CHAPTER 3: GLANDS

Glands are organs that are composed mainly of epithelial cells that are specialized for secretion. They can be classified in many different ways. One method depends on whether the gland secretes into the blood or into a duct system. Using this criterion, glands can be classified as either endocrine (secreting into the blood) or exocrine (secreting into a duct system).

In most cases, exocrine and endocrine glands both develop as an invagination of epithelial cells from a surface epithelium. This cord of cells grows downward into the underlying connective tissue and the gland develops at its distal end. In endocrine glands the cord becomes discontinuous so that the connection between the surface epithelium and the gland is lost. The products of an endocrine gland are secreted into the surrounding connective tissue, and then enter capillaries.

In exocrine glands the invaginating cord of epithelial cells persists and ultimately canalizes to form a duct with a lumen. The gland remains connected to the surface by the duct, which carries the secretions to the surface.

One additional variation occurs when the development of the gland does not involve epithelial invagination at all. In such cases it is the surface cells themselves that differentiate into secretory cells. One example would be the mucus-secreting surface cells that line the lumen of the stomach. Such cells would be considered a type of exocrine gland since they do not secrete into the bloodstream. Therefore we
can more precisely define an exocrine gland by saying that it secretes onto a free surface either directly or via a duct system.

There are many other ways that glands can be classified. For example they may be either unicellular or multicellular. Unicellular glands can be either exocrine (goblet cells) or endocrine (enteroendocrine cells of the GI tract). Similarly there are multicellular exocrine glands (salivary glands) and endocrine glands (thyroid).

Glands can also be classified according to the method by which they release their secretions (merocrine, apocrine, or holocrine). Protein-producing glands can be classified according to the viscosity of their secretory product (serous, mucous, or mixed mucoserous). Exocrine glands with ducts can be classified depending upon whether or not the duct branches (simple or compound). We will explore many of these concepts in the remainder of this section. For now we will limit our study to exocrine glands. The endocrine glands will be covered later in the course.

**UNICELLULAR EXOCRINE GLANDS**

Frame 21858  
Goblet Cell  
H&E  80x  
Goblet cells are unicellular exocrine glands that secrete a viscous mixture of glycoproteins called mucins, which mix with water to form mucus. The mucins are contained within vacuoles at the apical end of the cells, but are usually extracted during tissue preparation, leaving the apical end pale-staining. Goblet cells are found mainly in the respiratory and digestive tracts, where they are scattered individually among other cell types in the epithelium. The goblet cells develop from the same population of small basal stem cells that gives rise to the other differentiated cell types in the epithelium. In this image goblet cells are seen interspersed among the ciliated cells of the respiratory epithelium.

Frame 31069  
Goblet Cell  
H&E  80x  
Goblet cells are also common in the small and large intestine where they are scattered among the absorptive cells of the simple columnar epithelium.

Frame 30608  
Goblet Cell  
PAS  80x  
The periodic acid-Schiff (PAS) procedure for staining carbohydrates preserves the mucins of the goblet cells. Thus the apical end of a goblet cell, which appears pale in H&E preparations, is stained a distinctive magenta color with PAS. The microvilli on the absorptive cells are also PAS-positive due to the glycoproteins and glycolipids associated with the membrane. These form a layer called the glycocalyx.
MULTICELLULAR EXOCRINE GLANDS

In this example from the pyloric stomach, the surface mucous cells that line the lumen are an example of a multicellular exocrine gland that lacks a duct. These cells secrete the glycoprotein components of mucus directly onto the luminal surface. (Note that the word “mucous” is an adjective describing the cells. The word “mucus” is a noun describing their secretory product.)

Eccrine sweat glands are widely distributed in the skin, and secrete mainly in response to environmental heat. These multicellular glands are exocrine because they secrete onto the surface of the skin via a duct (arrow). The paler-staining secretory portion of the gland is visible at the bottom of the image.

Other examples of multicellular exocrine glands include the submucosal glands of the respiratory tract (seen here in the wall of the trachea), and the alveoli of mammary glands (the white circles are the lumens of individual alveoli), and the acini of the exocrine portion of the pancreas, and Brunner’s glands of the duodenum.

SEROUS VS. MUCOUS SECRETORY PRODUCT

Protein-producing cells can be classified as either serous or mucous depending on the viscosity of their secretory products. Serous cells secrete a watery mixture of glycoproteins. Mucous cells secrete a more viscous mix of glycoproteins. Serous and mucous cells also differ in morphology, as we will see. A gland can contain all mucous cells (a pure mucous gland), all serous cells (a pure serous gland), or a mixture of both (a seromucous or mucoserous gland).
The walls of the trachea and bronchi contain mixed seromucous glands and offer a good opportunity to compare the morphology of the two cell types. Serous cells (at the tip of the arrow) tend to have a darker staining cytoplasm due in part to the fact that the secretory products in their apical vacuoles are better preserved during tissue preparation, and can thus be stained by H&E. The mucous cells are much paler because most of the contents of the secretory granules have been extracted, leaving little or nothing in the apical cytoplasm to take up stain. A second useful feature is that a mucous cell is often so full of secretory granules that its nucleus becomes flattened at the basal end of the cell. A serous cell is more likely to have a rounder, less compressed nucleus.

The secretory units (acini) of the exocrine pancreas are composed of serous cells. The arrow indicates the approximate location of the lumen of an acinus (too small to be seen easily at this magnification). The individual acinar cells are arranged like the slices of a pie with their narrow apical ends near the lumen. Notice that the apical ends of serous cells stain acidophilic because of the proteins still present in their secretory granules. In pancreatic acinar cells the basal cytoplasm often stains basophilic (“basal basophilia”) due to the presence of extensive amounts of rough endoplasmic reticulum (RER), which is producing the secretory proteins. Thus there can be a marked difference between the staining affinities of different cytoplasmic regions within the same cell.

The arrow in this image points to a small duct in the connective tissue between pancreatic acini. Ignore that for the moment and concentrate on the serous acinar cells. In this micrograph the secretory granules are very well stained. Their localization at the apical end of the cells is obvious, and contrasts markedly with the more basophilic basal cytoplasm that contains the RER. The acinus near the center of the field demonstrates this well, and also has an easily visible lumen.

At high magnification, and using plastic-embedded sections, it is even possible to see individual secretory granules quite clearly (arrow). In pancreatic acinar cells, these granules contain zymogens (inactive precursors of digestive enzymes), and are thus often referred to as zymogen granules.
In contrast to the serous cells examined above, the secretory cells of Brunner’s glands (found in the duodenum) are mucous cells. The arrow rests in the lumen of a secretory unit, pointing at the apical plasma membrane of a secretory cell. The highly glycosylated mucins these cells produce are quite water-soluble, and are thus often lost during tissue preparation, leaving a pale or foamy appearance in H&E-stained sections. Note again the flattened nuclei at the basal end of the cells.

**SALIVARY GLANDS**

The three major salivary glands (parotid, submandibular, and sublingual) can be distinguished from one another based on their content of serous vs. mucous secretory cells.

The parotid gland is an entirely serous gland. The arrow points to one serous acinus composed of many individual serous cells. The lumen, which would be located in the middle of the acinus, is again too small to be seen at this magnification. This section also contains four relatively large branches of the parotid duct (lighter staining than the serous acini and with larger lumens), as well as several smaller branches of the duct system (one at the top of the image and two in the upper left corner). There are also several large venules in this field. They are lined by simple squamous epithelium (endothelium) and are filled with blood cells. Be sure you can distinguish these from the secretory acini and ducts.

The submandibular gland is a mixed seromucous gland in which the serous cells outnumber the mucous cells. When serous cells are abundant, they commonly form either serous demilunes or pure serous acini. The arrow indicates a pure serous acinus. A serous demilune is a multicellular structure shaped like a crescent moon, which is always located like a cap on the free end of a mucous secretory unit. On the left side of this image, pale-staining mucous secretory units predominate, and several are capped by a dark-staining serous demilune. The cells of a serous demilune release their secretions into the same lumen as the mucus cells.
The sublingual salivary gland is a mixed seromucous gland in which mucous cells predominate. Since the serous cells are relatively rarer, they are somewhat more likely to be found in serous demilunes (arrow) than in large pure serous acini.

**CLASSIFICATION BY GLAND SHAPE & BRANCHING PATTERN**

Exocrine glands are classified as simple glands if their duct does not branch and as compound glands if it does. Since you can't usually see the entire duct system in a single section, it is often not evident whether the gland is simple or compound from studying one slide. Serial sections might be needed to observe any branching. However, if the gland is large and composed of multiple lobules, then you can assume that the gland is compound since each lobule is at the end of a separate branch of the duct system. Lobules can be recognized because they are separated from one another by connective tissue sheets (septa) that may contain large ducts and blood vessels.

Glands can also be classified according to the shape of their secretory units. A tubular gland has elongated secretory units, while more spherical secretory units are characteristic of an acinar or alveolar gland (acinus = Latin for berry). Mucous secretory units tend to be tubular, while pure serous secretory units are likely to be acinar. A mixed seromucous gland that contains both types of units would be classified as a tubuloacinar gland. Some examples of classification using these criteria follow below.

The glands of the uterus are simple tubular glands. Each gland is formed by a separate invagination of the epithelium that lines the uterine lumen. There is no branching duct system, so it is a simple gland. It is tubular in shape, so a complete description would be that it is a simple tubular gland.

The exocrine pancreas has secretory units that are more spherical, hence it is an acinar gland. Since each acinus is drained by its own duct, with these ducts gradually merging to form larger and larger ducts, the gland must have a branched duct system. Hence the exocrine pancreas is an example of a compound acinar gland.
SWEAT GLANDS

Sweat glands are examples of simple coiled tubular glands, i.e., their duct is unbranched (simple) and their secretory unit has the shape of a coiled tubule. There are two types of sweat glands, eccrine sweat glands and apocrine sweat glands, which can be distinguished from one another by the morphology of their secretory units.

In eccrine sweat glands the secretory portion of the gland (arrow) is lighter staining and usually wider in diameter than the duct. The secretory portion and the duct both coil, so that a section through any one gland normally includes several sections through both secretory portion and duct. This image includes three sections through the secretory portion and many more sections through the smaller, darker ducts. The ducts are lined by a stratified cuboidal epithelium.

Myoepithelial cells are epithelial cells that are also specialized for contraction. They are located between the basal plasma membrane of the secretory cells and the basement membrane of the gland, and are found in both eccrine and apocrine sweat glands. They have elongated cytoplasmic processes that radiate out from the nucleus in many directions and are connected to the processes of neighboring myoepithelial cells, thus forming a basket-like network around the secretory portion of the gland. Their contraction helps to express the secretory product out into the duct. Because of their shape and arrangement, they are sometimes called stellate (star-shaped) cells or basket cells. Most sections pass through the slender cytoplasmic processes of these cells, which appear as small darker red triangles or streaks around the outer edge of the secretory portion of the gland. Myoepithelial cells are not found around the ducts in eccrine or apocrine sweat glands.

The ducts of apocrine and eccrine sweat glands resemble one another closely. However, the lumen of the secretory portion is much wider in an apocrine sweat gland (arrow) than in an eccrine sweat gland. The apocrine secretory epithelium varies from simple cuboidal to simple columnar, depending on the state of activity of the gland. This is in contrast to the more jumbled but consistent appearance of the cells in the secretory portion of an eccrine sweat gland.
SEBACEOUS GLANDS

Sebaceous glands (arrow) are found in the skin, and in most locations (as seen here) they are associated with a hair follicle. They secrete a waxy, oily substance (sebum) into the lumen of the follicle.

The stem cells for the secretory cells of a sebaceous gland are the small cells that rest on the basement membrane of the gland (arrow). As they mature they enlarge, accumulate lipid secretory products in their cytoplasm, and move toward the hair follicle, into which they secrete. Because the lipids are extracted during tissue fixation, these more mature cells have a paler, foamy cytoplasm. The nuclei also become pyknotic (i.e., shrunken, heterochromatic, and irregular in shape) and eventually disintegrate. The mature cells undergo lysis, releasing their secretion in a holocrine fashion, which means that the entire cell is lost as part of the secretory product. This is one of the three modes of secretion employed by secretory cells (see below).

MODE OF SECRETION

Exocrine and endocrine glands can be classified as merocrine, apocrine, or holocrine glands according to their mode of secretion.

In merocrine secretion, the secretory product is contained within a membrane-bounded vacuole in the cytoplasm of the cell and is released by exocytosis (fusion of the membrane of the vacuole with the plasma membrane of the cell). As a result, the secretory products are released, but there is no loss of any other part of the cytoplasm or membrane. This type of secretion occurs in eccrine sweat glands, salivary glands, pancreas, etc. It is the most common type of secretion.

In apocrine secretion, secretory product collects in the apical end of the cell. Part of the apical cytoplasm, surrounded by plasma membrane, then buds off of the cell. The membrane surrounding the released fragment of apical cytoplasm then breaks down to release the secretory product. The cell remains intact, but part of it has been lost along with the secretory product. This type of secretion occurs in the release of lipids by the lactating mammary gland. Controversy exists over whether any of the products of apocrine sweat glands are released by apocrine secretion or whether they employ only merocrine secretion.
Finally, in holocrine secretion, the entire cell is lost as part of the secretion. This is a very rare type of secretion. We have seen that it occurs in sebaceous glands, where the cell undergoes lysis during secretion. Some authorities also consider the release of sperm from the testis to be a type of holocrine secretion since the entire cell is lost into the secretion (i.e., into the semen). If you accept that view, then you have to stipulate that cell lysis is not a necessary part of holocrine secretion.

**TYPES OF COMPOUND DUCTS**

The branched duct system of a compound gland generally includes several different types of ducts such as intercalated ducts, striated ducts (both of which are types of intralobular ducts), interlobular ducts, and main or excretory ducts.

Frame 27544
Parotid Gland
Intercalated Duct
H&E 160x

Compound ducts begin as very small ducts that are directly continuous with the secretory units. These smallest ducts are commonly known as intercalated ducts, and are lined by a simple epithelium composed of low cuboidal cells. In this example from the parotid gland, the ducts stain lighter than the secretory acini. This is not the case with all glands and should therefore not be used as a criterion to distinguish duct from secretory unit. Recall, for example, that in the eccrine sweat glands the duct stains darker than the secretory unit.

Frame 28056
Sublingual Gland
Intralobular Duct
H&E 80x

The height of the epithelium and the width of the lumen gradually increase to form intralobular ducts with a simple cuboidal to columnar epithelium.
In some glands where the ducts extensively modify the ionic composition of the secretion, the large intralobular ducts are known as striated ducts. These are lined by simple cuboidal to columnar epithelial cells whose basal cytoplasm exhibits faint eosinophilic stripes (striations) oriented perpendicular to the basal plasma membrane (arrow). These striations are created by rows of eosinophilic mitochondria that line up in cytoplasmic pockets formed between the extensive infoldings of the basal plasma membrane. The mitochondria provide the energy for active transport of ions, while the membrane folds increase the surface area available to house the transporter proteins. Note that the nuclei of striated ducts tend to be near the middle of the cell rather than at the basal end because the basal folds exclude the nucleus from the basal region. This characteristic can help identify striated ducts even when the striations are not clearly visible.

Eventually the ducts within a lobule unite to form a duct that leaves the lobule and runs in the connective tissue septa between lobules. These are called interlobular ducts (arrow). As they unite to form larger and larger ducts, their epithelium changes from simple to pseudostratified or stratified, depending on the gland. Interlobular ducts are directly surrounded by connective tissue and tend to run with the larger blood vessels, whereas the intralobular ducts (e.g., intercalated ducts, striated ducts) are directly surrounded by secretory units. This image contains parts of three lobules. The large one on the right includes several good examples of intralobular ducts that you can contrast with the interlobular duct on the left.

The main duct of a compound gland (i.e., the one that opens onto the free surface) is also called the excretory duct. It has a large lumen and is lined by a pseudostratified or stratified epithelium (arrow). As it approaches the surface, the epithelium of the duct becomes more like the surface epithelium. In the case of the parotid gland, which empties into the mouth, the duct epithelium would become minimally keratinized stratified squamous, like that on the inner surface of the cheeks in the oral cavity.
### PRACTICE QUIZ #2: GLANDS

<table>
<thead>
<tr>
<th>Frame</th>
<th>H&amp;E</th>
<th>Magnification</th>
<th>Questions</th>
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<tr>
<td>27565</td>
<td>80x</td>
<td>1.</td>
<td>Identify this salivary gland.</td>
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<tr>
<td>21867</td>
<td>80x</td>
<td>2.</td>
<td>A. Identify the dark-staining cells indicated by the arrow.</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>B. What type of staining procedure was used on this section?</td>
</tr>
<tr>
<td>27770</td>
<td>160x</td>
<td>3.</td>
<td>The dark-staining structure indicated by the arrow is called a/an ________</td>
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<td>27571</td>
<td>160x</td>
<td>4.</td>
<td>This is a/an ________ duct</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>A. Intercalated</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>B. Interlobular</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>C. Striated</td>
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<tr>
<td>25311</td>
<td>80x</td>
<td>5.</td>
<td>This is a/an ________ gland.</td>
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<td></td>
<td></td>
<td></td>
<td>A. Apocrine sweat</td>
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<td></td>
<td></td>
<td></td>
<td>B. Eccrine sweat</td>
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<td></td>
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<td>C. Sebaceous</td>
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<tr>
<td></td>
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<td></td>
<td>D. Mammary</td>
</tr>
<tr>
<td>25347</td>
<td>80x</td>
<td>6.</td>
<td>Identify this cell as specifically as possible.</td>
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<tr>
<td>34186</td>
<td>160x</td>
<td>7.</td>
<td>Does the arrow indicate serous cells, mucous cells or sebaceous cells?</td>
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<tr>
<td>27945</td>
<td>80x</td>
<td>8.</td>
<td>Which salivary gland is this?</td>
</tr>
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<td>25830</td>
<td>40x</td>
<td>9.</td>
<td>Are these serous cells, mucous cells or sebaceous cells?</td>
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<tr>
<td>29486</td>
<td>80x</td>
<td>10.</td>
<td>Are these serous cells, mucous cells or sebaceous cells?</td>
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</tbody>
</table>
ANSWERS TO QUIZ #2: GLANDS

NOTE: Statements in brackets provide additional information, but that information is not required in order for the answer to be considered correct.

1. Parotid salivary gland [entirely serous]
   Frame 27565

2. Periodic acid-Schiff (PAS) reaction [staining mucins in goblet cells]
   Frame 21867

3. Serous demilune
   Frame 27770

4. A or Intercalated duct [a type of intralobular duct]
   Frame 27571

5. B or Eccrine sweat gland [because of its pale staining, small lumen, and “disorganized” epithelium]
   Frame 25311

6. Myoepithelial cell
   Frame 25347

7. Serous cells [pancreatic acinar cells]
   Frame 34186

8. Sublingual gland [mainly mucous, although there is often more serous component in the sublingual gland than is seen here]
   Frame 27945

9. Sebaceous cells [associated with a hair follicle where the hair shaft is missing]
   Frame 25830

10. Mucous cells [Brunner’s glands of the duodenum, although there is no way to know that at this high magnification]
    Frame 29486