MD Program
UNIVERSITY OF TORONTO

Histology

The Respiratory System

eMODULE TUTORIAL

CLICK TO BEGIN

H9 The Histology of the Respiratory System

All images are from Junqueira's Basic Histology, 13th ed., © 2013 by Mescher, denoted by "J", a recommended resource, unless otherwise noted.

Recommended online resources:

Western University Virtual Slide Box

University of Michigan Virtual Microscopy

University of Minnesota Histology Guide

University of Leeds Histology Guide

University of Illinois Cell and Tissue Biology

When you have learned the material presented here, you will be able to:

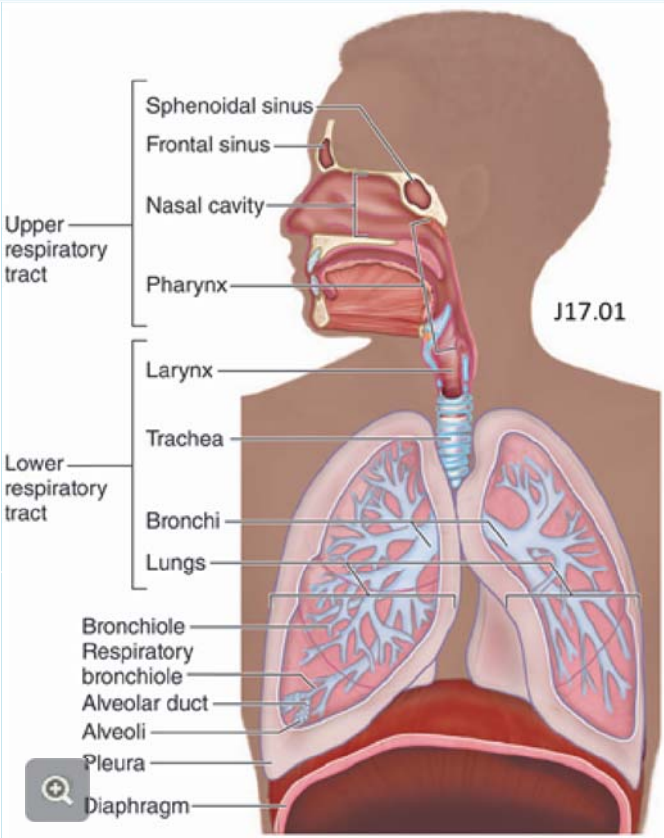
- describe the histological features of the upper respiratory tract, including the nose, paranasal sinuses and nasopharynx.
- compare and contrast the histological features of the lower respiratory tract, including the trachea, bronchi and bronchioles.
- describe the function of the various tissue layers that make up the walls of these passages.
- list the epithelial cell types that contribute to the lining of the airways and describe their function.
- describe the structure of the alveolus, including the function its epithelial cell types.
- describe the structure of the interalveolar septum.
- describe the blood-air barrier, or respiratory membrane.

The respiratory system functions to facilitate the exchange of oxygen (O_2) and carbon dioxide (CO_2) between air and blood. It can be divided a **conducting portion** and a **respiratory portion**.

The **conducting portion** moves air into and out of the lungs, bringing it to and from those surfaces specialized for gas exchange, which constitute the respiratory portion.

The conducting portion of the respiratory system includes all structures that conduct air into and out of the lungs. This includes the **nose, pharynx, larynx, trachea, bronchi, bronchioles and terminal bronchioles**. It is subdivided into the **upper respiratory tract** and the **lower respiratory tract** at the opening into the larynx, which is the point of bifurcation of the digestive and respiratory systems.

The **respiratory portion** of the respiratory system includes all structures in which gas exchange between air and blood takes place. This includes the **respiratory bronchioles, alveolar ducts and alveoli**. Alveoli make up most of the volume of the lungs.



Part I:
The Histology of the Conducting
Portion of the Respiratory System

The conducting portion of the respiratory system includes the **nose, pharynx, larynx, trachea, bronchi, bronchioles and terminal bronchioles.**

All surfaces that open to the outside of the body are lined by a **mucus membrane** or **mucosa**. This includes the respiratory system, digestive system and the genitourinary system. Mucus membranes consist of an **epithelial component** and an underlying connective tissue component, the **lamina propria**. **The epithelial component of a mucus membrane varies, depending on the function of the surface it lines**. For instance, the epithelial component of the mucosa of the small intestine is structurally specialized for nutrient absorption, while that of the seminiferous tubules is structurally specialized to produce spermatozoa.

In addition to moving air into and out of the lungs, the conducting portion of the respiratory system is structurally specialized to **condition inspired air**, which includes **warming**, **humidifying** and **filtering air** as it is drawn into the lungs toward the respiratory portion for gas exchange. **It is the mucosa of the conducting portion that is responsible for this function, as it is well-vascularized (to warm), wet (to humidify) and sticky with secreted mucus (to filter)**.

Respiratory epithelium consists of a pseudostratified, ciliated, columnar epithelium with goblet cells, as described in the eModule on epithelia.

The majority of the cells are ciliated columnar cells, with goblet cells interspersed. The goblet cells generate a sticky film of mucus that overlies the free surface of the respiratory epithelium. Particulate matter in inspired air becomes stuck in the mucus and the cilia beat toward the pharynx, propelling the mucus and particulate matter toward the upper esophageal sphincter, where it is swallowed. This is how respiratory epithelium cleans inspired air.

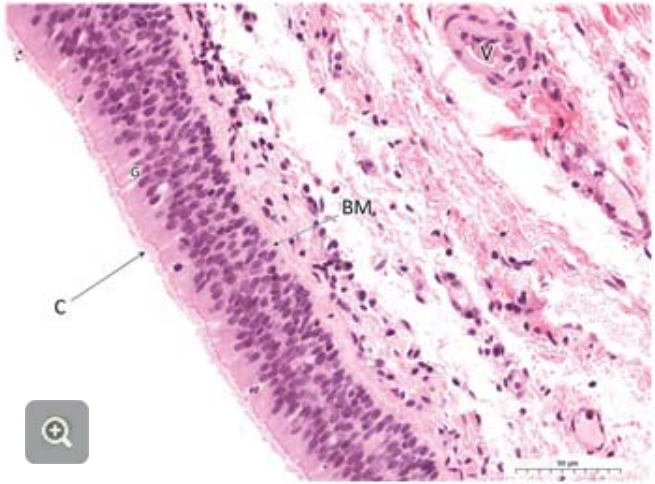
A small proportion of cells in respiratory epithelium are **small granule cells** or Kulchitsky cells. As part of the **diffuse neuroendocrine system** (DNES), small granule cells secrete their products across their basal aspect into the underlying interstitial fluid. Their cell products act in a paracrine manner to coordinate the function of adjacent cells and tissues.

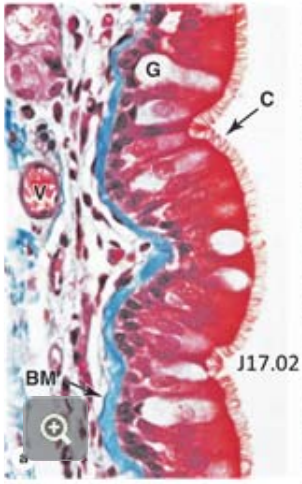
Dendritic cells present in the respiratory mucosa are **antigen-presenting cells**, similar to the Langerhan's cells of the skin. They are capable of migrating from the epithelium to the sub-adjacent lamina propria to present processed antigen to local lymphocytes.

Basal cells present in the respiratory epithelium are mitotically-active stem cells; they give rise to the various cells types present in the epithelium.

Respiratory Epithelium (from Module H2)

As seen in the **first two images**, respiratory epithelium lies on a thick **basement membrane** (BM). It is dominated by **ciliated cells** interspersed with **goblet cells** (G). Goblet cells produce a thick layer of mucus that overlies the epithelial surface. The cilia (C) propel the mucus layer, and any particulate matter trapped within it, toward the pharynx where it is swallowed. The underlying lamina propria is richly vascularized (V).





The third image shows a scanning electron micrograph of the luminal surface of a respiratory epithelium, after it has been washed of mucus. Goblet cells (G) are seen to be interspersed between the ciliated cells.

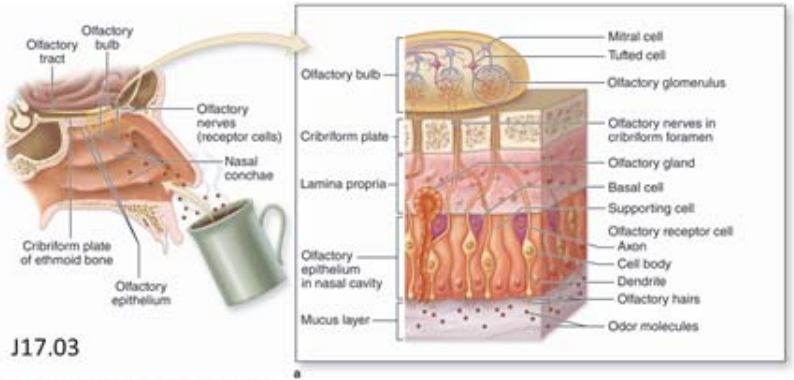
A well-vascularized respiratory mucosa lines most of the nasal cavity. The rich vascularity promotes the warming of inspired air, and **permits the rapid absorption of intranasally-administered drugs**. The nasal conchae promote turbulence in the inspired air, thereby enhancing the interaction between air and the moist, sticky, warm mucosal surfaces.

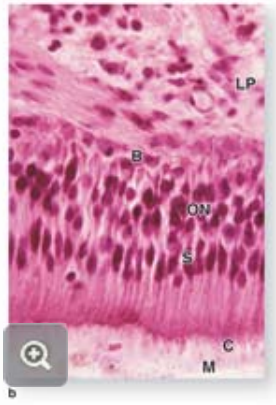
In the roof of the nasal cavity, including the superior conchae, the epithelium is specialized to detect odorant molecules in inspired air. This **olfactory epithelium** contains **chemosensitive olfactory neurons**, **support cells** and **basal cells**.

As you know from your study of the gross anatomy of the head and neck, the **paranasal sinuses** open into the nasal cavity. Mucus produced by the respiratory mucosa lining the paranasal sinuses is propelled by cilia through these openings, and thus drains into the nasal cavity.

The nasal cavities open posteriorly into the **nasopharynx**. This is the **only portion of the pharynx** that is lined by respiratory mucosa; the oropharynx and laryngopharynx, spaces shared by the respiratory and digestive system, are lined by typical oral mucosa, which includes a stratified squamous nonkeratinized epithelium.

Olfaction





The **dendritic ends of the olfactory neurons** (ON) extend into the mucus (M) coating the epithelial surface. Their nonmotile cilia (C) bear **receptors for specific odorant molecules**. Their **axonal ends** extend into the underlying lamina propria (LP), where they **form nerve bundles** which pass through the **cribriform plate of the ethmoid bone** to synapse onto second-order sensory neurons in the **olfactory bulb**, located inferior to the frontal lobes.

The **basal cells** (B) are **stem cells** that give rise to both the support cells (S) and the olfactory neurons. **Olfactory neurons are replaced every 2-3 months**, making the loss of smell (anosmia) or the reduced ability to smell (hyposmia) as a result of mucosal damage temporary. **Regeneration is an unusual property for neurons, and is best understood in olfactory neurons**.

The larynx opens into the **trachea**, a 10-12 cm long tube. From the lumen outward, the wall of the trachea consists of a **mucosa**, a **submucosa** and an **adventitia**.

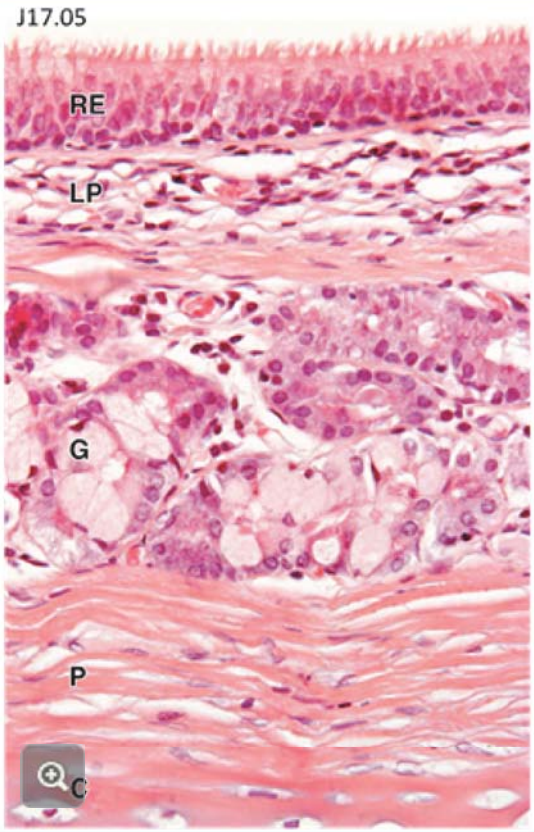
The respiratory **mucosa** lining the trachea includes a tall respiratory epithelium (RE) and lamina propria (LP).

Seromucous glands (G) in the **submucosa** produce watery mucus.

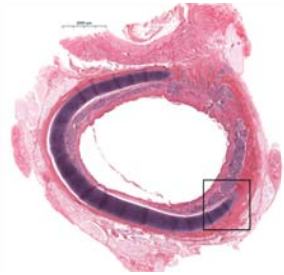
The trachea is kept patent (open) by a series of C-shaped cartilage rings (C) along its length, located **between the submucosa and adventitia**. **Perichondrium** (P) attaches these cartilaginous plates to the submucosa and adventitia.

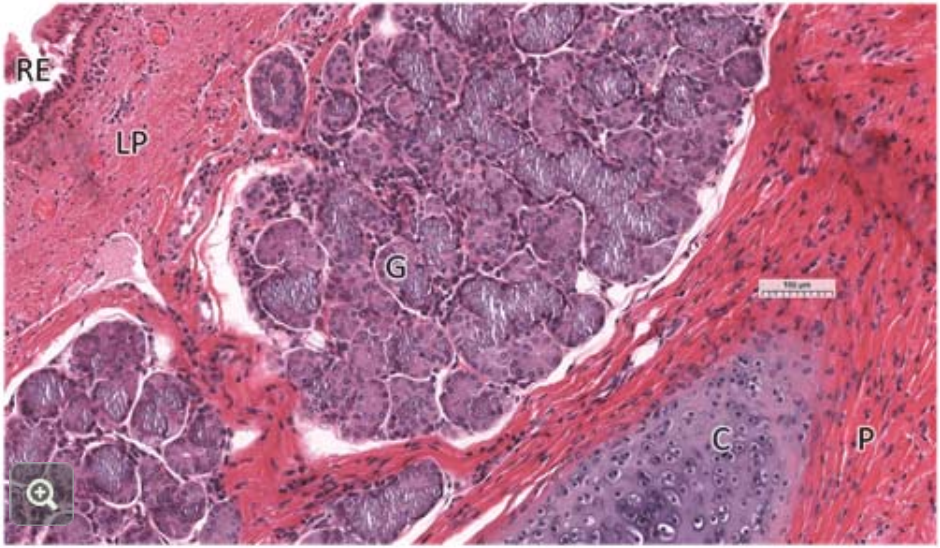
The opening in the "C" faces the esophagus, **posteriorly**. The two ends of the C-shaped cartilage are joined by a smooth muscle, the **trachealis**, the tone of which is under autonomic control. It **relaxes** during swallowing to allow the esophagus to bulge into the trachea with the passage of a bolus of food. It **contracts** during the cough reflex, narrowing the tracheal lumen and thereby increasing the velocity of expelled air.

The **adventitia** is **loose CT** that attaches the trachea to adjacent structures, such as the esophagus, posteriorly, and the thyroid gland, anteriorly and laterally.



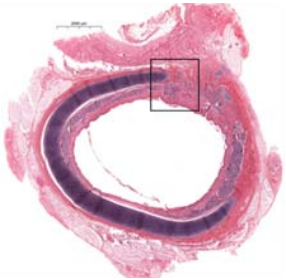
Trachea

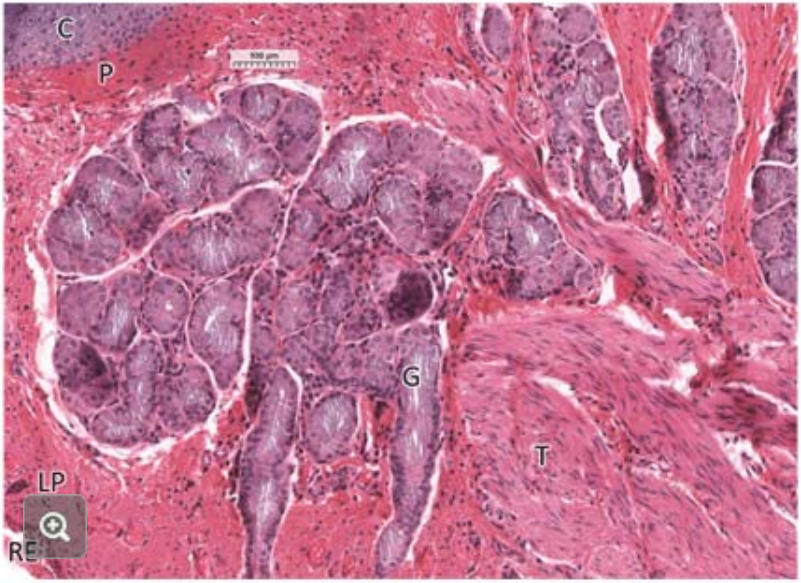




Histological section of the trachea showing the lumen lined by **respiratory epithelium** (RE) lying on a thick **lamina propria**. Within the submucosa are **seromucous glands** (G). C-shaped **hyaline cartilage** (C) surrounded by **perichondrium** (P) is also seen. A similar image demonstrating the **trachealis muscle** (T) can be seen here:

Trachea





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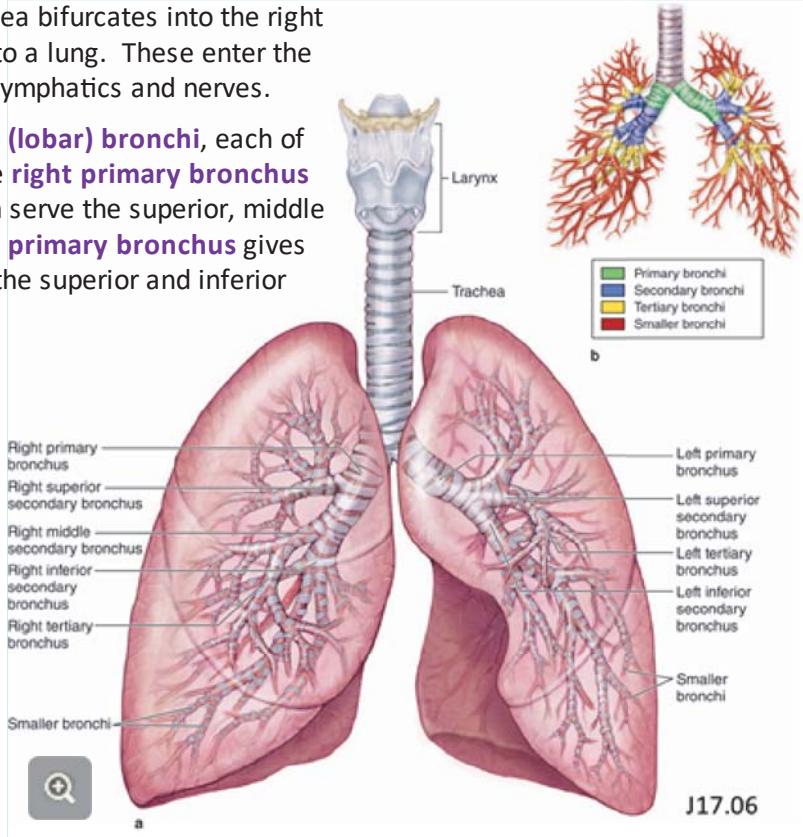
As you know from gross anatomy, the trachea bifurcates into the right and left **primary bronchi**, each dedicated to a lung. These enter the hilum of the lung with their blood vessels, lymphatics and nerves.

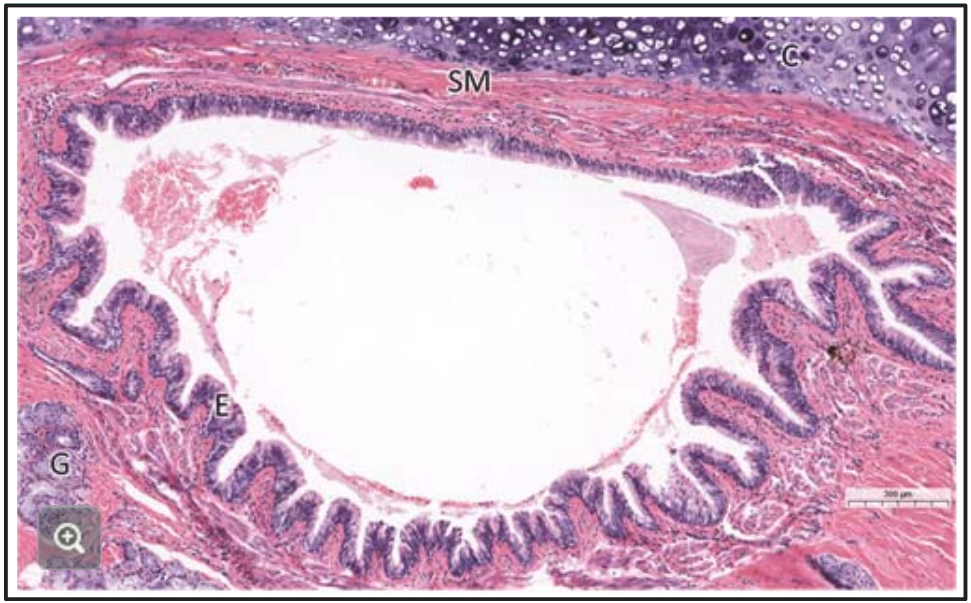
The primary bronchi branch into **secondary (lobar) bronchi**, each of which is dedicated to a lung lobe. Thus, the **right primary bronchus** gives rise to three secondary bronchi which serve the superior, middle and inferior lobes of the right lung. The **left primary bronchus** gives rise to two secondary bronchi which serve the superior and inferior lobes of the left lung.

Secondary bronchi branch to form **tertiary (segmental) bronchi**, each dedicated to a bronchopulmonary segment. **Bronchopulmonary segments** are independent subunits of lung tissue surrounded by a CT capsule, each having their own air, nerve and blood supply and lymphatic drainage.

Tertiary bronchi branch repeatedly, forming ever smaller **bronchi**, and ultimately forming **bronchioles**. The conducting portion of the respiratory system ends with the formation of **terminal bronchioles**.



Unlike the trachea, the cartilaginous support of primary bronchi includes **complete cartilaginous rings**. As the bronchi branch and luminal diameter decreases, the **cartilage transitions to a series of plates**. **Seromucous glands** remain abundant. Bundles of **smooth muscle and elastic fibres** appear in the lamina propria and increase in prominence as the bronchi branch and the cartilage decreases. **Lymphocytes** are present in the mucosa, as are lymphatic nodules of the mucosa-associated lymphoid tissue (MALT); these also increase with the branching of bronchi.



E – Respiratory epithelium
SM – Smooth muscle (increases as bronchi branch)
G – Seromucous glands
C – Hyaline cartilage
LP – Lamina propria
N – Nerve
LT – Lung tissue

Recall that as bronchi branch cartilage begins to disappear and SM becomes more prominent!

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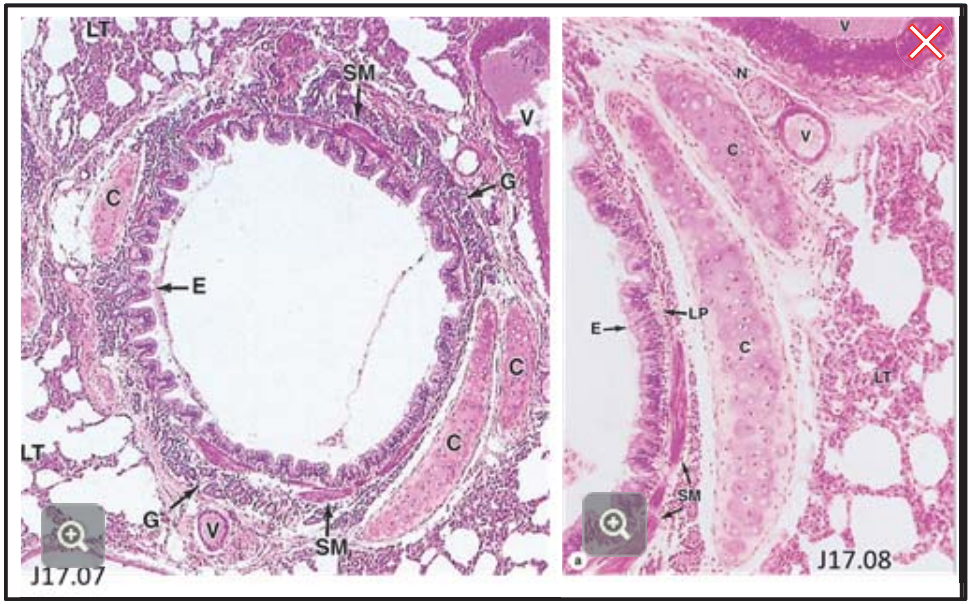

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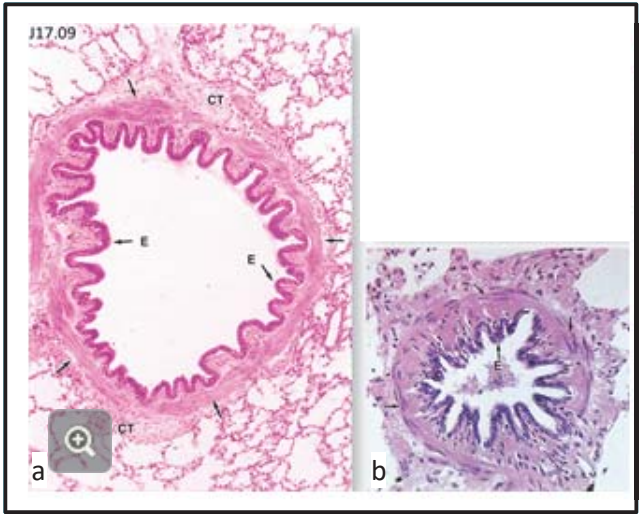
Bronchioles **lack both cartilage and seromucous glands**, and a **continuous layer of smooth muscle is their most prominent feature**. The submucosa and adventitia merge, and elastic fibres in this layer apply traction to the walls of these airways, **helping to maintain their patency**.

In the largest bronchioles, the mucosa includes a **typical respiratory epithelium**, as previously described. As the bronchioles branch and their diameter decreases, the **epithelium transitions to columnar ciliated cells, then cuboidal ciliated cells**. Goblet cells decrease in number, and cilia eventually disappear. This is thus **where the mucociliary apparatus begins**, which functions to clear airways of inspired particulate matter by propelling it toward the pharynx, adhered to the mucus covering the luminal surface.



In **bronchioles**, cartilage and glands are absent.

a. A large bronchiole has a typical respiratory epithelium (E) and prominent smooth muscle (arrows). The walls are supported by fibrous CT.

b. A small bronchiole has a ciliated cuboidal epithelium (E). The walls are dominated by several layers of smooth muscle.

A large bronchiole, seen here, has a typical respiratory epithelium (E) and prominent smooth muscle (SM). The walls are supported by fibrous CT.

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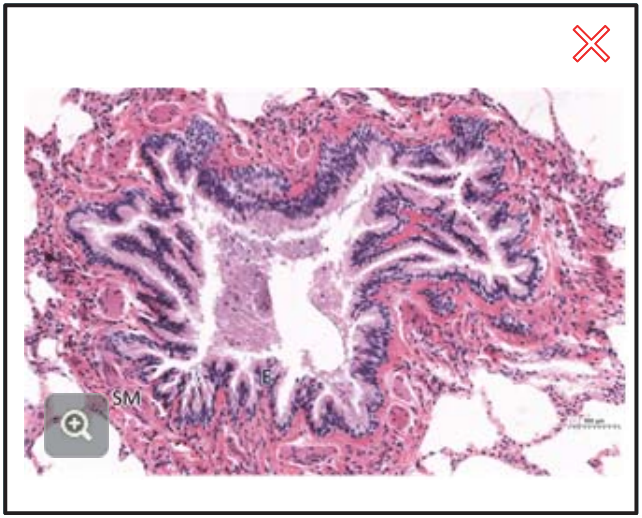

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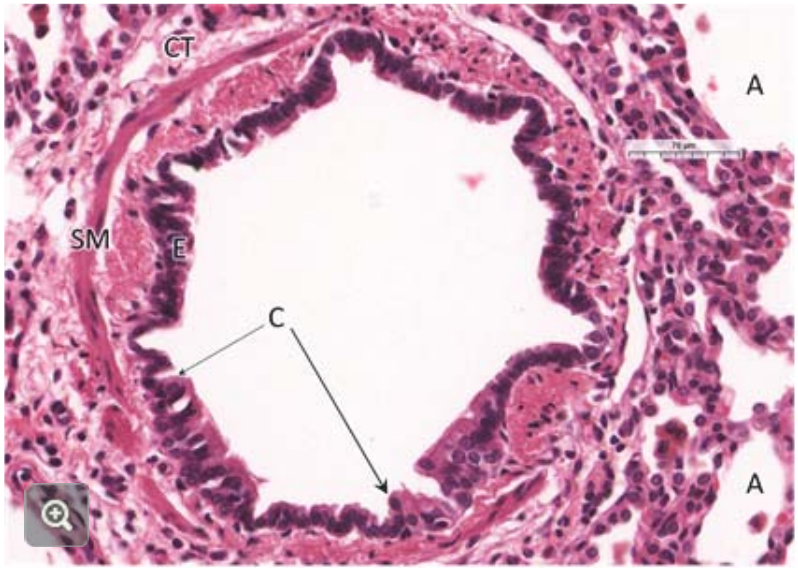
The conducting portion of the respiratory system ends with the **terminal bronchioles**. Here, the epithelium is **cuboidal** and includes **bronchiolar exocrine cells** (club cells, Clara cells) which secrete a surfactant-like substance that helps **maintain alveolar patency** and **antimicrobial peptides and cytokines** for local immune responses.



A terminal bronchiole is lined by a cuboidal to columnar epithelium that lacks cilia (E). It is surrounded by a thin but continuous layer of smooth muscle (SM) embedded in connective tissue (CT). Alveoli (A) surround the terminal bronchiole.

The epithelium is dominated by bronchiolar exocrine cells or club cells (C). They function to produce surfactant, as well as other molecules that function to defend against toxins and pathogens.

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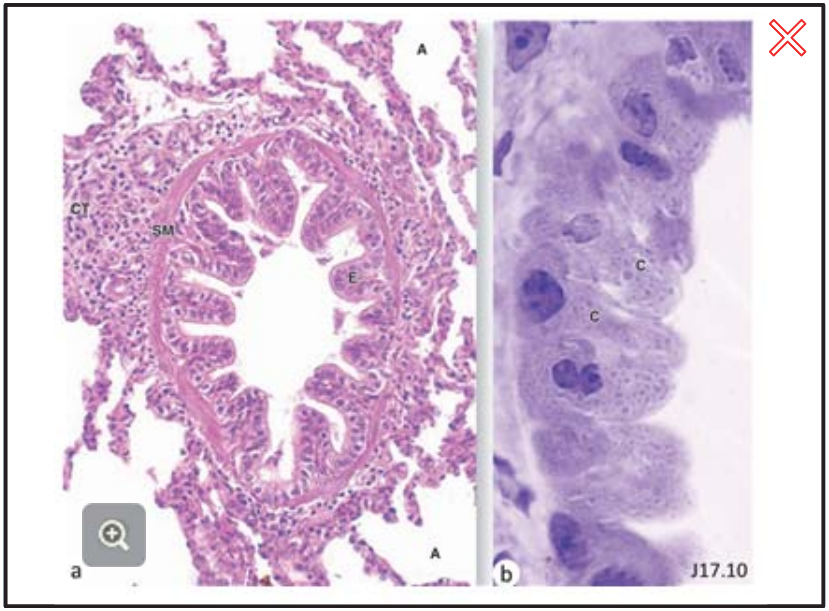

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Part II:
The Histology of the Respiratory
Portion of the Respiratory System

The respiratory portion of the respiratory system includes all structures in which gas exchange between air and blood takes place. This includes the **respiratory bronchioles, alveolar ducts and alveoli**.

Respiratory bronchioles are structurally similar to terminal bronchioles with the addition of occasional sac-like **alveoli** extending from their walls. Gas exchange occurs between air and blood across the walls of alveoli, and therefore respiratory bronchioles are the first part of the respiratory portion of the respiratory system.

As respiratory bronchioles branch, alveoli increase in number and begin to dominate the walls of the tubes. When the walls of the tubes consist entirely of openings into alveoli, they are then called **alveolar ducts**. Alveolar ducts open into expanded spaces called **alveolar sacs**, from which individual **alveoli** radiate in all directions.

Alveoli make up most of the volume of the lungs.

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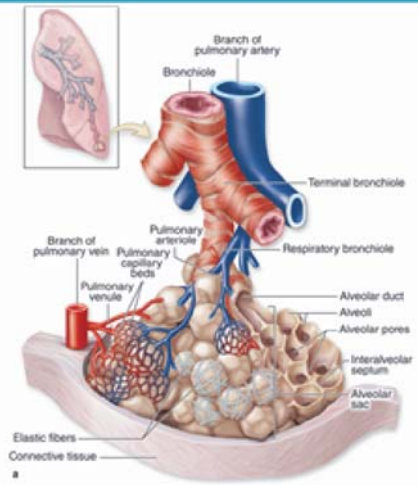

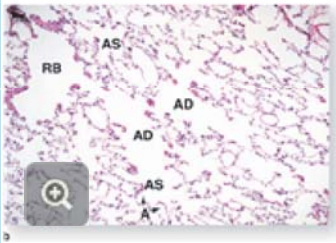

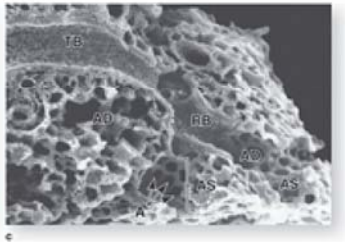

TB terminal bronchiole
RB respiratory bronchiole

AD alveolar duct
AS alveolar sac
A alveoli

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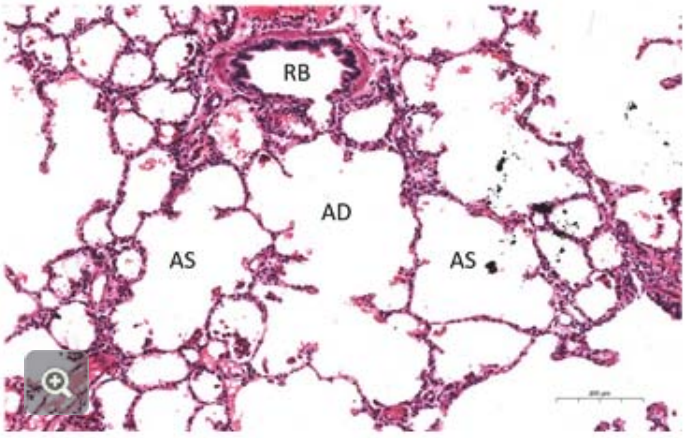
The Histology of Lung Tissue



In this histological image, one can see a **respiratory bronchiole** (RB) opening into an **alveolar duct** (AD), the alveolar duct in turn opens into expanded sac-like spaces referred to as **alveolar sacs** (AS).

As seen here, lung parenchyma is dominated by **alveoli** with **Type I pneumocytes** forming the majority of the surface area, and **Type II pneumocytes** dominating the cellular population (more later).

Lung tissue is often described as having the appearance of a sponge. It reminds me of an Aero Bar. (mmmm…chocolate….)

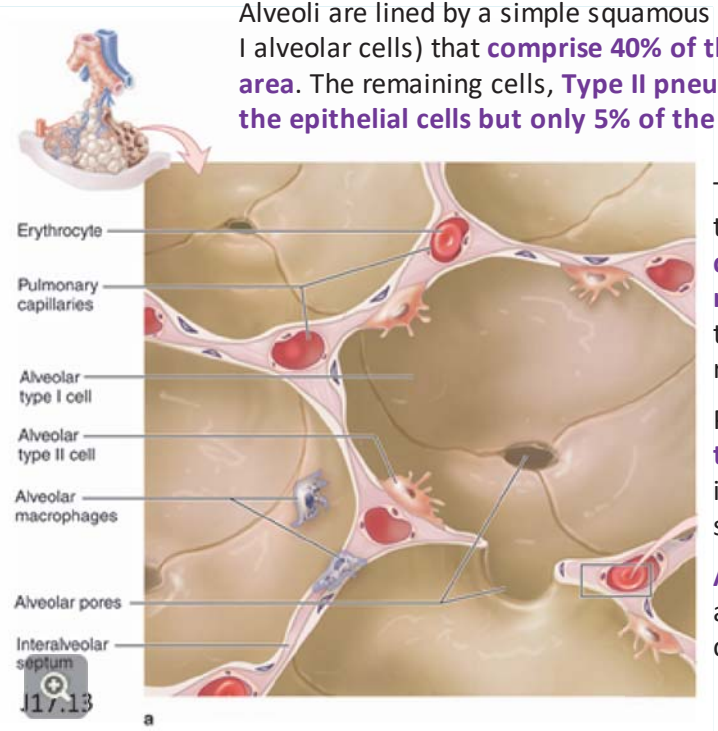
The air-filled spaces within the Aero bar represent the air-filled **alveoli**. The chocolate "septae" that separate the air-filled spaces represents the walls, or **interalveolar septae**, of the alveoli.

The interalveolar septae consist of **CT with elastic and reticular fibres in a small amount of extracellular matrix**, all produced by **fibroblasts**. The **elastic fibres** allow the alveoli to stretch on inspiration and to recoil on exhalation. The **reticular fibres** limit the amount of stretch that occurs on inhalation and help to prevent alveolar collapse on exhalation.

The CT of the interalveolar septae is riddled with **pulmonary capillary beds**, which are very thin-walled, but continuous, rather than fenestrated. In my Aero Bar analogy, they would be running within the chocolate septae, around the air-filled spaces. From these blood vessels, **macrophages** and other leukocytes gain access to the CT of the interalveolar septae.

The alveoli are lined by squamous epithelial cells called pneumocytes.

Adjacent alveoli are connected by **interalveolar pores** which provide collateral air flow between different bronchioles.



Alveoli are lined by a simple squamous epithelium. It includes **Type I pneumocytes** (Type I alveolar cells) that **comprise 40% of the epithelial cells but cover 95% of the surface area**. The remaining cells, **Type II pneumocytes** (Type II alveolar cells), **comprise 60% of the epithelial cells but only 5% of the surface area**.

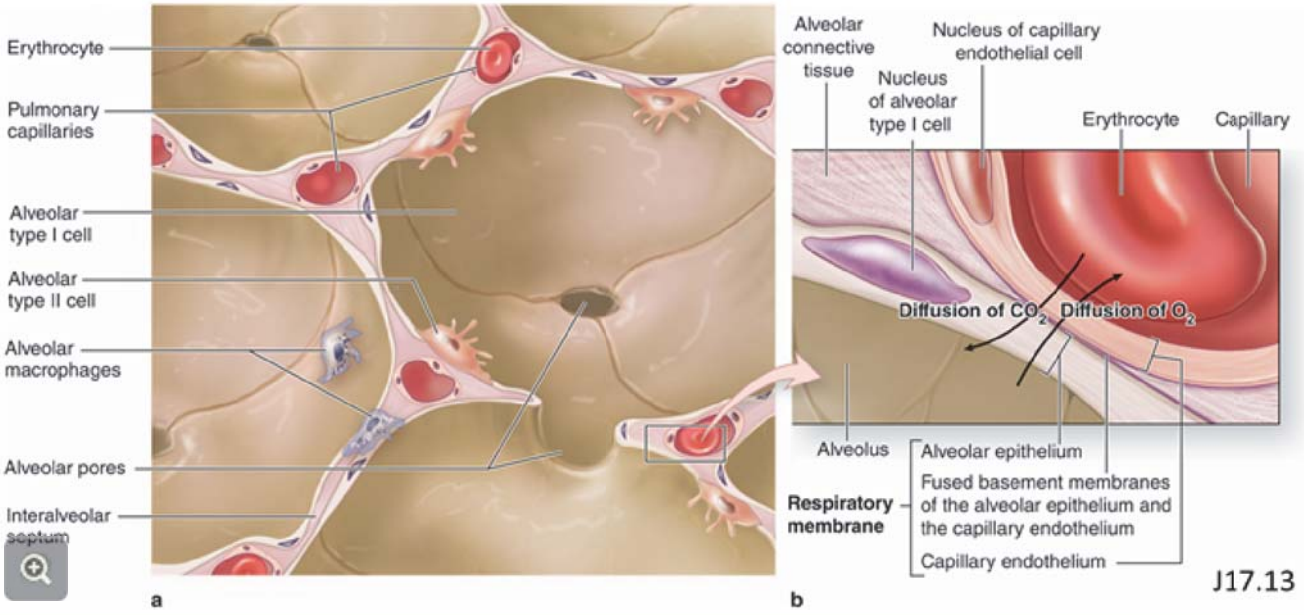
Type II pneumocytes produce **surfactant**, which they secrete onto the luminal surface. Surfactant **decreases alveolar surface tension** which helps **maintain alveolar patency**. They also **proliferate** to produce new Type I or Type II pneumocytes to repair or maintain the alveolar lining, as needed.

Pneumocytes are joined by **desmosomes and tight junctions**, the latter functioning to prevent interstitial fluid from passing into the alveolar space via the paracellular route.

Alveolar macrophages (dust cells) patrol for antigen that has eluded the defenses of the conducting portion of the respiratory system.

The **respiratory membrane** consists of the simple squamous **alveolar epithelium**, the simple squamous **capillary endothelium**, and an intervening **fused basement membrane**.

O_2 diffuses from air in the alveolar lumen, across the respiratory membrane to the capillary lumen. Here it bind hemoglobin within erythrocytes for transport throughout the body. CO_2 diffuses from blood within the capillary lumen, across the respiratory membrane and into the alveolar lumen.



Every day, tens of millions of blood **monocytes** migrate out of pulmonary capillaries into the CT of the interalveolar septum. There they differentiate into **alveolar macrophages, or dust cells**. Dust cells may phagocytose detritus in the interalveolar septum, or might migrate further, between the pneumocytes lining the alveolus, onto the luminal surface of the air sac. There they may phagocytose particulate matter and antigen that has eluded the defenses of the conducting portion of the respiratory system.

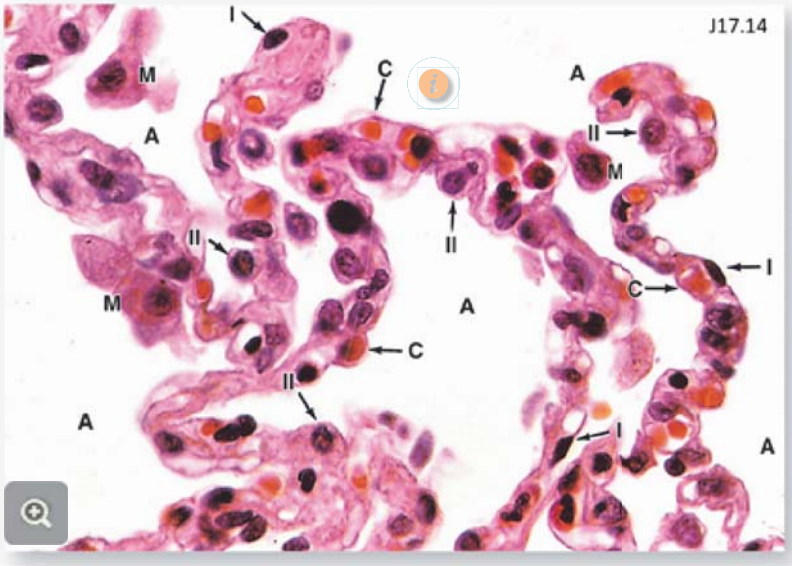
Macrophages are removed by three major means:

1) they might migrate up the airways to the bronchioles where they become trapped in the mucociliary apparatus and transported to the **pharynx** for elimination;

2) they might be carried from the lungs via **lymphatics**;

3) others die and remain as within the **CT** of the interalveolar septum for years.

You have seen evidence of 3) in the dissecting lab, in the form of the black material within the CT components of the lungs of your cadavers. This is dead macrophages filled with ingested particulate matter.



Press **Next** to start the Quiz or **Skip** to end H9

Which of the following are components of the interalveolar septum? Choose all that apply.

- [ ] smooth muscle
- [ ] reticular fibres
- [ ] cartilage
- [ ] seromucous glands
- [ ] elastic fibres

SUBMIT

Which of the following cell types are present in the respiratory portion of the respiratory tract? Choose all that apply.

- [ ] Type I pneumocytes.
- [ ] goblet cells
- [ ] ciliated epithelial cells
- [ ] Type II pneumocytes
- [ ] dust cells

SUBMIT

Conditioning of inspired air occurs in the lower respiratory tract but not the upper respiratory tract.

- True
- False

The presence of which structural feature distinguishes between terminal and respiratory bronchioles?

- [ ] Alveoli
- [ ] Cilia
- [ ] Exocrine bronchiolar cells
- [ ] Mucus glands in lamina propria
- [ ] Smooth muscle

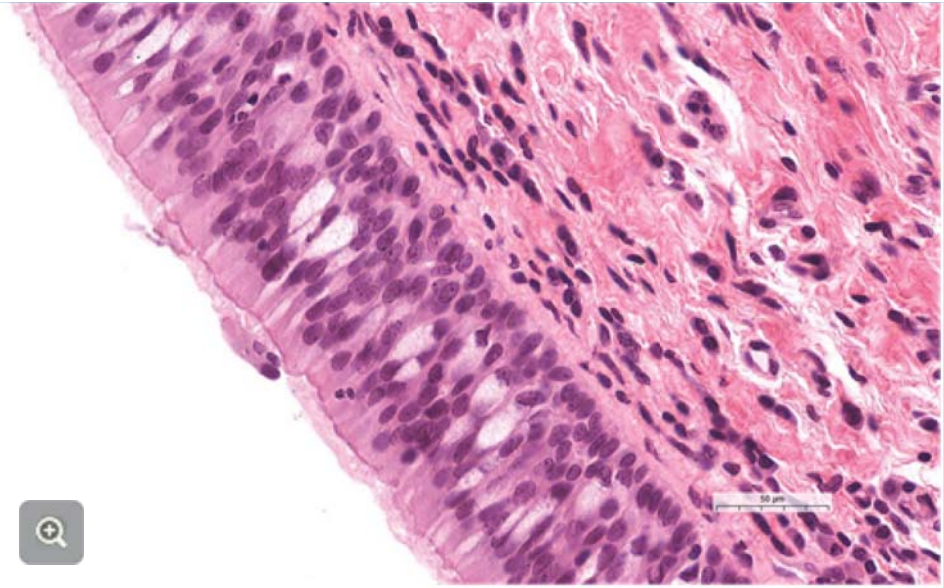
Which parts of the pharynx are lined by respiratory epithelium?
Choose all that apply.

- [ ] Nasopharynx
- [ ] Oropharynx
- [ ] Laryngopharynx
- [ ] None

SUBMIT

What type of epithelium is depicted in this image?

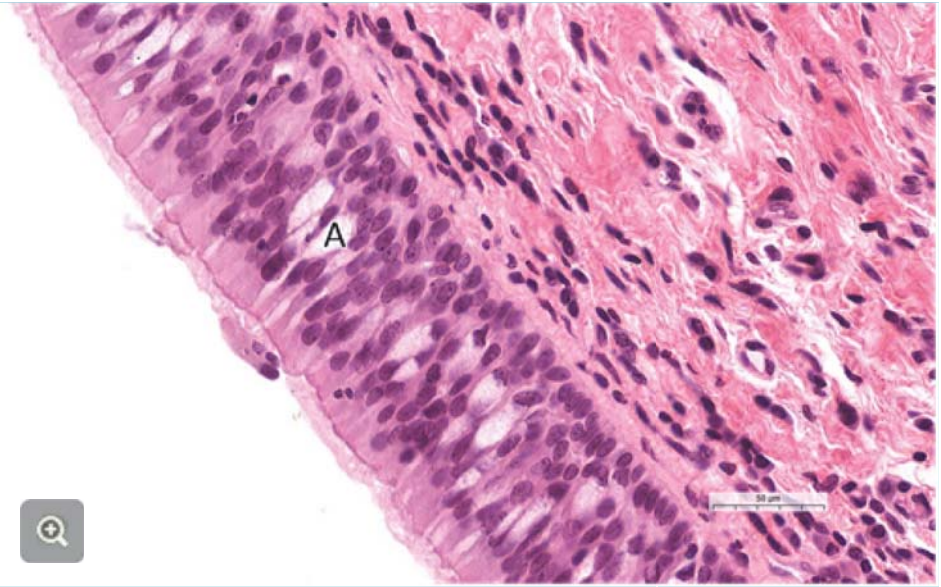
type your text here



SUBMIT

Identify cell type A. Be specific.

type your text here



SUBMIT

What structure is depicted in the image?

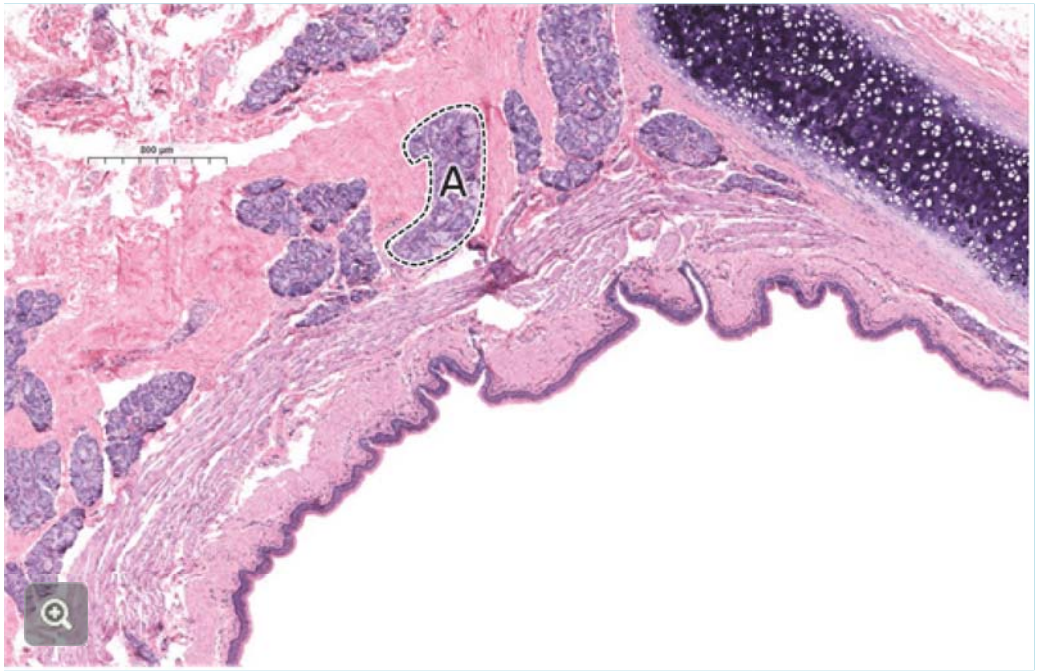
type your text here

SUBMIT

H9 Question 9

Identify structure A. Be specific.

type your text here

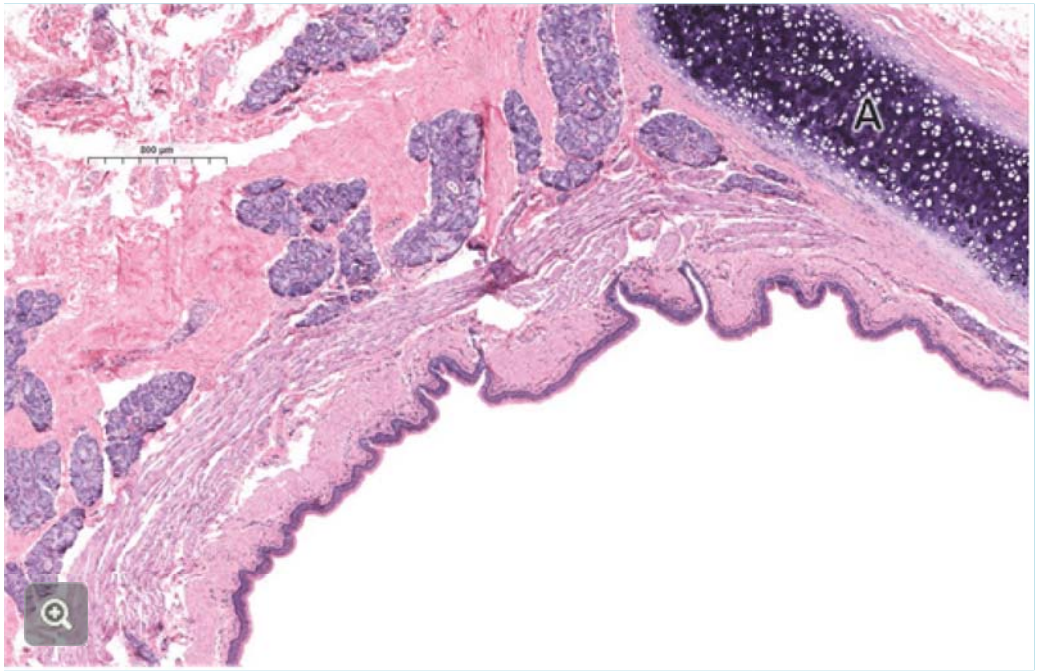


SUBMIT

H9 Question 10

Identify structure A. Be specific.

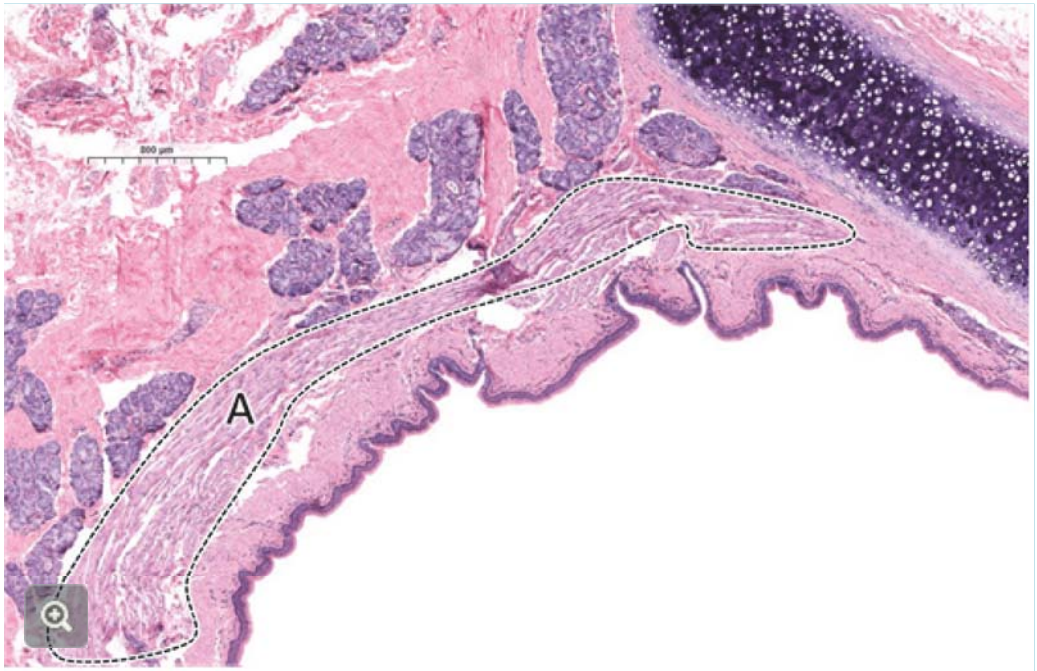
type your text here



SUBMIT

Identify structure A. Be specific.

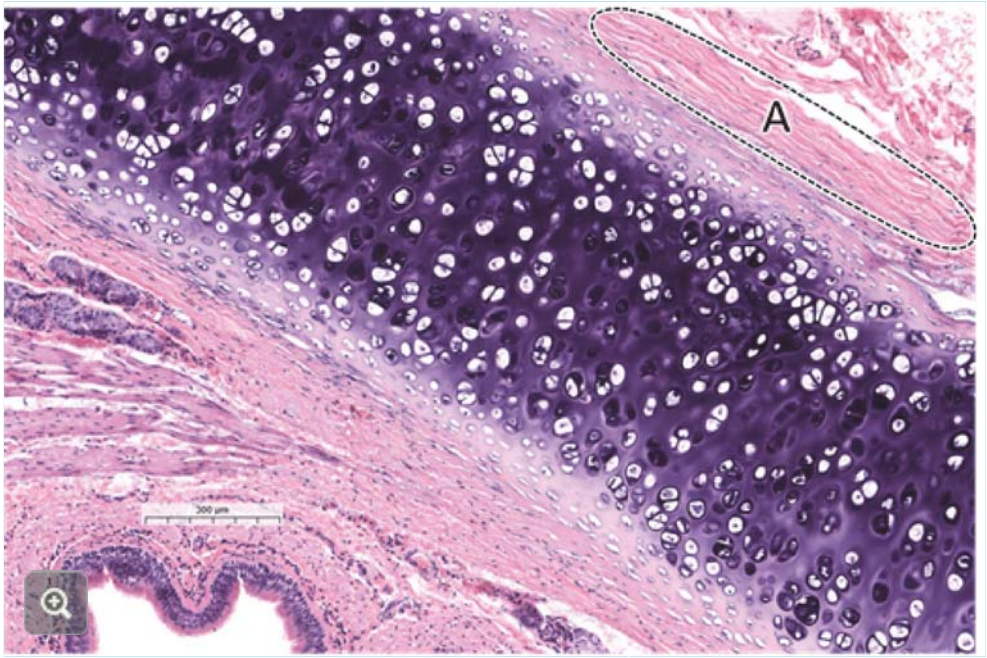
type your text here



SUBMIT

Identify layer A. Be specific.

type your text here

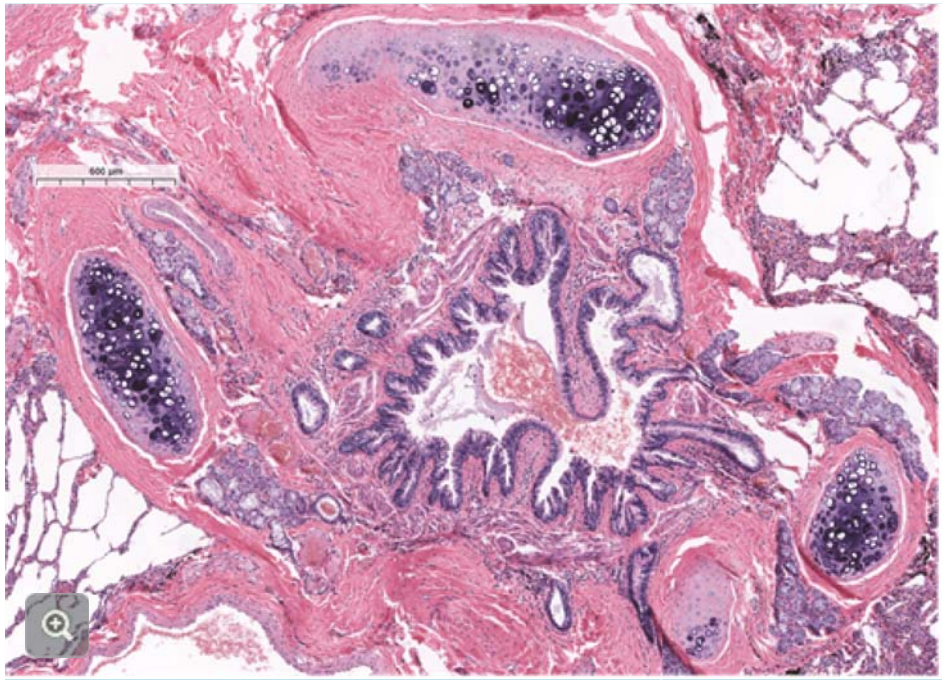


SUBMIT

H9 Question 13

What structure is seen in this image?

type your text here

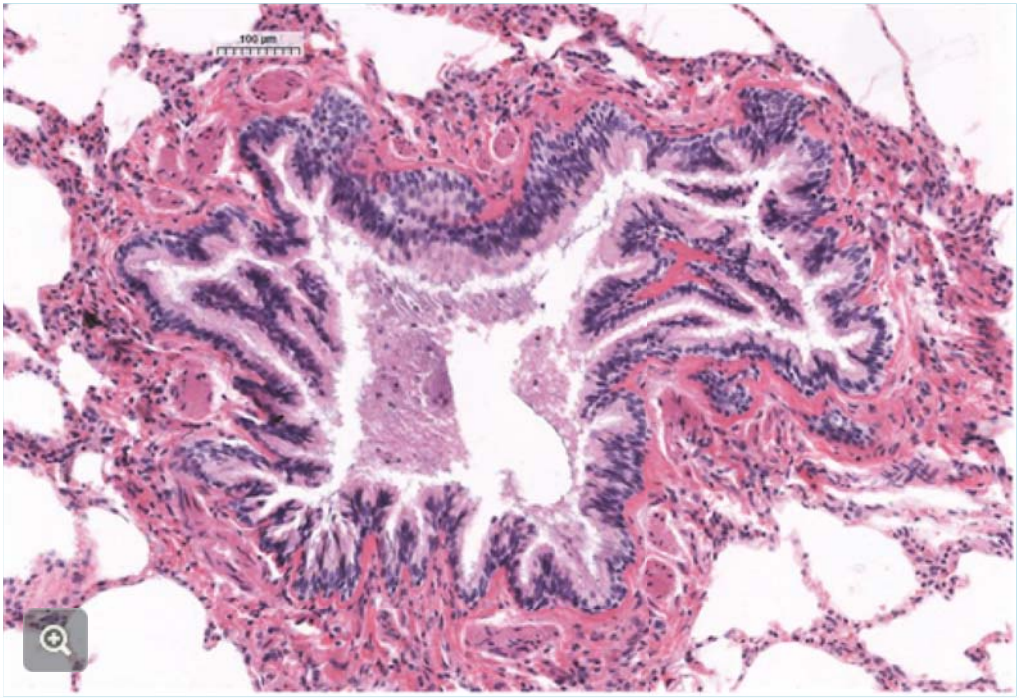


SUBMIT

H9 Question 14

What structure is seen in this image?

type your text here

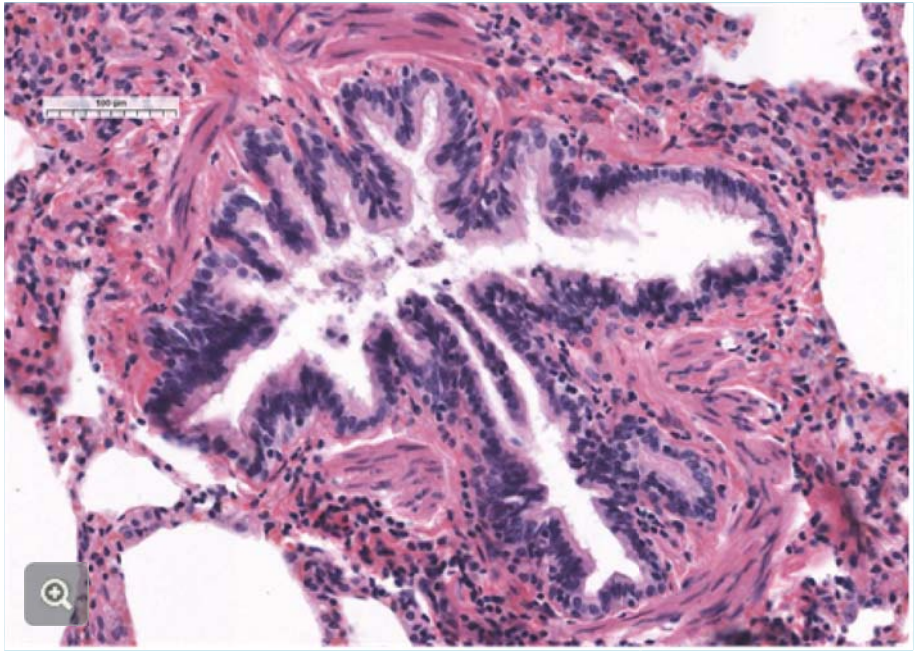


SUBMIT

H9 Question 15

What structure is seen in this image?

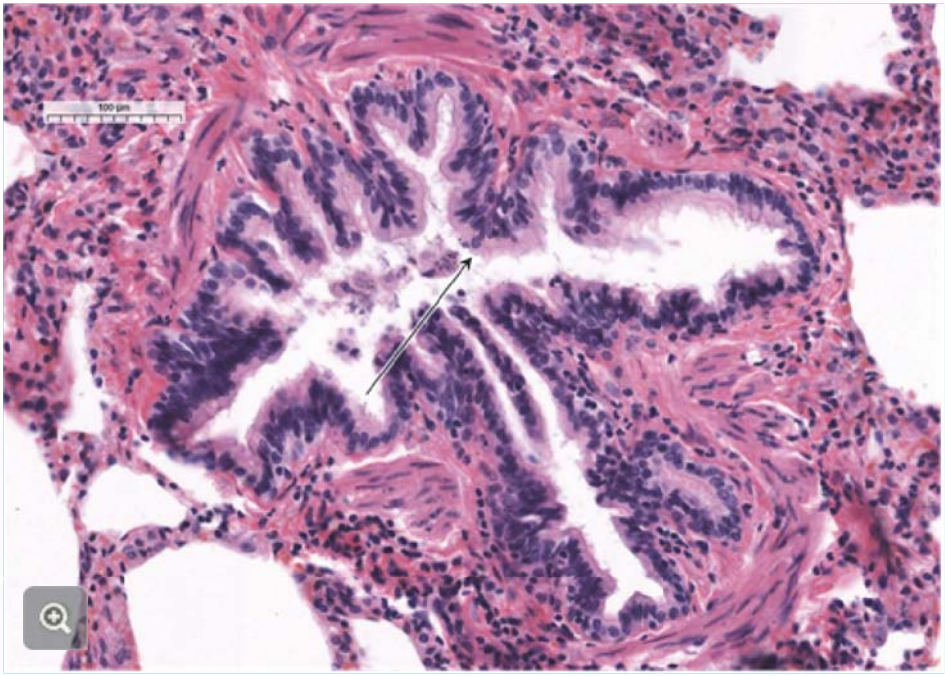
type your text here



SUBMIT

Identify the cell type indicated by the arrow.

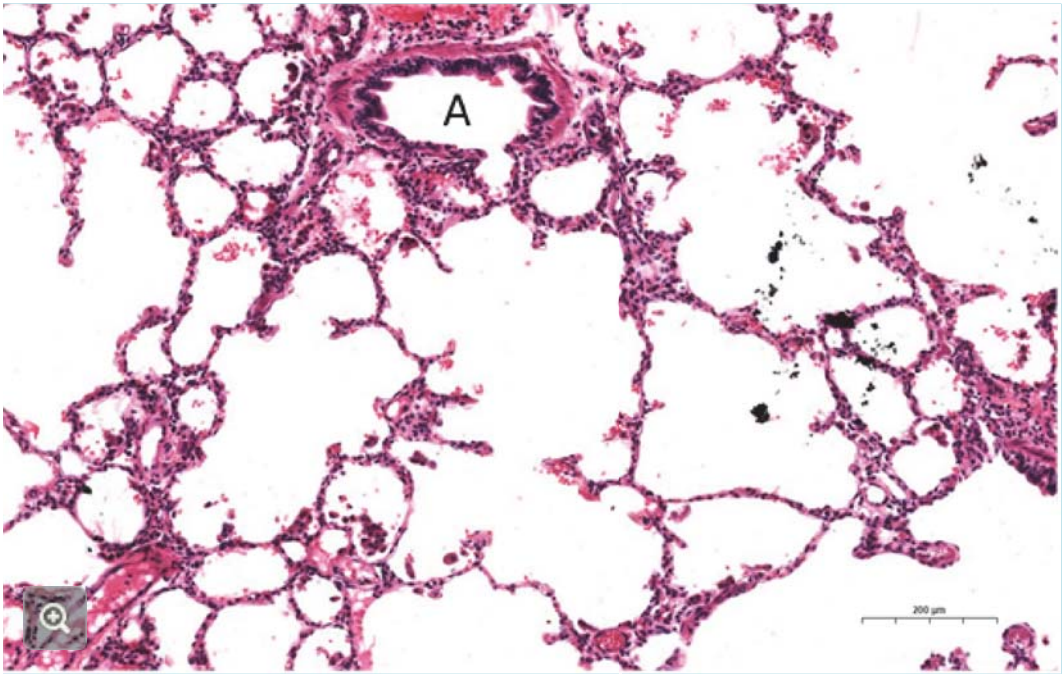
type your text here



SUBMIT

Identify structure A. Be specific.

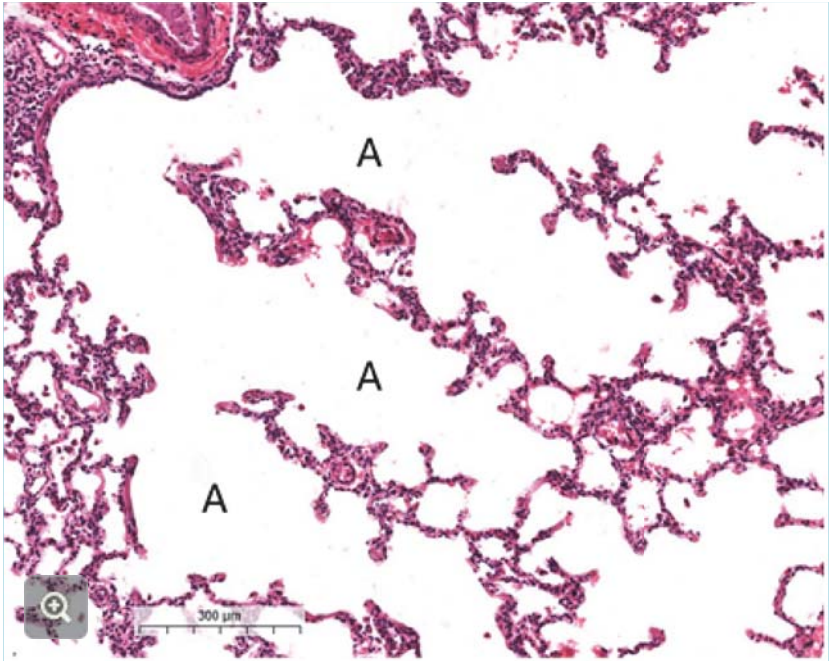
type your text here



SUBMIT

Identify structures A.

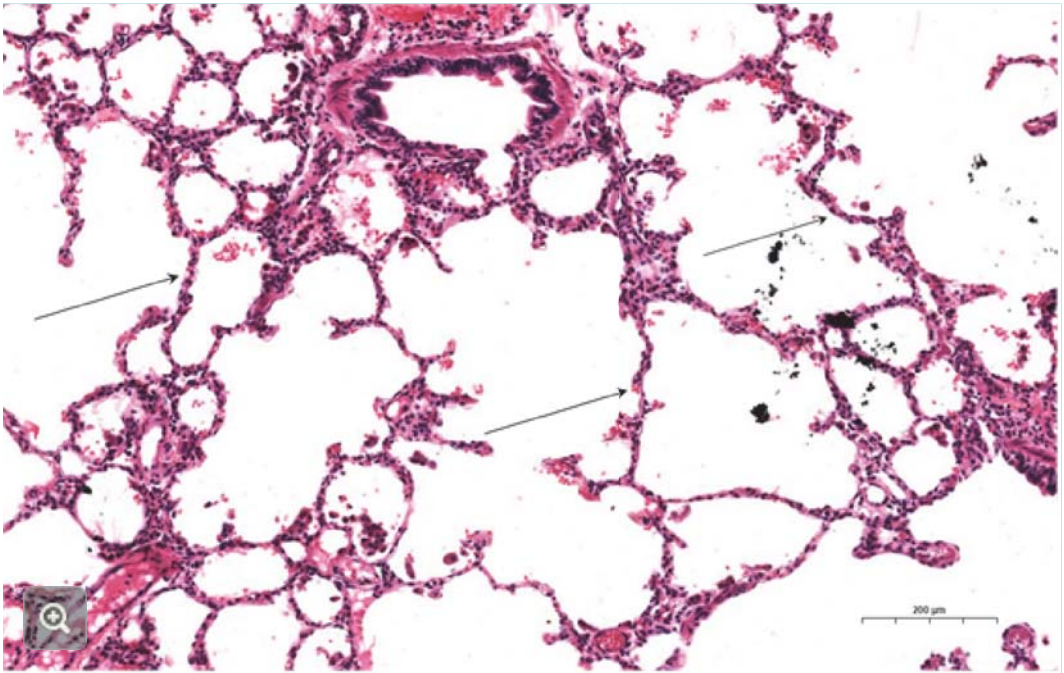
type your text here



SUBMIT

What structures are indicated by the arrows?

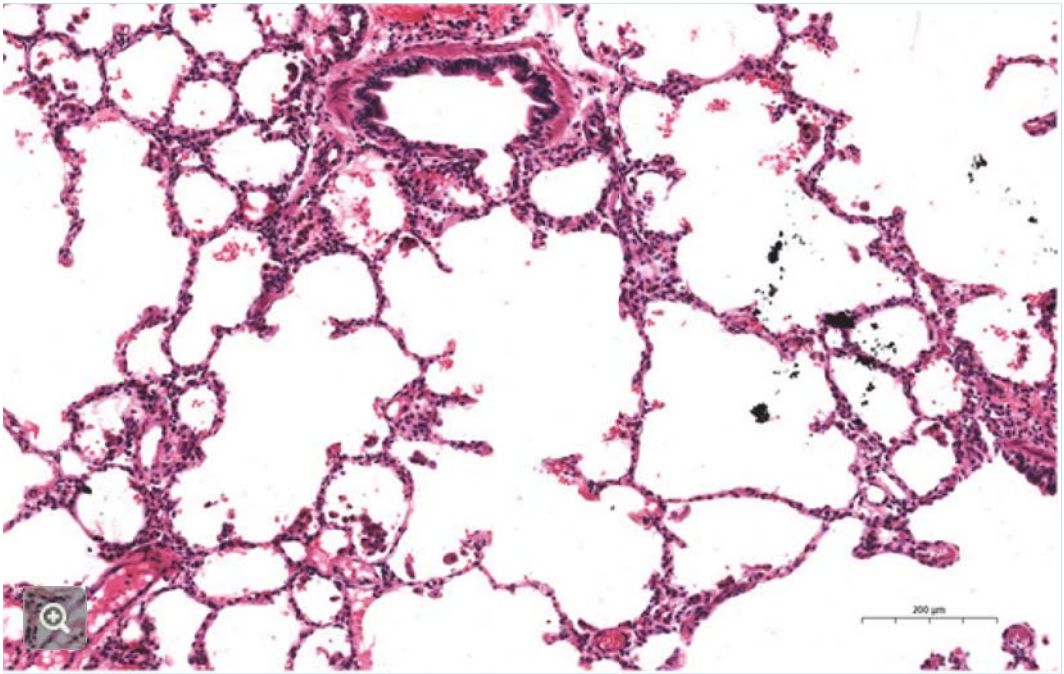
type your text here



SUBMIT

What cell dominates in this tissue, in terms of surface area? Be specific.

type your text here



SUBMIT

Congratulations on Finishing H9 The Histology of the Respiratory System!

REVIEW H9