PREFACE

Advertisers trying to describe a "new-and-improved" product face a dilemma: how to convince consumers that the item is better than it was, without disparaging its past value. The advertiser's dilemma aptly describes the challenge we confronted in revising John Hole's *Human Anatomy and Physiology*. How would we ever improve upon such a classic?

A New Team

We began where most revisions begin—addressing reviewers' concerns. We made corrections, updated terminology, and adjusted the writing style, while carefully retaining the flavor and breadth of coverage of the original. We added exciting opening vignettes to the chapters, sprinkled in many brand-new boxes, and weaved throughout the text cellular and molecular explanations of macroscopic structures and functions.

The three of us—a physiologist, a microbiologist, and a geneticist—were strangers when brought together just two summers ago. Immersed in this project, we became great friends, and a true collaboration was born. Our hope is that the result not only retains the comprehensiveness of John Hole's work, but also embraces our diverse training, our many teaching experiences, and our shared enthusiasm.

What's New

Hole's *Human Anatomy and Physiology* is still *Hole's Human Anatomy and Physiology*—but with a sharper focus and appearance. Here is what you will find.

Introductory Vignettes Readers are drawn immediately into the chapter's topic. Students will meet a fascinating cast of characters, from Judith R., a car accident victim in the emergency room of the hospital that opens chapter 1, to the final chapter's Orwell, a newborn in the year 2010 who undergoes a series of genetic tests—all of which are in experimental stages today. Along the way, readers will meet a carbohydrate-loading runner at the Boston marathon; Donald C., a survivor of a terrible fire; the 2 million-year-old skeleton of the Taung child; a famous violinist with incredibly flexible joints; a former president with Alzheimer's disease; Phineas Gage and Karen Ann Quinlan, whose tragic accidents taught us much about brain function; Christy Henrich, a gymnasi who died of anorexia; and the unforgettable story and photo of the first child to receive insulin to treat his diabetes.

Clinical Applications Many of these intriguing essays not only introduce the latest entrants in medical technology, but also dip back into history to reexamine the medicinal leech; analyze the dangers from weapons from past wars; and use DNA fingerprinting to identify royal remains in Russia. Clinical Applications discussing the new and sometimes controversial include tissue engineering; the polymerase chain reaction; breaching the blood-brain barrier; preimplantation diagnosis; joint replacements; growth hormone treatment; assisted reproductive technologies; and gene mapping.

Other Clinical Applications continue the theme of molecular and cellular explanations for physiological events. These include "Disease at the Organelle Level" and "Molecular Underpinnings of Cardiovascular Disease." Coverage of pathology highlights well-known disorders that have been in the news recently, such as migraines, chronic and cancer pain, respiratory illness from smoking, prostate enlargement, and breast cancer, as well as the unusual, such as smell and taste disorders, rapid aging conditions, and prophyria and King George III.

Breast Cancer Update

Finding the Lump

Few discoveries are as terrifying to a woman as finding a lump in her breast. The woman may first notice the irregularity as a small area of thickening, or, she may detect a dimple, a change in contour, or a nipple that is flatter than usual, points in an unusual direction, or produces a discharge.

The next step is having a thorough physical exam. The doctor palpates the breast and performs a mammogram, which is an X-ray scan that pinpoints the location and approximate extent of abnormal tissue (fig. 22C). An ultrasound scan might be done to distinguish between a cyst and a tumor. If an area might be cancerous, the next step is a biopsy, in which a very thin needle samples the affected tissue.

Eighty percent of the time, a breast lump is a sign of fibrocystic breast disease, which is benign. It may be a fluid-filled sac of glandular tissue (a cyst) or a solid, fibrous mass of connective tissue (a fibroadenoma). Treatment includes taking vitamin E or synthetic androgens under a doctor's care, or lowering caffeine intake and examining unusual lumps with mammograms or biopsies, because women with fibrocystic breasts are 1.6 times more likely to develop breast cancer than are other women.

Treatment

If biopsied breast cells are cancerous, treatment is usually surgical. A *lumpectomy* removes a small tumor and some surrounding tissue; a *modified mastectomy* removes an entire breast; and a *radical mastectomy* removes the breast and surrounding lymph and muscle tissue. Follow-up treatment varies depending upon the extent of the tumor. If abnormal tissue extends to nearby lymph nodes, chemotherapy and possibly radiation therapy will follow surgery. Chemotherapy is also indicated if a bone scan or other test reveals that the cancer has already spread. This happens in 7% of newly diagnosed cases of breast cancer.

The types of estrogen and progesterone receptors in the cancer cells determine, which drugs are used. Some drugs block estrogen or progesterone receptors, which blocks signals that tell the cells to divide. Tumor cells that lack hormone receptors are associated with a poor prognosis. Women with these tumors receive some type of chemotherapy even if the cancer has not spread to adjacent lymph nodes.

Causes of Breast Cancer

A woman who has a close relative who has had breast cancer is at a higher risk of developing the condition than a woman without a family history of breast cancer. Experimental genetic tests can tell whether a woman with a strong family history will develop the inherited form of the illness. This was the case for a young woman whose mother and sister had died of breast cancer. Another sister had recently been diagnosed. Just before she was to undergo breast removal to avoid her feared fate, a genetic test showed that she had not inherited the responsible gene. The woman's cousin, who thought she could not inherit breast cancer because her father was related to the affected family, found that she had indeed inherited the gene. A mammogram revealed a tiny tumor, and surgery saved her life.

Ten percent of all breast cancers are inherited, with the two major responsible genes—called BRCA 1 and BRCA 2—discovered in 1993 and 1994. Researchers are still searching for the environmental triggers of the remaining 90% of cases. One candidate is prolonged exposure to estrogen. The estrogen link was first recognized in the 1970s, when researchers realized that young women who had had their ovaries removed very rarely developed breast cancer. Did their lack of estrogen protect against breast cancer? It appears so.

Prolonged exposure to estrogen can occur in a variety of ways:

- Early menarche (first period) and late menopause (last period).
- Pesticide residues and other pollutants. These contaminants stimulate cell division like estrogens do. Wildlife populations exposed to environmental estrogens demonstrate reproductive problems, such as infertility, undersized genitalia, and thin egg shells.
- Having no children, or having a first child after the age of 30.
- Not breastfeeding. Women who do not breastfeed have a higher breast cancer risk than women who do.

Breast Cancer Statistics

Nearly 3 million women in the United States currently have breast cancer. People frequently misunderstand the oft-quoted figure that a woman's lifetime risk of developing breast cancer is 1 in 8, believing that at any given time 1 in 8 U.S. women have breast cancer. This figure, however, refers to the lifetime risk for women who live to be 95 (chart 22D).

Statistics indicate that breast cancer is on the rise. The lifetime risk of 1 in 8 was only 1 in 16 in the 1940s. It has increased by 1% a year since then, and by 4% a year since 1987. At least some of that rise is due to more widespread and earlier diagnosis, a result of public health programs to educate women about breast self-exam and mammography. Thanks to these efforts, most women will recover from breast cancer. However, the illness is the second most common cancer in women after lung cancer and causes 46,000 deaths in the United States each year.

Prevention

Health agencies advise mammograms once every two years for women aged 40 to 49, and yearly tests after that. A single "baseline" mammogram should be taken between age 35 and 40, as a basis of comparison. For a woman with a family history of breast cancer, this timetable is moved up. A mammogram can spot a tumor two years before a woman can feel it.

Thanks to the U.S. government's Women's Health Initiative, begun in 1993, we may soon learn enough about breast cancer to more effectively prevent and treat it. Some 70,000 women are participating in one or both of two investigations: The first study will test the ability of a diet low in fat and high in fruits and vegetables to prevent breast cancer. In the second study, healthy women with family histories of breast cancer are taking daily a drug called tamoxifen. This drug plugs up estrogen receptors in breast cells, preventing cell division.

Another candidate for breast cancer prevention is RU486, the drug used as an abortion pill because it prevents implantation by binding progesterone. This action may also prevent breast cancer. Tamoxifen and RU486 are currently being tested as breast cancer treatments too. Tamoxifen, for example, decreases risk of cancer recurrence by 30%.

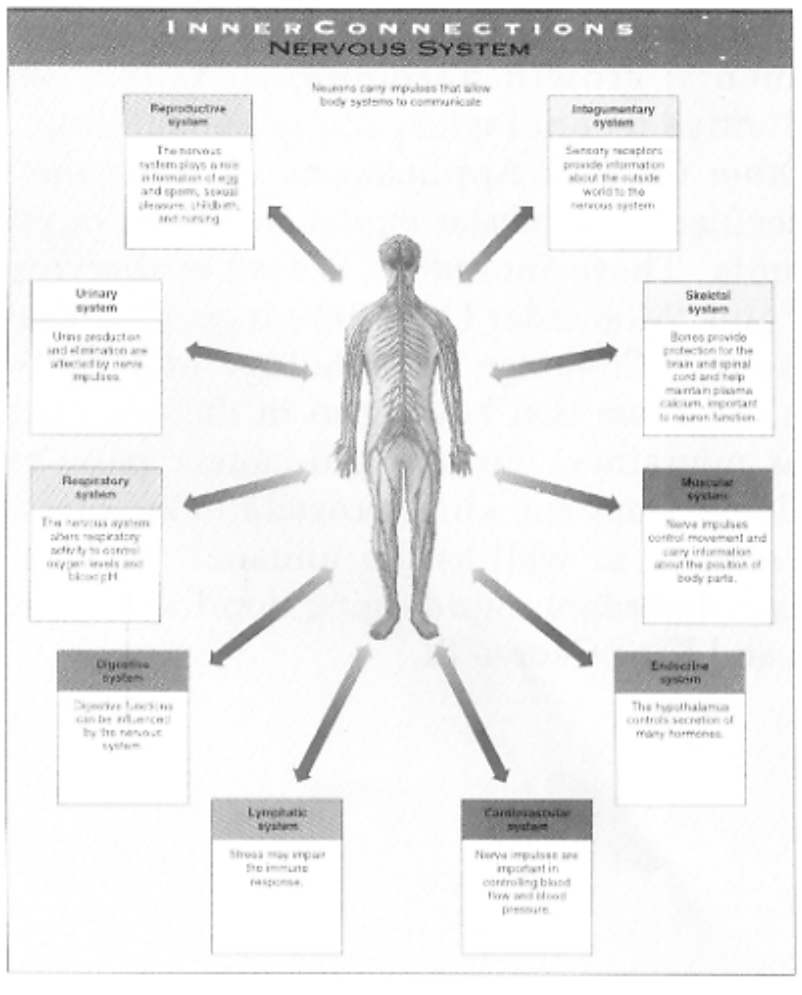
In addition, at least two dozen substances are being tested for their ability to direct the immune system to fight breast cancer cells. And the Women's Health Initiative is attempting to sort through the various purported environmental causes of breast cancer, including alcohol, pesticides, birth control pills, and electromagnetic fields.

Figure 22C
Mammogram (X-ray film) of a breast with a tumor (arrow).

Chart 22D Breast Cancer Risk

By Age	Odds	By Age	Odds
25	1 in 12,608	60	1 in 24
30	1 in 2,526	65	1 in 17
35	1 in 622	70	1 in 14
40	1 in 217	75	1 in 11
45	1 in 93	80	1 in 10
50	1 in 50	85	1 in 9
55	1 in 33	85 or older	1 in 8

InnerConnections These graphics appear at the end of selected chapters. They review the chapter material at a glance. More importantly, as their name states, they conceptually link the highlighted system to every other, reinforcing the dynamic interplays between groups of organs. InnerConnections can be used as springboards for class discussion, ideas for further study or term papers, review of chapter concepts, and reinforcement of the "big picture" in learning and applying the study of anatomy and physiology.



Chapter Order Following many reviewers' comments and our own instincts, we altered the chapter sequence to make more functional sense. The chapters are grouped as follows:

Levels of Organization

1. Introduction to Human Anatomy and Physiology
2. Chemical Basis of Life
3. Cells
4. Cellular Metabolism
5. Tissues

Support and Movement

6. Skin and the Integumentary System
7. Skeletal System
8. Joints and the Skeletal System
9. Muscular System

Integration and Coordination

10. Nervous System I: Basic Structure and Function
11. Nervous System II: Divisions of the Nervous System
12. Somatic and Special Senses
13. Endocrine System

Transport

14. Blood
15. Cardiovascular System
16. Lymphatic System and Immunity

Absorption and Excretion

17. Digestive System
18. Nutrition and Metabolism
19. Respiratory System
20. Urinary System
21. Water, Electrolyte, and Acid-Base Balance

The Human Life Cycle

22. Reproductive Systems
23. Human Growth and Development
24. Genetics

Content and Emphasis Changes

- The concept and theme of homeostasis are established firmly in chapter 1 and continue throughout the text in special figures featuring a normal range icon for quick identification.
- The presentation of chemistry and cells (chapters 2 and 3) is extensively updated, including greater detail in some areas, clearer discussion of transport across membranes, and several new figures.
- Cellular energetics and genetic information, two of the most difficult topics (chapter 4), have been redone, with new and clearer art. Detail has been clarified without compromising readability.
- Chapter 5, Tissues, has new micrographs and corresponding artwork, with fresh examples and added icons to help the student locate tissues in the human body.
- Chapter 6 presents an updated discussion of temperature regulation and fever in terms of the internal environment and hypothalamic setpoint, a theme also touched on in later chapters.
- Muscle, nerve, and endocrine functions are explained more clearly, focusing on mechanisms.
- The many new figures in chapter 15, Cardiovascular System, enable the student to integrate the various structures and functions of this complex organ system.
- Updated discussion of the relationships between T cells, B cells, and macrophages highlights chapter 16.
- Chapter 19 offers improved discussion of the role of intrapleural pressure in ventilation. Reworked figures present CO_2 transport and the chloride shift and various hemoglobin dissociation curves.
- Rewritten sections on the countercurrent multiplier system and control of glomerular filtration rate, along with new figures, make chapter 20 easier to comprehend.
- The chapters on reproduction, growth, development, and genetics (chapters 22–24) are substantially updated, including much material on current and future medical technology. The final chapter, Genetics, is completely new, emphasizing health care and bioethical challenges.

Illustration Program Perhaps the most obvious change in this edition is the revamped art program. Detail, clarity, and consistency have been added, with frequent use of icons to orient the reader and to establish a sense of scale. Color is consistent from chapter to chapter. If a lymphatic pathway is green in one chapter, it is green elsewhere, also. Careful selection of new micrographs and rendering of new art better correlate the two. The presentation of mitosis is a good example of the improved correspondence between micrographs and art.