# Respiratory Physiology

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**Hemisphere Publishing Corporation**
Washington New York London

**McGraw-Hill Book Company**
New York St. Louis San Francisco Auckland Bogotá
Düsseldorf Johannesburg London Madrid Mexico
Montreal New Delhi Panama Paris São Paulo
Singapore Sydney Tokyo Toronto

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**RESPIRATORY PHYSIOLOGY**



1 2 3 4 5 6 7 8 9 0 DODO 7 8 3 2 1 0 9

**Library of Congress Cataloging in Publication Data**
Jacquez, John A
Respiratory physiology.

Bibliography: p.
Includes index.
1. Respiration. I. Title. [DNLM: 1. Respiration.
WF102 J19r]
QP121.J32 612'.2 79-49
ISBN 0-07-032247-3

This book was set in Press Roman by Hemisphere Publishing Corporation. The editors were Rolfe W. Larson and Winfield Swanson; the production supervisor was Rebekah M. McKinney; and the typesetters were Shirley J. McNett and Peggy M. Rote.
R. R. Donnelley & Sons Company was printer and binder.

# Preface

This book is an introductory treatment of respiratory physiology for the graduate and postgraduate level. It evolved from my experience in teaching respiratory physiology to graduate students for well over the past decade. Aside from occasional work on topics that touch on respiratory physiology I have not done research in respiration. Consequently, this book is an overview of the field by an interested outsider who has taught the material at the introductory graduate level as well as in advanced graduate seminars. It is intended for the graduate student, the postdoctoral fellow, all scientists in the biological and medical sciences, and clinicians who are concerned with respiratory physiology.

There are many introductory texts available for medical students, but the time allocated to teaching respiratory physiology in the medical curriculum is now so short that most introductory treatments have become little more than brief synopses at the simplest level. At the other extreme are the detailed reviews of the different topics in respiratory physiology in the *Handbook of Physiology*, reviews written by research workers from the subfields of respiratory physiology. There is practically nothing intermediate available, and this book is intended to fall squarely between these two levels. The exposition is definitely at the graduate level. Although clinical applications are not emphasized, this text should be of interest to clinicians who specialize in pulmonary diseases.

Aside from the level of exposition how else does this book differ from others in respiratory physiology? First, there is an emphasis on basic physiological mechanisms rather than applications. Second, many ideas are developed in the context of the chronology of experimental results. Third, mathematical analysis at an introductory level is used where it seems appropriate. In quite a few areas of respiration mathematically based arguments are now an integral part of the research literature. We must expect of our graduate students that they have enough competence in calculus and introductory differential equations to be able to read the research literature. For this reason I have included many of the basic mathematical models and arguments. Finally, wherever possible I have introduced comparative aspects. Most medical scientists are trained in departments in medical schools where they learn mammalian physiology almost exclusively. It is by comparison across the different groups in the animal kingdom that one learns to appreciate the variety of solutions to physiological needs that have arisen in evolution.

The coverage of the subareas in a book on a large field often reflects the research interests of the author. I am not a respiratory physiologist and hope that as a result this book provides a fairly even-handed treatment of the major areas in respiratory physiology. There is, of course, the danger that an outsider will miss or misinterpret some important development. Consequently, I would appreciate any comments readers may have in this regard.

I want to thank the students who have contributed to the development of this book by listening to me and by questioning. My thanks go to the secretaries who typed the many versions of my class notes and to my wife who contributed so much in preparing the final manuscript.

*John A. Jacquez*

# Contents

Chapter 1

# Comparative Physiology of Respiration

## BASIC PROBLEMS

All animals depend on aerobic metabolism for their major source of energy. Anaerobic metabolism can serve in emergencies for shorter or longer periods depending on the species, but the generalization that all animals depend on aerobic metabolism remains true. As a result all animals have the same basic problems, namely 1) obtaining enough $O_2$, and 2) getting rid of $CO_2$ formed in oxidative metabolism. Water, the other product of oxidative metabolism, is handled by the mechanisms involved in maintaining osmotic balance and salt and water regulation and will not concern us.

Diffusion of gases across all or some portion of the interface between an animal and its environment is the basic physical process involved in gas exchange. Diffusion within the animal also plays a role, but when unaided by other means it places severe restrictions on the possible sizes of animals. For a sphere of tissue of radius $r$ cm with an $O_2$ consumption rate of $QO_2$ $cm^3$ $O_2$ (STPD)/$cm^3$-min, diffusion coefficient D $cm^2$/min, and solubility $\alpha$ $cm^3$ $O_2$ (STPD)/$cm^3$-atm, let $P_0$ be the partial pressure in atmospheres of $O_2$ at the surface required so that the $PO_2$ at the center of the sphere just falls to zero, then $P_0$ is given by Eq. (1-1) (1, 2).

$$P_0 = \frac{QO_2 r^2}{6\alpha D} \tag{1-1}$$

The combination $\alpha D = K$ is also known as Krogh's diffusion constant. Using Krogh's value (3) of $K$ of $1.4 \times 10^{-5}$ $cm^2$/min-atm for muscle at 20°C and a $QO_2$ of 0.013 $cm^3$ $O_2$/g-min, which is the value for the laboratory rat, assuming a density of 1, and that the $PO_2$ is that of $O_2$ in air, 0.197 atm, gives a value for $r$ of 0.36 mm. Thus, if $O_2$ exchange were entirely by diffusion, animals could not be thicker than one or at most a few millimeters, depending on the $QO_2$ and the environmental $PO_2$. For protozoans, poriferans, coelenterates, rotifers, platyhelminthes, and some small nematodes and annelids, diffusion may serve the purpose. For larger animals, it obviously is insufficient. Furthermore this calculation also tells us that approximately 0.5 mm is the maximum distance that any cell can be from a source of $O_2$ in larger animals and so represents a constraint that circulatory systems must satisfy.

## TYPES OF SOLUTIONS

The general evolutionary solution for the problems of exchange of $O_2$ and $CO_2$ involves the following features:

1 The development of special gas exchange surfaces. More than one such surface may be present in a species; one serving primarily for $O_2$ exchange, the other for $CO_2$ exchange.

2 The development of mechanisms to replenish or change the portion of the environment in contact with the exchanging surface. The process of moving part of the environment over the exchanging surface is called *ventilation.*

3 Development of circulatory systems that serve for the distribution of gases. This includes:

- a Modification of a portion of the circulation for perfusion of the exchanging surface.
- b Development of special mechanisms to transport the gases in the blood.
- c Distribution of the circulation in capillary beds in the peripheral tissues.

For insects and arachnids, the solution is fundamentally different. It is as though evolution attempted to capitalize on the much more rapid diffusion of gases in a gas phase (by a factor of $10^4$ or more) than in a liquid phase. The tracheal systems are systems of gas-filled tubes that ramify and bring the exchanging surface into the muscle and other cells of the organism. But diffusion in a gas phase also has its limits; in larger insects mechanisms to ventilate portions of the tracheal system have developed, and in some arachnids a circulation has developed as an intermediary between a modified tracheal system and the peripheral tissues.

In the main, then, we identify three major features of respiration in terms of which we can discuss the functional properties of respiratory systems. These are: 1) ventilation of the gas exchange surface, 2) diffusion across the gas exchange surface, and 3) circulatory mechanisms of distribution.

## GAS EXCHANGE ORGANS

There are four major types of gas exchange organs:

1 Body surface. All or part of the body surface may serve for gas exchange.
2 Gills. Gills are basically a method of increasing the exchanging surface by a folding out of the surface into many small projections or filaments. This is accompanied by special arrangements for ventilation and perfusion of the filaments.
3 Lungs. Lungs, like gills, are a mechanism for increasing the exchanging surface but arise by an infolding of the surface. There are both water lungs and air lungs, and ventilation may be to-and-fro or may involve a throughflow of medium.
4 Tracheae. These are infoldings of the surface into air-filled systems of tubes that eventually become many fine tubules ramifying into the tissues.

## RESPIRATORY MECHANISMS IN INVERTEBRATES

In this section we review the respiratory mechanisms found in the major groups of invertebrates. In the invertebrates there is a greater variety of respiratory mechanisms than in the vertebrates. The student who is particularly interested in the invertebrates should consult Mill (4).

### Protozoa, Porifera, Coelenterata, Platyhelminthes

In these groups diffusion across the general surface is the mechanism of gas exchange. In the coelenterates flagellae are used to circulate medium through the gastrovascular cavity, and in poriferans flagellae are used to ventilate the central colony cavity.

### Mollusca

**Pelecypoda (Bivalves)** Gills, enclosed by the mantle, are used to filter food from the water as well as for respiration. Water is pumped between the gill lamellae, which are ciliated; the cilia give rise to local ventilatory currents. The gill circulation is similar to that found in fishes, the blood flow being countercurrent to the water flow.

**Gastropoda (Snails)** For the most part, snails use gills, but the body surface also plays a role in gas exchange. In some snails that live in and out of the water rigid gills are present that function both in air and water. In the pulmonate (land) snails, the mantle cavity has been modified to form a diffusion lung, that is, an air cavity with a highly vascularized wall used for gas exchange. There is no cyclical or continuous ventilation of a diffusion lung. The lung communicates with the outside via an aperture under the edge of the shell; at intervals, the snail replenishes the air in the lung by ventilatory movements, between intervals the aperture remains closed.

**Cephalopoda (Squid, Octopus)** As in the bivalves ciliated gills that lie in a mantle cavity are used for respiration. Water is taken in by expansion of the mantle, ventilating the gills. Contraction of the mantle forces the water out of the funnel in a jet and serves for propulsion.

### Annelida

In the oligochaetes, the earthworm for example, gas exchange is via the surface, which is kept moist. In polychaetes, such as the sandworm *Nereis*, gill-like projections running along the side of the body (parapodia) are the primary means of gas exchange. In other polychaetes gills and branchial tufts serve for gas exchange.

### Arthropoda

The arthropods show a remarkable variety of gas exchange mechanisms.

**Crustacea** Gills with a circulation and a ventilation of water over them are the standard respiratory apparatus in the crustaceans.

**Insecta** The basic mechanism in the insects is a tracheal system, but this has undergone a number of modifications.

*Small Insects* Small insects use unmodified tracheal systems in which diffusion in the gas phase in the tracheae is the main mechanism of exchange. Tracheal systems open at the body surface via spiracles, the opening of which is in part dependent on the $PCO_2$.

*Larger Insects* In the larger insects diffusion alone is supplemented by ventilation of the large tracheae. Some species have air sacs, which are ventilated by movement of the abdomen. Ventilation becomes particularly important for flying insects because $O_2$ consumption in flight may increase by as much as 100-fold over that at rest. The flight muscles have a special system of air sacs and a high density of tracheoles. These air sacs as well as the primary and secondary tracheae of the flight muscles are ventilated by the movements of the thorax in flight (5).

*Aquatic Forms* The aquatic forms show the most remarkable modifications of the tracheal system. Some, such as the larval forms of the mosquito, must come to the surface at regular intervals to breathe through a special breathing tube. Some of the aquatic beetles take a bubble of air down to serve as a store of air. One remarkable development is plastron respiration, which occurs in the water bug, aphelocheirus. Basically this is a very thin layer of gas over the ventral body surface, which is held in place by a layer of fine hairs. The bug need not surface to replenish this air. The layer remains relatively constant in volume, its interface serving to exchange gases with the surrounding aqueous phase. Finally some aquatic forms have tracheal gills that are closed tracheal systems modified to provide a large surface area for diffusion of gases between the aqueous medium and the gas phase in the tracheae.

**Arachnida** The scorpions and spiders show another interesting modification of tracheal systems–book lungs. This is a gas cavity in the abdomen, with one wall folded into lamellae through which there is a blood circulation from the abdominal blood spaces. Thus here is the basic tracheal system modified into the general system of a specialized gas exchange surface with mechanisms for ventilation and a circulation for distribution of the gases to the cells of the body.

### Echinodermata

Echinoderms exhibit a number of modifications of the surface for gas exchange. In starfish, modifications of the dorsal surface give thin-walled skin gills or dermal branchiae for gas exchange and have a circulation of coelomic fluid through them. The tube feet, which are used in locomotion, also serve for gas exchange in some species. In holothurians, sea cucumbers, a water lung, which consists of branched tubes arising from the anal region, is used for gas exchange.

## EVOLUTION OF VERTEBRATE RESPIRATORY MECHANISMS

### Chordates to Fish

The prevertebrate chordates all use gills for respiration. All are filter feeders having many ciliated gills in the lateral wall of the pharynx. The cephalochordate amphioxus is a common example. The adult may have 180 gill slits, the gills being ciliated. Water passes through the gill slits and into a peribranchial chamber that has a posterior exit. The flow of water is quite high and serves for feeding as well as for gas exchange. Interestingly here at the chordate level we already have the typical vertebrate pattern of a crossing of the respiratory and feeding pathways with the pharynx as a common channel.

In the cyclostomes, the lamprey and hagfish, there are pouched gills in which water flow and blood flow is in a crude countercurrent arrangement as shown in Fig. 1-1. Some gas exchange also occurs through the skin in the cyclostomes. The countercurrent arrangement is highly developed in the teleosts in which each gill filament has numerous folds, the gill lamellae, on its upper and lower surfaces. A gill filament is shown schematically in Fig. 1-2*a* and *b*. Figure 1-2*b* is a longitudinal section along the axis of the gill filament and shows how the lamellae on the upper and lower surfaces are staggered in relation to one another.

A number of significant features of aquatic gill respiration are important in understanding functional aspects of respiration and circulation in fishes. First, there is only one circulation, the gills being in series with and preceding the systemic circulation that comes from the dorsal aorta (Fig. 1-3). The blood pressure in fishes is fairly low. Thus the gills must present a relatively low resistance to blood flow since systemic capillary beds are in series with the gills. Second, the relative and absolute solubilities of $O_2$ and $CO_2$ in water place significant constraints on gas exchange and thus affect acid-base balance. The low solubility of $O_2$ in water means that, in order to supply sufficient $O_2$ to the animal, ventilation must be much

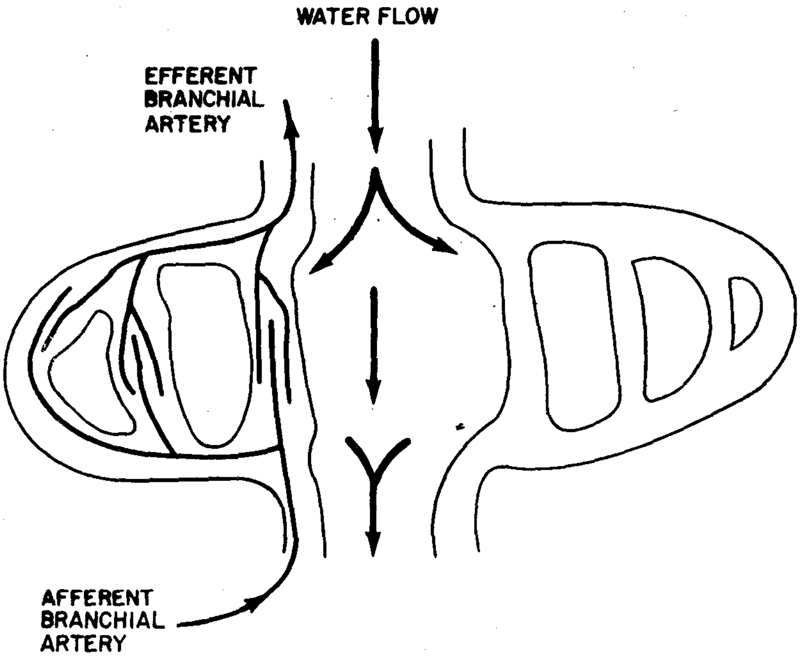


**Figure 1-1** Counterflow arrangement in gill pouch of hagfish (Myxine). [Modified from Hughes (6), with permission of Heinemann Educational Publishers Ltd. and Harvard University Press.]

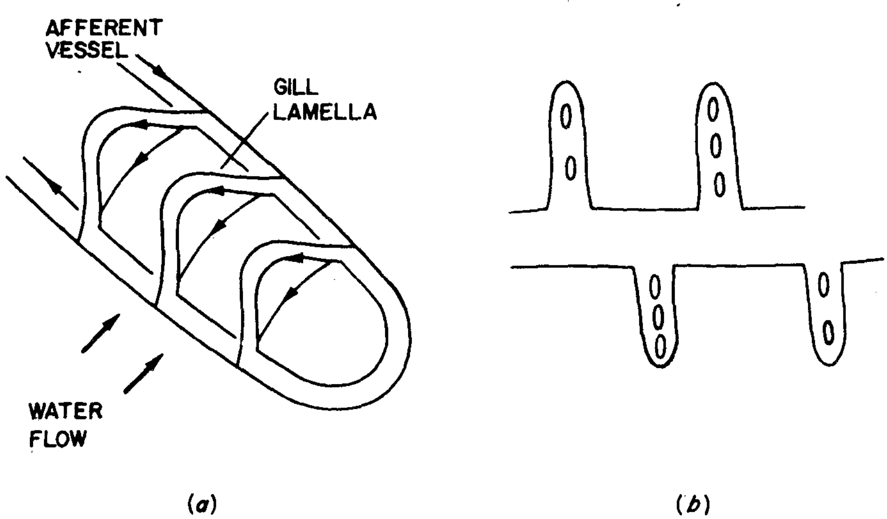


**Figure 1-2** Teleost gill filament. (*a*) Countercurrent flow of water and blood. (*b*) Longitudinal section along axis of gill filament.

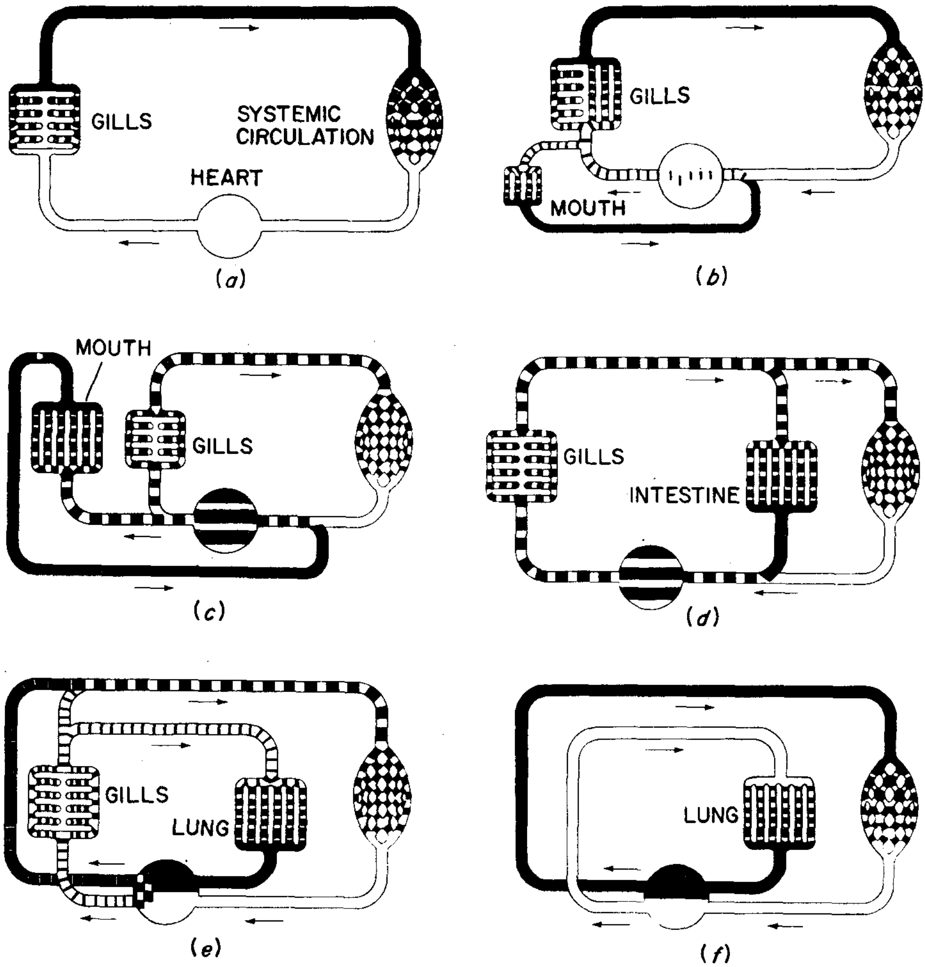


**Figure 1-3** Respiratory organs and circulation in different water and air breathers. (*a*) Typical fish with gills that are functional only in water. (*b*) *Symbranchus*: gills that function in air and water and surface of branchial cavity for exchange with air. (*c*) *Electrophorus*: vestigial gills that support some exchange with water and mucous membrane of mouth for exchange with air bubbles. (*d*) *Hoplosternum*: water gills and modified portion of intestinal tract for exchange with swallowed air bubbles. (*e*) Lungfish: gills and true lungs. (*f*) Mammals and birds: true lungs only. [Modified from Johansen (9), Air-breathing fishes. Copyright © 1968 by Scientific American, Inc. All rights reserved.]

higher in relation to blood flow to the gas exchange organ than in air breathers. In general, the ventilation/perfusion ratios (that is, ratio of medium passed over gas exchange surface per minute to blood perfusion of surface per minute) of fishes, are over 10-fold greater than those of mammals. Since solubility of $O_2$ in water decreases, while metabolic rates increase, with rise in temperature, fishes are better