**Pain Management Module**

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**Objectives:**

1. Review pain management objectives.
2. Understand use of opioids.
3. Review pain sensitization mechanism.

**INTRODUCTION**

Surgical practice consistently deals with the management of acute pain. Chronic pain is different from acute pain and often requires different approaches for management than chronic pain. This presentation will address managing acute pain and providing conscious sedation.

In 2001, standards for pain management were introduced by the Joint Commission. These standards identified pain as the “fifth vital sign.” These standards state that a patient should be properly assessed for pain, be given effective pain management, and be given appropriate education. Further, family members and hospital staff need to be educated in proper pain management.

The World Health Organization produced Treatment Guidelines on Pain (available at http://www.who.int/medicines/areas/quality_safety/guide_on_pain/en/). The goals of these pain management guidelines are to decrease patient pain and suffering, improve patient physical and mental functioning, and ensure improved quality of life for all patients. Measurement of pain is imperative, and each patient brings different perceptions to his or her pain. A visual analog scale of some type is usually used to assess pain. Most scales run from 0, indicating no pain, to 10, which indicates the worst pain ever perceived. One visual scale is the Wong-Baker Faces pain scale (http://www.wongbakerfaces.org/). These faces are used by nurses to assess pain and decide when pain medication should be given.

**Preemptive Analgesia**

The ability to decrease postinjury sensitization is the principle behind preemptive analgesia. If analgesia exists before a noxious stimulus (surgery) is delivered, postinjury hypersensitivity is prevented or blunted. The postinjury hypersensitivity is mediated via a central mechanism, which is prevented if the analgesia exists before the noxious stimulus. Without preemptive analgesia, hyperalgesia occurs, and allodynia is possible. Allodynia is the perception of pain secondary to a stimulus that did not produce pain before the insult (see image at http://www.aafp.org/afp/2001/0515/p1979.html).

**Conscious Sedation**

The Joint Commission standards for conscious sedation were developed at the same time as the pain standards. These standards place a new emphasis on the training and qualification of individuals administering sedation, monitoring the safety of patients during conscious sedation, and clarifying discharge criteria after conscious sedation. New definitions were also established.

1. **Minimal sedation** or **anxiolysis** is a drug-induced state during which patients respond normally to verbal commands. Ventilatory and cardiovascular functions are unaffected.
2. *Minimal sedation* or *anxiolysis* is a drug-induced state during which patients respond normally to verbal commands. Ventilatory and cardiovascular functions are unaffected.

3. *Moderate sedation/analgesia* or *conscious sedation* is a drug-induced depression of consciousness during which patients respond purposefully to verbal commands either alone or accompanied by light tactile stimulation. No intervention is required to maintain a patent airway, and spontaneous ventilation is adequate. Cardiovascular function is also maintained.

4. *Deep sedation/analgesia* is a drug-induced depression of consciousness during which patients cannot be easily aroused but respond purposefully after repeated or painful stimulation. These patients may require assistance in maintaining a patent airway, and spontaneous ventilation may be inadequate. Cardiovascular function is maintained.

5. *Anesthesia* consists of general anesthesia and spinal or major regional anesthesia. It does not include local anesthesia. General anesthesia is a drug-induced loss of consciousness during which patients are not arousable, even by painful stimulation. Maintenance of ventilatory function is often impaired. Cardiovascular function may also be impaired.

Conscious sedation requires preprocedural, procedural, and postprocedural responsibilities. During the procedure, a modified Ramsey Sedation Scale is helpful to assess levels of consciousness. The Modified Ramsey Sedation Scale is a 6-level scale that can be used to assess the patient’s conscious state.

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<thead>
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<th>Modified Ramsey Sedation Scale</th>
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**REGIONAL ANALGESIA**

Local anesthetics are commonly used via epidural, intrathecal, or peripheral routes. In epidural and intrathecal applications, they are often combined with opioids. Intrathecal injections are commonly used for anesthesia, whereas epidural injections are used to produce analgesia. Regional analgesia is used to reduce the dependence on opioids and to avoid opioid complications. The opioid complication most feared is respiratory depression from excessive medication.

Epidural techniques can improve postoperative analgesia and modify physiologic changes associated with surgery. Epidural analgesia is achieved when the agent is placed in the epidural space—in the bony spinal canal outside the dura mater. Drug administration is achieved in 3 ways with epidural placement. The first is by diffusion through the dura into the cerebrospinal fluid (CSF), then to the spinal cord or nerve roots. There is also some vascular uptake by the vessels in the epidural space into systemic circulation. Finally, there is fat within the epidural space where the drug can be absorbed, especially if lipophilic, which creates a drug depot from which the drug can eventually enter the CSF or the systemic circulation.

Epidural analgesia provides statistically improved pain relief at rest and with activity compared with parenteral analgesia in all surgical procedures. A proposed mechanism is that local
anesthetics in epidurals attenuate input into the central nervous system and, when combined with central opioids, lead to synergistic analgesic effects and improved pain control. In most studies, epidural analgesia is associated with fewer postoperative pulmonary and venous thromboembolism complications—a 30–40% reduction compared with systemic methods of relieving pain. Intraoperative blood loss is also reduced. When evaluating epidural analgesia in patients having abdominal surgery, ileus is shorter. Despite these advantages, many studies demonstrate no overall improved outcome comparing epidural with systemic pain control postoperatively.

Despite optimum pain control, epidural analgesia can have several unique complications, including increased levels of pruritus, increased numbness (epidurals placed in the lumbar position), and hypotension (epidurals using a local anesthetic and opioid mix in the thoracic position). Pruritus is present in 5–30% of patients; severe itching is present in approximately 9%. Pruritus is suspected to be secondary to a central opioid effect and can be difficult to manage. Antihistamines are routinely used, but their success rate is variable.

Hypotension is common and appears to be primarily related to the local anesthetic in the mixture. Treating the hypotension can require increasing fluid administration, reducing the drug dose, and adding a vasopressor. Epidural analgesia and therapeutic anticoagulation can lead to spinal hematoma and possible paralysis.

Epidurals can usually be placed in patients who will receive thromboprophylaxis with subcutaneous unfractionated heparin, as long as the heparin is delayed for 1 hour after catheter insertion. Patients receiving low molecular weight heparin (LMWH) should not have epidurals placed for at least 24 hours after the last LMWH dose. Current recommendations also suggest that heparin be stopped 12–25 hours before an epidural catheter is removed.

Another approach to regional analgesia is continuous paravertebral extrapleural infusions, especially for postthoracotomy pain management. This method allows continuous infusion of an opioid or a local anesthetic through a catheter placed in a paravertebral position. This technique may allow for less opioid use and fewer complications compared with epidural catheters.

Intercostal blocks for rib fractures represent a common use of a regional nerve block. Pain associated with rib fractures is the major cause of morbidity associated with this injury. Mortality rates of 12% have been documented with simple rib fractures. Relief of pain is the first step in the management of this injury. Placing these blocks in the anterior to mid-axillary line and using a small quantity of local anesthesia inferior to each rib achieves excellent analgesia. Other forms of intrapleural analgesia are appropriate when a pleural catheter is in place and the agent can be infused directly into the pleural space.

**APPROACH TO THE PATIENT WITH PAIN COMPLAINTS**

Several aspects of pain assessment are helpful:

1. **Location, duration, temporal pattern, modifiers (better/worse)**
2. **Quality**
   a. Somatic: dull/aching, well localized: fracture, bone met, muscle strain
   b. Visceral: dull/sharp/colicky; well localized or referred: gastritis, gallstones
   c. Neuropathic: burning, lancinating itching; radicular or stocking-glove distribution
   d. Numb: *Herpes Zoster*, spinal disc, diabetic neuropathy
3. **Intensity** can be measured by a visual analog scale (VAS).
4. Treatments: What has worked and what has not?
5. Impact: What is pain altering in the patient’s activities of daily living?
6. Causality: What does the patient think is causing the pain?
7. Patient goals: Where on the VAS would patient like to be?

**DRUG THERAPY**

1. Mild pain
   a. Over-the-counter drugs—aspirin, acetaminophen, ibuprofen, naproxen
   b. Side-effect profile and cost should determine choice of drug.
   c. No clear analgesic benefit of one drug compared with another
2. Moderate pain
   a. Single agents
      i. Codeine 30 mg, 60 mg (tablet or liquid)
      ii. Oxycodone 5 mg (tablet or liquid)
      iii. Propoxyphene 65 mg
      iv. Tramadol 50 mg, 100 mg
   b. Combination products
      i. Acetaminophen w/codeine 30 mg, 60 mg
      ii. Acetaminophen 325–500 mg or aspirin 325 mg w/oxycodone 2.5–10 mg
      iii. Acetaminophen 325–750 mg or aspirin 500 mg w/hydrocodone (5–10 mg)
      iv. Acetaminophen w/propoxyphene
3. Drug characteristics
   a. Potency: oxycodone = hydrocodone > codeine = tramadol > propoxyphene
   b. Duration: q3–4 for all products except tramadol (q6 hours)
   c. Cost: generic codeine or oxycodone << hydrocodone products
   d. The acetaminophen or aspirin in combination products limits dose escalation—do not exceed 3.0 g of acetaminophen or aspirin per 24 hours
4. Severe pain
   a. Short-acting drugs
      i. Morphine
      ii. Hydromorphone
      iii. Oxycodone
      iv. Oxymorphone (duration 4–6 hours)
      v. Meperidine: shortest acting—use only for procedure-related pain—duration <3 hours; use for <48 hours, no more than 600 mg/24 hours due to accumulation of toxic metabolite
   b. Long-acting drugs
      i. Morphine sustained release: peak effect ~2 hours; duration 8–12 hours
      ii. Oxycodone sustained release: peak effect ~1–2 hours; duration 8–12 hours
      iii. Oxymorphone sustained release: peak effect ~2–3 hours; duration 12 hours
      iv. Transdermal fentanyl: peak effect 18–24 hours; duration 48–72 hours; NOTE: 12–24 hours to wear-off once a patch is removed.
   c. Drug characteristics
      i. Oral administration: onset 15–30 minutes; peak effect 60–90 minutes; duration 2–4 hours
      ii. Parenteral administration: onset 2–15 minutes; peak effect 10–30 minutes; duration 1–3 hours
iii. Potency ratios: 30 mg oral morphine = 20–30 mg oral oxycodone = 7.5 mg oral hydromorphone = 10 mg IV/SQ morphine = 2 mg IV/SQ hydromorphone
iv. Dose escalation: Dose escalate by 50–100% for severe/uncontrolled pain; 25–50% for mild-moderate pain—irrespective of starting dose. Short-acting drugs can be dose escalated as often as every 1–2 hours; long-acting morphine/oxycodone every 24 hours; fentanyl patch or methadone no more frequently than every 48–72 hours

5. Methadone
a. Methadone has an extended terminal half-life, up to 190 hours. This half-life does not match the observed duration of analgesia (6–12 hours) after a steady state is reached.
b. This long half-life can lead to increased risk for sedation and respiratory depression, especially in the elderly or with rapid dose adjustments.
c. Methadone’s apparent potency, compared with other opioids, varies with the patient’s current exposure to other opioids.

6. Suggested Dosing Guide for Opioid-Tolerant Patients:

<table>
<thead>
<tr>
<th>Daily Oral Morphine Dose Equivalents</th>
<th>Conversion Ratio Oral Morphine to Oral Methadone</th>
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<tbody>
<tr>
<td>&lt;100 mg</td>
<td>3:1*</td>
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<tr>
<td>101–300 mg</td>
<td>5:1</td>
</tr>
<tr>
<td>301–600 mg</td>
<td>10:1</td>
</tr>
<tr>
<td>601–800 mg</td>
<td>12:1</td>
</tr>
<tr>
<td>801–1000 mg</td>
<td>15:1</td>
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<tr>
<td>&gt;1001 mg</td>
<td>20:1</td>
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*(i.e., 3 mg morphine:1 mg methadone)

OPIOID TOXICITY
1. Constipation: Prophylaxis with bowel stimulant (senna or milk of magnesia)
2. Nausea: not an allergy—will resolve after a few doses for most patients—use an antiemetic PRN (e.g., prochlorperazine)
3. Sedation/confusion: Will resolve after a few doses/days for most patients
4. Respiratory depression: Very rare with short-acting oral opioids, tolerance develops rapidly—risk factors include rapid IV push, new liver/renal dysfunction, severe lung disease, rapid dose escalation of fentanyl patch or methadone
5. Pruritus: Common, especially to morphine, least reported with fentanyl—not a true allergy; not a contraindication to opioid use; H₁/H₂ blockers usually not helpful; switch to opioid of a different pharmacological class.
6. Neurotoxicity: Multifocal myoclonus, delirium, and seizures are seen with morphine or hydromorphone, especially at high doses or in renal failure.
7. Prolonged QT interval: Risk of torsades de pointes with methadone

SUBSTANCE USE/ABUSE DEFINITIONS
1. Tolerance: Need to increase the amount of drug to obtain the same effect.
2. Physical dependence: Development of withdrawal reaction upon discontinuation or antagonism of drug
3. Pseudo addiction: Behavioral manifestations of addiction occurring because of undertreated pain; typically in the setting of severe continuous pain when drugs are administered at inadequate doses at excessive dosing intervals
4. Addiction
   a. Psychological dependence
   b. Overwhelming involvement in the acquisition and use of drugs for nonmedical purposes.
      Addiction is characterized by 1 or more of the following behaviors: impaired control over
drug use, compulsive use, continued use despite harm, and craving. Tolerance and
physical dependence may or may not be present. The presence of tolerance or physical
dependence does not prove psychological dependence.

KETAMINE

Ketamine is a phencyclidine derivative developed in the 1960s as a general anaesthetic.
Ketamine hydrochloride is given intravenously or intramuscularly for surgical anaesthesia.
Ketamine is also used as an adjuvant to opioids in the treatment of refractory pain in cancer
patients, in the treatment of neuropathic pain, and in the treatment of acute postoperative pain
(although it is not FDA approved for these conditions).

Ketamine acts on N-methyl-D-aspartate (NMDA) receptors as an antagonist. It is a
noncompetitive NMDA receptor antagonist that acts centrally where it modulates the sensory
processing of pain. The degree of analgesia is directly related to brain concentrations. It is
considered a dissociative agent, because it acts to dissociate the central nervous system from
outside stimuli. Its analgesic effect is accompanied by sedation and amnesia. However, it does
not depress respiratory or cardiovascular function.

Ketamine for postoperative pain may be administered before incision, after incision, or in the
postoperative period. It is usually given as an adjuvant to systemic opioid; for example, patient-
controlled analgesia (PCA). An intravenous route is most commonly used, although the drug can
be given by the intramuscular and subcutaneous route. Various doses are reported, but when used
for acute pain, a bolus of 0.5 mg/kg is used followed by an infusion of 2 µg/kg/min.

Studies in spinal surgery and major abdominal surgery demonstrate adequate pain control while
decreasing opioid use. In abdominal surgery, a 48-hour infusion was associated with less
postoperative nausea and vomiting. The ketamine patients had an incidence of 4% compared
with 27% in patients receiving hydroxyzine preoperatively. Many review papers show that
opioid dose reduction is a consistent finding.

Acute pain in the emergency department is another use for ketamine in children and adults.
Children are given 1.5–2 mg/kg and adults are given 1 mg/kg intravenously according to
emergency medicine guidelines.

Clinical use of ketamine has been limited due to possible psychotomimetic adverse effects, such
as hallucinations and bad dreams. Other common adverse effects include dizziness, blurred
vision, and elevation of intracranial pressure. However, overall, the drug is well tolerated at
commonly used doses.

References: Pain

1. Acute Pain Management Guideline Panel. Acute Pain Management: Operative or Medical
   Procedures and Trauma Clinical Practice Guideline. AHCPR Publication No. 92-0032. Rockville,
   MD: Agency for Health Care Policy and Research, US Department of Health and Human Services,


### Questions

1. A patient is scheduled to have a sigmoid colectomy. A preoperative epidural with a long-acting opioid is planned. Which of the following statements regarding preemptive analgesia is true?
   A. The incidence of hypotension is increased during the procedure.
   B. **Decreased alldynia and hyperalgesia will be present postoperatively.**
   C. Preemptive analgesia effects are mediated through peripheral pain receptor sensitization.
   D. Benefits are similar if the epidural is given at the end of the operation before the patient is awakened from general anesthesia.
   E. The benefit is mitigated by general anesthesia.

2. A patient has an epidural placed after a thoracotomy for pain control. On the first postoperative day, the patient is having excellent pain control based on a VAS score of 3 or 4. However, after every dose of drug via the epidural, a 30-minute period of hypotension occurs. The most likely cause of this hypotension is
   A. volume depletion.
   B. bleeding.
   C. the opioid dose is too high.
   D. **the local anesthetic dose is too high.**
   E. the patient is experiencing an allergic reaction to the epidural drugs.

3. Ketamine’s primary mechanism of action is as
   A. **An NMDA receptor antagonist.**
   B. a mu-receptor stimulant.
   C. a nitric oxide stimulant.
   D. a peripheral blocker of nociception.
   E. an alpha blockade in the brain.
4. A 35-year-old man is admitted with necrotizing pancreatitis. He complains of severe abdominal and back pain. He is receiving morphine sulfate parenterally at a dose of 5 mg every 2 hours. He states his VAS pain score is 8 to 9. A proper dose adjustment would be to
   A. increase the dose to 10 mg every 2 hours.
   B. increase the dose to 7.5 mg every 2 hours.
   C. change the opioid to hydromorphone at 1 mg every 2 hours.
   D. increase the dose 10–20 mg every 1 hour.
   E. switch to methadone at same dose.

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**Fluids and Electrolytes**

John A. Weigelt, MD, DVM, FACS

Objectives:
1. Describe body fluid compartments
2. List normal electrolyte concentrations of fluids
3. Review common fluid and electrolyte disorders

**BODY COMPARTMENTS**

Two-thirds of the body’s water is intracellular fluid (ICF). ICF is approximately 40% of a person’s body weight. The major ion is potassium. Extracellular fluid (ECF) is the remaining third of the body’s water and accounts for approximately 20% of a person’s weight. The primary ion is sodium. ECF consists of interstitial fluid (ISF) and plasma. ICF surrounds the cells but does not circulate and makes up three-quarters of the ECF. Plasma circulates as the extracellular component of blood and makes up one-quarter of the ECF.

Blood volume accounts for 7% of body weight, and 4% of body weight is from intravascular water. Blood has liquid and solid elements but behaves as a fluid in the body. An average adult body has approximately 5 L of blood. Intravascular solutes include Na, Cl, HCO₃, sugar, urea, and proteins, as well as the cellular elements of blood. Intracellular volume includes K, Mg, SO₄, and proteins.

Osmotic pressure is normally 280 mOsm and is caused by the number of osmotically active ions in any given compartment. The anions and cations in any compartment are equal in a steady state. This equilibrium in plasma is 154 mEq/L, in interstitial fluid is 153 mEq/L, and in intracellular fluid is 200 mEq/L. In the intravascular space, most of the osmotic activity is secondary to electrolytes.

1. Na ~ 140 mOsm (½ of total)
2. Cl and HCO₃ ~140 mOsm
3. Sugar, urea, creatinine ~ 10–20 mOsm
4. Proteins ~ 2 mOsm
COMMON FLUID CONCENTRATIONS

Composition of Intravenous Fluids

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<tr>
<th></th>
<th>Na⁺ (mEq/L)</th>
<th>K⁺ (mEq/L)</th>
<th>Ca²⁺ (mEq/L)</th>
<th>Cl⁻ (mEq/L)</th>
<th>HCO₃⁻ (mEq/L)</th>
<th>pH</th>
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<tbody>
<tr>
<td>Extracellular fluid</td>
<td>142</td>
<td>4</td>
<td>5</td>
<td>103</td>
<td>27</td>
<td>7.4</td>
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<tr>
<td>Lactated Ringer</td>
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<td>4</td>
<td>2.7</td>
<td>109</td>
<td>28</td>
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SODIUM

*Hyponatremia* is a decrease in the serum sodium concentration to less than 136 mmol/L. Hyponatremia can be associated with low, normal, or high osmolarity. Dilutional hyponatremia is the most common type and is associated with low osmolarity. Hypotonic hyponatremia represents an excess of water in relation to the body’s sodium stores, which may be low, normal, or increased. Impaired capacity for water excretion by the kidneys is the most common clinical condition—not excessive water intake. The abnormal water excretion is categorized by the relationship to the ECF. Diarrhea and diuretic agents are causes of hypotonic hyponatremia associated with a decreased volume of ECF. Hypotonic hyponatremia with congestive heart failure and cirrhosis is associated with an increased ECF. The condition is also seen with a normal ECF volume in adrenal insufficiency and use of vasopressin.

Central nervous system symptoms are seen with hyponatremia. Most patients with a serum sodium greater than 125 mmol/L are asymptomatic. Hypotonic hyponatremia causes cerebral edema and can produce seizures, coma, respiratory arrest, and death. Aggressive treatment of this type of hyponatremia can trigger demyelination of the pontine and extrapontine neurons, resulting in quadriplegia, seizures, coma, and death.

Euvolemic or hypervolemic patients who have concentrated urine can be managed with hypertonic saline. Patients who are symptomatic with low urine osmolarity can usually be managed by water restriction. The correction is calculated several different ways; one example is shown in the following case presentation:

A 66-year-old man has had severe diarrhea for 5 days. He has a low blood pressure and a serum sodium of 106 mEq/L with a potassium of 3.6 mEq/L. He is not mentally alert and may have had a seizure before admission. In addition to fluid resuscitation for hypovolemia, sodium correction is thought to be necessary. The patient weighs 70 kg.

\[
\text{Change in serum Na}^+ = \frac{\text{infusate Na}^+ - \text{serum Na}^+}{\text{Total Body Water (TBW)} + 1} = \frac{154 - 106}{42 + 1} = 1.1
\]

Thus, 1 L of normal saline (154 mEq Na⁺/L) will increase the serum sodium by 1.1 mEq/L. Given the patient’s hemodynamics, 12 L could be given over the next 24 hours with an expected rise in serum sodium of 12 mEq/L to 118–120 mEq/L. The caution is to not correct the hyponatremia too quickly, which can produce demyelination syndromes. Eight mEq/L/24 hours
is considered safe, and 12 mEq/L is considered the maximum change in sodium concentration that should be attempted.

*Hypernatremia* is defined as a serum sodium concentration of more than 145 mmol/L. Because serum osmolarity is primarily determined by ions, hypernatremia is always associated with hyperosmolarity. The most common cause of hypernatremia is net water loss. Pure water loss causes include unreplaced insensible losses and diabetes insipidus. Hypotonic fluid loss causes include nasogastric drainage and diuretic use. Sodium gain is less likely and is usually the result of errors in management with administration of fluids or supplements with excessive sodium concentrations, such as enteral feedings of hypertonic saline infusions.

Clinical symptoms include lethargy, stupor, and confusion. Treatment is hypotonic solutions, but correcting too rapidly can worsen central nervous system symptoms. Isotonic solutions should not be used to correct hypernatremia. Oral supplementation is preferred, if possible. Common solutions used include water, 5% dextrose, 0.2% sodium chloride, and 0.45% sodium chloride.

Urine osmolality is helpful in identifying a cause of hypernatremia. If the urine osmolality is more than 700–800 mOsm, then impaired water intake is a likely etiology. If the urine osmolality is less than 700–800 mOsm, impaired water intake and altered renal conservation is a likely cause. In this case, a diagnosis of diabetes insipidus is possible.

The formula used to calculate the amount of free water needed to correct the hypernatremia uses total body water (0.6 × weight in kg) and the difference between a normal serum sodium and the hypernatremic value. This formula is thought to be appropriate the closer the condition mimics a pure free water loss.

\[
\text{Free Water Deficit} = 0.6 \times \text{weight in kg} \times \frac{\text{Current serum Na}^+ - 1}{140}
\]

If the loss is secondary to hypotonic fluid losses, the recommended formula calculates the change in serum sodium desired. This formula will calculate the effect of 1 L of any infusate (with sodium) on serum sodium.

\[
\text{Change in serum sodium} = \frac{\text{infusate Na}^+ - \text{serum Na}^+}{\text{TBW} + 1}
\]

An example is helpful:

A 77-year-old woman is admitted with nausea and vomiting and abdominal pain for 3 days. Her mental status is depressed, and her serum sodium is found to be 159 mEq/L. She is tachycardic and afebrile, and she does not have peritonitis. Her potassium is 3.5 mEq/L. Her weight is 50 kg. A decision is made to correct her sodium by 10 mEq/L with 0.5% NaCl over 24 hours.

\[
\text{Change in serum sodium} = \frac{77 - 159}{30 + 1} = -2.6
\]

Thus, 1 L of 0.5% NaCl would correct her sodium by 2.6 points; 4 L are necessary to achieve a 10-point reduction, which would mean an hourly rate of 167 mL. Other losses the patient may
have must also be calculated into her total fluid requirements. The sodium should not be reduced by more than 10 mmol/L every 24 hours, especially if the hypernatremia is longstanding. When the free water deficit is calculated, usually one-half the volume is given in the first 24 hours.

**POTASSIUM**

Potassium balance is a function of intake and renal function. Only small amounts of potassium are lost in sweat and fecal excretions normally, but large losses can occur secondary to diarrhea, vomiting, or intestinal fistulas. A daily intake of 20–40 mEq is necessary for normal potassium homeostasis. Normal potassium levels are 3.5–4.5 mEq/L. Only 2% of the body’s potassium resides in the ECF, with the remaining located in the intracellular compartment. When a value of less than 3.6 mEq/L is used, more than 20% of hospitalized patients are considered hypokalemic, making it the most common electrolyte abnormality seen in hospitalized patients.

*Hypokalemia* is usually asymptomatic, especially with values between 3.0 and 3.5 mEq/L. An exception may be cardiac effects, where this level of hypokalemia can cause or exacerbate cardiac arrhythmias. Potassium levels less than 3.0 mEq/L are associated with weakness, glucose intolerance, and constipation. Values less than 2.5 mEq/L can cause muscle necrosis. The most common cause of hypokalemia is diuretic therapy. Alkalosis is another common cause of hypokalemia in hospitalized patients. This is usually the result of selective chloride depletion secondary to vomiting or nasogastric drainage. Treatment of the chloride deficiency is necessary to correct this type of hypokalemia. Primary hyperaldosteronism causes a hypokalemia independent of chloride depletion. Acidosis and hypokalemia occurs with distal renal tubular acidosis.

Treatment is administration of potassium. When given intravenously, potassium should not be given faster than 20 mEq/hour in an unmonitored situation or faster than 40 mEq/hour when cardiac monitoring is present. Oral administration is preferred, if possible.

*Hyperkalemia* is most commonly associated with renal failure. Potassium-sparing diuretics are also a cause. Minimal hyperkalemia is defined as serum values of 4.5–6.5 mEq/L, moderate is defined as 6.5–8.0 mEq/L, and severe is defined as greater than 8 mEq/L. Clinical signs and symptoms usually do not occur until the value exceeds 6.5 mEq/L.

Severe hyperkalemia is a life-threatening event because of the cardiovascular effect. Electrocardiogram (ECG) changes reflect potassium levels. Peaked T waves occur at a serum level of 5.5 mEq/L. QRS complexes widen as the potassium level exceeds 6.5 mEq/L. Between 7.5 and 8.0 mEq/L, P waves disappear and the QRS may resemble a sine wave. Ventricular fibrillation follows, and an inability to restore a normal sinus rhythm despite resuscitation technique is common. Treatment has an acute and chronic phase. Acute interventions should include administration of calcium gluconate or calcium chloride, an ampule of sodium bicarbonate, glucose, and insulin. Chronic treatments include ion exchange resins (sodium polystyrene), peritoneal dialysis, or hemodialysis.

**MAGNESIUM**

Magnesium is another intracellular ion. Only 1% of magnesium is in the ECF; 50% is intracellular, and the rest is located in bone. Hypermagnesemia is not a typical clinical concern,
although it is defined as an adverse event if magnesium replacement is excessive. A serum magnesium level of more than 2.7 mEq/L defines hypermagnesemia.

Hypomagnesemia is the more common clinically important condition. Hypomagnesemia has a 20–65% prevalence among critically ill patients. A value of less than 1.6 mEq/L defines hypomagnesemia. The most common cause is renal losses. Magnesium excretion is tied to the filtered sodium load. Because many critically ill patients receive saline solutions for resuscitation, this mechanism promotes magnesium loss. Loop diuretics also increase magnesium loss by interfering with magnesium resorption in the ascending loop of Henle. Glucose-induced diuresis associated with diabetes increases renal magnesium losses. Entero-cutaneous fistulas can also waste magnesium. Clinical manifestations include hypokalemia and hypocalcemia. Cardiac arrhythmias are seen, including torsade de pointes. Muscular weakness, tremors, and cramps may occur. In the critically ill, respiratory muscle weakness is a possible cause of failure to wean from mechanical ventilation. Treatment is usually intravenous in critically ill patients. One gram of magnesium sulfate contains 8 mEq of magnesium. A daily requirement is estimated to be 8–12 mEq. Thus, deficiency states must include the daily requirement and replacement amounts, which can easily reach 48–64 mEq in a 24-hour period. Renal excretion continues, which makes replacement difficult. When renal dysfunction is present, recommendations are to reduce the total estimated amount by 50%.

PHOSPHORUS

The skeleton is the location of 80–85% of body phosphorus. The rest is widely distributed throughout the body as organic phosphate compounds. In ECF, phosphorous is present mostly in the inorganic form. In serum, more than 85% of phosphorus is present as the free ion, and less than 15% is protein bound. The definition of hypophosphatemia is a serum level of less than 2.5 mEq/L. A value greater than 4.5 mEq/L is considered to be hyperphosphatemia. The daily requirements are 20–30 mmol/L. Phosphorus is necessary for numerous body functions related to adenosine triphosphate syntheses. Hypophosphatemia is the most common clinical condition seen, especially in critically ill patients. Hypophosphatemia can alter red cell oxygen transport and leukocyte function. A low phosphorus level can produce impaired diaphragmatic contractility, intermittent ventricular tachycardia, and insulin resistance.

Hypophosphatemia occurs in approximately 2% of hospitalized patients, but this percentage can increase to 35% in critically ill patients. Low serum phosphorus levels are caused by increasing renal excretion, probably as a result of volume expansion. Surgical patients who have large resuscitation volumes are especially at risk. Treatment is replacement, usually done intravenously. Care in administration is necessary, because hyperphosphatemia, hypotension, and renal failure have all been described with rapid replacements of phosphorus. Most protocols indicate that no more than 20 mmol be replaced over a 3-hour period. Others use 15 mmol doses given at a maximum of 3 times daily. Oral phosphorus replacements are poorly absorbed and may not be adequate when severe hypophosphatemia is present. In patients with phosphorus levels of 1–1.5 mEq/L, replacement with 60–80 mEq may be necessary, which will take 24 hours to administer. Another condition seen in malnourished patients is refeeding hypophosphatemia. This condition occurs as carbohydrates are reintroduced to a patient who has been catabolizing fat and muscle. Insulin release is stimulated by the carbohydrates, which enhances the intracellular uptake of glucose, phosphate, and potassium. This lowers serum phosphate; because low phosphorus levels were preexisting, hypophosphatemia occurs.
CALCIUM

Calcium is the most abundant mineral in the human body. The average adult body contains approximately 1 kg of calcium, but 99% is present in the skeleton as calcium phosphate. The ECF contains approximately 22.5 mmol, and 9 mmol is in serum. There is a constant turnover of 500 mmol calcium between bone and ECF every 24 hours. Serum calcium is closely regulated with a normal total calcium of 2.2–2.6 mmol/L or 9–10.5 mg/dL, which equates to a normal ionized calcium of 1.1–1.4 mmol/L or 4.5–5.6 mg/dL. Serum albumin levels affect serum calcium levels, as 50% of serum calcium is bound to albumin. Changes in serum albumin will cause proportional changes to serum calcium so that for every 1-g decrease in serum albumin, the serum calcium will fall 0.8 mg/dL. However, the biologic effect of calcium is mediated via ionized calcium, which does not change with serum albumin.

Hypocalcemia is uncommon, except as related to hypoparathyroidism, including postoperative hypoparathyroidism. The major signs are those of tetany, including Chvostek and Trousseau signs. ECG tracings are usually normal but may show a prolonged QRS interval. Acute treatment is administration of calcium as either calcium gluconate or chloride. The difference between the 2 is usually not clinically important, but the gluconate form needs to be metabolized by the liver before the calcium ion is released, whereas the chloride is immediately available on injection.

Chronic management of hypocalcemia requires calcium and Vitamin D. One important question is whether calcium supplementation is required during massive resuscitation with crystalloids and blood. These patients commonly have low serum albumin levels and low calcium levels. The data supporting routine calcium use are lacking. If low ionized calcium is present, supplementation may be necessary, but symptoms of hypocalcemia in these patients are difficult to identify.

Hypercalcemia is a common presenting sign for hyperparathyroidism as well as parathyroid hormone–secreting tumors. Approximately 20–40% of cancer patients will develop hypercalcemia sometime during their treatment course. These patients present with anorexia, nausea, vomiting, abdominal pain, constipation, polyuria, polydipsia, dehydration, psychosis, obtundation, and eventually coma. Treatment always begins with hydration. Saline is commonly used, because calcium excretion can be enhanced by a saline diuresis. Adding furosemide speeds the diuresis and excretion of calcium. Other drugs that can be used include corticosteroids, especially for malignant hypercalcemia; intravenous bisphosphonates; and calcitonin. Hemodialysis or peritoneal dialysis is occasionally needed.

References: Fluids and Electrolytes