PHYSIOLOGY

edited by

EWALD E. SELKURT, Ph.D.

LIBRARY OF CONGRESS CATALOG CARD NUMBER 61–16809

Third Printing

Published in Great Britain
by J. & A. Churchill Ltd., London

PRINTED IN THE UNITED STATES OF AMERICA

Foreword

This volume is intended to supply the basic core of physiology needed by students of medicine and the allied professions; it should also meet the needs, at the college level, of certain advanced courses in the biological sciences. As a collaborative effort by members of a department of physiology responsible for teaching the subject in a large state university medical complex, the text is comprehensive in its coverage and should meet the requirements of a wide variety of curricula.

The style is direct and didactic. Established facts are emphasized, and controversial issues have been minimized. Complementary subject matter taught by other disciplines, e.g., anatomy and biochemistry, has been limited to review of pertinent essentials. The text is particularly suited to fill the gap between oversimplified and synoptic works and the broad, detailed treatises which appeal more to the advanced student, investigator, and clinician.

The authors are active investigators in a variety of disciplines in physiology, and their contributions to this text are attuned to the latest developments in their respective fields. Although basic principles are stressed, the text has the advantage that clinical application has not been ignored. However, due to the rapid growth of knowledge in physiology, both at the basic level and at the clinical level, the teaching of clinical physiology is justifiably being handled to a greater and greater extent by teachers in the clinical disciplines, in departments of medicine, pediatrics, surgery, urology, neurology, etc. For this reason, the writers of this volume have concentrated their major efforts on providing a sound grounding in the fundamentals of mammalian physiology.

Acknowledgments

We wish to acknowledge the help of the following experts in certain specialized areas of physiology:

JAMES ASHMORE, Ph.D.
Professor, Department of Pharmacology, Indiana University School of Medicine, Indianapolis, Indiana

ALEX BLACK, Ph.D.
Associate Director, Agricultural Experiment Station, College of Agriculture, The Pennsylvania State University, University Park, Pennsylvania

STUART O. BONDURANT, M.D.
Associate Professor, Department of Medicine, Indiana University School of Medicine

ELSWORTH R. BUSKIRK, Ph.D.
Physiologist in Charge, Metabolic Chamber, National Institute of Arthritis and Metabolic Diseases, Bethesda, Maryland

WILLIAM P. DIESS, M.D.
Professor, Department of Medicine, Indiana University School of Medicine

HYMEN S. MAYERSON, Ph.D.
Professor, Department of Physiology, Tulane University School of Medicine, University Station, New Orleans

OSCAR D. RATNOFF, M.D.
Associate Professor, Department of Medicine, Western Reserve University School of Medicine, Cleveland, Ohio

WILLIAM E. SEGAR, M.D.
Associate Professor, Department of Pediatrics, Indiana University School of Medicine

Appreciation for their aid in the illustrating of the book is expressed to Mr. James F. Glore of the Illustrations Department of the Indiana University School of Medicine and to his staff, Mr. Joseph M. Demma and Mr. David Willoughby.

The help of our secretarial staff, which included Mrs. Patricia L. Anderson, Mrs. M. Helen Granger, and Mrs. Jane Fibiger, is gratefully acknowledged.

Particular acknowledgment is given to Mr. Fred Belliveau, Manager of the Medical Book Department of Little, Brown and Company, for the splendid cooperation of his firm, and to Miss Margaret Mutch for her invaluable work as copy editor.

Contents

FOREWORD vii

ACKNOWLEDGMENTS ix

1. PHYSIOLOGY OF THE CELL MEMBRANE 3
Julius J. Friedman

2. GENERAL PROPERTIES OF NERVE 18
Sidney Ochs

3. RECEPTORS AND EFFECTORS 43
Sidney Ochs

4. SPECIAL SENSES

The Eye 65
Paul C. Johnson

The Ear 84
Carl F. Rothe

The Ear: Vestibular Apparatus 95
Julius J. Friedman

5. REFLEXES AND REFLEX MECHANISMS 101
Sidney Ochs

6. ELECTRICAL PROPERTIES OF THE CEREBRUM AND UPPER SENSORY FUNCTIONS 124
Sidney Ochs

7. REGULATION OF VISCERAL FUNCTION BY THE AUTONOMIC NERVOUS SYSTEM 142
Carl F. Rothe

8. UPPER SOMATIC AND VISCERAL CONTROL 161
Sidney Ochs

9. HIGHER NERVOUS FUNCTIONS 177
Sidney Ochs

10. FUNCTIONAL PROPERTIES OF BLOOD 189
Julius J. Friedman

11. FLUID DYNAMICS 204
Carl F. Rothe

12. MICROCIRCULATION 225
Julius J. Friedman

13. THE HEART AS A PUMP; MECHANICAL CORRELATES OF CARDIAC ACTIVITY 246
Ewald E. Selkurt and Robert W. Bullard

14. CARDIAC EXCITATION, CONDUCTION, AND THE ELECTROCARDIOGRAM 266
Robert W. Bullard

15. CARDIODYNAMICS 285
Carl F. Rothe

16. PERIPHERAL BLOOD PRESSURES AND PULSES; VENOUS PRESSURE AND VENOUS RETURN 305
Ewald E. Selkurt

17. CONTROL OF THE CARDIOVASCULAR SYSTEM 327
Carl F. Rothe

18. CIRCULATION IN SPECIFIC ORGANS 343
Julius J. Friedman and Ewald E. Selkurt

19. PATHOLOGICAL PHYSIOLOGY OF THE CARDIOVASCULAR SYSTEM

Hypertension 376
Julius J. Friedman

Congestive Heart Failure 381
Ewald E. Selkurt

The Physiology of Shock 389
Ewald E. Selkurt

20. THE DYNAMICS OF RESPIRATORY STRUCTURES 399
Paul C. Johnson

21. RESPIRATORY GAS EXCHANGE AND TRANSPORT 417
Paul C. Johnson

22. NERVOUS AND CHEMICAL CONTROL OF RESPIRATION 444
Paul C. Johnson

23. RENAL FUNCTION 462
Ewald E. Selkurt

24. BODY WATER AND ELECTROLYTE COMPOSITION AND THEIR REGULATION 492
Ewald E. Selkurt

25. RESPIRATORY AND RENAL REGULATION OF ACID-BASE BALANCE 509
Paul C. Johnson and Ewald E. Selkurt

26. MOVEMENTS OF THE DIGESTIVE TRACT 524
Leon K. Knoebel

27. SECRETION AND ACTION OF DIGESTIVE JUICES; ABSORPTION 538
Leon K. Knoebel

28. ENERGY METABOLISM 564
Leon K. Knoebel

29. TEMPERATURE REGULATION 580
Robert W. Bullard

30. PHYSIOLOGY OF EXERCISE 596
Robert W. Bullard

31. PHYSIOLOGICAL PROBLEMS OF SPACE TRAVEL 616
Robert W. Bullard

32. GENERAL ENDOCRINOLOGY; HYPOPHYSIS 634
Ward W. Moore

33. ENDOCRINE FUNCTIONS OF THE PANCREAS 650
Ward W. Moore

34. FUNCTIONS OF THE PARATHYROID GLANDS 660
Ward W. Moore

35. THYROIDAL PHYSIOLOGY 666
Ward W. Moore

36. THE ADRENAL CORTEX 679
Ward W. Moore

37. ENDOCRINOLOGY OF REPRODUCTION 693
Ward W. Moore

INDEX 721

PHYSIOLOGY

edited by

EWALD E. SELKURT, Ph.D.

Professor and Chairman, Department of Physiology,
Indiana University School of Medicine

BY 8 AUTHORS

LONDON

J. & A. CHURCHILL LTD.

104 GLOUCESTER PLACE, W.1.

1

Physiology of the Cell Membrane

JULIUS J. FRIEDMAN

The fundamental unit of function is the cell, since virtually all tissue and organismal activity can be equated to the cellular level. The cell consists of a fluid system which includes all the constituents of protoplasm. It is surrounded by a membrane which represents a retaining wall acting to separate the fluid system inside the cell (the intracellular fluid) from the fluid which bathes the cell (the extracellular fluid).

In the process of normal cellular activity a variety of molecules and ions enter and leave the cell. This movement of particles must occur through the fluid system about the cell, as well as through the cell membrane. For this reason, knowledge and understanding of the factors which influence the movement of particles in solution and through the cell membrane are essential to the understanding of cellular activity and tissue function.

MOLECULAR KINETIC ACTIVITY

According to the molecular kinetic theory all molecules and ions are in a state of constant random motion. The extent and rate of this molecular movement are determined by the temperature of the system. As the temperature is increased, so is the molecular agitation. As the molecules move about in solution, they collide repeatedly with other molecules of the system and rebound. The frequency of collision between solute molecules is determined by the concentration of the molecules in solution. The greater the concentration, the greater the number of collisions per unit time. The force of collision is determined by the kinetic energies of the colliding particles. This is a function of their molecular weights and velocities. Particles possessing greater kinetic energies collide with greater force and rebound to a greater extent. Large molecules collide with great force but because of their great inertia are not easily deflected. As a result of molecular collisions molecules move along a very tortuous path from one region of the system to another.

DIFFUSION

The movement of molecules and ions in solution as a result of repeated intermolecular collisions is called diffusion. In a pure liquid which consists entirely of water molecules, there exists a continual thermal agitation of the molecules which leads to molecular diffusion. Therefore, molecules of water are continuously ejected from one region of the liquid to another. Since the molecules are uniformly distributed through the liquid, the frequency at which molecules are ejected from a region must be equal to the frequency at which molecules are introduced into that region.

If solute molecules are added to one region of the liquid, the concentration of molecules and the frequency of collisions at that region will be greater. As a result, solute molecules will be ejected from the region of high concentration to the region

of low concentration. There will be a net diffusion of solute molecules from a region of high concentration to one of low concentration.

When two regions of a system possess different concentrations, a concentration gradient is said to exist between the regions. The rate of diffusion of molecules is determined in part by the magnitude of the concentration gradient and also by the inherent ability of the molecules to move through a solution. This ability of a molecule to move through a solution is defined by its diffusion coefficient, D, which represents the number of moles of the substance that will traverse a unit area of solution when the concentration gradient is unity. This diffusion coefficient is inversely related to molecular weight. The greater the molecular weight, the lower the diffusion coefficient. This means that larger molecules diffuse through a solution at a lower rate than do smaller ones.

The rate of diffusion can be calculated by means of Fick's law of diffusion. It is written as:

$$\frac{ds}{dt} = -DA\ (C_1 - C_2)$$

and states that the amount of substance that will diffuse per unit time, ds/dt, is directly proportional to the diffusibility of the substance, D, the cross-sectional area of unit thickness through which the substance will diffuse, A, and the concentration gradient across the unit thickness of the system, $(C_1 - C_2)$. The expression is negative because the rate of diffusion is continually reduced. This results from the fact that as diffusion proceeds the concentration gradient becomes progressively reduced. As diffusion progresses, solute molecules are ejected from the region of high concentration to that of low concentration. Therefore, the concentration at the original solute region decreases progressively while the concentration at the original solvent region increases progressively. After adequate time has elapsed and sufficient diffusion has occurred, the concentration of solute at any one region of the solution is equal to that at any other region. Therefore, the concentration gradient no longer exists and no further net movement of molecules takes place. In such a case, the system is said to be at equilibrium. The term equilibrium is not intended to imply that the molecules of the system have ceased to diffuse. This would be contrary to the kinetic molecular theory. It simply indicates that the rate of movement in one direction is equal to the rate of movement in the opposite direction, so that no net transfer of molecules occurs.

CHARACTERISTICS OF THE CELL MEMBRANE

All cells of the organism are surrounded by membranes which separate the intracellular and extracellular environments. The continued functional existence of the cell depends on the ability of the membrane to permit some molecules and ions to pass while restricting the passage of others. In order to appreciate various functional characteristics of the cell membrane, a consideration of its chemical and physical characteristics is desirable.

Chemical analysis of a mass of red blood cell membranes has revealed that they consist primarily of lipid and protein. The lipid is represented by cholesterol, cephalin, and lecithin, while the main protein, stromatin, is a fibrous molecule with a high molecular weight. The concentration of lipid material is higher than that of the protein, and for each molecule of protein there are approximately 75 lipid molecules. There is presumably enough lipid in the cell membrane to form a bimolecular layer about the cell. In addition to lipids and protein, the cell membrane also contains salts, carbohydrates, water, and nucleic acids.

A variety of physical observations has confirmed the presence of lipid and protein in the cell membrane. All cells are preferentially wetted by lipids. Substances which are soluble in lipid are able to penetrate the cell membrane with ease, whereas substances which have a low lipid solubility penetrate the membrane with difficulty, if at all. Additional evidence of the lipid nature of the cell membrane is found in the high electrical impedance of the membrane which is a characteristic of lipid materials. Finally, the administration of substances which disrupt the structural integrity of lipid molecules also disrupts the integrity of the cell membrane. Evidence of the protein nature of the membrane may be found in the low surface tension which exists between the membrane and an aqueous phase. The presence of protein generally produces a low surface tension. The membrane behaves like a sieve and apparently possesses small openings or pores of molecular size through which small molecules can pass. A structure of this nature would be best formulated by polypeptide chains. In addition, membranes are very elastic and can accommodate changes in cell volume. The fibrous protein must account for this mechanical property since lipids lack mechanical strength. Finally, chemicals which act specifically on proteins to produce destruction of the molecule also act to disrupt the integrity of the membrane.

The structural organization of the lipid and protein molecules in the cell membrane has been inferred from its chemical and physical properties as well as the behavior of lipid-water interfaces. When lipid is placed over water, the lipid molecules orient themselves in such a manner that their polar groups are situated at the lipid-aqueous interface while the nonpolar tails of the molecules are oriented away from the aqueous medium. This alignment is due to the fact that polar groups of lipid molecules have an affinity for water, whereas the nonpolar tails of the lipid molecules do not. This behavior of lipid molecules at lipid-water interfaces has led some investigators to visualize the organization of the membrane as illustrated in Figure 1A, a bimolecular lipid layer with the polar groups oriented toward the aqueous phase and the nonpolar tails facing each other at the inside of the membrane. They have proposed further that the protein is distributed over the surface of the lipid layer, since proteins possess a high surface activity and when placed in contact with a lipid surface tend to cover it and reduce its tension. Thus, when viewed from either side the membrane should appear as a protein sieve covering an underlying lipid layer with spaces between the molecules (Fig. 1B) forming "pores."

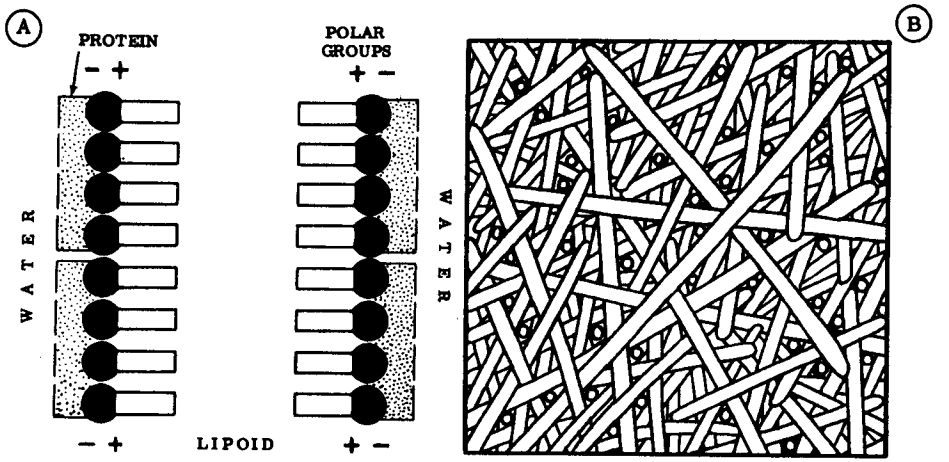

Figure 1. Hypothetical structure of the cell membrane. A, cross-sectional view. (From Davson and Danielli, 1943, p. 64.) B, surface view.

PERMEABILITY

In the course of normal cellular activity numerous substances enter and leave the cell by passing through the cell membrane. A membrane which permits substances to pass through is said to be permeable to those substances. The substances are said to permeate the membrane. A true semipermeable membrane is permeable to water but impermeable to all other substances. No such membrane exists in the living organism. Instead the biological cell membrane is said to be selectively permeable; i.e., in addition to being permeable to water and certain solute particles, it is also impermeable to other solute materials. Membrane permeability may be either passive or active. In passive permeability the driving force is the concentration gradient. No oxygen is utilized and metabolic energy is not expended in moving the particles through the membrane. On the other hand, active transport of particles through the membrane involves metabolic processes, which utilize a carrier mechanism and the expenditure of energy.

Among the various factors which determine the ability of a particle to pass through the membrane are molecular size, lipid solubility, ionic charge, and degree of ionic hydration.

Molecular Size and Permeability

The cell's plasma membrane is a sieve-like structure which contains numerous openings or pores of molecular dimension. Thus, a particle which possesses a dimension equal to or smaller than the pore should be able to traverse the membrane and gain access to the cell. The molecular weight of a substance often provides some indication of the molecular size. However, the effective molecular diameter is also determined by the molecular configuration. Thus, many large elongated molecules may be able to pass through the membrane pores while smaller symmetrical molecules cannot. Nevertheless, there is very good correlation between molecular weight and permeability. Accordingly, the greater the molecular weight, the lower the permeability. It is generally considered that the size of the membrane pore is slightly larger than the urea molecule. On this basis, one should expect molecules smaller than urea to pass through the membrane pores with ease, whereas molecules larger than urea should penetrate the membrane pores with great difficulty, if at all. Thus, molecules such as H_2O, O_2, CO_2, and NH_3, which are smaller than urea, pass through the membrane readily, whereas molecules of sugars, amino acids, and proteins, which are much larger than urea, are unable to pass through the membrane pores.

The rate of diffusion of all substances through the membrane pores is very low compared with the rate of diffusion in solution. The membrane, therefore, presents a barrier to virtually all particles. It is this feature of membrane permeability, no doubt, which has led to the conclusion that only about 1 per cent of the membrane surface area is occupied by pores.

Lipid Solubility and Permeability

While molecular weight is an important feature of membrane penetration, there are numerous molecules many times larger than urea which do pass through the cell membrane with ease. The characteristic which these substances have in common is lipid solubility. Because the cell membrane consists largely of lipid, molecules which are soluble in lipid can become dissolved in the substance of the membrane, diffuse through it, and thereby enter the cell. The ability of a molecule to penetrate

the membrane substance is determined by its partition coefficient, which is the ratio of the solubility of a molecule in lipid to that in water. The greater the lipid solubility, the greater the partition coefficient. As the partition coefficient increases, so does the membrane permeability. For this reason, high molecular weight alcohols have greater penetration rates than do lower molecular weight alcohols. It would appear that the partition coefficient of a substance is more important than its molecular size in determining its rate of penetration. However, this does not mean that molecular size does not influence penetration. When two molecules with equal partition coefficients are compared, the molecule with the lower molecular size will penetrate the membrane more rapidly.

Ionization and Permeability

Electrolytes in solution dissociate to form ions which may move independently through the membrane. However, the permeability of the membrane to ions differs markedly from that which might be expected on the basis of ionic size. Because of the charge at their surface, ions attract water molecules which become radially oriented about the ions. The ion with its surrounding water jacket is said to be hydrated. The relative ability of an ion to attract water molecules is determined by the density of electric charge at its surface. The surface charge of an ion is determined by the valence of the ion and the distance from the nucleus to the outer electron shell. Multivalent ions, which possess greater nuclear charge, take up more water than do univalent ions. As a result, multivalent ions possess greater hydrated radii than do univalent ions of similar size. If one compares two ions of the same valency, the smaller ion with fewer electron shells will have its outermost shell closer to the nucleus and will, therefore, possess a greater surface charge than the larger ion and will attract more water. Consequently, the smaller ion will have a greater hydrated radius than the larger ion.

The relationship can be simply illustrated by comparing Na^+ and K^+. Radii of Na^+ and K^+ with their hydration shell are illustrated in Figure 2. It is apparent that

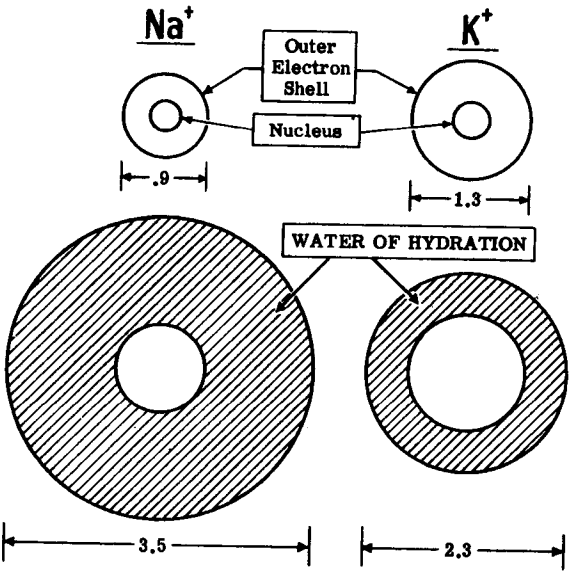

Figure 2. Ionic and hydrated radii of Na^+ and K^+.

the ionic size of Na^+ is smaller than that of K^+. Therefore, the Na^+ will possess a greater surface charge density than will K^+. Consequently, Na^+ will attract more water molecules than will K^+, and the hydrated size of Na^+ will exceed that of K^+. When one wishes to evaluate the ability of an ion to penetrate the membrane, the hydrated size of the ion must be considered, because the water molecules adhere to the ion as it attempts to pass through the membrane pores. Since the hydrated Na^+ is larger than the hydrated K^+, one would expect K^+ to diffuse through the membrane more rapidly. K^+ does, in fact, diffuse through the membrane about 50 times more rapidly than Na^+. However, K^+ diffuses through the cell membrane at a slower rate than does urea. Generally, because of their large hydrated size and their charge, ions have great difficulty in penetrating the membrane.

In order of their increasing hydrated size and decreasing ability to penetrate the membranes are:

$$H^+, OH^-, SCN^-, Cl^-, K^+, NH_4^+, NO_3^-, Ac^-, Na^+, Ca^{++}$$

Weak Electrolytes

Weak electrolytes are salts of weak acids and bases which when placed into solution undergo only partial dissociation. Therefore, weak electrolytes exist in solution as both ions and undissociated molecules. The concentration of each is determined by the dissociation constant of the salt. Cell membranes are generally more permeable to the undissociated molecule than they are to the ions, because of the difference in hydrated size and charge. Therefore, weak electrolytes penetrate the cell primarily in the undissociated form. When the hydrated ions are sufficiently small, the weak electrolytes enter as both the undissociated molecule and its ions. Thus, acetic acid enters the cell as the acid and as H^+ and acetate ion. Ammonium salts display an unusual behavior when placed in contact with red cell membranes. The NH_4Cl in solution dissociates partially into NH_4^+ and Cl^- and is also slightly hydrolyzed to form NH_3. The membrane is relatively impermeable to NH_4^+ but is highly permeable to NH_3, which enters the cell to form NH_4OH and NH_4^+ and OH^-. As $[OH^-]$ in the cell increases, it diffuses out of the cell, thereby upsetting electrical neutrality, and Cl^- exchanges with OH^- to re-establish electrical equilibrium. Thus, NH_4Cl gains access to the cell.

OSMOSIS AND OSMOTIC PRESSURE

When a solution is separated from pure water by a true semipermeable membrane, a situation exists initially wherein two gradients are present. There are a solute concentration gradient from the solution to the water and a solvent concentration gradient from the water to the solution. Because of these gradients, the solute and solvent molecules have a tendency to diffuse across the membrane. However, a true semipermeable membrane permits only water molecules to pass, while restricting the passage of the solute molecules. Therefore, the water molecules diffuse into the solution in accordance with the solvent gradient, and the volume of the solution increases while the volume of pure water decreases. This is illustrated in Figure 3.

The net movement of water across a membrane against a solute concentration gradient is osmosis. By means of osmosis the system tends to achieve a situation of uniform concentration. Thus, osmosis takes place whenever a concentration gradient

exists across a semipermeable membrane. This tendency for water to move in response to a solute concentration gradient develops a force called the osmotic pressure. The osmotic pressure may be measured as the height to which water rises in response to a concentration gradient across the membrane, and is expressed as centimeters of H_2O (Fig. 3). Osmotic pressure may also be defined as that

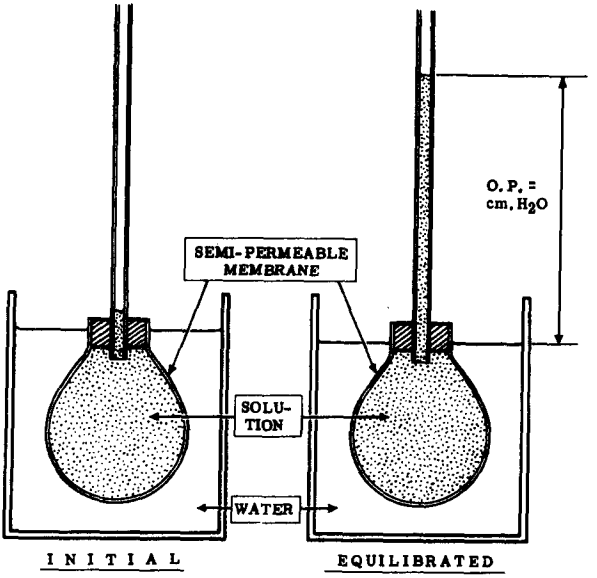

Figure 3. A simple osmometer which demonstrates the osmotic pressure developed by the presence of a solute on one side of a semipermeable membrane.

hydrostatic pressure which must be exerted upon a solution to prevent the movement of water into it through a semipermeable membrane from a less concentrated solution.

If this opposing pressure is increased to a level above the osmotic pressure of the solution, water is forced from the solution against the osmotic gradient. This event is called ultrafiltration and is an essential aspect of the movement of water and solute materials across the capillary endothelium (see Chapter 12).

It is also possible to calculate the osmotic pressure which exists across a membrane from a knowledge of the concentration of particles on either side of the membrane according to the expression:

$$\pi = RT\ (C_1 - C_2)$$

where π is the pressure in atmospheres, R is the gas constant (.082 liter-atmosphere per degree per mole), T is the absolute temperature, and $(C_1 - C_2)$ represents the concentration gradient across the membrane expressed in moles. The nature of the solute particles which constitute C in this expression is irrelevant. The osmotic pressure of a solution is determined by the total number of particles per unit volume and is independent of particle size or characteristics. Thus, large and small mole-

cules and ions contribute equally to osmotic pressure. For this reason, electrolytes which completely dissociate into at least two ions are capable of exerting at least twice the osmotic force of non-electrolytes of equal molarity. However, particles which permeate biological membranes slowly, if at all, are more effective as osmotic units than are those which penetrate more rapidly. Particles which diffuse rapidly through the membrane are able to equilibrate across the membrane quickly and thus exert no net osmotic force, whereas particles which are restricted to one side of a membrane continue to exert osmotic influences in that compartment. The most effective osmotic particles in the circulation are the plasma proteins. Because of their large size, they are essentially restricted to the circulatory system. They exert an osmotic force which aids in maintaining the circulating plasma volume (see Chapter 12). Since proteins are colloidal particles, this osmotic force is called colloidal osmotic pressure.

Solutions which possess equal concentrations of particles, when separated by a semipermeable membrane, possess equal osmotic pressures and are said to be isosmotic to each other. Thus, at zero time, a 1 molar solution of glucose is isosmotic to 1 molar urea. However, 1 molar glucose is not isosmotic to 1 molar NaCl because each mole of NaCl dissociates into two particles, so that one mole of NaCl produces the equivalent of two moles of particles, and therefore exerts about twice the osmotic force of an equimolar glucose solution. Solutions which, at zero time, possess greater osmotic pressure are hyperosmotic to solutions with lower osmotic pressures, which are hypoosmotic.

Because of this disparity between the number of moles and the number of osmotic particles, a more descriptive unit of particle concentration is used. This is the osmole, which represents the product of the number of moles and the number of particles contributed per mole. Thus:

1 molar glucose x 1 particle per mole = 1 osmolar glucose.

1 molar NaCl x 2 particles per mole = 2 osmolar NaCl.

The concentrations of constituents in biological fluids are low; therefore, for convenience of expression, the milliosmole (mOsm), which is one thousandth of an osmole, is used as the unit of particle concentration. The total osmolarity of the cellular constituents is approximately 300 mOsm per liter. Since the cells of the organism and the interstitial fluid are essentially at equilibrium, the osmolarity of the cellular fluids and the osmolarity of the extracellular fluids are probably approximately equal.

The term milliosmole per liter relates to the particle concentration of a solution. If one wishes to refer to the chemical concentration of the constituents of a solution, the suitable term is milliequivalent (mEq.). By comparison:

$$\text{mOsm/liter} = \frac{\text{mg. of particles/liter}}{\text{mol. wt.}}$$

$$\text{mEq./liter} = \frac{\text{mg. of particles/liter}}{\text{mol. wt.}} \times \text{valence}$$

It should be obvious that osmolarity and equivalency of univalent ions are identical.*

*Another appropriate unit of expression is the molal concentration, or molality, in which the concentration of the solute is expressed as moles (or osmoles) per 1000 gm. of solvent. This is important in circumstances where considerable variation in temperature occurs because of the expansion and contraction of liquid with changes in temperature. Because of this activity, the molarity of any given solution varies with temperature.

At low concentrations, such as occur in body fluids, the solutes may be expressed either in millimoles per kilogram (millimolal) or millimoles per liter (millimolar). The difference between molal and molar concentration is negligible in the range of temperature of the body fluid.

The definitions osmolality and osmolarity and osmolal and osmolar are similar, the unit of concentration being the osmole instead of the mole.