of hypokalemia requires correction of hypomagnesemia to prevent renal loss of K^+ (Answer B). Magnesium should be administered slowly to avoid hypotension and increased renal excretion caused by rapid administration. Continued K^+ should not be given until magnesium is administered (Answers A and C). Calcium correction will not have a large effect on K^+ correction (Answer D).

8. Answer: C

Enteral nutrition prevents gut mucosal atrophy and subsequent bacterial translocation (Answer C). Bacterial translocation is the crossing of bacteria from the GI tract into the systemic circulation. Enteral nutrition is associated with fewer infectious complications than PN, which may partly be because of a reduction in bacterial translocation (Answers A and B). Zinc does not affect atrophy and bacterial translocation (Answer D).

9. Answer: C

It is a common misconception that all patients with kidney failure need protein restriction (Answers A and B). This is true for chronic kidney disease patients who are not undergoing dialysis. Conversely, if they are undergoing dialysis, they do not need protein restriction and can receive AA at 1.2–1.5 g/kg/day (Answer C). Answer D is incorrect because too much protein is given.

