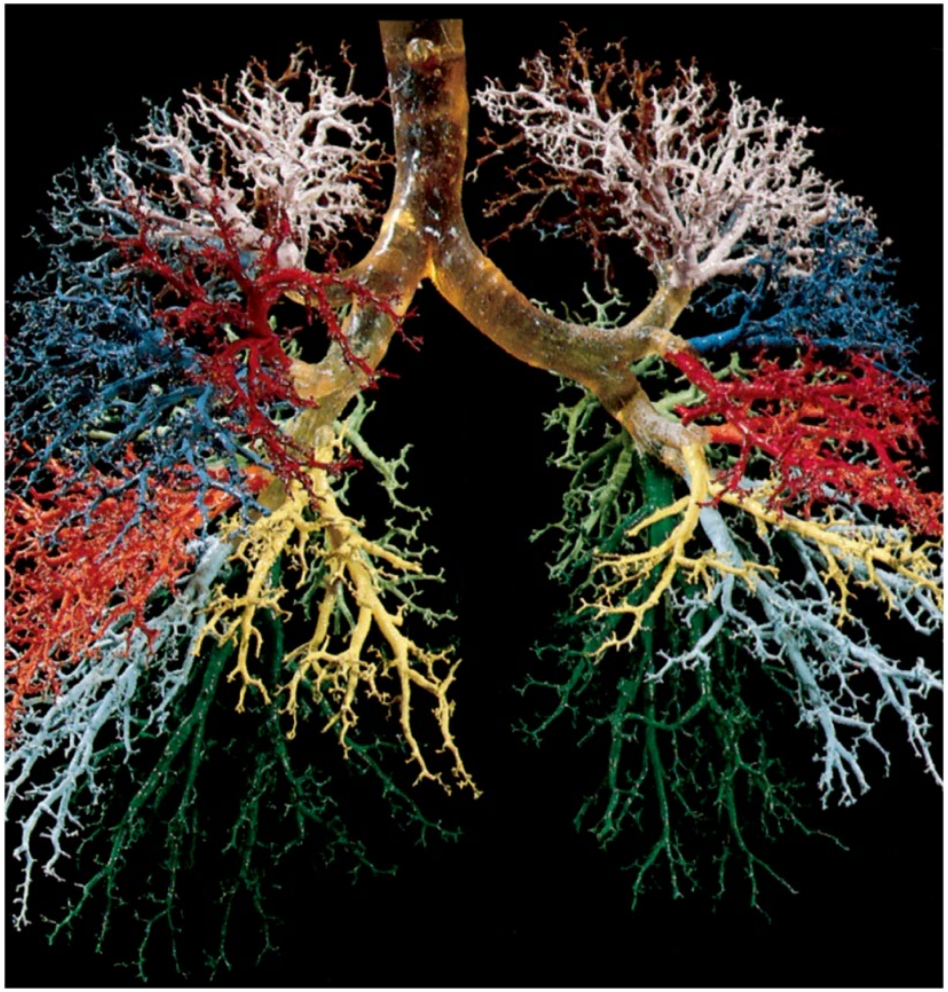
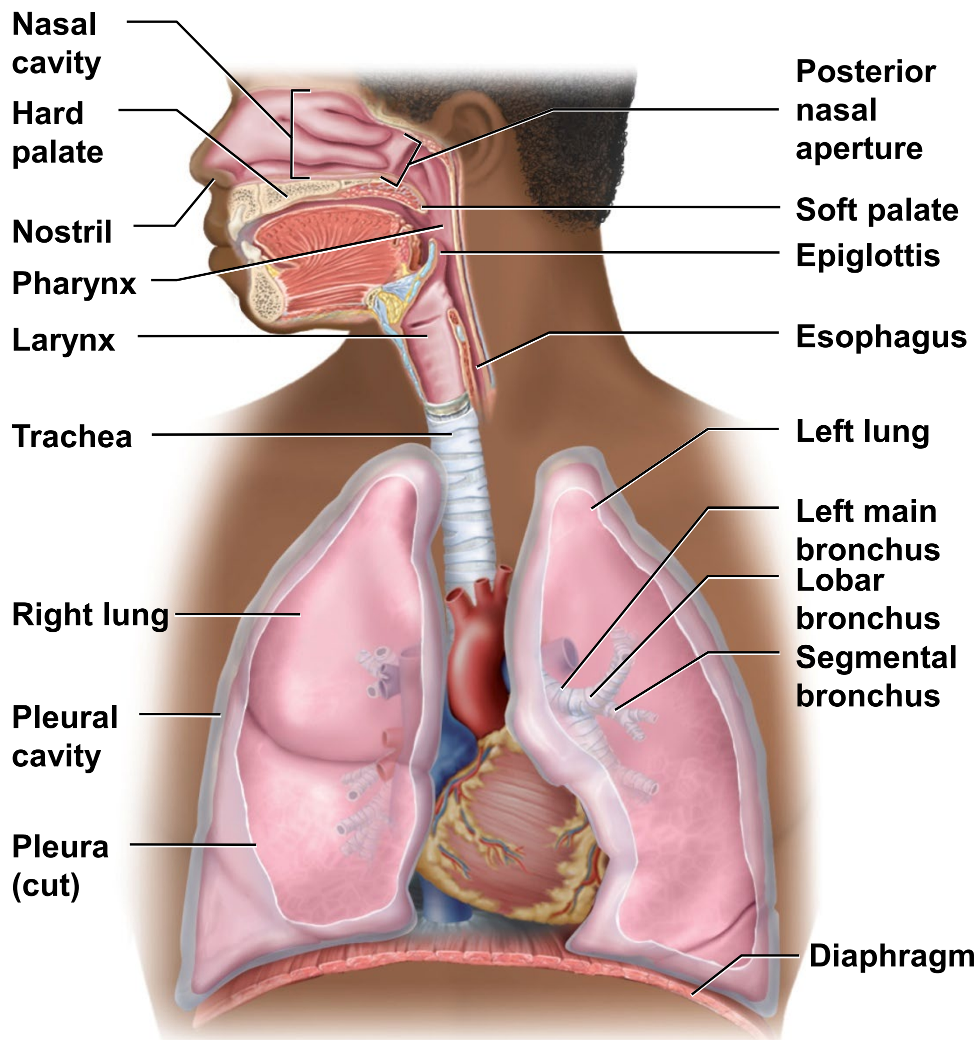
Chapter 22.1

# The Respiratory System



# Organs of Respiratory System




nose, pharynx, larynx, trachea, bronchi, lungs

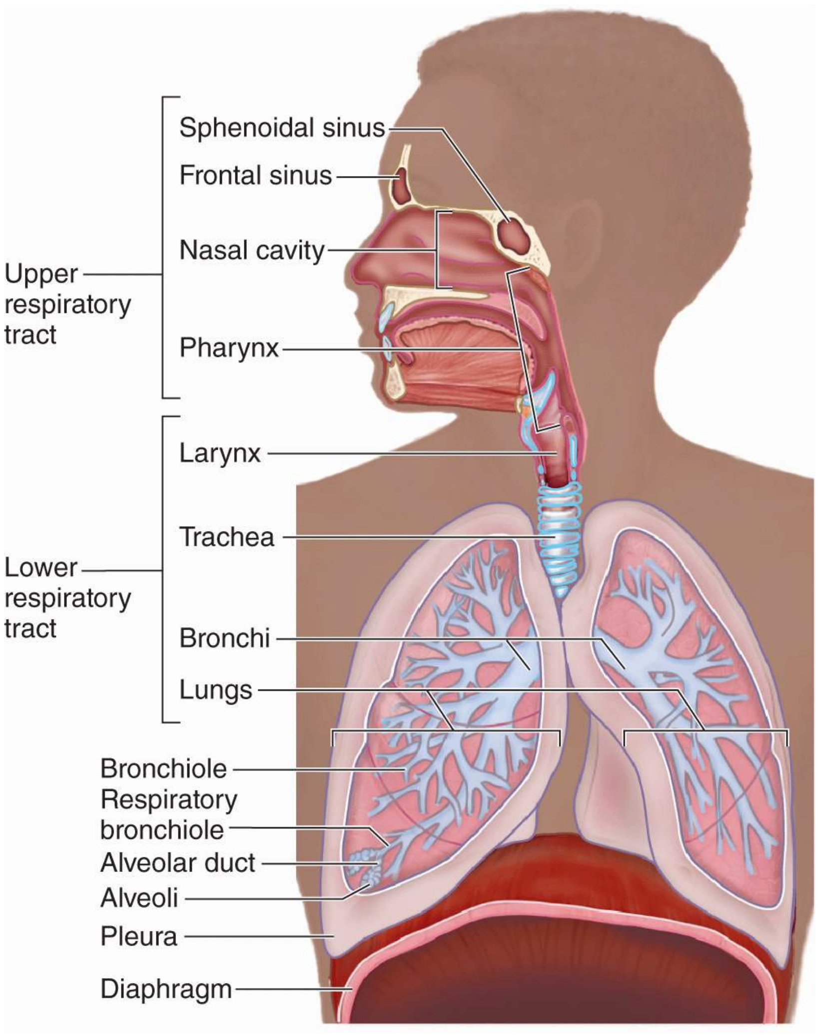
# Divisions of the Respiratory System

## Upper respiratory tract

- located in head and neck
- nose through laryngopharynx

## Lower respiratory tract

- organs of the thorax
- larynx through alveoli



# Conducting Division VS Respiratory Division

Conducting division of the respiratory system

> > those passages that serve only for airflow
> > no gas exchange
> > nostrils through major bronchioles

Respiratory division consists of alveoli and other gas exchange regions

- respiratory membrane // space between alveoli and capillary
- incoming air stops at the alveoli of the lungs
- 300 millions alveoli (150 million per lung)
- gases inside alveoli are exchanged with the gases in the bloodstream
- gas molecules ($O_2$ and $CO_2$) diffuse “down” concentration gradients
- 70 and 80 square meters of surface area

# Nasal Cavity

**Nasal conchae**

– nasal cavity occupied by three folds of tissue

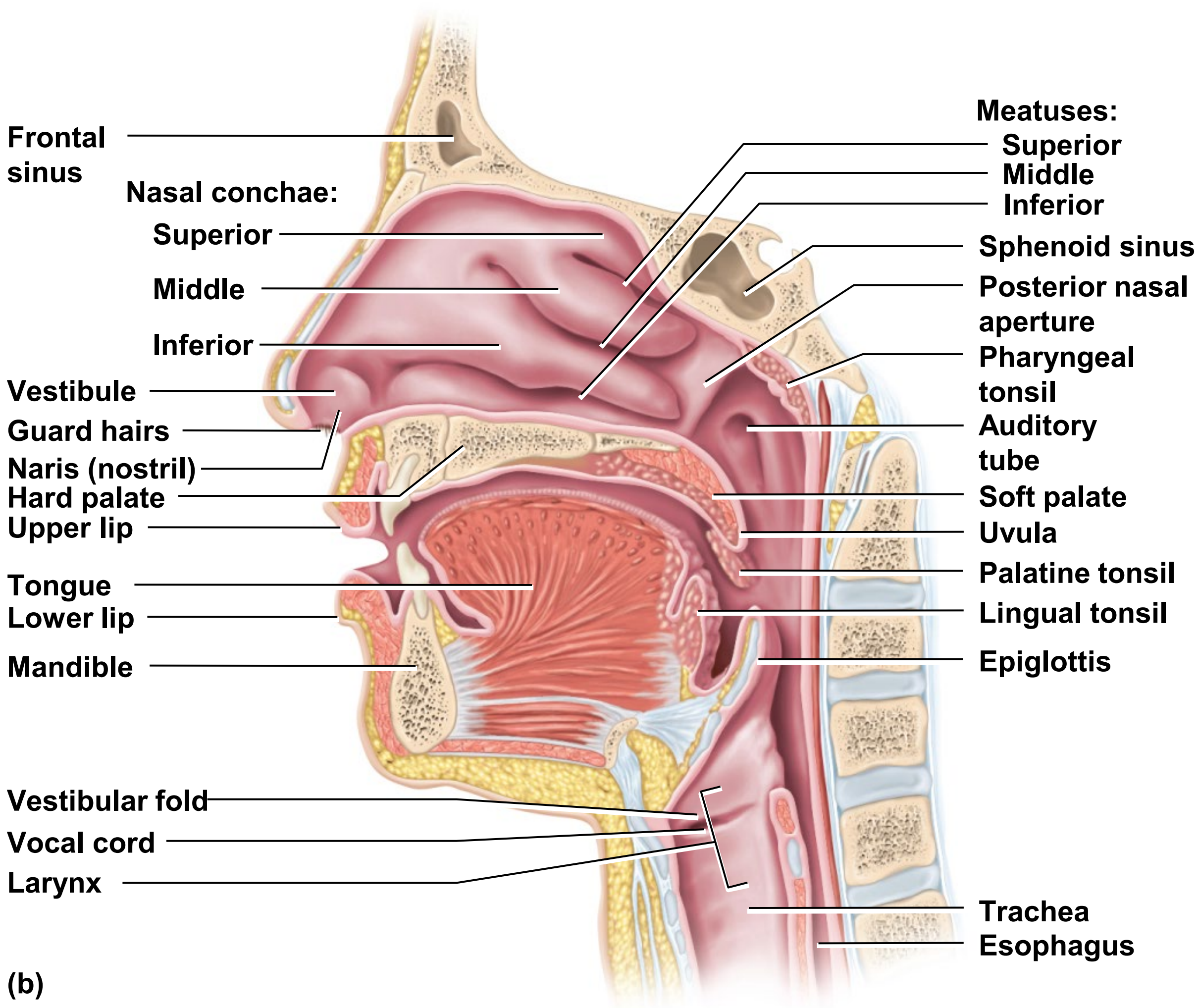
– **superior, middle, and inferior nasal conchae** (turbinates) // project from lateral walls toward septum

**- meatus** – narrow air passage beneath each concha // narrowness and turbulence ensure that most air contacts mucous membranes

- meatus function = cleans, warms, and moistens the air

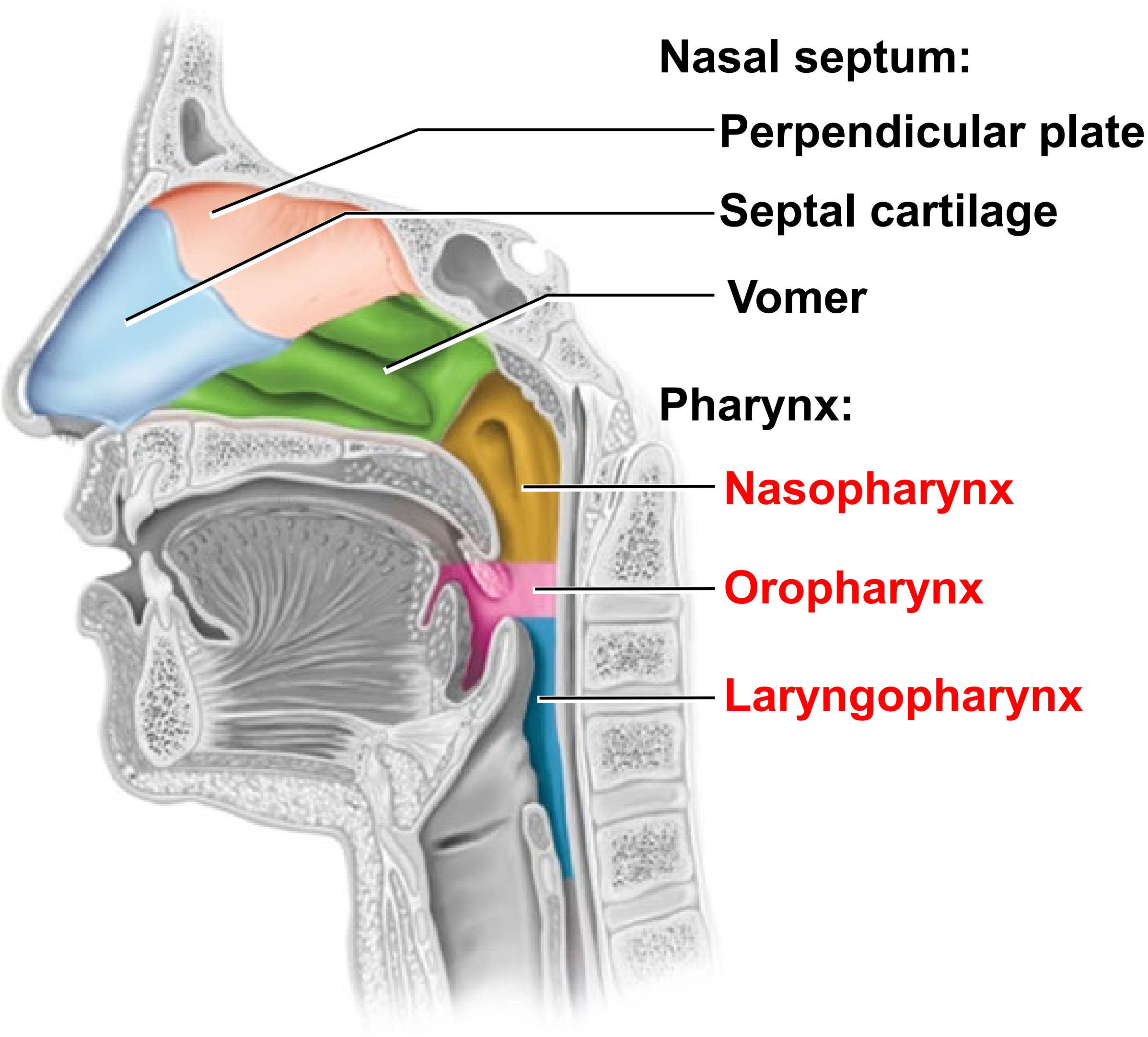
# Upper Respiratory Tract to Lower Respiratory Tract

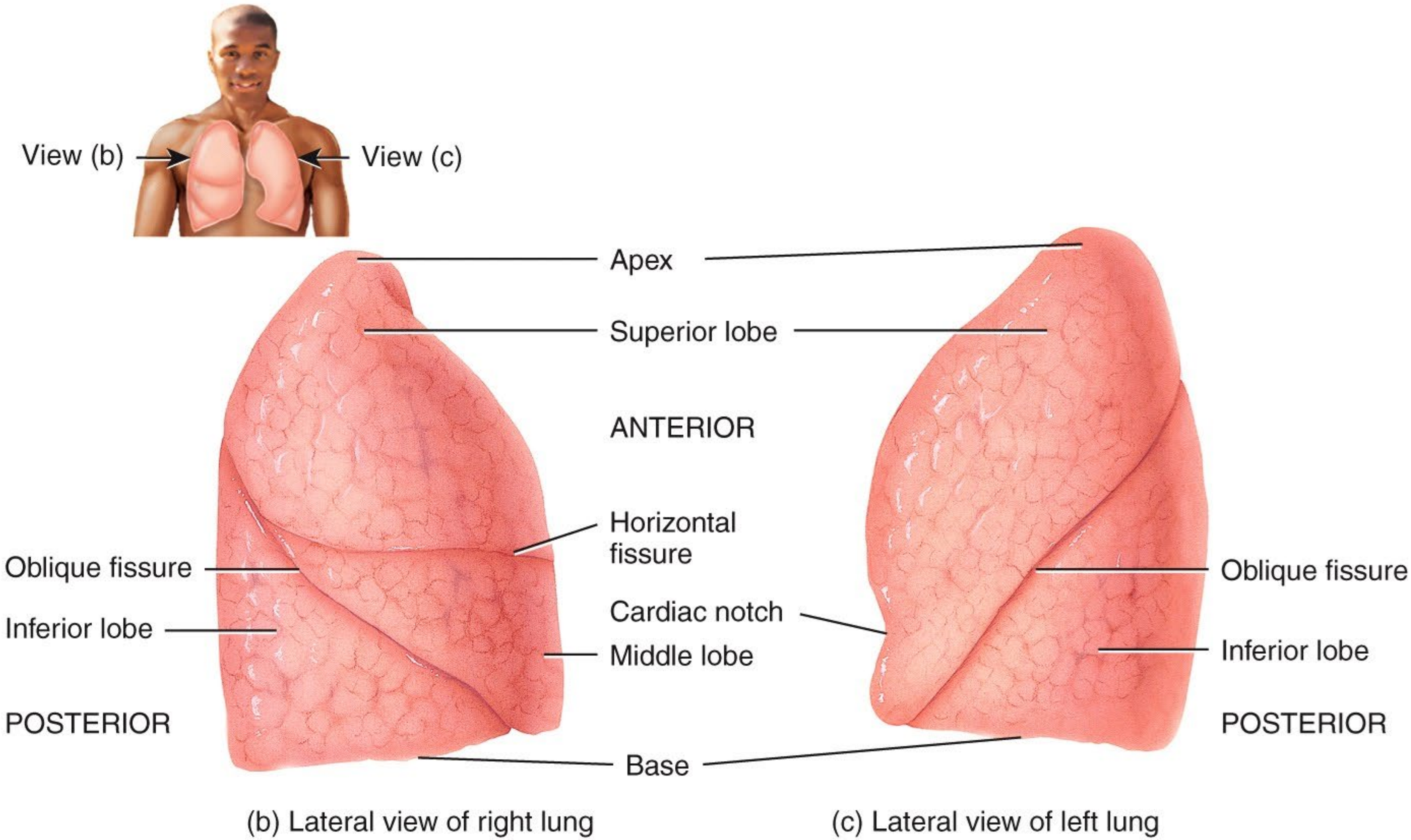
(respiratory organs in the head and neck / stop at entrance to larynx)




(b)

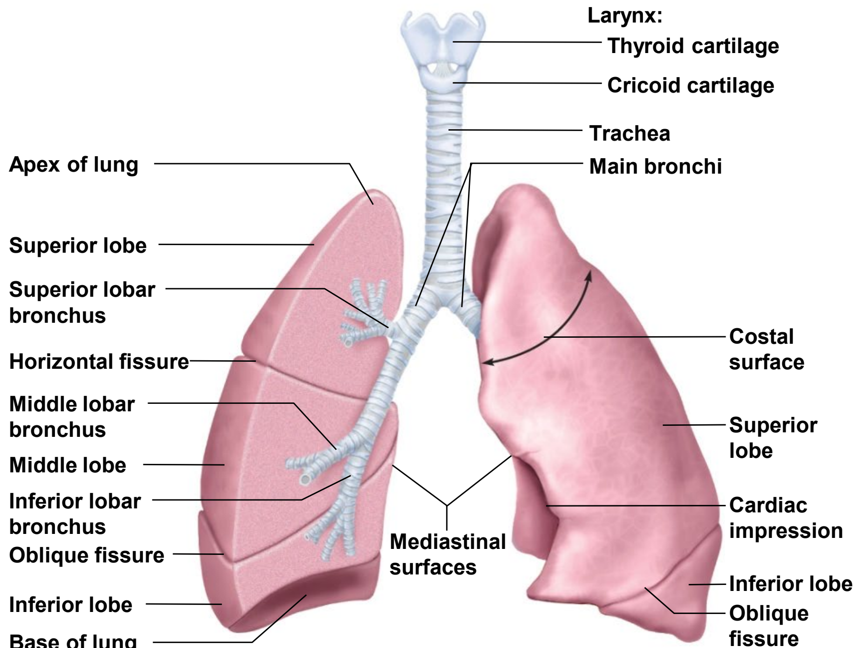
# Regions of Pharynx



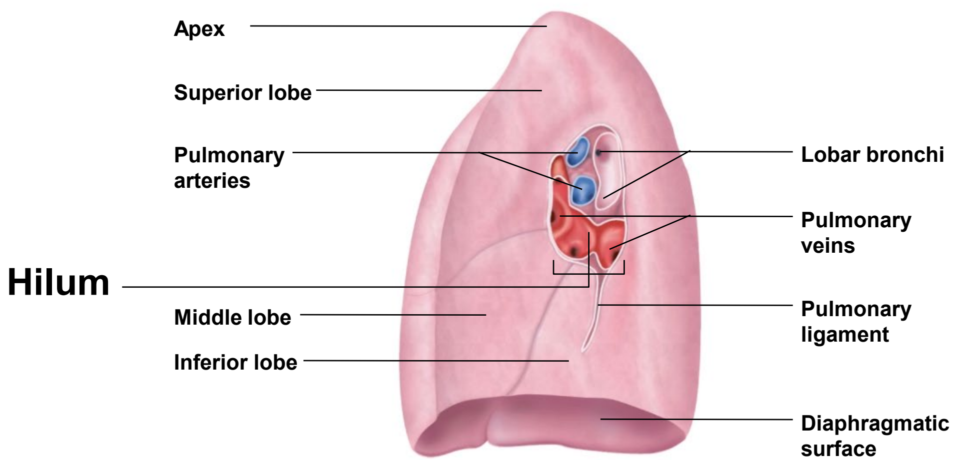



- Right lung three lobes and left lung two lobes
- Note: oblique fissures important lab learning objectives

# Lungs - Surface Anatomy




(a) Anterior view




(b) Mediastinal surface, right lung

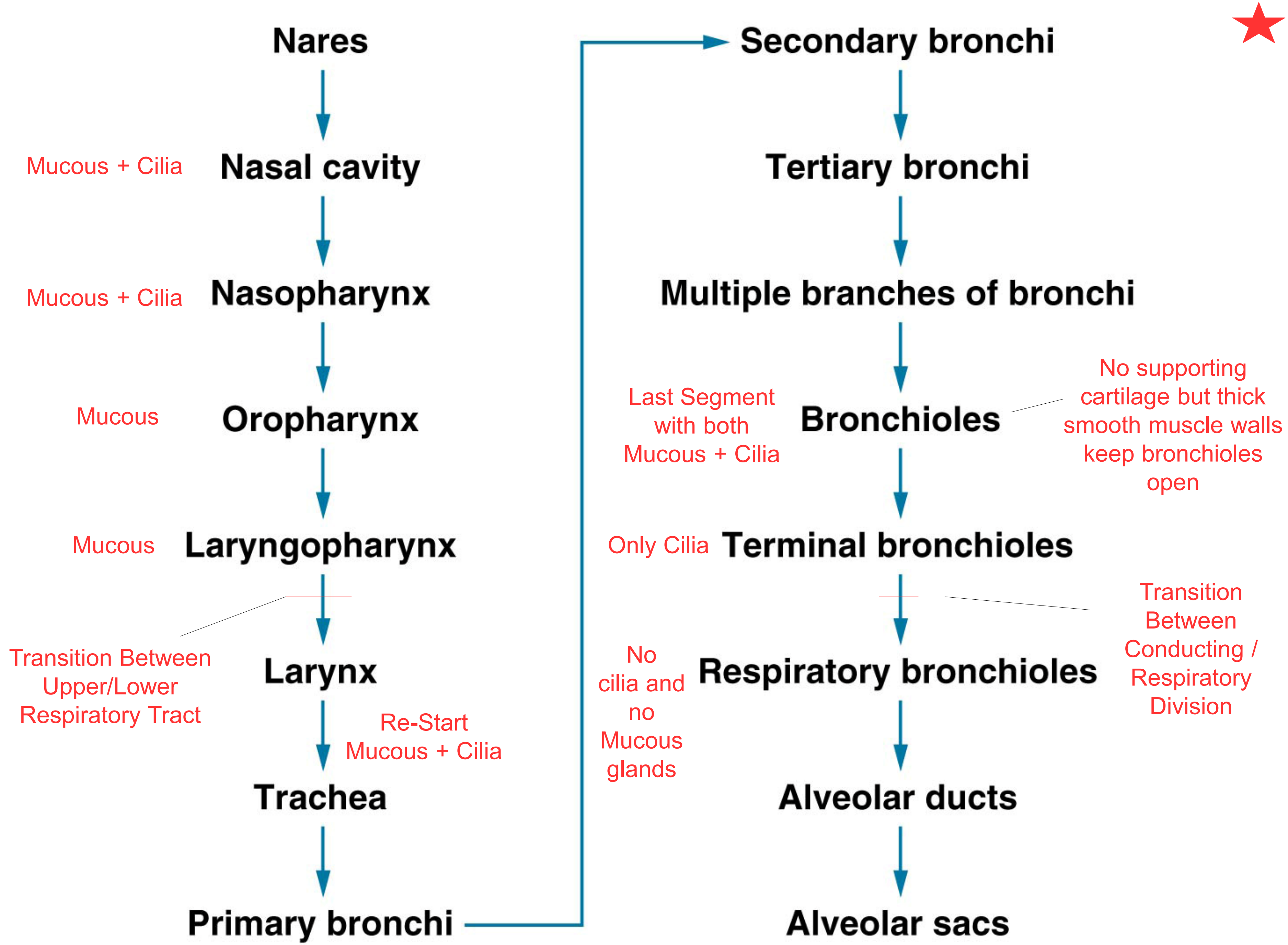
# Path of Air Flow

**Conducting Division**

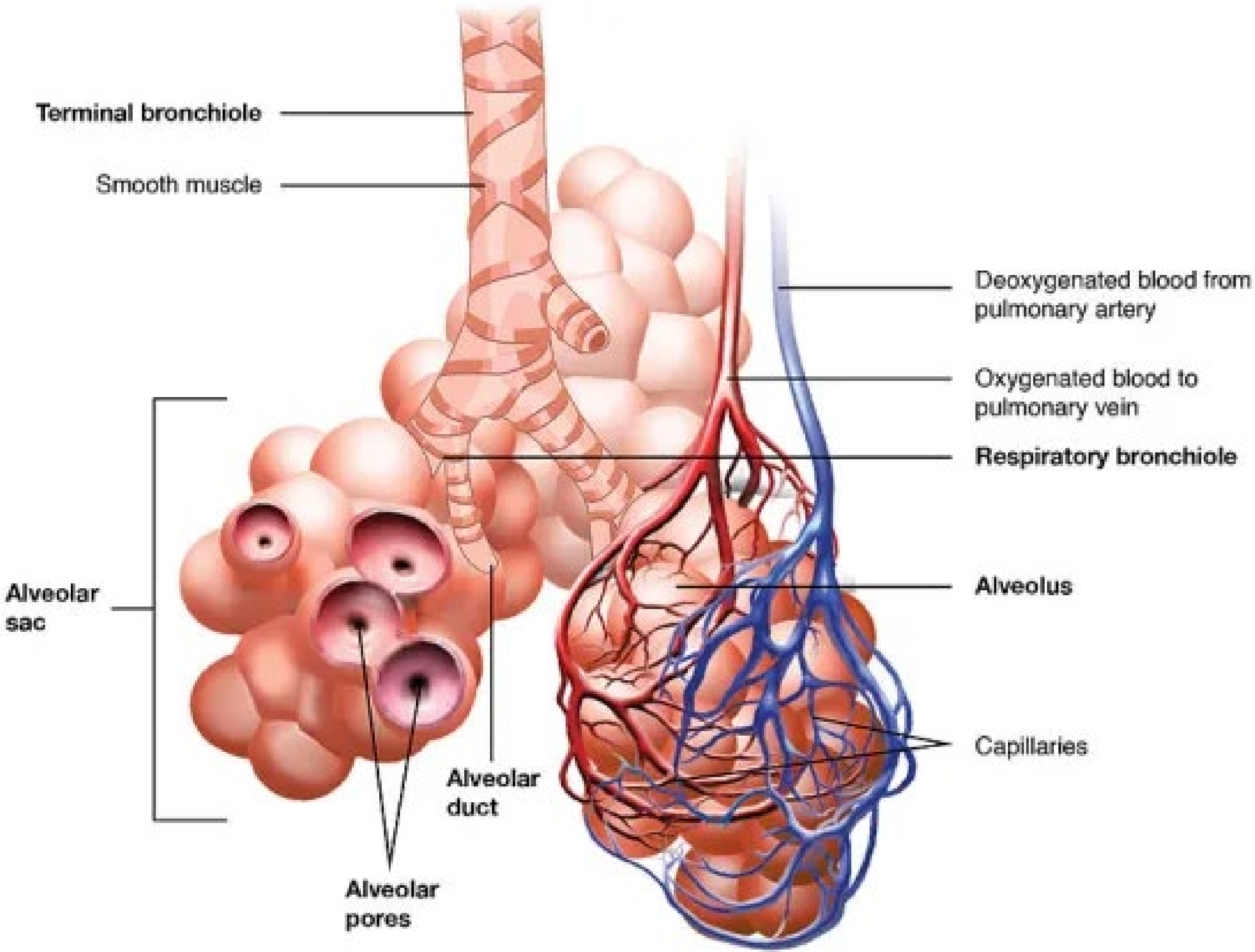
- nasal cavity
- pharynx
- larynx
- trachea
- main bronchus
- lobar bronchus
- segmental bronchus
- Bronchiole
- Terminal bronchiole

**Respiratory Division**

- respiratory bronchiole
- alveolar duct
- atrium
- alveolus



Nares
Nasal cavity
Nasopharynx
Oropharynx
Laryngopharynx
Larynx
Trachea
Primary bronchi
Mucous + Cilia
Mucous + Cilia
Mucous
Mucous
Transition Between Upper/Lower Respiratory Tract
Re-Start Mucous + Cilia
Secondary bronchi
Tertiary bronchi
Multiple branches of bronchi
Bronchioles
Terminal bronchioles
Respiratory bronchioles
Alveolar ducts
Alveolar sacs
Last Segment with both Mucous + Cilia
No supporting cartilage but thick smooth muscle walls keep bronchioles open
Only Cilia
Transition Between Conducting / Respiratory Division
No cilia and no Mucous glands




- Respiratory membrane formed by union of alveolar and capillary epithelial cells. These cells share a common basement membrane.

# Larynx

Larynx (voice box) – cartilaginous chamber about 4 cm  (1.5 in.)

- primary function is to keep food and drink out of the airway
- has evolved additional role – phonation – production of sound
- epiglottis – flap of tissue that guards the superior opening of the larynx

– at rest, stands almost vertically

– during swallowing, extrinsic muscles of larynx pull larynx upward

– tongue pushes epiglottis down to meet it

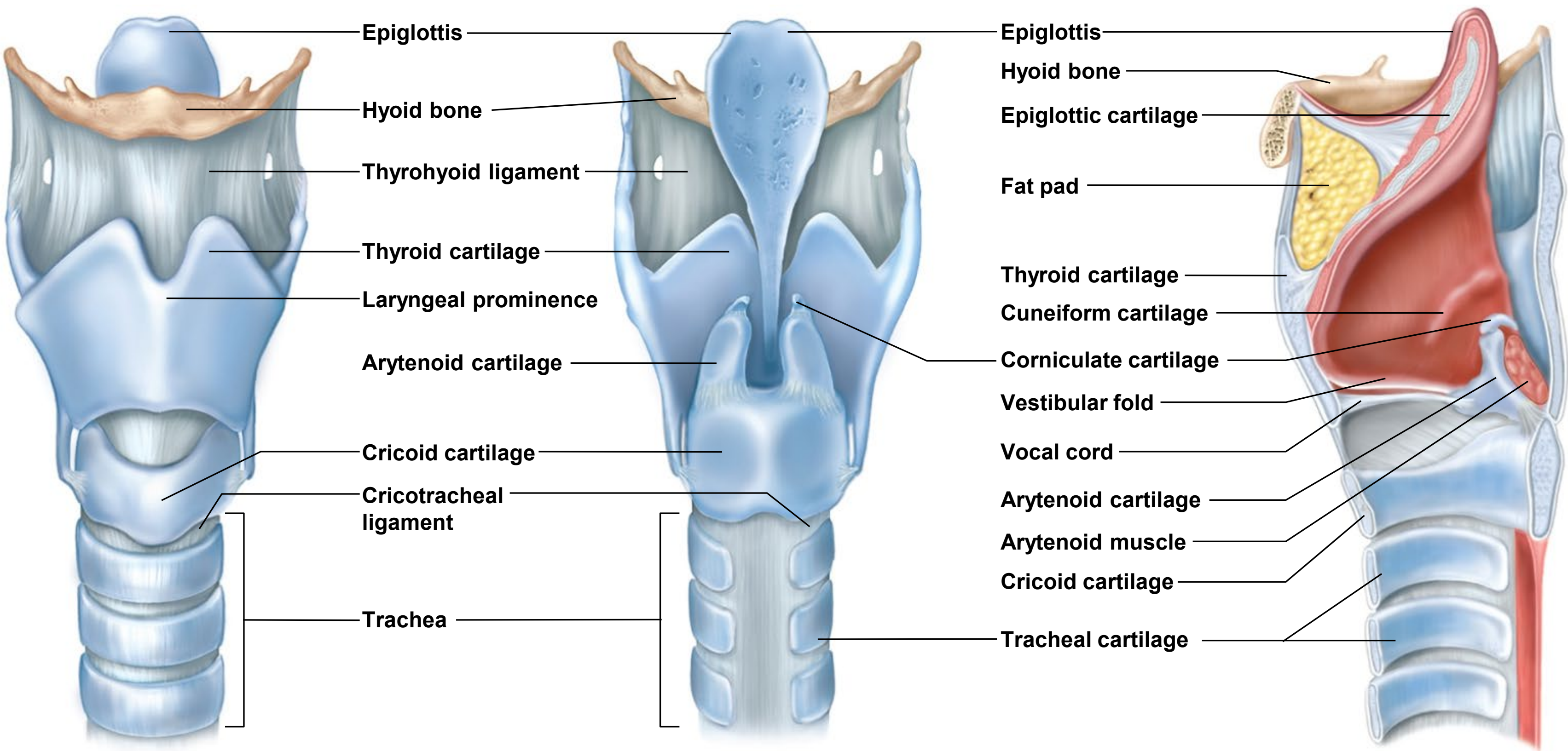
– closes airway and directs food to the esophagus behind it

– vestibular folds keeps food and drink out of  the airway

– vestibular ligaments (also called vocal cords)

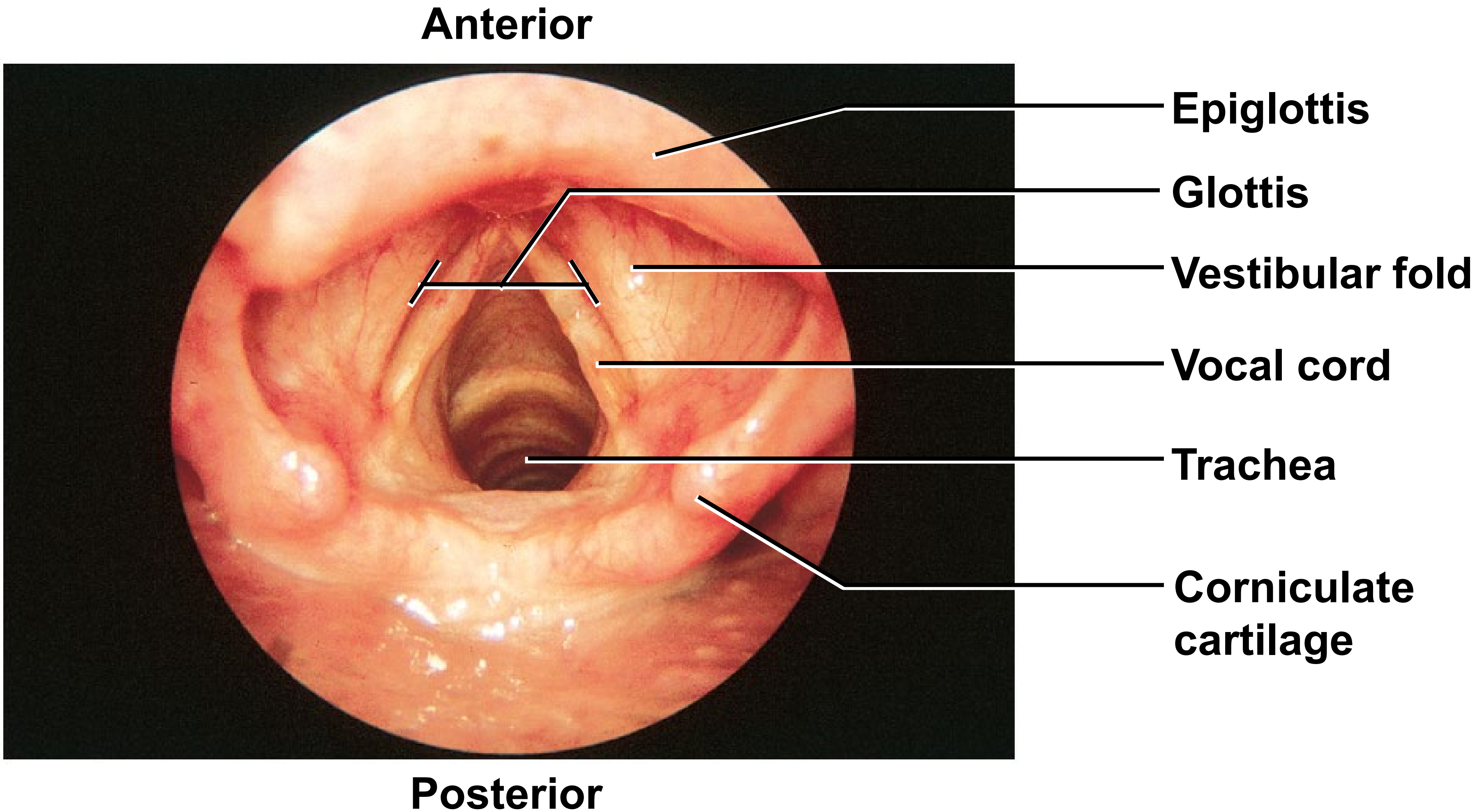
# Views of Larynx



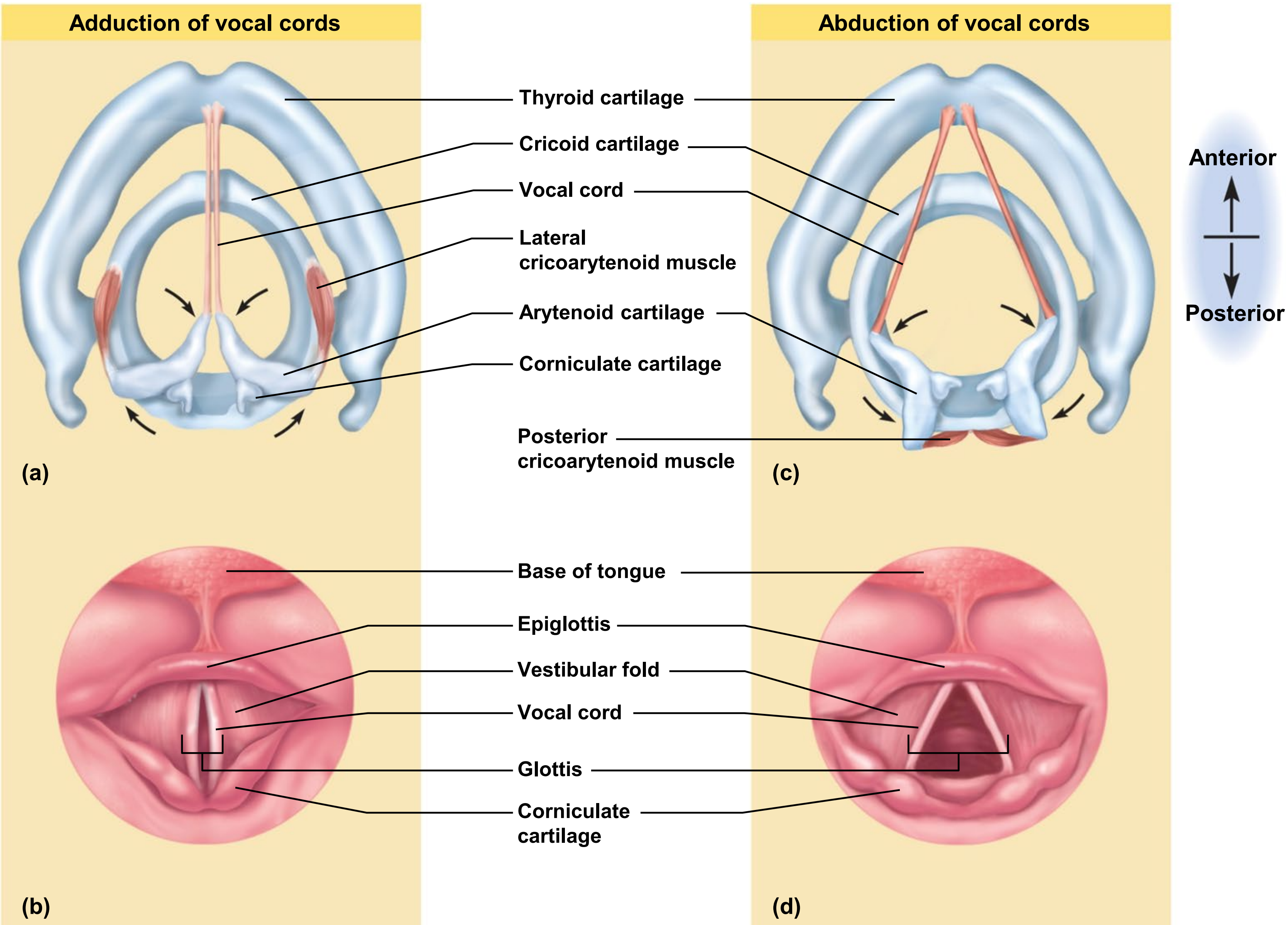



(a) Anterior (b) Posterior (c) Median

# Endoscopic View of the Larynx



# Action of Vocal Cords



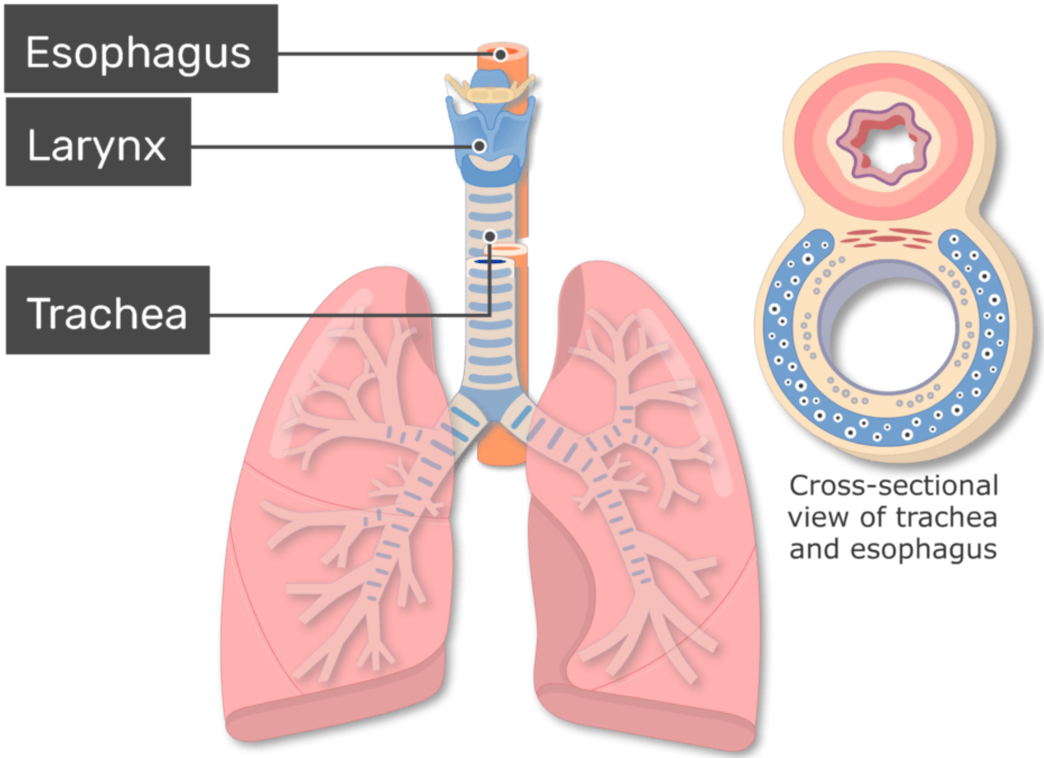
# Trachea (1 of 2)

**Trachea** (windpipe) – a rigid tube about 12 cm (4.5 in.) long and 2.5 cm (1 in.) in diameter

anterior to esophagus

supported by 16 to 20 **C-shaped** rings of **hyaline cartilage**

reinforces the trachea and keeps it from collapsing when you inhale




opening in rings faces posteriorly towards esophagus

**trachealis muscle** spans opening in rings

gap in C allows room for the esophagus to expand as swallowed food passes by

contracts or relaxes to adjust air flow

# Trachea (2 of 2)

inner lining of trachea is a ciliated pseudostratified columnar epithelium

composed mainly of mucus-secreting cells, ciliated cells, and stem cells

mucociliary escalator – mechanism for debris removal

mucus traps inhaled particles

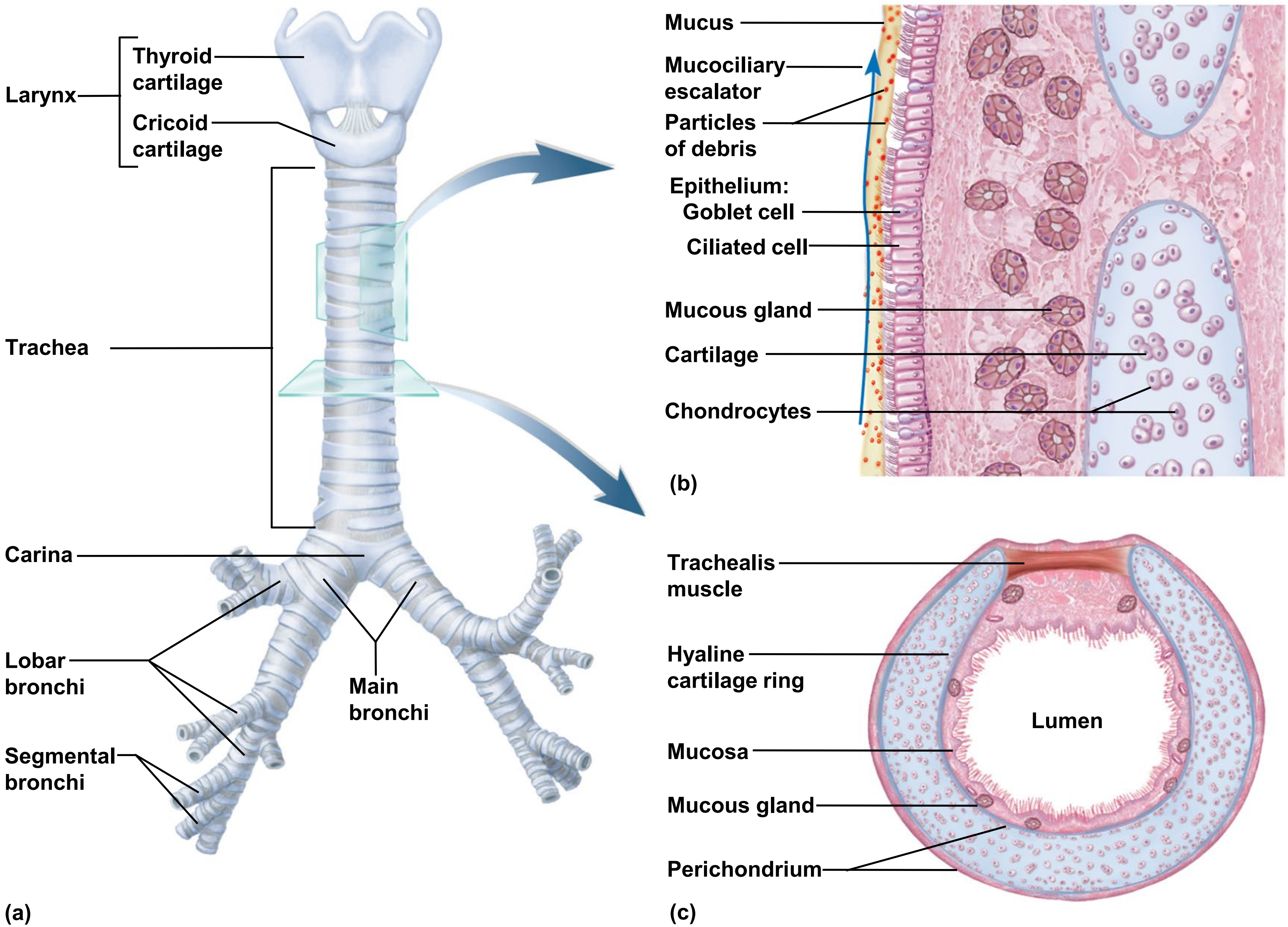
upward beating cilia drives mucus toward pharynx where it is swallowed

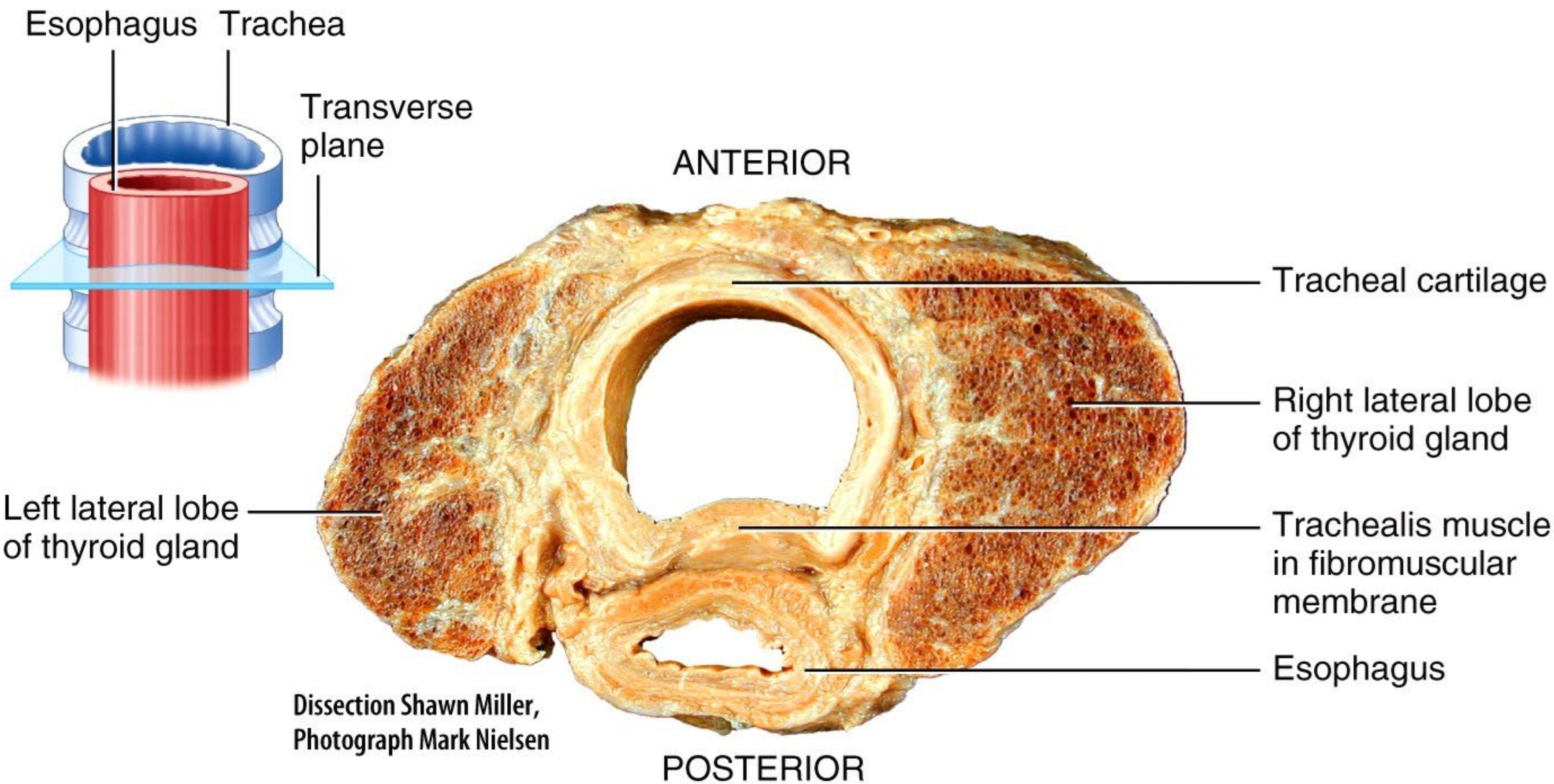
right and left main bronchi

trachea forks at level of sternal angle /// carina – internal medial ridge in the lowermost tracheal cartilage

directs the airflow to the right and left

# Lower Respiratory Tract

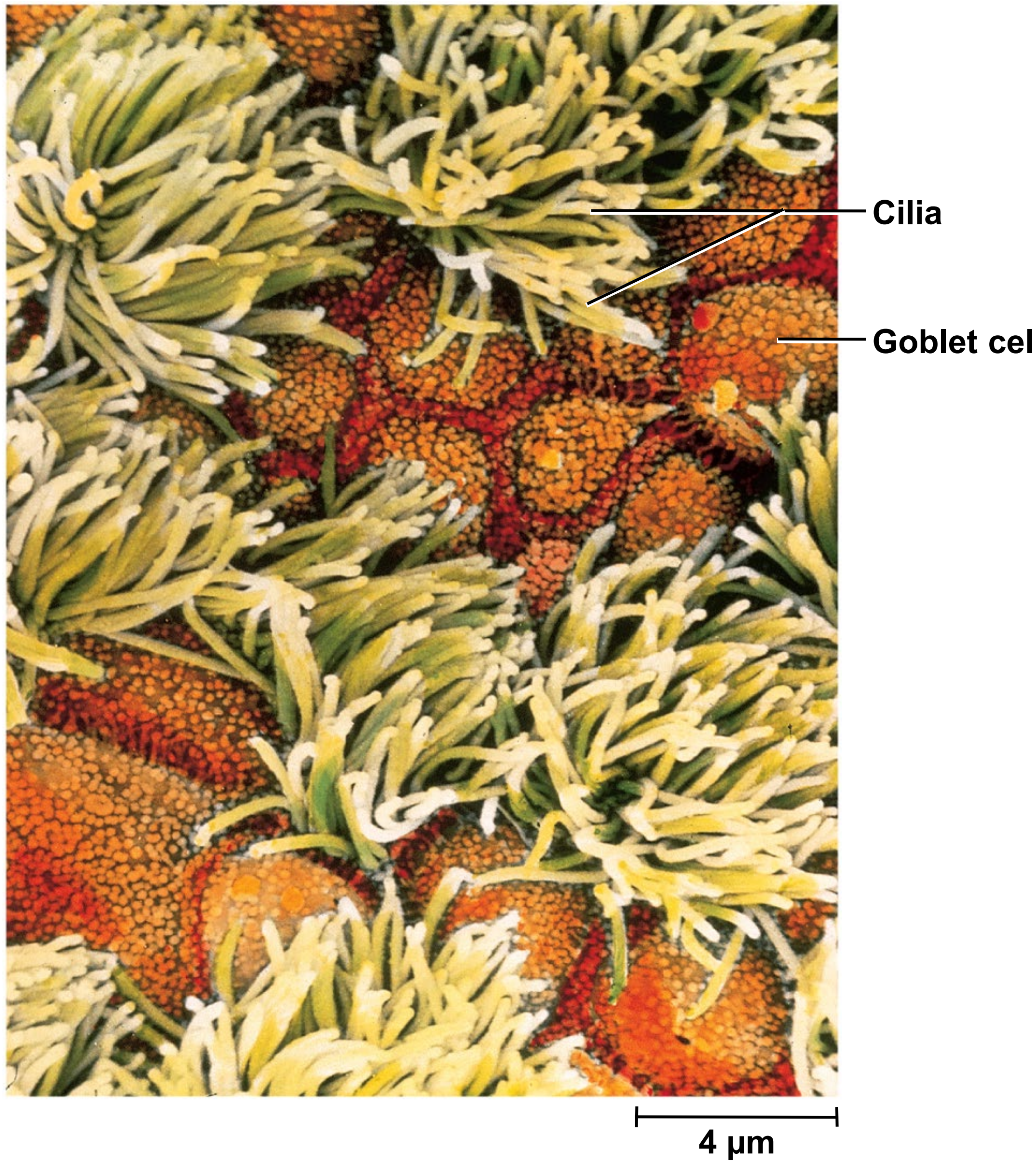





Superior view of transverse section of thyroid gland, trachea, and esophagus

# Tracheal Epithelium





# Blood Vessels Associated with Lung Tissue

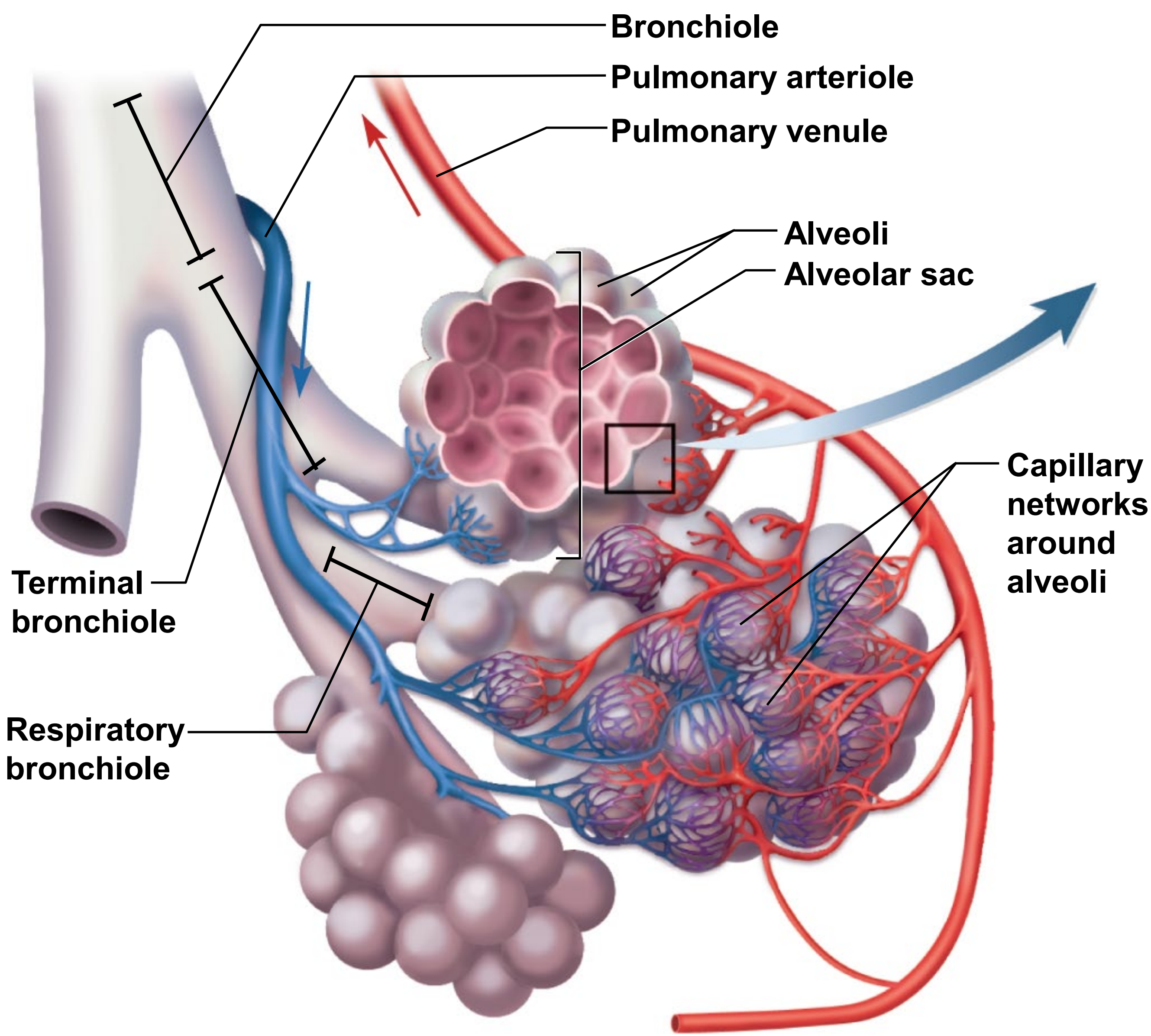
Pulmonary arteries & veins

These blood vessels closely follow the **bronchial tree** (air passageways) as they make their way to the alveoli /// pulmonary circuit = blood flow from right ventricle to left atria // pulmonary circuit

Bronchial arteries & veins

These blood vessels branch of thoracic aorta /// delivers oxygen and removes waste products from lung tissues /// systemic circuit

# Blood Supply to the Alveolar Sacs



# Bronchial Tree

## (Main Bronchi / Lobar Bronchi / Segmental Bronchi)

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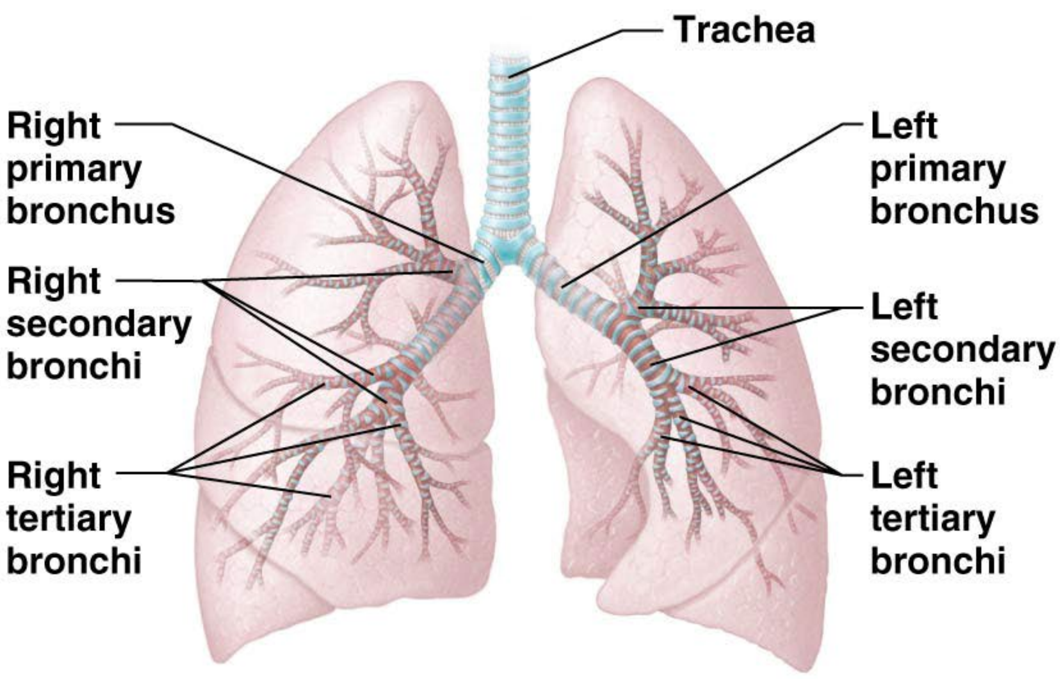
Bronchial tree – a branching system of air tubes located in each lung /// from one main bronchus extends 65,000 terminal bronchioles

Main bronchi (primary) – supported by c-shaped hyaline cartilage rings /// rt. main bronchus is a 2-3 cm branch arising from fork of trachea

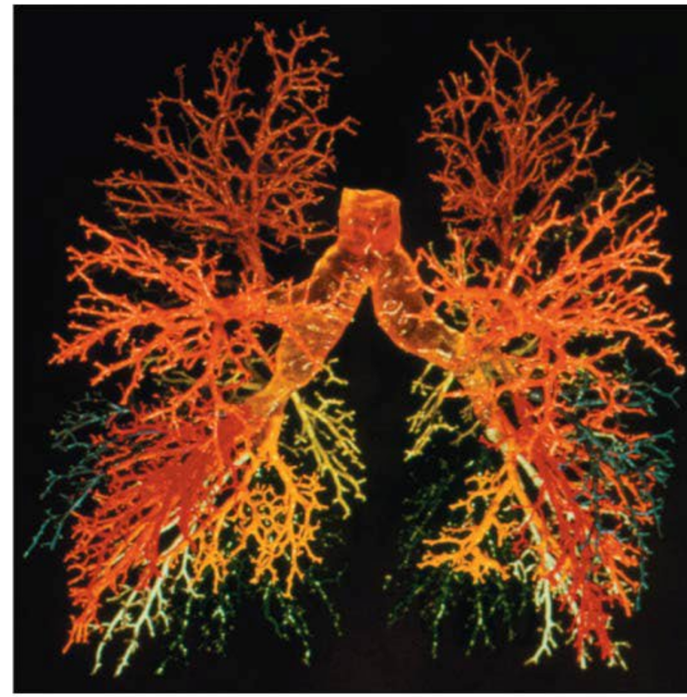
Right bronchus slightly wider and more vertical than left // this is why aspirated (inhaled) foreign objects lodge right bronchus more often the left

Left main bronchus is about 5 cm long /// slightly narrower and more horizontal than the right // less likely for food to end up in left bronchus

# Branching pattern of the bronchial tree.

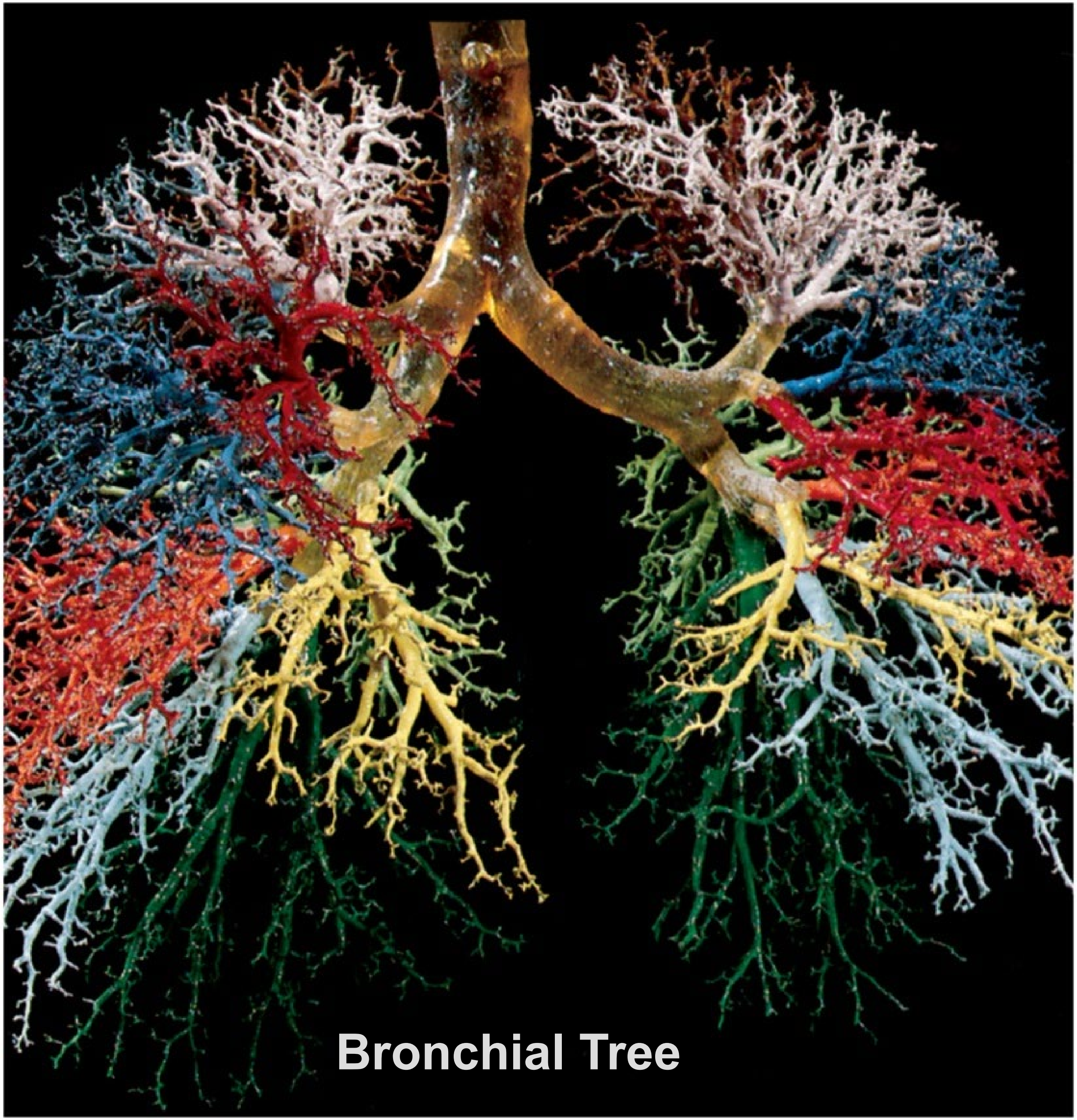



**(a) Conducting zone passages and bronchial tree**



**(b) Cast of bronchial tree**

Main Brochi = Primary Bronchi // Secondary = Lobar // Tertiary = Segmental Within Lobes



Bronchial Tree

# Bronchial Tree

## (Main Bronchi / Lobar Bronchi / Segmental Bronchi)

Lobar bronchi (secondary)  – supported by crescent shaped cartilage plates

three right lobar bronchi – superior, middle, and inferior  /// one to each lobe of the right lung

two left lobar bronchi - superior and inferior ///  one to each lobe of the left lung

Segmental (tertiary) bronchi - supported by crescent shaped cartilage plates

10 on right, and 8 on left

bronchopulmonary segment –functionally independent unit of the lung tissue

# Bronchial Tree
## (Main Bronchi / Lobar Bronchi / Segmental Bronchi)

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All segments of the bronchial tree including the “ bronchioles” are lined with a mucosa lined with  ciliated pseudostratified columnar epithelial cells

lamina propria = connective tissue /// has an abundance of mucous glands and lymphocyte nodules

bronchus-associated lymphoid tissue = BALT /// immediately deep to epithelium

all divisions of bronchial tree have a large amount of elastic connective tissue  ///  contributes to the recoil that expels air from lungs

the mucosa also has a well-developed layer of smooth muscle  /// muscularis mucosae which contracts or relaxes to constrict or dilate the airway, regulating air flow

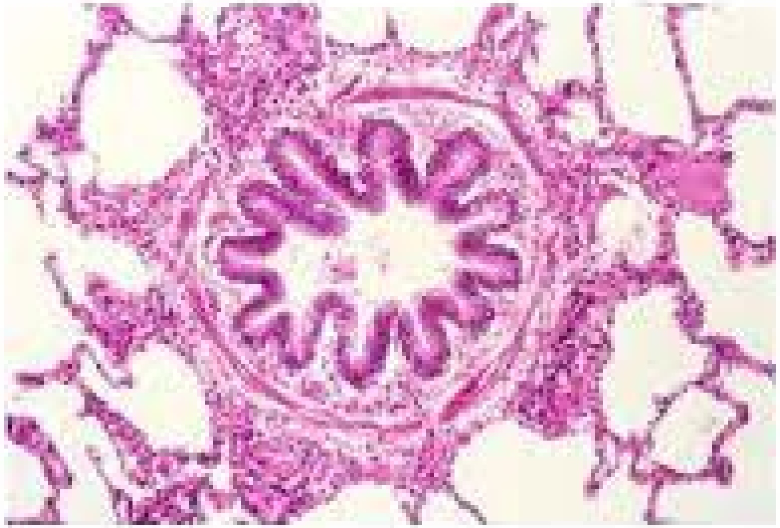
# The Distal Bronchiole Tree

## (Bronchioles / Terminal Bronchioles / Respiratory Bronchioles)

Bronchioles – first section of air conduction pathway without hyalin cartilage.

Thick smooth muscle walls prevent bronchioles from collapsing from negative pressure // only 1mm diameter

Pulmonary lobule = portion of lung ventilated by one bronchiole



Bronchioles have ciliated cuboidal epithelium and mucous glands

Terminal bronchioles have cilia but no mucus glands

Respiratory bronchioles do not have cilia and no mucous glands

Why does this make sense?

# The Distal Bronchiole Tree

**(Bronchioles / Terminal Bronchioles / Respiratory Bronchioles)**

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**Terminal bronchioles**

divides into 50 - 80 branches

final branches of conducting division

measure 0.5 mm or less in diameter

**no mucous glands** or goblet cells

**still have cilia** // move mucus draining into them from bronchioles towards larynx by mucociliary escalator (last segment with cilia)

each terminal bronchiole gives off two or more smaller respiratory bronchioles

# The Distal Bronchiole Tree

**(Bronchioles / Terminal Bronchioles / Respiratory Bronchioles)**

---

**Respiratory bronchioles**

**no cilia and no mucous glands**

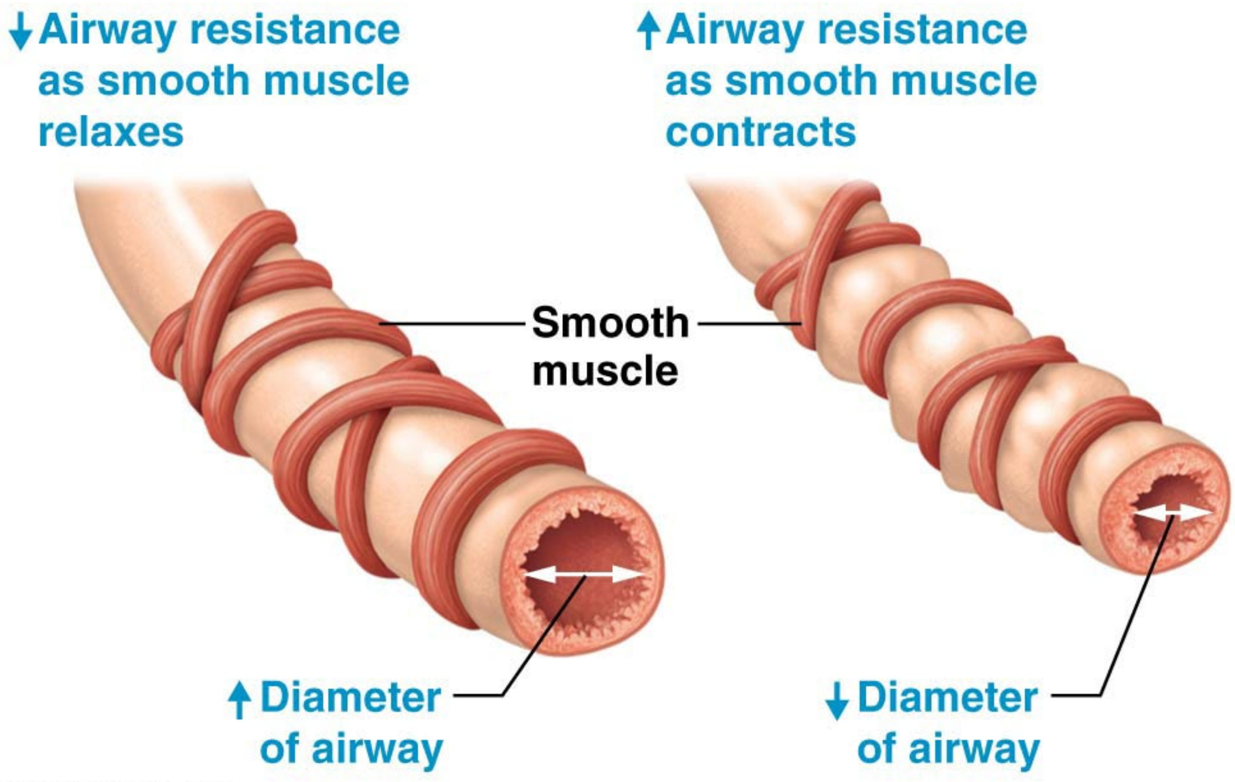
have alveoli budding from their walls

considered the **beginning of the respiratory division** since alveoli participate in gas exchange

divide into 2-10 **alveolar ducts**

end in **alveolar sacs** – grape-like clusters of alveoli arrayed around a central space called the **atrium**

# Relationship between airway resistance and airway diameter.




Histamine constricts bronchioles /// Epinephrine dilates bronchioles

What occurs when histamine is released by mast cells in the systemic tissues?

# Three Cell Types of the Alveoli 

150 million alveoli in each lung

Providing about 70 $m^2$ of surface for gas exchange

Three cell type in the alveolus (type I / type II / dust cells)

Squamous alveolar cells (type I)

thin, broad cells that allow for rapid gas diffusion between alveolus and bloodstream

cover 95% of alveolus surface area

# Three Cell Types of the Alveoli (2 of 3)

Great alveolar cells (type II)

round to cuboidal cells that cover the remaining 5% of alveolar surface

repair the alveolar epithelium when the squamous (type I) cells are damaged

secrete pulmonary surfactant /// a mixture of phospholipids and proteins that coats the alveoli and prevents them from collapsing when we exhale

# Three Cells of the Alveoli (3 of 3)

Alveolar macrophages (dust cells)

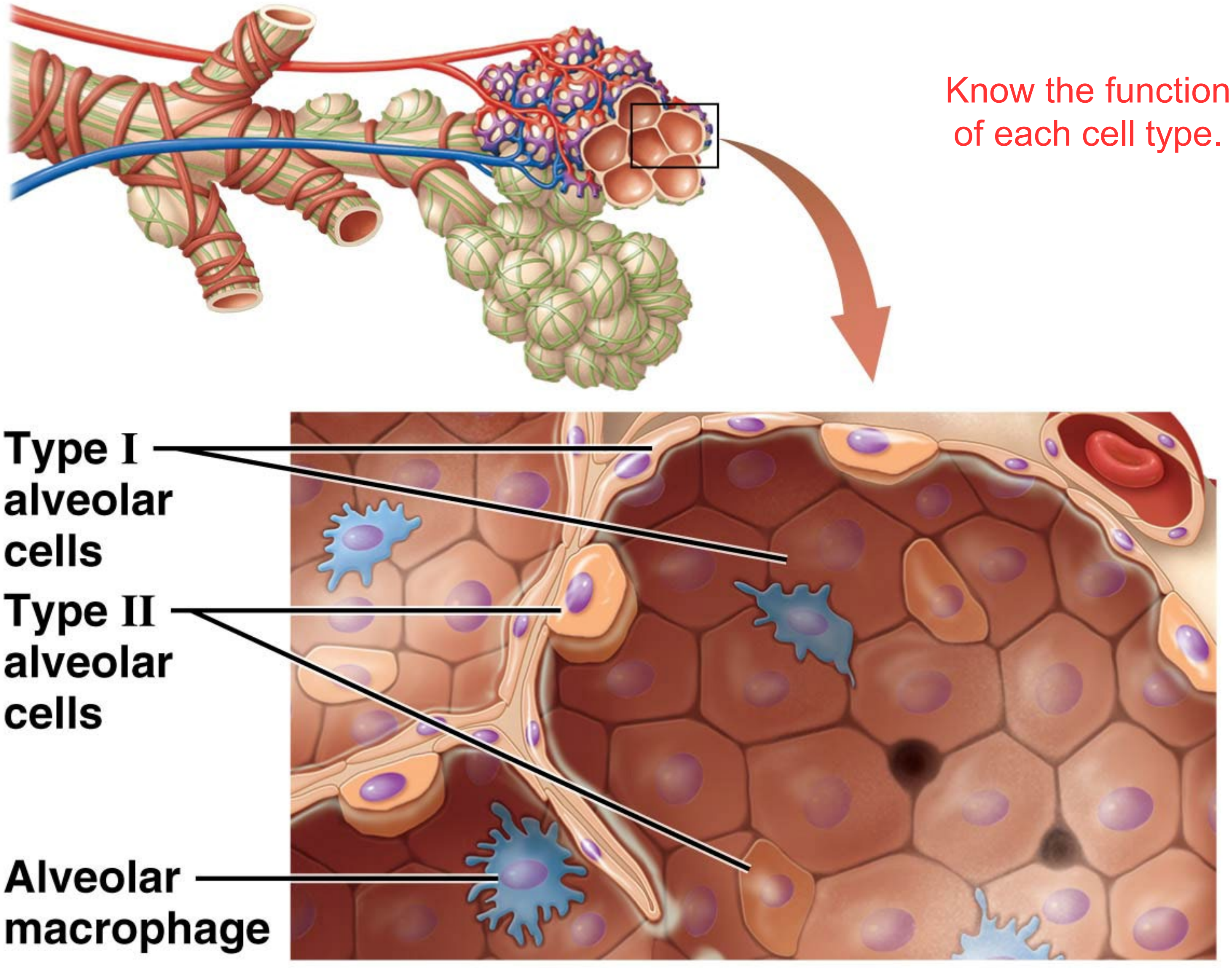
most numerous of all cells in the lung

wander the lumen and the connective tissue between alveoli

keep alveoli free from debris by phagocytizing dust particles

100 million dust cells perish each day as they ride up the mucociliary escalator to be swallowed and digested with their load of debris

# Three Alveolar Cell Types




Know the function of each cell type.

# Respiratory Membrane

Each alveolus surrounded by a basket like  capillary bed // network supplied with blood from pulmonary artery

Respiratory membrane – the barrier between the air inside the alveoli and and the blood inside the pulmonary capillary

Respiratory membrane consists of

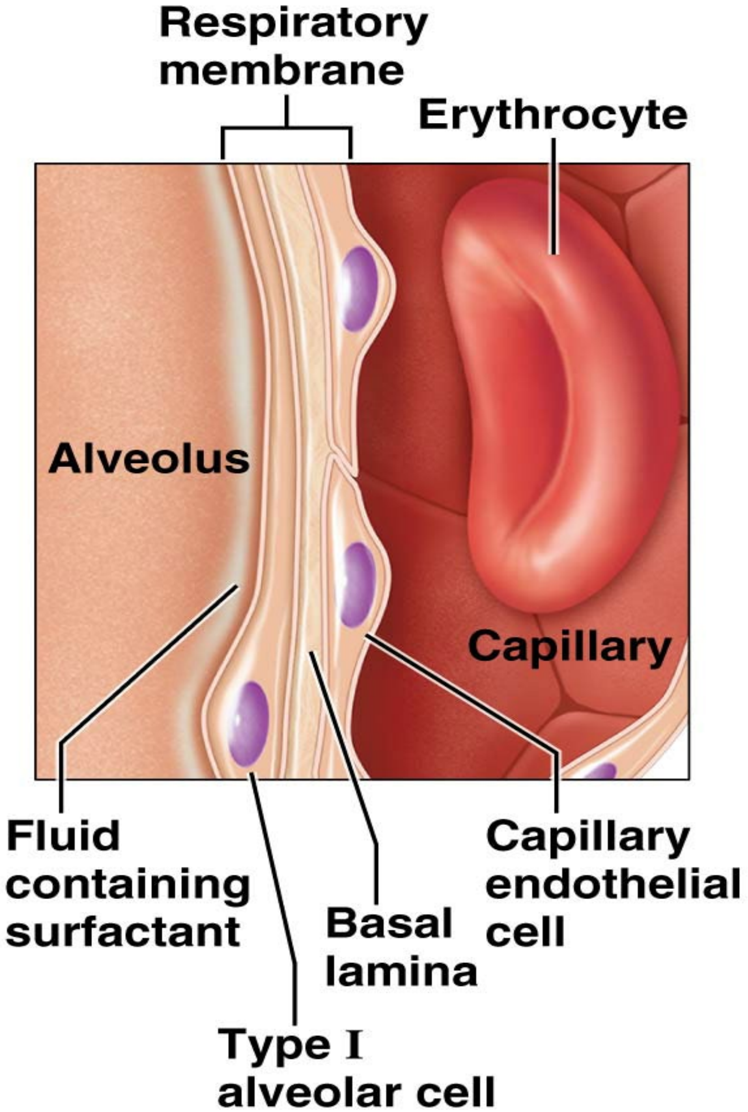
- squamous alveolar cells
- shared basement membrane
- endothelial cells of blood capillary

The shared basement membrane under certain conditions may swell due to edema.

Anything that increases distance across the respiratory membrane makes the diffusion on gasses slower

Anything that reduces the overall surface area of the  respiratory membrane makes the diffusion of gasses slower

# Structures of the respiratory membrane.




**(b) Respiratory membrane**

## How Will a Layer of Water on the Inner Surface of Alveoli Influences Inspiration and Expiration?

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Pulmonary surfactant produced by the great alveolar cells

Decreases surface tension by disrupting the hydrogen bonding in water

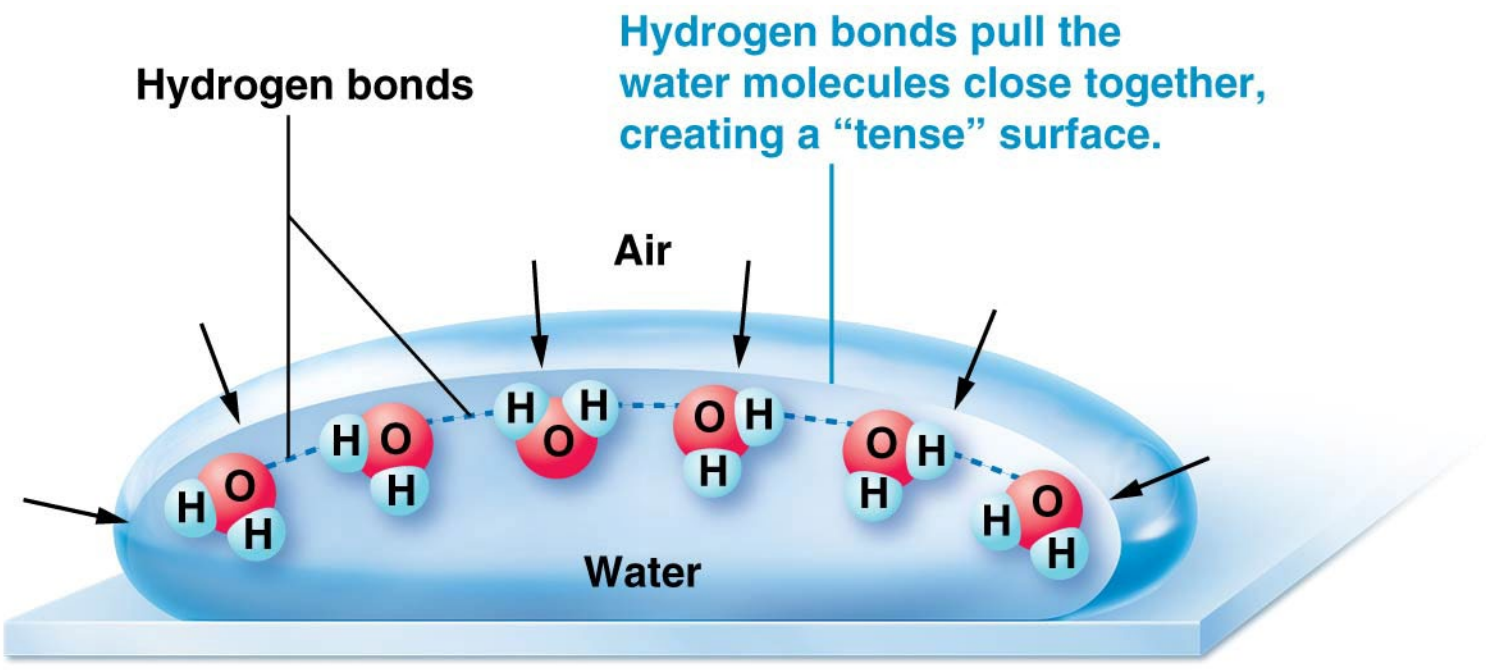
As lungs collapse, the water molecules on inner face of alveoli stack on top of each other.

These water molecules are connected by Hydrogen Bonds. /// surfactant disrupts Hydrogen Bonds, so it is easier to inflate lungs!!!

Because premature infants that lack surfactant they suffer from infant respiratory distress syndrome (IRDS) // great difficulty in breathing and may die

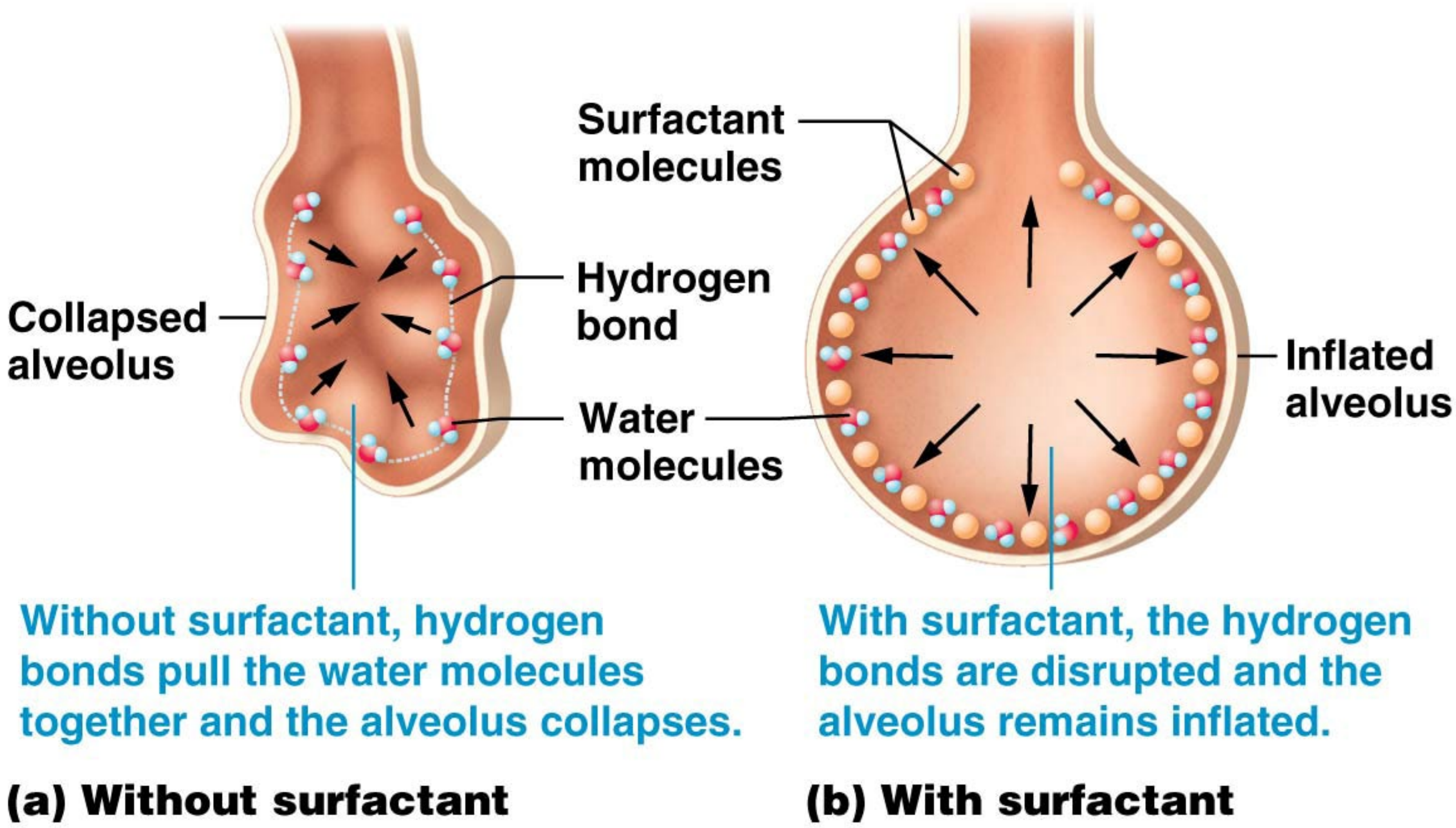
Knowledge about hydrogen bonding and the function of surfactant allows for treatment with artificial surfactant until lungs can produce Its own surfactant

# Water is a polar covalent molecule.




- It takes energy to separate water molecules
- This bonding helps to "deflate" the lungs.
- To reinflate the lungs these bonds must be broken.
- Pulmonary surfactant disrupts hydrogen bonds making it easier to inflate lungs.

# Effect of surfactant on alveolar surface tension.



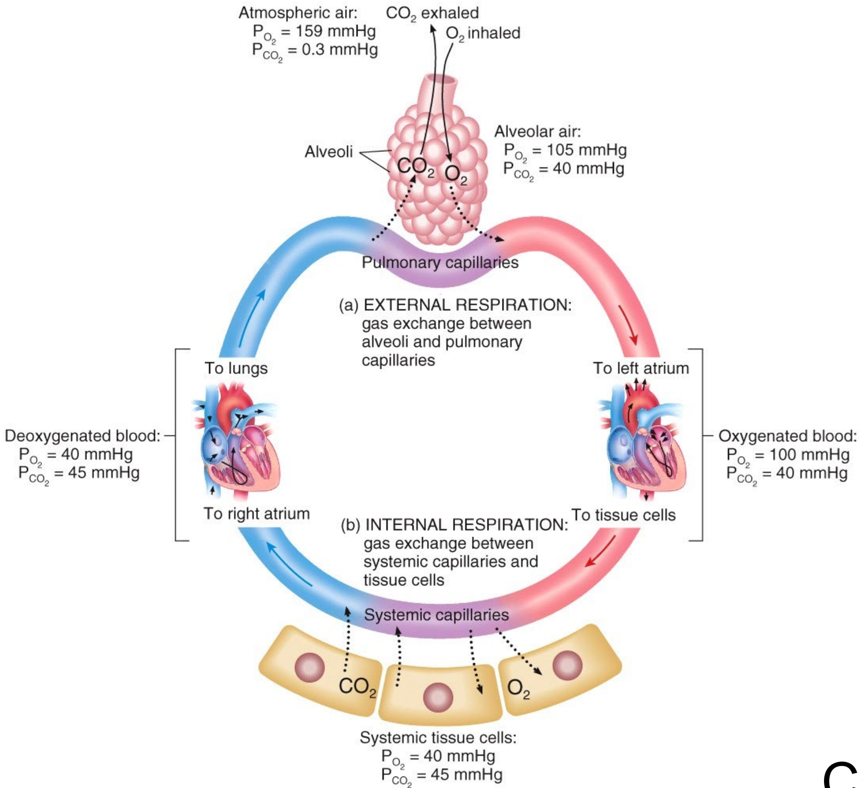

Without surfactant it will take more energy to inflate alveoli.

## TABLE 22.4 Composition of Inspired (Atmospheric) and Alveolar Air

| Gas | Inspired Air* | | Alveolar Air | |
|---|---|---|---|---|
| $N_2$ | 78.6% | 597 mm Hg | 74.9% | 569 mm Hg |
| $O_2$ | 20.9% | 159 mm Hg | 13.7% | 104 mm Hg |
| $H_2O$ | 0.5% | 3.7 mm Hg | 6.2% | 47 mm Hg |
| $CO_2$ | 0.04% | 0.3 mm Hg | 5.3% | 40 mm Hg |
| Total | 100% | 760 mm Hg | 100% | 760 mm Hg |

*Typical values for a cool clear day; values vary with temperature and humidity. Other gases present in small amounts are disregarded.

# How is the concentration of O2 and CO2 different between the atmosphere and systemic tissues?

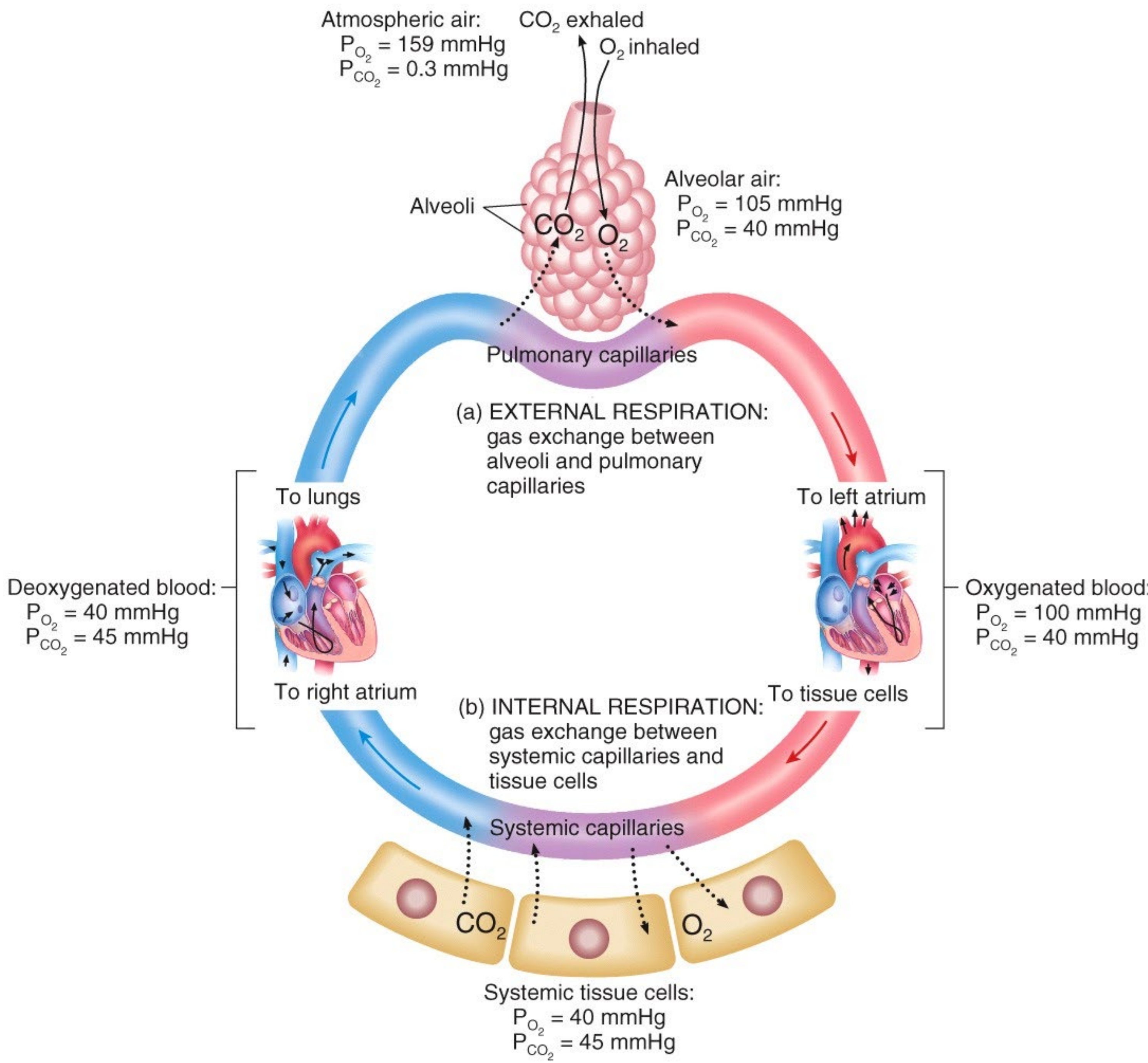



## Oxygen

159 mmHg - atmosphere
105 mmHg - alveolar
100 mmHg - blood arterial
040 mm Hg - systemic tissue
040 mmHg - blood venous

## Carbon Dioxide

.3 mmHg - atmosphere
40 mmHg - alveolar
40 mmHg - blood arterial
45 mmHg - systemic tissue
45 mmHg - blood venous


Atmospheric air:
$P_{O_2}$ = 159 mmHg
$P_{CO_2}$ = 0.3 mmHg
$CO_2$ exhaled
$O_2$ inhaled
Alveoli
$CO_2$
$O_2$
Alveolar air:
$P_{O_2}$ = 105 mmHg
$P_{CO_2}$ = 40 mmHg
Pulmonary capillaries
(a) EXTERNAL RESPIRATION:
gas exchange between
alveoli and pulmonary
capillaries
To lungs
To left atrium
Deoxygenated blood:
$P_{O_2}$ = 40 mmHg
$P_{CO_2}$ = 45 mmHg
Oxygenated blood:
$P_{O_2}$ = 100 mmHg
$P_{CO_2}$ = 40 mmHg
To right atrium
To tissue cells
(b) INTERNAL RESPIRATION:
gas exchange between
systemic capillaries and
tissue cells
Systemic capillaries
$CO_2$
$O_2$
Systemic tissue cells:
$P_{O_2}$ = 40 mmHg
$P_{CO_2}$ = 45 mmHg

# Pressure Gradients Determine Airflow

Respiratory airflow is governed by the same principles that regulates the flow of blood: pressure and resistance

Fluid movement is directly proportional to the pressure difference between two points

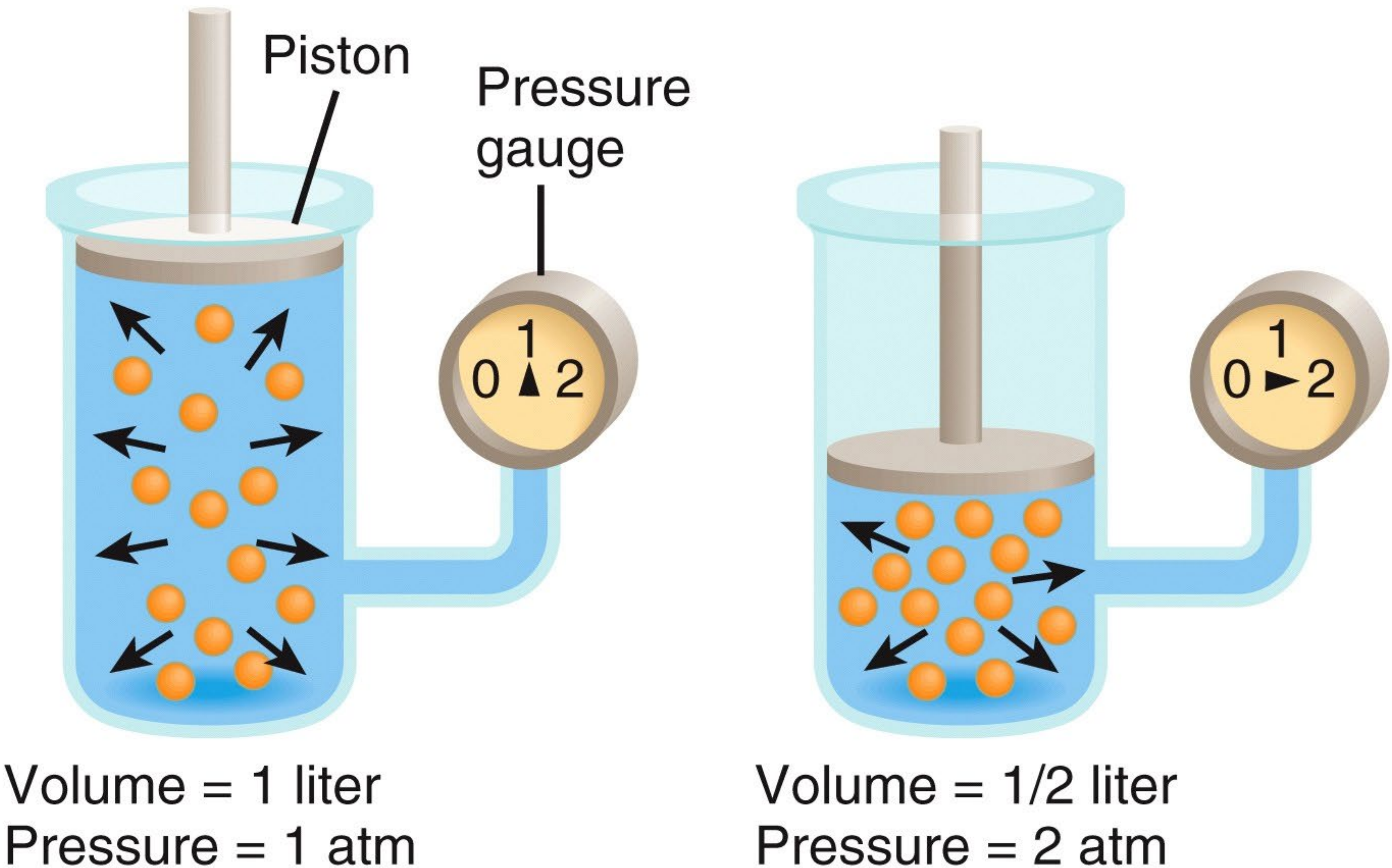
And fluid flow is inversely proportional to the resistance

So, if we want to ventilate the lungs (move air in and out) then we need to create a transient pressure gradient between the atmosphere and the lung tissue

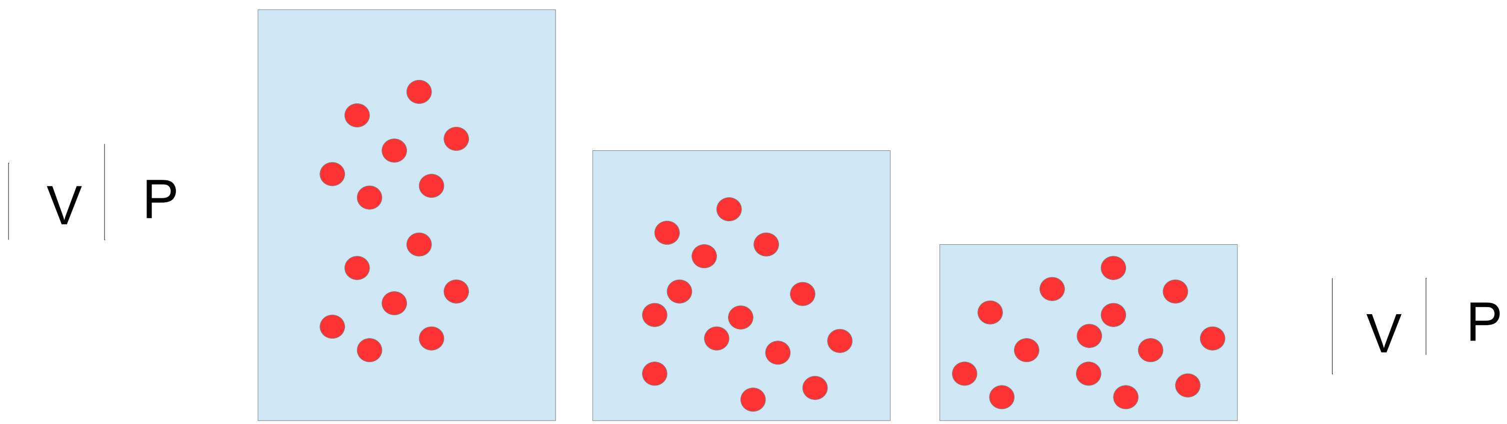
*Lower pressure in pleural cavity than the atmospheric pressure creates inspiration)  ///   greater pressure in pleural cavity than atmospheric pressure creates expiration*

**Laws of physic explain how the lungs move air!**

# Boyle's Law


Piston
Pressure gauge
1
0 2
1
0 2
Volume = 1 liter
Pressure = 1 atm
Volume = 1/2 liter
Pressure = 2 atm

# Boyle's Law




Assume constant temperature

Same number of gas atoms in each container

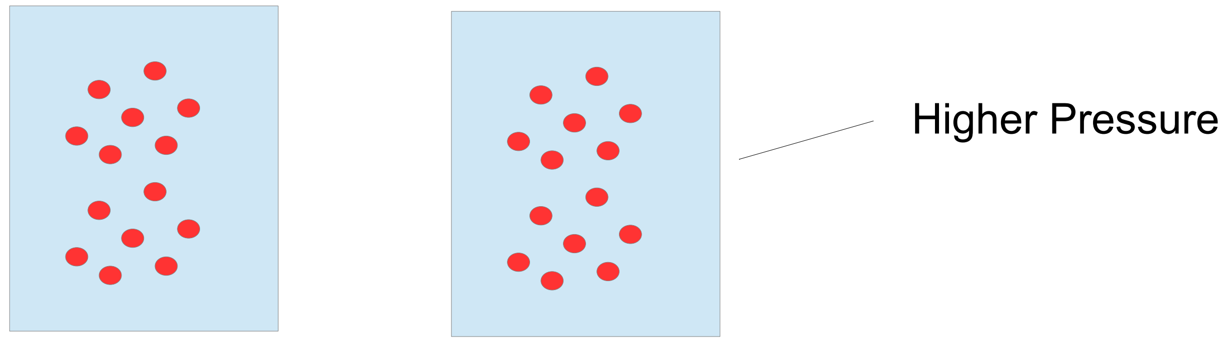
Fewer collisions in larger container (lower pressure)

More collisions in smaller container (higher pressure)

Pressure is inversely proportional to volume.

How does this help respiration?  Significance?

# Charles’ Law




25 degree Celcius

37 degree Celcius

Here the volume is constant but the temperature increases.

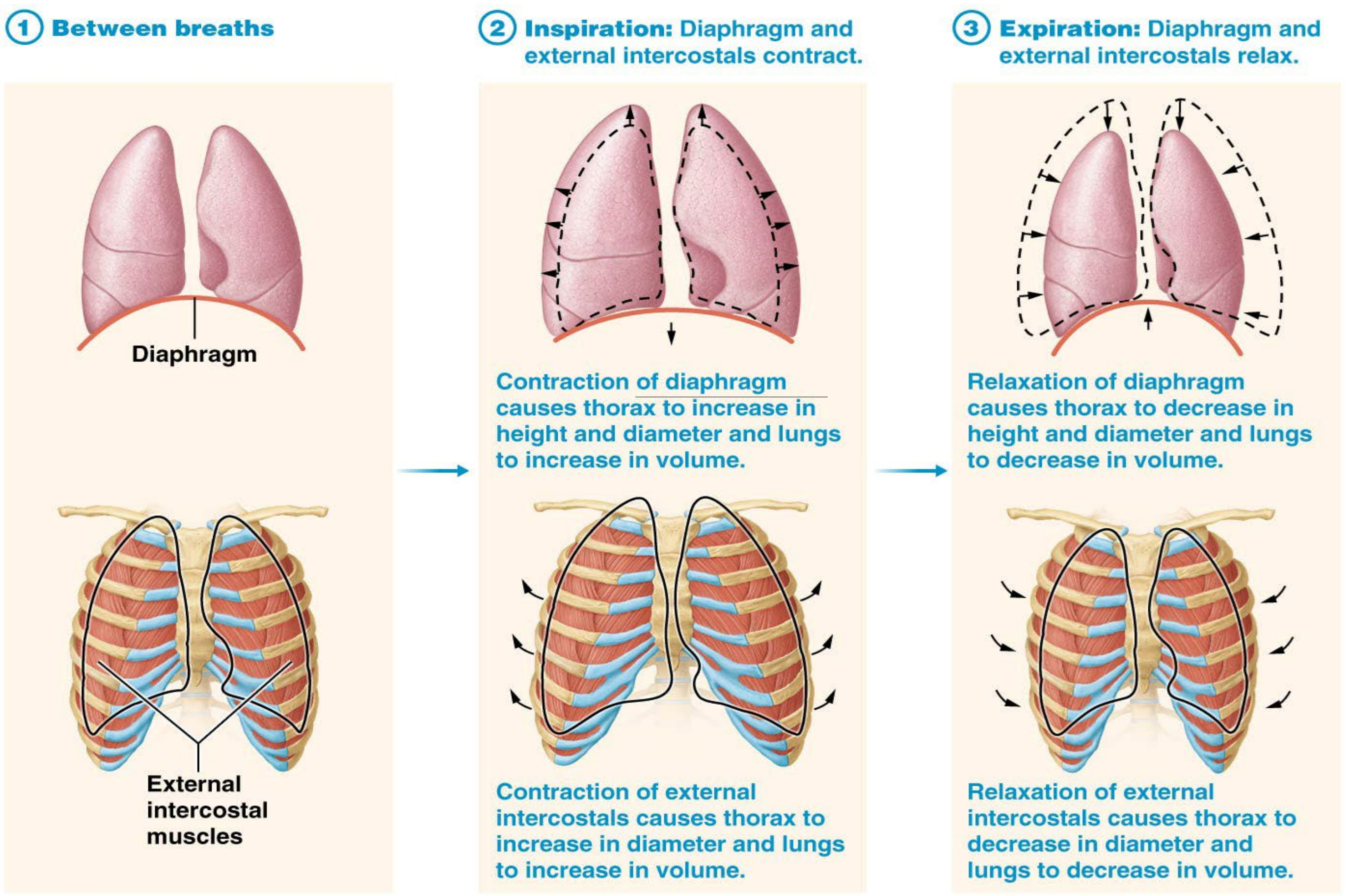
Since gas molecules move faster at a higher temperature, there are more gas molecule collisions against the sides of the container which results in an increase in pressure.  We did not increase the number of molecules, just the number of collisions.

When we breath in air, it is warmed by the mucosa.

How does this help respiration?  Significance?

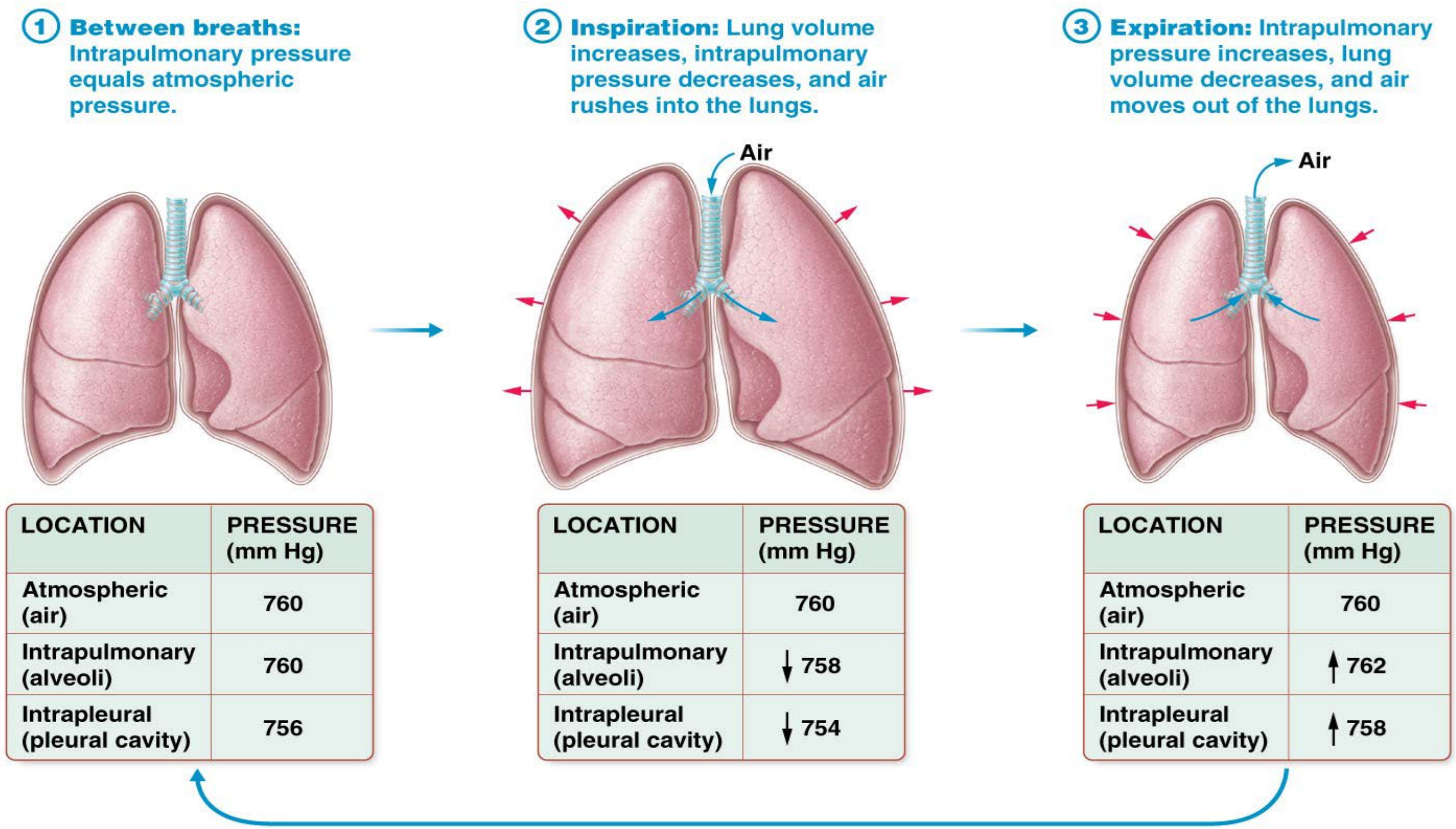
Note:  Dalton's Law of Gases and Henry’s Law also help to explain respiratory physiology (see reference video for more details)

## Volume changes in pulmonary ventilation: structure and function of the inspiratory muscles in quiet breathing.




- In "quiet breathing" inspiration is active and expiration is passive.
- Inspiration requires contraction of diaphragm and expiration occurs because of the recoil of elastic tissue expanded during inspiration.

# Pressure changes in pulmonary ventilation during respiratory cycle.



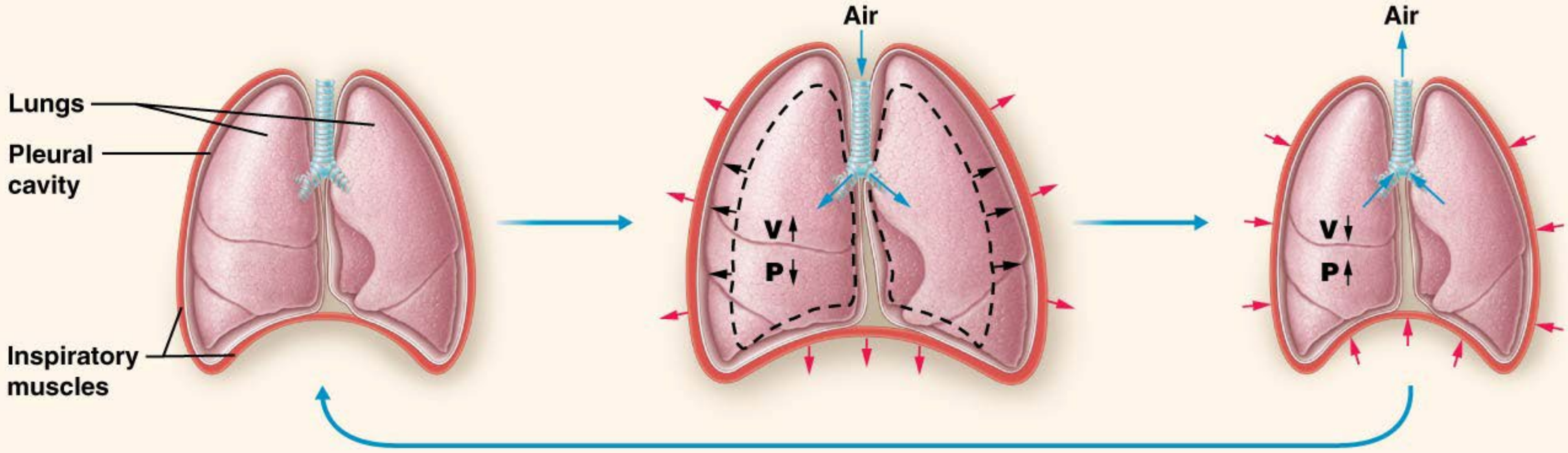

| LOCATION | PRESSURE (mm Hg) |
|---|---|
| Atmospheric (air) | 760 |
| Intrapulmonary (alveoli) | 760 |
| Intrapleural (pleural cavity) | 756 |

| LOCATION | PRESSURE (mm Hg) |
|---|---|
| Atmospheric (air) | 760 |
| Intrapulmonary (alveoli) | ↓ 758 |
| Intrapleural (pleural cavity) | ↓ 754 |

| LOCATION | PRESSURE (mm Hg) |
|---|---|
| Atmospheric (air) | 760 |
| Intrapulmonary (alveoli) | ↑ 762 |
| Intrapleural (pleural cavity) | ↑ 758 |

- Respiratory cycle is five seconds long.
- Inspiration occurs for two seconds as diaphragm contracts (active / volume).
- Expiration occurs for three seconds as diaphragm relaxes by elastic recoil.

# The Big Picture of Pulmonary Ventilation




**Between breaths**

- Intrapulmonary pressure equals atmospheric pressure.
- ↓
- No air movement occurs.

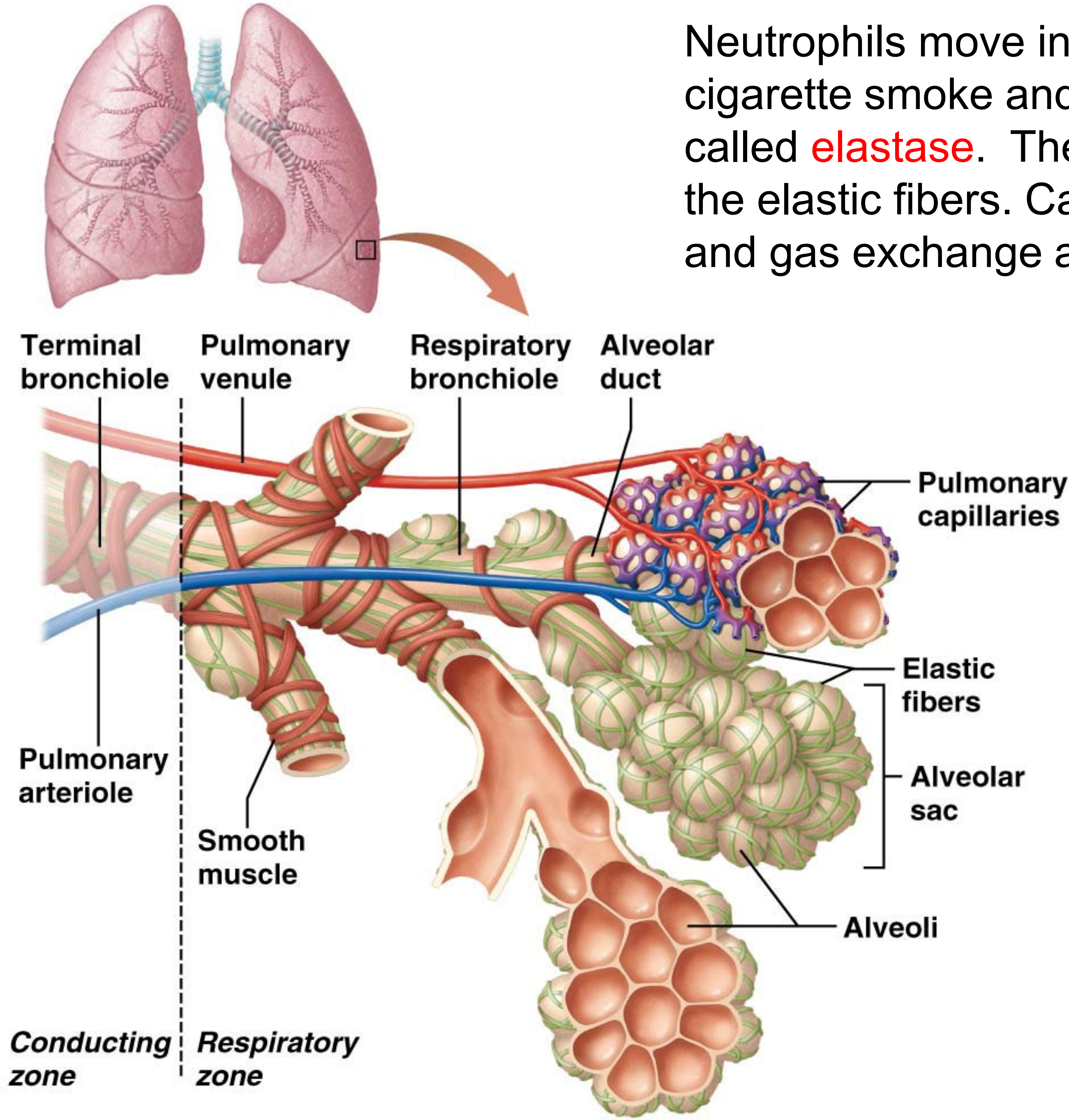
**Inspiration**

- Inspiratory muscles contract.
- ↓
- Thoracic volume increases.
- ↓
- Lung volume increases.
- ↓
- Intrapulmonary pressure decreases to below atmospheric pressure.
- ↓
- Air flows into lungs.

**Expiration**

- Inspiratory muscles relax.
- ↓
- Thoracic volume decreases due to elastic recoil. Passive
- ↓
- Lung volume decreases.
- ↓
- Intrapulmonary pressure increases to above atmospheric pressure.
- ↓
- Air flows out of lungs.

Neutrophils move into the area due to cigarette smoke and release an enzyme called elastase. The enzyme breaks down the elastic fibers. Causes reduced surface and gas exchange area.

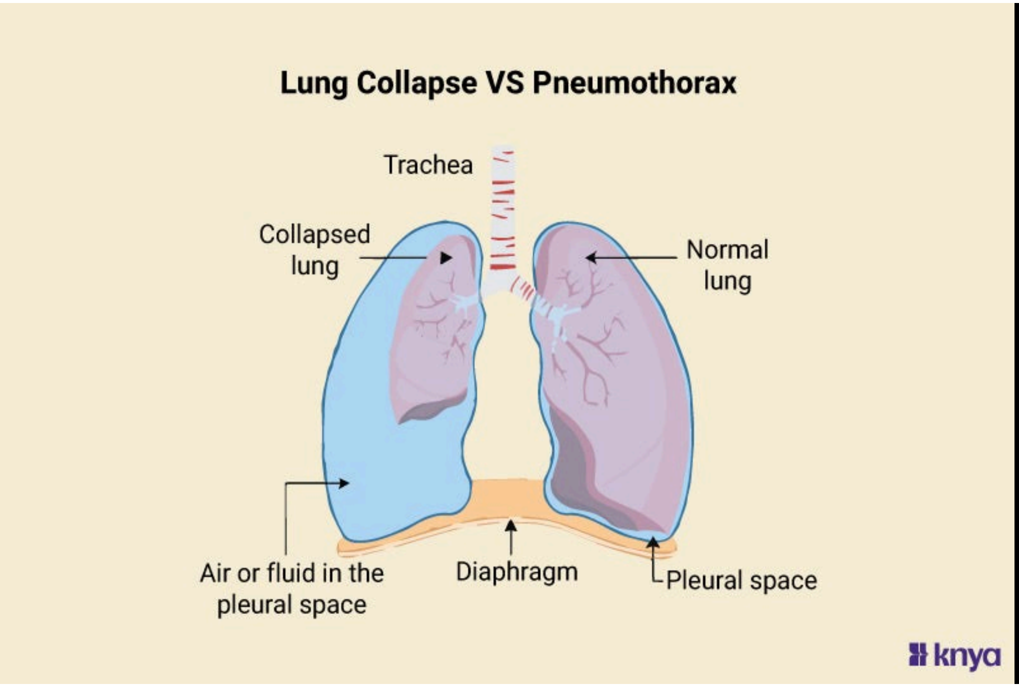



**(a) Structures of the respiratory zone**

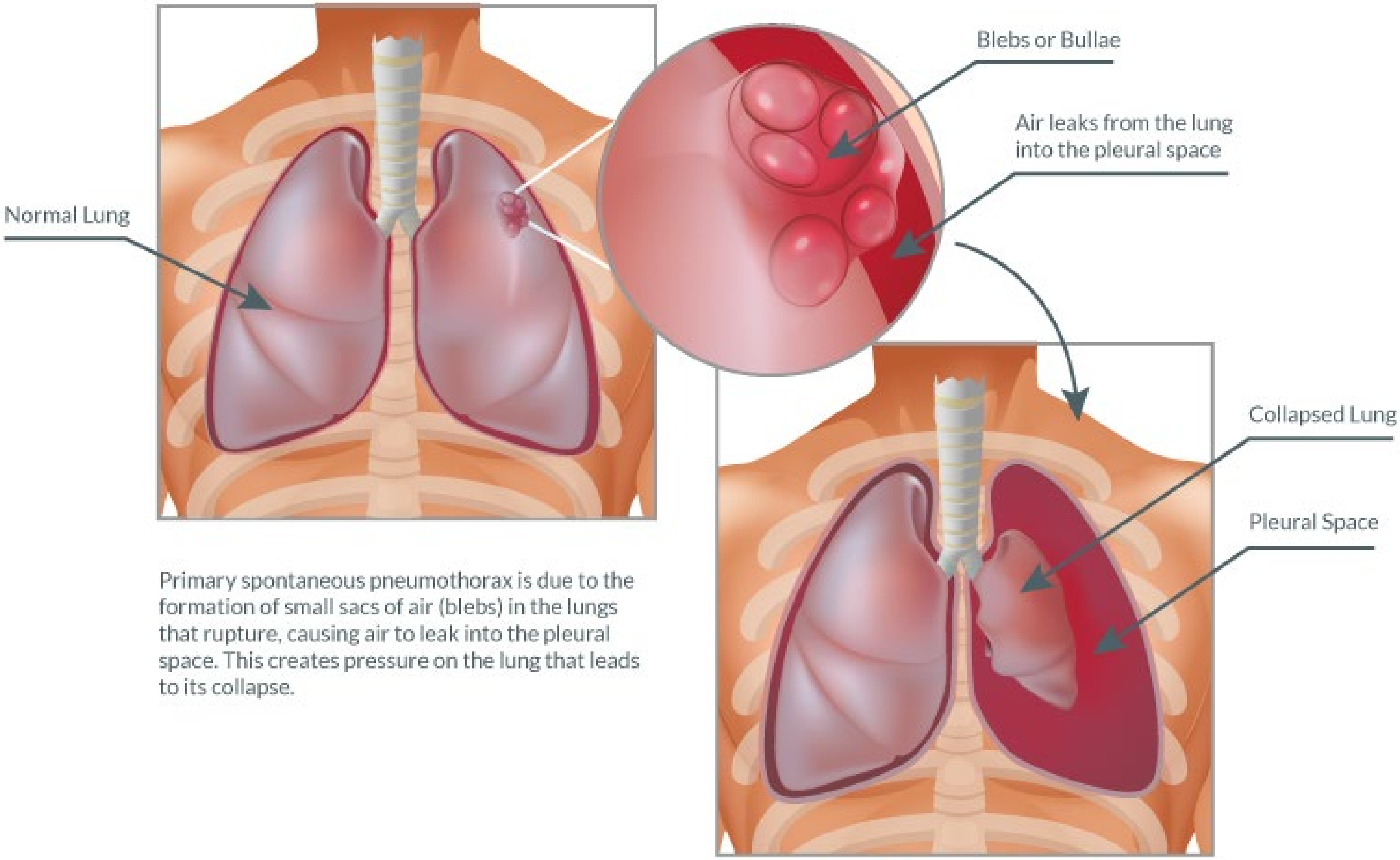
# Atelectasis VS Pneumothorax

Atelectasis and pneumothorax **both involve lung collapse** causing chest pain and breathing difficulty but differ in mechanism: **atelectasis** is a closure of air sacs (alveoli) often from blockages, while **pneumothorax** is air trapped in the chest cavity outside the lung, causing it to collapse.

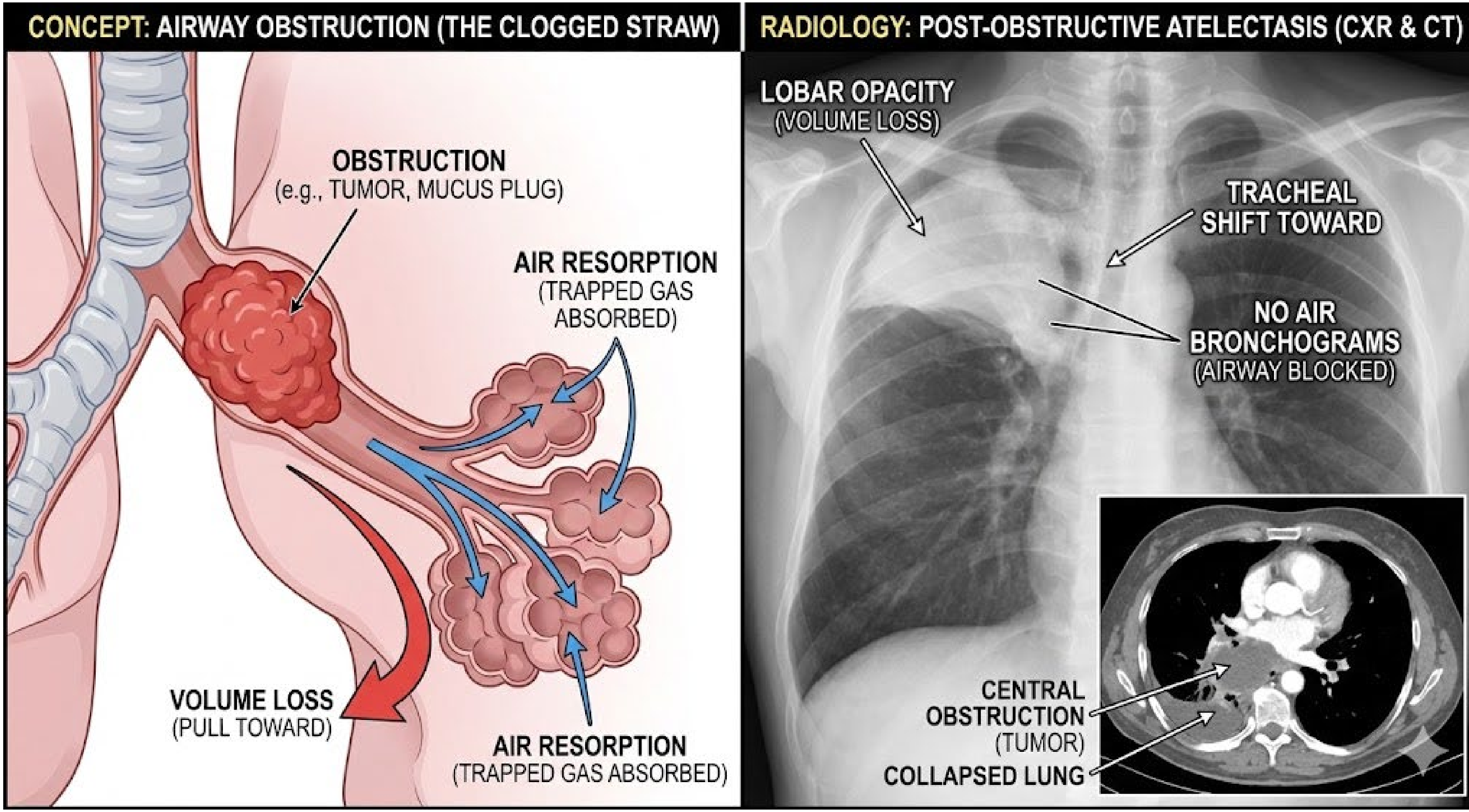
**Atelectasis**: Focuses on clearing airway blockages (deep breathing, chest physiotherapy, suctioning) and on clearing airway blockages. **Pneumothorax:** Focuses on removing trapped air via needle aspiration or chest tube insertion.

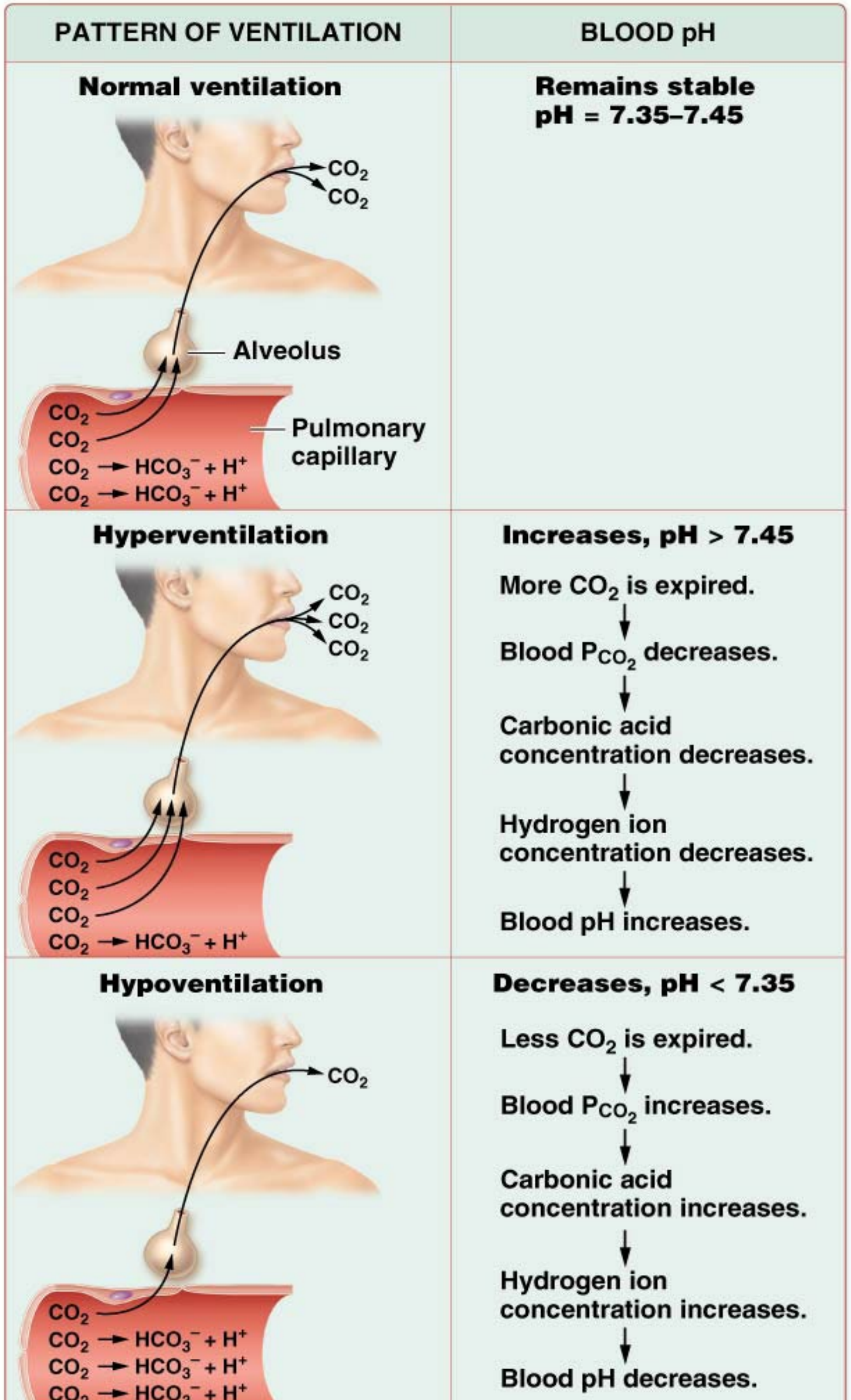



- **Atelectasis:** Appears white (radiopaque) on X-ray. P**neumothorax:** Shows as a dark (radiolucent) area with a visible pleural line (no lung markings).




Primary spontaneous pneumothorax is due to the formation of small sacs of air (blebs) in the lungs that rupture, causing air to leak into the pleural space. This creates pressure on the lung that leads to its collapse.


CONCEPT: AIRWAY OBSTRUCTION (THE CLOGGED STRAW)
OBSTRUCTION
(e.g., TUMOR, MUCUS PLUG)
AIR RESORPTION
(TRAPPED GAS
ABSORBED)
VOLUME LOSS
(PULL TOWARD)
AIR RESORPTION
(TRAPPED GAS ABSORBED)
RADIOLOGY: POST-OBSTRUCTIVE ATELECTASIS (CXR & CT)
LOBAR OPACITY
(VOLUME LOSS)
TRACHEAL
SHIFT TOWARD
NO AIR
BRONCHOGRAMS
(AIRWAY BLOCKED)
CENTRAL
OBSTRUCTION
(TUMOR)
COLLAPSED LUNG




# Effect of blood pH on ventilation patterns

$$CO_2 + H_2O \rightleftharpoons CH_2O_3 \rightleftharpoons H^{+} + CHO_3^{-}$$

Carbon dioxide plus water makes carbonic acid that then changes into proton plus bicarbonate

Carbonic acid is an acid because it can donate a proton

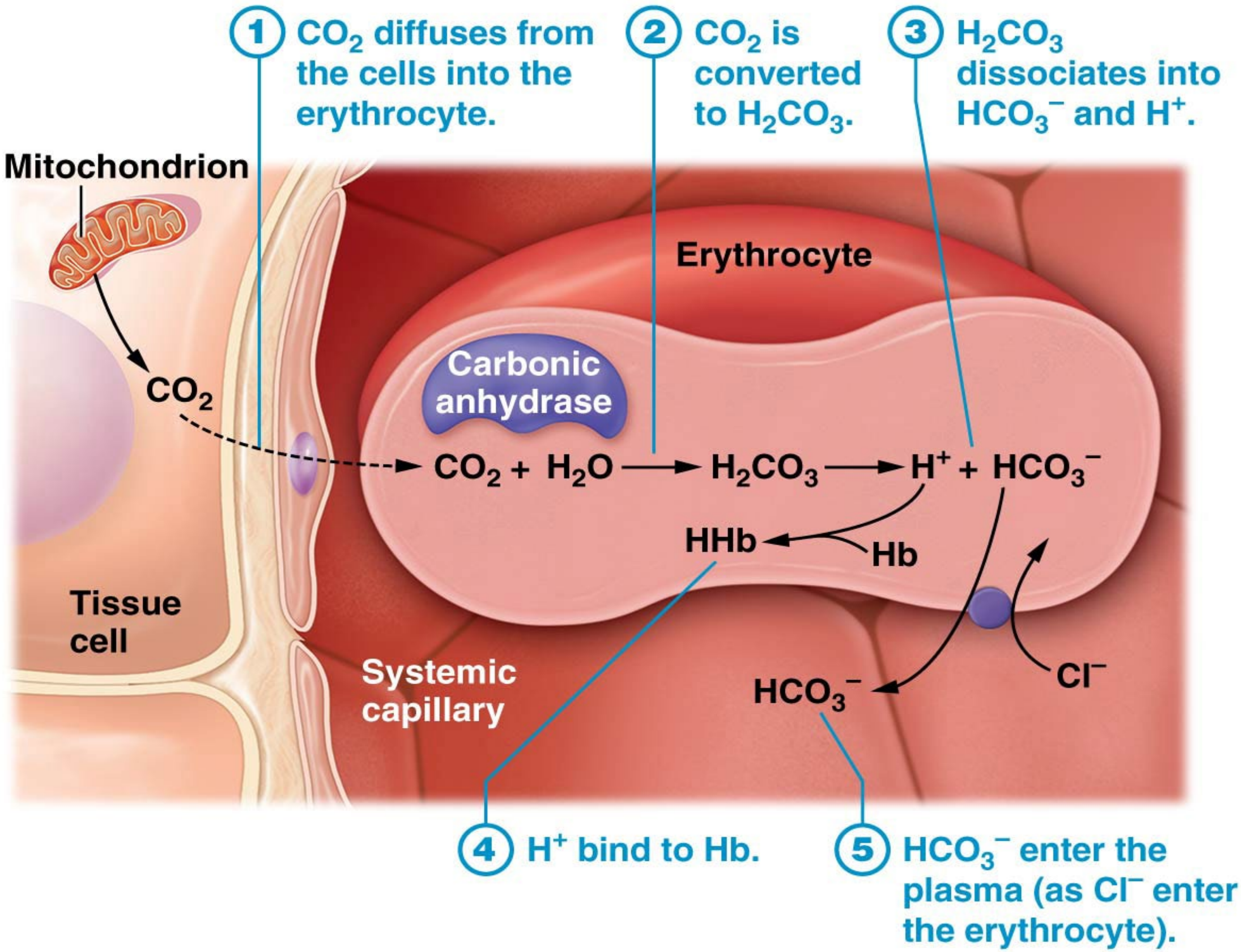
Bicarbonate is a weak base, and the proton is an acid

This chemical reaction occurs inside RBC and is catalyzed by carbonic anhydrase (CA)

Hyperventilate reduces ventilation

Hypoventilation stimulates ventilation

# Transport of carbon dioxide: the conversion of carbon dioxide and water into carbonic acid in erythrocytes.

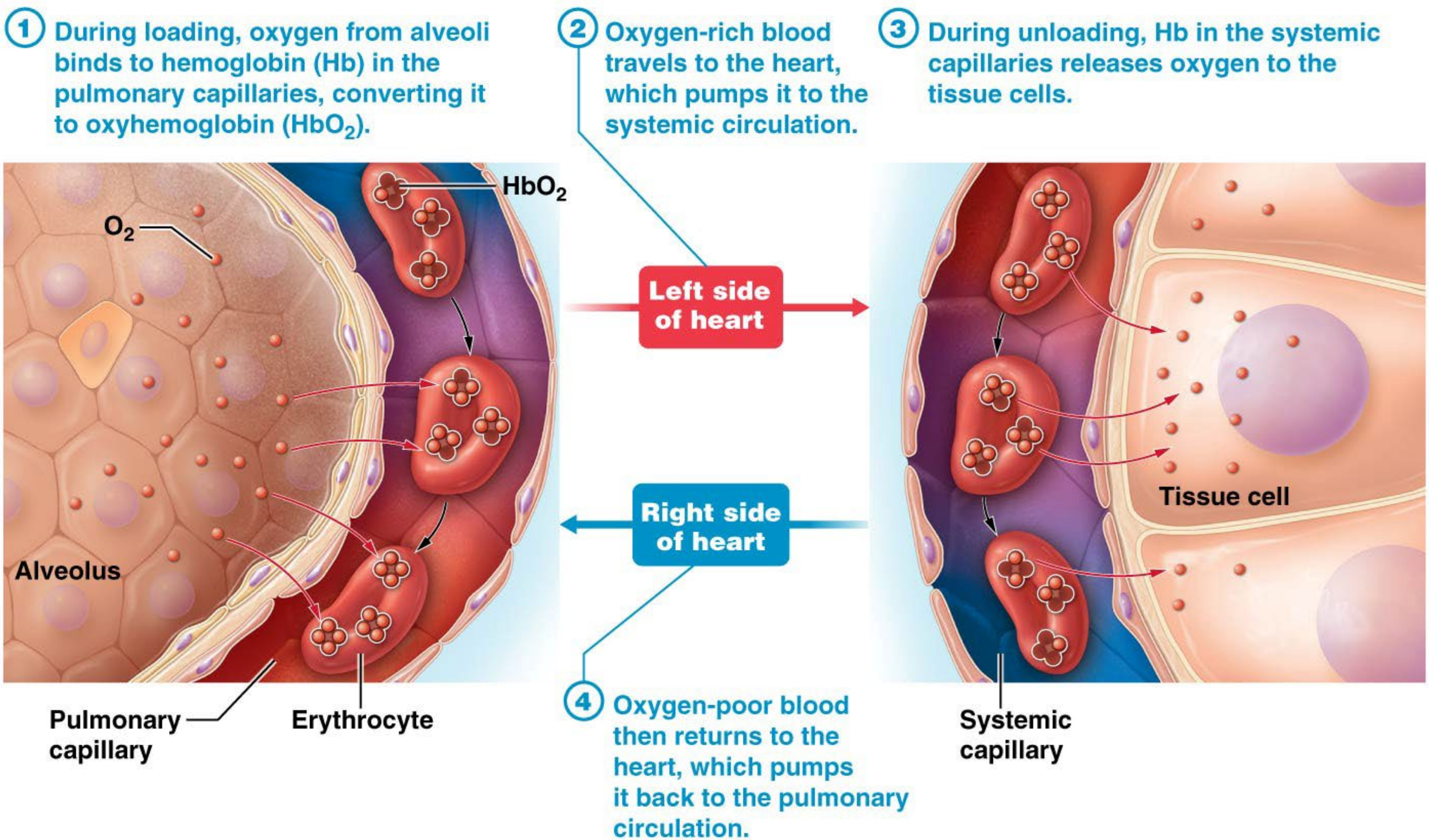



**(a) Bicarbonate formation in an erythrocyte in a systemic capillary**

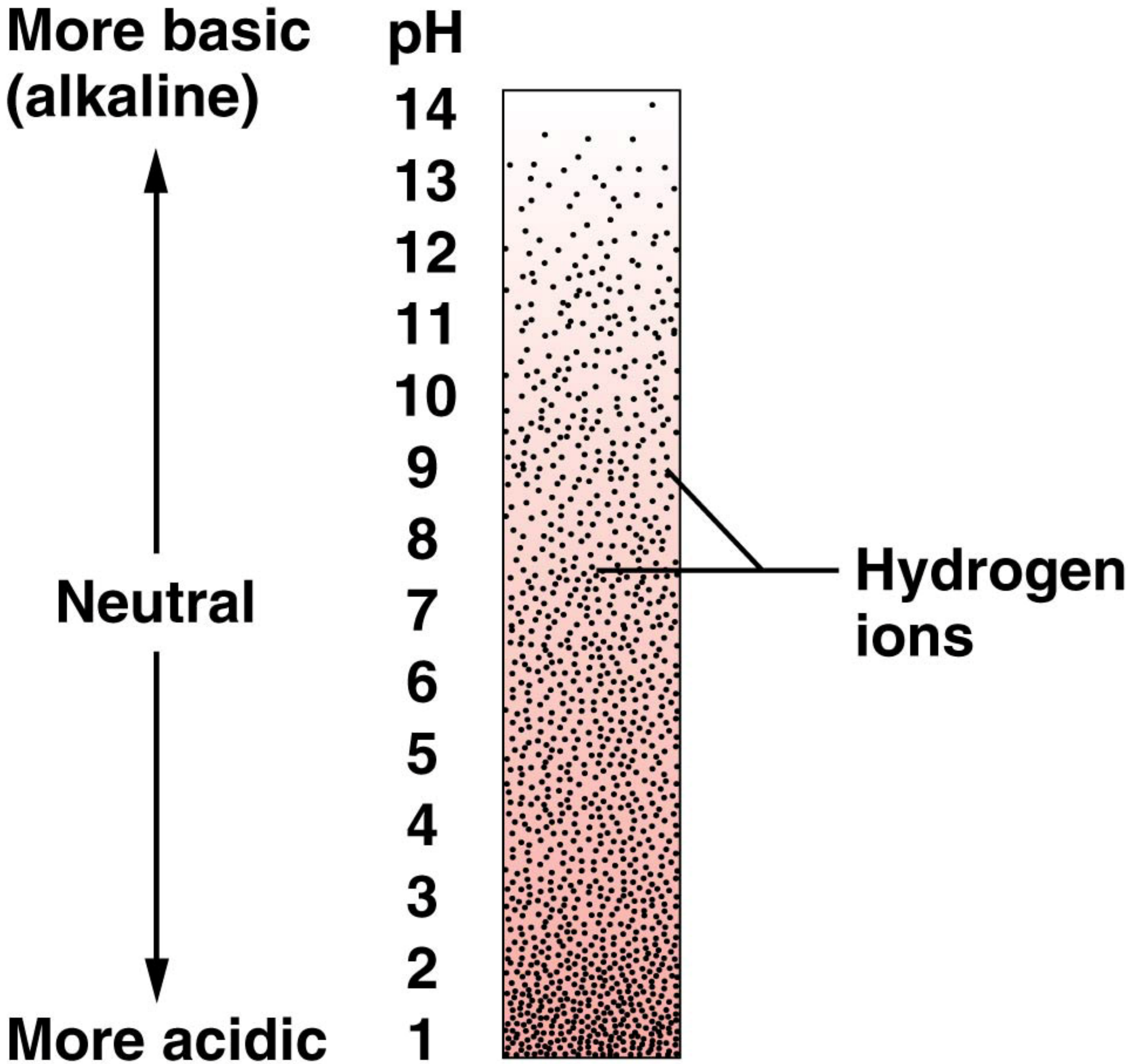
Bicarbonate forms ionic bond with sodium and is transported to lungs as sodium-bicarbonate

Hydrogen ion binds to Hb-O2 and causes oxygen to be released from Hb // oxygen now free to diffuse to mitochondria

# Transport of oxygen: loading and unloading of oxygen on hemoglobin in erythrocytes.



# pH



More basic
(alkaline)
Neutral
More acidic
pH
14
13
12
11
10
9
8
7
6
5
4
3
2
1
Hydrogen
ions

# Primary Control of Ventilation

The primary control centers for breathing (ventilation of lungs) are the chemoreceptors that respond to carbon dioxide levels in the blood. // Two locations

Central chemoreceptors // Located in the medulla

Peripheral chemoreceptors // Located in the carotid bodies and aortic arch

Both chemoreceptors detect changes in carbon dioxide level & hydrogen ions /// increase CO2 stimulates breathing

## Hypercapnia (high PCO2) Main Stimulus for Ventilation

As carbon dioxide levels in the blood increases // pH lower – blood becomes more acid like.

Carbon dioxide easily diffuses into cerebral spinal fluid within medulla oblongata (respiratory control centers).

This lowers pH and stimulates respiratory center

Increased rate and depth of respiration

# Hypercapnia (high $PCO_2$) Main Stimulus for Ventilation

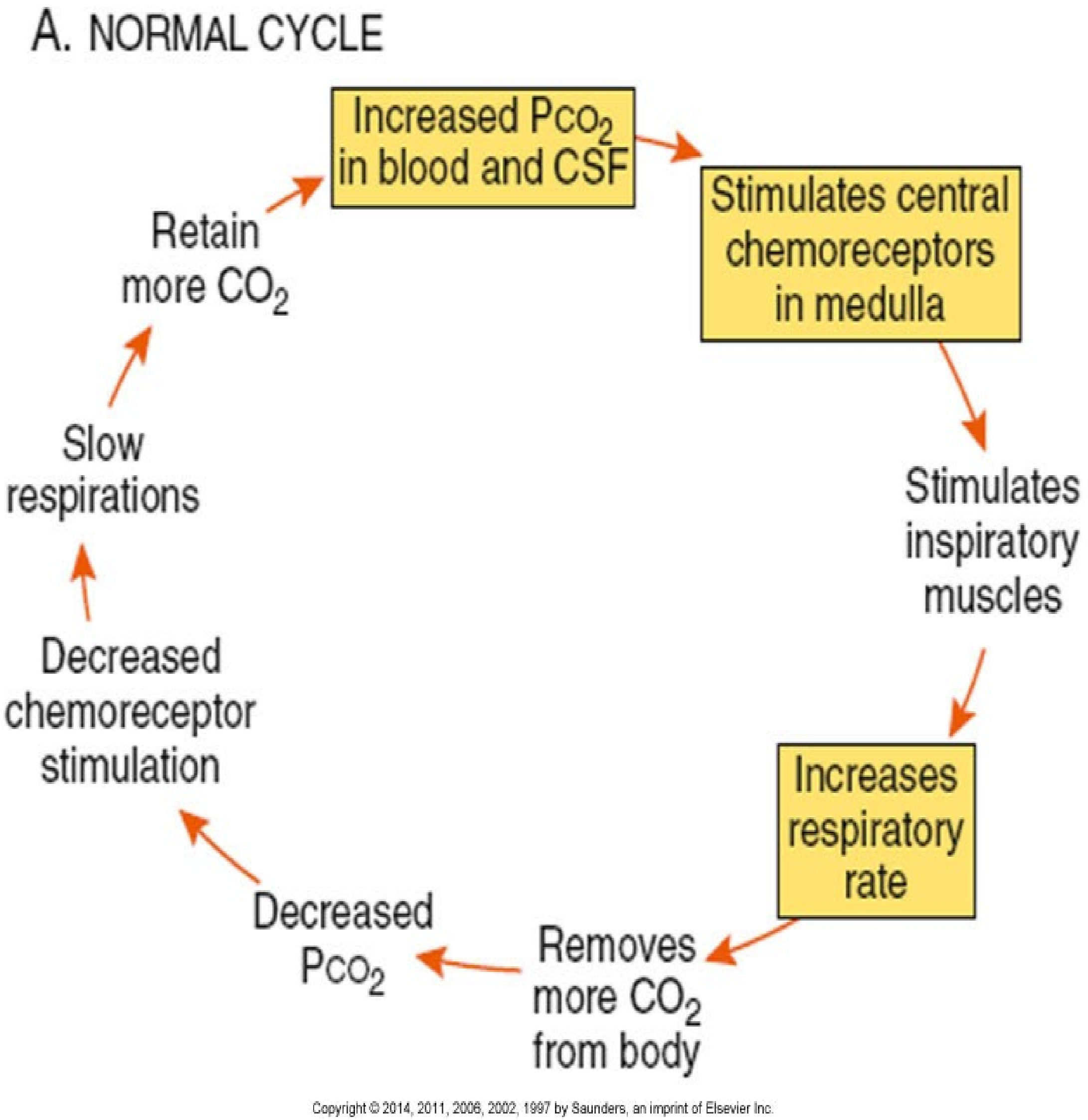
Hyperventilation is a condition in which you start to breathe very fast. Healthy breathing occurs with a healthy balance between breathing in oxygen and breathing out carbon dioxide.

You upset this balance when you hyperventilate by exhaling more $CO_2$. This upsets acid-base balance in blood.

Hyperventilation causes respiratory alkalosis, and this will depress central nervous system.

Swimmers often hyperventilate thinking this will add more oxygen to their blood so they can hold their breath longer, however. This is not true. The hyperventilation reduces carbon dioxide blood concentration so the swimmer may faint when they dive into the water. Very dangerous practice!

# Normal Respiratory Control



## Hydrogen Ions & Pulmonary Ventilation

Pulmonary ventilation is adjusted to maintain the pH within brain

Central chemoreceptors in the medulla oblongata produce about 75% of the change in respiration induced by pH shift

Yet $H^+$ does not cross the blood-brain barrier very easily

$CO_2$ crosses blood brain barrier rapidly and in CSF reacts with water and produces carbonic acid

Dissociates into bicarbonate and hydrogen ions /// most $H^+$ remains free and greatly stimulates the central chemoreceptors

Hydrogen ions also stimulate peripheral chemoreceptors which produce about 25% of the respiratory response to pH change

HOWEVER - peripheral chemoreceptors also sensitive to PO2 // *play important role in respiration after chronic high PCO2 or very low oxygen concentrations*

# Oxygen Secondary Control of Ventilation

Primary stimulus is under normal physiologic conditions with elevated $CO_2$ however...........

Extended period of high $CO_2$ will cause chemoreceptors to fatigue, and they will not respond elevated $CO_2$

Peripheral chemoreceptors now may react to low $O_2$ levels

*This is why $O_2$ becomes most important control mechanism in individuals with chronic lung disease (e.g. emphysema)*

This changes respiratory system into hypoxic drive

Central control centers no longer respond to $CO_2$ stimulus, and now peripheral chemoreceptors dominates with $PO_2$ as “controller”

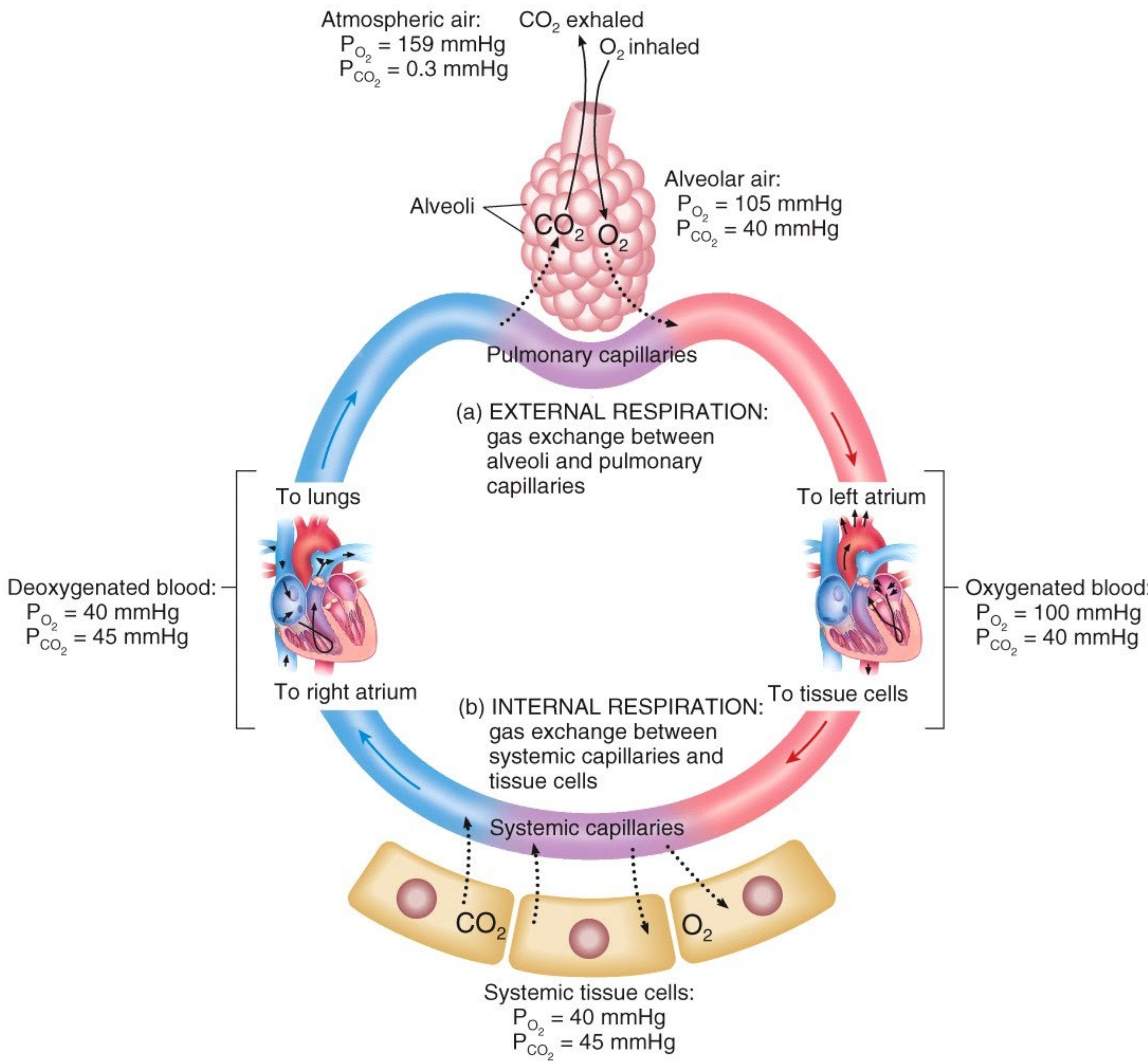
## When Peripheral Chemoreceptors Control of Ventilation

The peripheral chemoreceptors are stimulated by low oxygen levels (but not the central chemorecptors)

Occurs if PO2 falls below normal 100 mmHg and above 50 mmHg // within this range PO2 stimulates breathing rate (see next slide)

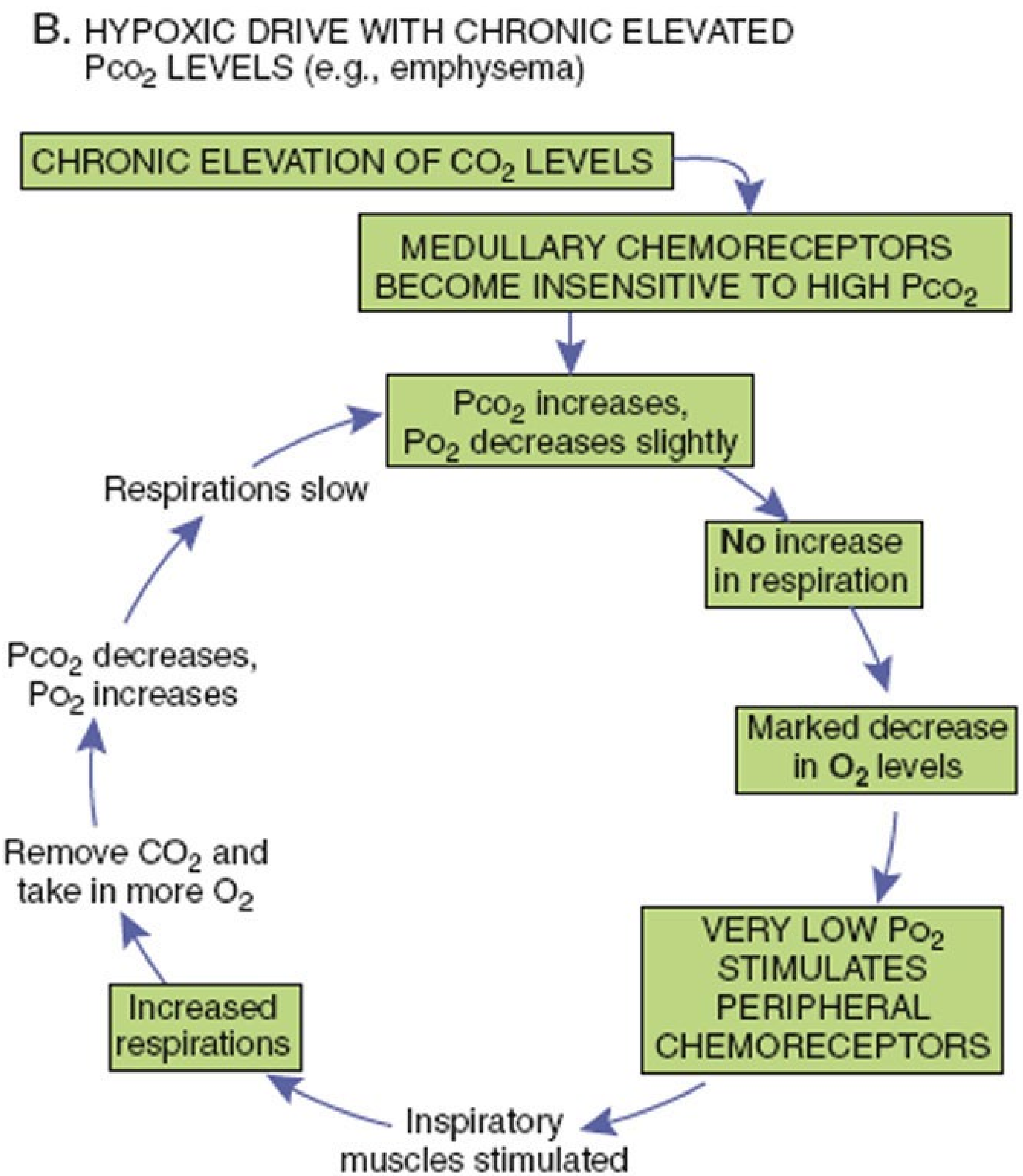
HOWEVER: Below 50 mmHg peripheral chemoreceptors do not stimulate inspiration

Severe PO2 deficiency will also now depress central chemorecptors // DRG do not respond to any inputs and sends fewer impulses to inhalation muscles // breathing slows – as O2 continues to drop this **starts a fatal positive feedback loop!**



Atmospheric air:
$P_{O_2}$ = 159 mmHg
$P_{CO_2}$ = 0.3 mmHg
$CO_2$ exhaled
$O_2$ inhaled
Alveoli
$CO_2$
$O_2$
Alveolar air:
$P_{O_2}$ = 105 mmHg
$P_{CO_2}$ = 40 mmHg
Pulmonary capillaries
(a) EXTERNAL RESPIRATION:
gas exchange between
alveoli and pulmonary
capillaries
To lungs
To left atrium
Deoxygenated blood:
$P_{O_2}$ = 40 mmHg
$P_{CO_2}$ = 45 mmHg
Oxygenated blood:
$P_{O_2}$ = 100 mmHg
$P_{CO_2}$ = 40 mmHg
To right atrium
To tissue cells
(b) INTERNAL RESPIRATION:
gas exchange between
systemic capillaries and
tissue cells
Systemic capillaries
$CO_2$
$O_2$
Systemic tissue cells:
$P_{O_2}$ = 40 mmHg
$P_{CO_2}$ = 45 mmHg

# Hypoxic Drive



The primary danger of admitting patients with **"hypoxic drive"** (typically chronic obstructive pulmonary disease, or COPD, retainers) to the emergency room is **oxygen-induced hypercapnia**, which <u>can lead to severe acidosis, coma, and respiratory arrest if they are given high-concentration oxygen</u>.

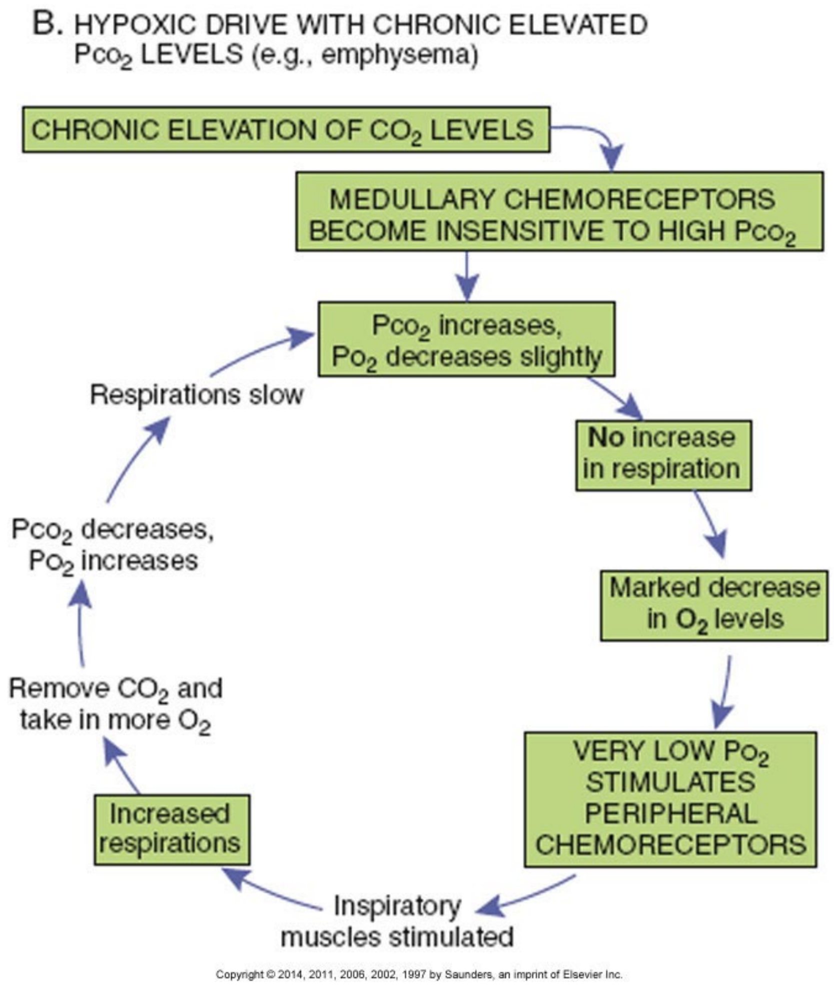
While the "hypoxic drive" theory suggests high oxygen levels turn off the signal to breathe, the more significant dangers in the ED are the disruption of oxygen-driven breathing mechanisms, worsening ventilation-perfusion mismatch, and the Haldane effect, which causes rapid $CO_2$ accumulation.

**Key Dangers and Risks:**

- **Oxygen-Induced Hypercapnia & Narcosis:** Excessive oxygen can cause an acute rise in carbon dioxide (), leading to narcosis (lethargy, confusion, coma).
- **Respiratory Arrest/Failure:** If the respiratory center is suppressed or overloaded by high oxygen, the patient may stop breathing or develop severe respiratory acidosis (pH $<7.25$).
- **Worsening V/Q Mismatch:** High-concentration oxygen reverses localized pulmonary vasoconstriction, causing blood to flow to poorly ventilated alveoli, which dramatically increases dead space and results in CO2 retention.
- **Haldane Effect:** High levels of oxygenated hemoglobin cannot bind as much CO2, leading to more CO2 dissolving back into the blood, increasing systemic acid.
- **Rebound Hypoxia:** Abruptly stopping high-flow oxygen can lead to a sudden, fatal drop in oxygen levels.

**Management Guidelines in the ED:**

To avoid these dangers, guidelines recommend **titrated oxygen therapy** rather than high-flow oxygen, specifically targeting an oxygen saturation of **88%–92%**. This reduces mortality and respiratory acidosis compared to high-concentration oxygen.



# Usable Air Within Lung Tissue

Anatomic dead space /// conducting division of airway where there is no gas exchange // 150 mL

This can be altered slightly by sympathetic and parasympathetic stimulation

Pulmonary diseases increases "dead space" (total dead space) also called physiologic dead space

Respiratory membrane thickened by edema or fibrosis

Some alveoli may be unable to exchange gases because they lack blood flow (perfusion and ventilation are not matched)

Some diseases reduce amount of respiratory membrane

These events all add to anatomic dead space to create total dead space

# Air Flow Into Lung Tissue and Gas Exchange

Only air that reaches the alveoli is available for gas exchange

Not all inhaled air gets to alveoli

500 mL moved into respiratory system // tidal volume

About 150 mL of the tidal volume fills the conducting division of the airway

Only 350 mL of air reaches the alveoli

# Usable Air Within Lung Tissue

Physiologic dead space = Sum of anatomic dead space and any pathological alveolar dead space caused by disease

If a person inhales 500 mL of air and 150 mL is in the anatomical dead space then only 350 mL reaches alveoli

Alveolar ventilation rate (AVR)

Air that ventilates alveoli (350 mL) X respiratory rate (12 bpm) = 4200 mL/min

Of all the measurements, this one is <u>most directly relevant to the body's ability to get oxygen</u> to the tissues and dispose of carbon dioxide

Lung diseases reduces AVR

# Measuring Ventilation Volumes

Spirometer – a device that recaptures expired breath and records such variables such as rate and depth of breathing, speed of expiration, and rate of oxygen consumption (view video)

Respiratory volumes (view video)

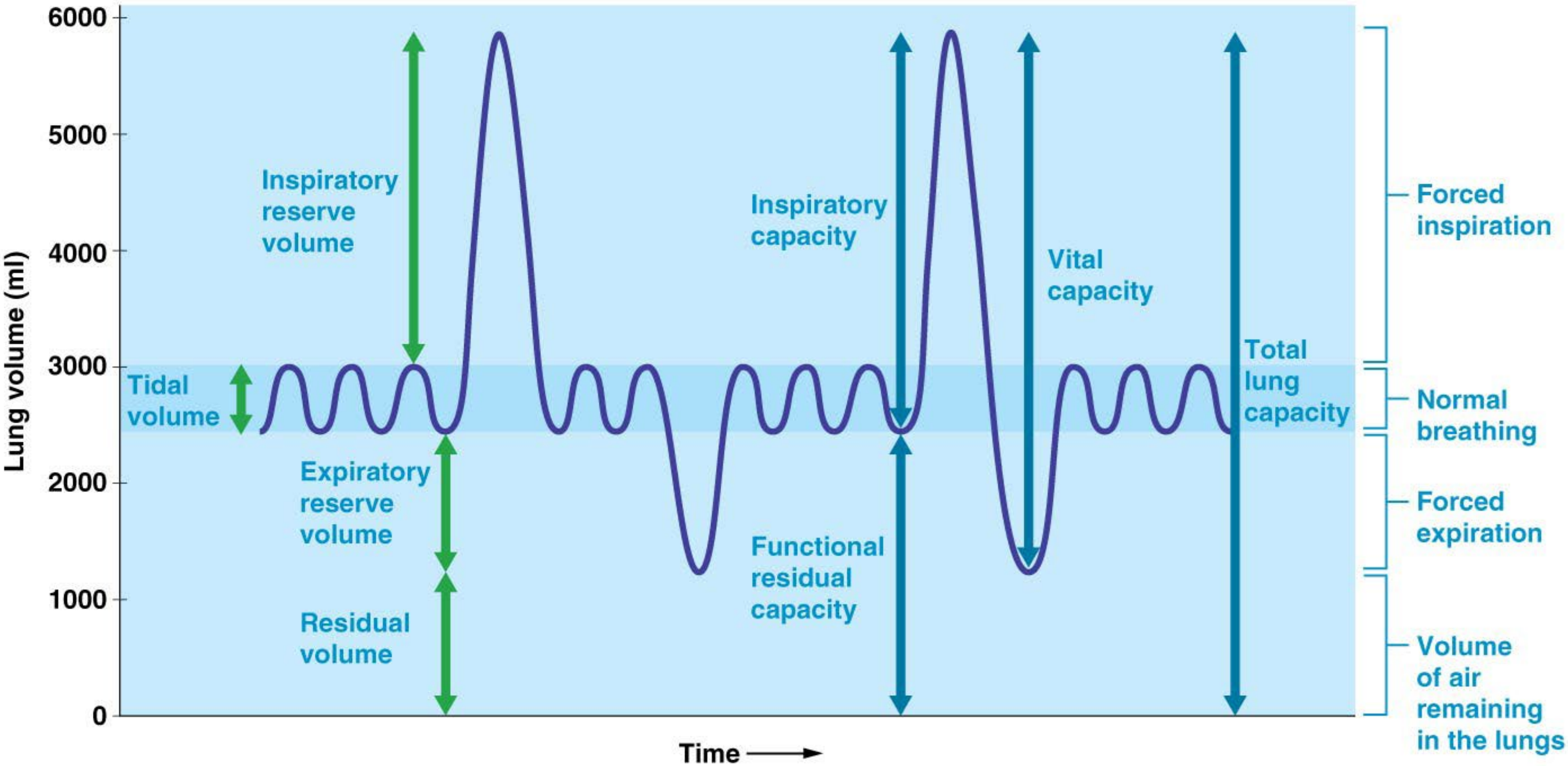
Tidal volume - volume of air inhaled and exhaled in one cycle during quiet breathing (500 mL)

Inspiratory reserve volume - air in excess of tidal volume that can be inhaled with maximum effort (3000 mL)

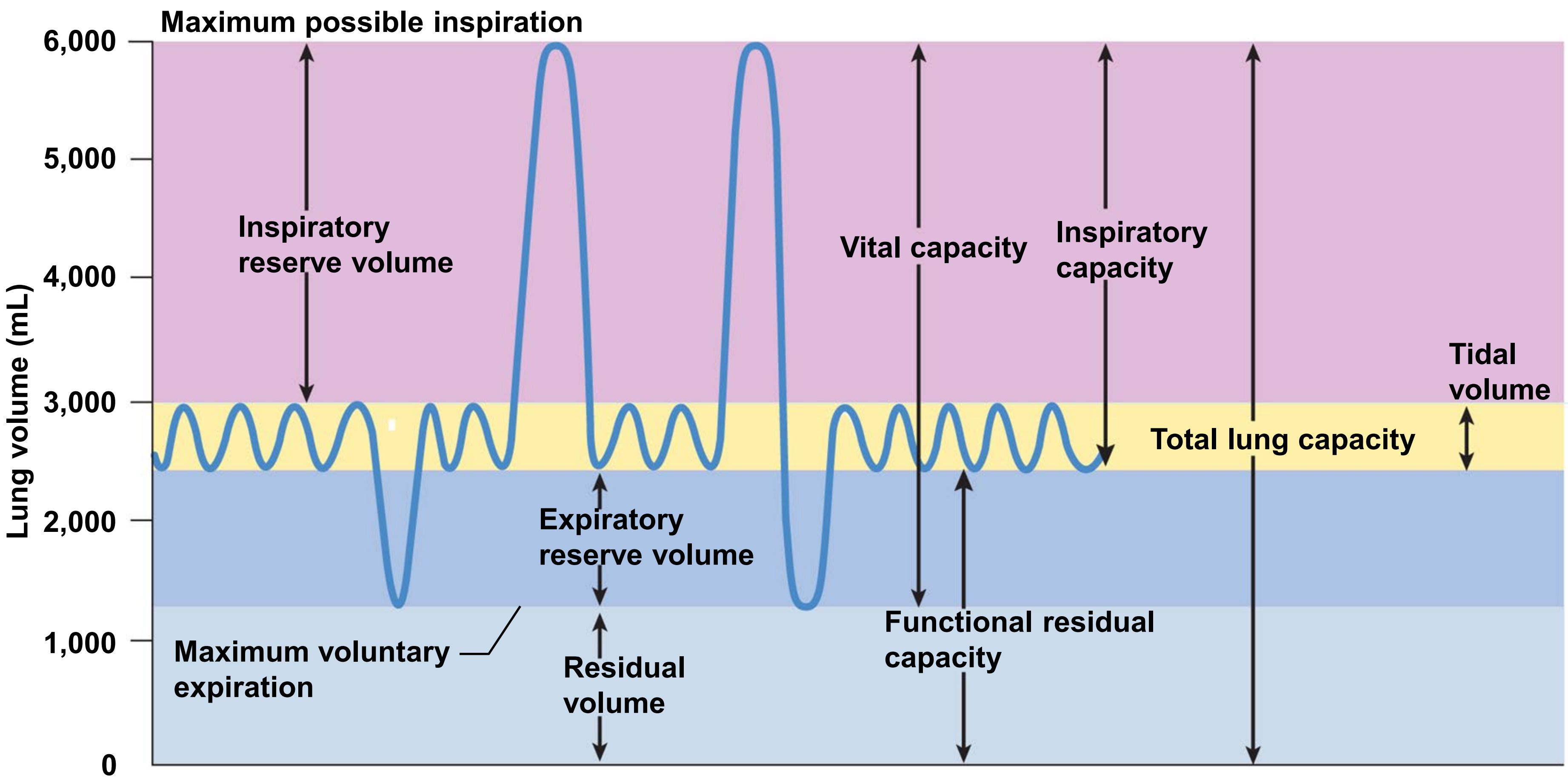
Expiratory reserve volume - air in excess of tidal volume that can be exhaled with maximum effort (1200 mL)

**Residual volume** - air remaining in lungs after maximum expiration (1300 mL)

# Graph of pulmonary volumes and capacities.



# Lung Volumes and Capacities



# Factors Affecting Gas Exchange

membrane thickness / membrane surface area / ventilation-perfusion coupling

---

Respiratory Membrane thickness

Only 0.5 μm thick

Presents little obstacle to diffusion

Pulmonary edema caused by left ventricular failure results in "thickening" of the respiratory membrane

Pneumonia also causes thickening of respiratory membrane

Results = greater distance for gases to travel between blood and air

Cannot equilibrate fast enough to keep up with blood flow

# Factors Affecting Gas Exchange

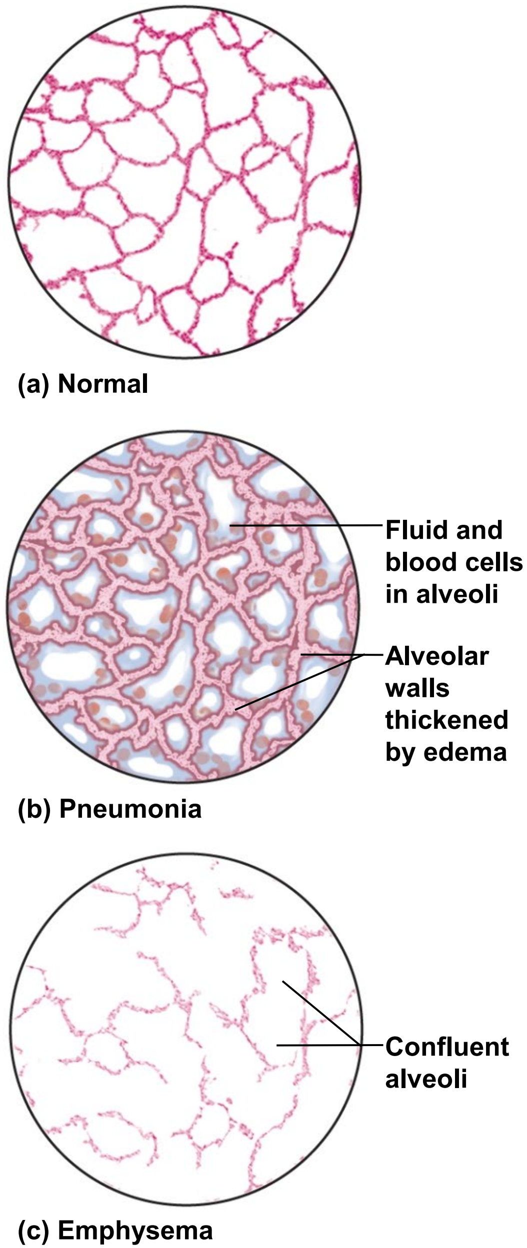
Membrane surface area

100 ml blood in alveolar capillaries, spread thinly over 70 $m^2$

Emphysema, lung cancer, and tuberculosis all decrease surface area for gas exchange

These conditions results in hypoxia

# Lung Disease Affects Gas Exchange




Abnormally few but large alveoli with total reduction of respiratory membrane.

## Autoregulation to Adjust Blood and Air Flows Within Lungs

Ventilation-perfusion coupling // the ability to match ventilation to perfusion (see next two slides)

Gas exchange requires both good ventilation of alveolus and good perfusion of the capillaries

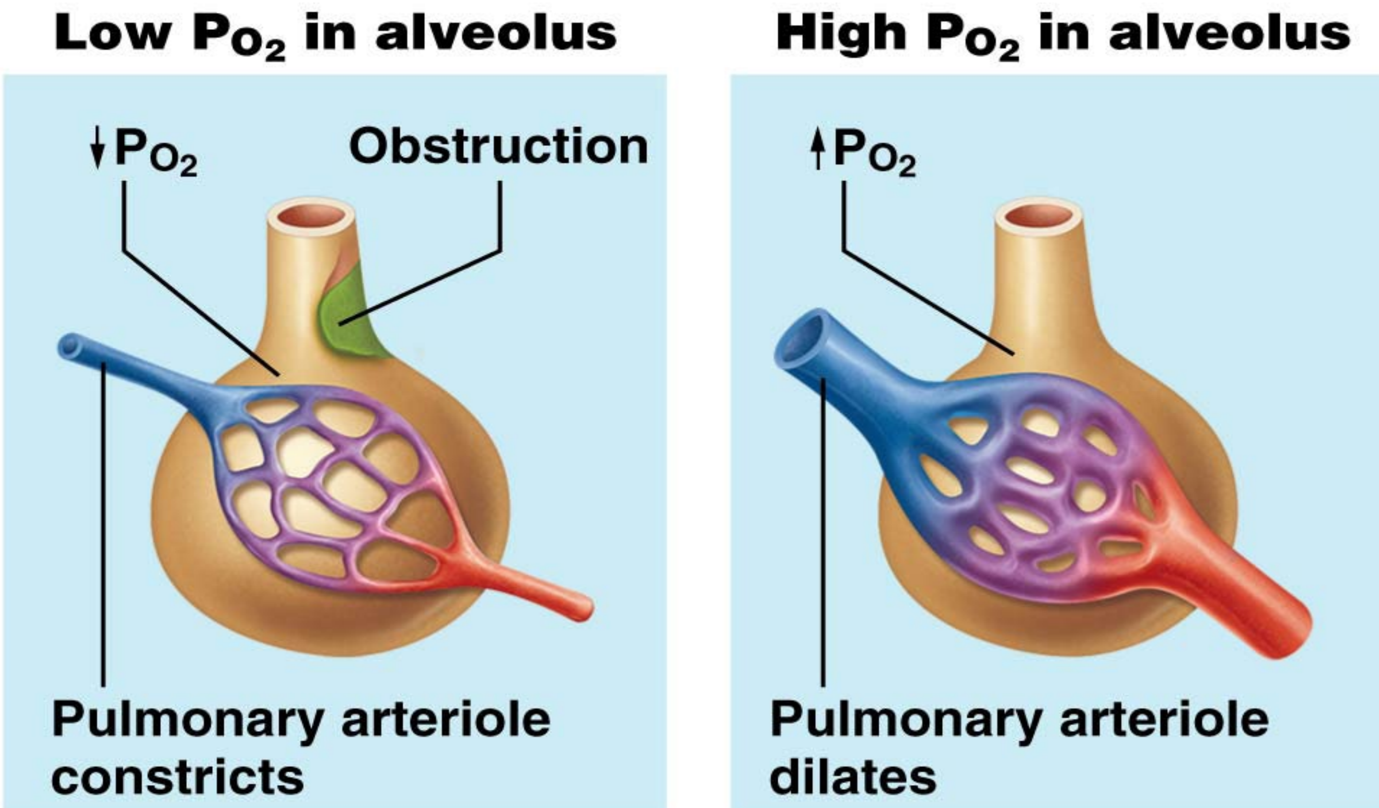
Ventilation-perfusion ratio of 0.8 (a flow of 4.2 L of air and 5.5 L of blood per minute at rest)

- Ventilation is air movement through alveoli
- Perfusion is blood flow through pulmonary capillary

Ventilation and perfusion is matched within the lung tissue by "autoregulation" // smooth muscles in bronchioles and pulmonary arterioles will selectively open and close to match ventilation to perfusion or perfusion to ventilation.

# Ventilation – Perfusion Coupling

*(Oxygen concentration in alveoli regulates smooth muscle in pulmonary arterioles.)*

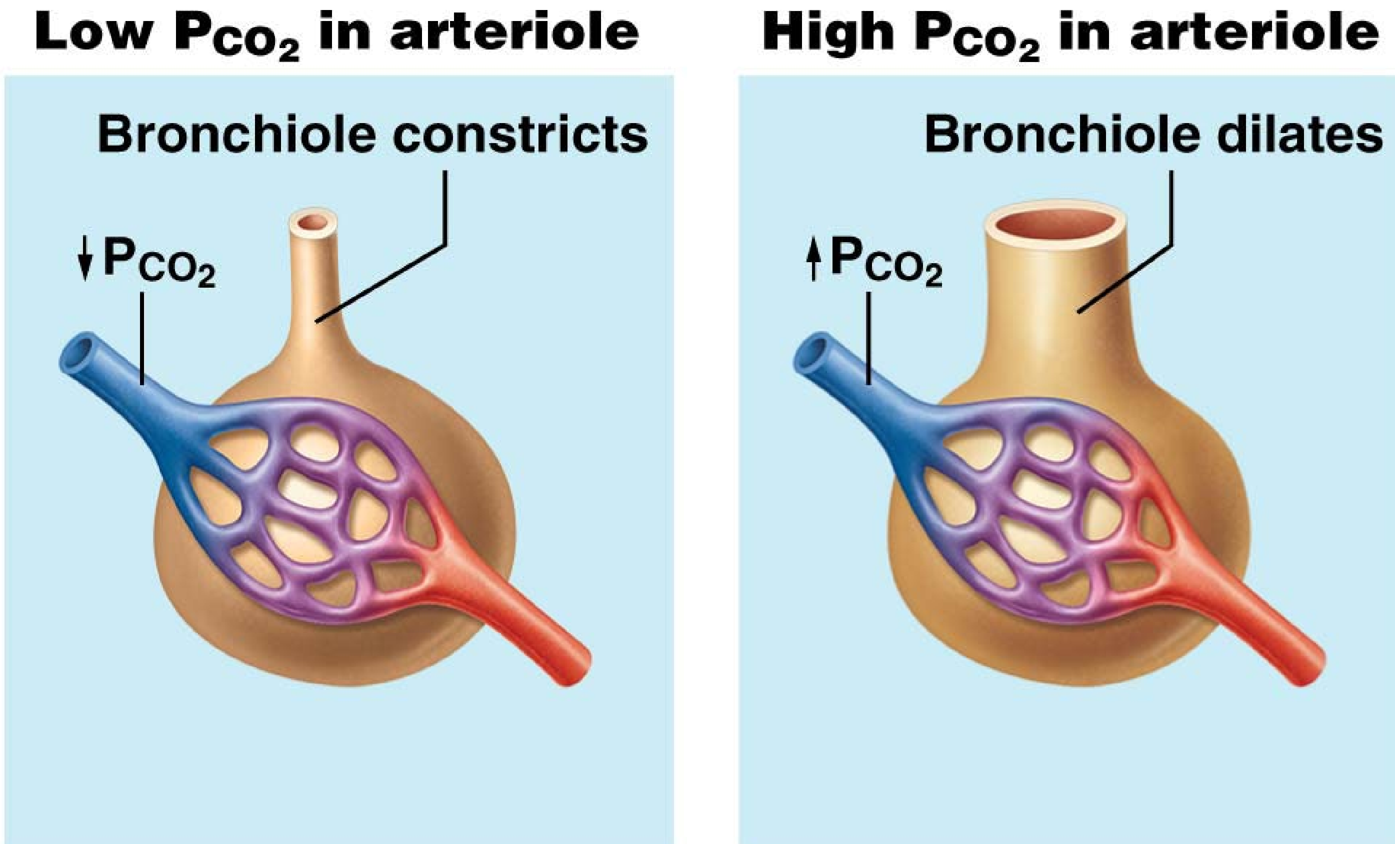



**(a) Changes in ventilation (alveolar $P_{O_2}$) lead to changes in perfusion.**

What happens when you change ventilation (bronchioles)?
You change smooth muscle tension in pulmonary arteriole.

# Perfusion - Ventilation Coupling

**(Carbon dioxide concentration in pulmonary arteriole reglate smooth muscle in bronchioles)**




**(b) Changes in perfusion (arteriolar $P_{CO_2}$) lead to changes in ventilation.**

What happens when you change perfusion (pulmonary arterioles)?
You change smooth muscle tension in bronchioles.

# Gas Transport

The process of carrying gases

- from the alveoli to the systemic tissues
- from the system tissues to the alveoli

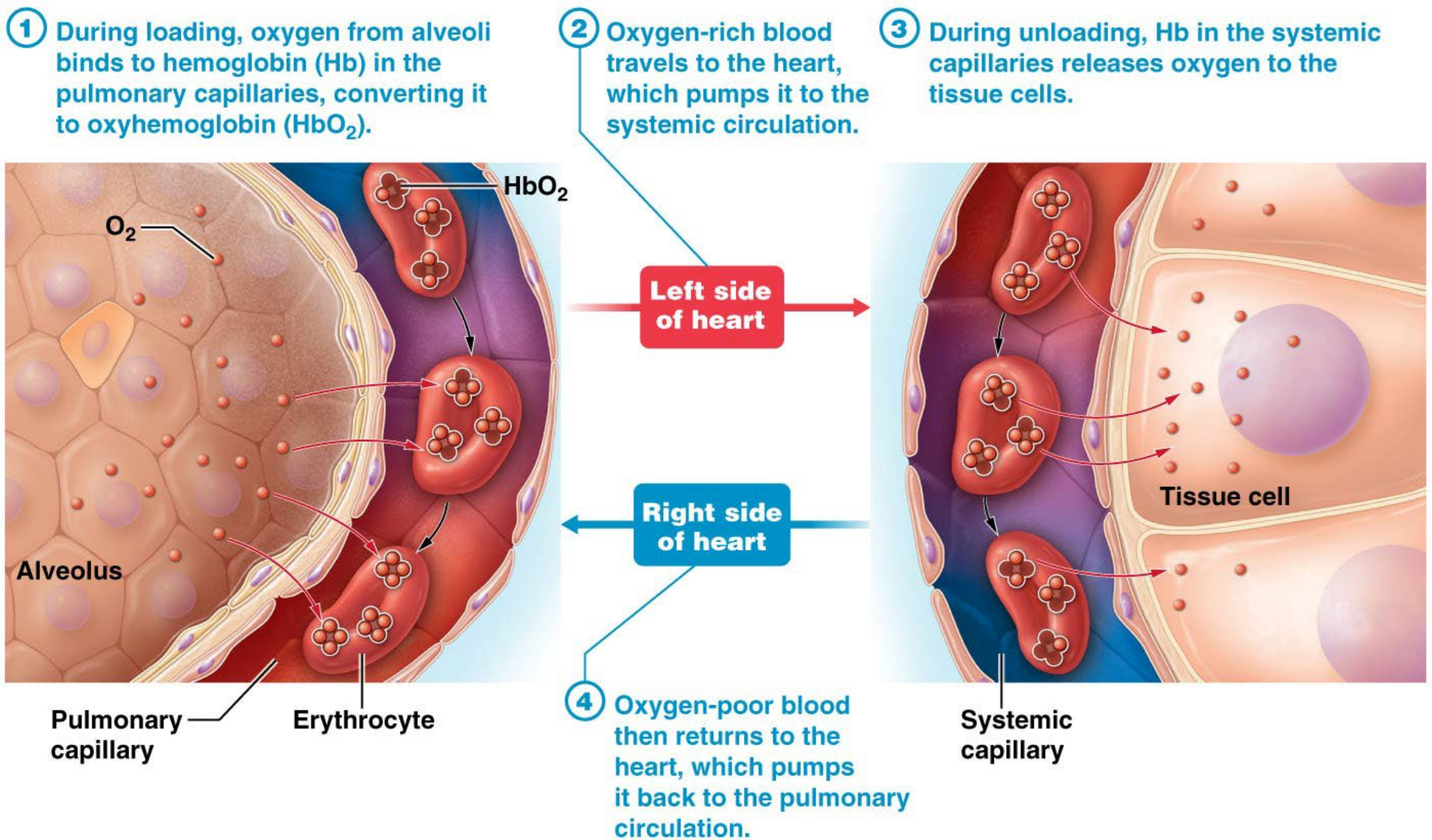
Oxygen transport

- 98.5% bound to hemoglobin
- 1.5% dissolved in plasma

Carbon dioxide transport

- 70% as bicarbonate ion
- 23% bound to hemoglobin (carbamino)
- 7% dissolved in plasma

# Transport of oxygen: loading and unloading of oxygen on hemoglobin in erythrocytes.



# Oxygen Transport

Hemoglobin (Hb) – molecule specialized in oxygen transport

Hb consist of four separate protein molecules (globulin)

Each globulin molecule has a heme group which binds one $O_2$ to its ferrous ion ($Fe^{2+}$)

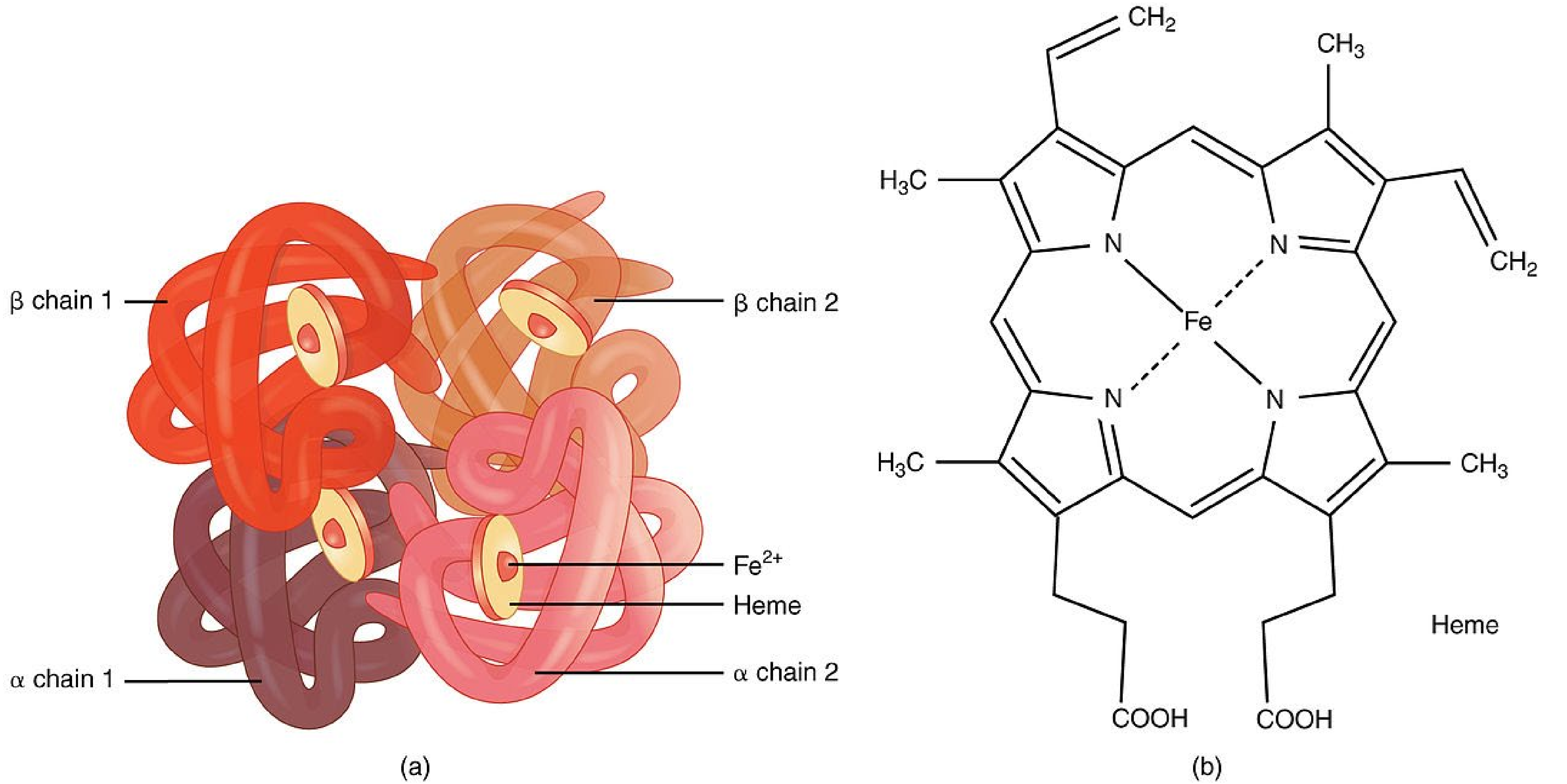
Therefore, one hemoglobin molecule can carry up to 4 $O_2$

100% oxyhemoglobin ($HbO_2$) – 4 $O_2$ bound to hemoglobin

Deoxyhemoglobin (HHb) – hemoglobin with no $O_2$

50% saturation Hb with 2 oxygen molecules

# Oxygen Transport



# Carbon Dioxide Transport

Carbon dioxide transported in blood using these three forms

- carbonic acid
- carbamino compounds
- dissolved in plasma

## How is oxygen and carbon dioxide load and unload during Systemic Gas Exchange?

Unloading of $O_2$ /// from blood into tissue

Loading $CO_2$ /// from tissue into blood

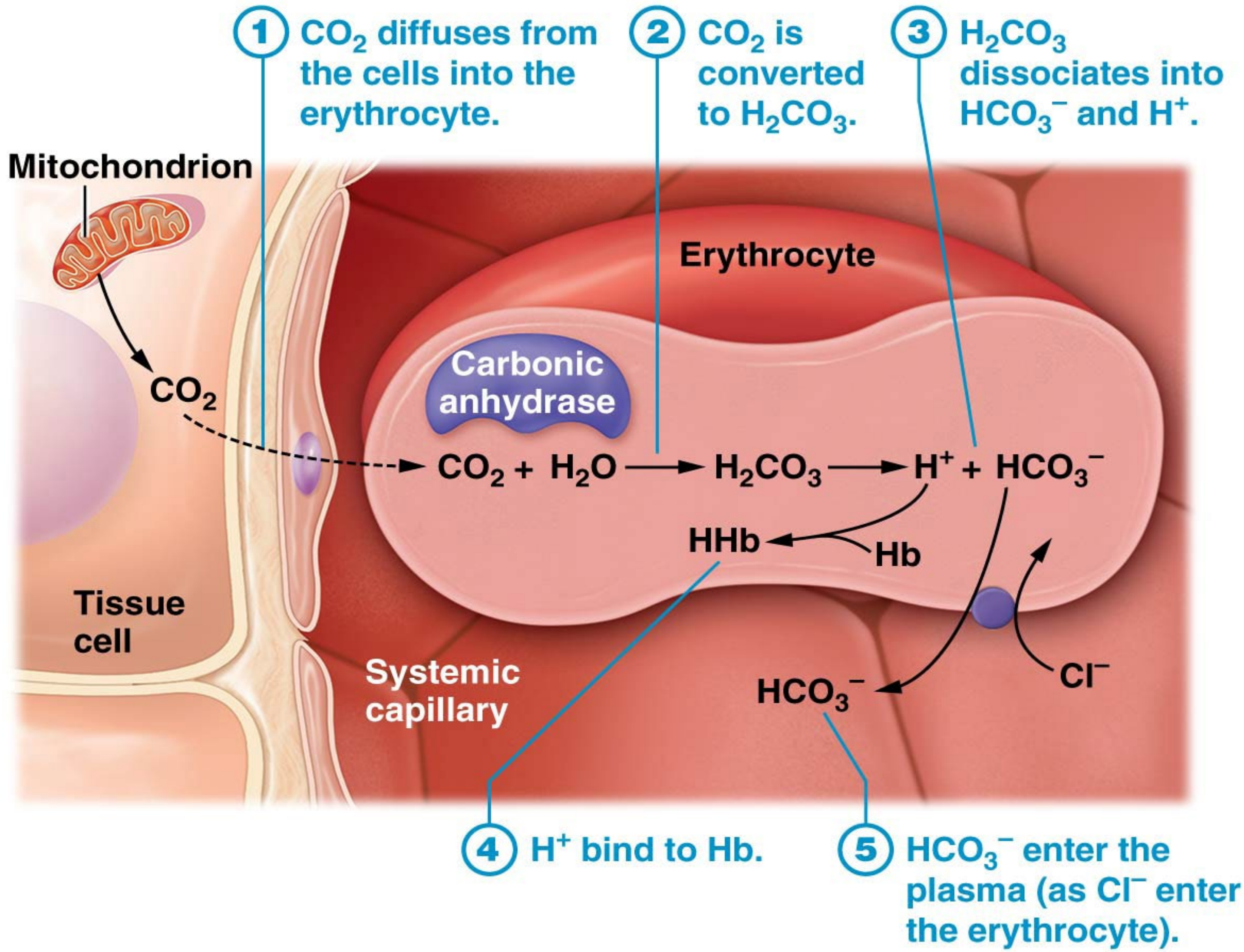
Key event occurs inside RBC // requires *carbonic anhydrase*

$$CO_2 + H_2O \rightarrow H_2CO_3 \rightarrow HCO_3^- + H^+$$

The “Chloride Shift”

- keeps reaction proceeding // exchanges $HCO_3^-$ for $Cl^-$
- $H^+$ binds to hemoglobin

# Transport of carbon dioxide: the conversion of carbon dioxide and water into carbonic acid in erythrocytes.

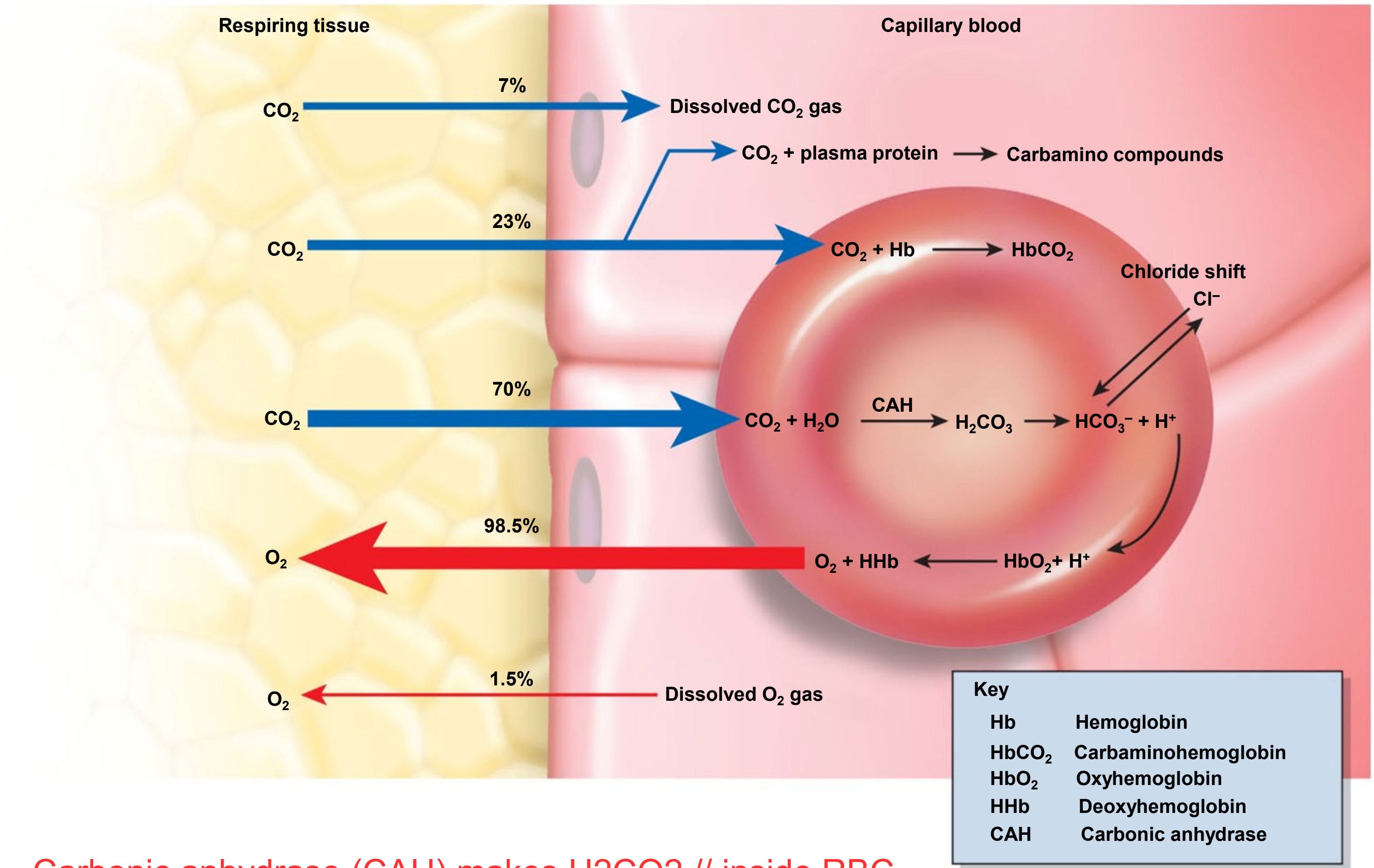



**(a) Bicarbonate formation in an erythrocyte in a systemic capillary**

Bicarbonate forms ionic bond with sodium and is transported to lungs as sodium-bicarbonate

Hydrogen ion binds to Hb-O2 and causes oxygen to be released from Hb // oxygen now free to diffuse to mitochondria

# Systemic Gas Exchange



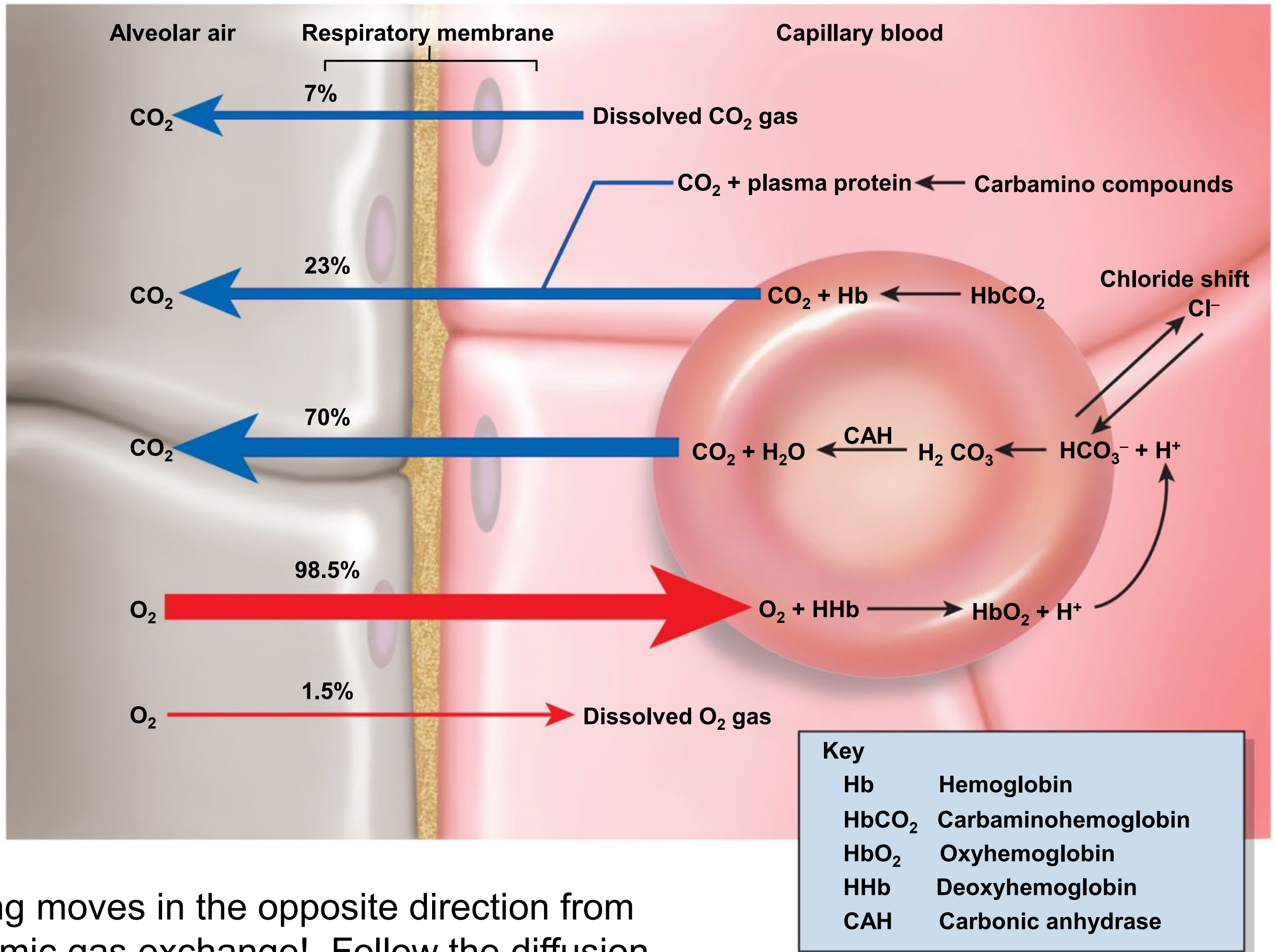

Carbonic anhydrase (CAH) makes H2CO2 // inside RBC

Hydrogen ion (H+) causes the release of O2 from Hb

What moves into cell as bicarbonate moves out?

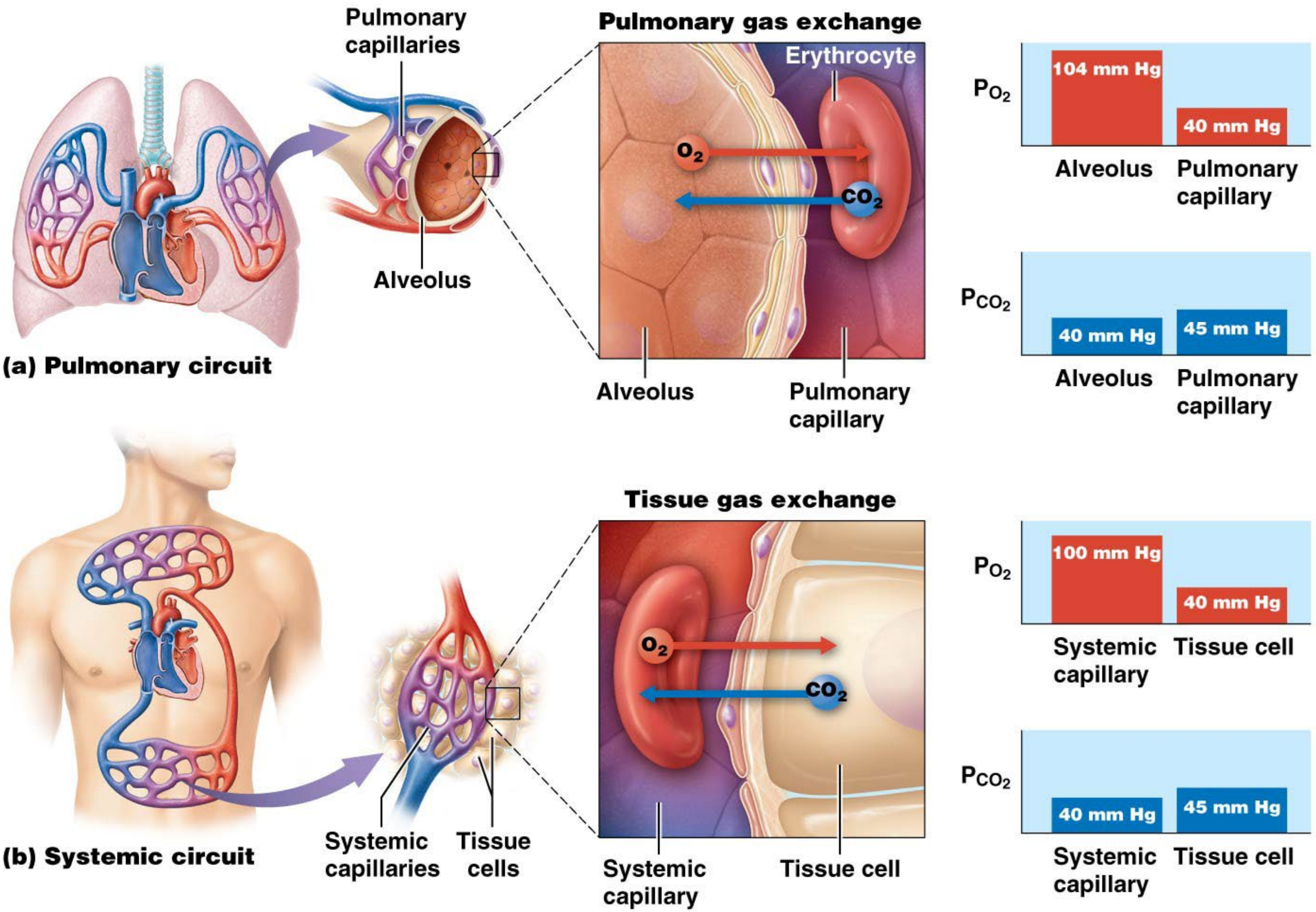
# Alveolar Gas Exchange






Everything moves in the opposite direction from the systemic gas exchange! Follow the diffusion of O2 into RBC and see outcome.

# Gas Transport in Systemic and Pulmonary Circuits



# How is oxygen unloaded from RBC in the Systemic Gas Exchange?

$O_2$ unloading

$H^+$ binding to $HbO_2$ reduces its affinity for $O_2$ /// $H^+$ responsible for release of $O_2$ from iron

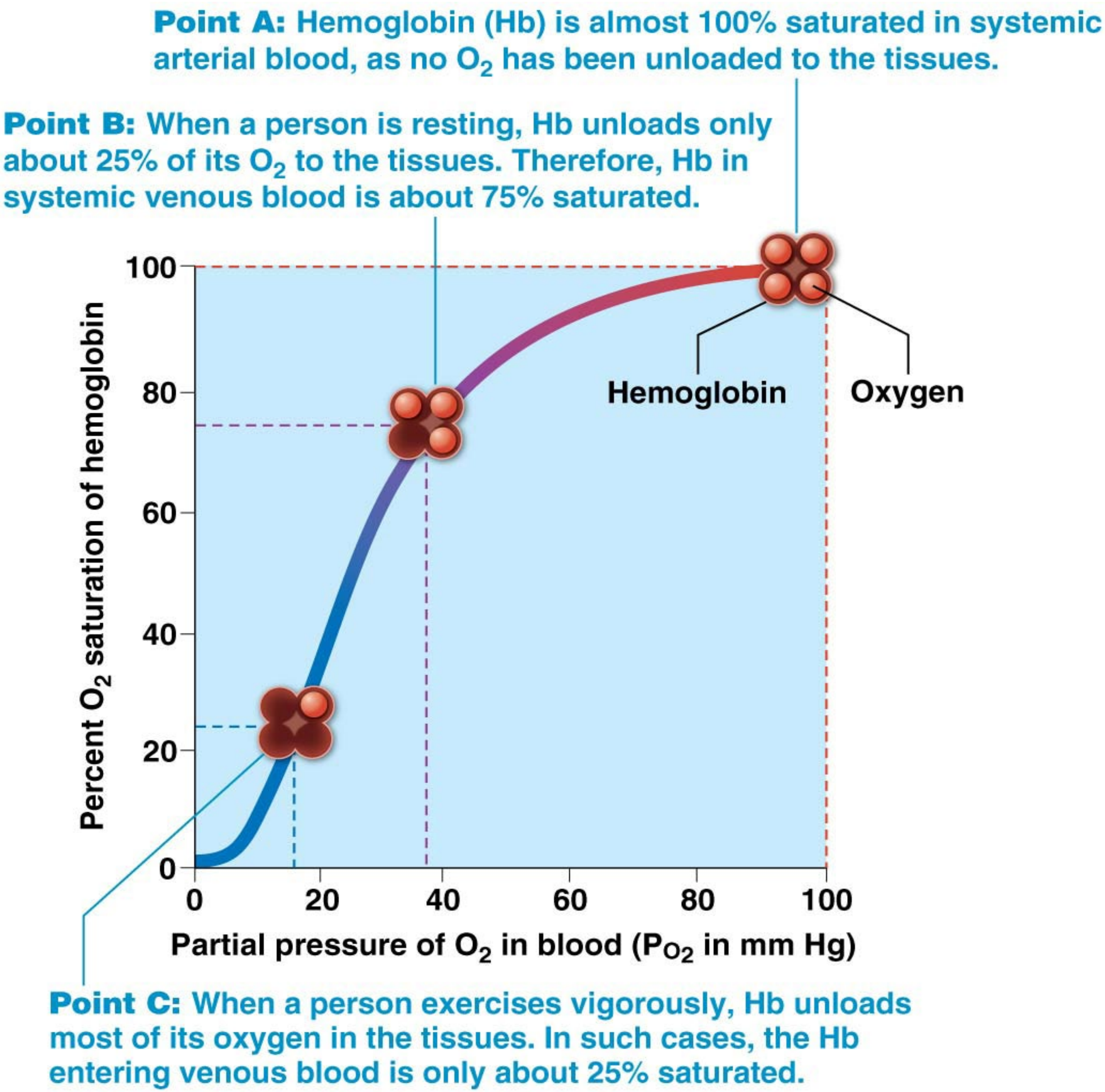
Iron in hemoglobin release oxygen

$HbO_2$ arrives at systemic capillaries 97% saturated (close to 100%!) /// leaves 75% saturated - unloads 25%

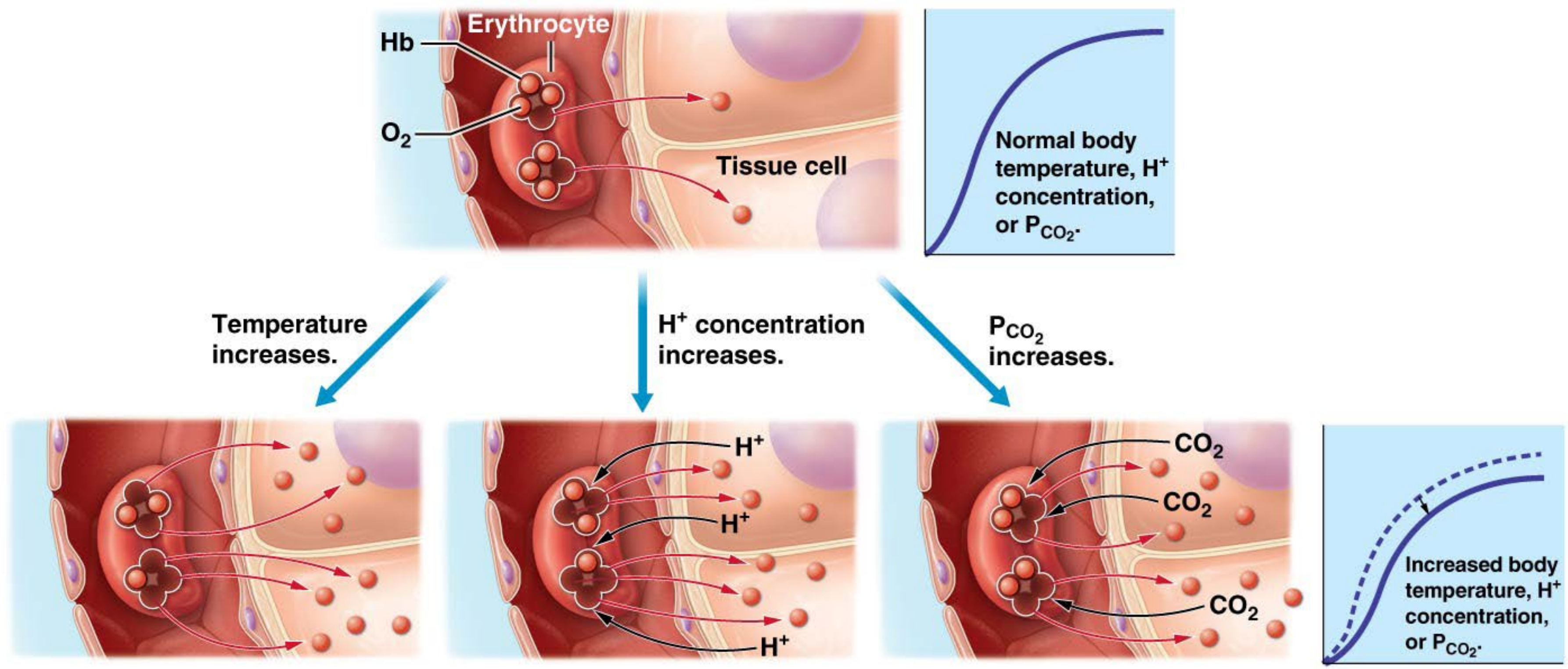
Venous reserve – oxygen remaining in the blood after it passes through the capillary beds

Utilization coefficient – gives up 22% of its oxygen load

**How much oxygen is unloaded during periods of rest or exercise?**



# Effect of temperature, hydrogen ion concentration, and PCO2 on oxygen unloading from hemoglobin.




**(a) Increased temperature causes more $O_2$ unloading.**

**(b) Increased $H^+$ causes more $O_2$ unloading.**

**(c) Increased $P_{CO_2}$ causes more $O_2$ unloading.**

These variables all increase when you exercise. This is when we need Hb to release more oxygen so we can deliver more O2 to our mitochondria (organelle that uses reduced coenzymes and oxygen) to make ATP

# Another Molecule Used to Unload Oxygen

Bisphosphoglycerate (BPG) – intermediate in glycolysis // as concentration of BPG increases it indicates high level of anarobic metabolism

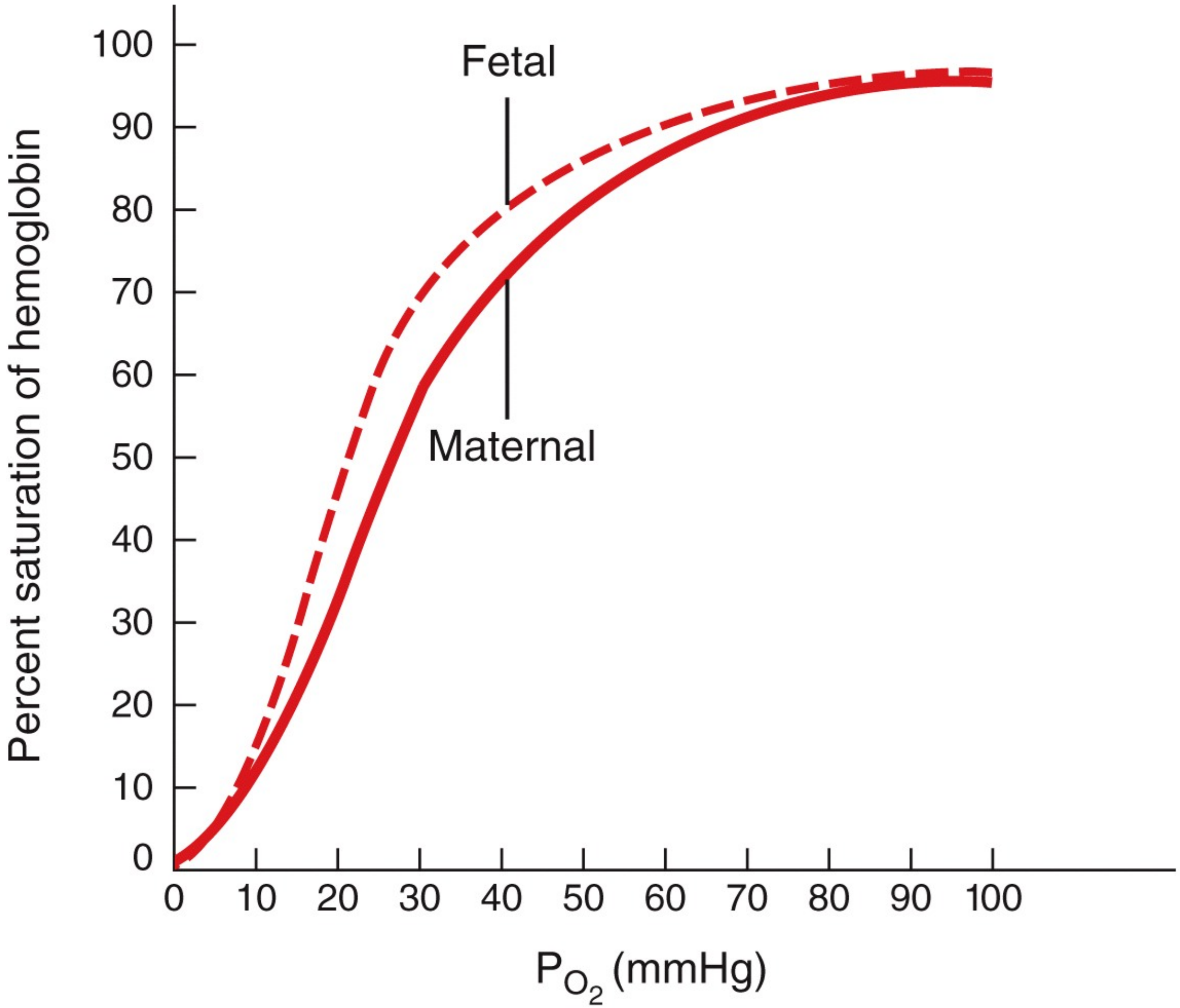
As RBCs produce more BPG, it binds to Hb and more $O_2$ is unloaded

↑ body temp (fever), thyroxine, growth hormone, testosterone, and epinephrine all raise BPG and cause more $O_2$ unloading

↑ metabolic rate requires ↑ oxygen

Haldane effect – rate of $CO_2$ loading is also adjusted to varying needs of the tissues /// low level of oxyhemoglobin enables the blood to transport more $CO_2$

# This Chart Shows Fetal Hb Has a Greater Infinity for O2 Than Maternal Hb



# Terminology: Variations in Respiratory Rhythm

eupnea – relaxed quiet breathing /// characterized by tidal volume 500 mL and the respiratory rate of 12 – 15 bpm

apnea – temporary cessation of breathing

dyspnea – labored, gasping breathing; shortness of breath

hyperpnea – increased rate and depth of breathing in response to exercise, pain, or other conditions

hyperventilation – increased pulmonary ventilation in excess of metabolic demand

hypoventilation – reduced pulmonary ventilation

Kussmaul respiration – deep, rapid breathing often induced by acidosis

respiratory arrest – permanent cessation of breathing

tachypnea – accelerated respiration rate

bradypnea – slow respiration rate