Chapter 5
Epithelial Tissue

Contents

General
One of the four basic tissue types

Structure
- Closely apposed cells facing free surfaces
- Abundant and well-developed cell junctions → cells adhere to each other
- Avascular
  - Nourished from blood vessels in underlying connective tissue
- Rests on basement membrane, which separates epithelial tissue from connective tissue
- Simple epithelia often have polarized cells:
  - Cell membrane is divided by tight junctions into:
    - Apical domain: face the free surface
    - Basolateral domain:
      - Lateral domain: communicate with neighboring epithelial cells
      - Basal domain: rests on the basement membrane

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Divided into
- Surface epithelium
- Glandular epithelium:
  - Forms the secretory portion of glands
  - Described in Chap. 6

Surface Epithelium

General
- Covers outer body surfaces, as the epidermis
- Lines body tubes, which communicate with the exterior, as the epithelium of mucous membranes
- Lines internal closed cavities, e.g.:
  - Blood and lymph vessels, as the endothelium
  - Pericardial, pleural, and peritoneal cavities, as the mesothelium
- Exposed to abundant mechanical stress
- Fast regeneration via stem cells

} High cell turnover rate

Divided into (Table 5.1)
Surface epithelium is classified by:
- Number of layers
  - Simple: one layer
  - Pseudostratified: one layer, but appears to have several layers
  - Stratified: multiple layers
- Shape of cells at surface
  - Squamous: height < width
  - Cuboidal: height ≈ width
  - Columnar: height > width

Function
- Simple epithelium:
  - Selective permeable barrier, e.g., in the endothelium
  - Absorption, e.g., in intestinal epithelium
  - Secretion, e.g., in kidney tubules
  - Transport:
    - Along epithelial surface (with the help of cilia), e.g., in respiratory epithelium
    - Across epithelium (transcytosis), e.g., in the endothelium
- Stratified epithelium:
  - Barrier function, e.g., in the epidermis (Chap. 20)
    - Mechanical barrier
    - Selective permeable barrier
    - Against microorganisms, evaporation, and UV radiation
  - Sensation, with the help of sensory receptors, e.g., in the epidermis (Chap. 20)

Light Microscopy

See Table 5.1.

Table 5.1 Surface epithelia and their location

		Squamous	Cuboidal	Columnar
Simple	Light microscopy	• Flat cells (height < width) • Central flattened nucleus	• Height ≈ width • Central round nucleus	• Height > width • Nuclei in same level in neighboring cells (commonly located basally)
	Location	For example, endothelium	For example, kidney tubule epithelium	For example, intestinal epithelium
Pseudostratified	Light microscopy	–	–	• Height > width • All cells touch basement membrane, but only some cells reach apical surface → nuclei in different levels in neighboring cells
	Location	–	–	For example, respiratory tract epithelium
Stratified	Light microscopy	Cells gradually flatten towards the surface: • Basal layer: one layer of basophilic cuboidal/ columnar cells • Middle layers: Polyhedral cells • Superficial layers: Squamous cells	• Multiple cell layers • Superficial cells are cuboidal	• Multiple cell layers • Superficial cells are columnar
	Location	Exists in two forms: • Keratinized: cells in superficial layers have lost their nuclei and are filled up with keratin, e.g., in the epidermis of the skin • Nonkeratinized: superficial cells contain nuclei, e.g., the epithelium the of esophagus	• Rare • For example, epithelium of large ducts of glands	• Rare • For example, epithelium of largest ducts of glands

Urothelium (Transitional Epithelium)

General
- Special stratified epithelium
- Not classified by the shape of cells at surface as other epithelia
- Lines the proximal part of the urinary tract, e.g., the urinary bladder

Structure
- Stratified epithelium.
- Cells of the middle layers have vacuolated cytoplasm and do not gradually flatten towards the surface.
- Superficial cells:
  - Large cells called "umbrella cells" as they cover several of the underlying cells
  - Contains:
    - Apical eosinophilic condensations, caused by many filaments
    - Plaques: areas of thickened apical cell membrane

Function
- Good at distending → found in places where large changes in organ volume occur
- Highly impermeable

Light Microscopy
Changes morphology with degree of distention (Table 5.2)

Table 5.2 Light microscopy of urothelium

		Relaxed state	Distended state
Low magnification		Mucous membrane folded	Mucous membrane smooth
High magnification	Basal layer	Several layers of basophilic cuboidal/ columnar cells	Few layers of basophilic cuboidal cells
	Middle layer	Several layers of pale polyhedral cells	Few/no layers of pale polyhedral cells
	Superficial layer	Large pale rounded cells, convex towards lumen	Large pale cuboidal or flattened cells

Cell Surface Specializations

General
Specializations of the cell surface, mediating various functions

Divided into
- Apical domain specializations:
  - Microvilli
  - Stereocilia
  - Cilia
  - Flagellum
- Lateral domain specializations:
  - Cell-to-cell junctions:
    - Occluding: tight junctions
    - Anchoring:
      - Zonulae adherentes
      - Fasciae adherentes (only in cardiac muscle cells)
      - Desmosomes
    - Communicating: gap junctions
- Basal domain specializations:
  - Basement membrane
  - Cell-to-extracellular matrix (ECM) junctions:
    - Anchoring:
      - Focal adhesions
      - Hemidesmosomes

APICAL DOMAIN SPECIALIZATIONS

Microvilli

General
Thin, small immotile extensions of the cell

Structure
- ⦸ 0.1 µm and 1–3 µm long
- Core made from bundle of 20–30 actin filaments, connected to cytoskeleton, and cross-binding proteins

Function
Increase apical surface area up to 20 times → improve absorption from and secretion to the free surface, e.g., in intestinal epithelium

Light Microscopy
- Single microvilli are too thin to be resolved in light microscope.
- Multiple microvilli are seen in the light microscope as a light refracting "striated/brush border."

Stereocilia

General
Thin, long immotile extensions of the cell

Structure
Long bendable microvilli of variable length

Function
- Increase apical surface area → improve absorption from the free surface, e.g., in the epididymis
- Special functions, e.g., in hair cells of the inner ear

Light Microscopy
Stereocilia are seen as long thin extensions in small bundles (resembling hairs of a paint brush) in the light microscope.

Cilia (Kinocilia)

Structure
⦸ 0.25 μm and 5–10 μm long

Consist of (Fig. 5.1)
- Core (axoneme):
  - Cylinder of nine microtubule doublets surrounding a center of two microtubules (9 + 2 structure)
  - Attached to a basal body
- Basal body:
  - Forms basis of cilium
  - Cylinder of nine microtubule triplets

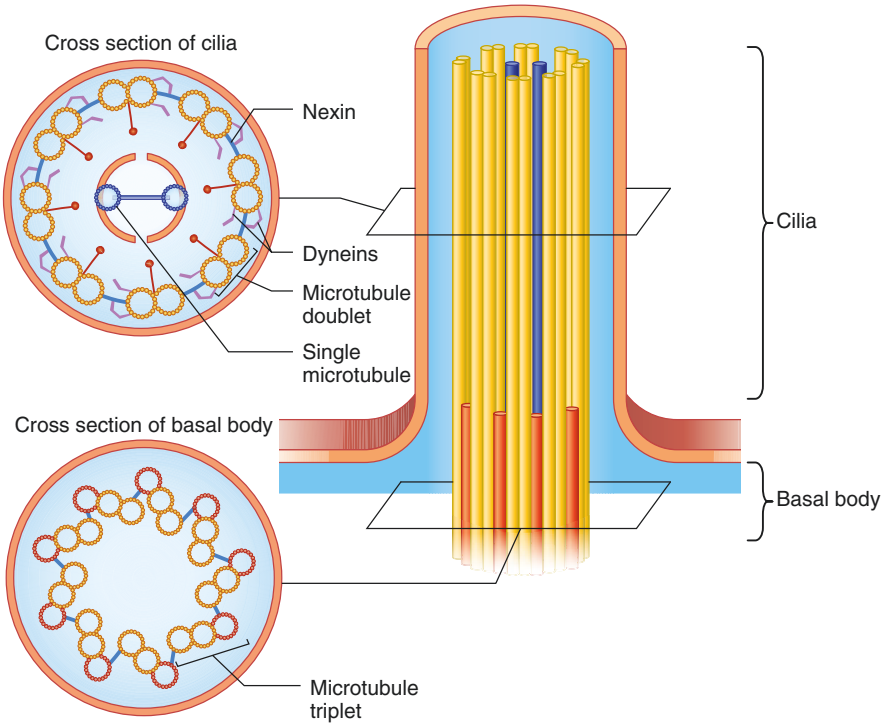


Fig. 5.1 Structure of the cilium: two cross sections, one of the axoneme and one of the basal body, show the structure of the cilium

Formation

- A basal body is formed from a centriole underneath the apical cell membrane.
- Microtubule doublets grow out from the microtubule triplets in the basal body to form the axoneme.

Function

Movement of fluid/mucous on cell surface in one direction, e.g., in the respiratory tract:

- Occurs via coordinated movements of cilia

Movement of cilia

- Microtubule doublets of axoneme are connected to each other with nexin.
- Two motor proteins (dyneins) are attached to each microtubule doublet → can bind to and move along the next microtubule doublet.
- When activated, the dyneins will try to slide one microtubule doublet relative to the other.
- As the microtubule doublets are connected to each other by nexin, the resulting movement is instead a bending of the whole axoneme → cilia bends.

Light Microscopy
Single cilia can be resolved in the light microscope as thin extensions of the apical cell surface.

Primary Cilia

General
Most cells contain one immotile and short primary cilia (9 + 0 structure), which function as a sensor of the extracellular environment.

Flagellum

General
In humans only present on sperm cells

Structure
A single long cilia

Function
Movement of the sperm cell, by undulating movements of the flagellum

LATERAL DOMAIN SPECIALIZATIONS

Light Microscopy
Lateral domain specializations as a group can sometimes be seen as a "terminal bar" in the light microscope, located at the most apical part of the lateral surface.

Occluding Cell Junctions (Tight Junctions, Zonulae Occludentes)

General
Cell junctions, which mainly act to seal off the intercellular space

Structure
- Most apically placed cell junction (Fig. 5.2)
- Form a 0.2 μm-wide belt (zonula) apically around the cell, analogous to the six-pack rings of beverage cans

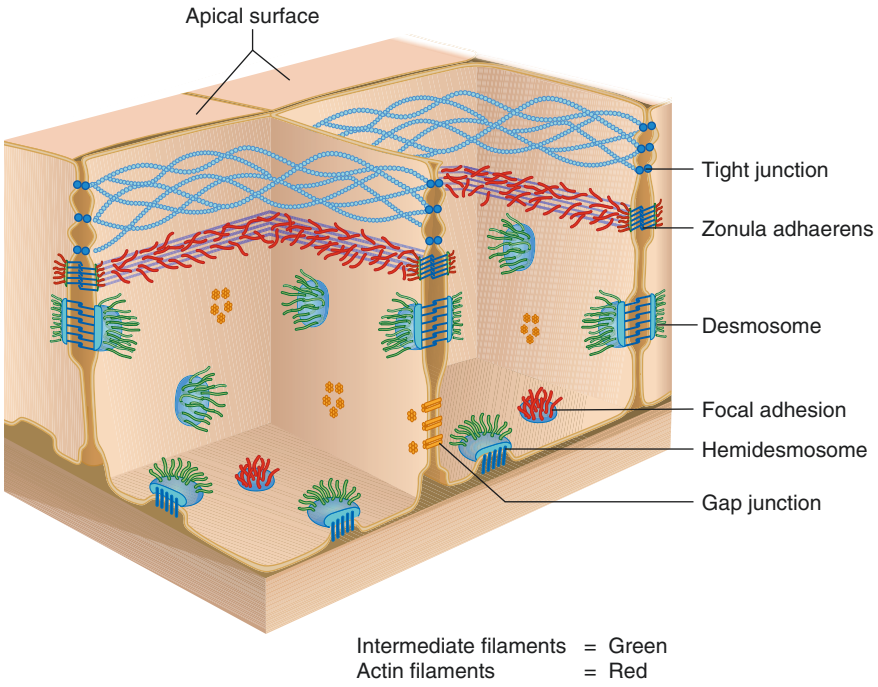


Fig. 5.2 Cell junctions: the cell junctions on the lateral and basal domains

Function

- Barrier of the intercellular space (paracellular pathway) between the cells: permeability depends on composition and amount of strands.
- Polarize cells: divides the cell membrane into an apical and basolateral domain → lateral diffusion of membrane lipids and membrane proteins is confined to each domain.

Consists of

- Transmembrane proteins:
  - Form strands in the plasma membrane
  - Connected intracellularly to the actin cytoskeleton
  - For example, occludins and claudins
- Strands from neighboring cells come together and seal off the intercellular space between the cells.

MEMO-BOX
OCCLUDing cell junction: zonula **OCCLUD**ens
Zonula oc**CL**udens: formed from oc**CL**udins and **CL**audins

Anchoring Cell Junctions

General
Cell junctions, which mainly act to adhere cells together

Function
Add mechanical strength to tissues: links cytoskeleton in neighboring cells together or to the extracellular matrix

Consist of
- Filaments:
  - Form the intracellular attachment to the cytoskeleton
  - Divided into:
    - Actin filaments
    - Intermediate filaments:
      - Cell junctions with intermediate filaments are stronger than those with actin filaments.
- Plaque:
  - Group of proteins, which form the connection between the filaments and cell adhesion molecules
- Cell adhesion molecules:
  - Transmembrane proteins, which form the contact to other cells or the extracellular matrix
  - Divided into:
    - Cadherins:
      - In cell–cell junctions
      - Form contact with cadherins in neighboring cells
      - Ca^{2+} dependent
    - Integrins:
      - In cell–extracellular matrix junctions
      - Form contact with multiadhesive glycoproteins, e.g., laminins and fibronectin

MEMO-BOX
Cadherins form **C**ell–**C**ell junctions and are **C**a^{2+} dependent

Divided into
- Cell–cell junctions
  - Zonula adherens
  - Fascia adherens (only in cardiac muscle cells)
  - Desmosome (macula adherens)
- Cell–extracellular matrix junctions (located in basal domain, but described with the other anchoring cell junctions here)
  - Focal adhesion
  - Hemidesmosome

MEMO-BOX
ADHEring contacts: almost all contain **ADHE**sion/**ADHE**rens in their name.

Zonula adherens

General
Forms a belt (zonula) around cells, basal to the tight junction belt (Fig. 5.2)

Consist of
- Actin filaments
- Plaque
- Cadherins

Fascia adherens

General
- Similar to zonula adherens, but only forms a sheet (fascia) in a part of the membrane and not a belt around the entire cell
- Only found in the intercalated discs of cardiac muscle cells

Consist of
- Actin filaments
- Plaque
- Cadherins

Desmosome (macula adherens)

Structure
Point-shaped contact, ⦸ 0.1–0.2 µm (Fig. 5.2)

Consist of
- Intermediate filaments
  - Intermediate filaments are looping through the plaque.
- Plaque
- Cadherins

Focal adhesion

General
- Point-shaped contact at the basal domain (Fig. 5.2).
- Assembly and disassembly of focal adhesions provide basis for cell migration.

Consist of
- Actin filaments
- Plaque
- Integrins

Hemidesmosome

Structure
- Point-shaped contact, ⦸ 0.1–0.2 µm (Fig. 5.2)
- Resembles the desmosome

Consist of
- Intermediate filaments
  - Intermediate filaments are ending in the plaque.
- Plaque
- Integrins

Communicating Cell Junctions (Gap Junctions, Nexuses)

General
Cell junctions, which form channels for transport of small molecules between cells (Fig. 5.2)

Structure
- Group of channels between adjacent cells.
- Each channel is formed from two connexones, one from each cell, which align in the intercellular space.
- Connexones are formed from six circularly arranged connexins.

Function
- Channels for small molecules, e.g., ions.
  - Opening/closing of channels is regulated.
- Allows coordination of adjacent cells, e.g., contraction in cardiac muscle cells.

MEMO-BOX
NEXus consists of six con**NEX**ins, which form one con**NEX**one.

Intercellular Space

General
Spaces between cells

Structure
Intercellular spaces between neighboring cells are formed, as the glycocalyx (negatively charged) on each cell repels each other.

Function
- Site of fluid transfer
- Space for free nerve endings and leukocytes

Lateral surface folds

General
In some epithelial cells, lateral surface folds are found, e.g., in some cells of the intestinal epithelium.

Function
Increase the lateral surface area → improve absorption from and secretion to the intercellular space

BASAL DOMAIN SPECIALIZATIONS

Basement Membrane

Function
- Anchors epithelia to underlying connective tissue
- Passive filter for molecules and cells, e.g., leucocytes
- Affects organization, polarization, and differentiation of epithelial cells
- Forms a structural basis for regeneration of epithelium

Consist of
- Basal lamina (similar to external lamina in non-epithelial tissues)
  - Lamina lucida (preparation artifact)
  - Lamina densa
    - Type IV collagen (≈50 % of protein in basal lamina)
    - Proteoglycans
    - Multiadhesive glycoproteins, e.g., laminins and fibronectin, which bind to both integrins of cell-to-extracellular matrix junctions and collagen → anchors cells to the extracellular matrix
  - Epithelial cells produce the contents of the basal lamina.
- Reticular lamina (lamina reticularis):
  - Reticular fibers in ground substance
  - Anchoring fibrils from the basal lamina loop around the reticular fibers → attach basal lamina to underlying connective tissue.
  - Fibroblasts produce the contents of the reticular lamina, which is a part of the underlying connective tissue.

Light Microscopy
- Rarely seen in HE stain
- Stained with PAS and silver stains → visible in the light microscope

Anchoring Cell Junctions

General
Hemidesmosomes and focal adhesions are described together with the other anchoring cell junctions, under lateral domain specializations (see above).

Basal surface infoldings

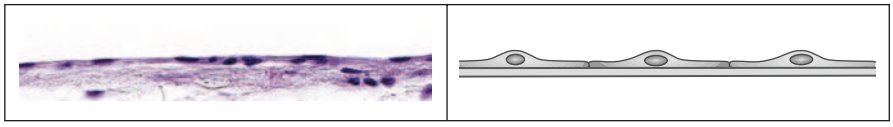
General
In some epithelial cells, basal surface infoldings are found, e.g., in kidney tubule epithelium.

Function
Increase the basal surface area → improve absorption and secretion across basal domain of the plasma membrane

Guide to Practical Histology: Surface Epithelium

General
- Avascular
- The cells are densely packed.
- Line "free" surfaces, i.e., always face a lumen or an exterior surface.

Simple Squamous Epithelium

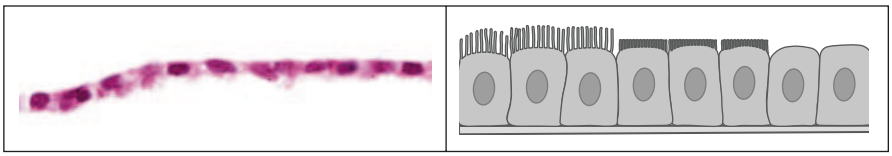


Left: photomicrograph of simple squamous epithelium. Magnification: high. Stain: HE (Courtesy of professor Jørgen Tranum-Jensen, University of Copenhagen). *Right*: simplified illustration of simple squamous epithelium

Characteristics
- Flat cells.
- Height < width.
- Sometimes a small central prominence is seen, containing the flattened nucleus.

Location
For example, endothelium of blood vessels

Simple Cuboidal Epithelium



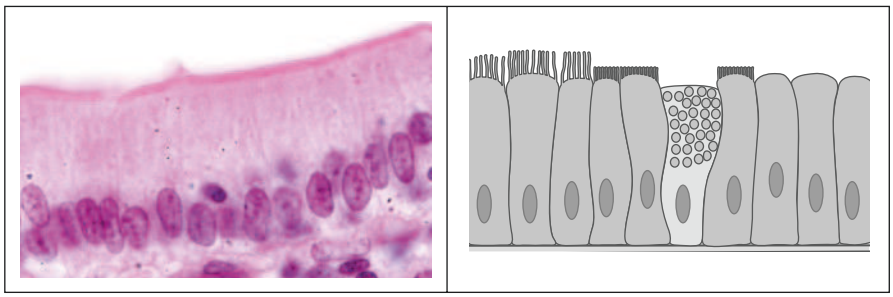
Left: photomicrograph of simple cuboidal epithelium. Magnification: high. Stain: HE (Courtesy of professor Jørgen Tranum-Jensen, University of Copenhagen). *Right*: simplified illustration of simple cuboidal epithelium with apical cilia (left), apical brush border (microvilli) (middle), and without apical specializations (right).

Characteristics
- Height ≈ width
- Central round nucleus, which fills up most of the cell

Location
- Without apical specializations, e.g., in small ducts of glands
- With an apical brush border, e.g., in the kidney tubules
- With apical cilia, e.g., as the ependymal cells of the central nervous system

Can be mistaken for
Low simple columnar epithelium:
- There is a smooth transition between the two types of epithelium.

Simple Columnar Epithelium



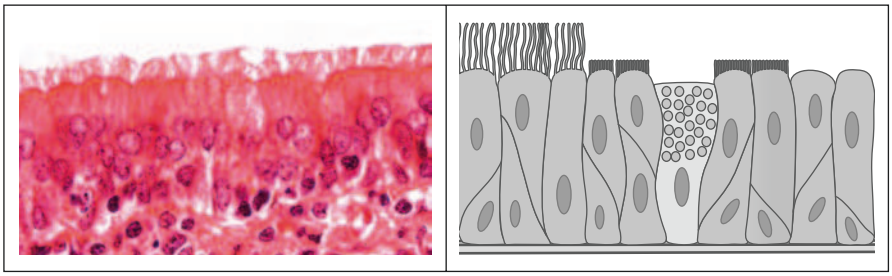
Left: photomicrograph of simple columnar epithelium with a brush border. Magnification: high. Stain: PAS-hematoxylin (Courtesy of professor Jørgen Tranum-Jensen, University of Copenhagen). *Right*: simplified illustration of simple columnar epithelium with apical cilia (left), apical brush border (microvilli) and an interspersed goblet cell (middle), and without apical specializations (right).

Characteristics
- Height > width
- Nuclei in same level in neighboring cells (commonly basally located)

Location
- Without apical specializations, e.g., in smaller ducts of glands
- With an apical brush border and interspersed goblet cells, e.g., in intestinal epithelium
- With apical cilia, e.g., in the uterine tubes

Can be mistaken for
- Pseudostratified columnar epithelium:
  - Cells are normally taller
  - Nuclei in different level in neighboring cells
- High simple cuboidal epithelium:
  - There is a smooth transition between the two types of epithelium.

Pseudostratified Columnar Epithelium



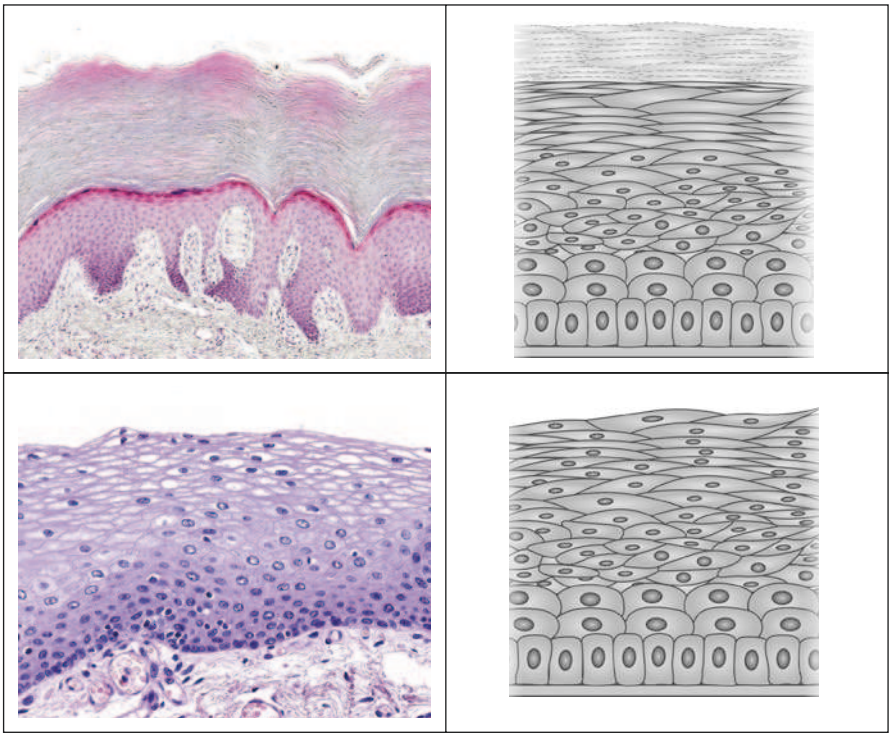
Left: photomicrograph of pseudostratified columnar epithelium with cilia. Magnification: high. Stain: HE (Courtesy of professor Jørgen Tranum-Jensen, University of Copenhagen). *Right*: simplified illustration of pseudostratified columnar epithelium with apical cilia (left), apical brush border (microvilli) and an interspersed goblet cell (middle), and without apical specializations (right).

Characteristics
- Height > width
- All cells touch the basement membrane.
- Only some of the cells reach the apical surface.
- Nuclei are located in different levels in neighboring cells.

Location
- Without apical specializations, e.g., in part of the penile urethra
- With apical cilia and interspersed goblet cells, e.g., in the upper respiratory tract
- With apical stereocilia, e.g., in the ductus epididymidis

Can be mistaken for
- Simple columnar epithelium:
  - Cells are normally shorter.
  - Nuclei are located in the same level in neighboring cells (commonly basally located).
- Stratified columnar epithelium:
  - Not all cells touch the basement membrane.

- Do not have apical cilia or stereocilia.



Top left: photomicrograph of stratified squamous keratinized epithelium. Magnification: low. Stain: HE (Courtesy of associate professor Steen Seier Poulsen, University of Copenhagen). *Top right*: simplified illustration of simple squamous keratinized epithelium. *Bottom left*: photomicrograph of stratified squamous nonkeratinized epithelium. Magnification: high. Stain: HE (Courtesy of associate professor Steen Seier Poulsen, University of Copenhagen). *Bottom right*: simplified illustration of simple squamous nonkeratinized epithelium

Stratified Squamous Epithelium

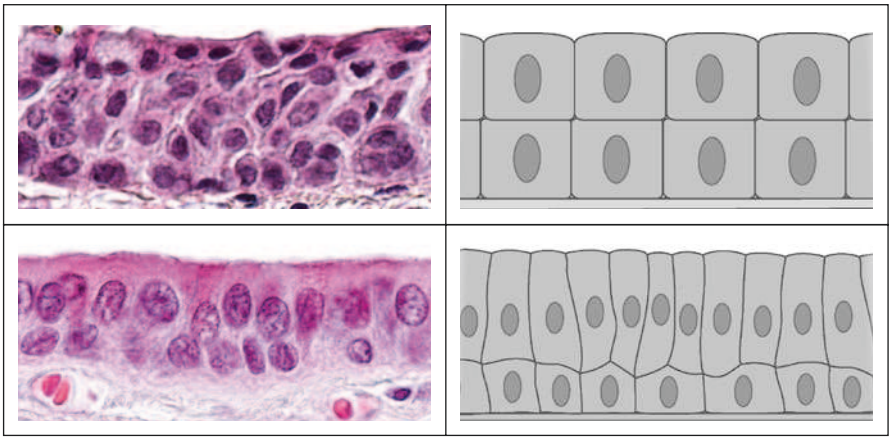
Characteristics

- Cells gradually flatten towards the surface:
  - Basal layer: one layer of basophilic cuboidal/columnar cells
  - Middle layers: polyhedral cells
  - Superficial layers: squamous cells
- Can be keratinized or nonkeratinized:
  - Keratinized:
    - Cells in the superficial layers:
      - Have lost their nuclei
      - Are filled up with keratin → stain eosinophilic
      - Have unclear cell borders
    - Seen as a homogenous mass of parallel eosinophilic cell layers
      - The mass sometimes detaches from the underlying cell layers in specimens.

- Nonkeratinized:
  - Superficial cells contain nuclei

Location
- Keratinized, e.g., in the epidermis of the skin
- Nonkeratinized, e.g., the epithelium of the esophagus

Can be mistaken for
Urothelium:
- Cells do not gradually flatten towards the surface.
  - Only a single superficial layer of flattened cells can be seen.
- Middle and superficial layers contain pale cells with a vacuolated cytoplasm.



Top left: photomicrograph of stratified cuboidal epithelium. Magnification: high. Stain: HE (Courtesy of professor Jørgen Tranum-Jensen, University of Copenhagen). *Top right*: simplified illustration of stratified cuboidal epithelium. *Bottom left*: photomicrograph of stratified columnar epithelium Magnification: high. Stain: HE (Courtesy of professor Jørgen Tranum-Jensen, University of Copenhagen). *Bottom right*: simplified illustration of stratified columnar epithelium

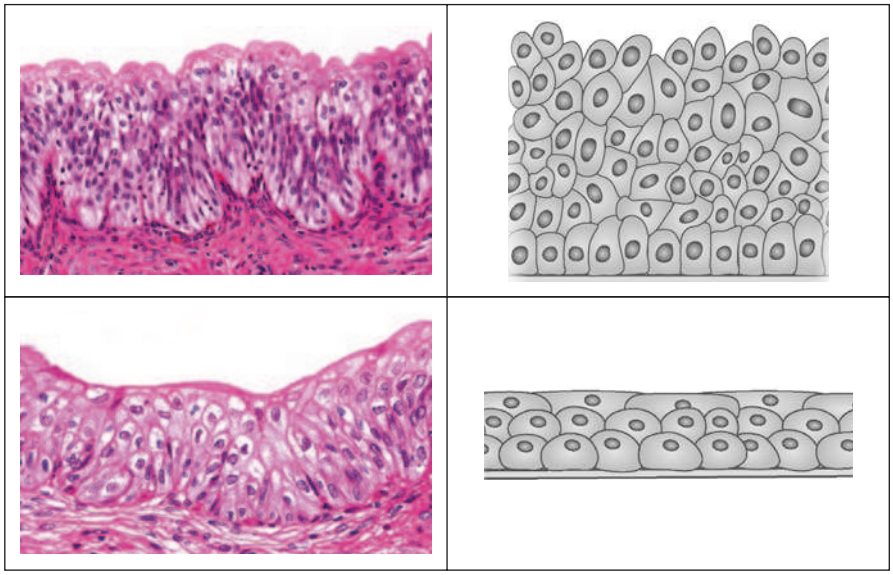
Stratified Cuboidal/Columnar Epithelium

Characteristics
- Multiple cell layers.
- Superficial cells are cuboidal/columnar.

Location
- Without apical specializations, e.g., in larger ducts of glands
- With interspersed goblet cells, e.g., in the conjunctiva

Can be mistaken for
Pseudostratified columnar epithelium:
- All cells touch the basement membrane.

- Often found with apical cilia or stereocilia, which are not seen in stratified



Top left: photomicrograph of urothelium in relaxed state. Magnification: high. Stain: HE (Courtesy of professor Jørgen Tranum-Jensen, University of Copenhagen). *Top right*: simplified illustration of urothelium in relaxed state. *Bottom left*: photomicrograph of urothelium in distended state. Magnification: high. Stain: HE (Courtesy of professor Jørgen Tranum-Jensen, University of Copenhagen). *Bottom right*: simplified illustration of urothelium in distended state

epithelium.

Urothelium (Transitional Epithelium)

Characteristics

- Cells do not gradually flatten towards the surface:
  - Basal layers: basophilic cells
  - Middle layers: pale polyhedral cells with a vacuolated cytoplasm
  - Superficial layer:
    - A single layer of large pale cells
    - Each cell covers several underlying cells.
    - Cells change morphology with the degree of distension:
      - Relaxed state: a single layer of rounded cells, convex towards lumen
      - Distended state: a single layer of cuboidal or flattened cells

Table 5.3 Microscopic characteristics of urothelium

		Relaxed state	Distended state
Low magnification	Mucous membrane	Folded	Smooth
	Underlying layers of smooth muscle tissue	Thick	Thin
High magnification	Superficial layer of large, pale cells	Rounded cells, convex towards lumen	Cuboidal or flattened cells
	Middle layers of pale polyhedral cells	Several layers	Few/no layers
	Basal layers of basophilic cells	Several layers	Few layers

- Changes morphology with degree of distention (Table 5.3)

Location
Only found lining the proximal part of the urinary tract, e.g., the ureters and the urinary bladder

Can be mistaken for
Stratified squamous nonkeratinized epithelium:
- Cells gradually flatten towards the surface
- Several layers of superficial flattened cells.

References

5, 33, 34.

Chapter 6
Glandular Epithelium and Glands

Contents

Glandular Epithelium

Function

- Epithelial cells that are highly specialized for secretion:
  - Secretion is the release of specific products synthesized within the cell
- Other cell types also secrete products, e.g.:
  - Fibroblasts: secrete extracellular matrix components
  - Plasma cells: secrete antibodies

A. Rehfeld et al., *Compendium of Histology*, DOI 10.1007/978-3-319-41873-5_6

Formation
Glandular epithelium is formed from an ingrowth of surface epithelium:
- Exocrine glandular tissue
  - Maintains a connection to the surface epithelium during development, i.e., has a duct system
- Endocrine glandular tissue
  - Does not maintain a connection to the surface epithelium during development, i.e., lacks a duct system

Mechanisms of secretion

Divided into
- Constitutive secretion, found in all cell types
  - Unregulated exocytosis of small vesicles
  - Vesicles are not visible in the light microscope
  - This is the standard route out of the trans-Golgi network for proteins not sorted to other destinations, e.g., growth factors and procollagen
- Regulated secretion, only found in specialized cells, e.g., glandular epithelial cells
  - Exocytosis of large stored vesicles in response to a stimulus.
  - Vesicles are normally visible in light microscope.
  - Only specific protein products are sorted to this pathway out of the trans-Golgi network.
  - Regulated by:
    - The autonomous nervous system
    - The endocrine system

Glands

General
Cell or organ specialized for secretion of products that are used in another location

Divided into
- Exocrine glands
- Endocrine glands

Consist of
Most multicellular glands consist of:
- Parenchyma of epithelial tissue
  - Glandular epithelium
    - Forms the secretory part
  - Surface epithelium
    - Forms the duct system
    - Only in exocrine glands
- Stroma of connective tissue
  - Supports and organizes epithelial tissue parts

Exocrine Glands

General
- Secretory cells that secrete products to the free apical cell surface.
- Glandular epithelium is connected to the surface epithelium directly or via a duct system.
  - Products are secreted either directly or transported to a surface epithelium through the duct system.

Divided into
Exocrine glands are classified by:
- Number of gland cells
  - Unicellular exocrine glands
  - Multicellular exocrine glands
- Secretory product
  - Mucous
  - Serous
  - Mixed mucoserous
- Structure of gland
  - Duct system organization
  - Shape of end pieces
- Method of secretion
  - Merocrine secretion
  - Apocrine secretion
  - Holocrine secretion

Number of Gland Cells

Unicellular Exocrine Glands (Goblet Cells)

General

- Virtually the only unicellular exocrine gland in humans
- Found dispersedly in, e.g., respiratory and intestinal epithelium

Light Microscopy

- Flask-shaped cell, with nucleus placed in the narrow basal part of the cell.
- Apical broad cell part is filled with mucin-containing vesicles.

Multicellular Exocrine Glands

Divided into

- Exocrine glands within surface epithelium:
  - Secreting epithelial surface
    - Looks like an epithelium composed solely of goblet cells
    - Only found in the epithelium of the stomach
  - Intraepithelial glands
    - Invagination of glandular epithelium within a normal surface epithelium
    - For example, in the male urethra and on the internal surface of the eyelid
- Exocrine glands within connective tissue:
  - Most common multicellular gland type, e.g., parotid gland.
  - Glandular epithelium is arranged in end pieces, connected to the surface epithelium via a duct system.

Secretory Product

General

Glands are named after their secretory product:

- Glands with purely mucous or serous secretions are called mucous glands or serous glands, respectively.
- Mixed glands are called mucoserous or seromucous glands, depending on the major content.

Divided into

- Mucous product: viscous secretion, made from mucin and H_2O
- Serous product: thin, aqueous secretion, containing various enzymes
- Mixed product: mixed mucous/serous secretion

Structure of Gland

General

Glands are named after structure:

- Depending on the organization of the duct system, the glands are named simple straight, simple coiled, or compound.
  - When a single duct has >1 end pieces, it is named simple branched.
- Depending on the shape of the end pieces, the glands are called tubular, alveolar, or acinar.
  - Glands with end pieces of different shapes are named tubuloacinar or tubuloalveolar.

Divided into (Fig. 6.1)

- Duct system organization
  - Simple (unbranched) duct
    - Straight
    - Coiled
  - Compound (branched) duct
- End piece
  - Shape:
    - Tubular
      - Tube-shaped lumen and outer surface
      - For example, in eccrine sweat glands
    - Alveolar
      - Sac-shaped lumen and outer surface
      - For example, in mammary glands
    - Acinar
      - Tube-shaped lumen and sac-shaped outer surface → cone-/pyramid-shaped cells
      - Most common type, e.g., in parotid glands
  - Organization:
    - Single: a single end piece at the end of the duct
    - Branched: several end pieces on a simple (unbranched) duct
    - Coiled (only tubular end pieces)

Type of Secretory Method

General

Glands are named after their type of secretory method.

- Merocrine glands: most glands
- Apocrine glands: primarily in the lactating mammary glands (Chap. 27)
- Holocrine glands: only sebaceous and modified sebaceous glands (Chap. 20)

Duct system and end piece organization

Simple (unbranched) duct	Simple Tubular	Simple branched tubular (Multiple end pieces on an unbranched duct)	Simple coiled tubular
Compound (branched) duct	Compound tubular		

End piece shape

	Tubular end piece	Acinar end piece	Alveolar end piece
Longitudinal section			
Cross section			

Fig. 6.1 Duct system and end pieces: the different types of duct system organizations and end piece shapes

Divided into
- Merocrine secretion
  - Exocytosis of vesicles
  - Most common type, e.g., in parotid gland
- Apocrine secretion
  - Ligation of an apical cell part, containing the secretory product (e.g., lipid droplets) and a surrounding envelope of cytoplasm and cell membrane
  - Primarily found in the lactating mammary gland (Chap. 27)
- Holocrine secretion
  - Extrusion of the whole cell, containing secretory product
  - Only found in sebaceous glands and modified sebaceous glands (Chap. 20)

MEMO-BOX
- M**E**rocrine secretion: secretion by **E**xocytosis
- **A**pocrine secretion: secretion by ligation of **A**pical cell part
- **H**olocrine secretion: secretion by extrusion of w**H**ole cells

Exocrine Glands Within Connective Tissue

General
Most common type of multicellular exocrine gland

Consists of (Fig. 6.2)
- Parenchyma
  - Secretory end pieces
  - Duct system (by some considered a part of the stroma)
- Stroma

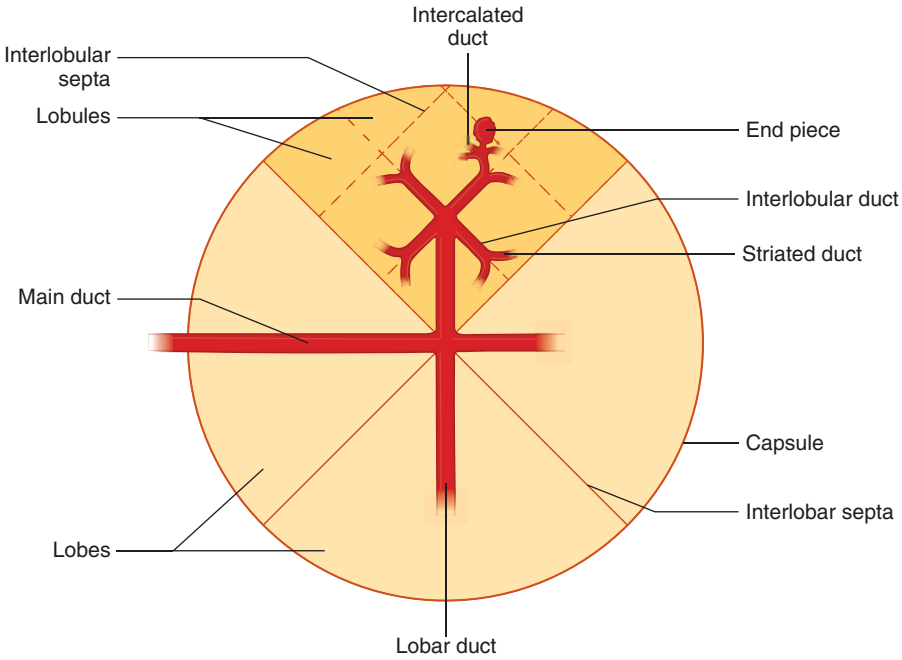


Fig. 6.2 Organization of a multicellular exocrine gland within connective tissue

PARENCHYMA

Secretory End Pieces

Structure

- Glandular epithelial cells in end pieces.
- End pieces form the blind ends of the duct system.

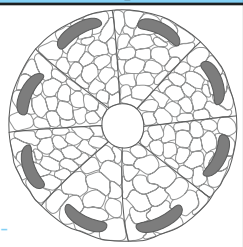
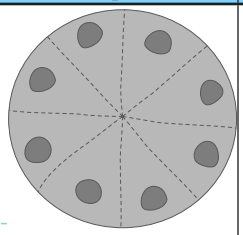
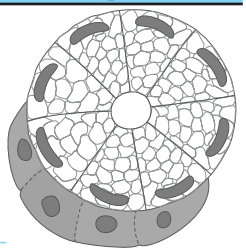
Function

Secretory (functional) part of gland

Light Microscopy

- End pieces are seen in cross sections as small rounded units (Fig. 6.1).
- Morphology of end pieces varies with type of secretory product (Table 6.1).

Table 6.1 Microscopic characteristics of serous, mucous, and mixed acinar end pieces

	Mucous end piece	Serous end piece	Mixed end piece
Illustration of cross section			
End piece morphology	• Large and irregular • Distinctly separated	• Small and rounded • Hard to distinguish from each other	Same as mucous end piece, but with clumps of serous cells located peripherally
Cells			
• Nucleus	Flat and basal	Round and basal	• Mixture of mucous and serous cells • Artifact during preparation → serous cells swell and displace to the outside of the mucous cells the in end piece as "demilunes"
• Cytoplasm	• Filled with mucin vesicles • Mucin is lost during routine preparation → weakly stained cytoplasm with a vacuolated appearance	• Well-developed rER → basophilic near nucleus • Apical vesicles, often acidophilic	
• Vesicles	Visible	± Visible	• Visible in mucous cells • ± Visible in serous cells
Cell borders	Visible	Indistinct	Visible between mucous cells
Lumen	Large, normally visible in the light microscope	Small, normally not visible in the light microscope	Large, normally visible in the light microscope
Location	For example, in sublingual glands	For example, in parotid glands	For example, in glands of epiglottis

MEMO-BOX

- **S**erous acinar end pieces look like "**S**alami pizzas" with their round nuclei (salami slices).
- **M**ucous acinar end pieces look like "**M**agnolia flowers" with their large lumen (green center of flower) and light cells, with visible borders (petals).

Myoepithelial cells

General

- Thin layer of contractile cells found between:
  - Glandular epithelial cells and their basal lamina in end pieces
  - Surface epithelium and their basal lamina of some ducts
- Found in sweat, tear, mammary, and salivary glands

Structure

- Flat cells with long cell extensions
- Surround end pieces and ducts

Function

Contraction → assist in squeezing out the secretory products from gland

Duct System

Structure (Table 6.2)

- Composed of surface epithelium.
- Epithelium changes with the ⦸ of the duct.

Function

- Transports secretory products from end pieces to the surface.
- The duct epithelium of some glands modifies the secretory product during the passage, e.g., in the salivary glands.

Light Microscopy

See Table 6.2.

STROMA

Structure (Table 6.3)

Connective tissue containing blood vessels and nerves

Function

Supports and organizes the parenchyma

MEMO-BOX

- "Inter" means between: **INTER**lobular ducts runs in the **INTER**lobular septae, between lobuli.
- "Intra" means within: intralobular ducts runs within lobuli.
- End pieces: the pieces at the very end of the duct system.

Table 6.2 Duct system

Duct part	Path	⦸	Epithelium
Main duct ↓	Transverse capsule of gland, ends at epithelial surface	Large	Stratified cuboidal/columnar with multiple layers
Lobar ducts ↓	Run in lobes	↓	Fewer layers
Interlobular ducts ↓	Run in interlobular septae		Fewer layers
Intralobular ducts: • Striated ducts ↓	Run in lobules		Simple columnar
• Intercalated ducts	Run in lobules and connect directly with end pieces	Small	Simple cuboidal

Table 6.3 Stroma of glands

Connective tissue part	Location
Capsule ↓	Surrounds the gland
Interlobular septa ↓	Divide the gland into lobes
Interlobular septa ↓	Divide the lobes into lobules
Reticular connective tissue	Surrounds intralobular ducts and end pieces

Endocrine Glands

General

- Contain no duct system or secretory end pieces.
- Cells secrete their products (hormones) to intercellular space, from where they diffuse into the blood stream of adjacent capillaries.
- The tissue is densely vascularized, commonly with fenestrated capillaries.

Function

Secretion of hormones:

- Hormones can, via distribution through the blood circulation, affect target cells in the whole body.
  - Hormones act via receptors in target cells.
- Secretion is regulated by negative and positive feedback mechanisms (Chap. 24).

Divided into

Endocrine glands are classified by:

- Number of cells
  - Unicellular endocrine glands, e.g., the enteroendocrine cells of the gastrointestinal tract
  - Multicellular endocrine glands, e.g., the adrenal gland
- Histology
  - Trabecular endocrine tissue.
    - Anastomosing plates/strings of cells, separated by densely vascularized loose connective tissue.
    - Unlike normal epithelial cells, the cells lack an apical free surface (named epithelioid cells).
    - Make up all endocrine tissues, except in the thyroid gland.
  - Follicular endocrine tissue
    - Simple (one layered) epithelium, surrounding fluid-filled cavities (follicles).
    - Epithelial height varies with secretory activity.
      - Passive gland: squamous/cuboidal epithelium
      - Active gland: columnar epithelium
    - Only found in the thyroid gland
- Secretory product
  - Peptide hormones
    - For example, insulin
    - Secreted by merocrine secretion
  - Steroid hormones
    - For example, testosterone and estrogens
    - Diffuse freely out of the cells after production
  - Amine hormones
    - For example, adrenalin and thyroxin.
    - Thyroid hormones are transported across the cell membrane by carrier proteins.
    - Remaining amine hormones are secreted by merocrine secretion.

Endocrine Cells

Structure

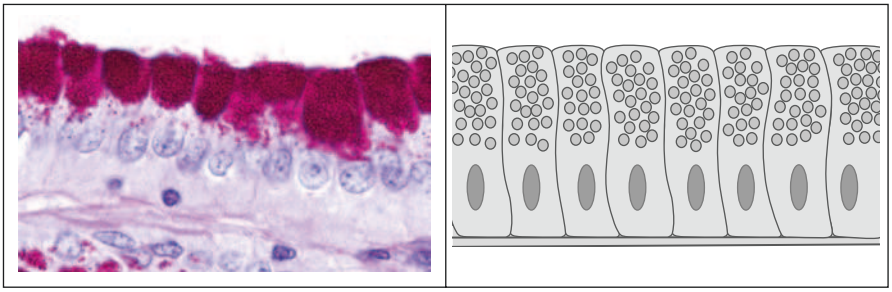
Morphology varies with the type of hormones produced:

- Peptide/amine hormone-producing cells commonly contain:
  - Well-developed rER, Golgi apparatus, and multiple secretory vesicles
- Steroid hormone-producing cells contain:
  - Well-developed organelles and inclusions needed for the synthesis of steroid hormones
    - Abundant sER
    - Mitochondria with tubular cristae
    - Abundant lipid droplets
      - Contain precursor molecules for steroid hormone synthesis, e.g., cholesterol
      - Seen as cytoplasmic vacuoles in the light microscope

Guide to Practical Histology: Glandular Epithelium

EXOCRINE GLANDS WITHIN SURFACE EPITHELIUM

Secreting Epithelial Surface

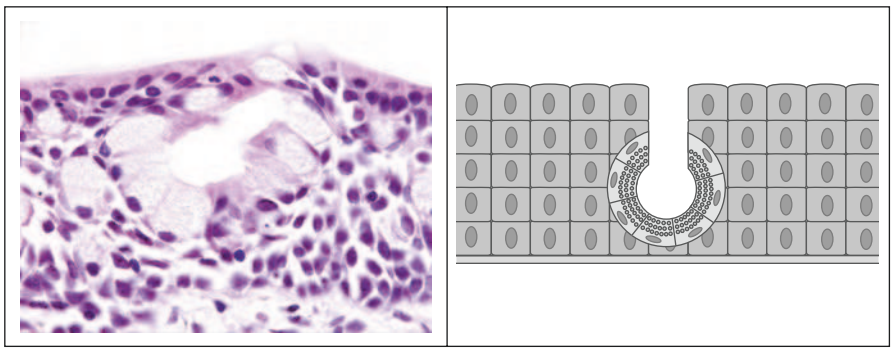


Left: photomicrograph of secreting epithelial surface. Magnification: high. Stain: PAS, hematoxylin and aurantia (Courtesy of associate professor Steen Seier Poulsen, University of Copenhagen). Right: Simplified illustration of secreting epithelial surface

Characteristics
Epithelium of mucous secreting cells:
- Epithelial cells resemble goblet cells.

Location
Only found in the epithelium of the stomach

Intraepithelial Glands



Left: photomicrograph of intraepithelial glands. Magnification: high. Stain: HE (Courtesy of professor Jørgen Tranum-Jensen, University of Copenhagen). *Right*: simplified illustration of intraepithelial glands

Characteristics
A small invagination of glandular epithelium, within "normal" surface epithelium

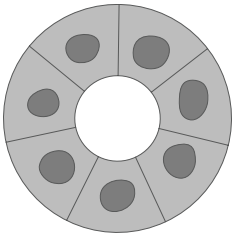
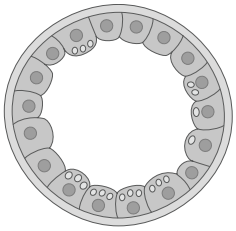
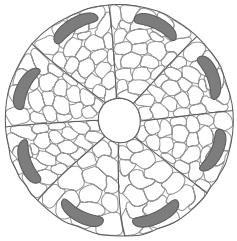
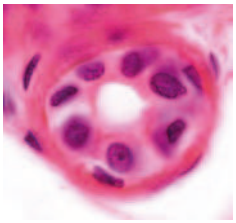
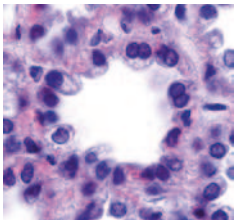
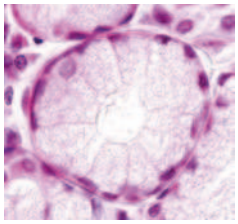
Location
For example, in the conjunctiva of the internal surface of the eyelid

EXOCRINE GLANDS WITHIN CONNECTIVE TISSUE

Characteristics
- Cross sections of:
  - Secretory end pieces
  - Ducts
- Shape of secretory end pieces differs between glands (Table 6.4):
  - Tubular
  - Alveolar
  - Acinar, the most common type

Divided into
- Merocrine glands, the most common type
- Apocrine glands
- Holocrine glands

Table 6.4 Microscopic characteristics of tubular, alveolar, and acinar end pieces

	Tubular end piece	Alveolar end piece	Acinar end piece
Illustration of cross section			
Photo-micrograph of cross section			
Location	For example, in sweat glands	For example, in mammary glands	For example, in the parotid gland

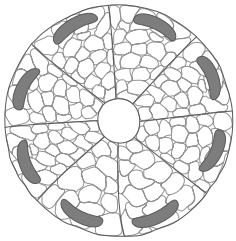
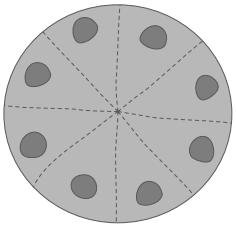
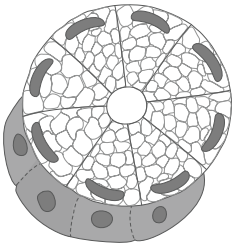
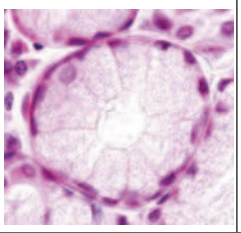
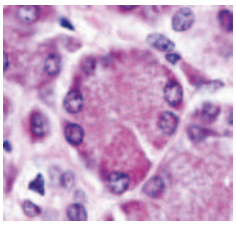
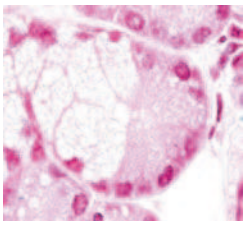
Top left: simplified illustration of tubular end piece. Top center: simplified illustration of alveolar end piece. Top right: simplified illustration of acinar end piece. Middle left: photomicrograph of tubular end piece. Magnification: high. Stain: HE (Courtesy of associate professor Steen Seier Poulsen, University of Copenhagen). Middle center: photomicrograph of alveolar end piece. Magnification: high. Stain: HE (Courtesy of associate professor Steen Seier Poulsen, University of Copenhagen). Middle right: photomicrograph of acinar end piece. Magnification: high. Stain: HE (Courtesy of professor Jørgen Tranum-Jensen, University of Copenhagen)

Merocrine Glands

Characteristics

- Cross sections of secretory end pieces:
  - Commonly numerous and densely packed
  - Can be tubular, alveolar, or acinar (Table 6.4)
  - Morphology differs according to secretory product (Table 6.5):
    - Serous
    - Mucous
    - Mixed
- Cross sections of ducts
  - Seen scattered within the cross sections of secretory end pieces
  - Lined with simple/stratified, cuboidal/columnar epithelium
  - Visible lumen

Table 6.5 Microscopic characteristics of serous, mucous, and mixed acinar end pieces

	Mucous end piece	Serous end piece	Mixed end piece
Illustration of cross section			
Photo-micrograph of cross section			
End pieces	• Large and irregular • Distinctly separated	• Small and rounded • Hard to distinguish from each other	As the mucous end piece, but with clumps of serous cells located peripherally
Cells:			
• Nucleus	Flat and basal	Round and basal	Mixture of mucous and serous cells
• Cytoplasm	Light and vacuolated → light cells	• Basophilic basally → dark cells • Apical vesicles, often acidophilic	
• Vesicles	Visible	± Visible	• Visible in the mucous cells • ± Visible in serous cells
Cell borders	Visible	Indistinct	Visible between mucous cells
Lumen	Large, normally visible in the light microscope	Small, normally not visible in the light microscope	Large, normally visible in the light microscope
Location	For example, duodenal glands	For example, parotid gland	For example, glands of epiglottis

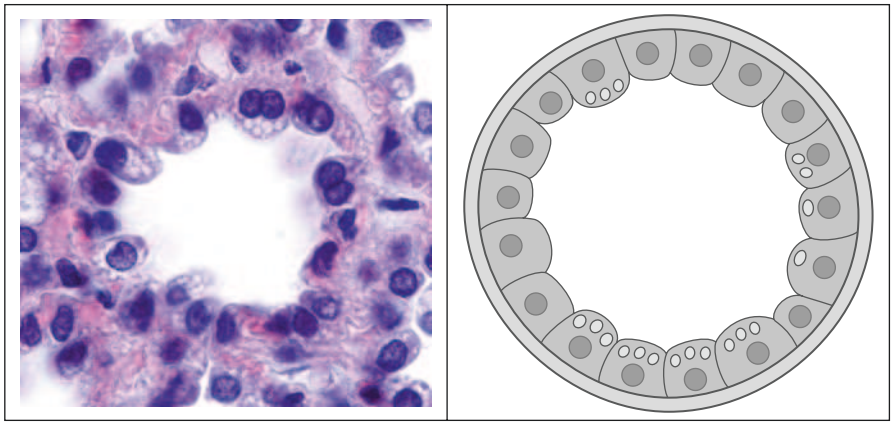
Top left: simplified illustration of mucous end piece. *Top center*: simplified illustration of serous end piece. *Top right*: simplified illustration of mixed end piece. *Second row left*: photomicrograph of mucous end piece. Magnification: high. Stain: HE (Courtesy of associate professor Steen Seier Poulsen, University of Copenhagen). Second row center: photomicrograph of serous end piece. Magnification: high. Stain: HE (Courtesy of associate professor Steen Seier Poulsen, University of Copenhagen, University of Copenhagen). Second row right: photomicrograph of mixed end piece. Magnification: high. Stain: HE (Courtesy of professor Jørgen Tranum-Jensen, University of Copenhagen)

Location

Merocrine glandular tissue makes up most multicellular exocrine glands:

- Shape of end pieces differs between glands:
  - Tubular end pieces, e.g., sweat glands
  - Alveolar end pieces, e.g., prostate gland
  - Acinar end pieces, e.g., parotid glands
- The product of most glands is mixed, i.e., the glands contain both serous, mucous, and mixed end pieces, in varying ratios.
  - Exceptions:
    - Pure serous glands, e.g., the parotid glands
    - Pure mucous glands, e.g., the Brunner glands of the duodenum

Apocrine Glands



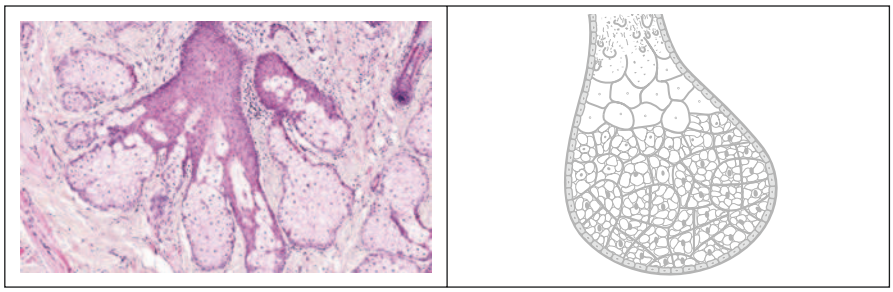
Left: photomicrograph of alveolar end piece of a lactating mammary gland. Magnification: high. Stain: toluidine blue (Courtesy of associate professor Steen Seier Poulsen, University of Copenhagen) *Right*: simplified illustration of alveolar end piece of a lactating mammary gland

Characteristics

- Cross sections of secretory end pieces
  - Numerous and densely packed alveolar end pieces with:
    - Simple cuboidal epithelium
    - Large lumen, often containing eosinophilic secretions
  - The cells of the end pieces
    - Are convex towards lumen
    - Often contain apical lipid droplets
- Cross sections of ducts
  - Seen scattered within the cross sections of secretory end pieces
  - Lined with simple/stratified, cuboidal/columnar epithelium
  - Visible lumen

Location
- Apocrine secretion is primarily seen in the lactating mammary glands
- Apocrine sweat glands (apocrine secretion here is debated)

Holocrine Glands



Left: photomicrograph of sebaceous gland. Magnification: High. Stain: HE (Courtesy of associate professor Steen Seier Poulsen, University of Copenhagen). Right: simplified illustration of sebaceous gland

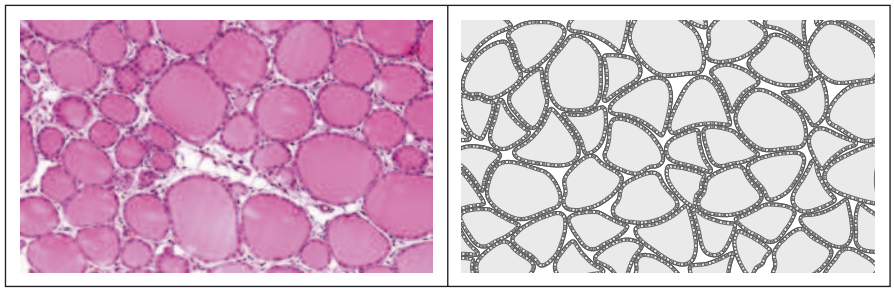
Characteristics
- One to several large acinar end pieces
  - End pieces are seen as a large aggregation of cells, which resembles a "grape cluster."
  - Basal layer
    - Smaller cuboidal basophilic cells
  - Middle layers
    - Pale polyhedral cells with a vacuolated cytoplasm and gradually smaller nuclei (cells resemble fish eyes)
  - Luminal layers
    - Pale cells breaking into pieces
- Ducts are often not seen.
- Often seen adjacent to a hair follicle, i.e., in dermis of the skin.

Location
Only found as the sebaceous glands and modified sebaceous glands, e.g., in the skin

ENDOCRINE GLANDULAR TISSUE

General
- Without cross sections of secretory end pieces and ducts
- Cells in cords/groups/follicles
- Contains multiple capillaries
  - Seen as narrow white spaces with multiple eosinophilic erythrocytes

Follicular Endocrine Tissue

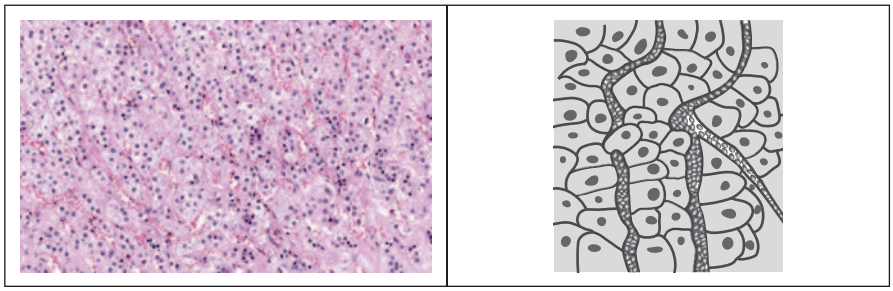


Left: photomicrograph of follicular endocrine tissue. Magnification: low. Stain: HE (Courtesy of professor Jørgen Tranum-Jensen, University of Copenhagen). *Right*: simplified illustration of follicular endocrine tissue

Characteristics
- Consists of multiple follicles
  - Rings of simple epithelium
  - Epithelium surrounds a lumen with homogenous eosinophilic material (colloid).
- Connective tissue with capillaries is seen between the follicles.

Location
Only found in the thyroid gland

Trabecular Endocrine Tissue



Left: photomicrograph of trabecular endocrine tissue. Magnification: low. Stain: HE (Courtesy of professor Jørgen Tranum-Jensen, University of Copenhagen). *Right*: simplified illustration of trabecular endocrine tissue

Characteristics

- Anastomosing strands of cells forming a disorganized network
- Separated by loose connective tissue with numerous capillaries
- Morphology differs depending on hormonal product:
  - Steroid hormone-producing tissue
    - Cells are large and pale.
    - Contain many small lipid droplets, seen as empty vacuoles → "popcorn-/foam"-like cells.
  - Peptide/amine hormone-producing tissue
    - Cells are small and dark.

Location

Areas of both types are found, e.g., in the adrenal gland.

- Cortex: steroid hormone-producing endocrine tissue
- Medulla: peptide/amine hormone-producing endocrine tissue

Can be mistaken for

Brown fat

- Cells in aggregations, not in strands.
- Cells contain larger lipid droplets.
- Not divided into morphologically different areas, as many trabecular endocrine tissues are.

References

5, 12, 20, 33, 34.