## Cases AND Problems

# Physiology

FOURTH EDITION

- 62 cases covering the most relevant physiology concepts
- Thought-provoking questions with full explanations
- Problem-solving exercises and solutions

Linda S. Costanzo

### **Physiology** Cases and Problems

FOURTH EDITION

#### Linda S. Costanzo, Ph.D.

Professor of Physiology and Rioph Medical College of Virginia Virginia Com noriwe Richmond, Vi



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Fourth Edition

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#### **Preface**

This book was written for first- and second-year medical students who are studying physiology and pathophysiology. In the framework of cases, the book covers clinically relevant topics in physiology by asking students to answer open-ended questions and solve problems. This book is intended to complement lectures, course syllabi, and traditional textbooks of physiology.

The chapters are arranged according to organ system, including cellular and autonomic, cardiovascular, respiratory, renal and acid-base, gastrointestinal, and endocrine and reproductive physiology. Each chapter presents a series of cases followed by questions and problems that emphasize the most important physiologic principles. The questions require students to perform complex, multistep reasoning, and to think integratively across the organ systems. The problems emphasize clinically relevant calculations. Each case and its accompanying questions and problems are immediately followed by complete, stepwise explanations or solutions, many of which include diagrams, classic graphs, and flowcharts.

This book includes a number of features to help students master the principles of physiology.

- Cases are shaded for easy identification.
- Within each case, questions are arranged sequentially so that they intentionally build upon each other.
- The difficulty of the questions varies from basic to challenging, recognizing the progression that most students make.
- When a case includes pharmacologic or pathophysiologic content, brief background is provided to allow first-year medical students to answer the questions.
- Major equations are presented in boldface type, followed by explanations of all terms.
- Key topics are listed at the end of each case so that students may cross-reference these topics with indices of physiology texts.
- Common abbreviations are presented on the inside front cover, and normal values and constants are presented on the inside back cover.

Students may use this book alone or in small groups. Either way, it is intended to be a dynamic, working book that challenges its users to think more critically and deeply about physiologic principles. Throughout, I have attempted to maintain a supportive and friendly tone that reflects my own love of the subject matter.

I welcome your feedback, and look forward to hearing about your experiences with the book. Best wishes for an enjoyable journey!

Linda S. Costanzo, Ph.D.

#### Acknowledgments

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Finally, heartfelt thanks go to my husband, Richard, our children, Dan and Rebecca, my daughter-in-law, Sheila, and my granddaughter, Elise, for their love and support.

Linda S. Costanzo, Ph.D.

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#### CASE 1

#### **Permeability and Simple Diffusion**

Four solutes were studied with respect to their permeability and rate of diffusion in a lipid bilayer. Table 1–1 shows the molecular radius and oil–water partition coefficient of each of the four solutes. Use the information given in the table to answer the following questions about diffusion coefficient, permeability, and rate of diffusion.

table <b>1</b> -	b I e 1-1 Molecular Radii and Oil-Water Partition Coefficients of Four Solutes		
Solute	Molecular Radius, Å	Oil-Water Partition Coefficient	
А	20	1.0	
В	20	2.0	
С	40	1.0	
D	40	0.5	

#### Questions

- 1. What equation describes the diffusion coefficient for a solute? What is the relationship between molecular radius and diffusion coefficient?
- 2. What equation relates permeability to diffusion coefficient? What is the relationship between molecular radius and permeability?
- 3. What is the relationship between oil—water partition coefficient and permeability? What are the units of the partition coefficient? How is the partition coefficient measured?
- 4. Of the four solutes shown in Table 1-1, which has the highest permeability in the lipid bilayer?
- 5. Of the four solutes shown in Table 1-1, which has the lowest permeability in the lipid bilayer?
- **6.** Two solutions with different concentrations of Solute A are separated by a lipid bilayer that has a surface area of 1 cm<sup>2</sup>. The concentration of Solute A in one solution is 20 mmol/mL, the concentration of Solute A in the other solution is 10 mmol/mL, and the permeability of the lipid bilayer to Solute A is  $5 \times 10^{-5}$  cm/sec. What is the direction and net rate of diffusion of Solute A across the lipid bilayer?
- 7. If the surface area of the lipid bilayer in Question 6 is doubled, what is the net rate of diffusion of Solute A?
- **8.** If all conditions are identical to those described for Question 6, except that Solute A is replaced by Solute B, what is the net rate of diffusion of Solute B?
- 9. If all conditions are identical to those described for Question 8, except that the concentration of Solute B in the 20 mmol/mL solution is doubled to 40 mmol/mL, what is the net rate of diffusion of Solute B?

#### ANSWERS ON NEXT PAGE



#### Answers and Explanations

1. The Stokes-Einstein equation describes the diffusion coefficient as follows:

$$D = \frac{KT}{6\pi r \eta}$$

where

D = diffusion coefficient

K = Boltzmann's constant

T = absolute temperature (K)

r = molecular radius

 $\eta$  = viscosity of the medium

The equation states that there is an inverse relationship between molecular radius and diffusion coefficient. Thus, small solutes have high diffusion coefficients and large solutes have low diffusion coefficients.

2. **Permeability** is related to the diffusion coefficient as follows:

$$P = \frac{KD}{\Delta x}$$

where

P = permeability

K = partition coefficient

D = diffusion coefficient

 $\Delta x = \text{membrane thickness}$ 

The equation states that permeability (P) is directly correlated with the diffusion coefficient (D). Furthermore, because the diffusion coefficient is inversely correlated with the molecular radius, permeability is also inversely correlated with the molecular radius. As the molecular radius increases, both the diffusion coefficient and permeability decrease.

3. The oil–water **partition coefficient** ("K" in the permeability equation) describes the solubility of a solute in oil relative to its solubility in water. The higher the partition coefficient of a solute, the higher its oil or lipid solubility and the more readily it dissolves in a lipid bilayer. The relationship between the oil–water partition coefficient and permeability is described in the equation for permeability (see Question 2): the higher the partition coefficient of the solute, the higher its permeability in a lipid bilayer.

The partition coefficient is a dimensionless number (meaning that it has no units). It is measured by determining the concentration of solute in an oil phase relative to its concentration in an aqueous phase and expressing the two concentrations as a ratio. When expressed as a ratio, the units of concentration cancel each other.

One potential point of confusion is that in the equation for permeability, K represents the partition coefficient (discussed in Question 4); in the equation for diffusion coefficient, K represents the Boltzmann constant.

**4.** As already discussed, permeability in a lipid bilayer is inversely correlated with molecular size and directly correlated with partition coefficient. Thus, a small solute with a high partition coefficient (i.e., high lipid solubility) has the highest permeability, and a large solute with a low partition coefficient has the lowest permeability.

Table 1-1 shows that among the four solutes, Solute B has the highest permeability because it has the smallest size and the highest partition coefficient. Based on their larger molecular radii and their equal or lower partition coefficients, Solutes C and D have lower permeabilities than Solute A.

- 5. Of the four solutes, Solute D has the lowest permeability because it has a large molecular size and the lowest partition coefficient.
- 6. This question asked you to calculate the net rate of diffusion of Solute A, which is described by the Fick law of diffusion:

$$J = P A (C_1 - C_2)$$

where

net rate of diffusion (mmol/sec)

= permeability (cm/sec)

A = surface area (cm<sup>2</sup>)

 $C_1$  = concentration in solution 1 (mmol/mL)

concentration in solution 2 (mmol/mL)

In words, the equation states that the net rate of diffusion (also called flux, or flow) is directly correlated with the permeability of the solute in the membrane, the surface area available for diffusion, and the difference in concentration across the membrane. The net rate of diffusion of Solute A is:

=  $5 \times 10^{-5}$  cm/sec  $\times 1$  cm<sup>2</sup>  $\times$  (20 mmol/mL – 10 mmol/mL)

 $= 5 \times 10^{-5} \text{ cm/sec} \times 1 \text{ cm}^2 \times (10 \text{ mmol/mL})$ 

 $= 5 \times 10^{-5} \text{ cm/sec} \times 1 \text{ cm}^2 \times (10 \text{ mmol/cm}^3)$ 

 $5 \times 10^{-4}$  mmol/sec, from high to low concentration

Note that there is one very useful trick in this calculation:  $1 \text{ mL} = 1 \text{ cm}^3$ .

- 7. If the surface area doubles, and all other conditions are unchanged, the net rate of diffusion of Solute A doubles (i.e., to  $1 \times 10^{-3}$  mmol/sec).
- 8. Because Solute B has the same molecular radius as Solute A, but twice the oil-water partition coefficient, the permeability and the net rate of diffusion of Solute B must be twice those of Solute A. Therefore, the permeability of Solute B is  $1 \times 10^{-4}$  cm/sec, and the net rate of diffusion of Solute B is  $1 \times 10^{-3}$  mmol/sec.
- 9. If the higher concentration of Solute B is doubled, then the net rate of diffusion increases to  $3 \times 10^{-3}$  mmol/sec, or threefold, as shown in the following calculation:

 $1 \times 10^{-4} \text{ cm/sec} \times 1 \text{ cm}^2 \times (40 \text{ mmol/mL} - 10 \text{ mmol/mL})$ 

 $1 \times 10^{-4} \text{ cm/sec} \times 1 \text{ cm}^2 \times (30 \text{ mmol/mL})$   $1 \times 10^{-4} \text{ cm/sec} \times 1 \text{ cm}^2 \times (30 \text{ mmol/cm}^3)$ 

 $3 \times 10^{-3}$  mmol/sec

If you thought that the diffusion rate would double (rather than triple), remember that the net rate of diffusion is directly related to the difference in concentration across the membrane; the difference in concentration is tripled.

#### **Key topics**

Diffusion coefficient

Fick law of diffusion

Flux, or flow

Partition coefficient

Permeability

Stokes-Einstein equation

#### Chapter 1

#### CASE 2

#### Osmolarity, Osmotic Pressure, and Osmosis

The information shown in Table 1–2 pertains to six different solutions.

t a b l e 1-2 Comparison of Six Solutions				
Solution	Solute	Concentration (mmol/L)	g extension	g viet out
1	Urea	1 was true of an interest	1.0	0
2	NaCl	and the second second second	1.85	0.5
3	NaCl	2	1.85	0.5
4	KCI	1	1.85	0.4
5	Sucrose	1	1.0	0.8
6	Albumin		1.0	1.0

g, osmotic coefficient; o, reflection coefficient.

#### Questions

- 1. What is osmolarity, and how is it calculated?
- 2. What is osmosis? What is the driving force for osmosis?
- 3. What is osmotic pressure, and how is it calculated? What is effective osmotic pressure, and how is it calculated?
- **4.** Calculate the osmolarity and effective osmotic pressure of each solution listed in Table 1–2 at 37°C. For 37°C, RT = 25.45 L-atm/mol, or 0.0245 L-atm/mmol.
- 5. Which, if any, of the solutions are isosmotic?
- 6. Which solution is hyperosmotic with respect to all of the other solutions?
- 7. Which solution is hypotonic with respect to all of the other solutions?
- **8.** A semipermeable membrane is placed between Solution 1 and Solution 6. What is the difference in effective osmotic pressure between the two solutions? Draw a diagram that shows how water will flow between the two solutions and how the volume of each solution will change with time.
- **9.** If the hydraulic conductance, or filtration coefficient  $(K_p)$ , of the membrane in Question 8 is 0.01 mL/min-atm, what is the rate of water flow across the membrane?
- 10. Mannitol is a large sugar that does not dissociate in solution. A semipermeable membrane separates two solutions of mannitol. One solution has a mannitol concentration of 10 mmol/L, and the other has a mannitol concentration of 1 mmol/L. The filtration coefficient of the membrane is 0.5 mL/min-atm, and water flow across the membrane is measured as 0.1 mL/min. What is the reflection coefficient of mannitol for this membrane?



#### Answers and Explanations

1. Osmolarity is the concentration of osmotically active particles in a solution. It is calculated as the product of solute concentration (e.g., in mmol/L) times the number of particles per mole in solution (i.e., whether the solute dissociates in solution). The extent of this dissociation is described by an osmotic coefficient called "g." If the solute does not dissociate, g=1.0. If the solute dissociates into two particles, g=2.0, and so forth. For example, for solutes such as urea or sucrose, g=1.0 because these solutes do not dissociate in solution. On the other hand, for NaCl, g=2.0 because NaCl dissociates into two particles in solution, Na $^+$  and Cl $^-$ . With this last example, it is important to note that Na $^+$  and Cl $^-$  ions may interact in solution, making g slightly less than the theoretical, ideal value of 2.0.

#### Osmolarity = g C

where

g = number of particles/mol in solution

C = concentration (e.g., mmol/L)

Two solutions that have the same calculated osmolarity are called **isosmotic**. If the calculated osmolarity of two solutions is different, then the solution with the higher osmolarity is **hyperosmotic** and the solution with the lower osmolarity is **hyposmotic**.

2. Osmosis is the flow of water between two solutions separated by a semipermeable membrane caused by a difference in solute concentration. The driving force for osmosis is a difference in osmotic pressure caused by the presence of a solute. Initially, it may be surprising that the presence of a solute can cause a pressure, which is explained as follows. Solute particles in a solution interact with pores in the membrane and in so doing lower the hydrostatic pressure of the solution. The higher the solute concentration, the higher the osmotic pressure (see Question 3) and the lower the hydrostatic pressure (because of the interaction of the solute with pores in the membrane). Thus, if two solutions have different solute concentrations (Fig. 1–1), then their osmotic and hydrostatic pressures are also different, and the difference in pressure causes water flow across the membrane (i.e., osmosis).

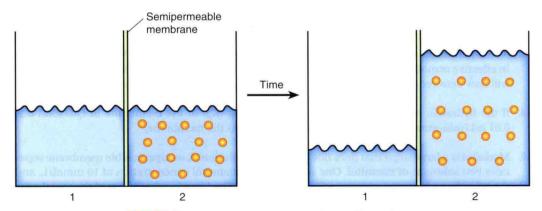


FIGURE 1–1. Osmosis of water across a semipermeable membrane.

#### 3. The osmotic pressure of a solution is described by the van't Hoff equation:

#### $\pi = g C RT$

where

 $\pi$  = osmotic pressure [atmospheres (atm)]

g = number of particles/mol in solution

C = concentration (e.g., mmol/L)

R = gas constant (0.082 L-atm/mol-K)

T = absolute temperature (K)

In words, the van't Hoff equation states that the osmotic pressure of a solution depends on the concentration of osmotically active solute particles. The concentration of solute particles is converted to a pressure by multiplying this concentration by the gas constant and the absolute temperature.

The concept of "effective" osmotic pressure involves a slight modification of the van't Hoff equation. Effective osmotic pressure depends on *both* the concentration of solute particles *and* the extent to which the solute crosses the membrane. The extent to which a particular solute crosses a particular membrane is expressed by a dimensionless factor called the reflection coefficient ( $\sigma$ ). The value of the reflection coefficient can vary from 0 to 1.0 (Fig. 1–2). When  $\sigma$  = 1.0, the membrane is completely impermeable to the solute; the solute remains in the original solution and exerts its full osmotic pressure. When  $\sigma$  = 0, the membrane is freely permeable to the solute; solute diffuses across the membrane and down its concentration gradient until the concentrations in both solutions are equal. In this case, where  $\sigma$  = 0, the solutions on either side of the membrane have the same osmotic pressure because they have the same solute concentration; there is no difference in effective osmotic pressure across the membrane, and no osmosis of water occurs. When  $\sigma$  is between 0 and 1, the membrane is somewhat permeable to the solute; the effective osmotic pressure lies somewhere between its maximal value and 0.

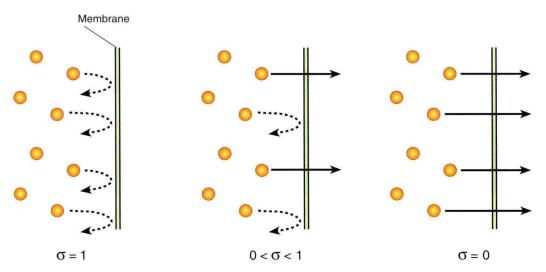


FIGURE 1-2. Reflection coefficient. σ, reflection coefficient.

Thus, to calculate the **effective osmotic pressure** ( $\pi_{\text{eff}}$ ), the van't Hoff equation for osmotic pressure is modified by the value for  $\sigma$ , as follows:

#### $\pi_{\text{eff}} = g C \sigma RT$

where

 $\pi_{\text{eff}}$  = effective osmotic pressure (atm)

g = number of particles/mol in solution

C = concentration (e.g., mmol/L)

R = gas constant (0.082 L-atm/mol-K)

T = absolute temperature (K)

 $\sigma$  = reflection coefficient (no units; varies from 0 to 1)

**Isotonic** solutions have the same effective osmotic pressure. When isotonic solutions are placed on either side of a semipermeable membrane, there is no difference in effective osmotic pressure across the membrane, no driving force for osmosis, and no water flow.

If two solutions have different effective osmotic pressures, then the one with the higher effective osmotic pressure is **hypertonic**, and the one with the lower effective osmotic pressure is **hypotonic**. If these solutions are placed on either side of a semipermeable membrane, then an osmotic pressure difference is present. This osmotic pressure difference is the driving force for water flow. Water flows from the hypotonic solution (with the lower effective osmotic pressure) into the hypertonic solution (with the higher effective osmotic pressure).

#### 4. See Table 1-3.

t a b l e 1-3 Calculated Values of Osmolarity and Effective Osmotic Pressure of Six Solution			
Solution	Osmolarity (mOsm/L)	Effective Osmotic Pressure (atm)	
1	1	0	
2	1.85	0.0227	
3	3.7	0.0453	
4	1.85	0.0181	
5	1	0.0196	
6	1.0	0.0245	

- **5.** Solutions with the same calculated osmolarity are **isosmotic**. Therefore, Solutions 1, 5, and 6 are isosmotic with respect to each other. Solutions 2 and 4 are isosmotic with respect to each other.
- Solution 3 has the highest calculated osmolarity. Therefore, it is hyperosmotic with respect to the other solutions.
- 7. According to our calculations, Solution 1 is hypotonic with respect to the other solutions because it has the lowest effective osmotic pressure (zero). But why zero? Shouldn't the urea particles in Solution 1 exert *some* osmotic pressure? The answer lies in the reflection coefficient of urea, which is zero: because the membrane is freely permeable to urea, urea instantaneously diffuses down its concentration gradient until the concentrations of urea on both sides of the membrane are equal. At this point of equal concentration, urea exerts no "effective" osmotic pressure.
- 8. Solution 1 is 1 mmol/L urea, with an osmolarity of 1 mOsm/L and an effective osmotic pressure of 0. Solution 6 is 1 mmol/L albumin, with an osmolarity of 1 mOsm/L and an effective osmotic pressure of 0.0245 atm. According to the previous discussion, these two solutions are *isosmotic* because they have the same osmolarity. However, they are *not isotonic* because they have different effective osmotic pressures. Solution 1 (urea) has the lower effective osmotic pressure and is hypotonic. Solution 6 (albumin) has the higher effective osmotic pressure and is hypertonic. The