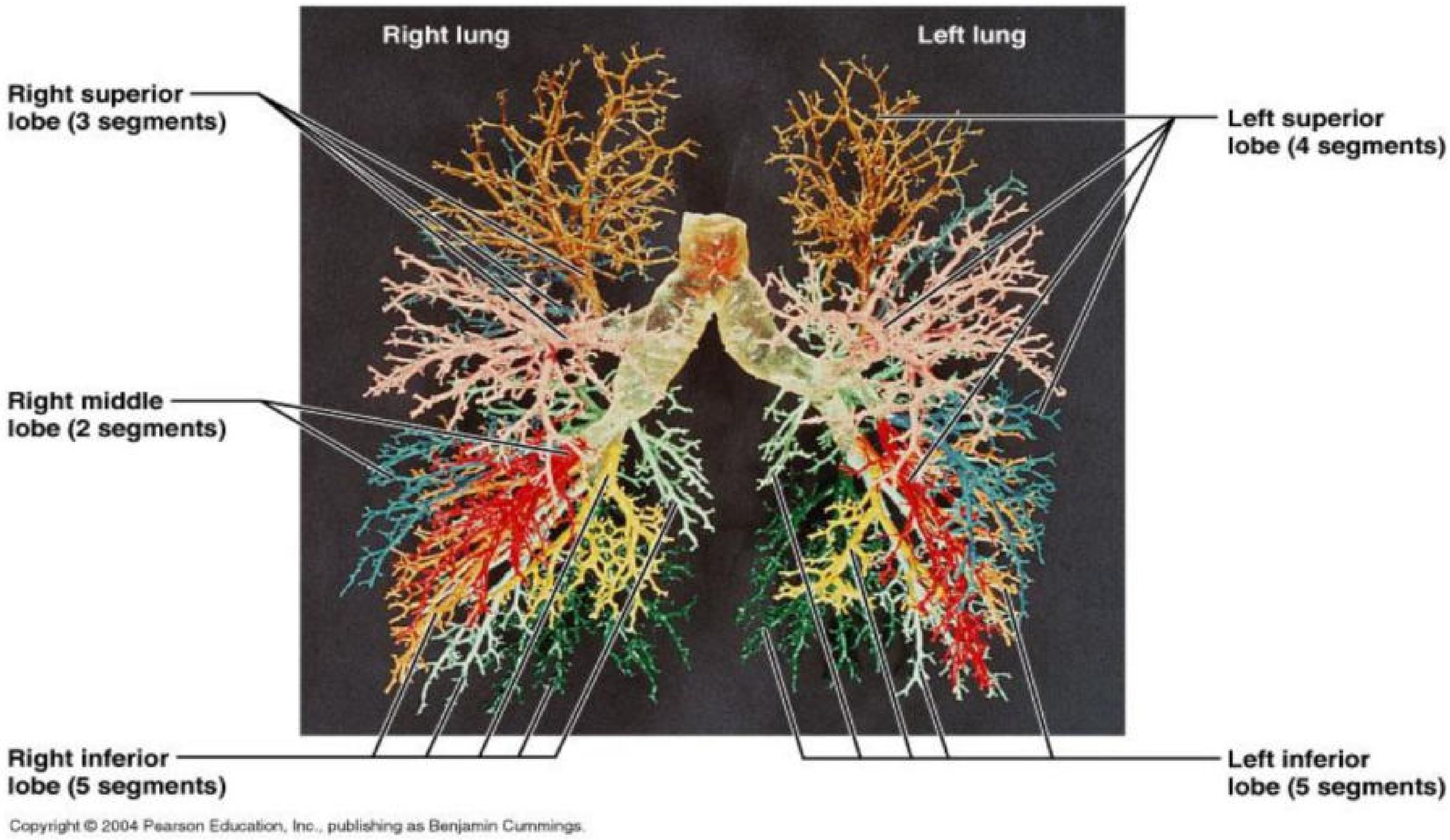
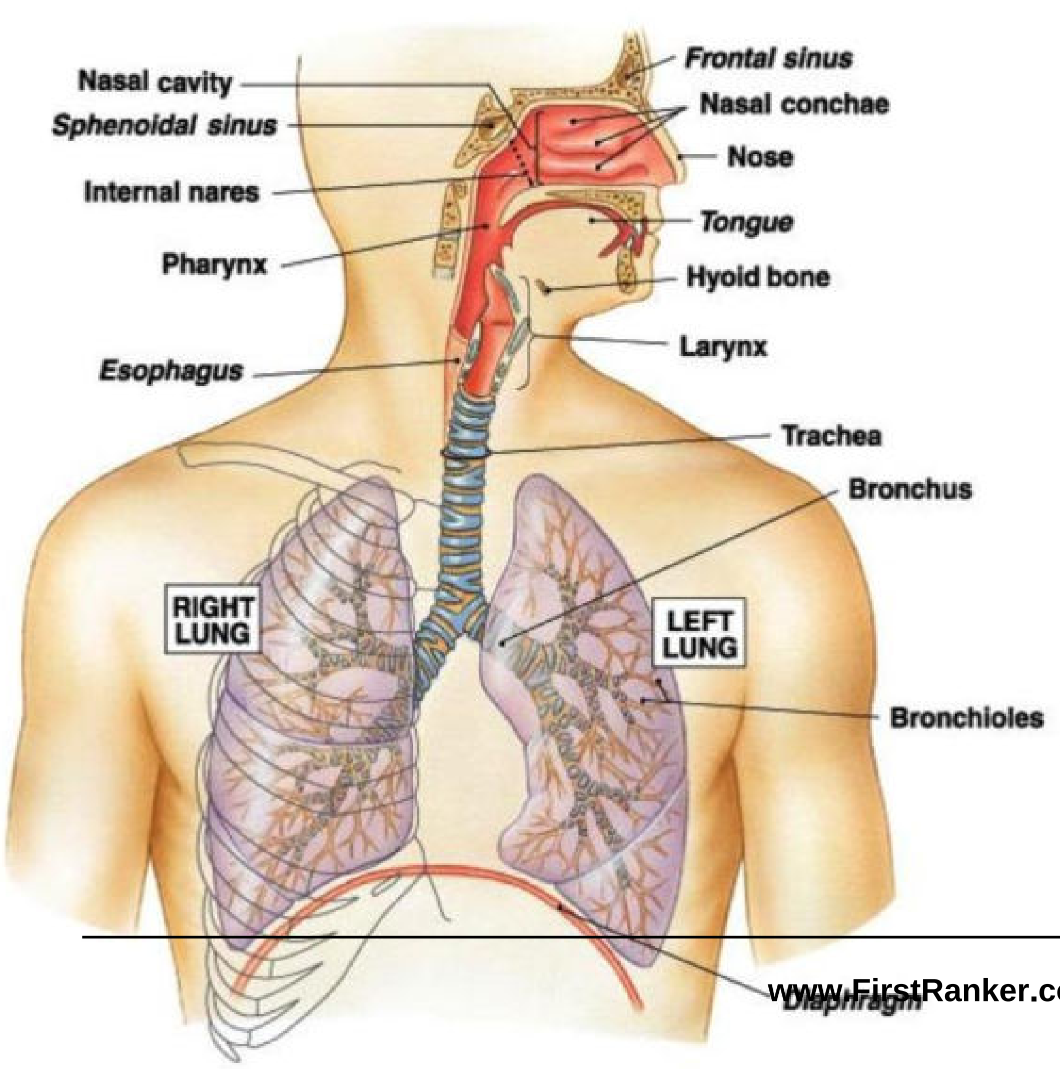
Functional anatomy of the respiratory system

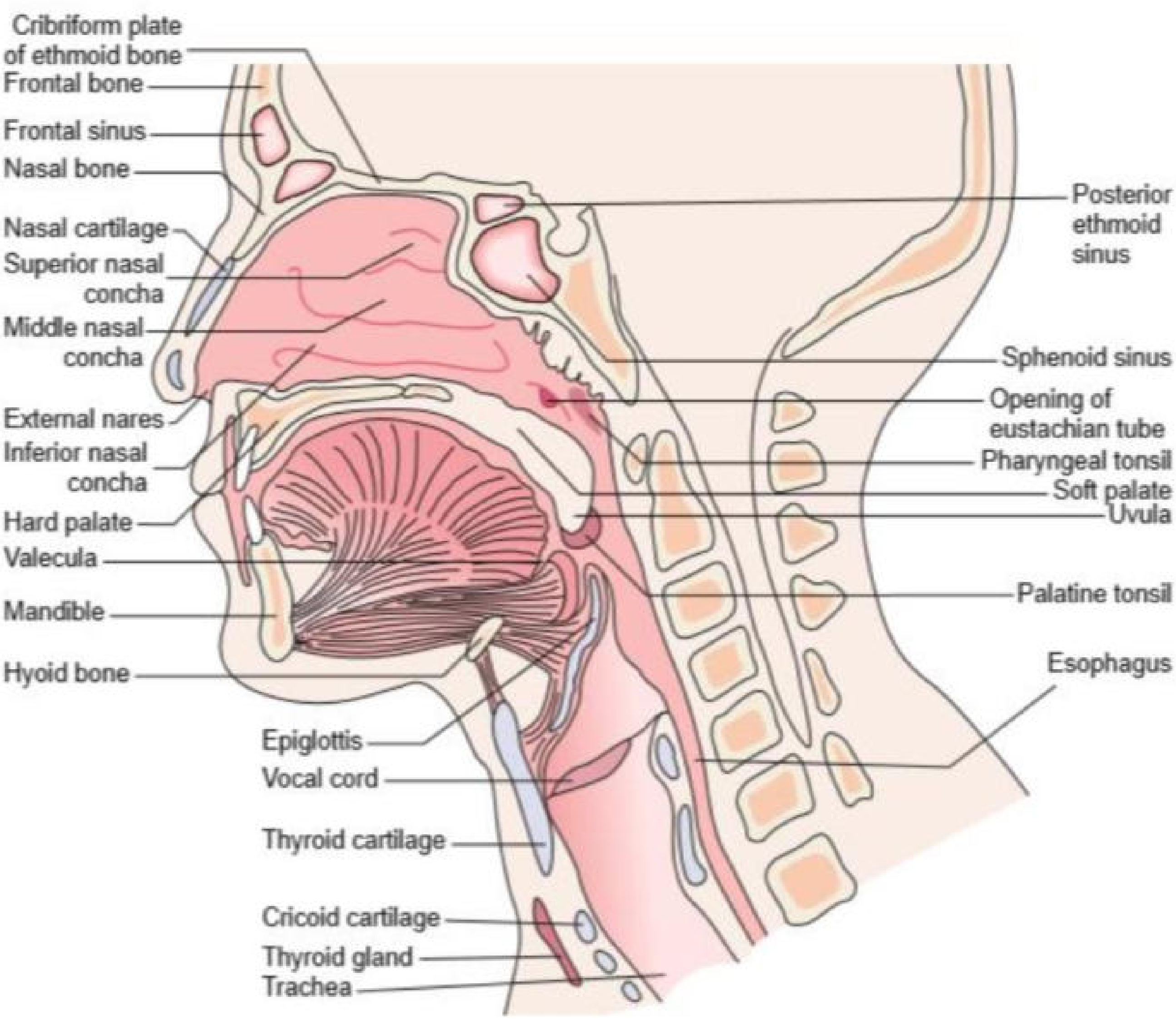


Respiratory System Divisions



- Upper Airway
  - Nose, pharynx, larynx and associated structures
- Lower Airway
  - trachea, bronchi, lungs

Midsagittal section through the upper airway



Functions of the upper airway

- Passageway for gas flow
- Filter
- Heater
- Humidification
- Sense of smell and taste
- Phonation
- Protection of lower airways

Size of Particles Entrapped in the Respiratory Passages.

No particles larger than 6 micrometers in diameter enter the lungs through the nose.
Of the remaining particles, many that are between 1 and 5 micrometers settle in the smaller bronchioles as a result of gravitational precipitation. For instance, **terminal bronchiolar disease is common in coal miners because of settled dust particles**.
Some of the still smaller particles (smaller than 1 micrometer in diameter) diffuse against the walls of the alveoli and adhere to the alveolar fluid.
But many particles smaller than 0.5 micrometer in diameter remain suspended in the alveolar air and are expelled by expiration. For instance, the **particles of cigarette smoke** are about 0.3 micrometer.
Almost none of these particles are precipitated in in the respiratory passageways before they reach the alveoli. Unfortunately, up to one third of them do precipitate in the alveoli by the diffusion process, with the balance remaining suspended and expelled in the expired air.
Many of the particles that become entrapped in the alveoli are removed by alveolar macrophages

Nasal breathing v/s oral breathing

Breathing is normally possible through either the nose or the mouth, the two alternative air passages converging in the oropharynx.

Deflection of gas into either the nasal or the oral route is under voluntary control and accomplished with the soft palate, tongue and lips.

Nasal breathing is the norm and has two major advantages over mouth breathing:

1. filtration of particulate matter by the vibrissae hairs and
2. Better humidification of inspired gas.

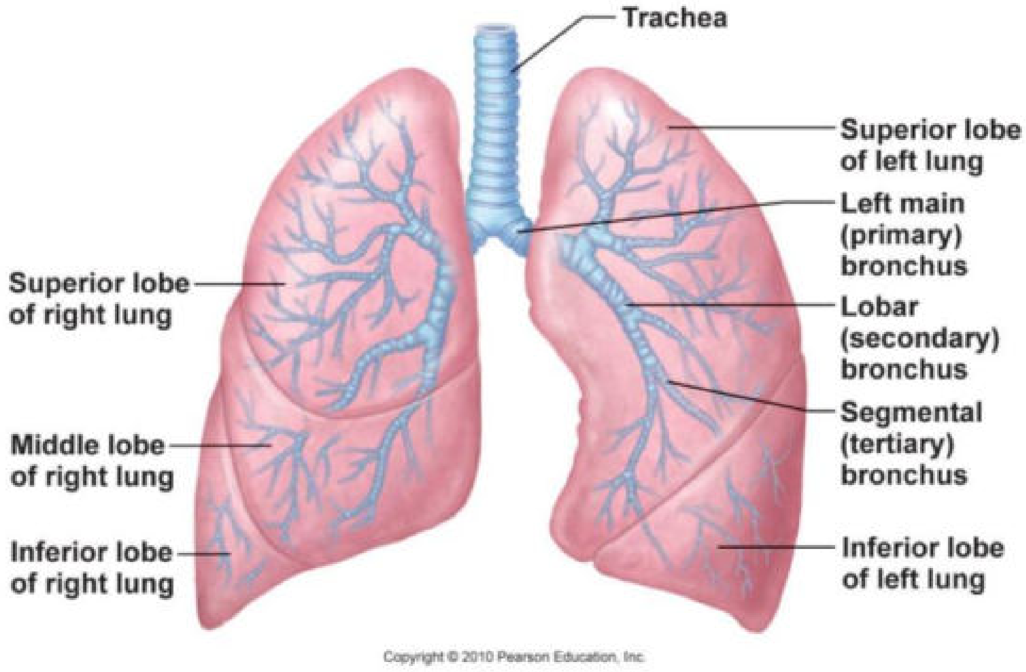
Humidification by the nose is highly efficient because the nasal septum and turbinates greatly increase the surface area of mucosa available for evaporation.

Nasal resistance to airflow when obstructed by polyps, adenoids or congestion of the nasal mucosa.

With increasing levels of exercise in normal adults, the respiratory minute volume increases, and at a level of ~35 L/min−1 the oral airway comes into play.

Lower respiratory tree

1. The airways of the tracheobronchial tree extend from the larynx down to the airways participating in gas exchange.
2. Each branching of an airway produces subsequent generations of smaller airways.
3. The first 15 generations are known as **conducting airways** because they convey gas from the upper airway to the structures that participate in gas exchange with blood.
4. The microscopic airways beyond the conducting airways that carry out gas exchange with blood are classified as **the respiratory airways.**

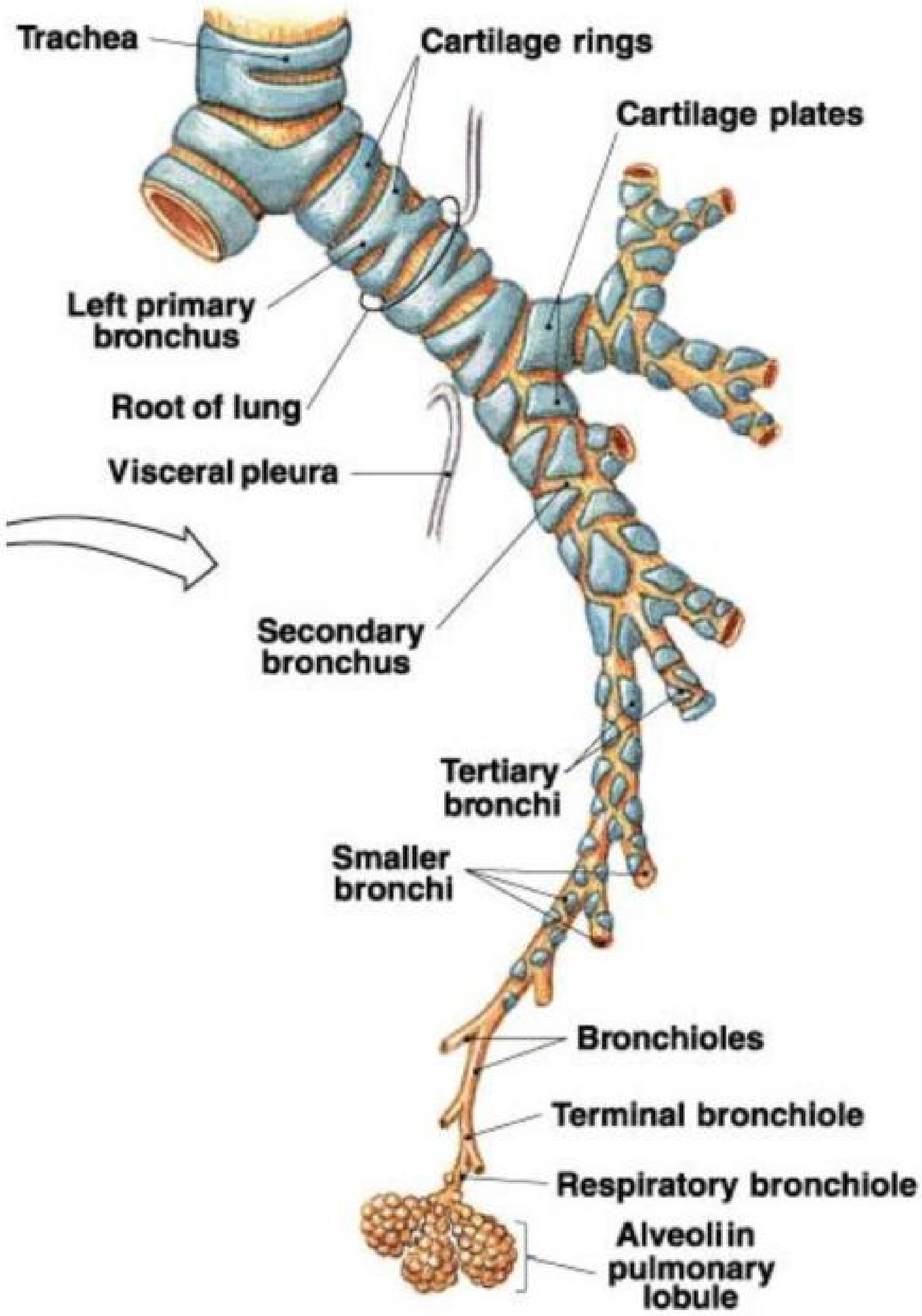


7

Tracheobronchial Tree

Conducting zone: 1st 16 generations (Trachea to terminal bronchioles)

- Passageway for air movement; **No gas exchange occurs in the conducting zone.**
- The smallest airways in the conducting zone are the terminal bronchioles.
- **Trachea and main bronchi**: Cartilage consists of U-shaped rings. **The lobar and segmental bronchi**: small plates of cartilage.
- **Bronchioles**: Cartilage disappears. *Bronchioles are suspended by elastic tissue in the lung parenchyma, and the elasticity of the lung tissue helps keep these airways open.*
- The first four generations of the conducting zone are subjected to changes in negative and positive pressures and contain cartilage to prevent airway collapse.
- The conducting zone has its own separate circulation, the bronchial circulation, which originates from the descending aorta and drains into the pulmonary veins.



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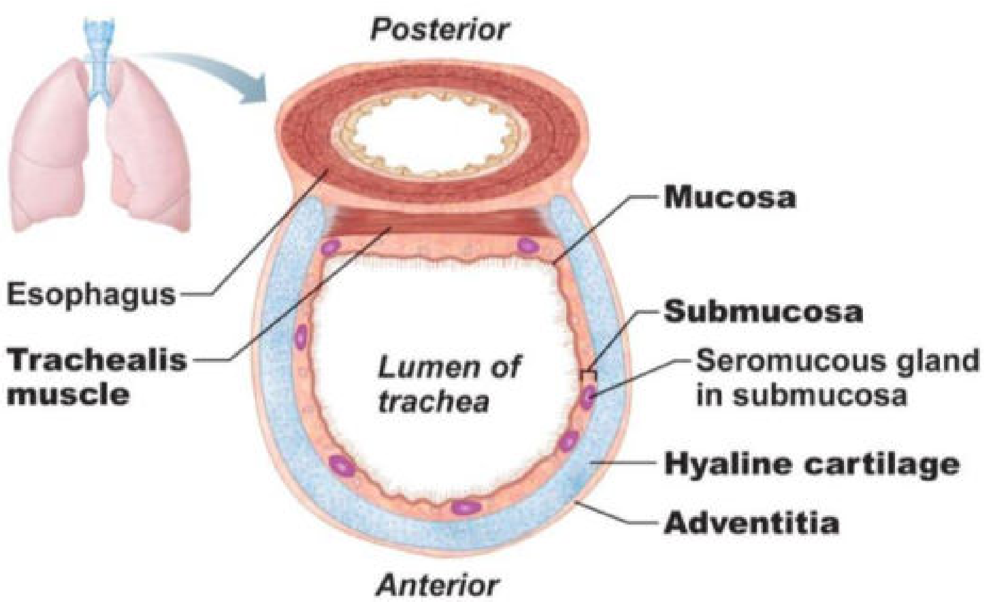
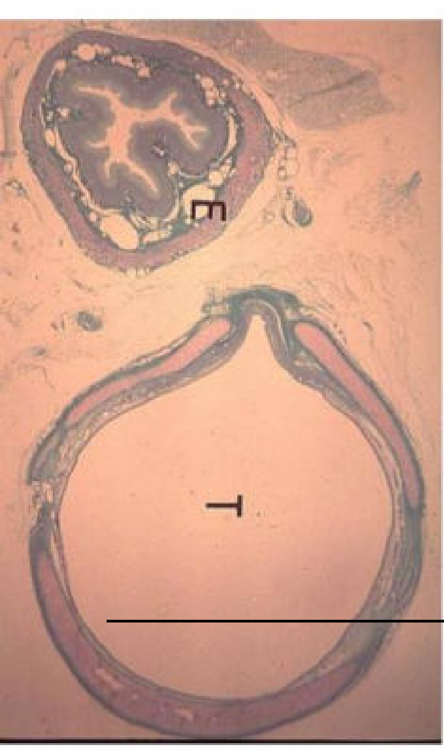
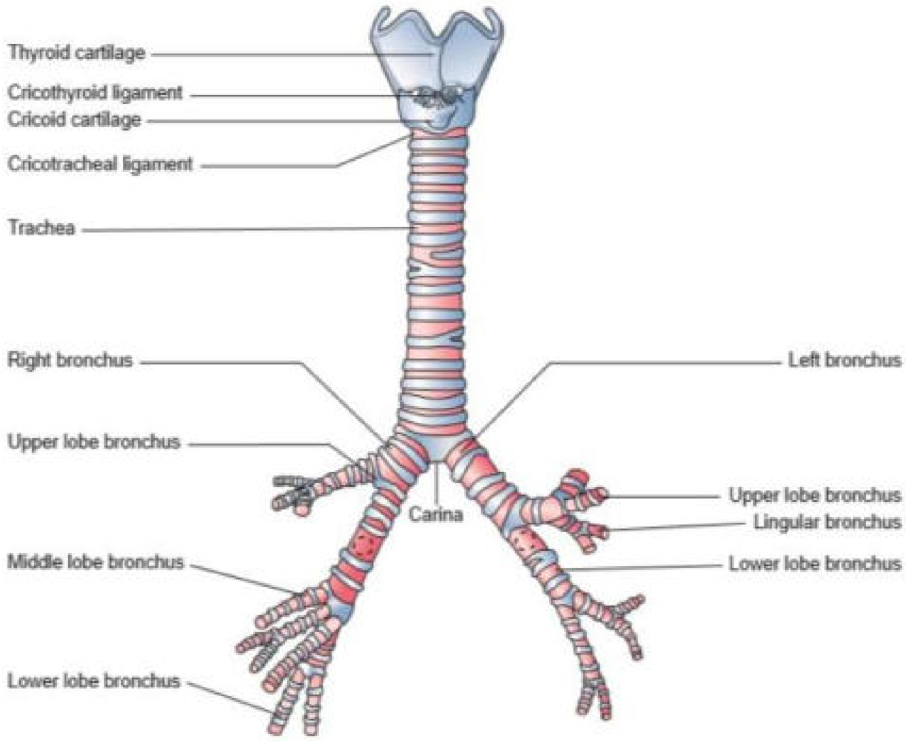
Tracheal: generation 0





<u>The normal trachea as viewed during a rigid bronchoscopy</u>. The ridges of the cartilage rings are seen anteriorly and the longitudinal fibres of the trachealis muscle are seen posteriorly, dividing at the carina and continuing down both right and left main bronchi.

Major airways of the tracheobronchial tree



The trachea bifurcates asymmetrically, and the right bronchus is wider and makes a smaller angle with the long axis of the trachea.

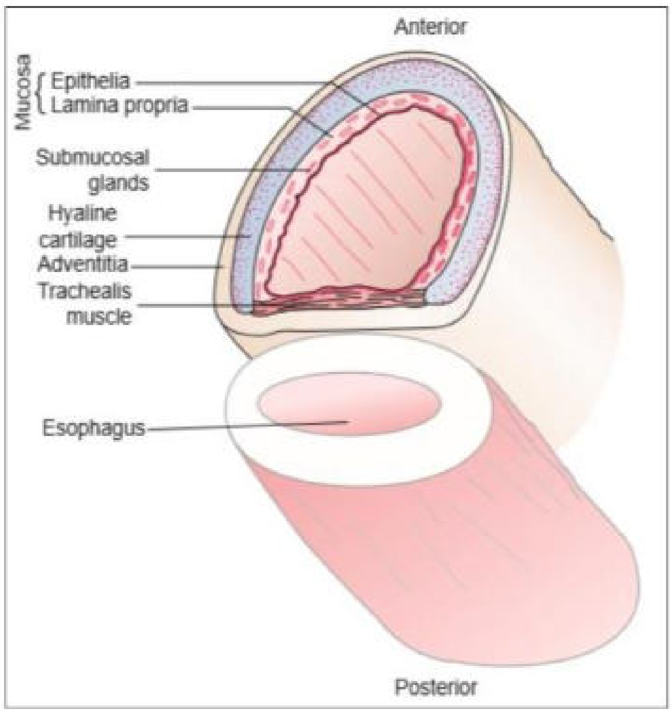
The trachea is positioned **midline** in the upper mediastinum and branches into right and left main stem bronchi.
At the base of the trachea, the last cartilaginous ring that forms the bifurcation for the two bronchi is called the **carina**.
The carina is an important landmark used to identify the level where the two main stem bronchi branch off from the trachea; this is normally at the base of the aortic arch.

Trachea

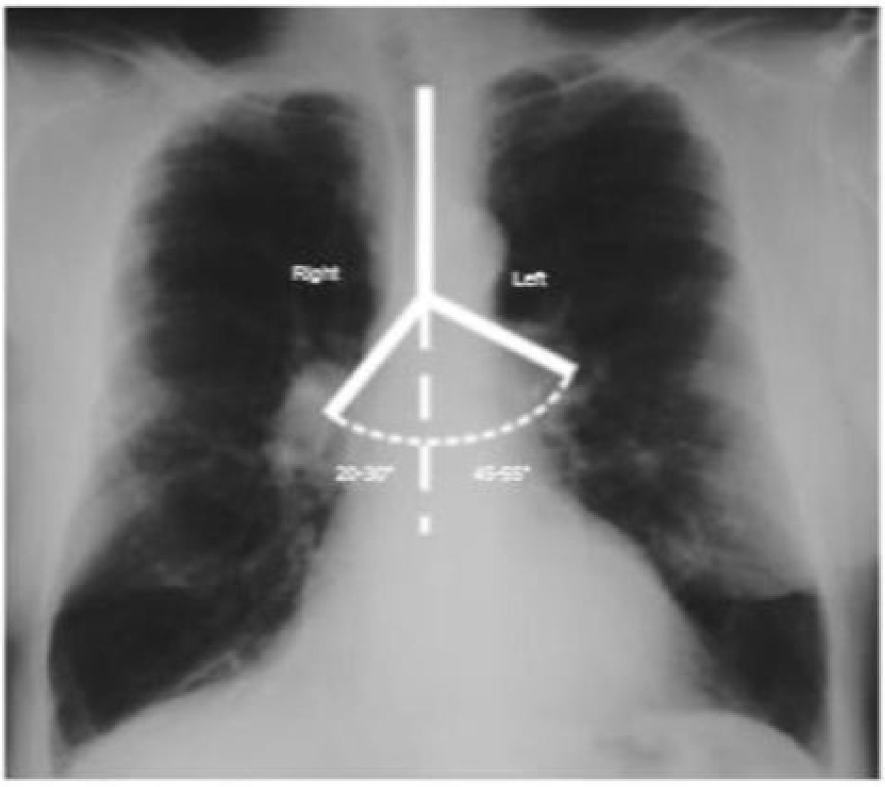
- extends from its connection to the cricoid cartilage down through the neck and into the thorax to the articulation point between the manubrium and body of the sternum (angle of Louis).
- The adult trachea is approximately 12 cm long and has an inner diameter of about 2 cm.
- The cartilaginous rings support the trachea so it does not collapse during exhalation. Some compression occurs when the pressure around the trachea becomes positive. During a strong cough, the trachea is capable of some compression and even collapse when the decreased diameter increases the linear velocity of gas flow and therefore the efficiency of removal of secretions.
- The negative pressure generated around the trachea during inhalation causes it to expand and lengthen slightly.
- The part of the trachea in the neck **is not subjected to intrathoracic pressure** changes, but it is very vulnerable to pressures arising in the neck . An external pressure of the order of **4 kPa (40 cmH2O**) is sufficient to occlude the trachea.

Cross-sectional view through the trachea and esophagus

- The outermost layer is a thin connective tissue sheath.
- Below the sheath are 16 to 20 C-shaped cartilaginous rings that provide support and maintain the trachea as an open tube.
- The inner surface of the trachea is covered with a mucous membrane.
- In the posterior wall of the trachea is a thin band of tissue, called the trachealis muscle that supports the open ends of the tracheal rings.
- The esophagus lies just behind the trachea.



Course of trachea and right and left main stem bronchi, superimposed on a standard chest radiograph



- The right bronchus branches off from the trachea at an angle of approximately 20 to 30 degrees, and the left bronchus branches with an angle of about 45 to 55 degrees.
- The lower angle branching (closer to mid-line) of the right bronchus results in a greater frequency of foreign body passage into the right lung because of the more direct pathway

The placement of an endotracheal tube through the upper airway and into the trachea is a common airway management technique to facilitate artificial airway placement.

- PROBLEM: After placement of an endotracheal tube in a patient with a 70-kg predicted body weight (PBW), it is noted that breath sounds are heard in the right chest only and that the patient's oxygenation is deteriorating. Is the airway placement the cause of the problem? How can this problem be avoided?
- ANSWER: An endotracheal tube (ET) of proper diameter should be placed in the trachea so the tip is 3 to 5 cm above the carina. If the ET is advanced too far, it often enters the right main stem bronchus because of the straighter path this bronchus offers. A right main stem intubation results in right lung ventilation only. The left lung continues to receive pulmonary blood flow but does not oxygenate adequately. To avoid this problem the ET generally should not be advanced more than 24 cm past the lips in a 70-kg PBW patient. At this point, auscultation is done with a stethoscope to confirm breath sounds in both lungs. A chest radiograph can be taken to confirm the ET position.

RULE OF THUMB : The 60-to-40 Rule

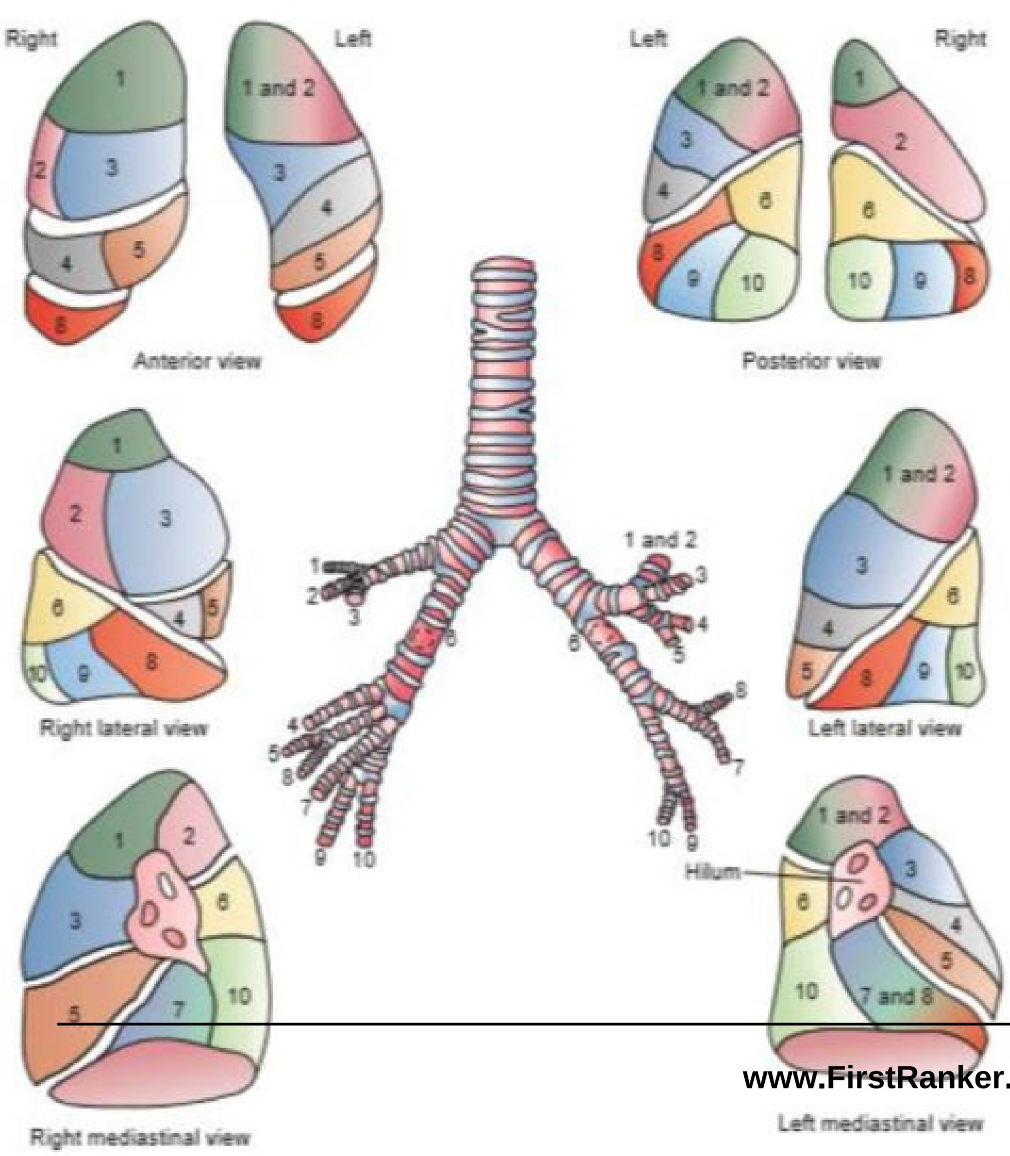
- The right lung is slightly larger than the left lung because of the location of the heart.
- The right lung has a sizable middle lobe and the left lung has a smaller lingular segment in the left upper lobe.
- For purposes of estimating the contribution of the right and left lungs to ventilation and gas exchange, the 60-to-40 rule is used.

- The right lung is assumed to provide 60% of the ventilation/gas–exchange capacity, and the left lung is assumed to provide the remaining 40%.
- If a patient requires removal of the entire left lung (pneumonectomy), a 40% decrease in lung volume would be expected.

Lobar and Segmental Pulmonary Anatomy

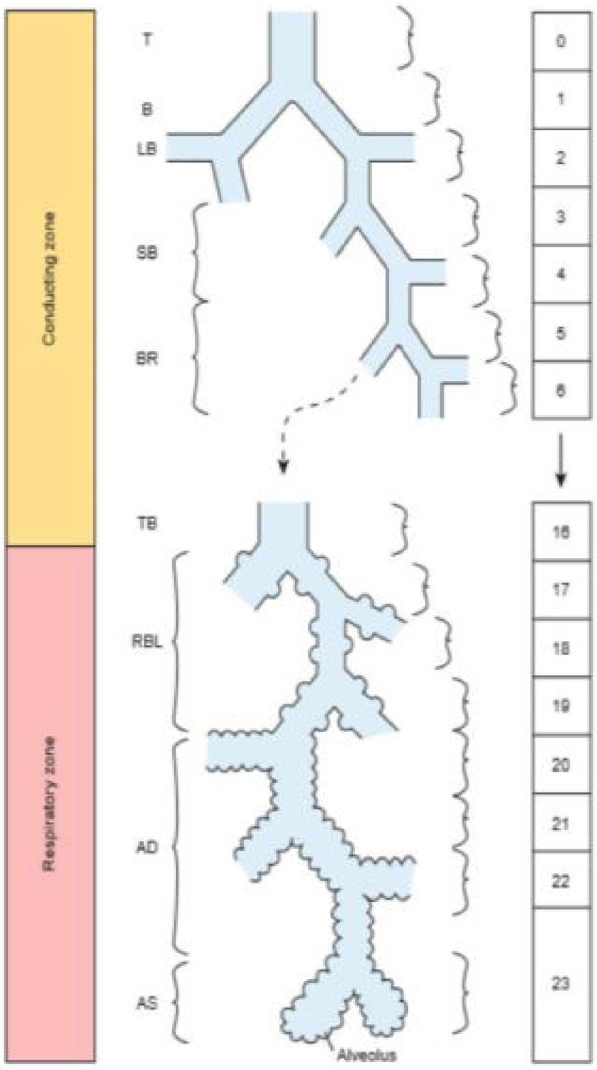
- The lungs: an apex and a base and are subdivided by fissures into lobes. The lobes are subdivided further into **bronchopulmonary segments** (functional anatomic unit of the lung
- Each segment is supplied with gas from a single segmental bronchus.
- the right lung has 10 and the left lung has 8 segments.
- The airways continue to divide as they penetrate deeper into the lungs. The segmental bronchi bifurcate into approximately 40 subsegmental bronchi, and these divide into hundreds of smaller bronchi. Thousands of bronchioles branch from the smaller bronchi. Tens of thousands of terminal bronchioles arise from the bronchioles.

Bronchopulmonary segmental divisions of the lungs



Bronchopulmonary Segments*

Segment	Number	Segment	Number
Right Upper Lobe		**Left Upper Lobe**	
Apical	1	Upper division	
Posterior	2	Apical-posterior	1 and 2†
Anterior	3	Anterior	3
Right Middle Lobe		**Lower Division (Lingula)**	
Lateral	4	Superior lingula	4
Medial	5	Inferior lingula	5
Right lower lobe		Left lower lobe	
Superior	6	Superior	6
Medial basal	7	Anterior basal	7 and 8
Anterior basal	8	Lateral basal	9
Lateral basal	9	Posterior basal	10
Posterior basal	10		



Bronchi down to generation 4 are sufficiently regular to be individually named.

Total cross-sectional area of the respiratory tract is minimal at the third generation.

The small bronchi (5-11) extend through about seven generations with their diameter falling from 3.5 to 1 mm.

At the level of the smallest true bronchi, air passages lie close to branches of the pulmonary artery in a sheath containing pulmonary lymphatics, which can be distended with oedema fluid giving rise to the characteristic 'cuffing' responsible for the earliest radiographic changes in pulmonary oedema.

These smaller bronchi rely for their patency on cartilage within their walls and on the transmural pressure gradient, which is normally positive from lumen to intrathoracic space.

Respiratory epithelium: Cell types

Ciliated Epithelial Cells:

- The most abundant cell type in the respiratory epithelium.
- In the nose, pharynx and larger airways: are pseudostratified, gradually changing bronchi: single layer of columnar cells; bronchioles : cuboidal cells and finally type I alveolar epithelial cells.
- are characterized by the presence of around 300 cilia per cell.
- The ratio of secretory to ciliated cells in the airway decreases in more distal airways from (equal in the trachea and three quarters ciliated in the bronchioles).

Goblet Cells : A density of approximately 6000 per mm^2 (in the trachea) and produce the thick layer of mucus that lines all but the smallest conducting airways.

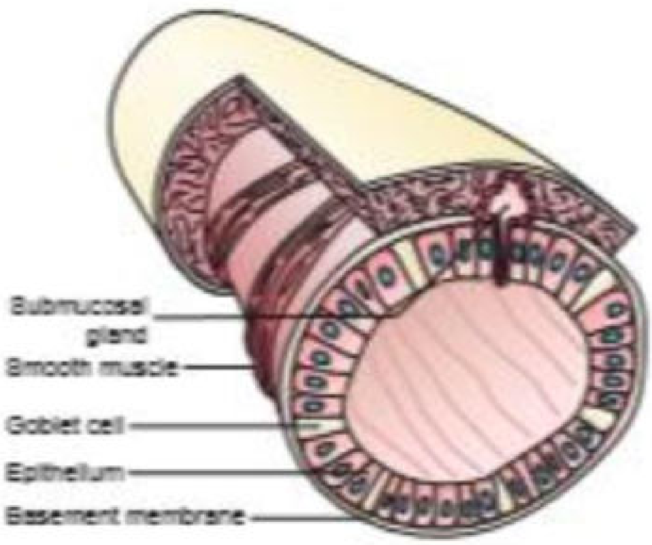
Submucosal Secretory Cells

- Submucosal glands occur in the larger bronchi and in the trachea (10 submucosal openings per mm^2).
- Comprise both serous cells (gland acinus) and mucous cells (closer to the collecting duct).
- The serous cells have the highest levels of membrane-bound cystic fibrosis transmembrane conductance regulator in the lung, Antiprotease enzymes and a variety of other proteins of uncertain function.

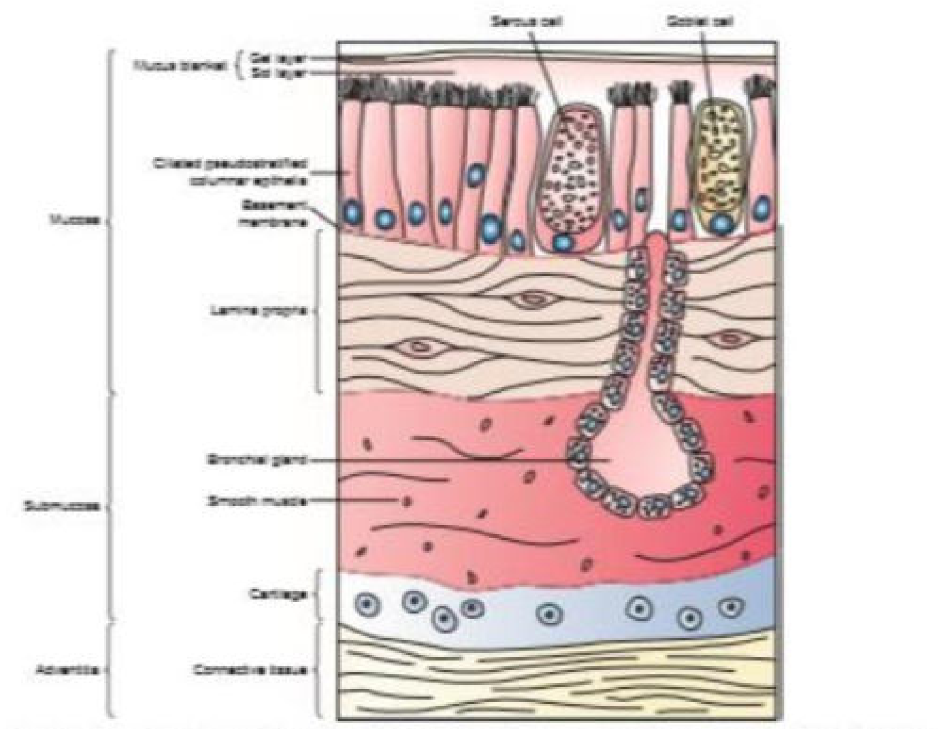
Neuroepithelial Cells

- found throughout the bronchial tree, (larger numbers in the terminal bronchioles).
- found individually or in clusters.
- Present in foetal lung tissue in a greater number (might control lung development).

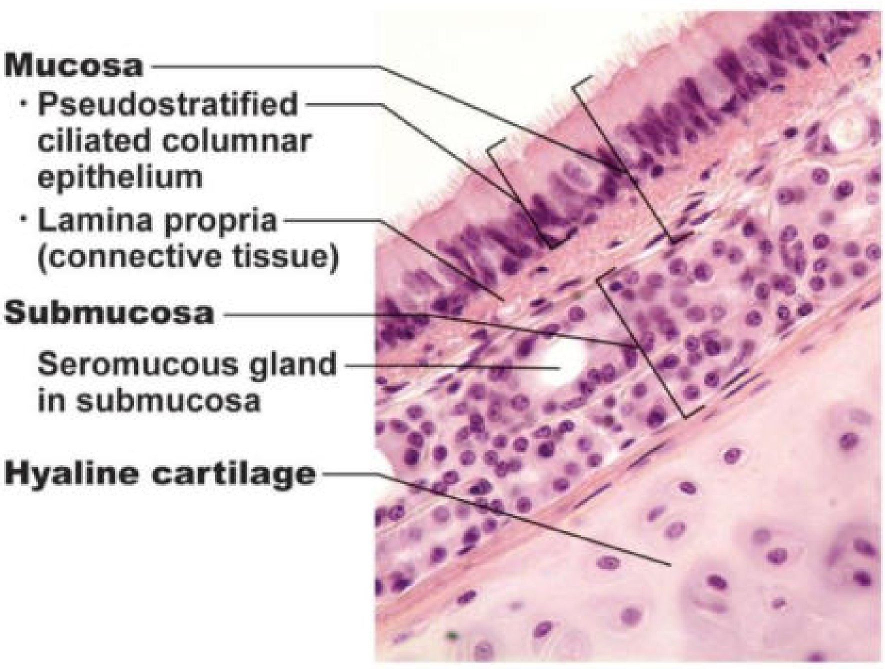
Cross-sectional view through a bronchiole



Microscopic view of mucous membrane



Tracheal Anatomy



(b) Photomicrograph of the tracheal wall (320x)

(c) Scanning electron micrograph of cilia in the trachea (2500x)

Under the electron microscope, the surface of the mucus membrane looks like a “shag carpet” of cilia with approximately 1 to 2 billion cilia per square centimeter.

- The cross-sectional area of the conducting system increases exponentially. At the level of the terminal bronchioles, the cross-sectional area is approximately 20 times greater than that at the trachea.
- Increased cross-sectional area reduces the velocity of gas flow during inspiration.
- At the level of the terminal bronchiole, its average velocity falls to speed of diffusing gas molecules which is physiologically important for two reasons.

1. **Laminar flow develops minimizing resistance in the small airways and decreases the work associated with inspiration.**
2. **Low gas velocity facilitates rapid mixing of alveolar gases. This mixing provides a stable partial pressure of O_2 and CO_2 in the alveolar environment that supports stable diffusion and gas exchange.**

Mucus secretion…

- The various secretory cells (primarily goblet cells) of the mucosa and bronchial glands of the submucosa contribute to the production of mucus.
- Approximately 100 ml of mucus per day is produced. Most of the mucus formed in the larger airways is produced by the bronchial glands.
- The amount and composition of mucus produced can increase and change with airway irritation and diseases such as chronic bronchitis and asthma.
- Mucus is spread over the surface of the mucus membrane to a depth of approximately 7 µm and is propelled by the ciliated epithelia toward the pharynx.
- The outer layer of mucus is more gelatinous and is called the **gel** layer. The inner layer is much more fluid-like and is referred to as the **sol** layer.
- The mucus normally produced is a nearly clear fluid with greater viscosity than water. It is a mixture of 97% water and 3% solute.
- The solute portion is produced primarily by goblet cells and bronchial glands; it is called mucin and is composed of protein and minerals. The glycoprotein, lipid, and water content of mucus provide its viscoelastic gel properties.

Mucus secretion…

- Mucus functions to protect the underlying tissue.
- It helps prevent excessive amounts of water moving into and out of the epithelia.
- It shields the epithelia from direct contact with potentially toxic materials and microorganisms.
- It acts like sticky flypaper to trap particles that make contact with it. This makes mucus an important part of the pulmonary defenses.
- The production of mucus is stimulated by local mechanical and chemical irritation, release of proinflammatory mediators (e.g., cytokines), and parasympathetic (vagal) stimulation.

Ciliary epithelium

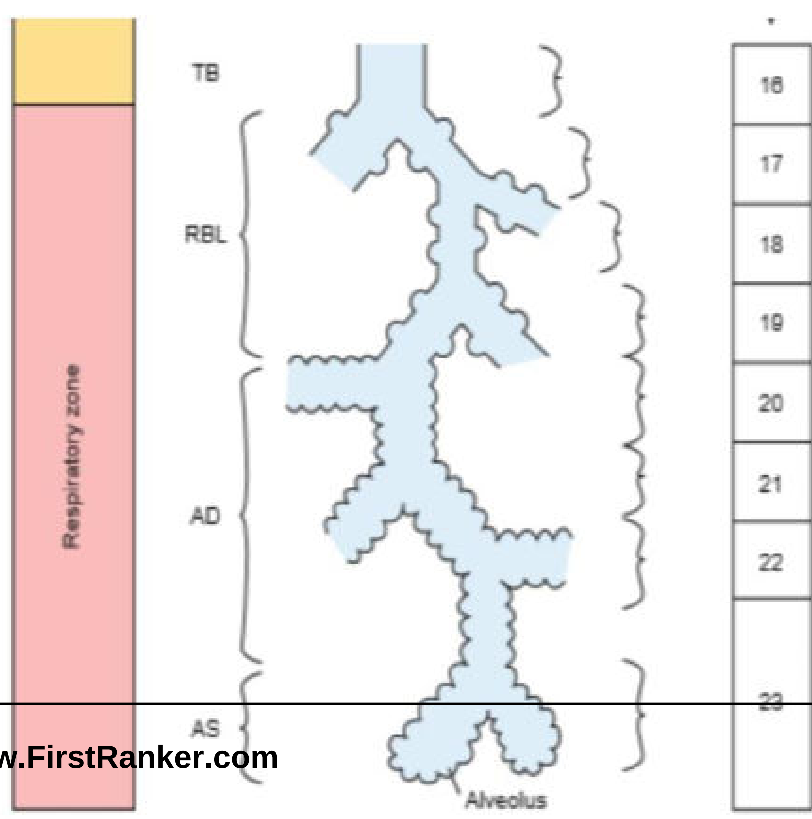
Ciliated cells are found in the nasal cavity and all the airways from the larynx to the terminal bronchioles.
Each of the pseudostratified cells possesses approximately 200 cilia on its luminal surface.
Each cilium is an extension of the cell with an average length of about 6 µm and diameter of about 0.2 µm.
The cilia “stroke” at a rate of approximately 15 times per second, producing a sequential motion of the cilia called a metachronal wave whose “wavelength” is approximately 20 µm and propels surface material in a specific direction.
Ciliary beating can be effectively slowed or stopped if the viscosity of the sol layer is increased by exposure to dry gas.
Ciliary motion is also slowed or stopped after exposure to smoke, high concentrations of inhaled O_2, and drugs such as atropine.

Bronchioles (Generations 12 to 14)

- The internal diameter is ~1 mm.
- **Patency** : Cartilage disappears from the airway wall below this level . The air passages are directly embedded in the lung parenchyma, the elastic recoil of which holds the air passages open .
- The total cross-sectional area increases which makes the flow resistance of these smaller air passages (less than 2 mm diameter) negligible under normal conditions.
- The resistance of the bronchioles can increase to very high values when their strong helical muscular bands are contracted.
- The conducting airways derive their nutrition from the bronchial circulation and are influenced by systemic arterial blood gas levels.
- The acinar airways and rely upon the pulmonary circulation for their nutrition.

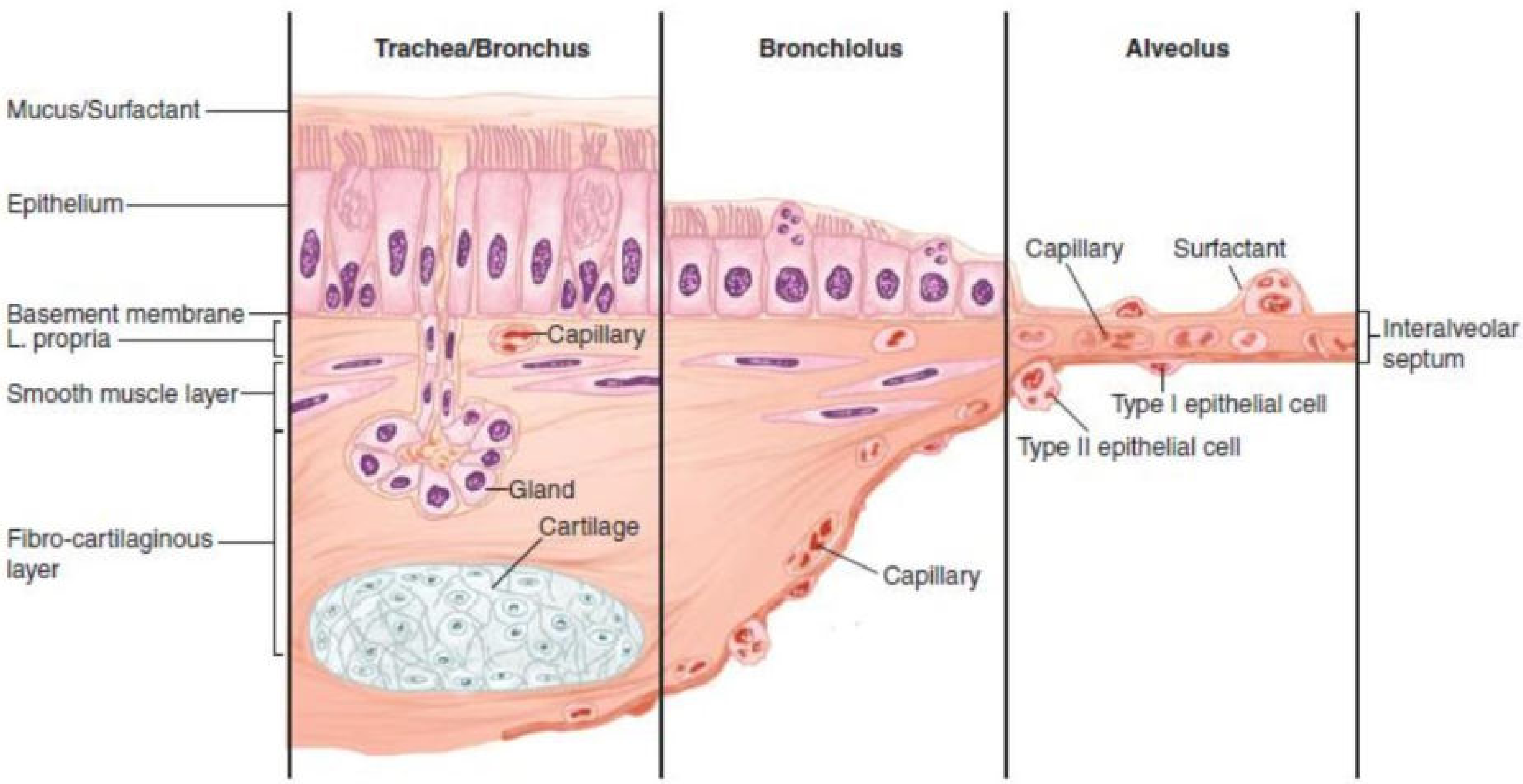
Transition to Respiratory Bronchioles (Generations 15 to 18)

- The functions of the air passages are solely conduction and humidification. Beyond this point there is a gradual transition from conduction to gas exchange.
- In the four generations of respiratory bronchioles there is a gradual increase in the number of alveoli in their walls.
- Like the earlier bronchioles, the respiratory bronchioles are embedded in lung parenchyma.
- There is no significant change in calibre of advancing generations of respiratory bronchioles (~0.4 mm diameter).



Alveolar Ducts (Generations 19 to 22) and Alveolar Sacs (Generation 23)

- Arise from the terminal respiratory bronchiole, from which they differ by having no walls other than the mouths of mural alveoli (approximately 20 in number).
- The alveolar septa comprise a series of rings forming the walls of the alveolar ducts and containing smooth muscle.
- Approximately 35% of the alveolar gas resides in the alveolar ducts and the alveoli that arise directly from them.
- The last generation of the air passages differs from alveolar ducts solely because they are blind.
- It is estimated that about 17 alveoli arise from each alveolar sac and account for about half of the total number of alveoli which occurs in larger airways. Millions of alveolar ducts branch off the respiratory bronchioles.
- Alveolar ducts are tiny airways only 0.3 mm in diameter, and their walls are composed entirely of alveoli.
- Each alveolar duct ends in a cluster of alveoli, which is frequently referred to as an alveolar sac.
- Each alveolar sac opens into about 16 or 17 alveoli, and about one-half the total number of alveoli are found in this region.



Cellular transition from conducting airway to the alveolus. The epithelial layer transitions from pseudostratified layer with submucosal glands to a cuboidal and the to a squamous epithelium. The underlying mesynchyme tissue and capillary structure also changes with the airway transition. The cells of the respiratory mucosa change as they progress into the smaller airways. As the thickness of the airway walls decreases, bronchial glands become fewer in number. At the bronchiolar level, the number of ciliated cells decreases.

Transition from conducting airway to the alveolus

- As the conducting airway transitions to terminal and transitional bronchioles, the histological appearance of the conducting tubes change.
- Secretory glands are absent from the epithelium of the bronchioles and terminal bronchioles, smooth muscle plays a more prominent role and cartilage is largely absent from the underlying tissue.
- **Clara cells, nonciliated** cuboidal epithelial cells that secrete important defense markers and serve as progenitor cells after injury, make up a large portion of the epithelial lining in the latter portions of the conducting airway

Epithelial cells in the conducting airway secrete a variety of molecules that aid in lung defense: Secretory immunoglobulins (IgA), collectins (including surfactant protein (SP) –A and SP-D), defensins and other peptides and proteases, reactive oxygen species, and reactive nitrogen species.

These secretions can act directly as antimicrobials to help keep the airway free of infection.

Airway epithelial cells secrete a variety of chemokines and cytokines that recruit traditional immune cells and other immune effector cells to site of infections.

The smaller particles that make it through the upper airway, ~2–5 µm in diameter, generally fall on the walls of the bronchi as the airflow slows in the smaller passages.
There they can initiate reflex bronchial constriction and **coughing.**

Circulation in lung

- **The conducting zone** has its own separate circulation, the bronchial circulation, which originates from the descending aorta and drains into the pulmonary veins.
- The respiratory zone has its own separate and distinct circulation, **the pulmonary circulation**.
- The lungs have the most extensive capillary network of any organ in the body. Pulmonary capillaries occupy 70% to 80% of the alveolar surface area.
- The pulmonary circulation receives all of the cardiac output and, therefore, blood flow is high.
- One pulmonary arterial branch accompanies each airway and branches with it.
- Red blood cells can pass through the pulmonary capillaries in less than 1 second.

Smooth muscle of the airways

- The smooth muscle of the airways varies in location and structure. In the large airways (e.g., the trachea), smooth muscle is bundled in sheets. In smaller airways, smooth muscle forms a helical pattern that wraps the airway in bundles in decreasing quantities as the airways branch and become smaller.
- Muscle fibers crisscross and spiral around the airway walls. This placement reduces the diameter of the airway and shortens it when the muscle contracts.
- This pattern of smooth muscle continues but thins out on reaching the smallest bronchioles.
- The tone of the smooth muscle is increased and results in bronchospasm by the activity of the parasympathetic nervous system (release of acetylcholine) and proinflammatory mediator release from mast cells, inflammatory cells, and neuroendocrine cells.

Nervous and Local Control of the Bronchiolar Musculature

The walls of the bronchi and bronchioles are innervated by the autonomic nervous system.

Nerve cells in the airways sense mechanical stimuli or the presence of unwanted substances in the airways such as inhaled dusts, cold air, noxious gases and cigarette smoke.

These neurons can signal the respiratory centers to contract the respiratory muscles and initiate sneeze or cough reflexes.

The receptors show rapid adaptation when they are continuously stimulated to limit sneeze and cough under normal conditions.

— "Sympathetic" Dilation of the Bronchioles. Direct control of the bronchioles by sympathetic nerve fibers is relatively weak because few of these fibers penetrate to the central portions of the lung. However, the bronchial tree is very much exposed to norepinephrine and epinephrine released into the blood by sympathetic stimulation of the adrenal gland medullae. Both these hormones, especially epinephrine because of its greater stimulation of beta-adrenergic receptors, cause dilation of the bronchial tree.

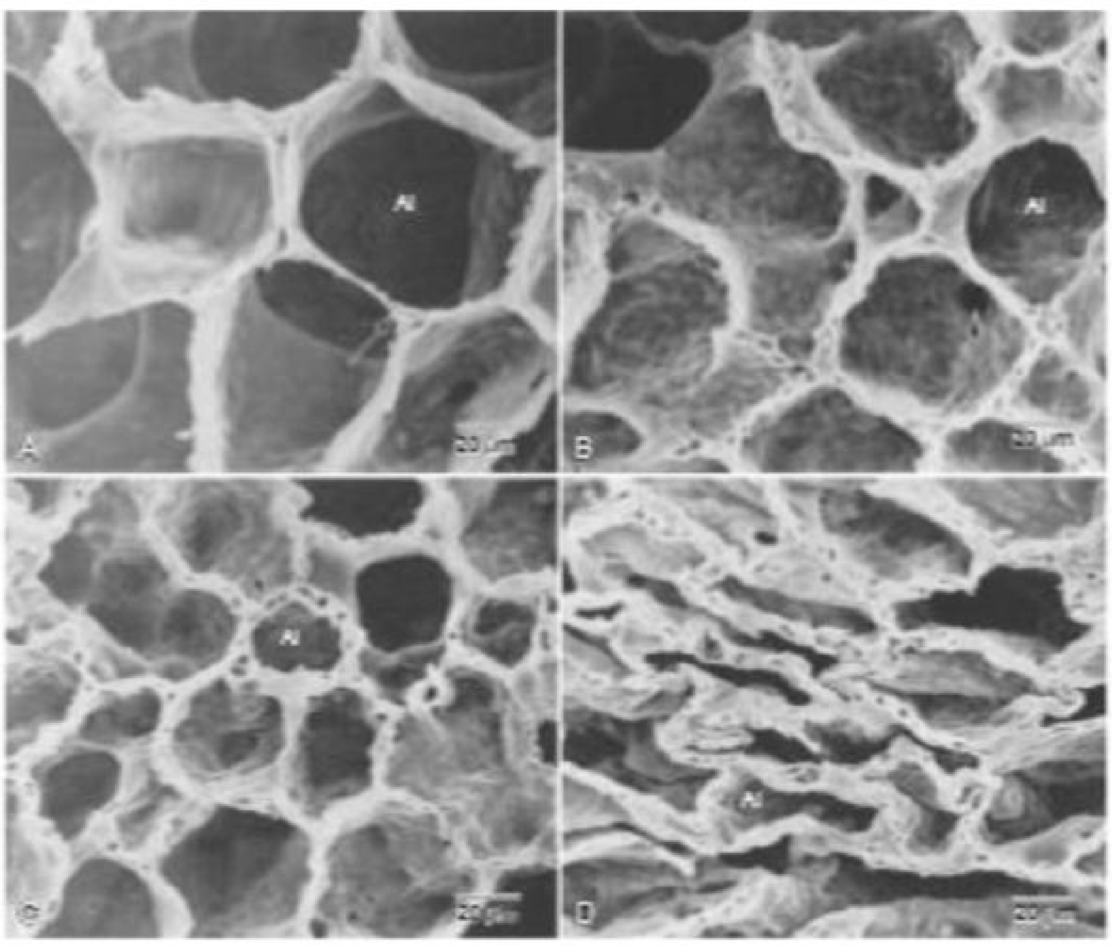
Parasympathetic Constriction of the Bronchioles. A few parasympathetic nerve fibers derived from the vagus nerves penetrate the lung parenchyma. These nerves secrete acetylcholine and, when activated, cause mild to moderate constriction of the

Local Control of the Bronchiolar Musculature

- Local Secretory Factors Often Cause Bronchiolar Constriction.
- Several substances formed in the lungs are often quite active in causing bronchiolar constriction.
- Two of the most important of these are histamine and slow reactive substance of anaphylaxis. Both of these are released in the lung tissues by mast cells during allergic reactions, especially those caused by pollen in the air.
- Therefore, they play key roles in causing the airway obstruction that occurs in allergic asthma; this is especially true of the slow reactive substance of anaphylaxis.
- The same irritants that cause parasympathetic constrictor reflexes of the airways—smoke, dust, sulfur dioxide, and some of the acidic elements in smog—often act directly on the lung tissues to initiate local, non-nervous reactions that cause obstructive constriction of the airways.

The Alveoli

- The mean total number of alveoli has been estimated as 400 million, but ranges from about 270 to 790 million, correlating with the height of the subject and total lung volume.
- The size is dependent on lung volume but due to gravity they are normally larger in the upper part of the lung, except at maximal inflation when the vertical gradient in size disappears.
- At functional residual capacity the mean diameter of a single alveolus is 0.2 mm and the total surface area of the alveoli is ~130 m^2.
- Intrinsic shape of alveoli (Al) is maintained from FRC to TLC.
- Alveolar walls are flat with sharp corners where the adjacent walls meet.



A 30 cm H2O [TLC]).
B 8 cm H2O 50% TLC).
C 4 cm H2O [FRC]).
D 0 cm H2O (minimum volume).

Scanning electron photomicrographs at the same magnification of perfusion-fixed normal rat lung at different degrees of inflation pressure.

The Alveolar Septa

They are **generally flat, making the alveoli polyhedral rather than spherical**. The septa are perforated by small fenestrations known as the **pores of Kohn**, which provide collateral ventilation between alveoli.

Collateral ventilation also occurs between small bronchioles and neighbouring alveoli, adjacent pulmonary acini and occasionally intersegmental communications, (Canals of lambert) and is more pronounced in patients with **emphysema**.

The 'active' side: The alveolar wall, the capillary endothelium and the alveolar epithelium are closely apposed, with almost no interstitial space, such that the total thickness from gas to blood is ~0.3 µm.
The 'service' side: is more than 1- to 2-µm thick and contains a recognisable interstitial space containing elastin and collagen fibres, nerve endings and occasional migrant polymorphs and macrophages.
The distinction between the two sides of the capillary has considerable pathophysiological significance as the active side tends to be spared in the accumulation of both oedema fluid and fibrous tissue.

Highly magnified cross-sectional sketch of the cells and organization of the alveolar septa