

INTRODUCTION TO

HUMAN DISEASE

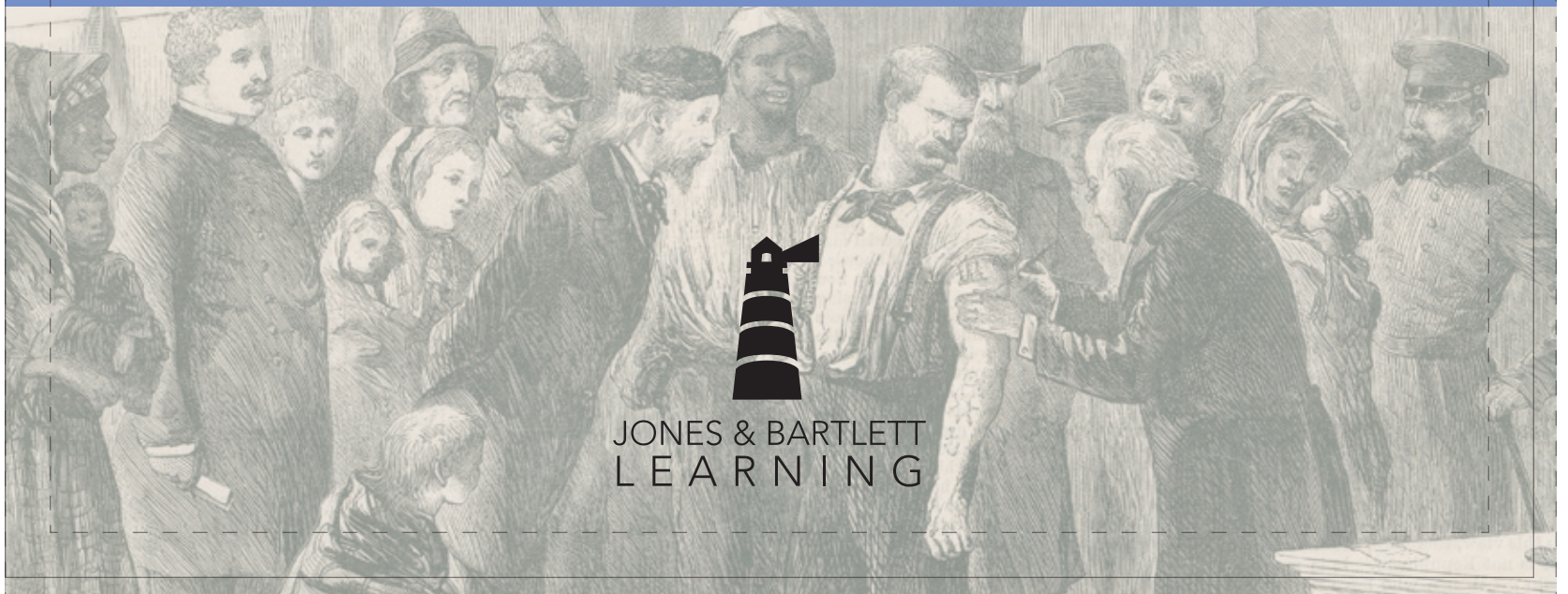
Pathophysiology for Health Professionals
SEVENTH EDITION

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*This book is dedicated to students beginning their
careers in the allied health sciences.*



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Preface

The scope and purpose of this text have not changed since it was first published in 1979, and the intentions expressed in the preface to the first edition are just as applicable to the Seventh Edition. *Introduction to Human Disease: Pathophysiology for Health Professionals* introduces the basic principles of disease to allied health professions students. Our intent is to provide comprehensive information on all aspects of human disease with minimal requirements for prerequisite knowledge. Over the course of the previous six editions, we have noticed that lay people and medical students—overwhelmed by the volumes of detailed and technical information delivered to them in print and, increasingly, on the Internet—turn to this text for a basic outline of how the health profession approaches particular diseases or where a specific disease fits into the medical nosological scheme. While we are happy they derive benefit from the discussions of diseases laid forth in this text, the intended readership is students wishing to pursue a career in nursing, pharmacy, dentistry, physical or occupational therapy, nutrition, or other allied health professions fields who require a broad understanding of disease epidemiology, cause, diagnosis and treatment, and a basic grounding in the specialized medical lexicon.

We have been pleased by the continued use of previous editions by instructors who teach pathology courses to a variety of allied health professions students. We believe all health professions students have a need for a common vocabulary and a broad-based understanding of human disease. Thus, we define terms as clearly and specifically as possible and attempt to describe the most common and important diseases of humans, including mental illnesses. In fact, a special effort is made in this text's format to make the reader aware of the most frequent and significant diseases in each organ category.

The basic format of this text, which has made it so popular over the course of editions, has been retained, including the comprehensive list of learning objectives at the beginning of each chapter and a set of practice questions at the end of each chapter. Each chapter has

been critiqued by pathophysiology instructors for content, accuracy, and presentation. Based on reviewers' and readers' suggestions for each successive edition, we have added more clinical information, including general and specific treatments for diseases. Consequently, although *Introduction to Human Disease* remains primarily a pathology text, the clinical information provides a more comprehensive foundation for the reader.

New to the Seventh Edition

In this Seventh Edition, new illustrations have been added, and the content has been updated to reflect the current state of medical knowledge and practice. Specifically,

- Previous edition Chapters 5, Hyperplasias and Neoplasm, and Chapter 6, Cancer, are now combined into one chapter—Chapter 5, Neoplasia.
- Chapter 16, Kidney, Lower Urinary Tract, and Male Genital Organs, has now been split into two new chapters: Chapter 15, Kidney, Lower Urinary Tract, and Chapter 16, Male Genital Organs.

How This Text Is Organized

This text is divided into four sections:

- **Section I** provides fundamental vocabulary and concepts, a broad analysis of the most common and significant diseases, and a discussion of the tools and processes of diagnosis.
- **Section II** provides a framework for the basic types of human disease: reactions to injury, neoplasia, genetically determined disease, and intrauterine injury.
- In **Section III** each chapter discusses the diseases of a specific organ system. We review the anatomy and physiology of that organ, provide an overview of the most frequent and important diseases encountered, discuss diagnostic techniques (symptoms, signs, laboratory tests, and radiological and clinical procedures), profile the diseases, and discuss the consequences of failure of the organ to function.

■ **Section IV** presents diseases that tend to affect multiple organs and share causative mechanisms within each group. Included topics are infections, immune reactions, external injury by physical and chemical agents, and disorders caused by nutritional deprivations and excesses. We believe these chapters are easier to learn after diseases of the organs have been studied; however, they can be inserted earlier in a course without any prerequisites other than Sections I and II.

We hope that this Seventh Edition continues to be of use to students embarking on a career in the allied health professions. The sheer volume of medical knowledge can appear overwhelming, and the technical vocabulary used can seem like a foreign language to students at the beginning of their studies. By reading and studying the content in *Introduction to Human Disease*, students should be well on their way to gaining the basic foundation they need for a rewarding and exciting career in medicine.

How to Use This Text

Pedagogy

Introduction to Human Disease: Pathophysiology for Health Professionals, Seventh Edition, incorporates a number of engaging pedagogical features to aid in the student’s understanding and retention of the material.



Each chapter begins with a framework for learning the most important topics covered, utilizing an **Outline** of material to be discussed, a list of learning **Objectives**, and an inventory of the **Key Terms** defined in the content.

the lungs fail to remove secretions, allowing bacteria to proliferate and cause pneumonia. Infections of the genitourinary tract are also common in terminally ill patients. Whatever the initial site of the infection, many patients eventually develop bacteremia, or the presence of bacteria in blood, which leads to spread of the infectious organisms to other organs. The predisposing factors for terminal infections are the previously

mentioned immune and white cell deficiencies, immobilization, obstruction of body passageways, and general debilitation. Cachexia, metabolic and endocrine effects, and hemorrhage all contribute to death in cancer patients. Often, a single immediate cause of death in a patient with terminal cancer is not identifiable; the various adverse results of the tumor burden collectively lead to death.

Practice Questions 87

Practice Questions

- Which of the following statements about the epidemiology of cancer is correct?
 - The incidence of cancers in the population is the same regardless of age, race, and sex.
 - The types of cancers that affect children are different from those that affect adults.
 - All cancers have the same survival statistics.
 - Carcinomas are less frequent than sarcomas.
 - Cancers are most common in the pediatric population.
- A 63-year-old woman develops breast cancer. Which of the following tests would not provide information regarding the stage of her disease?
 - A CT scan demonstrating nodules in the lung
 - A biopsy of a suspicious nodule in the liver
 - Removal and microscopic examination of the axillary lymph nodes on the same side as the breast cancer
 - Counting the number of mitotic figures in the breast cancer
- Which of the following is the most common cause of death from cancer?
 - Obstruction
 - Hemorrhage
 - Pathologic fracture
 - Anemia
 - Infection
- Which of the following statements about carcinogenesis is correct?
 - It usually takes only one mutation to cause cancer.
 - Viruses, chemicals, and radiation are types of promoters.
 - Mutations that cause transformation of a cell must be transmitted to the cell's progeny for progression to occur.
 - Mutations in oncogenes result in slowing down of the cell cycle, so more mutations can accumulate.
- Tumor suppressor genes are
 - rarely mutated in cancers.
 - more commonly mutated in carcinomas than in sarcomas.
 - genes that are involved in accelerating or enhancing growth.
 - genes that encode proteins that regulate cell growth.
 - rarely implicated in genetic forms of cancer.
- So that appropriate therapy can be given for any cancer, which of the following is necessary?
 - The presence of a mass
 - X-ray diagnosis
 - The presence of systemic manifestations
 - A tissue diagnosis
 - The presence of metastases
- An old adage in medicine is "iron-deficiency anemia in an adult man is colon cancer until proven otherwise." Why do you think colon cancer would cause anemia?
 - Colon cancer metastasizes to bone, replacing the blood-forming elements in the marrow.
 - The cells of the colon carcinoma require iron, so they "steal" it from the blood.
 - Red blood cells are lysed (killed) as they pass through the malignancy.
 - Blood is lost across the surface of the cancer.

Each chapter concludes with **Practice Questions** to assess comprehension of concepts.

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as a food additive; it imparts a chewy, elastic quality to foods, thickens sauces, and stabilizes foods. Gluten is added to a wide variety of products, from baked beans to ice cream and ketchup, to shampoo and toothpaste, and it is even used as a "filler" in multivitamin pills and other medications. Gluten does not need to be disclosed on food labels, so people with celiac disease need to become experts at detecting gluten lurking in the ingredients listed on food labels. For patients with very severe celiac disease, "gluten-free" products that were processed in the same plant or with the same machinery as wheat products can contain enough trace gluten to cause disease symptoms. Even toasting gluten-free and wheat bread in the same toaster can cause problems.

BOX 30-4 Celiac Disease

Causes
Immunologically mediated reaction to ingested gluten

Lesions
Short intestinal villi causing malabsorption
Some patients may develop skin manifestation (dermatitis herpetiformis)

Manifestations
Bloating
Diarrhea
Abdominal pain
Irritability, weakness
Failure to thrive

Another autoimmune disease linked to digestion and absorption is **pernicious anemia**. Epithelial cells in the stomach produce a protein called intrinsic factor, which binds to vitamin B₁₂ in the duodenum and facilitates its absorption in the ileum. Without intrinsic factor, its absorption is absorbed very poorly. In pernicious anemia, an autoimmune reaction destroys the epithelial cells in the stomach, so the production of intrinsic factor declines. Once the body uses up its stores of vitamin B₁₂, the patient begins to develop symptoms of vitamin B₁₂ deficiency. Pernicious anemia is most common in the elderly population (the median age of diagnosis is 60 years), and it can develop in conjunction with other conditions in which the epithelial cells of the stomach are damaged (e.g., achlorhydria, chronic inflammation) or surgically removed (e.g., for **bariatric surgery**).

Pernicious anemia develops insidiously and, if untreated, progresses relentlessly to cause irreversible neurologic damage and death. Before overt symptoms develop, routine laboratory testing may detect megaloblastic anemia. The diagnosis is confirmed with additional laboratory findings: leukopenia, low serum vitamin B₁₂, and increased levels of metabolites usually processed by the enzyme of which vitamin B₁₂ is the

cofactor. If the diagnosis is made early enough and treatment begun quickly, the symptoms may never develop. The classic triad of symptoms associated with pernicious anemia is glossitis (large, sore, and red tongue with a smooth surface), paresthesias (numbness and tingling of the hands and feet), and weakness. This type of anemia can also cause fatigue, rapid heart rate, heart murmurs, shortness of breath, and, if severe and prolonged, frank congestive heart failure. The neurologic damage is due to degeneration of axons in the spinal tract. It initially causes paresthesias in the hands and feet, which then progresses to absent reflexes, difficulty walking, and eventually paraplegia.

There is no cure for pernicious anemia; the epithelial cells of the stomach, once irreparably damaged, cannot be stimulated to produce intrinsic factor again. Also, because oral vitamin B₁₂ is absorbed very poorly in the absence of intrinsic factor, oral administration of this nutrient alone is insufficient to bring the body stores of vitamin B₁₂ back up to safe levels. Patients with vitamin B₁₂ deficiency are initially treated with daily, intramuscular injections of high doses of vitamin B₁₂. Once the serum levels of vitamin B₁₂ are sufficiently high, the patient can be maintained on monthly injections. If caught early enough, pernicious anemia is reversible, and signs of anemia and neurological damage do not develop.

BOX 30-5 Pernicious Anemia

Causes
Autoimmune destruction of cells in the stomach that produce intrinsic factor
Decreased absorption of vitamin B₁₂

Lesions
Autoimmune gastritis
Leukopenia
Low serum vitamin B₁₂

Manifestations
Glossitis
Paresthesias, progressing to paraplegia
Weakness
Cardiac abnormalities (rapid heart rate, murmurs)

Enzyme Deficiencies

Digestion and absorption of nutrients require the action of numerous enzymes, as well as lubrication by secretions produced by various glands in the upper digestive tract and participation of the indigenous intestinal flora. Amylase, an enzyme that digests starch, is produced by the salivary glands and begins to digest food while it is being masticated in the mouth. Destruction of the salivary glands—for example, by an autoimmune disorder—can lead to problems with nutrition, both because of

Throughout the text, key points are illustrated and important information is highlighted in **Boxes** to ensure comprehension and to aid the study of critical materials. **Key Terms** also are bolded throughout the chapters for ease of discovery.

A colorful and engaging layout enables easy reading and supports the retention of important concepts. Additionally, more than 400 full-color, medically accurate **photographs, illustrations, and tables** provide valuable insight into disease epidemiology and diagnosis.

50 CHAPTER 4 Adaptation, Injury, Inflammation, and Repair

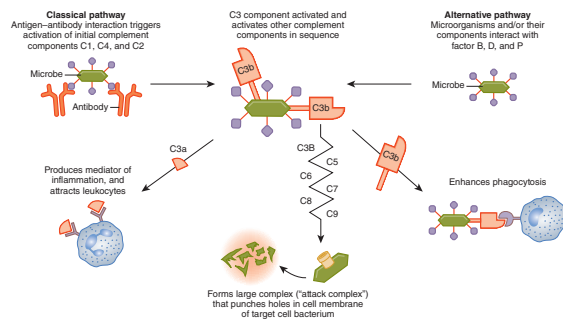


FIGURE 4-19 Complement system.

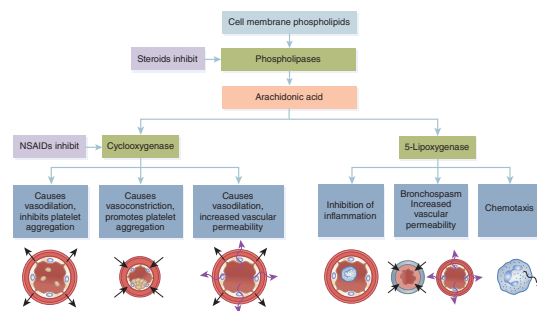


FIGURE 4-20 Arachidonic acid system.

or opsonize foreign material, and some can induce fever. Their exact effect depends on the cell that produces them and the context in which they are produced. For example, one type of leukotriene, produced by endothelial cells, maintains vascular smooth muscle at a steady state of constriction at all times. During an acute inflammatory event, a different leukotriene, produced by leukocytes, counteracts this effect and causes the vessel to dilate. Arachidonic acid metabolites are very potent mediators of inflammation, and some of the most potent anti-inflammatory pharmaceutical drugs we have interfere with arachidonic acid metabolism. *Non-steroidal anti-inflammatory drugs*

TABLE 4-3 Cytokines

Pro-inflammatory (T Regulators)	IL-1 IL-6 TNF IL-8 IFN- γ	a) Systemic effects ↑ Slow-wave sleep Neutrophilia ↓ Appetite Fever
Attenuating	TGF- β IL-10	b) Endothelial effects ↑ Leukocyte adhesion ↑ Procoagulant activity ↑ PD $_E$ synthesis
		c) Fibroblast effects ↑ Proliferation ↑ Collagen synthesis

such as aspirin and ibuprofen prevent the production of prostacyclins, and steroids inhibit the first step in arachidonic acid metabolism, so that neither leukotrienes nor prostaglandins can be produced in sufficient quantity to sustain an inflammatory response.

In addition to the plasma-derived and cell-derived mediators of inflammation, a variety of polypeptide cytokines and chemokines regulate inflammation (Table 4-3). Tumor necrosis factor (TNF), interleukin-1 (IL-1), IL-8, and IL-6 are cytokines produced by leukocytes and endothelial cells; they enhance the acute inflammatory process locally by increasing leukocyte adhesion to endothelium, increasing blood coagulation properties, and stimulating the further production of prostaglandins. Systemically, these cytokines elicit fever and neutrophilia, increase sleep, and decrease appetite. Other cytokines, such as IL-10 and transforming growth factor (TGF), have a down-regulating effect and consequently aid in the resolution of acute inflammation.

We have already mentioned, in passing, some important variations in the inflammatory process. Reactions with lots of neutrophils cause tissue destruction but are important in containing pyogenic bacteria. Macrophages are prominent when there is dead tissue to remove or foreign substances to contain. Edema predominates when lots of histamine is released, as in atopic allergy and immune complex reactions. Fibrin is a prominent part of the inflammatory process if a protective barrier is needed on injured surfaces. Chronicity, or prolonged duration, of inflammation introduces even more variations.

Chronic Inflammation

Chronic means persistent for a long time. Chronic inflammation may result from acute inflammation that persists because the cause is not completely eliminated, or it may be associated with a cause that never was acute but present at a low level for a long time.

The term *chronic inflammation* is also used as a label for the histologic picture typically associated with prolonged inflammation. As will be discussed later, some

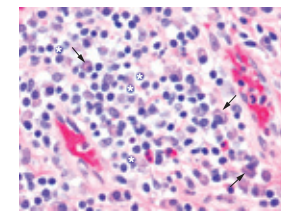


FIGURE 4-21 Chronic inflammation is characterized by an infiltrate composed of lymphocytes (white dots), plasma cells (black arrows), and macrophages. Eosinophils are also present in this focus of chronic inflammation. Notice also the vascular congestion (bright red areas represent red blood cells in capillaries).

chronic inflammations have a more specific appearance (e.g., granulomatous inflammation) and some clinically acute inflammations mimic chronic inflammation histologically. Let us first describe the typical appearance of chronic inflammation and then deal with the variations and their pathogenesis.

Because the injury in chronic inflammation is usually low grade, edema and hyperemia are less pronounced than in acute inflammation and few or no neutrophils are present. The area is infiltrated predominantly by lymphocytes, plasma cells, and, less conspicuously, macrophages (Figure 4-21). Plasma cells are often prominent and easily recognized. They are derived from B-lymphocytes in the tissue, and their primary function is to produce antibodies. These attach to foreign material in the area as opsonins, priming neutrophils and macrophages to phagocytose this material. Lymphocytes, which morphologically consist mostly of a nucleus with a small rim of cytoplasm, play a much larger role than their innocuous appearance suggests. Different types of lymphocytes can perform various functions. They can recognize foreign material, kill host cells in the area of foreign antigens to isolate the foreign substance, transform into plasma cells to produce antibodies, and direct the traffic of other inflammatory cells, especially macrophages. However, in routine histologic sections, it is not possible to tell which lymphocytes are doing what and why. Macrophages may play the same role as they do in acute inflammation (phagocytosis and digestion of debris), but they may also become directly cytotoxic to host cells under certain conditions. Lymphocytes produce cytokines and chemokines that attract macrophages to the area of inflammation, and macrophages in turn secrete cytokines and chemokines that attract and activate lymphocytes.

Another hallmark of chronic inflammation, regardless of type, is the creation of fibrous tissue, or **fibrosis**

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Acknowledgments

Foremost, we want to acknowledge the contributions of Thomas Kent, MD, who was the senior author of *Introduction to Human Disease* through the first four editions. Dr. Kent was a leading medical educator for many years and was cofounder of the Group for Research in Pathology Education (GRPE), a consortium that shares pathology education materials amongst more than 75 medical schools. In 1975, Dr. Kent had students at the University of Iowa’s College of Medicine take tests on the computer, a further example of his prescience in education. Dr. Kent is now retired from pathology teaching, but the success of the first four editions of this text is in no small measure the result of his vision in creating the style and format of the text, plus his insistence that

the content be directed to an understanding of the most common and important diseases. We strive to carry forward his vision into the Seventh Edition.

In June 2008, we received a letter from Jones & Bartlett Learning. The publisher had received a note from a person who “was extremely sad” to see *Introduction to Human Disease* “leave the shelves” after the fourth edition, and we were asked if we would consider revising the book. Thus began our relationship with Jones & Bartlett Learning; and we have been extremely pleased with the help we have received along the way, most recently from Cathy Esperti, Rachael Souza, Nora Menzi, Rob Boder, Troy Liston, and other members of the editorial, marketing, and production teams.

