Preface

This case study book provides an opportunity for integrative thinking in the areas of physiology, pathophysiology, and pharmacy. It provides students with an early introduction to the case-based nature of their future careers as practicing pharmacists and health care professionals.

The cases are straightforward and short and they are written at a level appropriate for student pharmacists in the first professional year of study. Written primarily as a review of fundamental physiological principles, these cases are also designed to illustrate the physiological basis of medicine and pharmacotherapeutics as well as to strengthen problem-solving skills.

The book is intended as a supplemental text for courses in physiology and pathophysiology. It begins with cases related to cellular physiology and nerve cell function. These are followed by cases involving the two major regulatory systems in the body: (1) the nervous system, including the brain, spinal cord, pain, and autonomic nervous system and (2) the endocrine system. The book then continues with cases concerning muscle physiology and the cardiovascular, respiratory, digestive, renal, and immune systems. Finally, an appendix provides brief descriptions of various diagnostic tests mentioned in some of the case studies and a glossary provides definitions of clinical terms that may be unfamiliar to student pharmacists in their first professional year.

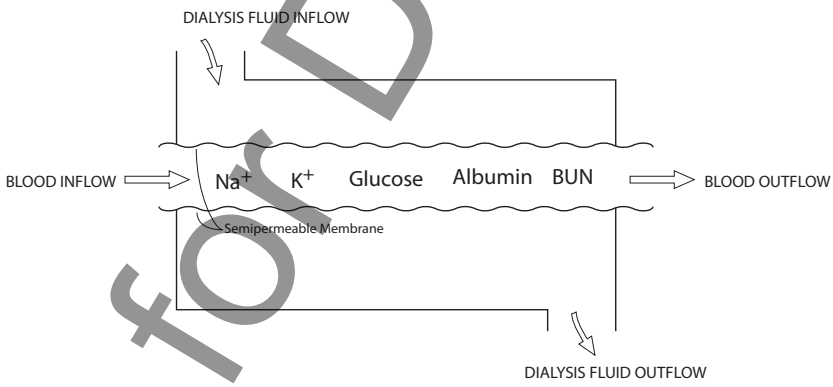
chapter one

Cellular Physiology

Hemodialysis

SP is a 42-year-old male with end-stage renal disease (ESRD). He goes for dialysis at the hospital out-patient clinic three times per week for 3 to 4 hours per visit. The hemodialysis system has three components (as illustrated in the figure below):

- Dialysis fluid compartment
- Blood compartment
- Semipermeable cellophane membrane



This membrane is permeable to all molecules except plasma proteins and blood cells. The dialysis fluid is a salt solution with ionic concentrations similar to those in normal plasma. The fluid surrounding the membrane is constantly drained and replenished. A sample of the patient's blood prior to dialysis revealed the following:

	Blood Sample	Normal Reference Range
• Plasma osmolarity	285 mOsm/L	280–290 mOsm/L
• Potassium	5.2 mEq/L	3.5–5.0 mEq/L
• Sodium	145 mEq/L	135–145 mEq/L
• Glucose	90 mg/dL	70–110 mg/dL
• Albumin	4.3 g/dL	3.5–5.0 g/dL
• Blood urea nitrogen	25 mg/dL	7–18 mg/dL

1. Define diffusion and osmosis. Describe the factors that affect the rate of diffusion and the magnitude of osmosis.

2. There has been significant fluid retention in this patient due to the ESRD and the inability of the kidneys to excrete a sufficient volume of urine. In order to reduce this fluid buildup, should the dialysis fluid be isosmotic, hypoosmotic, or hyperosmotic compared to the plasma?

3. Which of the following would be an expected component of the dialysis fluid: potassium, sodium, glucose, albumin, blood urea nitrogen? Explain why or why not for each substance.

4. Which of these substances may diffuse out of the blood compartment into the dialysis fluid compartment?

5. Which of these substances will diffuse out of the blood compartment into the dialysis fluid compartment resulting in a net loss of the substance?

6. Explain why the dialysis fluid surrounding the cellophane membrane must constantly be drained and replenished.

Hyponatremia

NG is a 24-year-old male athlete who ran the Boston marathon. The day of the race was sunny and the temperature was 83°F. NG sweated profusely and replaced the lost fluids with spring water as often as possible. After running approximately 18 miles, he became confused and disoriented. Other symptoms included muscle weakness, abdominal cramps, headache, and muscle cramps. He was forced to discontinue the race when he experienced vomiting and diarrhea. NG was brought to the emergency room where lab tests revealed a marked decrease in plasma osmolarity and a serum sodium of 120 mmol/L. Treatment included intravenous administration of a hypertonic saline solution and the loop diuretic furosemide. (Hyponatremia is also discussed in Chapter 8: Renal System, p. 145.)

1. What is hyponatremia?

2. What is the normal value for serum sodium?

3. With this condition, is the extracellular fluid likely to be isosmotic, hyperosmotic, or hypoosmotic compared to the intracellular fluid? Explain.

4. In terms of the extracellular and intracellular compartments, describe the effect hyponatremia has on osmotic and hydrostatic pressures.

5. Does water move into or out of the body's cells? What other signs or symptoms may result from this shift in water?

6. Does hyponatremia cause any change in the resting membrane potential of the body's cells? Why or why not?

7. How does the administration of hypertonic saline solution alleviate this condition?

8. What is the advantage of the intravenous administration of a solution such as hypertonic saline versus the oral administration?

9. How could NG have avoided the development of hyponatremia?

Membrane Potentials in Hyperkalemia

JB is a 62-year-old female who visited her primary care physician. Her symptoms included muscle cramps, weakness, and dizziness as well as gastrointestinal distress (nausea, vomiting, and diarrhea). Previous medical history includes diabetes mellitus and progressively impaired renal function. Her physician withdrew blood for a series of lab tests. The results indicated that the patient had a serum potassium level of 6.2 mmol/L. Other serum electrolytes were within the normal ranges.

1. What is hyperkalemia?

2. What are the average concentrations of potassium in the intracellular fluid (ICF) and the extracellular fluid (ECF)?

3. What is the relative permeability of K^+ ions in unstimulated cells?

4. What effect does hyperkalemia have on the movement of K^+ ions across cell membranes?

5. What are the average concentrations of sodium in the ICF and the ECF?

6. What is the relative permeability of Na^+ ions in unstimulated cells?

7. What effect does hyperkalemia have on the movement of Na^+ ions across cell membranes?

8. Will hyperkalemia cause the membrane potential to become more negative or less negative? Is this change referred to as depolarization or hyperpolarization?

9. What types of cells are affected by changes in membrane potential?

10. Initially, the changes in membrane potential led to the development of muscle cramps in the patient. How has the excitability of the skeletal muscle fibers been affected?

11. Muscle cramps are followed by muscle weakness. Explain how changes in membrane potential and ion flux cause subsequent skeletal muscle weakness.

12. The most serious effect of hyperkalemia is cardiac arrest. Is it likely that the heart will stop beating during a heartbeat (while the cardiac muscle is stimulated to contract) or in between beats? Why?

Membrane Potentials in Hypokalemia

JM is a 64-year-old female who had been experiencing generalized fatigue, weakness and difficulty breathing. Over time, these symptoms became steadily worse and she went to her primary care physician. Physical examination revealed distension of the jugular veins, ascites and edema in the lower extremities. Further testing led her physician to a diagnosis of congestive heart failure. JM was treated with digoxin to enhance the strength of contraction of her heart and with the diuretic hydrochlorothiazide to relieve the edema. After taking the hydrochlorothiazide for a few days, JM experienced extreme weakness and muscle twitching. She returned to her doctor who also observed depressed neuromuscular reflexes and a decrease in neuromuscular tone (loss of firmness of the skeletal muscles). JM was informed by her physician that thiazide diuretics have several potential adverse effects including hypokalemia. A blood test was performed to confirm this diagnosis.

1. What is hypokalemia?

2. What is the normal distribution of potassium in the extracellular fluid and the intracellular fluid?

3. What effect does hypokalemia have on the movement of potassium across the cell membrane? Why?

4. What effect does hypokalemia have on the membrane potentials of neurons and muscle cells?

5. Explain how hypokalemia led to the symptoms observed in this patient.

6. The patient's hypokalemia was treated with the intravenous administration of potassium. Which of the following methods of administration is recommended: the rapid infusion of a concentrated potassium solution or the slow infusion of a dilute potassium solution? Why?

Action Potentials in Tetrodotoxin Poisoning

PS is a 23-year-old man who had been dining in a sushi restaurant. Approximately 15 minutes after eating several pieces of fugu (puffer fish), he noticed a tingling sensation in his tongue and the inside of his mouth. These symptoms were followed by lightheadedness, dizziness, and vomiting. When he tried to leave the restaurant, he felt weakness in his legs and he collapsed. Upon examination in the emergency room, the patient was observed to be hypotensive (blood pressure 105/60 mmHg) and bradycardic (heart rate 58 beats per minute). His superficial and deep reflexes were markedly suppressed. When a painful stimulus was applied to his hand, no withdrawal reflex was elicited. An electromyogram and a nerve conduction velocity test were ordered. These tests involve the placement of microelectrodes in the patient's arm. It was revealed that the generation of action potentials in the sensory fibers of the ulnar nerve was impaired. A diagnosis of tetrodotoxin poisoning was made and the patient received therapy aimed at restoring blood pressure to the normal range.

1. Which ion channels are blocked by tetrodotoxin?

2. Why does this blockade impair the generation of action potentials in the sensory nerve fibers?

3. What effect does the blockade of these ion channels have on the resting membrane potential in the sensory nerve fibers?

4. Vigorous stimulation of the hand results in the low frequency generation of action potentials. What changes are observed in these action potentials?

5. The duration of the action potentials is normal. Why?

6. What is the cause of muscle weakness?

7. What is a potential cause of death for a patient with tetrodotoxin poisoning?

Neuronal Physiology in Multiple Sclerosis

SK is a 28-year-old female who has had recurrent episodes of neurological dysfunction. Four years ago, she experienced visual clouding and ataxia that persisted for several days before completely resolving. Eighteen months ago, she developed an intension tremor in her left hand that also resolved within a few weeks. Currently, SK is experiencing fatigue, a loss of balance, impaired gait, nystagmus, and mood swings. Magnetic resonance imaging (MRI) studies revealed multiple lesions in the white matter of the brain, spinal cord, and the optic nerve.

1. At what age are patients typically diagnosed with multiple sclerosis? Is this disease more prevalent in men or women?

2. What is the source of myelin in the central nervous system? In the peripheral nervous system?

3. Why are neuronal axons covered with myelin referred to as white matter? What is the composition of this substance?

4. What is the function of myelin? How does the molecular composition of myelin cause this effect?

5. Compare and contrast local current flow and saltatory conduction. Which type of electrical conduction would normally occur in the affected neurons?

6. What types of nerve fibers are myelinated? Unmyelinated? Explain.

7. Describe the lesions observed in the white matter. What is the clinical term for these lesions?

8. Define ataxia and nystagmus. What is the cause of these symptoms?

9. How has the transmission of electrical impulses been affected by the demyelination?

Synaptic Transmission in Seizure Disorder

DP is a 24-year-old male who had his first tonic–clonic seizure at the age of 15. At the beginning of the seizure, this patient experiences an immediate loss of consciousness and often incontinence. A common disorder encountered in pediatric neurology, this form of seizure begins with sharp tonic contraction of the muscles characterized by extension of the extremities. This is followed by the clonic phase which is characterized by rhythmic bilateral contraction and relaxation of the extremities. The tonic–clonic phases persist for approximately 60 to 90 seconds. For several years, DP has controlled his seizures with a single medication, carbamazepine. However, during the last 6 months, he has experienced a marked increase in seizure activity. His neurologist has now prescribed a second medication, topiramate, to be taken along with the carbamazepine.

1. Seizures are the result of spontaneous, uncontrolled activity of neurons in the cerebral cortex of the brain. Explain how this neuronal hyperexcitability in the brain can lead to contraction of skeletal muscles.

2. What is the absolute refractory period (ARP) in neurons? The relative refractory period (RRP)?

3. The mechanism of action of carbamazepine involves a decreased rate of recovery of voltage-gated Na^+ channels from their inactivation state. What effect does carbamazepine have on the ARP? The RRP?

4. What effect does carbamazepine have on the frequency of action potential generation in these neurons?

5. Compare and contrast temporal summation and spatial summation of postsynaptic potentials.

6. How is temporal summation in postsynaptic neurons likely to be altered by carbamazepine? Spatial summation?

7. Explain why carbamazepine is the primary drug used for the treatment of tonic–clonic seizures.

8. Compare and contrast excitatory postsynaptic potentials (EPSPs) and inhibitory postsynaptic potentials (IPSPs).

9. In addition to its inhibitory effects on Na^+ channels, topiramate enhances γ-aminobutyric acid (GABA)-mediated chloride conductance. Does this latter effect of topiramate increase the number of EPSPs or IPSPs generated in the neurons? Explain.

10. Is topiramate likely to affect temporal summation or spatial summation? Why?

11. How does topiramate affect the generation of action potentials in these neurons?