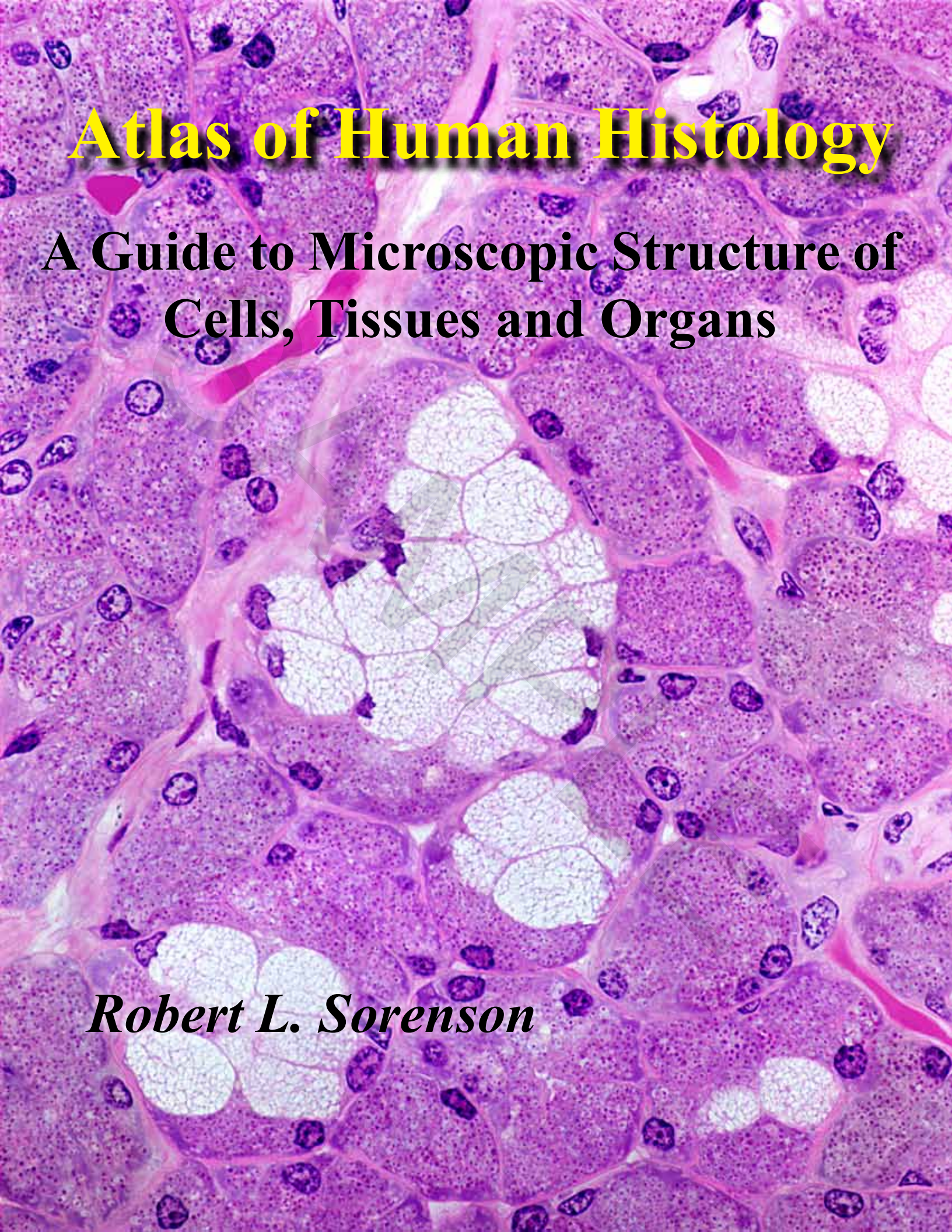

Atlas of Human Histology

A Guide to Microscopic Structure of Cells, Tissues and Organs

Robert L. Sorenson

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This atlas is a series of photographs ranging from low to high magnifications of the individual tissue specimens. The low magnification images should be used for orientation, while the higher magnification images show details of cells, tissues, and organs. Although every effort has been made to faithfully reproduce the colors of the tissues, a full appreciation of histological structure is best achieved by examining the original specimens with a microscope. This atlas is a preview of what should be observed.

The photomicrographs found in this atlas come from the collection of microscope slide used by medical, dental and undergraduate students of histology at the University of Minnesota. Most of these slides were prepared by Anna-Mary Carpenter M.D., Ph.D. during her tenure as Professor in the Department of Anatomy (University of Minnesota Medical School).

Each tissue specimen, in its entirety, has been digitized with a high resolution 40X or 60X lens to generate virtual microscope slides. The Virtual Microscope Collection includes additional slides which complement and extend the core slide collection. Producing the virtual slide collection and developing the web site for their presentation was done with the very capable assistance of Todd C. Brelje Ph.D.

The drawings that appear in the atlas are the product of Jean E. Magney, who is accomplished both as an histologist and an artist. Her talented interpretation of biological structure and its artistic rendering greatly facilitate the learning and comprehension of histology. These drawings first appeared in “Color Atlas of Histology” Stanley L. Erlandsen and Jean E. Magney, Mosby 1992.

Robert L. Sorenson, Ph.D.

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INTRODUCTION:

What is histology? Histology is the study of cells, tissues and organs as seen through the microscope. Although this atlas is a guide to biological structure that can be observed through the light microscope, histology also includes cellular detail down to the molecular level that can be observed using an electron microscope. The importance of histology is that it is the structural basis for cell, tissue and organ biology and function (physiology) and disease (pathology).

What is the plan for the study of cells, tissues and organs? Histology is organized into four basic types of tissues.

1. Epithelium
2. Connective tissue including

   Cartilage and bone

   Blood and blood formation
3. Muscle
4. Nervous tissue

Chapters 2-8 are concerned with the features of the four basic tissues. The remaining chapters focus on features of organs. Organs are typically made up of more than one type of tissue and cells with varying degrees of differentiation.

The light microscope, tissue preparation, limits and challenges.

The bright field light microscope is a two lens compound optical instrument. The two lenses are the objective and the oculars. The oculars have a 10 fold magnification and the objectives range from 10X, 20X, 40X to 100X. Thus the total magnification typically ranges from 100 fold to 1000 fold. In practice this means that while using the 10X objective you have a wide field of view, but with low resolution. While using the 100X objective you have high resolution, but with a very small field of view. To use a metaphor what this means is that when using the low power objective you can see the forest but not the trees and while using the high power objective you can see the leaves on the trees but not the forest. Therefore when examining a specimen it is essential to start with the low power objective to gain perspective and then work up to the highest power magnification as needed to observe the necessary detail.

Examination of tissues requires that they be prepared for viewing with a microscope. This is a multi-step process that includes fixation (preserves the tissue), embedment (stabilizes the tissue for sectioning), sectioning (cuts the specimen into thin slices of about 5 um) then placing the sections on a glass slide so they can be stained for viewing.

A note about resolution and detection. Resolution refers to the ability to discriminate between two adjacent objects. For the light microscope with optimal lenses and sample preparation this approaches 0.2 um, which is the theoretical limit for light microscopes. [The eye can resolve about 250-500 um and the electron microscope can resolve about 1 nm) Detection refers to the ability to detect something and this can be much smaller than the limit of resolution. For fluorescence molecules this can be as little as a few molecules!

Structure	Size	Light Microscope
Human ovum	120 um	
Most cells	10-30 um	
Red blood cell (RBC)	7 um	
Mitochondium	0.4-1.0 um	
Cilium	0.3 um	
Microvillus	100 nm	**Electron Microscope**
Microtubule	24 nm	
Myosin filaments	15 nm	
Intermediate filaments	10 nm	
Plasma membrane	9 nm	
Microfilaments (actin)	5 nm	

There are several challenges in learning histology. The first being that the view observed through a microscope gives you a perspective that you are unlikely to have experienced previously. It is a complex data set – one with a broad range of shapes and sizes, with varying shades of red and blue. This complex image offers very few clues that are intuitive. Also, the tissue specimen is a two dimensional slice of a complex three dimensional

structure. So, once the two dimensional image has been ascertained you still have the challenge of imagining its three dimensional elaboration. The ideal situation is to have the student and teacher viewing the same specimen simultaneously such as in a dual view microscope. Since this is not always possible, this atlas was written as if a teacher was always at your side to help guide you from low power to the highest power necessary to observe the essential features of the tissue specimens. Thus you will notice that images of all of the slides range from a macroscopic view of the microscope slide itself and then progress through higher magnifications as needed.

How to study microscope slides:

1. Know what structures are important to learn. This atlas shows and identifies the structures and how to find them.
2. The next task in learning is to see if you can identify the structures when examining a slide. Always start at the lowest power (this is important for context and orientation). Increase the magnification as needed so that additional features of the specimen can be observed.
3. Take notes on the features that are observed in the slide. This is best done by drawing pictures and writing a description of the specimen. As in any science laboratory, it is essential that observations be recorded. Not only is this good practice but in research and medicine it is also a legal requirement.
4. Each chapter has a section “Observe and note”. This lists the features that are essential to learning histology and are noteworthy.

How to take Histology Laboratory Notes:

A. Draw a picture of the object of interest. (A blue and red pencil is sufficient for nearly all drawings)

B. Write notes about its appearance, characteristics and features.

Nearly every cell can be described by taking note of:

1. Size
2. Shape
3. Nuclear size and shape and nuclear/cytoplasmic ratio
4. General Staining properties (H&E)
    a. Basophilia & eosinophilia
    b. Hetero- and euchromatin
5. Special staining properties
    a. Verhoeff, Azan, silver etc.
6. Cellular specializations
    a. Microvilli, cilia, secretion granules, myofilaments etc.
    b. Unusual amounts of mitochondria, RNA etc
7. Cellular constituents such as secretion granule contents (hormones, enzymes)
8. Polarity
9. Extracellular material
    a. Extent
    b. Appearance

10. Location
    a. Example
        i. Adjacent to similar cells
        ii. Borders a lumen
        iii. Surrounded by extensive extra-cellular matrix
        iv. Etc.
11. Organization (cells, tissues and organs)
    a. Arrangement of cells of similar and different types
    b. Arrangement of cells with respect to extracellular material
12. Compare and contrast with similar/different cells.
13. Heterogeneity among homologous cells:
    a. Cell development and differentiation
    b. Cell Cycle
    c. Active and resting cycles
    d. Exposure to a concentration gradient of nutrients
        i. Example
            1. Skin cells
            2. Liver hepatocytes

C. Include questions in the notes.

Carefully formulated questions can often reveal the answer.

D. Drawing (and taking notes) is a way of thinking, seeing and understanding.

Chapter 1 Introduction and Cell

The first chapter is an exercise in examining histological tissue specimens through the microscope. A variety of cells, tissues and organs are provided as samples. Also, several different histological stains are used.

A note about stains:

Biological material is inherently of low contrast and provides little to see in the standard bright-field microscope unless treated with a histological stain.

Hematoxylin and Eosin (H&E):

1. This is the most commonly used stain for histology and histo-pathology.
    a. Hematoxylin: Cationic, positively charged, blue dye complex.
        i. Reacts with negatively charged groups:
            1. COO^- - in proteins
            2. SO_4^- - in proteoglycans (GAGs)
            3. PO_4^- - in nucleic acids
        ii. Reacts with basophilic structures: basophilia
    b. Eosin: Anionic, negatively charged red dye
        i. Reacts with positively charged groups:
            1. NH_3^+ - in proteins
            2. mitochondria
        ii. Reacts with acidophilic structures: acidophilia, eosinophilia

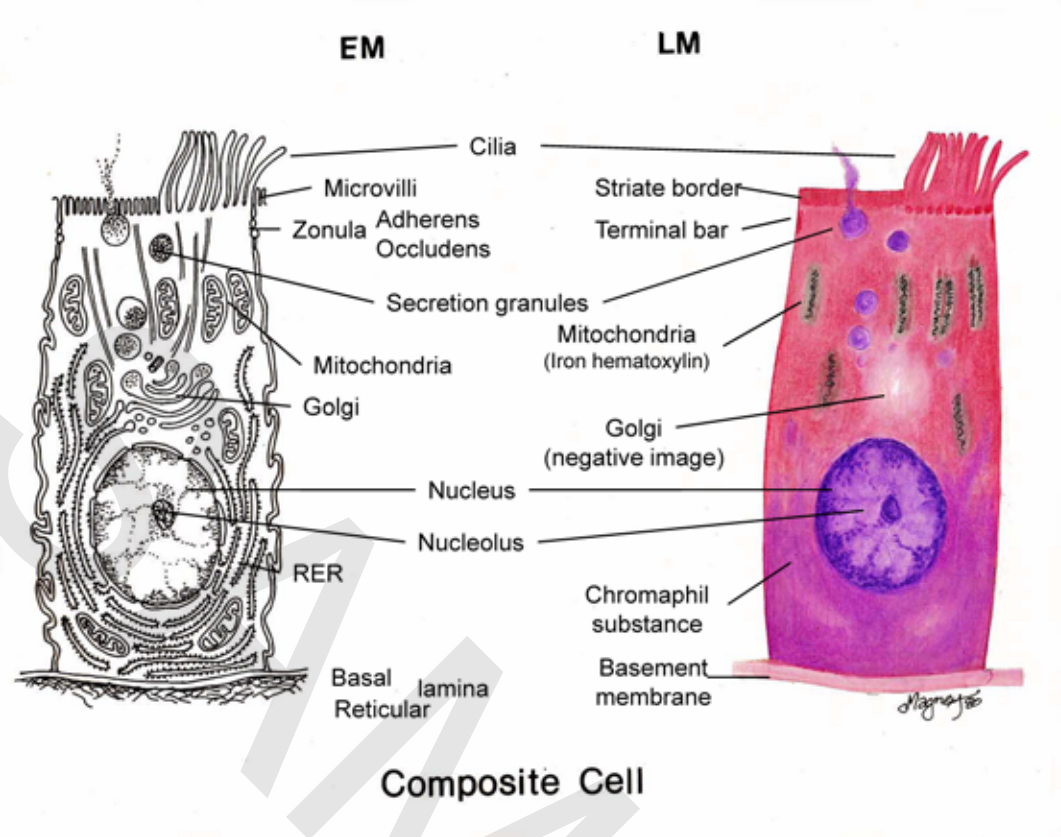
Other stains:

1. Azan: stains collagen blue
2. Silver: stains reticular fibers (collagen type III) black
3. Golgi stain: stains Golgi apparatus
4. Toluidine blue: stains RNA blue and stains mast cells purple
5. Verhoeff: stains elastic protein black
6. Feulgen: stains DNA
7. Sudan: stains lipids
8. PAS (periodic acid Schiff): stains glycogen
9. Aldehyde fuchsin: stains insulin, mast cell granules and elastic fibers purple

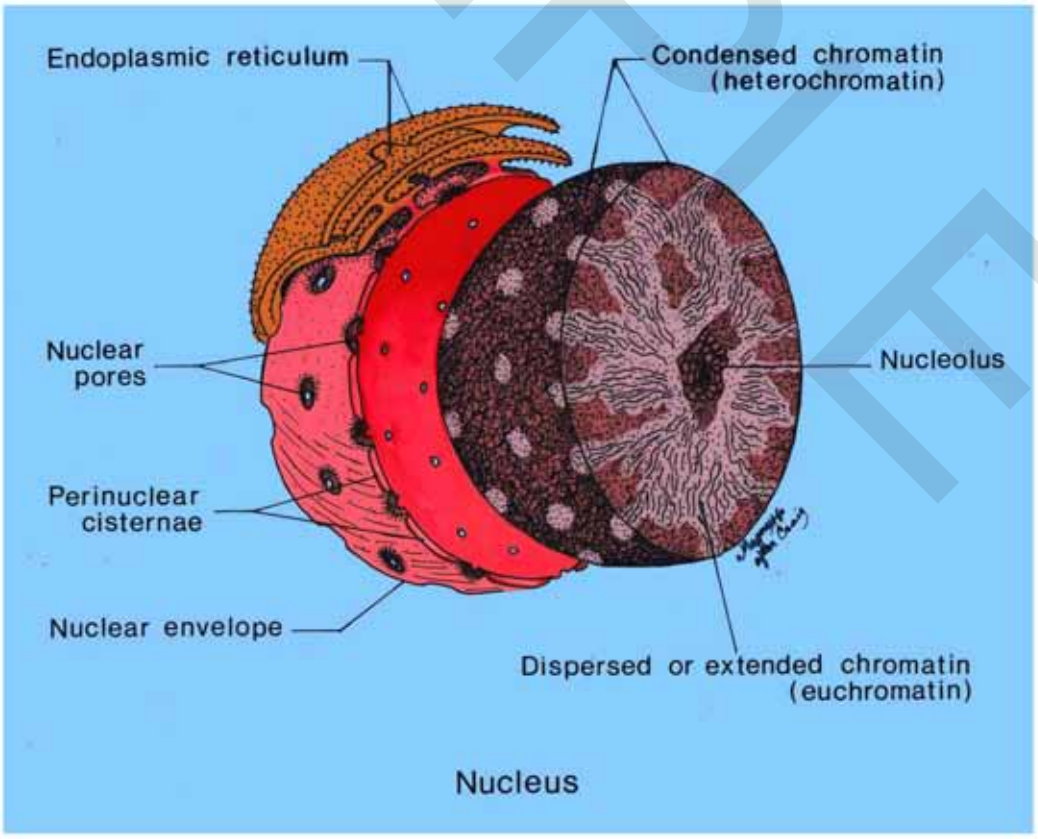
Observe and note:

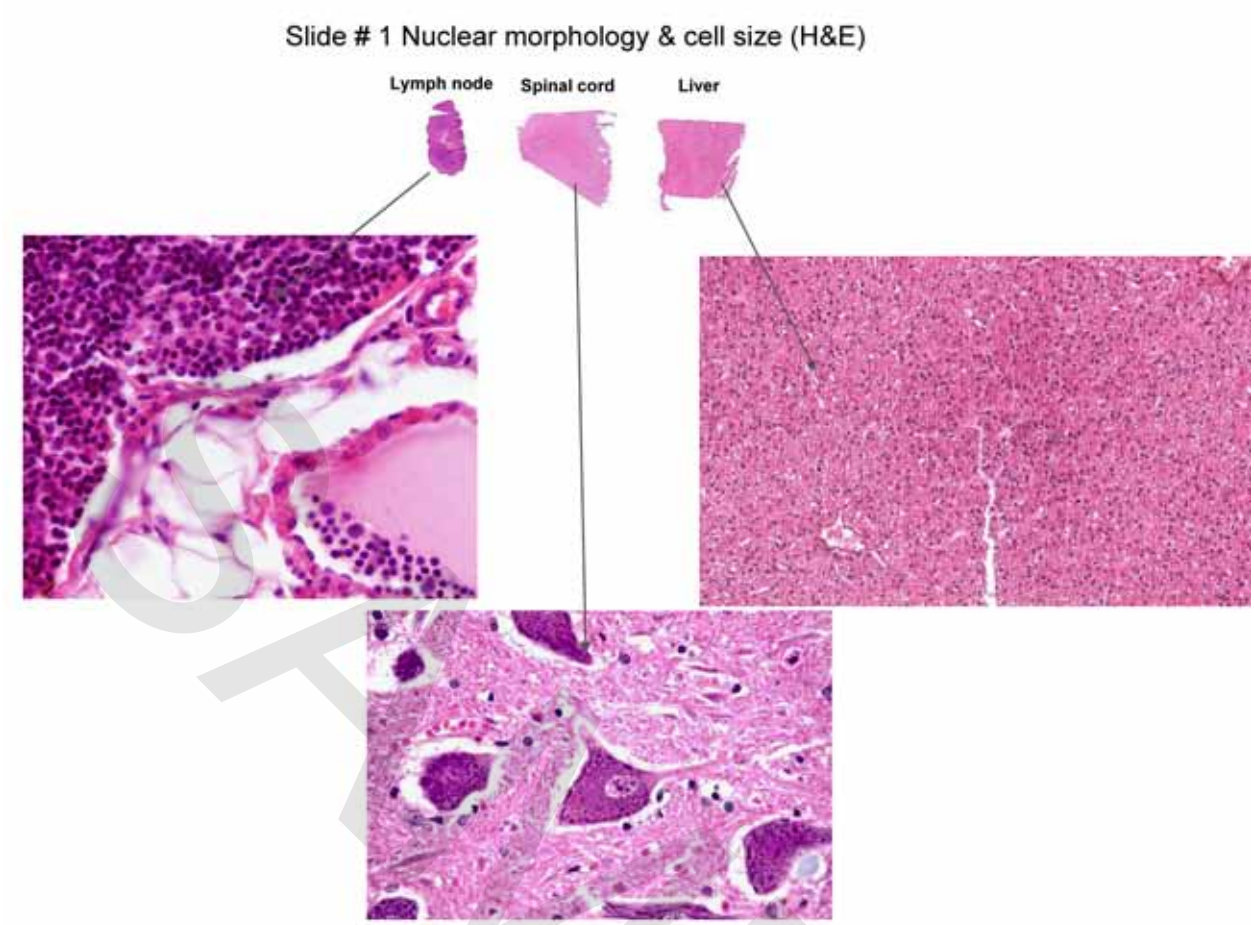
1. Staining characteristics of various cells and tissues.
2. Cell size using red blood cells (7um) as an internal metric.
3. Cell size, shape, nuclear size and shape and nuclear/cytoplasmic ratios.
4. Eosinophilia and basophilia.
5. Euchromatin and heterochromatin.
6. Cellular versus extracellular material such as collagen.
7. Characteristics of different histological stains.

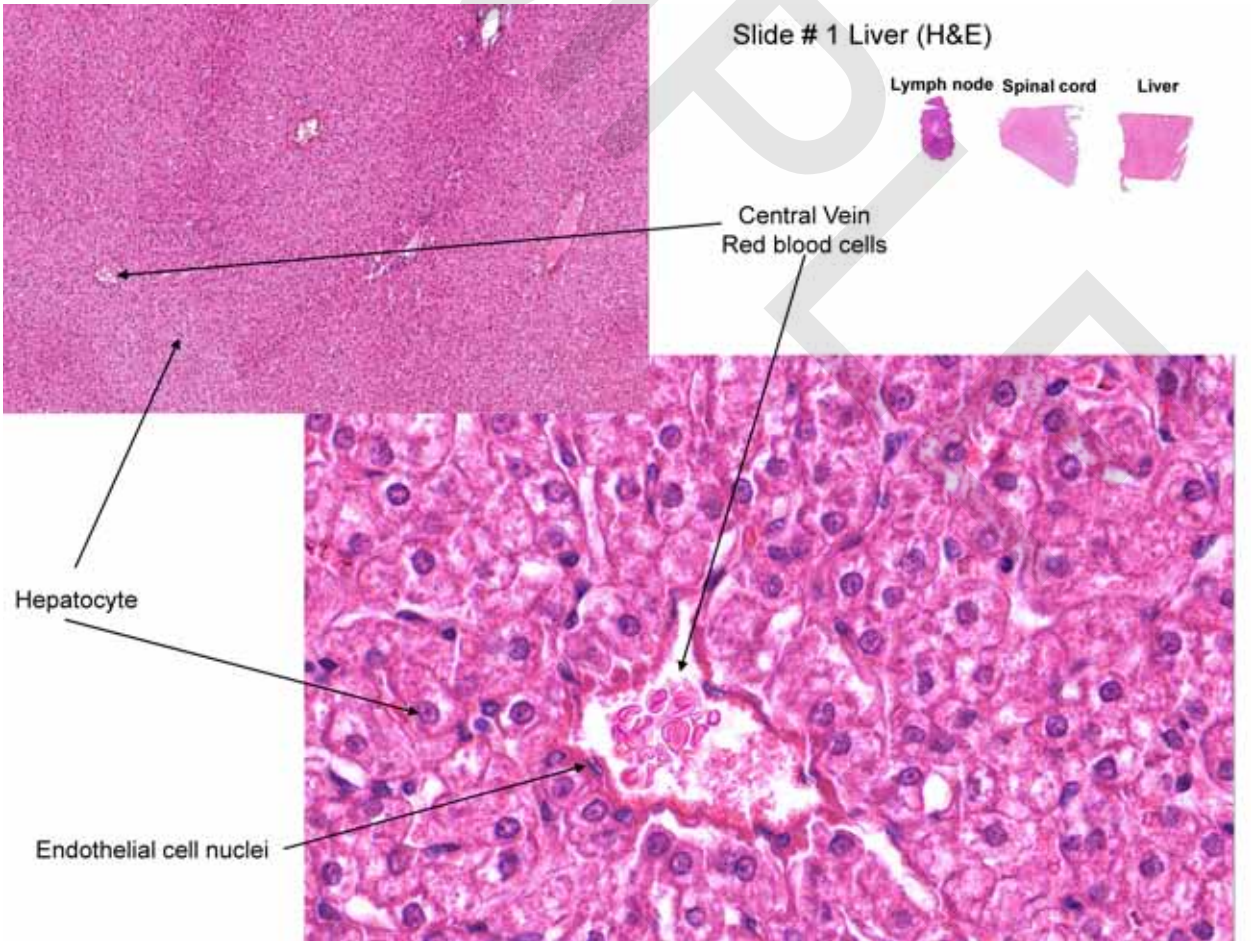
Cell structure & staining

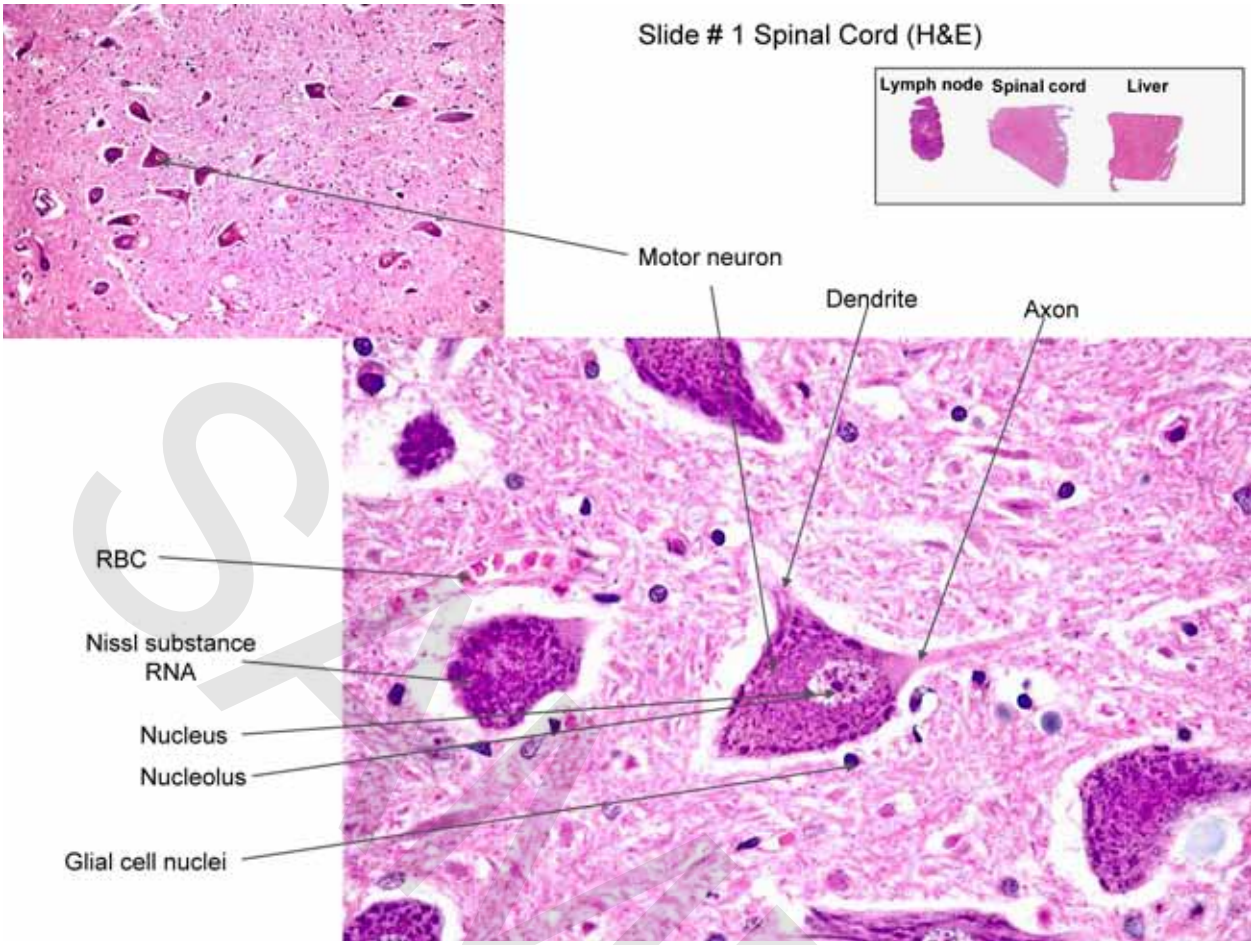


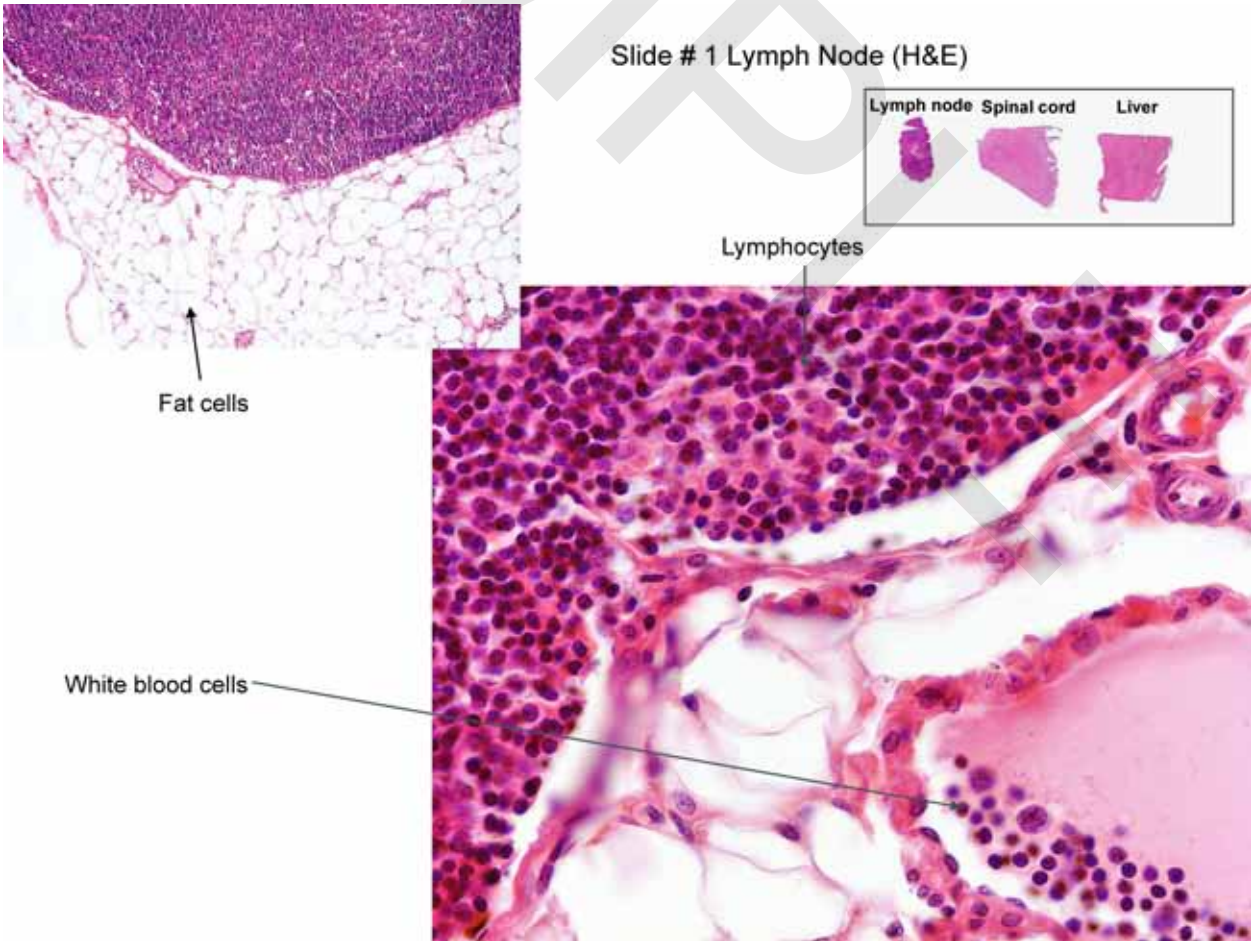
Nucleus Structure (Euchromatin & Heterochromatin)

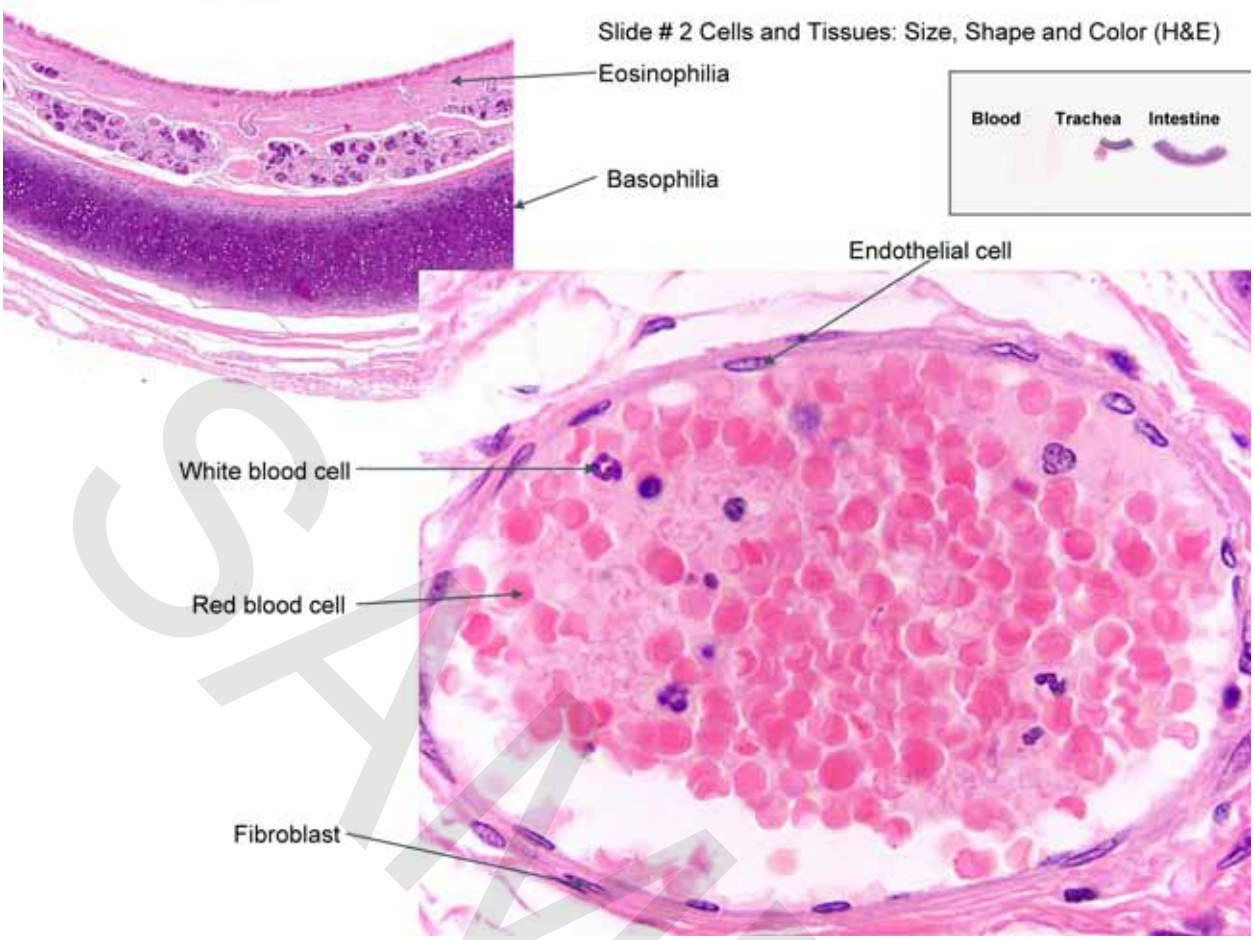


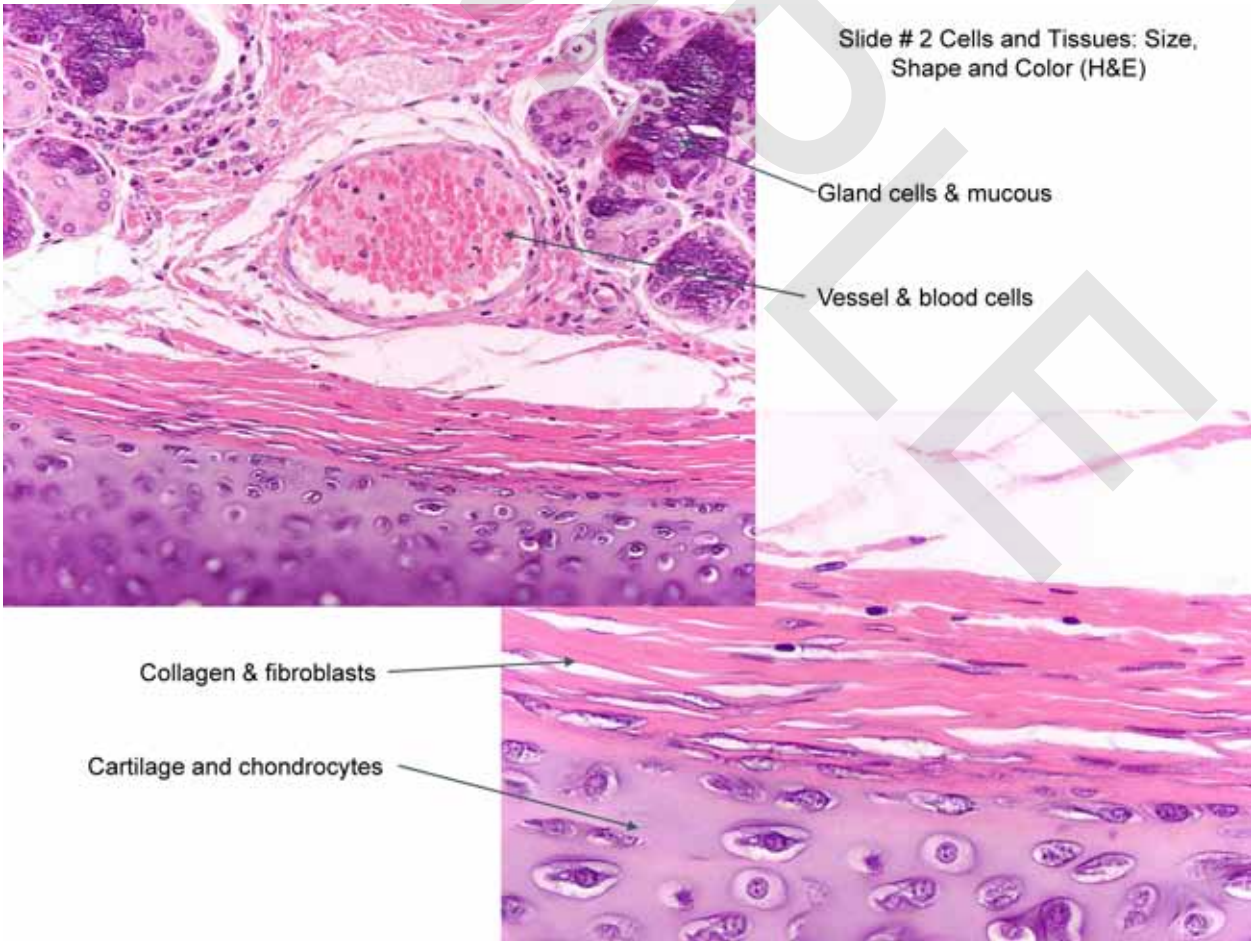

Slide # 1 Nuclear morphology & cell size (H&E)
Lymph node
Spinal cord
Liver


Slide # 1 Liver (H&E)
Lymph node
Spinal cord
Liver
Central Vein
Red blood cells
Hepatocyte
Endothelial cell nuclei

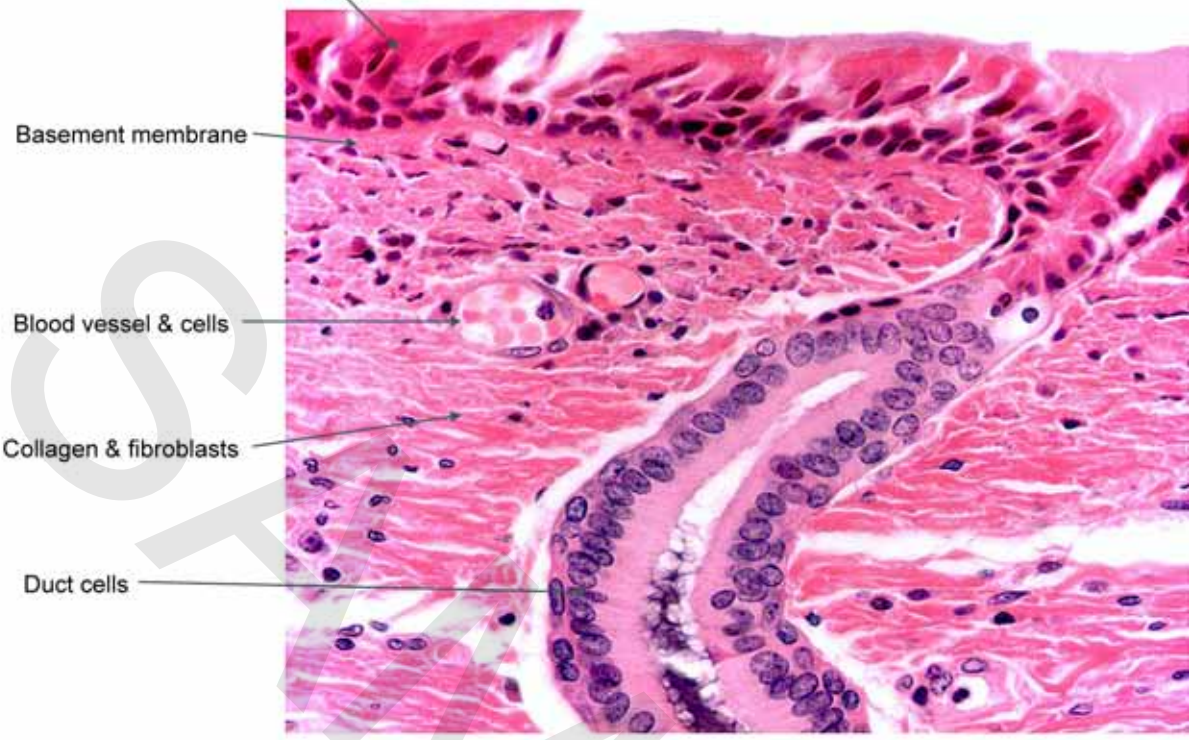

Slide # 1 Spinal Cord (H&E)
Lymph node
Spinal cord
Liver
Motor neuron
Dendrite
Axon
RBC
Nissl substance
RNA
Nucleus
Nucleolus
Glial cell nuclei


Slide # 1 Lymph Node (H&E)
Lymph node
Spinal cord
Liver
Lymphocytes
Fat cells
White blood cells

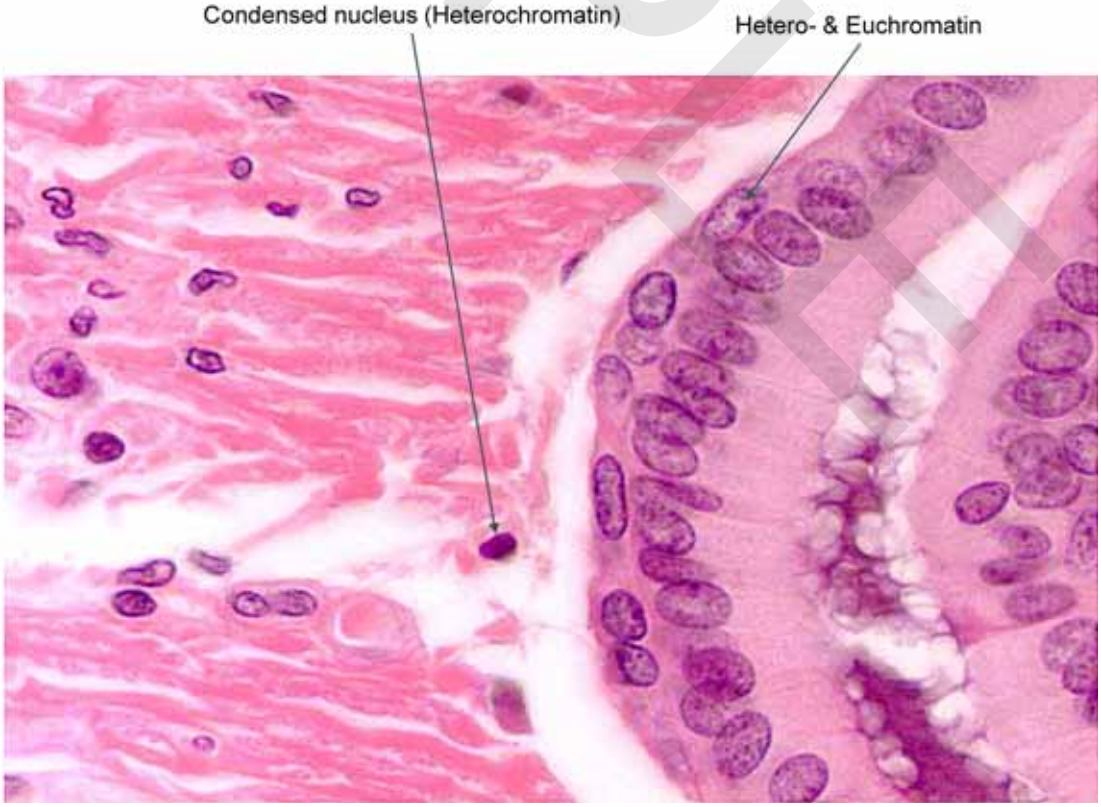

Slide # 2 Cells and Tissues: Size, Shape and Color (H&E)
Eosinophilia
Basophilia
Blood
Trachea
Intestine
Endothelial cell
White blood cell
Red blood cell
Fibroblast


Slide # 2 Cells and Tissues: Size, Shape and Color (H&E)
Gland cells & mucous
Vessel & blood cells
Collagen & fibroblasts
Cartilage and chondrocytes

Slide # 2 Cells and Tissues: Size, Shape and Color (H&E)

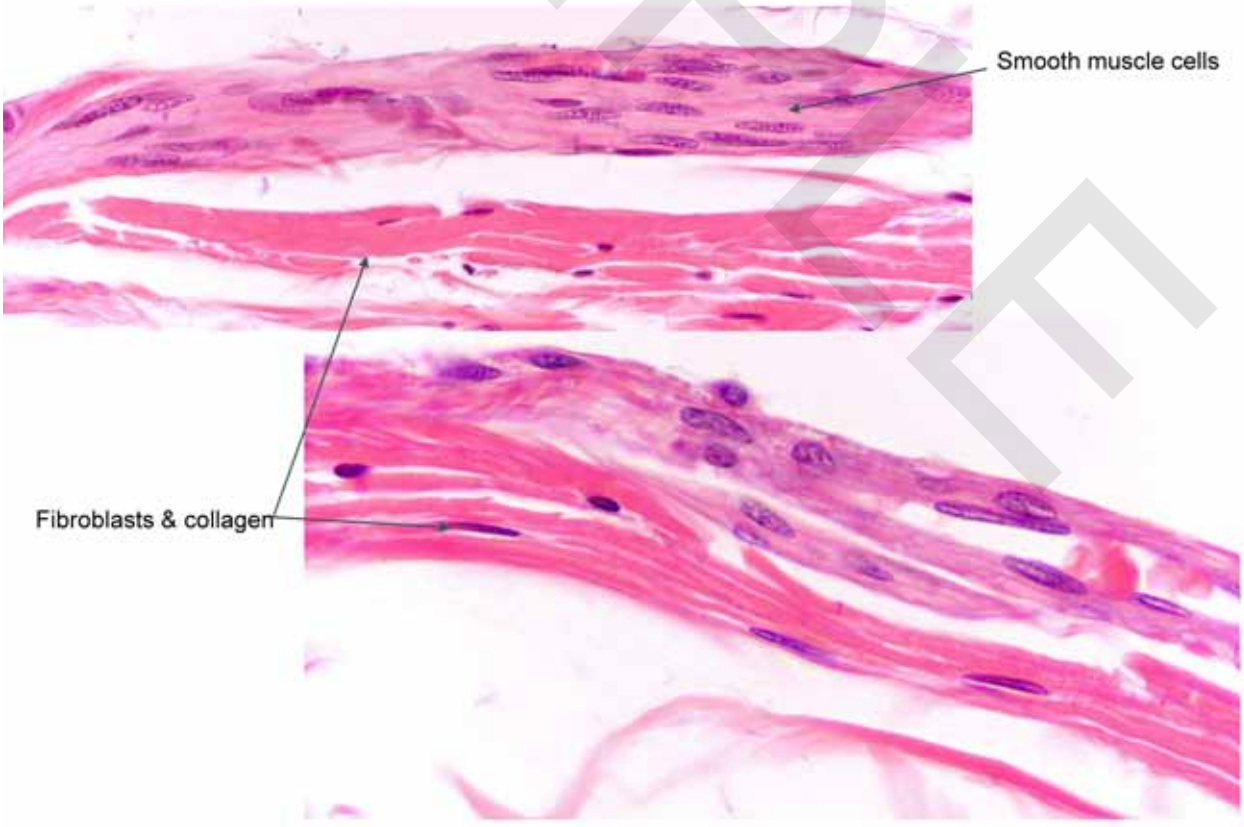


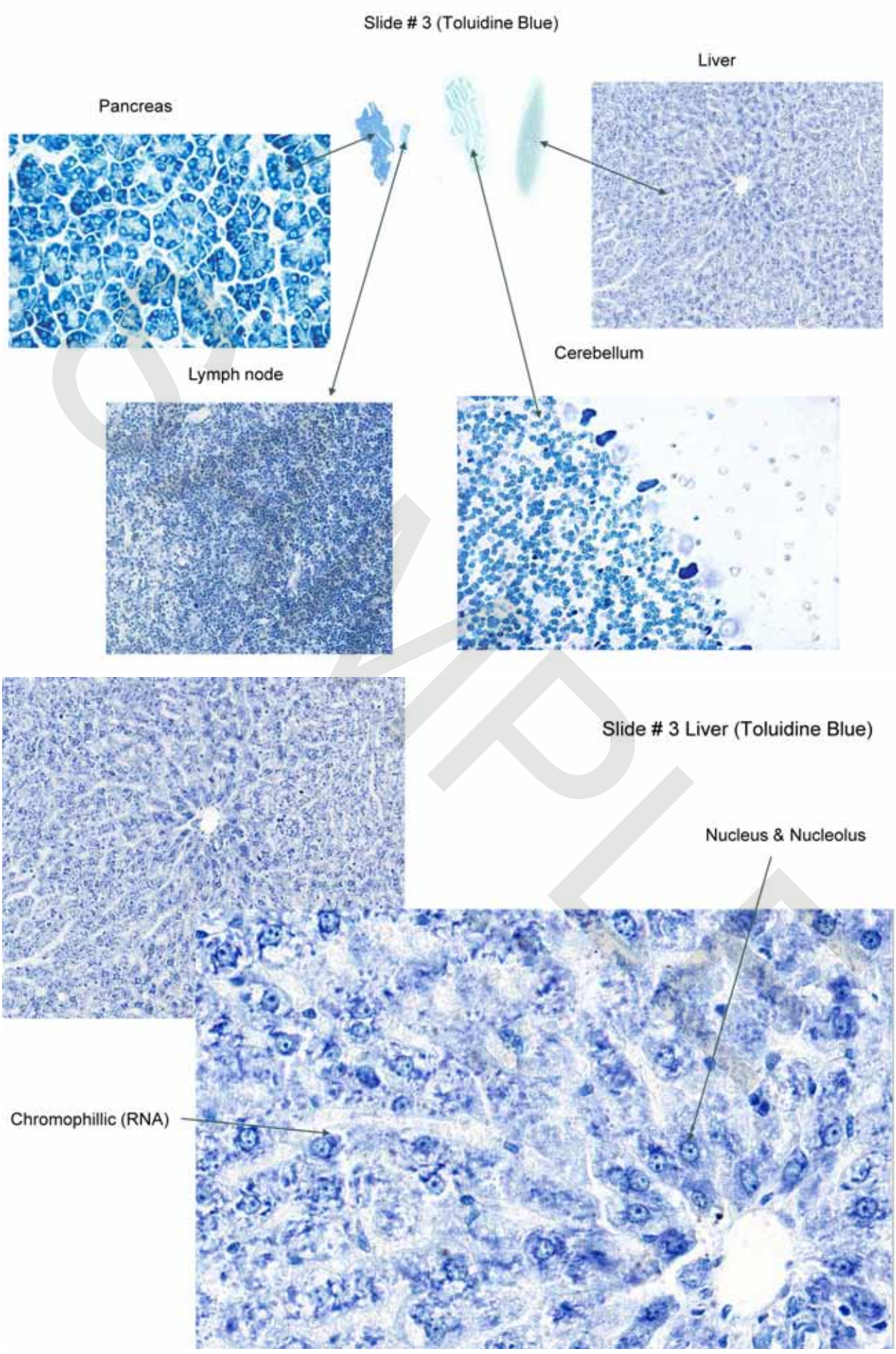
Slide # 2 Cells and Tissues: Size, Shape and Color (H&E)

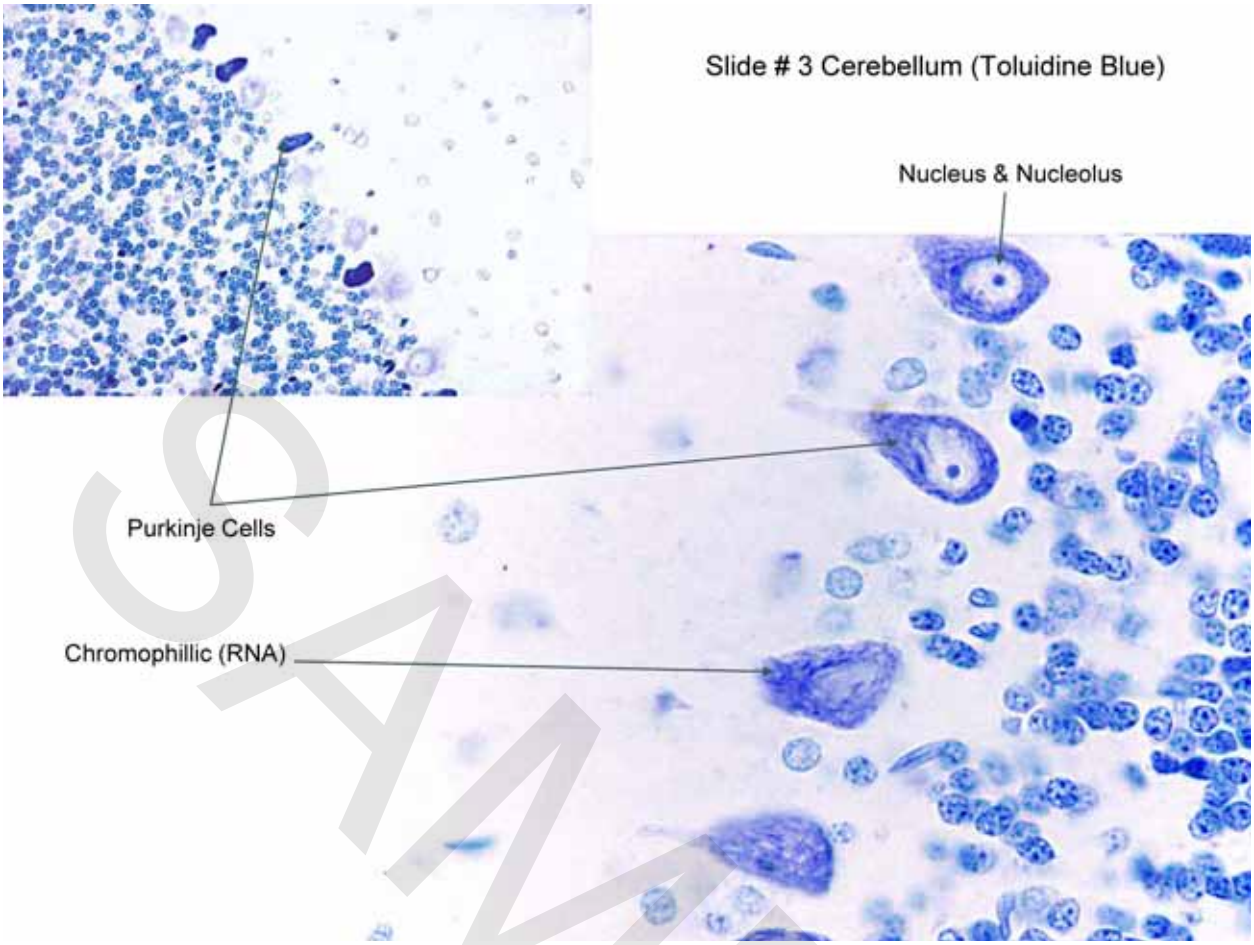


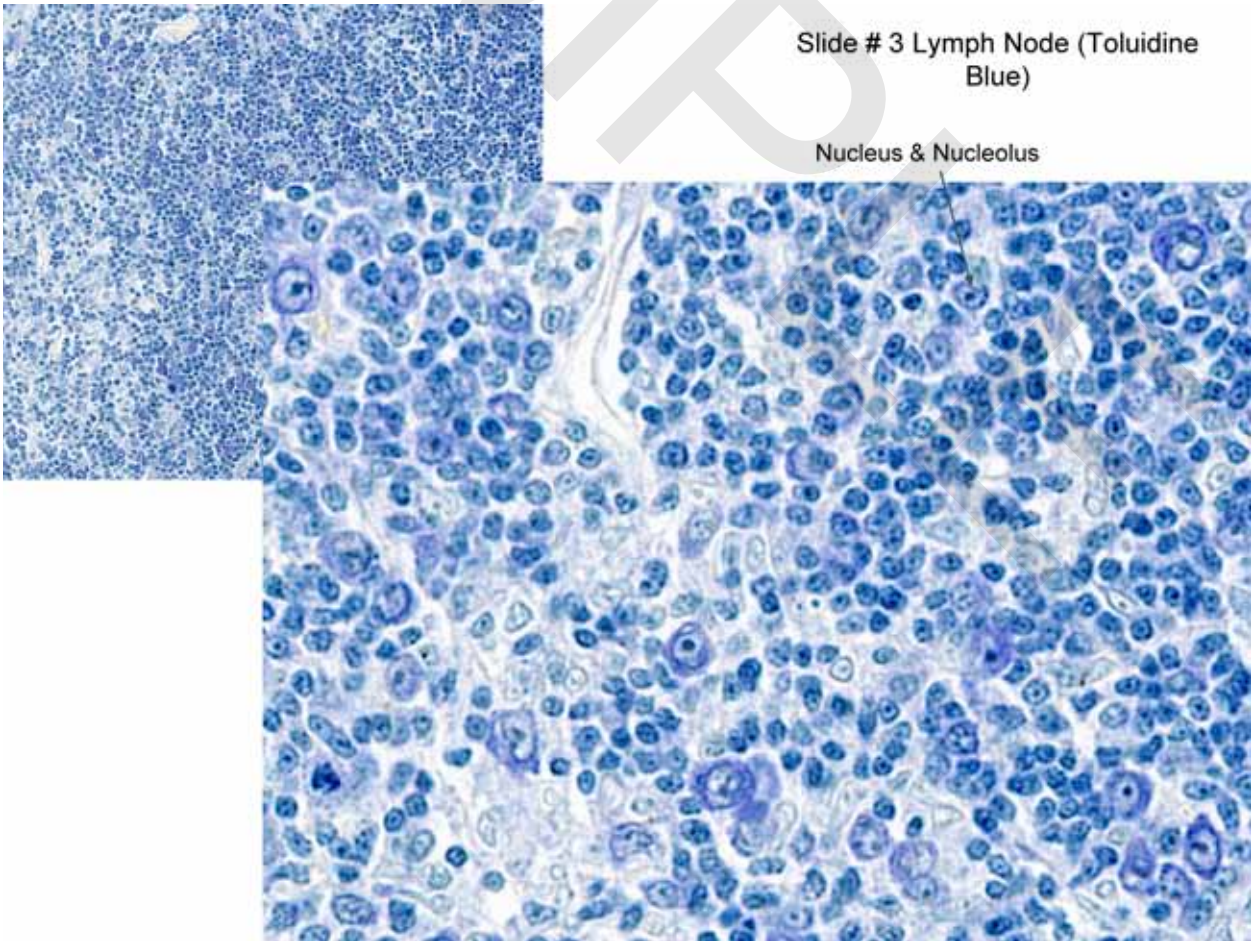
Slide # 2 Cells and Tissues: Size, Shape and Color (H&E)

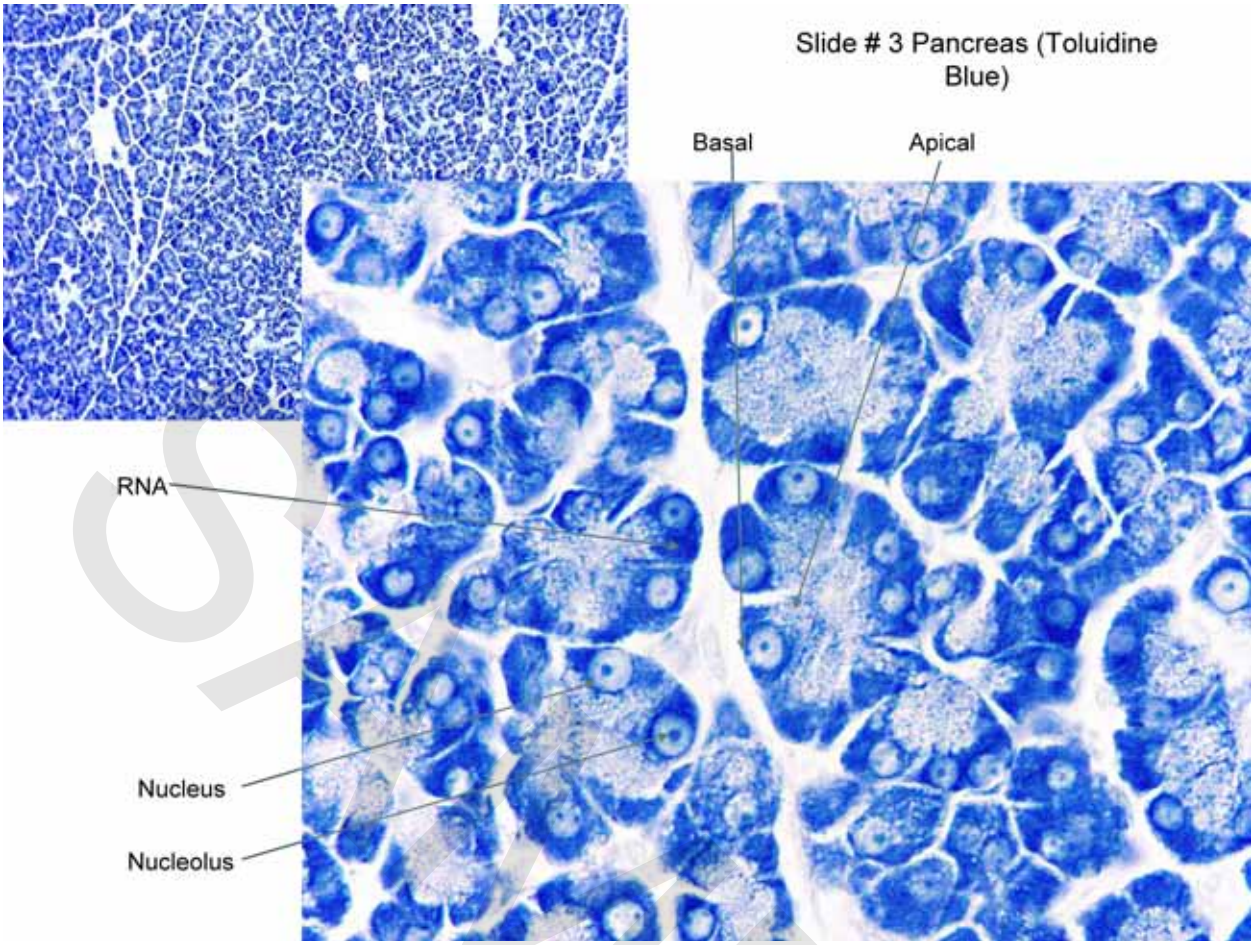
Slide # 2 Cells and Tissues: Size, Shape and Color (H&E)

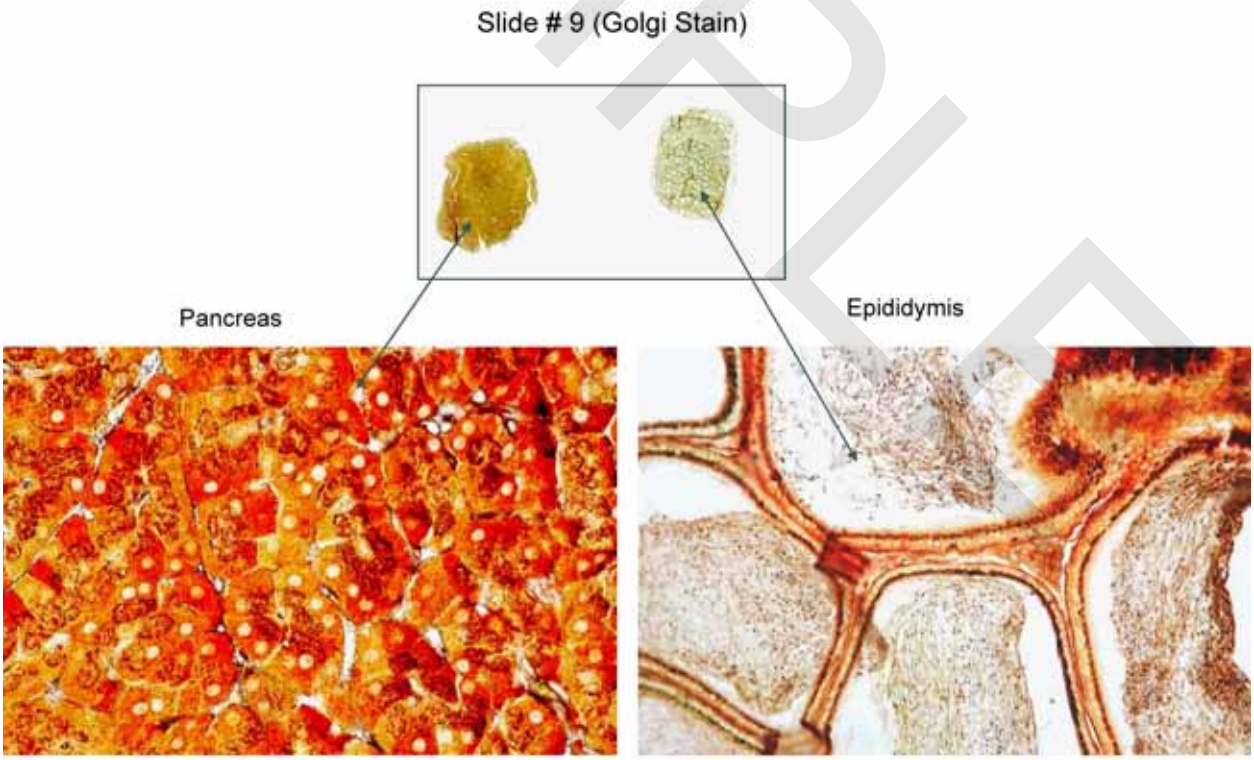



Slide # 3 (Toluidine Blue)
Liver
Pancreas
Cerebellum
Lymph node
Slide # 3 Liver (Toluidine Blue)
Nucleus & Nucleolus
Chromophillic (RNA)

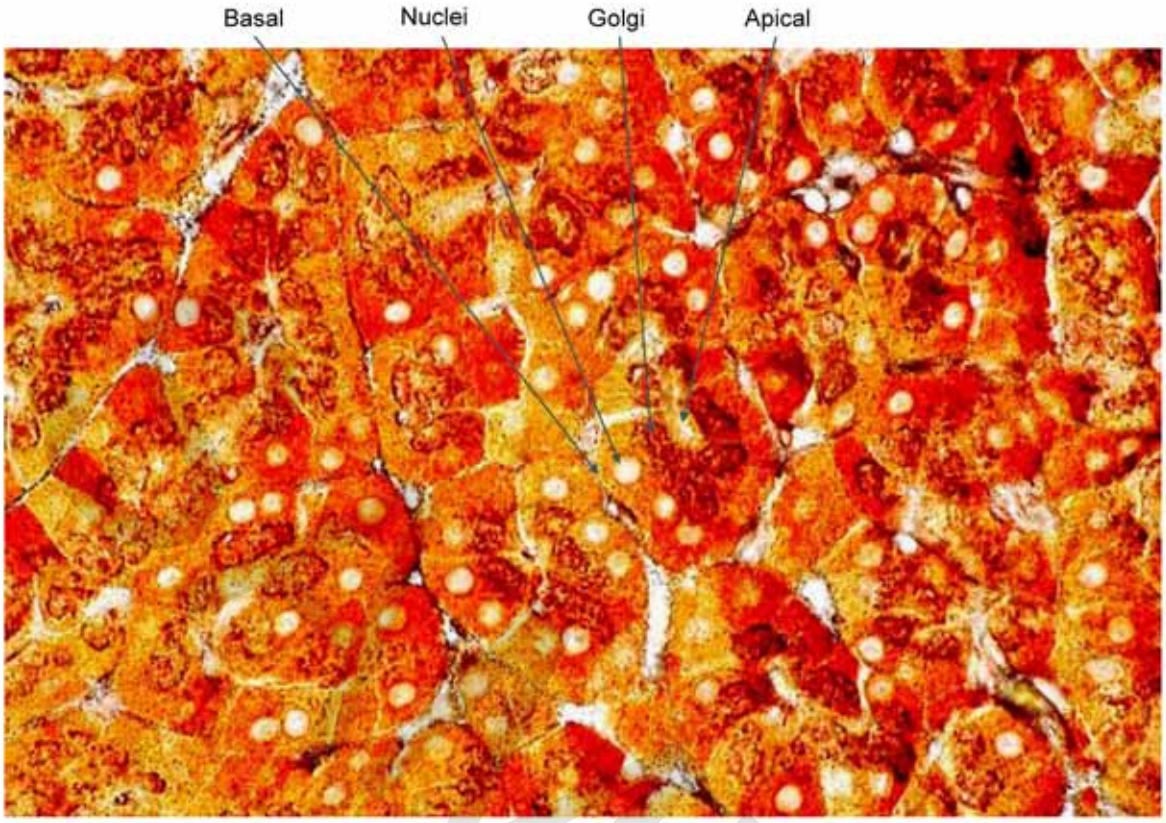

Slide # 3 Cerebellum (Toluidine Blue)
Nucleus & Nucleolus
Purkinje Cells
Chromophillic (RNA)


Slide # 3 Lymph Node (Toluidine Blue)
Nucleus & Nucleolus

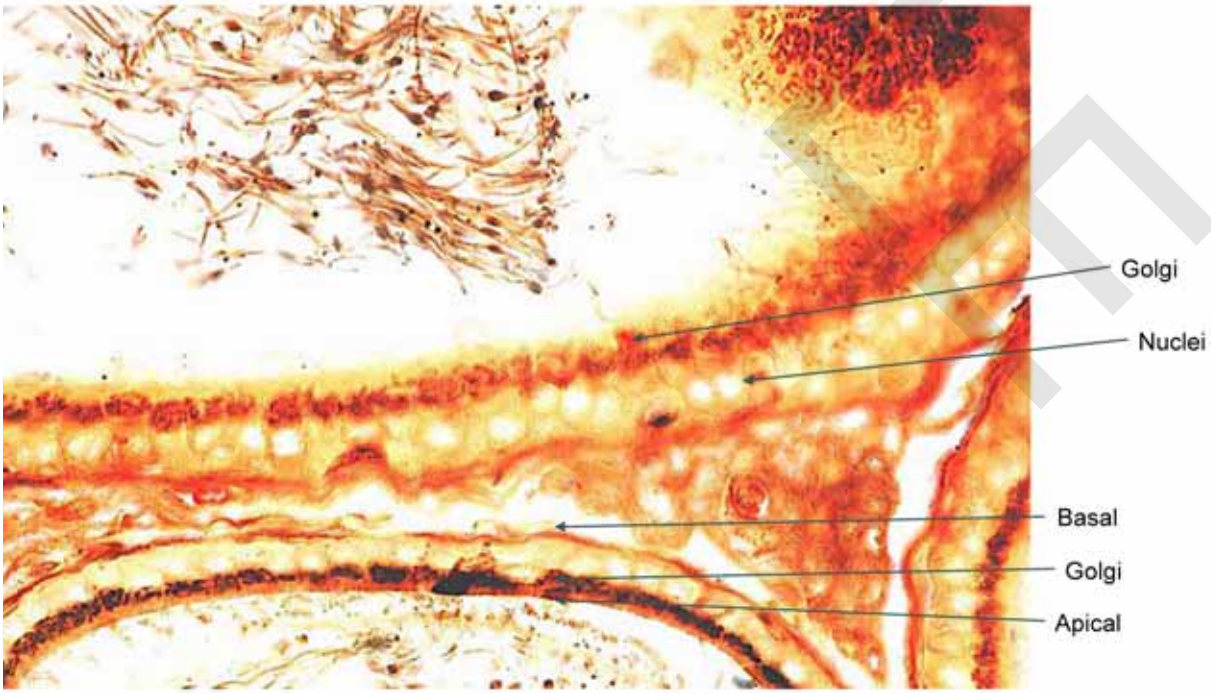

Slide # 3 Pancreas (Toluidine Blue)
Basal
Apical
RNA
Nucleus
Nucleolus

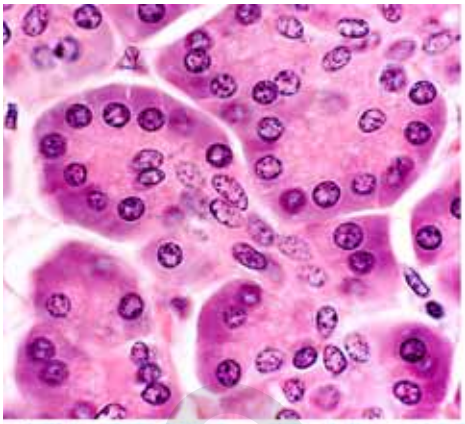

Slide # 9 (Golgi Stain)
Pancreas
Epididymis

Slide # 9 Pancreas (Golgi Stain)

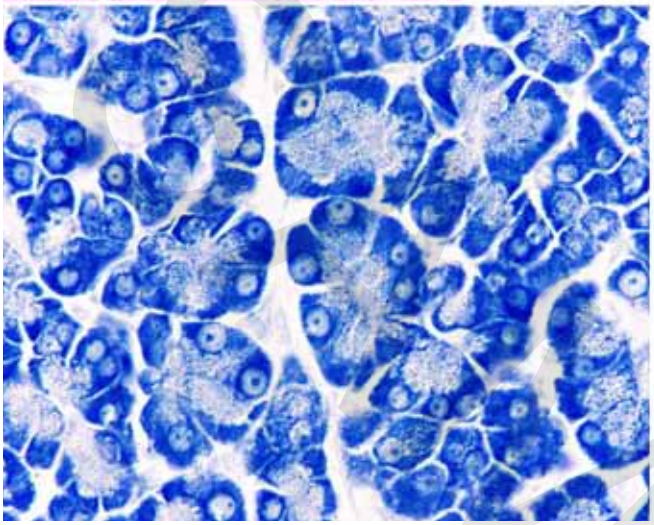


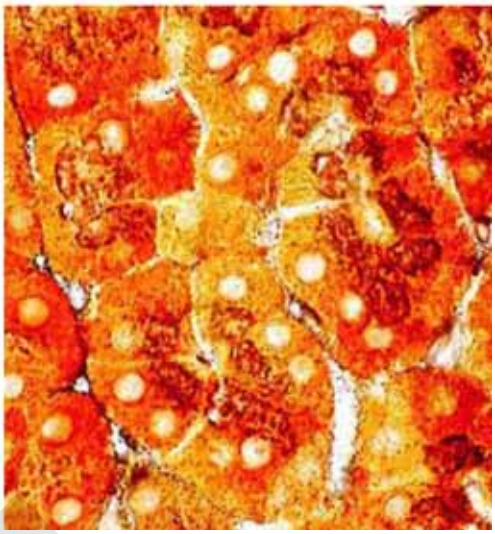
Slide # 9 Epididymis (Golgi Stain)





Same cells (Pancreas) with 3 stains
(H&E, Toluidine blue, Golgi)

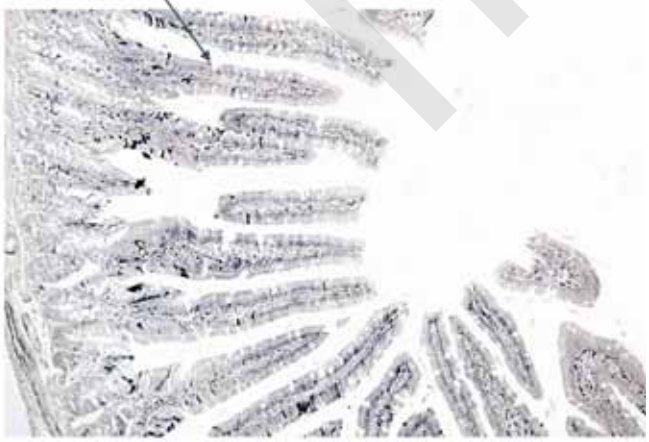


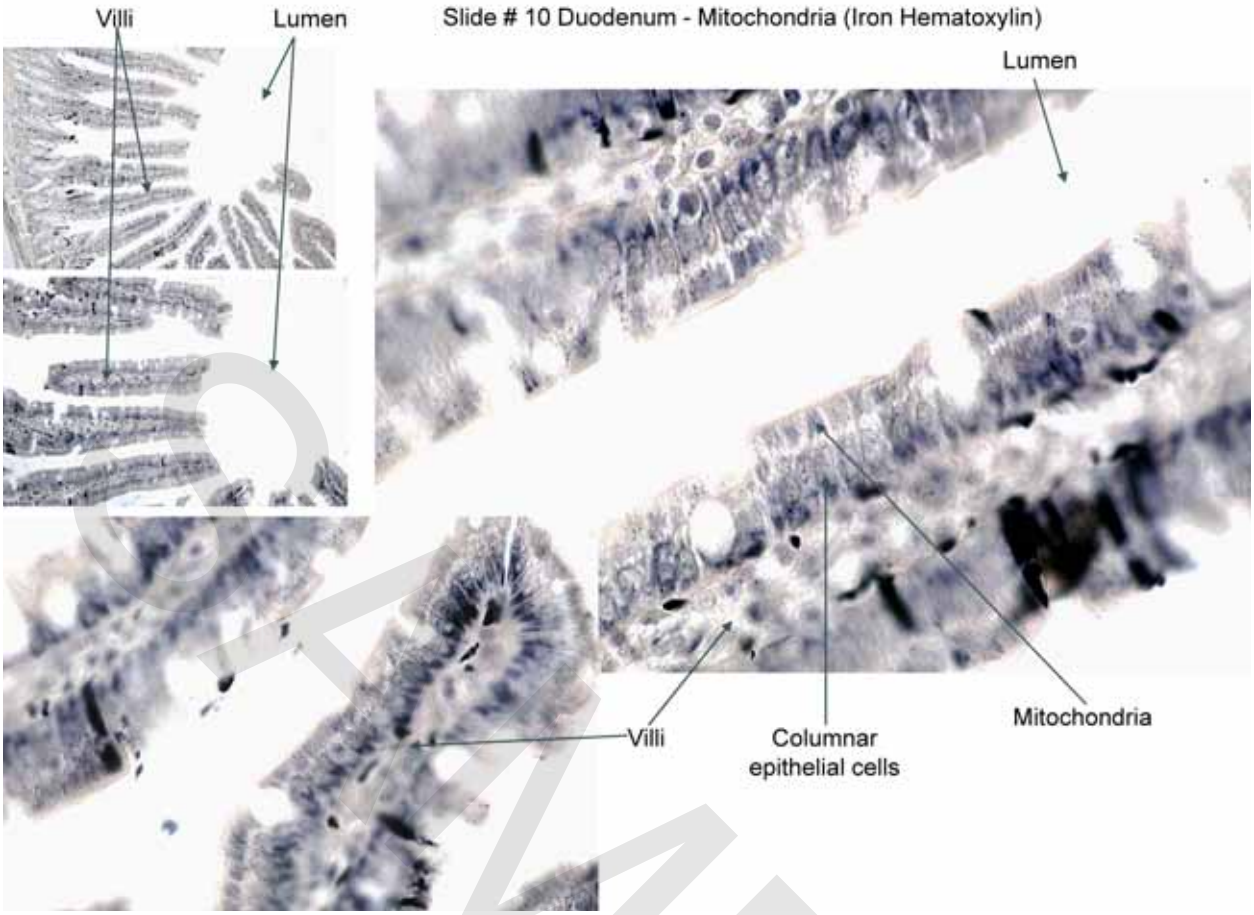


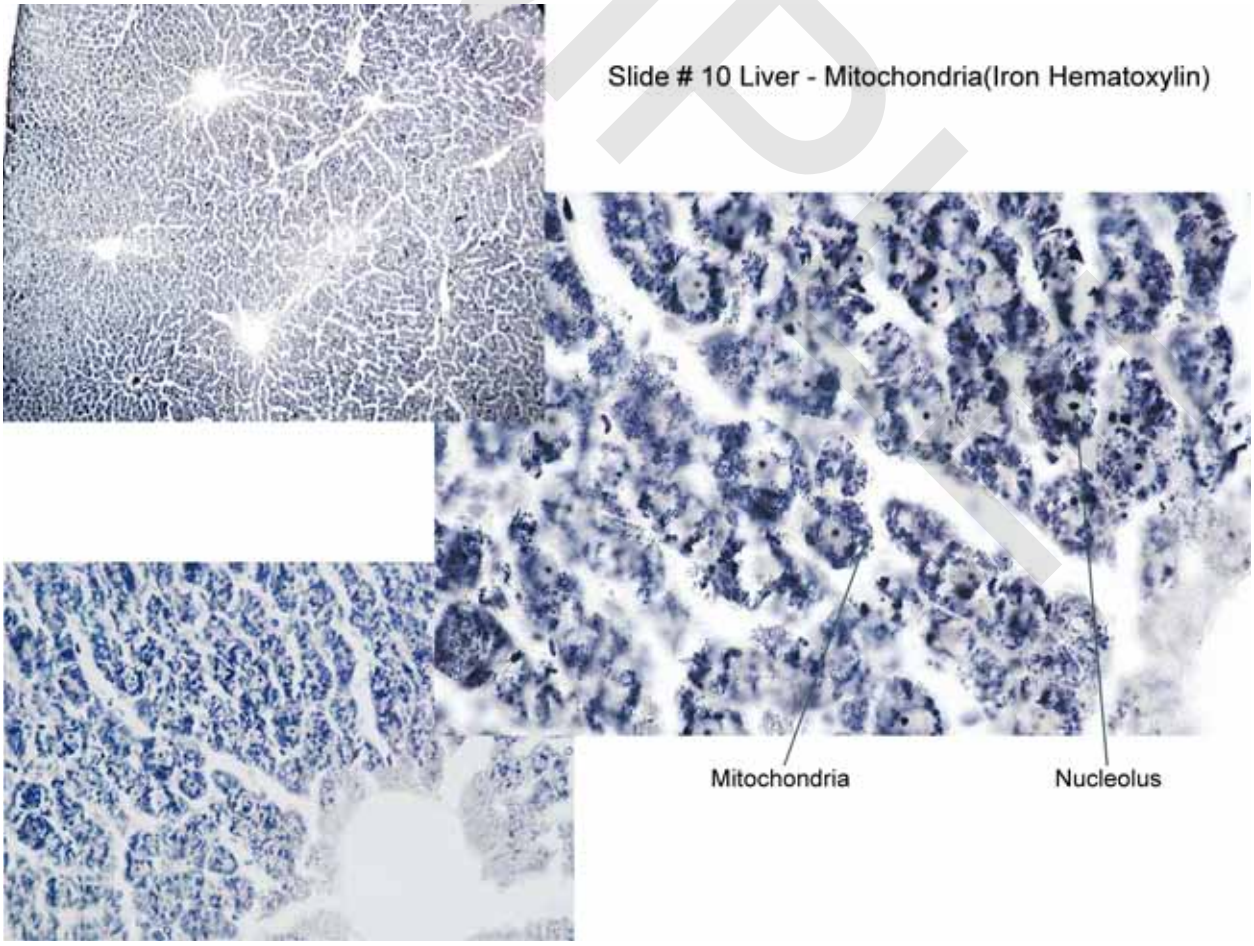
Slide # 10 Mitochondria (Iron Hematoxylin)

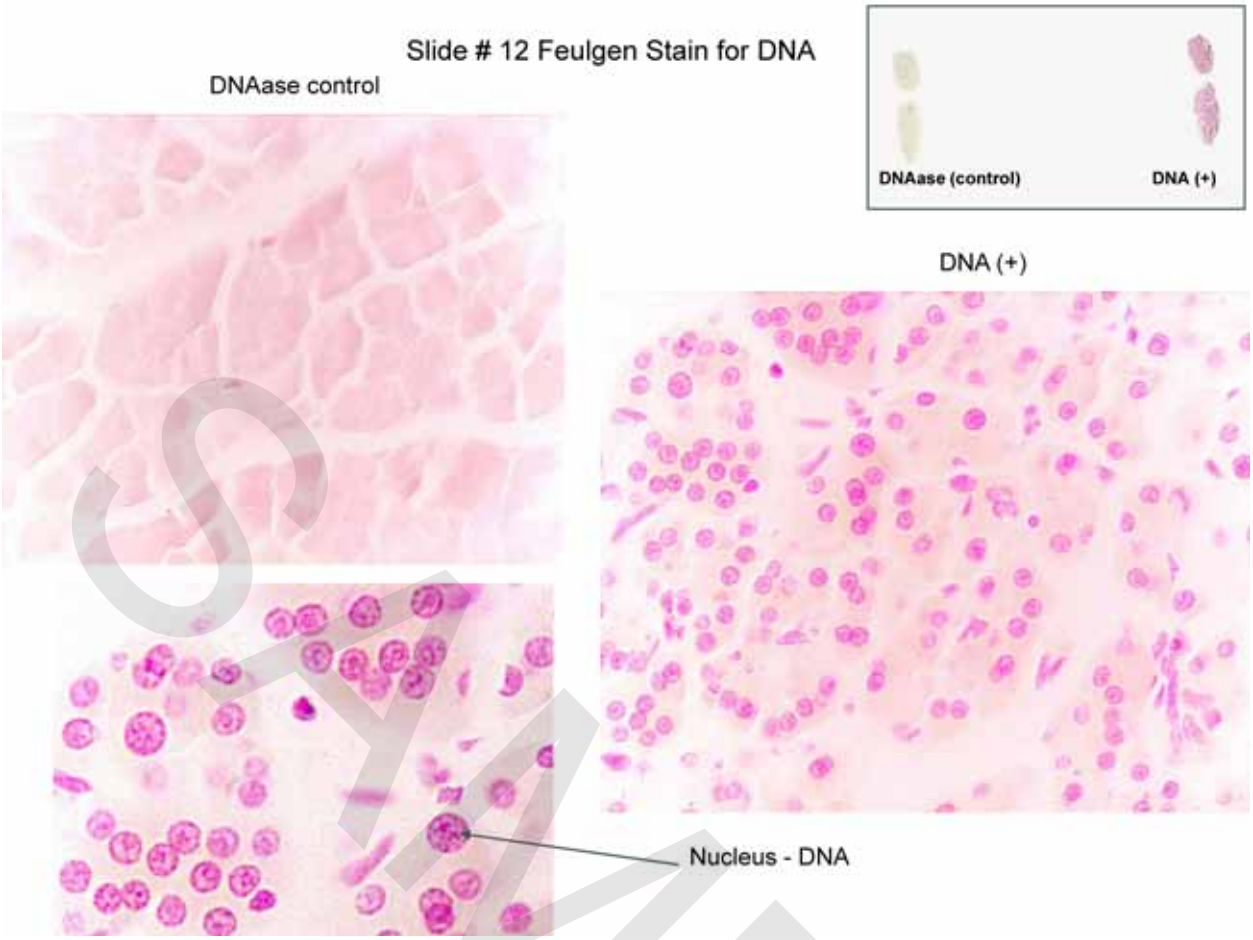
Liver

Intestine




Villi
Lumen
Slide # 10 Duodenum - Mitochondria (Iron Hematoxylin)
Lumen
Villi
Columnar
epithelial cells
Mitochondria


Slide # 10 Liver - Mitochondria(Iron Hematoxylin)
Mitochondria
Nucleolus


Slide # 12 Feulgen Stain for DNA
DNAase control
DNAase (control)
DNA (+)
DNA (+)
Nucleus - DNA

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