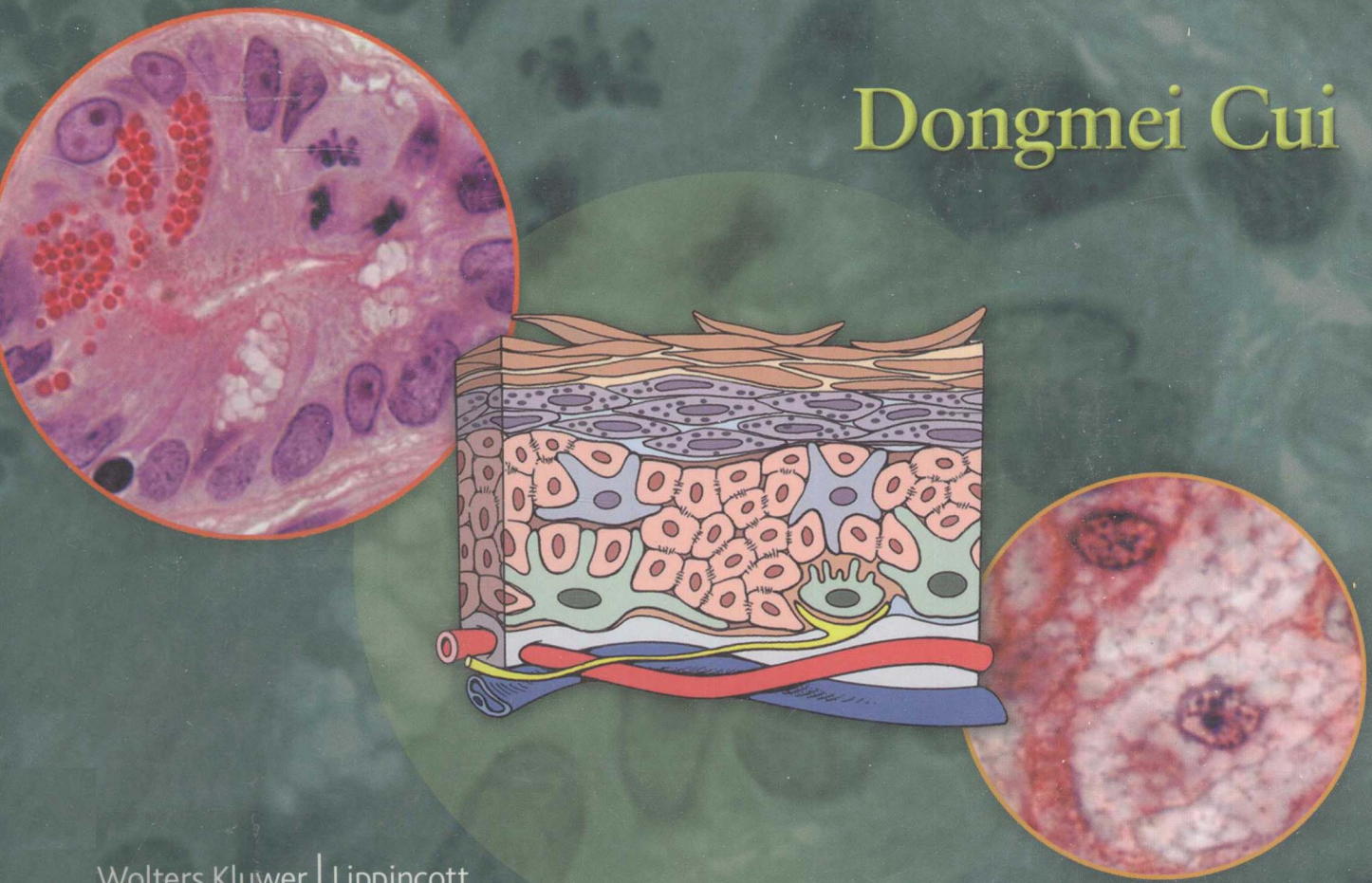
Atlas of Histology

with Functional & Clinical Correlations

Dongmei Cui



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Atlas of Histology with Functional and Clinical Correlations

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Dedication

To my husband Gongchao and my son Tong for their love, understanding, and constant support during my academic journey.

To my students for their enthusiasm, which inspired me to embark on this book.

To my colleagues and friends who have encouraged, supported, and helped me bring this project to fruition.

—Dongmei Cui

Preface

At the beginning of his course, an accomplished pathologist said, and we paraphrase:

> *All we are going to look at in this course is altered histology. If you have mastered histology, you have mastered pathology. You see within a pathologic specimen remnants of the tissue from which it came.*

Though it could be argued that this is an overly simplistic view, there is nevertheless a great deal of truth in it.

Successful and productive careers in the healthcare professions are the result of an interconnected educational process. An understanding of basic science is greatly enhanced by considering it within an appropriate clinical context, and, conversely, a successful diagnosis requires an understanding of how disease has altered the structure and function of the normal body. Recognition of this interconnectedness has been an important consideration in the development of this book.

A variety of issues have influenced the educational playing field in recent years. These include (1) a changing population of basic biomedical instructors, (2) pressures for premedical and medical education curriculum change, and (3) the compelling need to integrate basic science courses with clinical medicine. The latter point is especially important. Even as curricula are being revised, there is a clear expectation that the clinical relevance of basic science information should be emphasized. Clinical correlations, when appropriately integrated, result in a more effective learning experience, which promotes the understanding of the relationships between the normal and the abnormal as well as between the healthy state and the diseased state. Clinical correlations also facilitate learning clinical concepts and enhance students' understanding of basic science information, especially as they relate to their specific career objectives.

The goal of *Atlas of Histology with Functional and Clinical Correlations* is not only to provide a practical and useful source of fundamental information concerning basic histology but also to do so using an innovative approach that shows how tissues can be modified by a pathological process. This integrated approach emphasizes learning both normal structure *and* how the same tissues would appear in an abnormal state. We believe this approach will provide a bridge for students between knowledge of basic histology and information that will directly contribute to their future understanding of clinical concepts.

This "Atlas with Extras" functions much like a combination atlas and text. These "extras" consist of many structure and function correlations, expanded and informative figure descriptions, text boxes offering additional relevant information, the extensive use of clinical examples and their correlation with histological constructs, and relevant electron micrographs integrated throughout. Taken collectively, these features form a flexible educational tool that can be adapted to a wide variety of teaching and learning environments.

Atlas of Histology with Functional and Clinical Correlations comprises 21 chapters in 3 units—beginning with "Basic Principles of Cell Structure and Function" and then progressing to "Basic Tissues" and, finally, to "Organ Systems." Using a proven-effective building-block approach, this book starts with an introduction to the cell using light and electron microscopic images—"visual definitions" of the terms that will be used throughout the book. The remaining chapters flow in a logical manner through increasingly more complex tissues and organs, illustrating the essentials in color photos and drawings (normal and abnormal) and in electron micrographs.

The three general concepts that have been followed in this book are to arrange related information on facing pages; to emphasize the interrelation of structural, functional, and clinical information; and to use meaningful clinical examples. More specifically, the concepts informing the creation of this atlas are as follows.

First, the figure numbers are color coded: Those for histological sections and for TEM and SEM are yellow, those for line drawings are highlighted in purple, and those for clinical

images are highlighted in blue. In addition, all clinical information—images and text—is highlighted in blue, allowing the user to easily identify it.

Second, as consistently as possible, a structure or tissue is represented in at least three or four ways and arranged to fit on a single page or on facing pages. This unique format gives students a complete visual impression in an integrated, correlated style of (1) light and electron micrographic images, (2) diagrammatic representations of the same tissue or structure, and (3) examples of how that tissue or structure might be modified by a pathological process. This provides histology students an effective and efficient way both to learn basic histology and to recognize tissues altered by a disease process.

Third, most photomicrographs in this atlas have a high-power inset that was taken from the same slide as the primary photograph for comparison of tissues and structures in both low and high magnifications, thus facilitating the learning process.

Fourth, in this atlas, structures are clearly labeled with their complete names instead of with initials or numbers keyed to a list of abbreviations. This approach saves time and, therefore, greatly expedites learning.

Fifth, we have included information on a wide variety of tissues and structures in order to provide a useful learning tool for medical and dental students and other healthcare professionals. For instance, Chapter 14, "Oral Cavity," contains not only an extensive description of the mouth soft tissues but also appropriate details of tooth structure to aid those in the field of dentistry, and in "Eye" (Chapter 20), we have included detailed photographs and illustrations for the eye and retina for those in the field of ophthalmology. Moreover, a special effort has been made to arrange this book in a sequence that will accommodate a wide range of curricula.

Sixth, a brief introduction and an overview, including key concepts integrating structure and function, begin each chapter. Chapters and topics are organized in the general sequence corresponding to that used by most textbooks and histology courses.

Seventh, tables summarizing the key features of cells, tissues, and organs and synopses of their key structural and functional characteristics appear in each chapter. This allows for an efficient use of study and review time.

Eighth, important phrases and key terms are presented in **bold** in the text and in the figure descriptions for emphasis.

Over the years, many of the color photomicrographs included in this atlas have been used in our histology laboratory demonstrations. Students have found them very useful and have expressed their interest in acquiring hard copies for their personal study. This was the seminal reason that motivated us to embark on this project. We hope this atlas will fulfill students' needs as they progress toward their clinical careers; it would never have evolved without their encouragement.

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James C. Lynch
Duane E. Haines
Gongchao Yang
Jonathan D. Fratkin
Jackson, Mississippi 2010

Acknowledgments

The completion of a project of this scope relies on the ideas and inspiration that represent its beginning and on the kindness and expertise of colleagues who have graciously given suggestions and comments and offered reviews, both formal and informal, during its progress. These two factors have been brought together by the cooperation of many.

This book would not have been possible without the full support and encouragement of Dr. Duane E. Haines and Dr. James C. Lynch during the initial proposal. I am grateful to Dr. Haines for his vision of integrating clinical correlations into this book.

I would like to express my sincere appreciation to the expert consultants who contributed to this project both through their insightful review of chapters and many constructive suggestions and by providing tissue samples, slides, or other images. I especially appreciate Dr. Ben R. Clower and Dr. March D. Ard for their initial and continued support and encouragement. Special thanks are due to Dr. Steven Bigler, chairman of the Pathology Department, University of Mississippi Medical Center, for his generous support during this project. We have also benefitted greatly from, and are grateful for, the helpful comments (especially regarding applicability to the classroom setting) made by faculty and student reviewers. Each of these individuals is listed in the prefatory pages.

My coauthors and I offer special thanks to Ms. Varie Lynch for her careful and excellent editing, reviewing, and proofreading of each chapter. We are grateful to Mr. Glenn Hoskins, who was the main source of electron micrographs (TEM and SEM) and who willingly prepared new images as necessary. Tissue prepared by Ms. Dianne Holmes and Ms. Betty Chen was used in this project. We also thank Mr. Tong Yang, who created many original line drawings and helped with the preparation of the computer files for submission to the publisher. Mr. Jerome Allison provided invaluable advice and assistance in computer-related matters. In addition, helpful comments were provided by Mr. David Lynch, who reviewed some of the chapters, and Dr. Eddie Perkins, who offered a number of suggestions on various phases of the project. We also thank Ms. Melanie Casey, a dental student, who organized a group of her colleagues to review the chapter on the oral cavity. They did an excellent job.

The inclusion of pathological photomicrographs and MRI and CT images in this work is made possible by the outstanding cooperation of our clinical and basic science colleagues. We express our sincere thanks to the following individuals: Dr. Kay Allen, Dr. Alexandra Brown, Dr. Michael F. Flessner, Dr. Roland F. Garretson, Dr. J. Mark Reed, Dr. Gary W. Reeves, Dr. Jennifer Schulmeier, Dr. Billy Walker, Dr. Niping Wang, and Dr. Bob Wineman. In addition, a number of other individuals generously offered or, in some cases, granted us permission to use their images. They are recognized on the Figure Credits page. We greatly appreciate their professional courtesy.

Many new line drawings, both great and small, were created for this work. These were largely the work of Mr. Michael Schenk (Director of Biomedical Illustration Services) and Mr. Walter Kyle Cunningham (Medical Illustrator). We are enormously appreciative of their time, energy, and dedication to creating the best possible artwork for this book. They went out of their way to accommodate our requests, and we are very happy with the results.

The completion of this work would not have been possible without the interest and support of the publisher, Lippincott Williams & Wilkins. We would like to thank Ms. Crystal Taylor (acquisitions editor), Ms. Kelley Squazzo (product manager), Ms. Jennifer Clements (art director), and Ms. Kelly Horvath (freelance development and copy editor). Lastly, but certainly not least, Ms. Lisa Boyd and Ms. Mary Ann Albin, who both work in the main office of the Department of Anatomy at the University of Mississippi, helped with many administrative tasks that were collectively a great help.

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Contents

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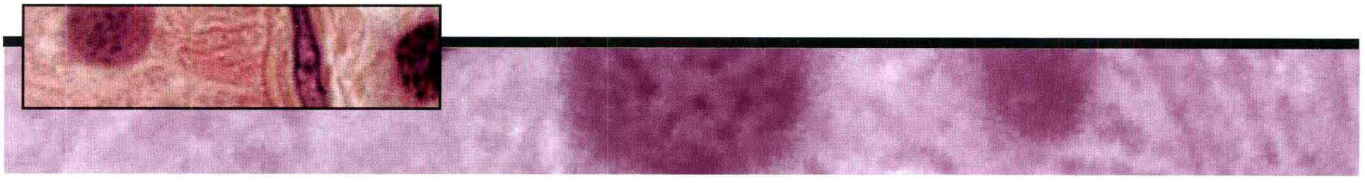


Descriptive Terms for Normal Cells

- Cell Shape
- Cytoplasm Features
- Nucleus Features
- Cell Size

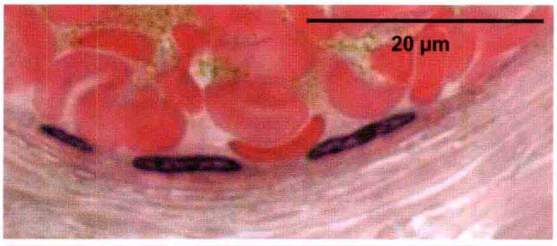
Descriptive Terms for Abnormal Cells and Tissues

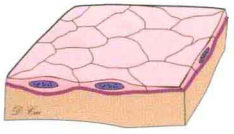
- Acute Inflammation
- Apoptosis
- Atrophy
- Calcification
- Chronic Inflammation
- Cellular Accumulations
- Granulomatous Inflammation
- Hyperplasia
- Hypertrophy
- Hydropic Change
- Karyorrhexis
- Metaplasia
- Monomorphism
- Multinucleation
- Pleomorphism
- Pyknosis
- Scar
- Necrosis
- Pigments
- Ulcer

Descriptive Terms for Normal Cells

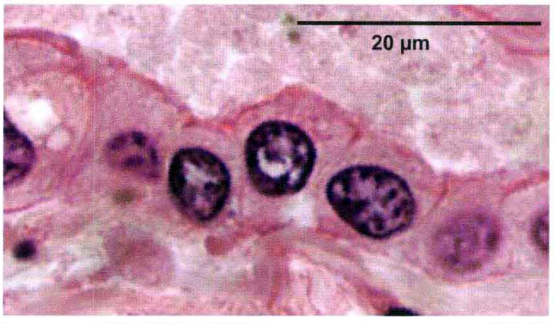
Cell Shape

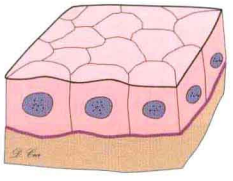
Squamous: This is an epithelial cell that has a flattened, "squamous" shape. Usually, the squamous cells we see in sections are cut edgewise so that they appear very thin, and about all we see is the flattened nucleus. The example here shows nuclei of three endothelial cells lining a vein full of erythrocytes.



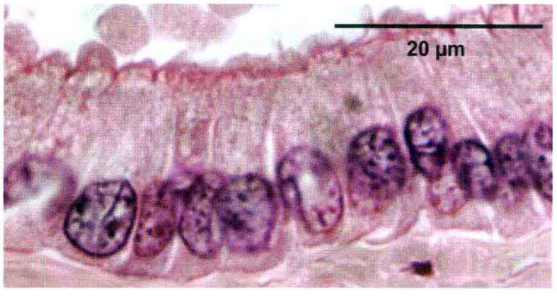


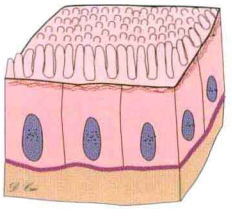
Cuboidal: This is an epithelial cell with equal height and width. The example here is a layer of cuboidal epithelial cells lining a small duct in the pancreas.



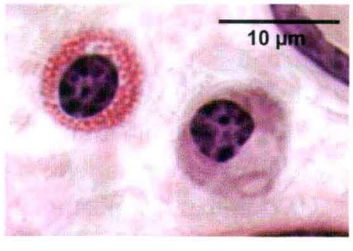


Columnar: This is an epithelial cell with the height distinctly greater than the width. The example here is a layer of columnar cells lining a large duct in the pancreas.

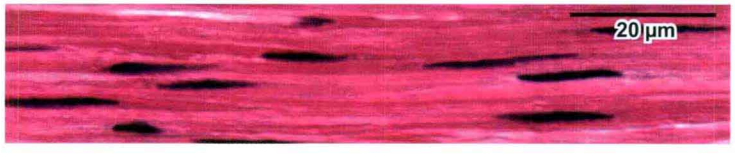




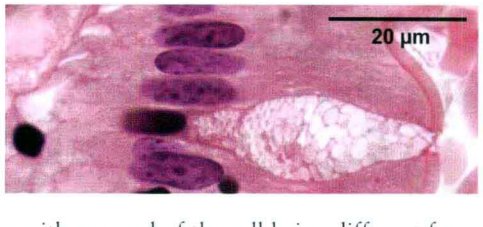
Spherical or ovoid: These terms describe ball-shaped or egg-shaped cells, respectively. The examples here are two spherical cells, a mast cell on the left and a plasma cell on the right. These residents of connective tissue can assume other shapes depending on pressures from neighboring structures.

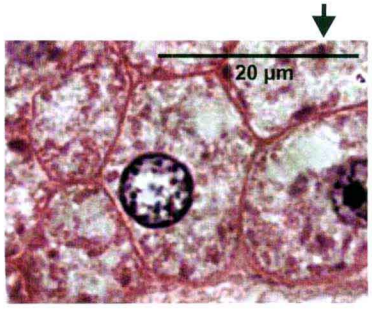


Fusiform: These cells are elongated and tapering at the two ends. The examples here are smooth muscle cells packed together in parallel. The elongated nucleus of each cell is easy to see, but the boundaries of the long spindle-shaped cells are difficult to distinguish.



Polyhedral: Multiple flattened surfaces give the appearance of a pentagon, hexagon, and so on. The hepatocyte shown displays six sides.

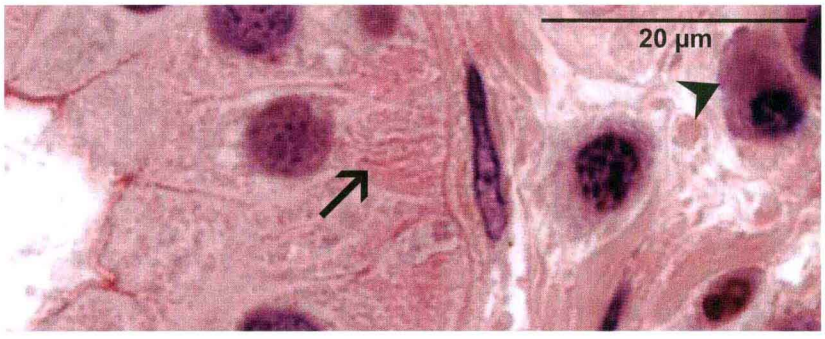




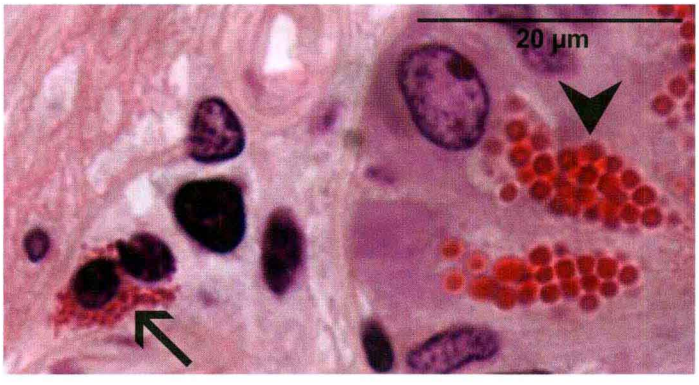
Polarized: These cells have a distinct orientation with one end of the cell being different from the other. Each columnar cell in the above example of intestinal epithelium has an apical end on the right that is different than the basal end on the left. The apical ends are exposed to the lumen. Most of the cells are absorptive cells that have a brush border and a dense row of microvilli extending from their apical surfaces. The cell that appears to have vacuoles filling the apical two thirds of its cytoplasm is a goblet cell, a mucus-secreting cell. What appear to be vacuoles are actually secretory vesicles that lost their contents during processing of the tissue.

Cytoplasm Features

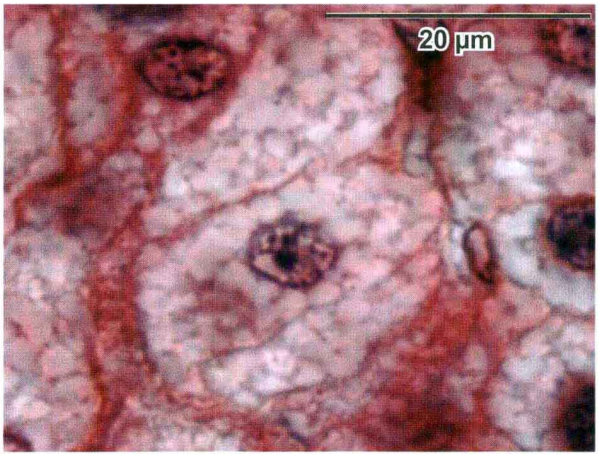
Basophilia versus acidophilia (eosinophilia): In a hematoxylin and eosin (H&E)–stained section, basophilic components stain blue-purple; acidophilic components stain pink-red. The *arrow* indicates the basal part of the cytoplasm of a cell of a salivary gland duct. The acidophilic (*pink*) staining results from a concentration of mitochondria in this part of the cell. The *arrowhead* indicates the cytoplasm of a plasma cell. The basophilic (*bluish*) staining results from a concentration of rough endoplasmic reticulum.



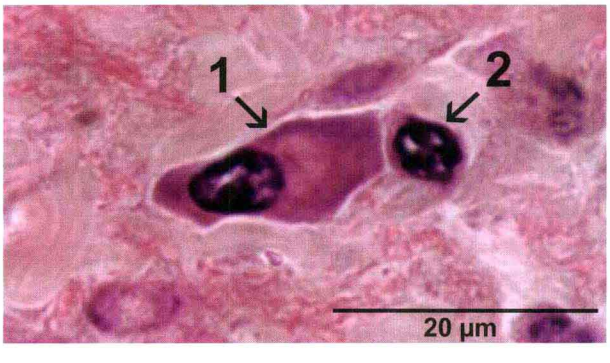
Granules: These vesicles stain because they retained at least some of their contents during tissue preparation. The *arrow* indicates small acidophilic granules filling the cytoplasm of an eosinophil. The *arrowhead* indicates large acidophilic secretory granules in the apical cytoplasm of a Paneth cell. Note that the basal cytoplasm surrounding the nucleus of the Paneth cell stains basophilic, indicating large amounts of rough endoplasmic reticulum in this region of the cell.



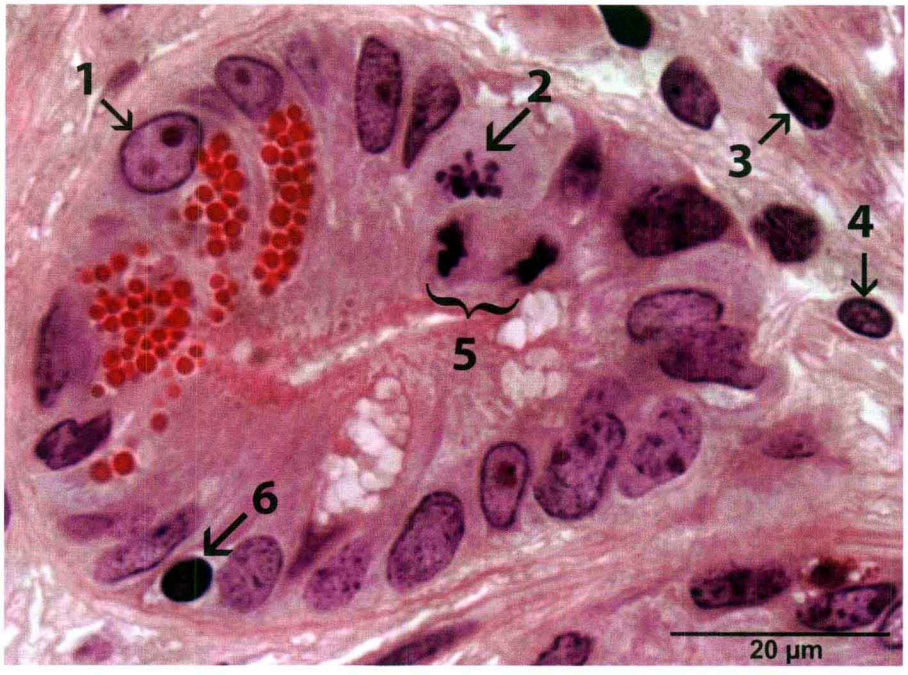
Vacuolated cytoplasm: This type of cytoplasm contains what appear to be empty holes. Usually, these represent either lipid droplets or vesicles whose contents were washed out during processing of the tissue. What appear to be empty spaces in the cells from the adrenal cortex shown here were actually occupied, in the living state, by droplets of lipid (cholesterol) that were extracted during tissue preparation.



Abundant versus scant: This pair of terms describes a substantial amount (volume) of cytoplasm (*cell 1*) or a slight amount of cytoplasm (*cell 2*) surrounding the nucleus. These are inexact terms but are sometimes useful in describing a cell.



Nucleus Features



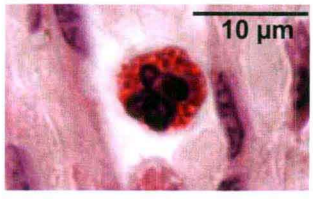
Large versus small: This is another imprecise set of terms, but useful if it's possible to make comparisons with nuclei of other cells in the field of view. *Label 1* indicates a relatively *large* nucleus; *labels 3*, *4*, and *6* indicate *small* nuclei.

Euchromatic versus heterochromatic: Nuclei of most cells show us a mixture of *euchromatin* (dispersed, lightly stained, accessible to transcription) and *heterochromatin* (condensed, darkly stained, inactive). However, there is a wide variability in the relative proportions of the two forms. *Nucleus 1* has mostly euchromatin. *Nucleus 6* is highly heterochromatic. *Nuclei 3* and *4* have mixes of heterochromatin and euchromatin. Notice that the size of a nucleus is roughly proportional to its content of euchromatin.

Nucleoli prominent: Presence of an obvious nucleolus (*nucleus 1*) or nucleoli indicates that the cell is actively synthesizing ribosomes and, therefore, proteins. Typically, nucleoli are present in a nucleus that has most of its chromatin in the form of euchromatin, but there are exceptions (for example, some malignant tumor cells).

Mitotic nucleus: When a cell divides, the nuclear envelope dissolves, and the chromosomes are dark, condensed particles. *Label 2* indicates the chromosomes of a metaphase cell. Label 5 indicates two clusters of chromosomes in an anaphase cell.

Simple versus segmented: A *simple* nucleus appears as a single structure that can have a variety of shapes (round, oval, indented, fusiform, irregular). All the nuclei in this photomicrograph are simple nuclei. A *segmented* nucleus, which is typical of some types of white blood cells, appears in sections as two or more distinct parts (lobes), as seen in the cell in the center of this small panel.



Inferences from nucleus appearance: The appearance of the nucleus provides some clues about the state of the cell's activity. Cells that are active in protein synthesis will usually have fairly large nuclei, prominent nucleoli, and a preponderance of euchromatin. Examples of such cells are rapidly dividing cells (which are busy duplicating cell constituents to be divided among daughter cells), cells that secrete proteins, and cells that have a very large area of membrane and a large volume of cytoplasm to maintain (e.g., neurons).

Cell Size

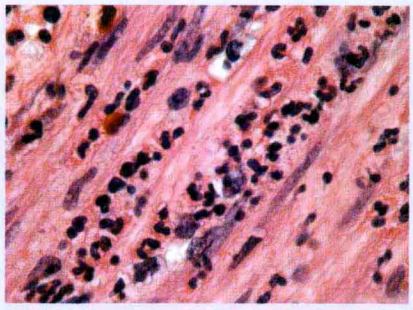
Large versus small: Although many cell types have diameters falling in the range of 10 to 20 µm, the total spectrum of cell sizes is much broader. There are cells much smaller (e.g., inactive lymphocyte at about 6 µm) or much larger (e.g., megakaryocyte at about 100 µm). If cell volume and surface area are considered things can get pretty tricky, because many cells are not compact spheres or simple geometric shapes but have other shapes that can be extremely complex.

Descriptive Terms for Abnormal Cells and Tissues

Acute Inflammation. H&E, ×388

Acute inflammation is an immediate response by the immune system due to tissue injury from many causes including infection, necrosis, and trauma. It results in a local increase in blood flow, tissue edema due to increased vascular permeability, and an increased number of acute inflammatory cells (chiefly polymorphonuclear leukocytes or neutrophils). A confluent collection of neutrophils is an **abscess**.

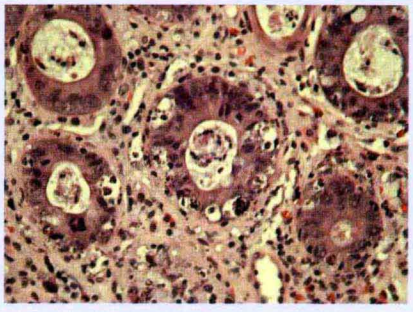
Image: Acute appendicitis showing an infiltration of neutrophils within layers of smooth muscle in the appendiceal wall is shown.



Apoptosis. H&E, ×155

Apoptosis is the process of cell death initiated by either physiologic or pathologic causes. Pathologic apoptosis may be seen in malignant neoplasms, cells damaged by radiation or chemicals, tissues infected by viruses, and immunologic damage as seen in graft-versus-host disease.

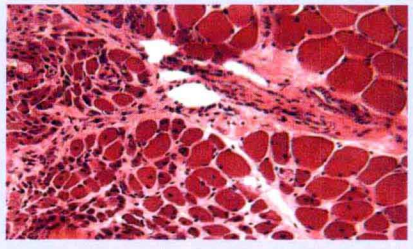
Image: Colonic mucosa demonstrating marked apoptosis of the crypt epithelial cells is shown in a patient with graft-versus-host disease following a bone marrow transplant.



Atrophy. H&E, ×99

Pathologic **atrophy** refers to a decrease in cell size as a result of various factors including denervation, decreased use, aging, decreased blood supply and nutrients, and pressure.

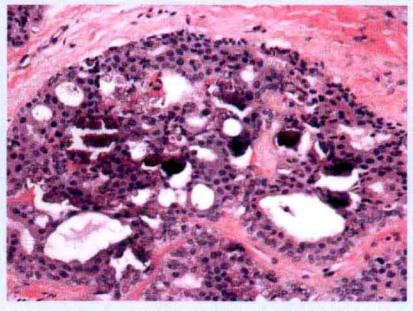
Image: Skeletal muscle showing denervation atrophy is pictured here. Note the larger, normal myocytes in the *right portion* of the image, and the smaller, atrophic myocytes in the *left portion* of the image. In this case, damage to a motor neuron or axon caused atrophy of a group of muscle fibers it served.



Calcification. H&E, ×199

Tissue **calcification** is abnormal and is broadly divided into **metastatic calcification** and **dystrophic calcification**. *Metastatic calcification* occurs in normal, healthy tissues in patients who are hypercalcemic due to vitamin D intoxication, renal failure, or increased parathyroid hormone or in patients with bone destruction. *Dystrophic calcification* occurs in dying or necrotic tissues in patients with normal serum calcium.

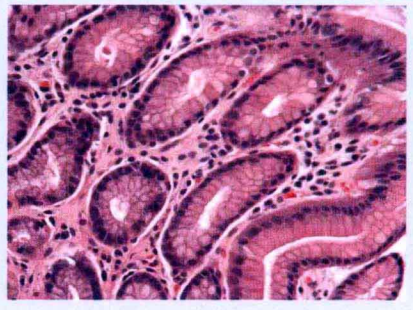
Image: Dystrophic calcification in an intraductal papilloma of the breast is shown. Tissues that assume a papillary morphology tend to develop calcifications at the tips of degenerating papillae. Other examples include papillary thyroid carcinoma and serous papillary neoplasms of the ovaries. Round, lamellated calcifications are called **psammoma bodies**.



Chronic Inflammation. H&E, ×199

Chronic inflammation is an ongoing inflammatory process, typically weeks to months in duration. It may be seen in infectious processes, like viral hepatitis, autoimmune disease, and toxic exposures. **Acute** and **chronic inflammations** commonly coexist, as in active chronic gastritis due to infection of the gastric mucosa by the bacteria *Helicobacter pylori*. The inflammatory cells participating in chronic inflammation include lymphocytes, plasma cells, mast cells, and eosinophils.

Image: This stomach biopsy shows chronic gastritis; note the plasma cells within the lamina propria. No neutrophils are seen, which would indicate a concomitant active, acute inflammatory process.

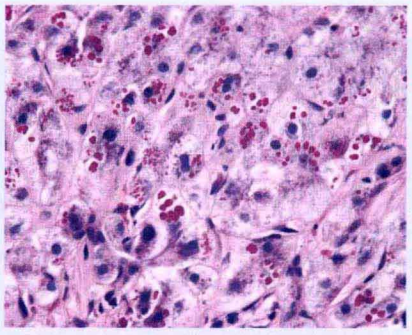


Cellular Accumulations

Alpha 1-Antitrypsin. PASD (periodic acid-Schiff with diastase digestion), ×173

Alpha 1-antitrypsin deficiency is an autosomal recessive disorder characterized by low serum concentrations of the enzyme *alpha 1-antitrypsin*, which inhibits or inactivates proteases and elastases. Alpha 1-antitrypsin deficiency may cause neonatal hepatitis with later cirrhosis and pulmonary panacinar emphysema.

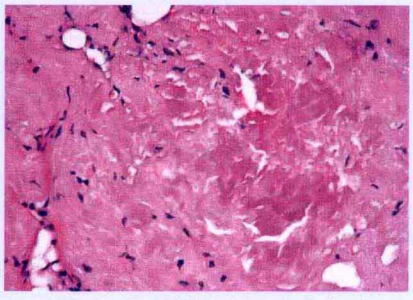
Image: A liver biopsy in a patient with alpha 1-antitrypsin deficiency shows accumulated alpha 1-antitrypsin as hyaline globules in this PAS stain. The globules remain after the tissue has been treated with diastase (diastase resistant).



Amyloid. H&E, ×173

Amyloid is an abnormal protein caused by many pathological conditions, the most common of which include **AL amyloid,** caused by light chains secreted by plasma cells in plasma cell myeloma or monoclonal B-cell neoplasms; **AA amyloid,** seen in chronic inflammatory conditions; and **Aβ amyloid** in Alzheimer disease. Many other types of amyloids exist.

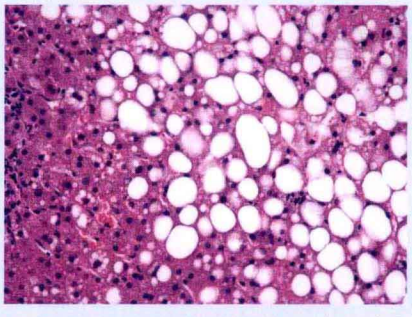
Image: A lymph node containing AL amyloid in a patient with small lymphocytic lymphoma is shown. In H&E-stained preparations, amyloid is amorphous and eosinophilic. Amyloid stained with Congo red shows a characteristic green birefringence when viewed with polarized light.



Fatty Change. H&E, ×173

Fatty change, or **steatosis**, is the abnormal intracellular accumulation of lipid. Although it can occur in many organs, it is most commonly seen in the liver because of a variety of causes including alcohol abuse, hepatitis C, genetic predisposition, medications, toxins, and diabetes mellitus.

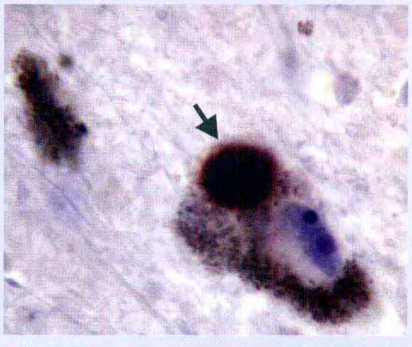
Image: This liver biopsy shows marked steatosis with intracellular lipid vacuoles.



Lewy Body. Immunohistochemistry for alpha-synuclein, ×431

A *Lewy body* is an intracytoplasmic oval with a halo, formed in neuromelanin-containing neurons in patients with idiopathic Parkinson disease.

Image: In this immunoperoxidase preparation, brown pigment indicates the presence of alpha synuclein (*arrow*), the main protein in the inclusion.



Neurofibrillary Tangles. Silver stain, ×173

In patients with Alzheimer disease, microtubule-associated protein tau and abnormally phosphorylated neurofilaments form *neurofibrillary tangles* within neurons.

Image: This silver-stained slide shows a twisted, black helix (*arrows*) in the cytoplasm of a neuron from a patient with Alzheimer disease.