2ND EDITION

Physiology of the Heart & Circulation

ROBERT C. LITTLE

Preface to the First Edition

THIS BOOK is based on the material I have used in presenting cardiovascular physiology to medical and beginning graduate students. The organization and depth of coverage of each topic are designed to outline the essentials of the subject in a form that will be useful for individuals at that level. Physicians, more advanced graduate students and others may find it useful as a concise review of the field. In the compilation of this material, it has been assumed that the reader has some knowledge of anatomy, biochemistry and elementary physics. Basic biophysical and structural aspects of cardiovascular function are discussed in Part I. Students without a background in these areas and who wish a less rigorous discussion of the heart and circulation may elect to skip parts of this first section and concentrate on the more descriptive coverage in the remaining chapters that deal with the function of the heart and the circulation.

In the interest of brevity, a moderately dogmatic approach has been used, and extensive documentation or presentation of research results has been avoided. If a fuller discussion of the data base that underlies these explanations is desired, larger encyclopedic texts and research monographs should be consulted. In adopting this method I have not meant to suggest that the explanations discussed are always settled or that there are not other viewpoints. Nevertheless, when the data appeared to justify such an approach and the explanation utilized appeared to be generally accepted, only one opinion is given. Discussion of alternate explanations is left for the course instructor or outside reading by the student. A few pertinent references that I have found to be helpful are listed at the end of each chapter. The serious student may find them, along with the credits listed for some of the illustrations, an access point to the literature.

Our knowledge of cardiovascular physiology stems from the work of many investigators. The names of a few individuals who have made significant contributions to the development of the field have been included in this discussion to provide historical relevance. I regret that space has not permitted the listing of many others who perhaps have made even greater contributions to our understanding of cardiovascular physiology.

Since this book is directed largely to medical students and others in the health care field, reference, where appropriate, is made to disease conditions as part of the discussion of normal cardiovascular physiology. In addition, a somewhat more detailed discussion of such clinical matters as heart sounds, the electrocardiogram and cardiac arrhythmias is included than is usual for a basic science text. These areas are discussed to provide an understanding of the underlying physiologic principles and how they are modified by disease conditions. No attempt, however, has been made to cover these areas in a comprehensive clinical fashion.

Many individuals have helped in the preparation of this book. My thanks go to many colleagues and students who have encouraged me in this venture and have given valuable help and criticism during the preparation of the manuscript. Special thanks go to Drs. Gene L. Colborn, Jack M. Ginsburg, Mary Ella Logan and Vernon T. Wiedmeier of the Medical College of Georgia and to Dr. Carleton H. Baker and the members of the Department of Physiology of the School of Medicine, University of South Florida, who reviewed sections of the manuscript and made helpful suggestions. Final responsibility must, however, remain with the author. I am indebted to Shirl Melton for preparation of the finished typescript and to Jim Wilson and his staff of the Department of Medical Illustration at the Medical College of Georgia for original drawings and illustrations.

ROBERT C. LITTLE

Preface to the Second Edition

THIS BOOK continues to be directed to medical and first-year graduate students and others who need an understanding of the function of the heart and circulation. The basic coverage remains unchanged from the first edition; however, each section has been carefully revised and new information added as needed to bring them up to date. A new chapter devoted to the response of the heart and circulation to stress has been included. In addition, a number of illustrations have been revised and several new ones added. This revision and update has been accomplished without undue expansion of the book by shortening some sections and deleting outdated material and controversial explanations.

I am indebted to students and colleagues who provided helpful criticisms and suggestions. It is my hope that readers will continue to provide such input. Special acknowledgment is due Drs. G. C. Bond, J. F. Delahayes, J. M. Ginsburg, R. E. Godt, T. M. Nosek, and V. T. Wiedmeier for their constructive comments, and to Debra Montgomery for secretarial assistance.

ROBERT C. LITTLE

CONTENTS

PART II: THE HEART

Physiology of the Heart and Circulation

SECOND EDITION

Robert C. Little, M.D.

Professor and Chairman, Department of Physiology, and
Professor of Medicine, Medical College of Georgia
School of Medicine, Augusta, Georgia

YEAR BOOK MEDICAL PUBLISHERS, INC.
CHICAGO • LONDON

First edition, 1977
Second edition, 1981

Library of Congress Cataloging in Publication Data

Little, Robert C
Physiology of the heart and circulation.

Includes bibliographies and index.
1. Cardiovascular system. I Title [DNLM
1. Cardiovascular system – Physiology 2. Heart
– Physiology. WG202 L778p]
QP102.L57 1981 612'.1 80-21864
ISBN 0-8151-5476-3

Part I

PHYSIOLOGIC PRINCIPLES

Chapter 1 • INTRODUCTION TO CARDIOVASCULAR PHYSIOLOGY

A DISCUSSION of the forces that cause water (solvent) and its dissolved materials (solute) to move from one part of the body to another is a logical starting point for a text on cardiovascular physiology. Accordingly, these factors, along with a listing of some of the characteristics of blood that are important to the function of the vascular system, will be summarized in this chapter.

Movement of Fluid and Dissolved Solute in the Body

Body water is usually subdivided into three general compartments: *intracellular*, *interstitial* (outside both the cell and vascular system), and *vascular*. Other classifications can be used (Fig 1–1). Water and its dissolved solute move more or less independently within and among these compartments by the processes of diffusion, osmosis (a special case of diffusion), ultrafiltration, and carrier-mediated transport, which can be either active or facilitative in nature. In addition, the fluid inside the vascular system (blood) is circulated by the pumping action of the heart. This hydraulic movement of fluid (bulk flow) will be discussed in subsequent chapters.

Diffusion

The process of diffusion is important for the function of the vascular system. For example, most of the interchange in the capillary bed between blood plasma and body cells takes place by diffusion through the bounding membranes of each compartment and the intervening interstitial fluid. Diffusion can be simply defined as the spontaneous movement of particles as a consequence of thermal agitation from areas of high concentration to areas of low concentration. This movement is specific for each species of particles and is independent of the movement of other particles in the medium.

In the macroscopic sense, the basic molecular energy of a substance

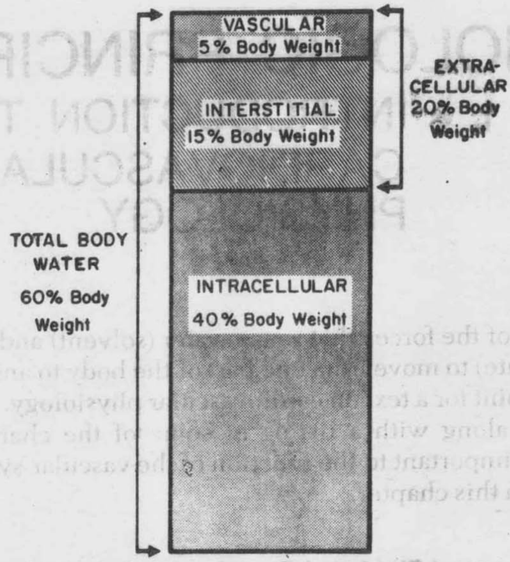

Fig 1–1.—Body water compartments showing approximate distribution of total body water for an adult male. The vascular volume does not include cellular elements of the blood.

(assuming there are no chemical bonds or other forms of extraneous energy) exists primarily as the kinetic energy of its component molecules due to their motion and the electrostatic forces (van der Waal forces) among adjacent particles. The intermolecular distances in a gas are normally so great that significant internal force fields do not develop in that medium and the molecules are relatively free to move. In contrast, the molecules of a liquid are close together and are more likely to form intermolecular combinations. As a result, their motion is restrained. Some molecules (the number varies with the temperature) have sufficient energy to break away from these restraining forces and are able to move about in a random, straight-line manner until they hit another particle. When this happens, kinetic energy is transferred to the less active member. The consequence of many such collisions is a relatively uniform distribution of kinetic energy among all the particles in the bulk phase of a homogeneous solution.

The kinetic energy of a moving particle can be determined by the following equation:

$$KE = \frac{mV^2}{2} \qquad (1-1)$$

where m is the mass of the particle and V is the linear velocity. The temperature and the average kinetic energy of a system are directly related. It follows, therefore, that at a given temperature (i.e., level of kinetic energy), particle velocity is inversely related to the square root of the mass (Graham's law). The water molecules in an aqueous solution of glucose will, for example, move three times as fast as the glucose molecules, which are approximately ten times heavier. In addition, the greater the density of the medium, the greater the probability that a moving particle will strike another particle and thereby shorten the length of its free path of movement. For this reason, other things being equal, the net linear velocity of a particle is inversely related to the density of the medium.

These factors have physiologic significance. With the exception of the pulmonary system, diffusion in the body takes place primarily in solutions. Even apparently solid structures such as membranes act as if they were liquids. As a result, lipid-soluble particles that are too large to travel through the aqueous channels that apparently penetrate the membrane are able to move from one side to the other. This is accomplished by their dissolving in the lipoid center of the membrane and diffusing to the opposite side before reentering the aqueous phase. Because of the greater density of the lipid interior compared to body fluids, the diffusion velocity through the membrane will be considerably slower than in the bulk aqueous phase on either side (Fig 1–2). As a consequence, significant concentration gradients in the body occur primarily across cell or epithelial membranes. Appreciable concentration differences within a local fluid compartment are observed only in conjunction with unique vascular arrangements such as the countercurrent system of the kidney, which supports a solute concentration gradient within the renal extracellular fluid.

The diffusion process can be illustrated (Fig 1–3) by separating sucrose solutions by means of a freely permeable divider. There is a greater probability that a sucrose molecule during its random movement will move from solution A (high concentration) to solution B (low concentration) than vice versa. Although some sucrose molecules will move through the divider in both directions, the net movement will be from the area of high concentration to the area of low concentration. It should be noted that, due to the random motion of the water molecules, there will also be a net diffusion of water (osmosis) in the direction opposite to the movement of sucrose as water moves from an area of high water concentration to one of lower water concentration.

The rate of diffusion for a single species of particles was described

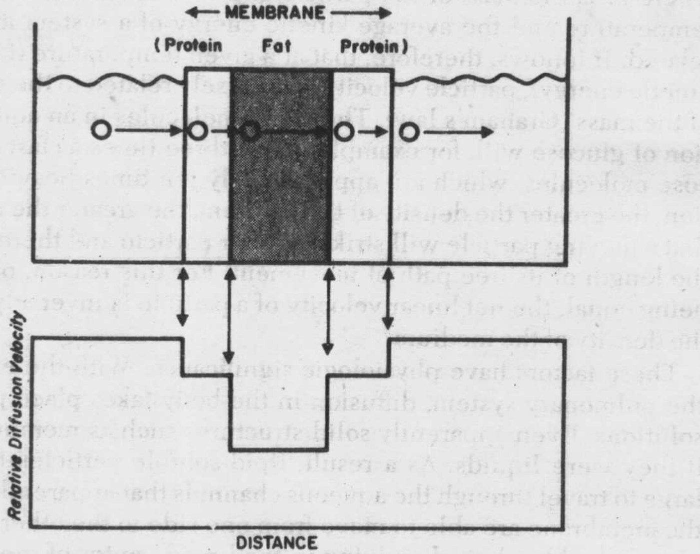

Fig 1–2.—**Top,** schematic diagram showing movement of a diffusing particle in the aqueous phase on each side of a membrane and in each of the three layers of the membrane. For purposes of illustration, the random walk of the diffusing particles is shown as a net forward movement through the membrane. **Bottom,** graph showing the relative velocity of movement of the particle in each membrane phase.

in 1855 by the German biophysicist Adolph Fick, and formulated into what is known as Fick's law.* In a simplified form this law states:

$$\dot{Q} = -\left(\frac{dc}{dx}\right)AD \qquad (1-2)$$

where $\dot{Q}$ is the rate of flow of solute at right angle to the interface (milligrams per second), dc/dx is the concentration gradient (i.e., the change in the concentration [milligrams per cubic centimeter] across the interface [centimeters] separating the two solutions), A is the area of the interface (square centimeters), and D is the diffusion coefficient (square centimeters per second). The magnitude of D is dependent on the temperature and the properties of the diffusing substance and the medium through which diffusion occurs. The negative sign is used because diffusion is downhill, i.e., from areas of high concentration to areas of low concentration.

Physiologists are interested in the diffusion of substances across a wide variety of membranes. The width of the membrane (analogous to

*This should be distinguished from the Fick principle, discussed in chapter 7.

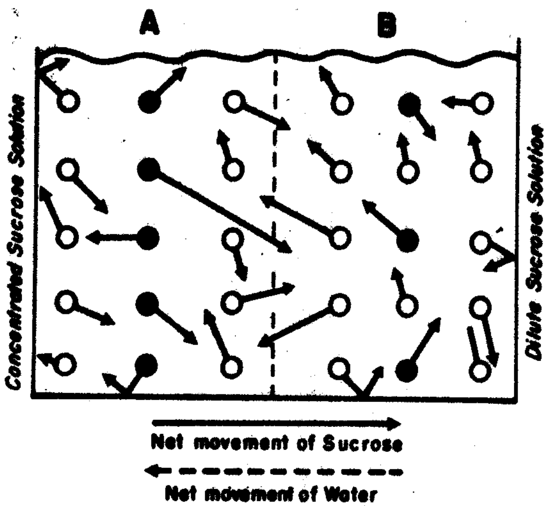

Fig 1–3.—Schematic diagram showing a concentrated sucrose solution *(A)* separated from a dilute sucrose solution *(B)* by a freely permeable divider. *Open circles* represent water molecules; *closed circles* represent sucrose molecules. See text for further discussion.

dx in equation 1–2) can be included as part of the diffusion coefficient to form a permeability constant (P) as follows:

$$P = \frac{D}{d} \qquad (1-3)$$

where d is the width of the membrane. An average value of 75 A is frequently assumed for cell membranes. The permeability constant for a species of particles has the units of a velocity (centimeters per second) and gives the diffusion rate per unit membrane area when exposed to a unit concentration difference.† This value will be utilized in chapter 3 as part of the discussion of the electric activity of the heart.

When the permeability constant is substituted into equation 1–2 and the assumption is made that there is a linear drop in concentration of the diffusing substance as it travels through the membrane (Fig 1–4), Fick's law becomes

$$\dot{Q} = -PA([c_1] - [c_2]) \qquad (1-4)$$

where $[c_1]$ and $[c_2]$ are the concentrations of the solute on each side of the membrane. (Technically, activities should be used instead of con-

† Diffusion and permeability constants are temperature dependent. As body temperature is normally closely regulated, this factor will not be considered in the discussion presented here.

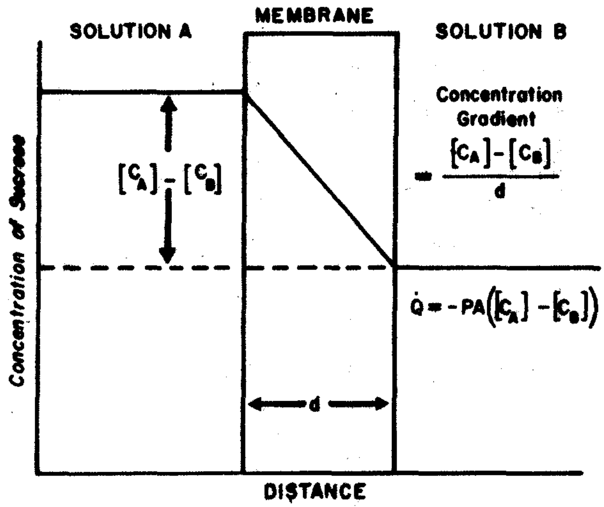

Fig 1–4.—Diagrammatic representation of the diffusion of sucrose through a membrane that separates a more concentrated sucrose solution from a dilute sucrose solution. The concentration of sucrose in each solution is indicated by $[C_A]$ and $[C_B]$, respectively. See text for description of other mathematical terms.

centrations, but for dilute solutions the two values are almost identical.)

This relationship between the concentration of dissolved particles on each side of a membrane and their rate of diffusion becomes of particular importance in the microcirculation where it underlies much of the movement of nutrients and metabolites in and out of the capillary bed. This aspect of diffusion will be covered in chapter 9 as part of the discussion of capillary function. It is worthwhile to point out here that diffusion is only practical for the transport of biologic substances over short distances as its effectiveness decreases with the square of the diffusion path. As a result, the time required for equilibrium to occur over a distance of a few microns is usually measured in seconds, while this interval may become hours when the diffusion distance is increased to millimeters.

Osmosis

As indicated earlier, *osmosis* is the special case of diffusion where movement of solvent is studied. It usually is defined in terms of the solute concentration. Therefore, osmosis is the movement of water from solutions of *low solute* concentration to those of *high solute* con-