

# Pathophysiology

Edited by

A. A. Buehlmann • E. R. Froesch

With contributions by

G. Baumgartner • P. G. Frick •

M. Knoblauch • P. Lichtlen •

W. A. Scheitlin • M. Schmid • P. W. Straub

# Pathophysiology

Edited by

A. A. Buehlmann • E. R. Froesch

With contributions by

G. Baumgartner • P. G. Frick •

M. Knoblauch • P. Lichtlen •

W. A. Scheitlin • M. Schmid • P. W. Straub

Translated by Terry Telger

Includes 74 figures



Springer-Verlag  
New York • Heidelberg • Berlin

Prof. Dr. med. Albert A. Buehlmann†  
Prof. Dr. med. E. Rudolf Froesch  
Departement für Innere Medizin, Universität Zürich  
CH-8091 Zürich

Prof. Dr. med. Günter Baumgartner  
Neurologische Klinik und Poliklinik, Universität Zürich  
CH-8091 Zürich

Prof. Dr. med. Paul G. Frick  
Priv.-Doz. Dr. med. Walter A. Scheitlin†  
Departement für Innere Medizin, Universität Zürich  
CH-8091 Zürich

Priv.-Doz. Dr. med. Markus Knoblauch  
Kreisspital, CH-8708 Männedorf

Prof. Dr. med. Paul Lichtlen  
Medizinische Hochschule, 3000 Hannover

Prof. Dr. med. Martin Schmid  
Medizinische Klinik, Stadtspital Waid, CH-8006 Zürich

Prof. Dr. med. P. Werner Straub  
Medizinische Klinik, Universität Bern  
CH-3010 Bern

† Deceased.

#### Library of Congress Cataloging in Publication Data

Buehlmann, Albert A. 1923-  
Pathophysiology.

Translation of Pathophysiologie.

Bibliography: p.

Includes index.

1. Physiology, Pathological. I. Froesch, E. Rudolf,  
1929- joint author. II. Title.

RB113.B8413 616.07 79-408

Title of the German Original Edition: *Pathophysiologie*. Springer-Verlag,  
Berlin-Heidelberg-New York, 1972, 1974, 1976.

All rights reserved.

No part of this book may be translated or reproduced in any form without  
written permission from Springer-Verlag.

© 1979 by Springer-Verlag New York Inc.

Printed in the United States of America.

The use of general descriptive names, trade names, trademarks, etc., in this  
publication, even if the former are not especially identified, is not to be taken as  
a sign that such names, as understood by the Trade Marks and Merchandise  
Marks Act, may accordingly be used freely by anyone.

9 8 7 6 5 4 3 2 1

ISBN 0-387-90370-4 Springer-Verlag New York Heidelberg Berlin  
ISBN 3-540-90370-4 Springer-Verlag Berlin Heidelberg New York

## Preface

No doubt, there are many ways to practice "good" medicine, whatever this may be. Forty years ago the history, observation, and clinical examination of a patient led to diagnosis and therapy. Since then, we have learned a great deal about the biochemical and physiologic processes in the human body and about the pathogenetic mechanisms by which they are disturbed and lead to disease.

Today, the basis of clinical judgment and patient management is the understanding of pathogenetic mechanisms of disease. This concise and basic text of pathophysiology introduces the medical student to the basic pathophysiologic mechanisms. Each chapter begins with a short outline of the general physiologic and biochemical principles of an organ, a system, or a metabolic process; their possible derangements are described, with emphasis on the more important and more frequently occurring diseases. Although the primary purpose is to convey a basic understanding of clinical medicine to first-year medical students, many students have used this book as a convenient reference up to and after graduation.

In many medical schools, the student's introduction to clinical medicine is a pathophysiology course, lying between biochemistry and physiology on the one hand and bedside teaching on the other. This course has proved to be particularly useful when given in conjunction with courses covering other aspects of pathogenesis, such as immunology, pathology, and psychology, as well as basic principles of patient care. In addition, nurses, dieticians, laboratory technicians, and other medical personnel involved in patient care have found this book rewarding; the course of teaching in these professions too often does not impart sufficient insight into pathogenetic mechanisms.

We hope that this book will help medical students and physicians understand pathogenetic mechanisms in general terms. Its content is limited to what we consider essential: It is an introduction and must be followed by the study of more thorough textbooks, reviews, and original articles.

A. A. Buehlmann  
E. R. Froesch

# Contents

## 1 The Lungs and Respiration *A. A. Buehlmann*

Physiology	1
Regulation of Breathing	2
Pulmonary Volumes and Distensibility of Lungs and Thorax	2
Resistance to Flow; Ventilatory Reserves	4
Ventilation and Circulation	5
Gas Exchange	6
Alveolar Ventilation; Dead-Space Ventilation	6
Alveolar Ventilation and Pulmonary Perfusion	7
Pulmonary Gas Diffusion	7
Gas Transport in Blood	9
Pathophysiology	10
Abnormal Atmospheric Conditions	10
Hypoxia	10
Hyperoxia	12
Hyperbaric Conditions	13
CO <sub>2</sub> Enrichment of Inspiratory Air	14
Acceleration	15
Pathophysiologic Syndromes	15
Periodic Breathing	15
Restriction and Obstruction	17
Hyperventilation	19
Nonuniform Ventilation-Nonuniform Perfusion	20
Alveolar Hypoventilation	21
Impairment of Diffusion	23
Dead-Space Hyperventilation	25
Increased Venous Admixture (Right-to-Left Shunt)	25
Pulmonary Vascular Obstruction	26
Increased Pulmonary Perfusion (Left-to-Right Shunt)	26
Reduction of Cardiac Output	27
Pulmonary Congestion; Alveolar and Interstitial Pulmonary Edema	27

## 2 The Heart and Circulation A. A. Buehlmann • P. Lichtlen

Physiology (A. A. Buehlmann)	33
The Heart	33
Regulation of Myocardial Contraction	33
Pressure Changes in Heart and Vessels; Cardiac Valves	36
Blood Volume, Cardiac Output, Vascular Resistances, and Cardiac Work	38
Myocardial Energy Metabolism	43
Peripheral Circulation	44
Coronary Circulation	44
Peripheral Arteries and Veins	46
Regulation of Circulation	47
Circulation during Pregnancy	49
Effects of Regular Vigorous Exercise ("Athletic Heart")	49
Pathophysiology (A. A. Buehlmann)	50
The Heart	50
Heart Failure; Disturbances in Myocardial Function	50
Congestion in the Systemic and Pulmonary Circulation	52
Shock	53
Congenital Cardiovascular Anomalies	56
Acquired Heart Diseases	62
Disturbances of Cardiac Rhythm (P. Lichtlen)	67
Peripheral Circulation (P. Lichtlen)	73
Coronary Insufficiency	73
Hypertension	77

## 3 Temperature Regulation and Heat Balance A. A. Buehlmann

Physiology	81
Pathophysiology	83
Hyperthermia	83
Hypothermia	83
Burning and Freezing	84
Fever	85

## 4 Blood P. G. Frick • P. W. Straub

Erythrocytes and Hemoglobin (P. G. Frick)	87
Physiology and Biochemistry	87
Pathophysiology	89
Anemias	89
Polycythemia and Erythrocytosis	105
Leukocytes (P. G. Frick)	106
Physiology	106
Pathophysiology	107
Leukocytosis and Leukopenia	107

Eosinophilia	108
Lymphocytosis	108
Leukemia	108
Plasmacytoma or Multiple Myeloma	110
Macroglobulinemia (Waldenström's Disease)	110
Malignant Lymphomas	111
The Immune System (P. G. Frick)	112
Physiology	112
The Cellular Basis of Immunologic Processes	112
Pathophysiology	113
Immunologic Deficiencies	113
Plasma Proteins (P. G. Frick)	114
Physiology and Biochemistry	114
Pathophysiology	115
Hypoproteinemia	115
Dysproteinemia	117
Paraproteinemia	117
Selective Protein Deficiencies	119
Porphyria (P. G. Frick)	119
Physiology and Biochemistry	119
Pathophysiology	119
Blood Coagulation and Hemostasis (P. W. Straub)	121
Normal Hemostasis	121
Pathophysiology	126
Abnormalities of Hemostasis	126
Thrombosis	128

## 5 The Kidney

W. A. Scheitlin • A. A. Buehlmann

Physiology	129
Renal Blood Flow	129
Glomerular Filtration	131
Tubular Function	134
The Concentration of Urine and Its Disorders	135
Tests for Renal Function	137
Acidification of the Urine	138
Diuretics	138
Pathophysiology	138
Acute Renal Failure	138
Renal Parenchymal Lesions	139
Prerenal Disturbances	141
Postrenal Causes	141
Chronic Renal Insufficiency	142
Kidney Function	143
Uremia; Extrarenal Complications	145
Tubular Syndromes	147
Water Reabsorption	147
Amino Acid Reabsorption	148

Phosphate Reabsorption	148
Glucose Reabsorption (Renal Glucosuria)	148
H <sup>+</sup> Ion Excretion	149
Nephrotic Syndrome	150
Edema in Renal Disease	150
The Kidneys and Hypertension	151
Renovascular Hypertension	151
Hypertension in Chronic Renal Insufficiency	152
Hypertension in Acute Glomerulonephritis	153

## 6 Water and Electrolyte Balance

### A. A. Buehlmann

Physiology	155
Water Balance	155
Electrolyte Balance	157
Capillaries-Interstitium Fluid Transfer	159
Regulation of Water and Electrolyte Balance	160
Pathophysiology	161
Overhydration and Dehydration	161
Isotonic Overhydration: Excess of Extracellular Water and Sodium	162
Isotonic Dehydration: Lack of Extracellular Water and Sodium	163
Hypertonic Overhydration: Sodium Excess	163
Hypertonic Dehydration: Water Deficiency	164
Hypotonic Overhydration: Water Excess	165
Hypotonic Dehydration: Sodium and Water Deficiency	165
Disturbances of Electrolyte Balance	165
Sodium, Potassium, and Chloride	165

## 7 Acid-Base Balance

### A. A. Buehlmann

Physiology	169
Disturbances of Acid-Base Balance	172
Respiratory Acidosis and Alkalosis	173
Metabolic Acidosis and Alkalosis	174

## 8 Bone, Calcium, and Phosphate Metabolism

### E. R. Froesch

Physiology	175
Disturbances of Bone Metabolism	177
Osteoporosis	177
Hypoparathyroidism	177
Primary Hyperparathyroidism	178
Secondary Hyperparathyroidism	179
Osteomalacia	179



## 9 Endocrinology *E. R. Froesch*

Physiology	181
The Concept of Hormones	181
Biosynthesis, Storage, and Secretion of Hormones	181
Hormone Transport in Blood	183
Mode of Action of Hormones	184
Breakdown, Half-Life, and Excretion of Hormones	185
Regulation of Hormone Secretion	187
Pathophysiology of Endocrine Disorders	188
Congenital Disorders of Hormone Biosynthesis and Secretion	188
Storage and Secretion of Hormones	189
Abnormalities of Hormone Transport	189
Disturbances of Hormone Actions	189
Disturbances in Breakdown and Excretion of Hormones	190
Disturbances of the Control Mechanism	191
Autonomous Hormone Production by Endocrine Gland Tumors	191
Autonomous Ectopic Hormone Production	191
Endocrine Hyperfunction Syndromes due to Endocrine Gland Destruction	191
Endocrine Disorders and the Brain	193
Special Pathophysiology of Endocrine Glands	195
Hypofunction of Endocrine Glands	195
Growth and Development	195
Pituitary Dwarfism	196
Hypogonadotropic Hypogonadism	197
Combined Lack of Various Anterior Pituitary Hormones	197
Diabetes Insipidus	200
Decreased Function of the Thyroid Gland	201
Hypofunction of the Adrenal Cortex	204
Hypofunction of the Adrenal Medulla	207
Insufficiency of the Gonads	208
Endocrine Hyperfunction Syndromes	210
Gigantism and Acromegaly	210
Hyperthyroidism	212
Adrenal Cortex	216
Adrenal Medulla	220

## 10 Metabolism *E. R. Froesch*

Regulation of Glucose and Fat Metabolism	223
Metabolism and Food Ingestion: Substrate Storage and Anabolic Processes	223
Transition from Energy Storage to Mobilization	227
Regulation of Insulin Secretion	230
Pathophysiology	231
Diabetes Mellitus	231
Acute Metabolic Disorders in Diabetes	231

Water and Electrolyte Disturbances in Acute Diabetic	
Metabolic Derangement	232
Clinical Symptoms of Diabetic Precoma and Coma	233
Diagnosis of Diabetic Coma	234
Treatment of Diabetic Coma	234
Etiology of Insulin Deficiency	236
Definition of Diabetic Stages	238
Late Complications	240
Treatment	242
Nondiabetic Melliturias	244
Renal Glucosuria	244
Other Melliturias	244
Hypoglycemia	245
Reactive Hypoglycemia with Hyperinsulinism	245
Reactive Hypoglycemia without Hyperinsulinism	246
Fasting Hypoglycemia with Hyperinsulinism	247
Fasting Hypoglycemia without Hyperinsulinism	248
Tumor Hypoglycemia	250
Fat Metabolism and Its Disorders	252
Physiology of Blood Lipids	252
Essential Familial Hyperlipidemias	253
Secondary Hyperlipidemias	257
A- $\beta$ -Lipoproteinemia	258
Lipidoses of the Central Nervous System	258
Disturbances of Purine and Pyrimidine Metabolism	259
Primary Gout	259
Secondary Forms of Gout	259

## 11 Digestive Organs

*M. Schmid • M. Knoblauch*

The Gastrointestinal Tract (M. Schmid)	261
The Esophagus	261
Physiology	261
Methods of Investigation	262
Pathophysiology	262
The Stomach	265
Physiology	265
Investigation of the Stomach	269
Pathophysiology	269
The Intestine	272
Physiology	272
Pathophysiology	276
Tests for Absorption in and Function of the Small Intestine	279
The Colon	280
Physiology	280
Pathophysiology	281
The Liver (M. Schmid)	283
General Physiology and Structure	284

Bile and Bile Acids	285
Physiology	285
Pathophysiology	288
Bilirubin Metabolism	289
Physiology	289
Pathophysiology	292
Hepatic Blood Flow	296
Physiology	296
Pathophysiology	296
Ascites	298
Hepatic Insufficiency	300
The Bile Ducts (M. Knoblauch)	302
Physiology and Anatomy	302
Pathophysiology	304
The Exocrine Pancreas (M. Knoblauch)	308
Physiology and Anatomy	308
Pathophysiology	310

## 12 The Nervous System

*G. Baumgartner*

Introduction	317
General Remarks	317
Membrane Potential; Action Potential	318
Signal Conduction	318
Axonal Flow	321
Signal Transmission	321
Data Processing	322
Motoneuron, Muscle Spindle, Muscular Contraction, and Stretch Reflex	323
Pathophysiology	325
Motor Disturbances	325
General Motor Concept	325
Neuromuscular Diseases	326
Supranuclear Paresis	336
Lesions of Basal Ganglia	341
Lesions of the Cerebellum	344
Motor Disturbances due to Afferent Nerve Lesions	348
Sensory Disturbances	348
Afferent Control	348
Superficial and Proprioceptive Sensation	349
Pain	352
Disturbances of Special Sensory Systems	356
Vision	356
Vestibulo-Oculomotor System	362
Hearing	367
Epileptic Seizures	368
Neuronal Mechanisms	368
Causes of Epileptic Seizure	369
Focal and Generalized Seizures	370

xii CONTENTS

Neuropsychology	372
General Organization of the Cortex	372
Asymmetry of Hemispheric Functions	374
Speech and Higher Cortical Functions	375
Memory and Its Disturbances	378
Consciousness	380
Sleep	380
Disturbances due to Brain Diseases and Metabolic Disorders	380
Trauma-Induced Disturbances of Consciousness	381
Disturbances of Autonomic Innervation	382
Sweat Secretion	382
Neurogenic Bladder Disturbances	382
Disturbances of Energy Metabolism, Cerebral Blood Flow, and	
Cerebrospinal Fluid	383
Energy Metabolism	383
Cerebral Blood Flow	384
Cerebrospinal Fluid and Intracranial Pressure	385
Literature	387
Index	391

# 1

## The Lungs and Respiration

A. A. Buehlmann

### Physiology

The exchange of  $O_2$  and  $CO_2$  between air and blood is made possible by pulmonary ventilation and pulmonary blood flow. With the release of  $CO_2$ , the lungs also help regulate the acid-base balance.

Five factors are involved in the performance of these tasks. Abnormalities can occur in each of these factors, with resulting disturbances of pulmonary function:

1. The regulation of breathing, innervation of respiratory musculature, and the contractility of respiratory muscles
2. Pulmonary ventilation and its regional distribution as the result of airway resistance and the distensibility of the pulmonary parenchyma
3. The gas-exchange surface area
4. Resistance to diffusion between alveolar gases and the blood
5. Pulmonary blood flow and its regional distribution

The control circuit encompassing the arterial blood gases, respiratory centers, and respiratory musculature regulates the ventilation of the lungs via supplementary afferent nerves in such a way that the  $PO_2$ ,  $PCO_2$ , and pH of the arterial blood remain fairly constant. At the same time, the uptake of  $O_2$  and release of  $CO_2$  may vary considerably in accordance with muscular

activity. The autonomous regulation of breathing can be voluntarily suspended for a limited time and is subject to psychic influences as well.

### *Regulation of Breathing*

Two functions that share many of the same regulatory centers and pathways can be distinguished in the regulation of breathing:

1. The coordination of muscular innervation for rhythmic breathing
2. The regulation of ventilation to keep arterial blood gases constant

Unlike the myocardium, the respiratory musculature has no intrinsic rhythm. The interaction of various nerve centers is necessary for its coordinated periodic innervation. The "apneusis center" located in the lower pons region prolongs the activity of inspiratory stimulation. The "pneumotaxic center," which is located in the upper pons region and is influenced by numerous afferent inputs, excites the expiratory and inhibits the inspiratory stimulation of the bulbar respiratory center. Expansion of the lungs sends inhibitory impulses to the apneusis center via the vagus nerve, thereby increasing the stimulation of expiration. Excision of the pneumotaxic center combined with vagal transection results in cessation of breathing following inspiration.

A fall of the arterial  $P_{O_2}$  below 70 mm Hg leads to a marked increase in ventilation by excitation of chemoreceptors in the carotid bodies. The  $P_{CO_2}$  acts peripherally at the same sites as the  $P_{O_2}$ , but also exerts a central effect. Ventilation is increased by a rise in the  $P_{CO_2}$ . A decrease in pH has the same effect. Humoral regulation by the  $P_{O_2}$  and  $P_{CO_2}$  is probably accomplished by intracellular pH changes in the peripheral and central receptors. The two phrenic nerves arising from cervical segments C3 to C5 supply the diaphragm, which is essential for inspiration, while intercostal nerves I to XII innervate the intercostal muscles, which are actively involved in both inspiration and expiration.

The initial adaptation of breathing during muscular efforts is probably controlled by mechanical receptors in joints and muscles. During steady state the ventilation is regulated by the arterial  $P_{CO_2}$  and  $P_{O_2}$ . Oxygen breathing during exercise reduces the ventilation more than during rest.

Pregnancy, fever, and thyrotoxicosis elevate the threshold for  $O_2$ , increase the sensitivity to  $O_2$ , and increase the stimulation by the carotid bodies at a given  $P_{O_2}$ , so that ventilation is augmented and arterial  $P_{CO_2}$  decreased. Myxedema, hypothermia, and starvation have the opposite effect.

### *Pulmonary Volumes and Distensibility of Lungs and Thorax*

The uniform unfolding of the lungs at the onset of spontaneous respiration after birth is facilitated by a phospholipid surface film known

as the *surfactant*. A deficiency of surfactant promotes the formation of *hyaline membranes*, which may cause severe respiratory disorders in infants.

The *vital capacity*, or the volume of air between maximal inspiration and expiration, can be measured with a simple spirometer. This parameter is of great practical importance in assessing the ventilatory reserves. The *residual volume*, or the volume of gas remaining in the lungs after maximal expiration, is measured indirectly by a gas mixing method or by body plethysmography. Vital capacity plus residual volume give the *total lung capacity*. Normal values for total lung capacity depend primarily upon age, body size, and gender. Total lung capacity and vital capacity are about 15% lower in women than in men of equal size and age. These capacities continue to increase after the cessation of longitudinal growth, attain a maximum at age 23–25, and remain more or less constant through age 50 (Fig. 1-1).

Aging is normally accompanied by an increase in the compliance of the lungs. The declining recoil force of the pulmonary parenchyma leads to an increase in the residual volume and the gas content of the alveoli, which impairs gas mixing (Fig. 1-1).

The recoil tendency of the lungs is always expiratory, while that of the thoracic cage is expiratory during deep inspiration and inspiratory during deep expiration. This results in a resting position that corresponds to the *functional residual capacity*. The functional residual capacity is normally equal to 40%–50% of the total lung capacity and is greater in a sitting or standing position than in recumbency. It normally decreases with increasing abdominal content, as during pregnancy.

The distensibility, or *compliance*, of the pulmonary parenchyma is described in terms of the quotient  $dV/dP_{el}$ . In the absence of gas flow in the airways, the *pleural pressure* is equal to the elastic pressure,  $P_{el}$ . The quotient is not constant over the entire range of vital capacity, but decreases

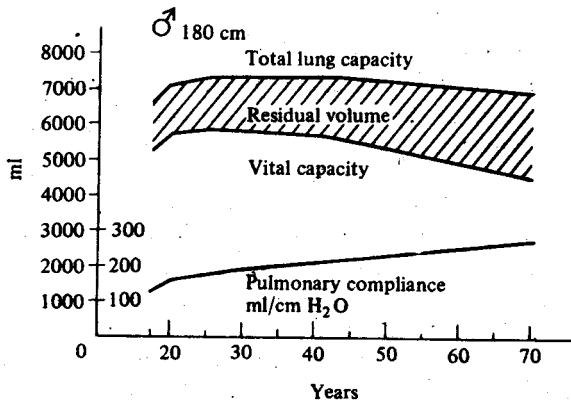


FIG. 1-1. Age dependence of pulmonary compliance and lung volumes.

with increasing inflation of the lungs. However, the surfactant between the alveolar gases and lung tissues alters the surface tension of pulmonary fluids in such a way that this volume/pressure ratio remains nearly linear for the individual alveolae and thus for the lung as a whole in the range of functional residual capacity with a respiratory volume less than one-half the vital capacity. Pulmonary compliance increases during growth, paralleling the increase in total lung capacity and vital capacity, and continues to increase with age in the adult (Fig. 1-1).

The compliance of the lungs is also influenced by their blood content. In an upright position the blood-rich basal regions of the lung have a lower compliance than the apical regions, which are characterized by low perfusion but good ventilation during rest.

The pleural pressure corresponds to the *intrathoracic pressure* and exhibits slight local variations. During inspiration it is 1–2 cm H<sub>2</sub>O more negative in the basal region than the apical region. The respiratory changes in the intrathoracic pressure are transmitted to the esophagus where they can be measured by the intraesophageal-balloon technique.

The *dynamic compliance* is given by the quotient  $dV/dP_{el}$  during spontaneous respiration at respiratory volumes of approximately 1000 ml in the adult. The zero flow occurring at the interphase between respiratory excursions lasts only a fraction of a second. The *static compliance* is the quotient obtained during a prolonged cessation of breathing at the end of an inspiration. The statically measured compliance is greater than the dynamically measured value, especially when strongly divergent airway resistances are juxtaposed.

The compliance of the thoracic cage is of the same order of magnitude as that of the lungs. It is difficult to measure and of no clinical importance. The thoracic compliance is greatly increased during artificial respiration during paralysis or relaxation of respiratory and abdominal muscles by drugs.

### *Resistance to Flow; Ventilatory Reserves*

The resistance to flow (viscance), given by the quotient  $(P_{pl} - P_{el})/\text{flow rate}$ , is composed of the *aerodynamic airway resistance*, or simply resistance, and the *lung-tissue deformation resistance*. During normal respiration the resistance is 70%–80% of the viscance. The airway resistance corresponds to the quotient alveolar pressure/flow rate and can be measured by whole-body plethysmography with minimal patient discomfort. It is a function of gas viscosity, gas density, and airway geometry. Normally 75% of the resistance is localized in the larynx (glottis). Its numerical value in the adult is of the order of 1.5–2.5 cm H<sub>2</sub>O/liter/sec. Flow resistance is doubled during nasal respiration. The primary pressure drop thus takes place in the extrathoracic airways under normal conditions. The diameter of the airways varies with the expansion of the lungs, increasing



somewhat during inspiration and decreasing during expiration. At high rates of flow both the inspiratory and expiratory resistances are increased because of turbulence. For the turbulent component of flow, the resistance increases with the square of the flow rate. When the turbulent component is strong, the resistance at a given flow rate decreases with air density at higher altitudes or if the  $N_2$  in the respiratory air is replaced by the lighter He.

Ventilatory breathing reserves are described in terms of the maximum possible ventilation per minute. The maximum breathing capacity (MBC) is obtained at a respiratory frequency of 40–50/min and it is 25–30 times the vital capacity. During maximal physical exertion for a period of several minutes, ventilation levels off at 65%–75% of the MBC.

In spontaneous respiration the airway pressure is negative during inspiration and positive during expiration. Without external anatomical stabilization the extrathoracic airways would collapse during inspiration while the intrathoracic airways remain open due to the negative intrathoracic pressure. However, the positive intrathoracic and alveolar pressure, which is particularly marked during forced expiration, may lead to collapse of the intrathoracic airways if the primary pressure drop is not extrathoracic (in the larynx and nose) for pathologic reasons.

The flow resistance accompanying forced inspiration and expiration can be determined simply by measuring the forced inspiratory and forced expiratory volume ( $FIV_{1.0}$ ,  $FEV_{1.0}$ ). In this test the patient is instructed to inhale (exhale) as rapidly as possible after maximal expiration (inspiration). From 80%–90% of the vital capacity is normally inhaled in 1 sec, and 70%–80% percent exhaled. These relative values are independent of the vital capacity and generally do not decrease until after age 70. The maximum flow rate, or peak flow, is attained at the onset of forced expiration, the flow rate decreasing steadily thereafter. During forced inspiration a high flow rate is maintained over most of the vital capacity. The peak flow of forced expiration is not attained.

### *Ventilation and Circulation*

The rhythmic changes produced in the intrathoracic, intra-alveolar, and intra-abdominal pressure by the respiratory muscles influence the circulation. The respiratory changes in intrathoracic pressure amount to approximately 5 mm Hg during quiet respiration and are transmitted to the heart, the superior vena cava, the aorta, and the intrapulmonary-pre-alveolar arteries and the veins. The alveolar capillaries are subjected to alternating positive and negative alveolar pressure. The intrathoracic pressure is positive only during forced expiration. The intra-abdominal pressure transmitted to the inferior vena cava and to its area of blood influx assumes positive values and increases during inspiration.

The venous return to the right heart is promoted during inspiration