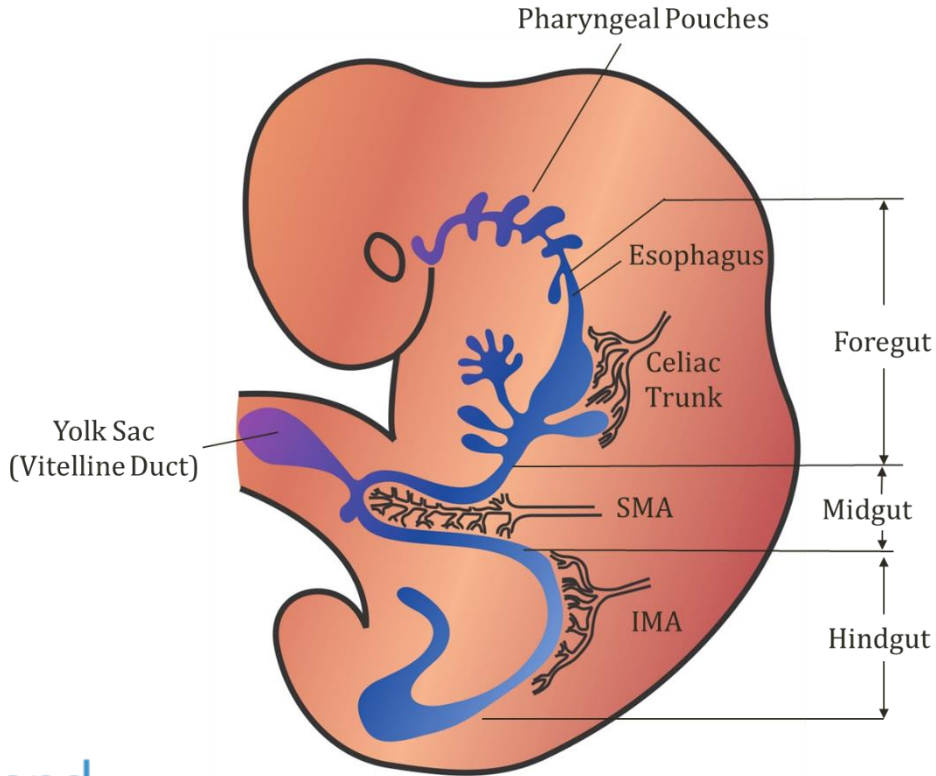
Pulmonary Embryology

Jason Ryan, MD, MPH

Lung Embryology

- Lung bud ("respiratory diverticulum")
  - Outgrowth of **foregut** (future esophagus)
  - Forms during **4th week of development**



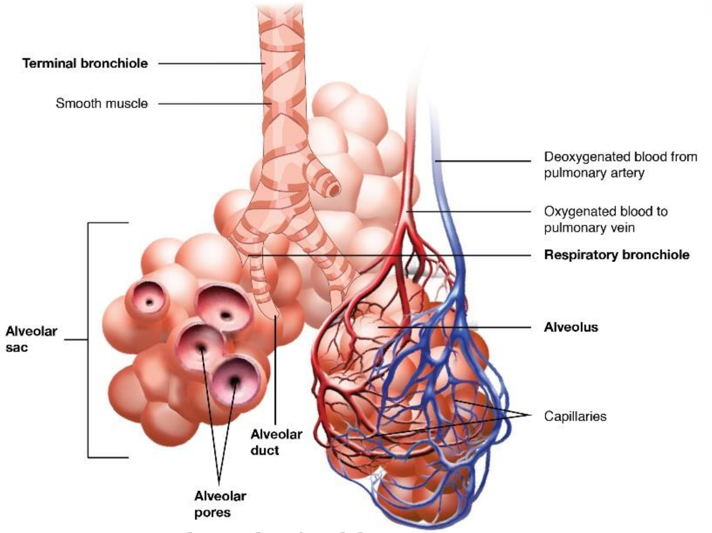
Lung Maturation

Stages/Periods

- Psuedoglandular (5-16wk)
- Canalicular (16-26wk)
- Saccular (26wk-birth)
- Alveolar (after birth)

Lung Anatomy

- Bronchi
  - Hyaline cartilage
- Bronchioles
  - No cartilage
  - Terminal → respiratory
- Alveoli
  - Capillaries
  - Gas exchange



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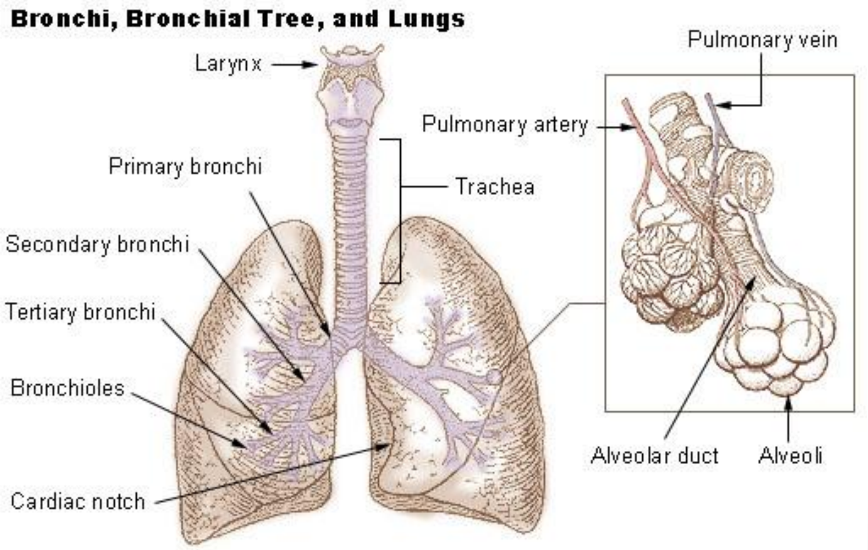

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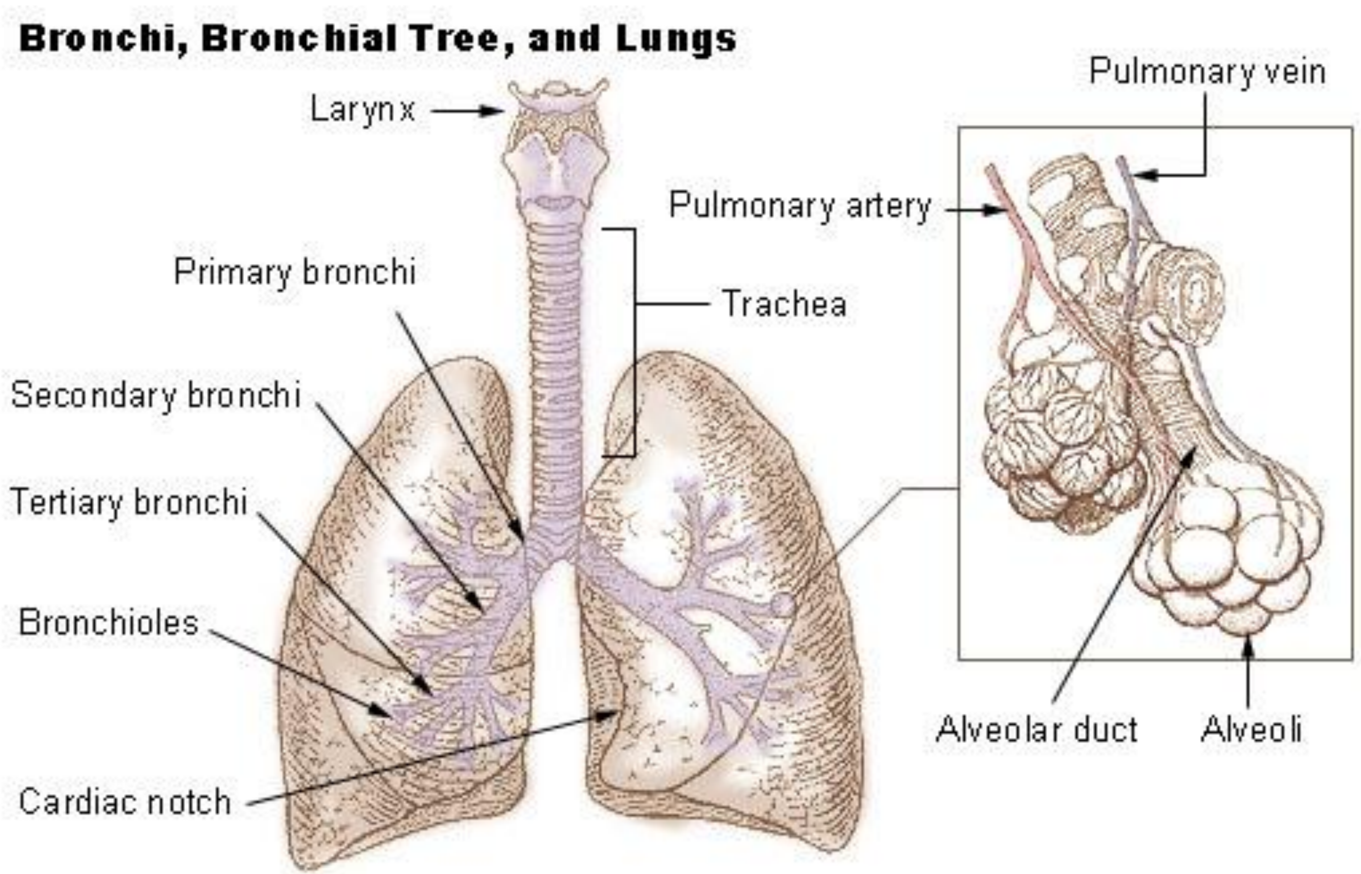
Lung Anatomy



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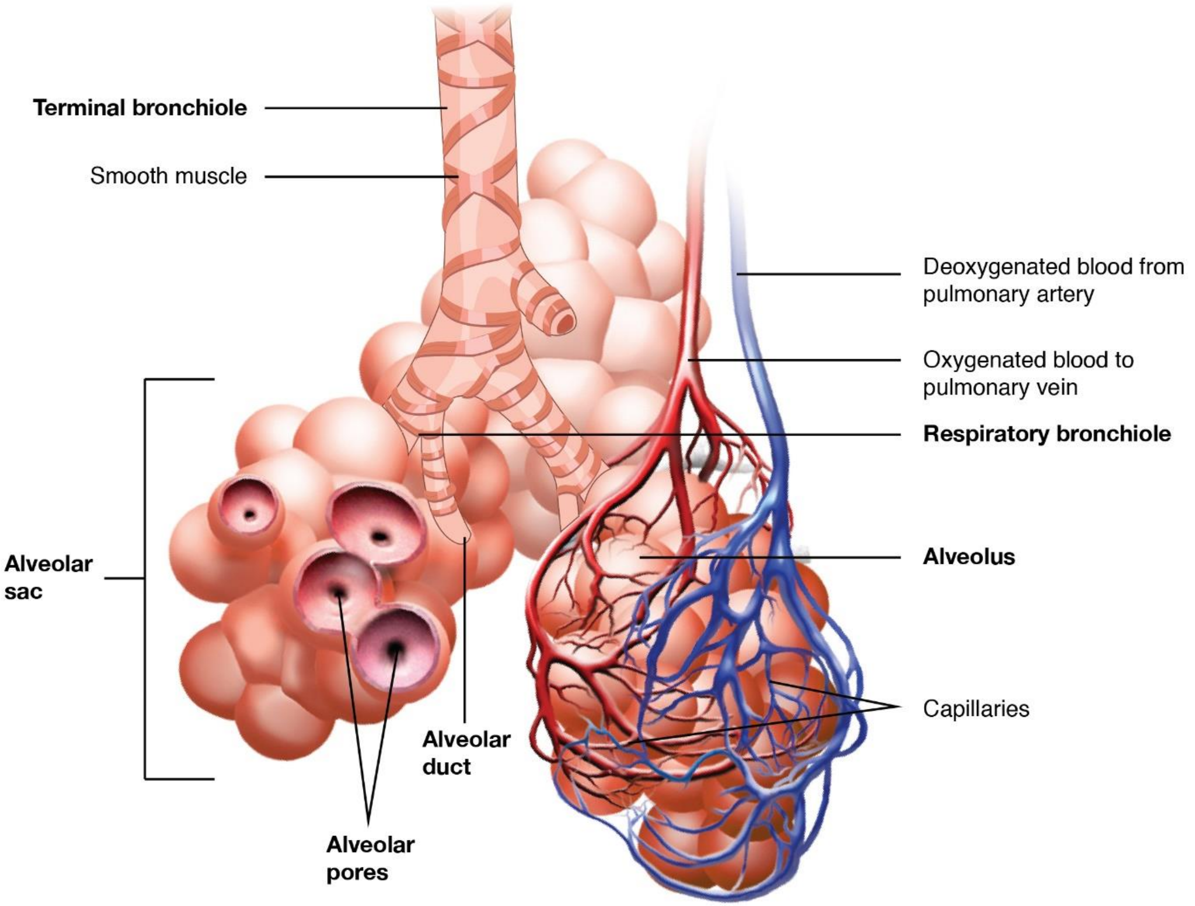
Boards&Beyond STUDY SMARTER

Lung Anatomy



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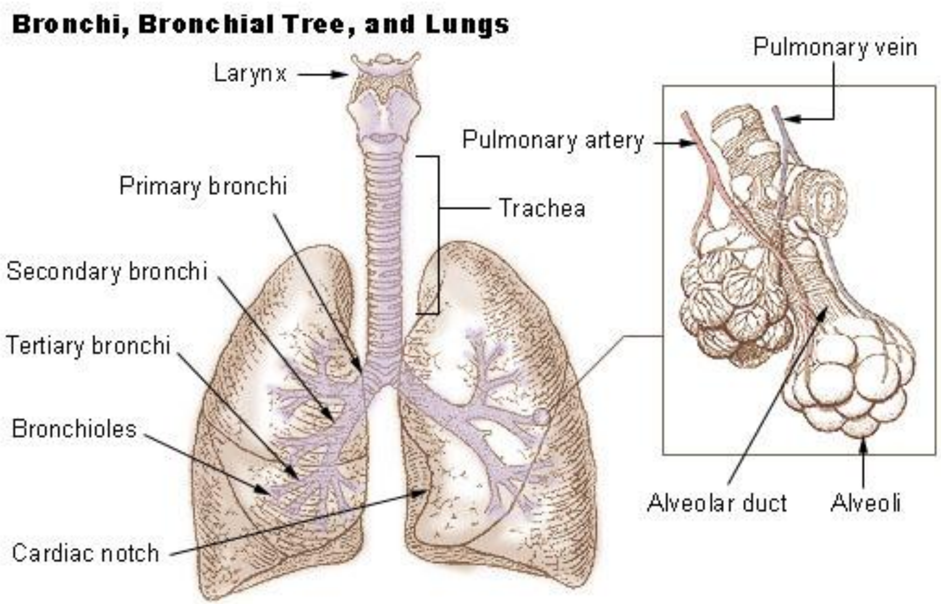
Pseudoglandular Period

5-16 weeks

- Lungs resemble a gland
- Branching to level of terminal bronchioles
- No respiratory bronchioles or alveoli present



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Fetal Respiration

- **Fetal breathing** movements occur in utero
- Baby **aspirates amniotic fluid**
- Stimulates **lung development**
- Growth of respiratory muscles
- Important for growth during pseudoglandular phase

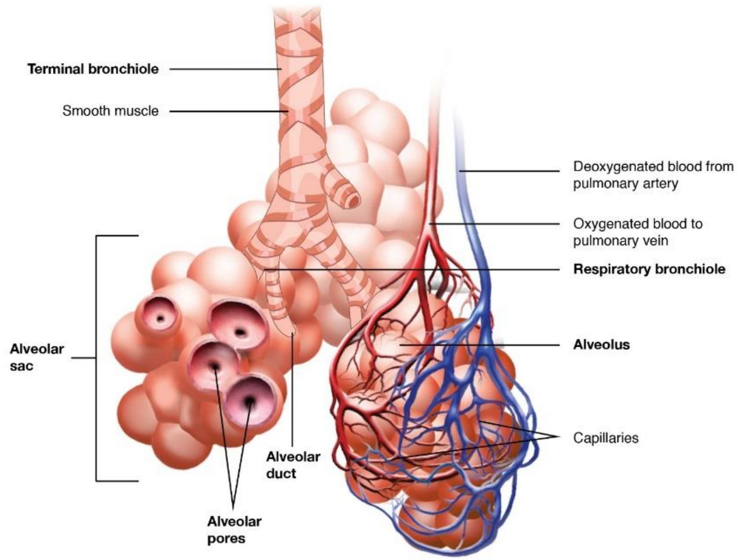
Fetal Respiration

- **Oligohydramnios:**
  - Pulmonary hypoplasia
  - Part of Potter's sequence
  - Caused by fetal kidney abnormalities

Canalicular Period

16-26 weeks

- Terminal bronchioles divide
- Form respiratory bronchioles
- Respiratory bronchioles divide into alveolar ducts
- Survival after birth possible at end of period



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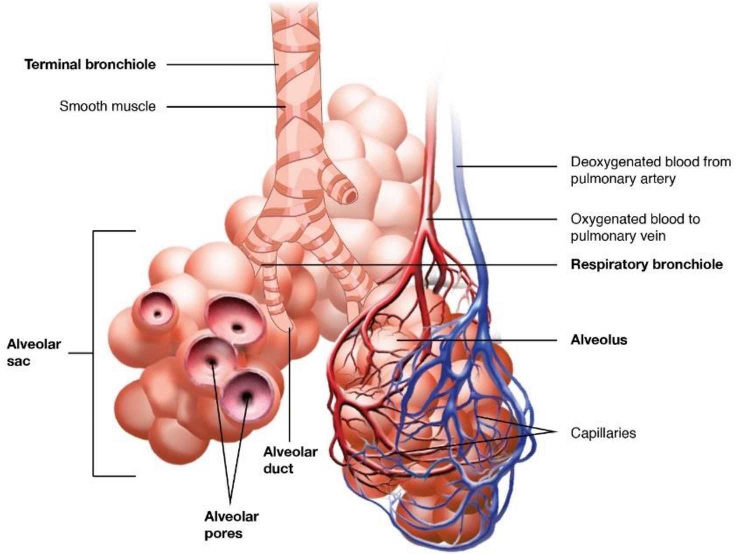
Canalicular Period

16-26 weeks

- Airway lumens become larger
- **Type II pneumocytes** form
  - Produce surfactant
  - Lowers surface tension
  - Keeps alveoli open



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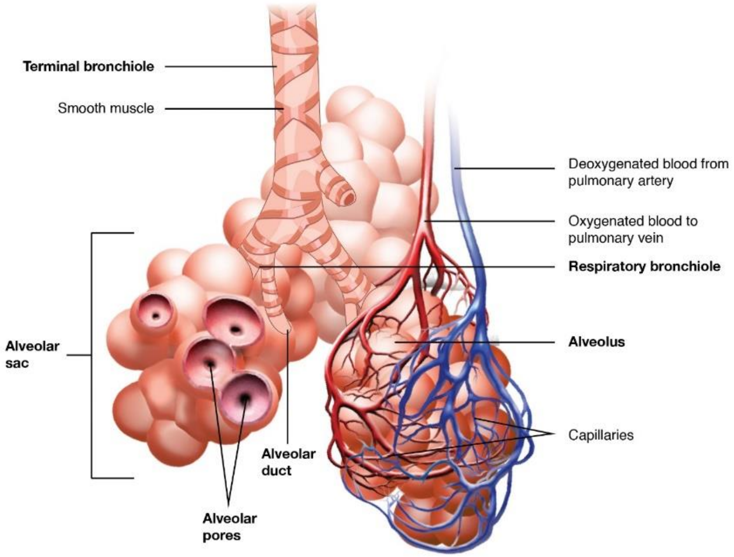
Saccular Period

26 weeks - birth

- Terminal sacs (primitive alveoli) form
- Capillaries multiply in contact with alveoli



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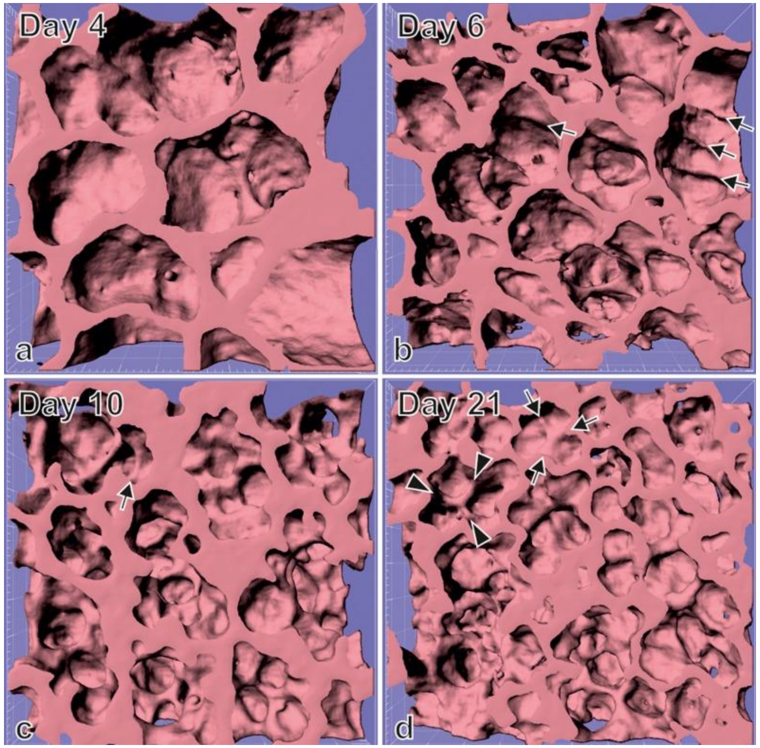
Alveolar Period

After birth

- At birth, only about 1/3 of alveoli present
- Following birth:
  - ↑ number of respiratory bronchioles and alveoli
- **Continued lung development** through age 10

Alveolarization

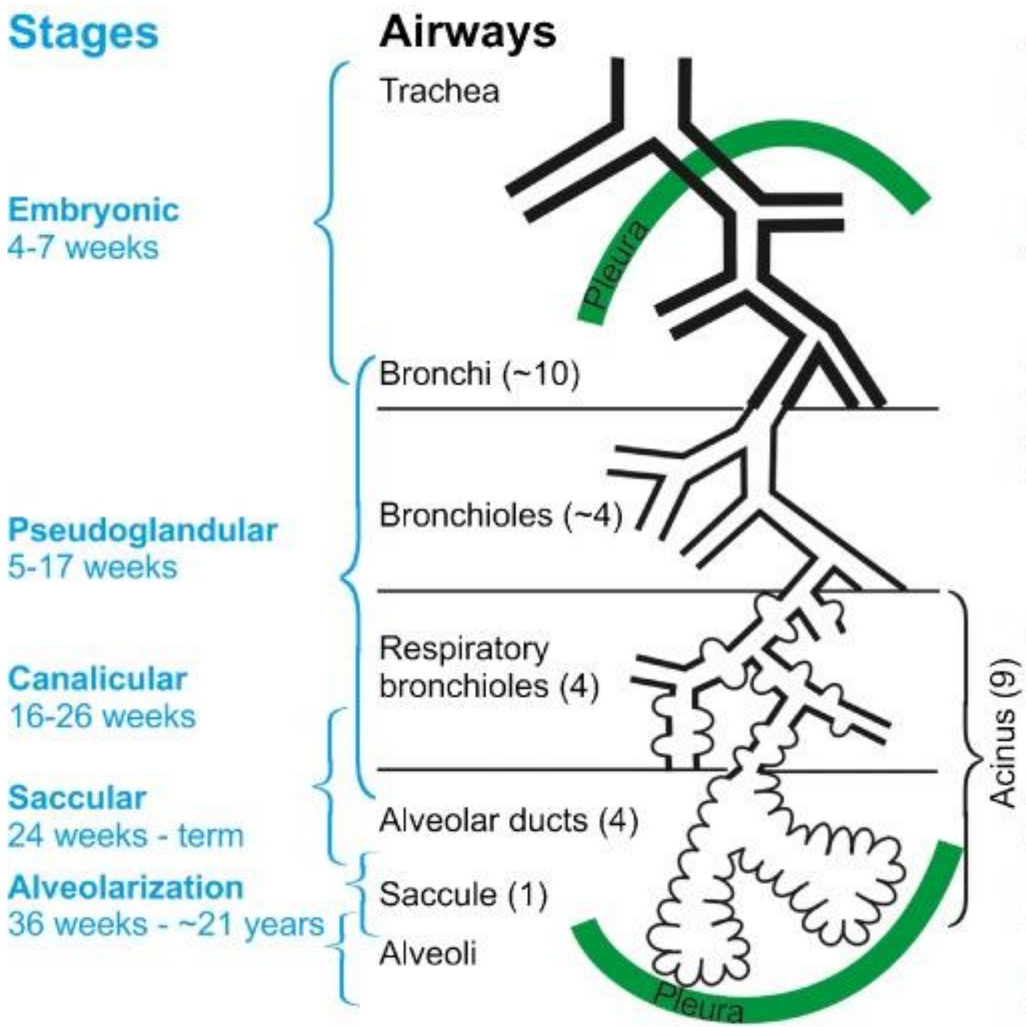
- Airspaces subdivided
- New walls formed (septa)



Johannes Schittny. Cell Tissue Res. 2017; 367 (3) 427

Bronchopulmonary Dysplasia

- Occurs in premature infants
- Treated in NICU
- Surfactant, oxygen, mechanical ventilation
- Oxygen toxicity and lung trauma
- **Alveolarization** does not progress normally
- Respiratory problems during infancy
- Often improves during childhood



Johannes Schittny. Cell Tissue Res. 2017; 367 (3) 427

Pulmonary Hypoplasia

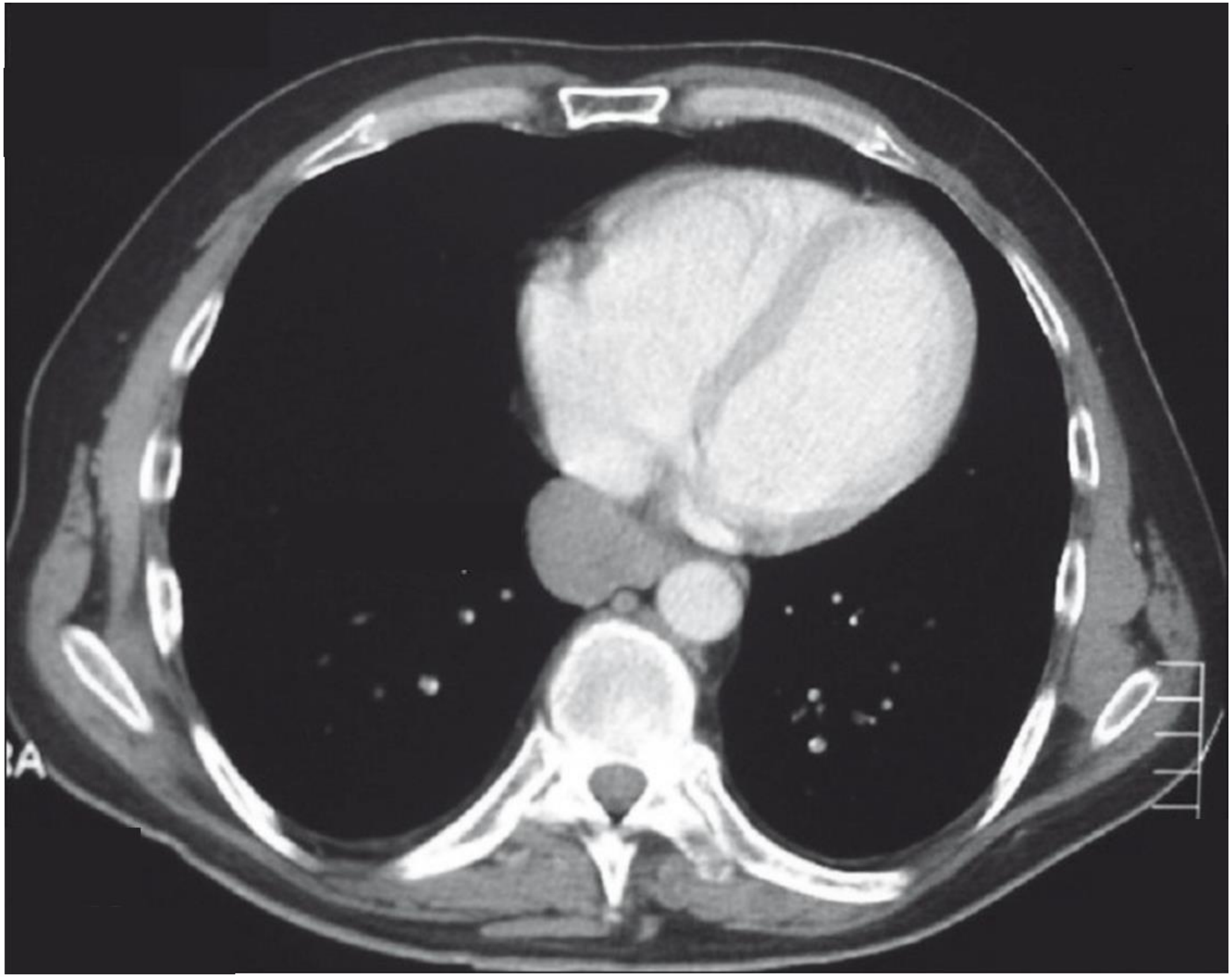
- Oligohydramnios (Potter's sequence)
- Congenital diaphragmatic hernia
  - Defective formation **pleuroperitoneal membrane**
  - Hole in diaphragm
  - Abdominal organs herniate into chest
  - In utero herniation → **pulmonary hypoplasia**
  - Often fatal

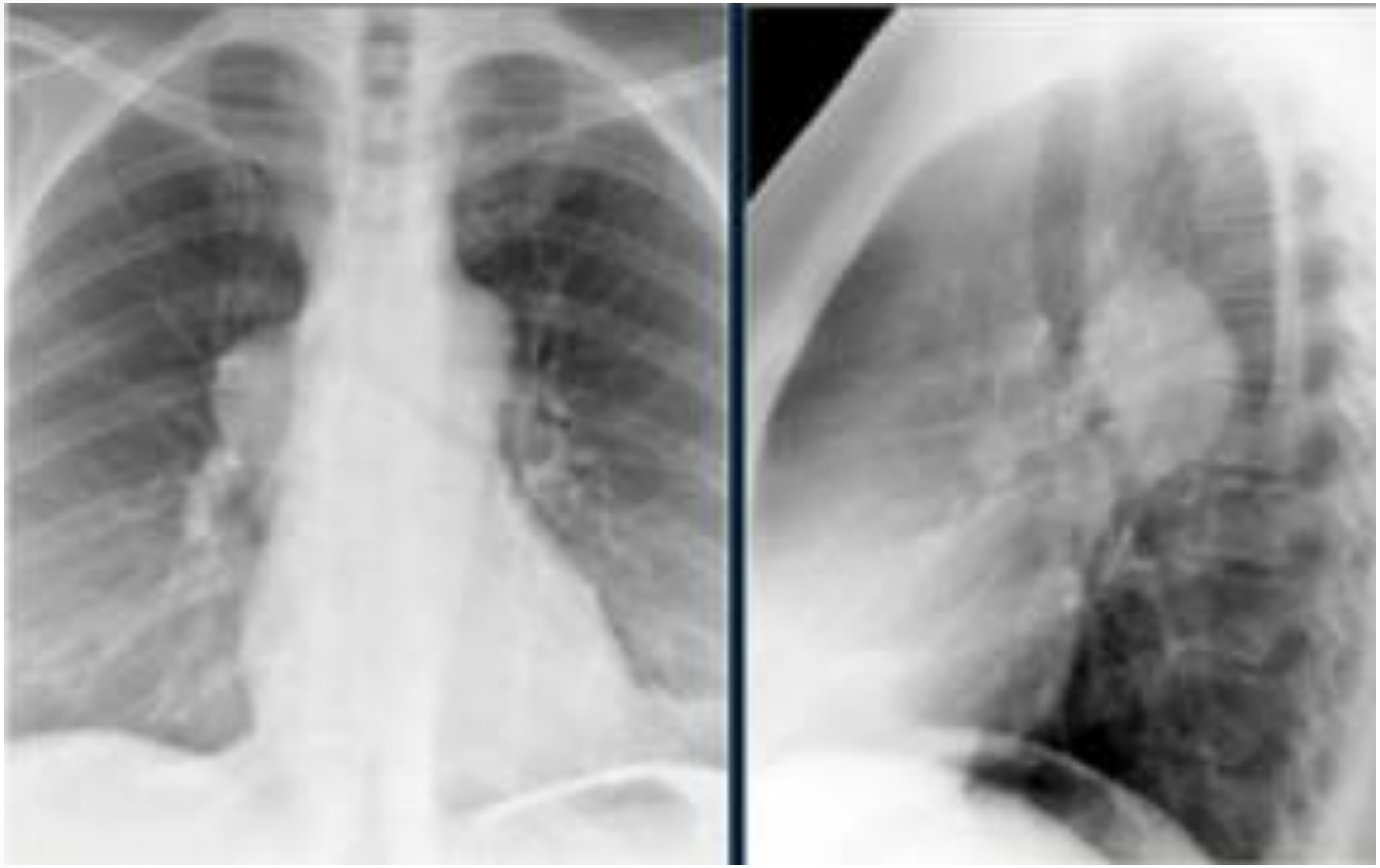
Bronchogenic Cysts

- Abnormal budding of **foregut**
- Usually found in mediastinum
- Contain clear fluid
  - Air seen when infected

Bronchogenic Cysts

- Do not communicate with lungs
- Lined by **respiratory epithelium**
  - Columnar, ciliated
- Walls contain **cartilage** (diagnostic criteria)
- Often asymptomatic
- May lead to pneumonia, compression of airway





The Radiology Assistant

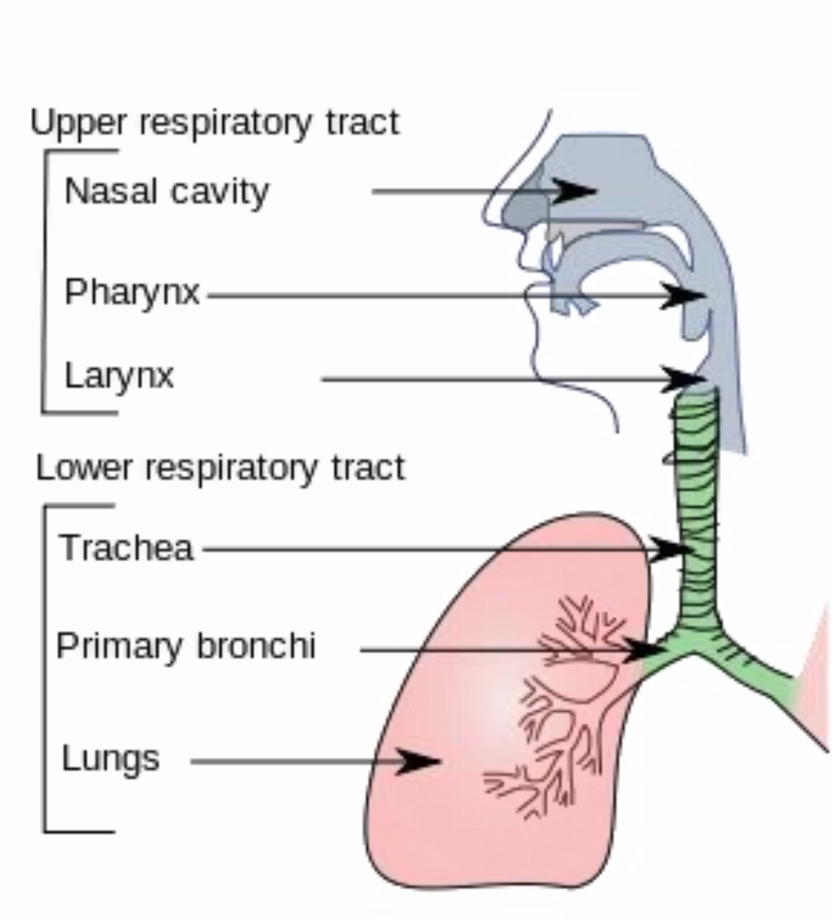
Pulmonary Vascular Resistance

- In utero
  - **PVR is high**
  - Canalicular stage: few/no pulmonary capillaries
  - Later stages: hypoxemia → vasoconstriction
  - Umbilical venous blood: PaO_2 30mmHg; O_2sat=80%
  - Only about 10% of cardiac output to lungs
- **At birth**
  - **PVR falls** significantly
  - 100% cardiac output through lungs

Pulmonary Anatomy

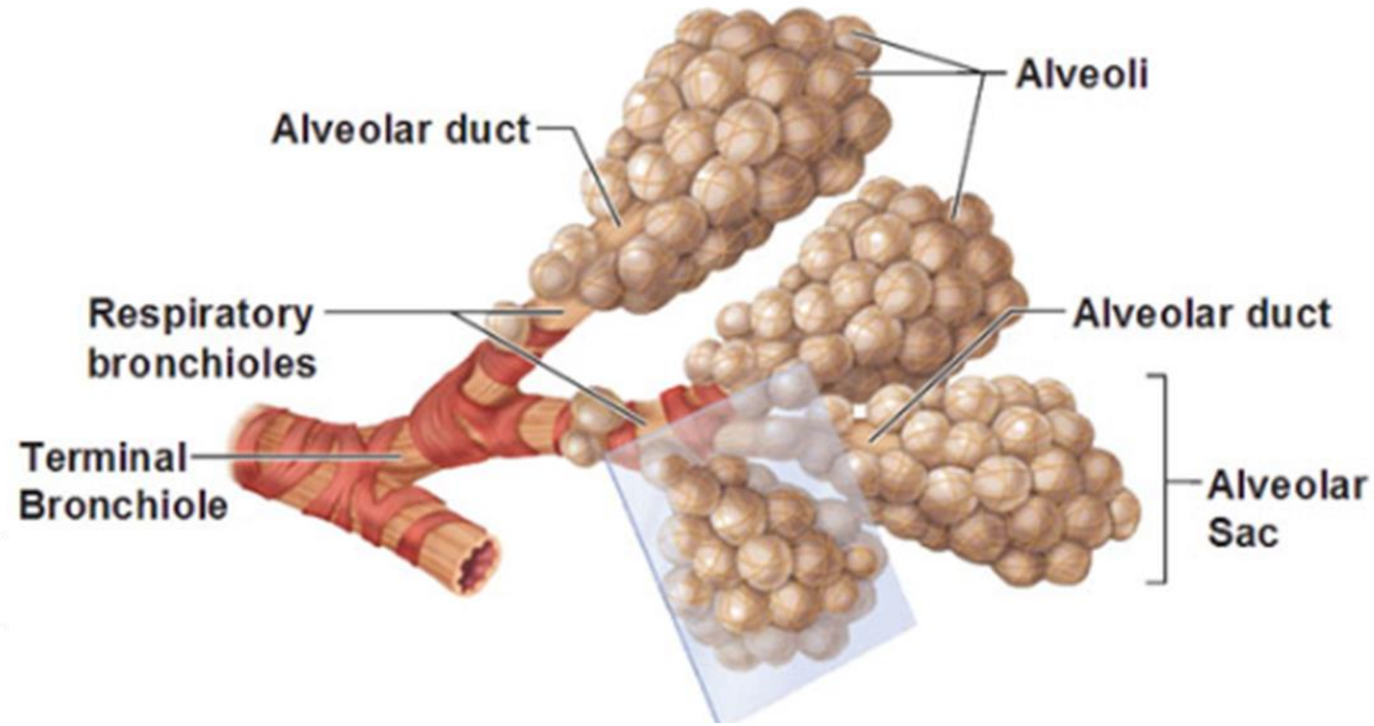
Jason Ryan, MD, MPH

Respiratory Tract



Zones

- **Conducting Zone**
  - No gas exchange
  - Large airways, nose, pharynx, trachea, bronchi
  - Filters, warms, humidifies air
  - Anatomic dead space
- **Respiratory Zone**
  - Gas exchange
  - Respiratory bronchioles, alveolar ducts, alveoli



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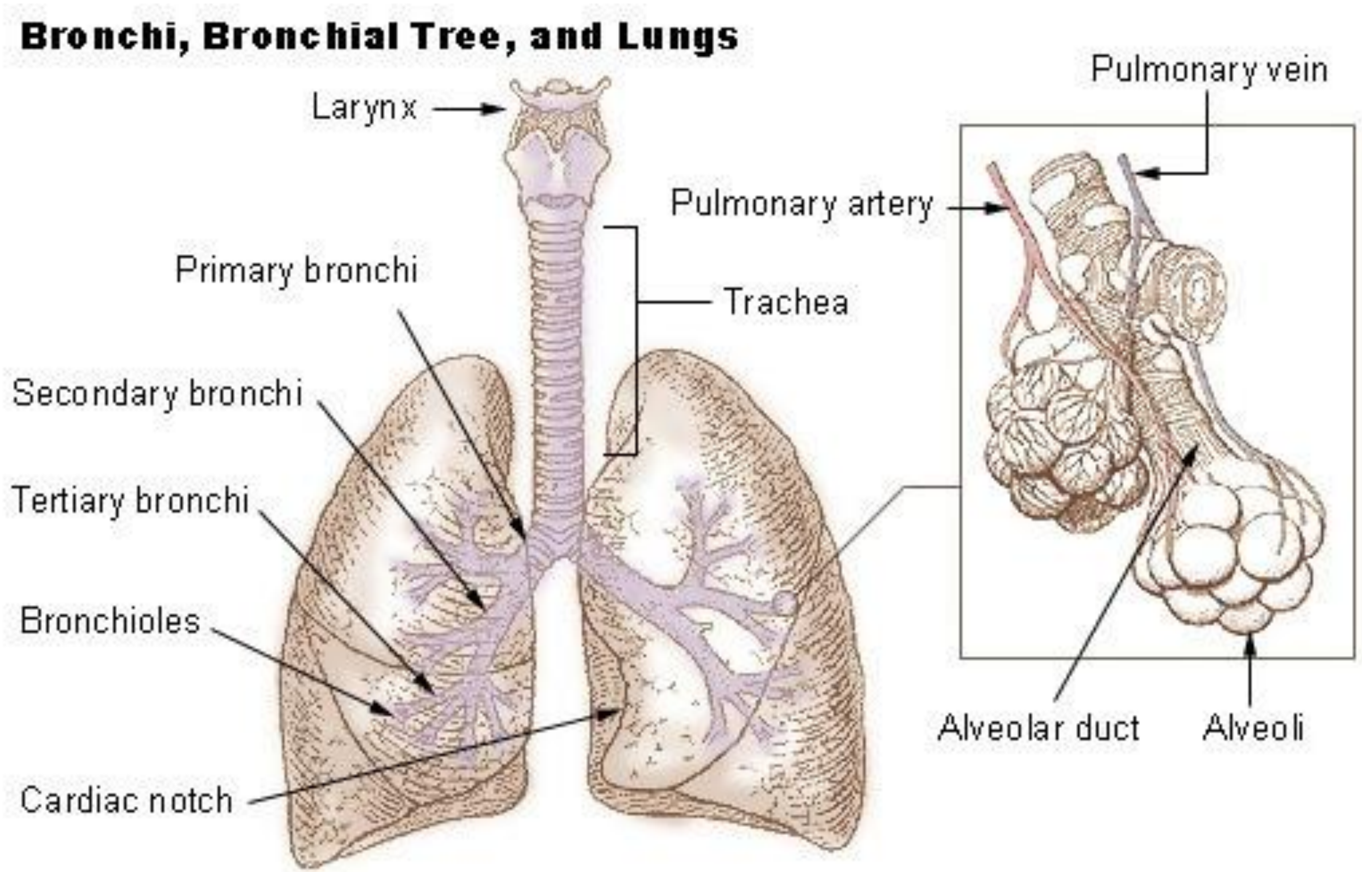
Lung Anatomy

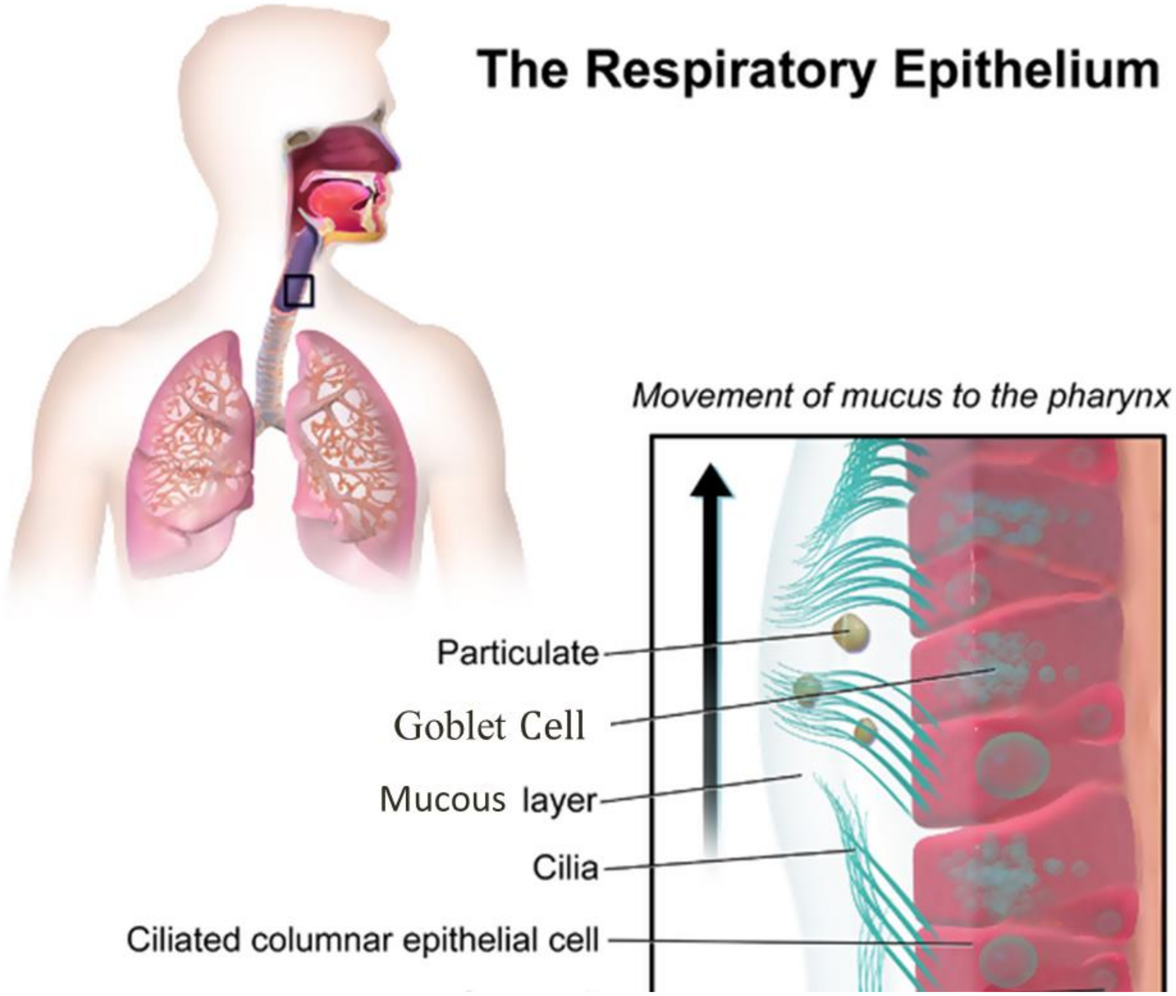


Bronchi and Bronchioles

- **Bronchi (cartilage)**
  - Primary (left and right)
  - Secondary/lobar
  - Tertiary/segmental
- **Bronchioles (no cartilage)**
  - Lobular/large
  - Terminal
  - Respiratory (feeds alveoli)

Airway Cells

- **Goblet cells**
  - Secrete **mucus**
  - Mostly glycoproteins and water
  - Protects against particulates, infection
- **Ciliated epithelial cells**
  - Beating cilia move mucus to epiglottis
  - Mucus swallowed
- **Club cells (bronchioles)**
  - Non-ciliated epithelial cells
  - Secrete protective proteins
  - Detoxification (P450 enzymes)



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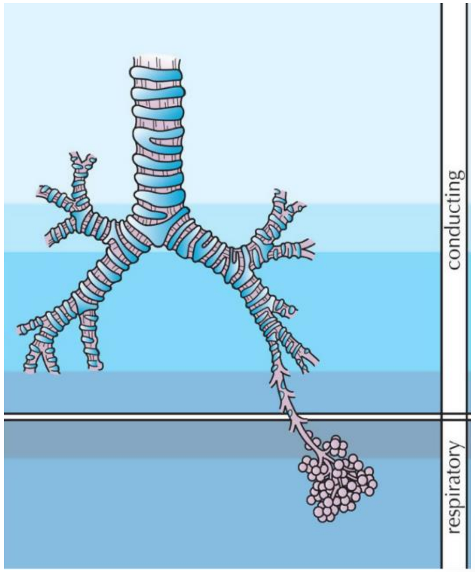
Respiratory Epithelium

- **Trachea and bronchi**
  - Ciliated pseudostratified columnar epithelial cells
  - Goblet cells
- **Bronchioles**
  - Epithelium transitions
  - Forms ciliated simple cuboidal epithelium
  - Club cells (terminal bronchioles)



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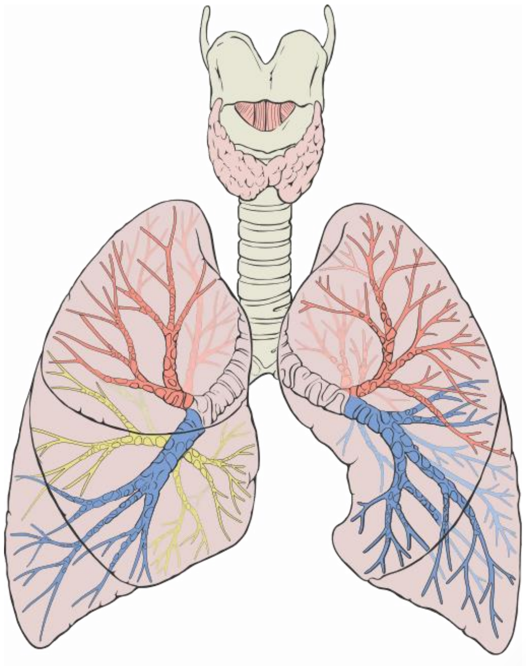
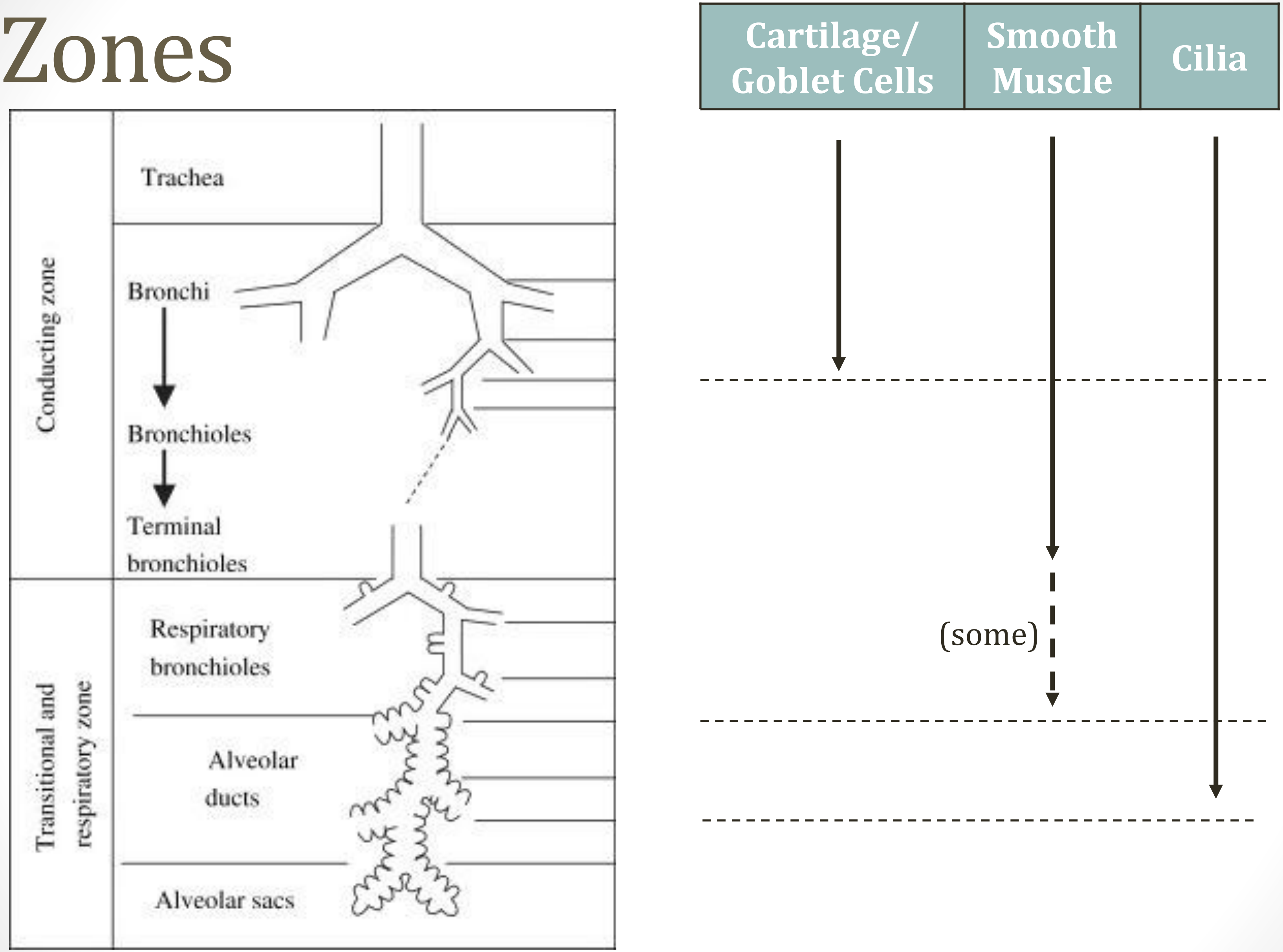
Smooth Muscle

- **Conducting airway** walls contain smooth muscle
- Sympathetic activation (beta-2)
  - Bronchodilation
- Parasympathetic activation (M3)
  - Bronchoconstriction



Patrick Lynch/Wikipedia

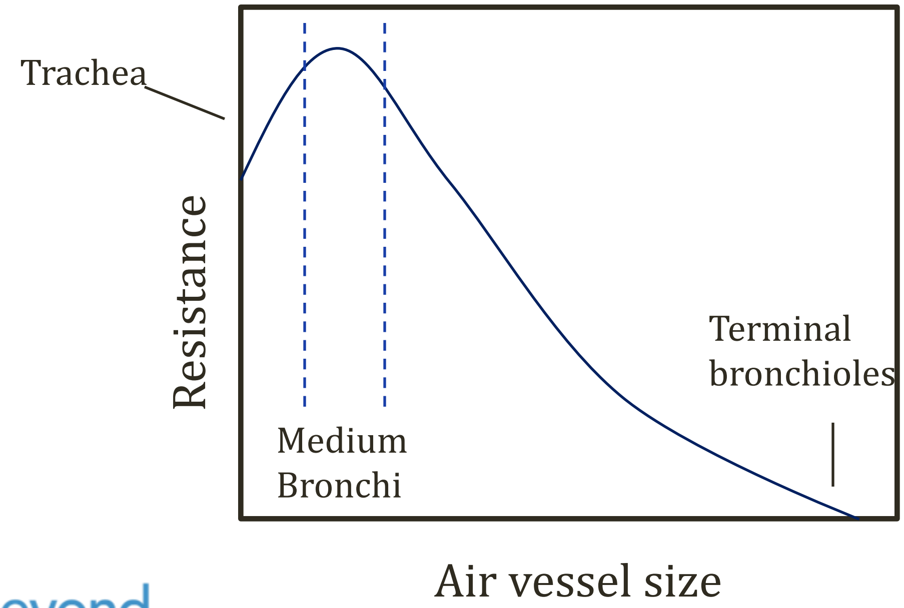
Zones



Conducting zone
Trachea
Bronchi
Bronchioles
Terminal bronchioles
Transitional and respiratory zone
Respiratory bronchioles
Alveolar ducts
Alveolar sacs
Cartilage/ Goblet Cells
Smooth Muscle
Cilia
(some)

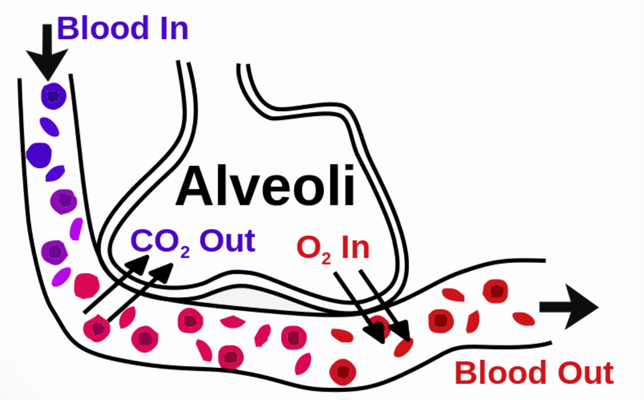
Resistance to Air Flow

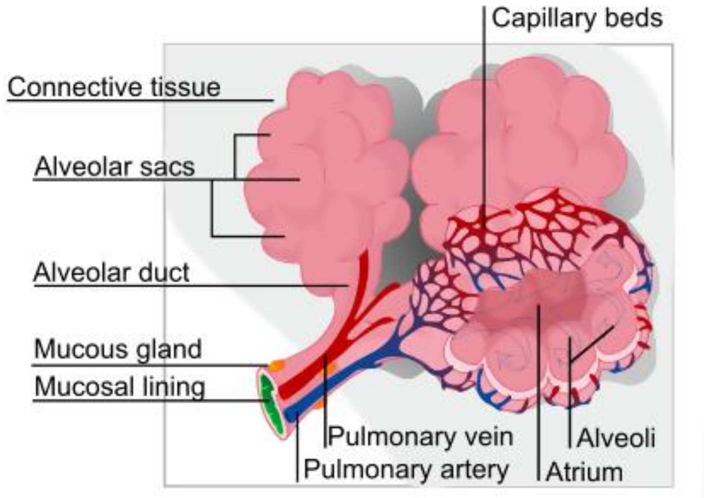
- Upper airways about 50% resistance
  - Nose, mouth, pharynx
- Lower airway resistance
  - Highest in **medium bronchi** (turbulent flow)
  - Lowest in terminal bronchioles - slow laminar flow



Alveoli

- Small sacs
- Separated by septa
- Simple squamous epithelium (pneumocytes)
- Gas exchange
- Surrounded by capillaries





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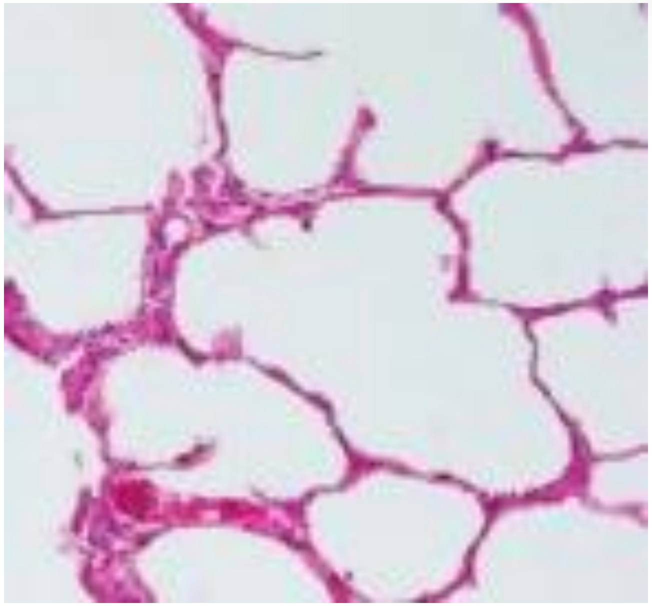
Pneumocytes

Alveolar Epithelial Cells

- Type 1
  - Most common (97% of cells)
  - Thin for gas exchange
- Type 2
  - Produce **surfactant**
  - Can proliferate to form other cell types
  - Key for **regeneration** after injury
- Alveolar macrophages



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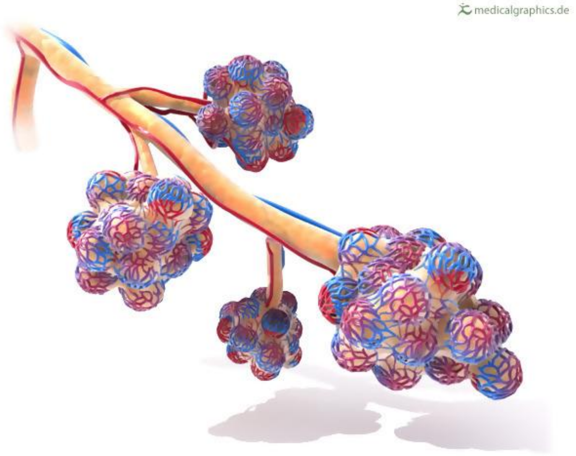
Surfactant

- Exhale → alveoli shrink
- Collapse → atelectasis
- ↓ efficiency gas exchange
- Surfactant prevents collapse of alveoli



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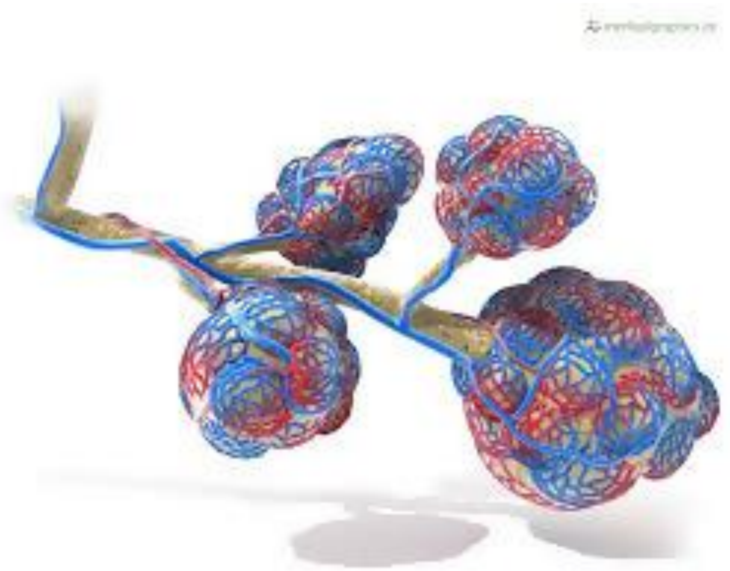
Surfactant

- Secreted by **type 2 pneumocytes**
- Mix of **lecithins** (lipid substance)
- Especially **dipalmitoylphosphatidylcholine**



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Surface Tension

- Alveoli lined with film of liquid
- Liquid-liquid forces shrink surface area into sphere
- **Surface tension** = liquid-liquid forces

Law of Laplace

- Determines collapsing pressure
  - Forces tending to collapse alveoli
  - Low collapsing pressure = easy to remain open
  - High collapsing pressure = difficult to remain open

$$\text{Collapsing Pressure} = \frac{2 * (\text{surface tension})}{\text{radius}}$$

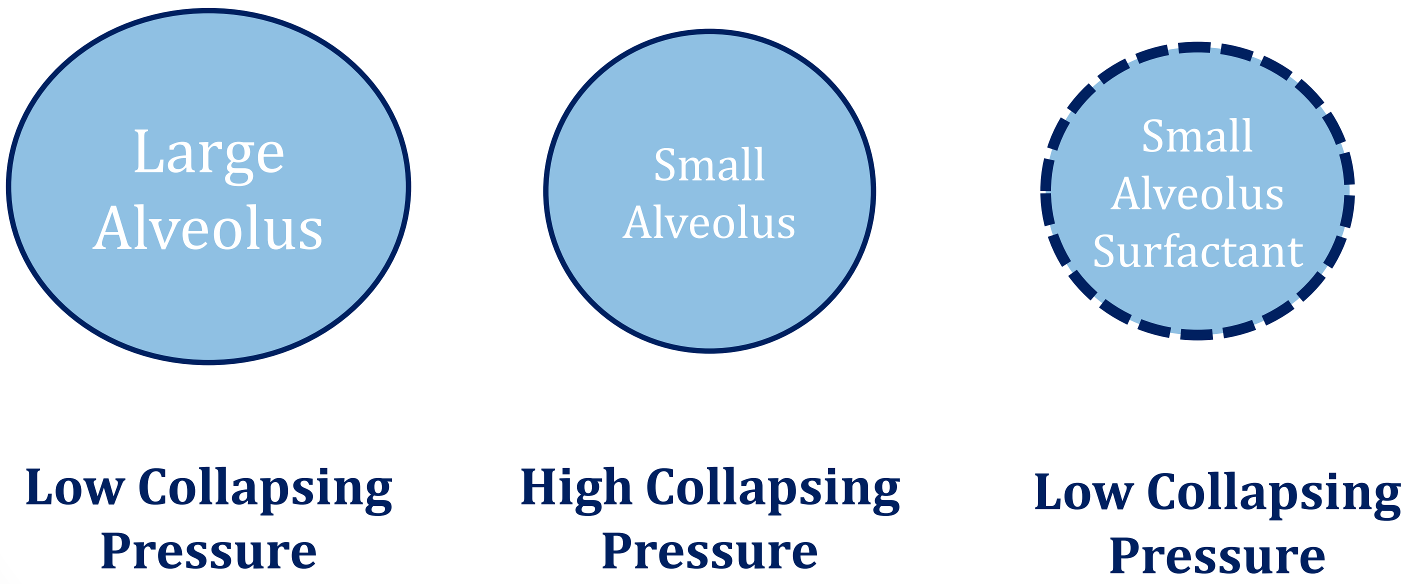
Law of Laplace

- Lungs contain many small alveoli
- Small radius = high distending pressure
- Need low surface tension to remain open
- Surfactant **reduces surface tension**
- Increases lung compliance (less stiff, more floppy)

$$\text{Collapsing Pressure} = \frac{2 * (\text{surface tension})}{\text{radius}}$$

Law of Laplace

$$\text{Collapsing Pressure} = \frac{2 * (\text{surface tension})}{\text{radius}}$$



Fetal Lung Maturity

- Lungs **"mature"** when adequate surfactant present
- Occurs around **35 weeks**
- Lecithin–sphingomyelin ratio (L/S ratio)
- Both produced equally until ~35 weeks
- Ratio >2.0 in amniotic fluid suggests lungs mature

Neonatal RDS

Neonatal Respiratory Distress Syndrome

- **Surfactant deficiency**
- High surface tension
- Atelectasis
- Decreased lung compliance
- Hypoxemia/↑ $pCO2$ (poor ventilation)
- Poorly responsive to O_2
  - Lungs collapsed (alveoli)
  - Intrapulmonary shunting

Neonatal RDS

Risk Factors

- Prematurity
- Maternal diabetes
  - High insulin levels decrease surfactant production
- Cesarean delivery
  - Baby spared stress response at delivery
  - Reduced fetal cortisol
  - Reduction in surfactant

Neonatal RDS

Complications

- Bronchopulmonary dysplasia
  - Oxygen toxicity
  - **Alveolarization** does not progress normally
  - Respiratory problems during infancy
- Patent ductus arteriosus
  - Hypoxia keeps shunt open
- Retinopathy of prematurity
  - Oxygen → free radical formation
  - Neovascularization in the retina
  - Retinal detachment → blindness

Neonatal RDS

Prevention and Treatment

- Preterm delivery: **betamethasone**
  - Corticosteroid
  - Given to mother to stimulate surfactant production
- Treatment: surfactant
  - Administered via endotracheal tube

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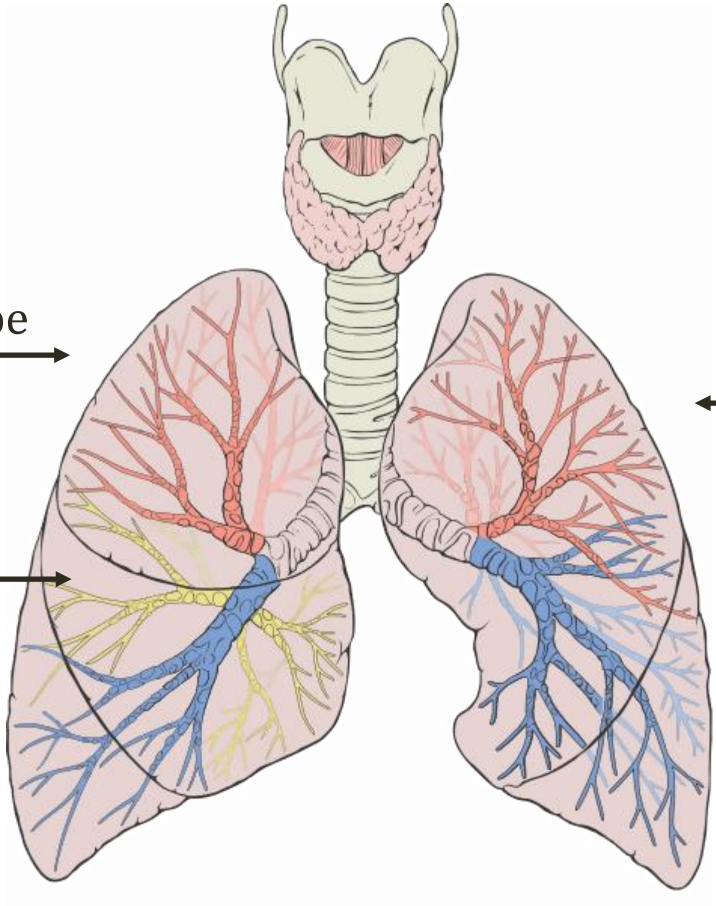
Lobes



Right Upper Lobe

Right Middle Lobe

Right Lower Lobe

Left Upper Lobe

Left Lower Lobe

Image courtesy of Patrick J. Lynch, medical illustrator

Right Upper Lobe

Right Middle Lobe

Right Lower Lobe

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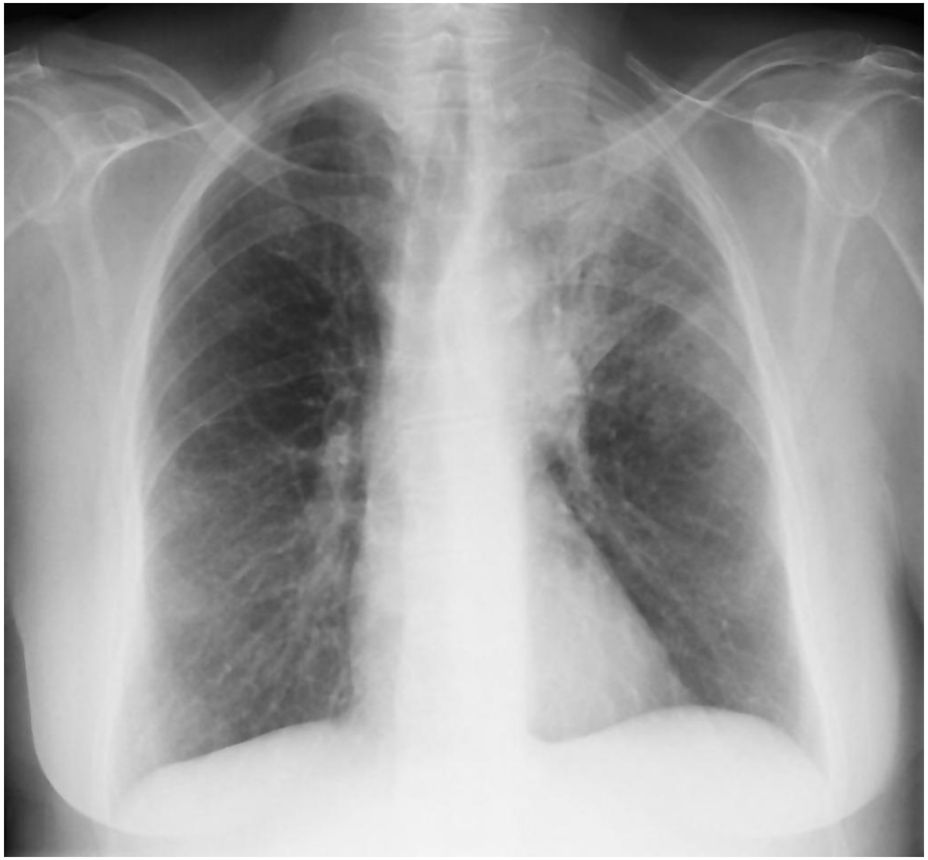
Left Upper Lobe



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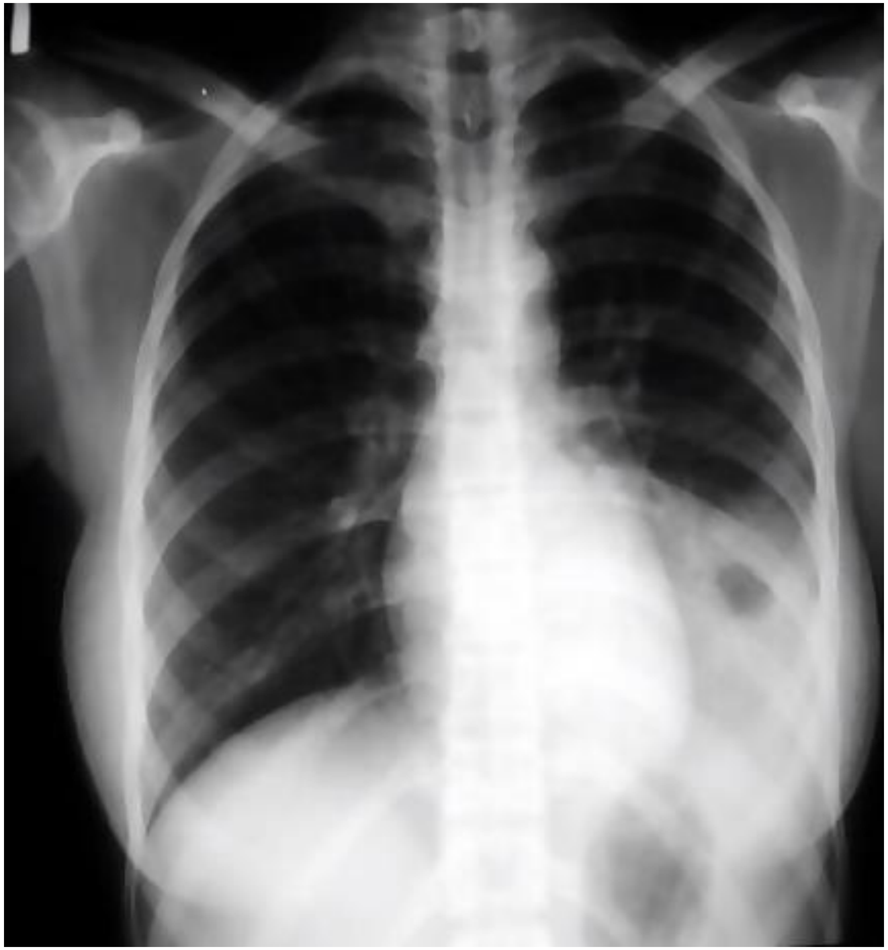
Left Lower Lobe



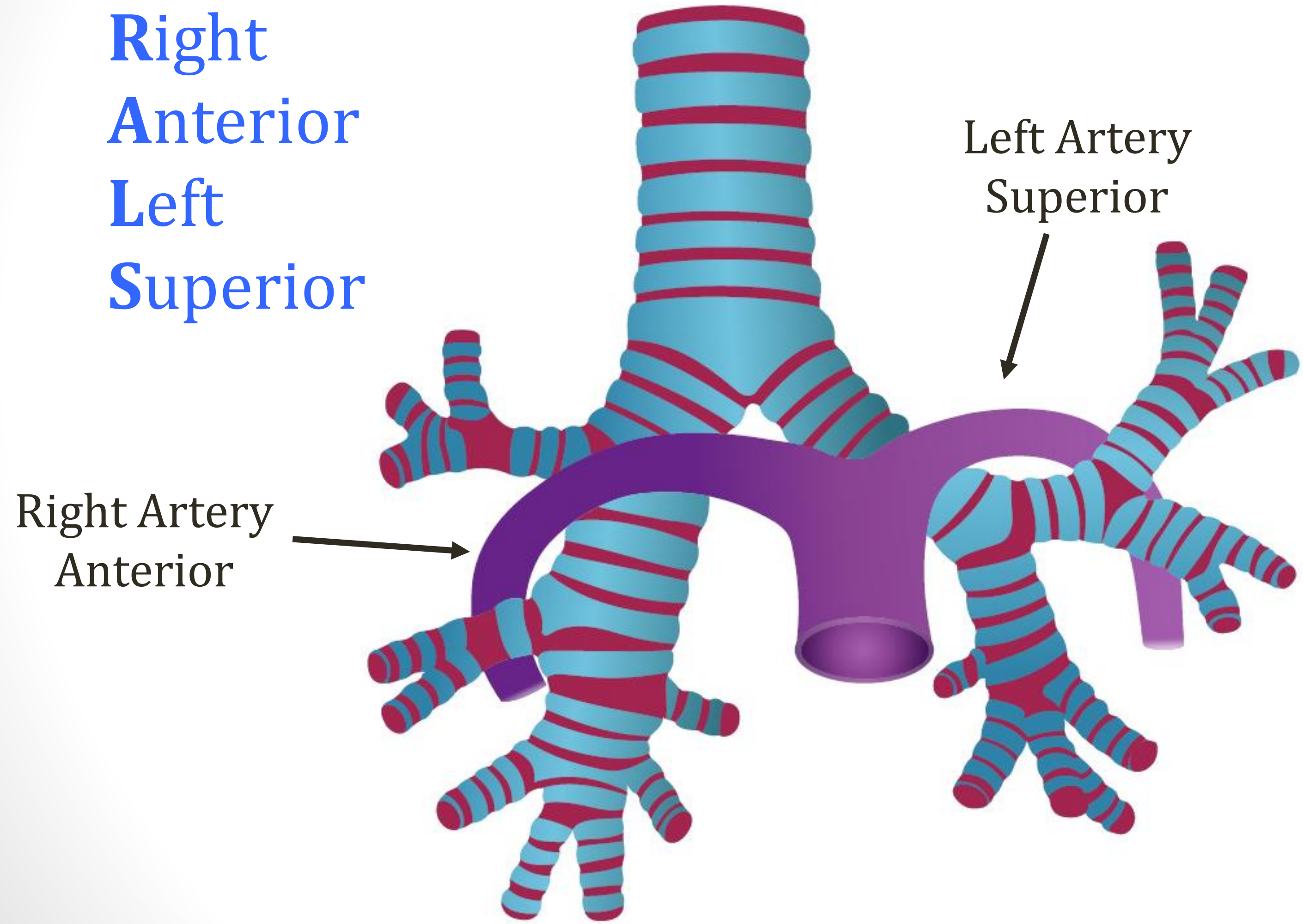
Foreign Body Aspiration

- Commonly occurs in children (peanuts)
- **Right lung** is more common site of aspiration
  - Right bronchus wider with less angle
  - More vertical path to lung
- Right lung: 60% cases
  - Majority in main bronchus
  - Small number in right lower lobe bronchus
- Left lung: 23% cases
  - Majority in main bronchus
  - Small number in left lower lobe bronchus

Source: Eren et al. Foreign body aspiration in children: experience of 1160 cases. Ann Trop Paediatr. 2003;23(1):31.

Mediastinal Anatomy

Right
Anterior
Left
Superior



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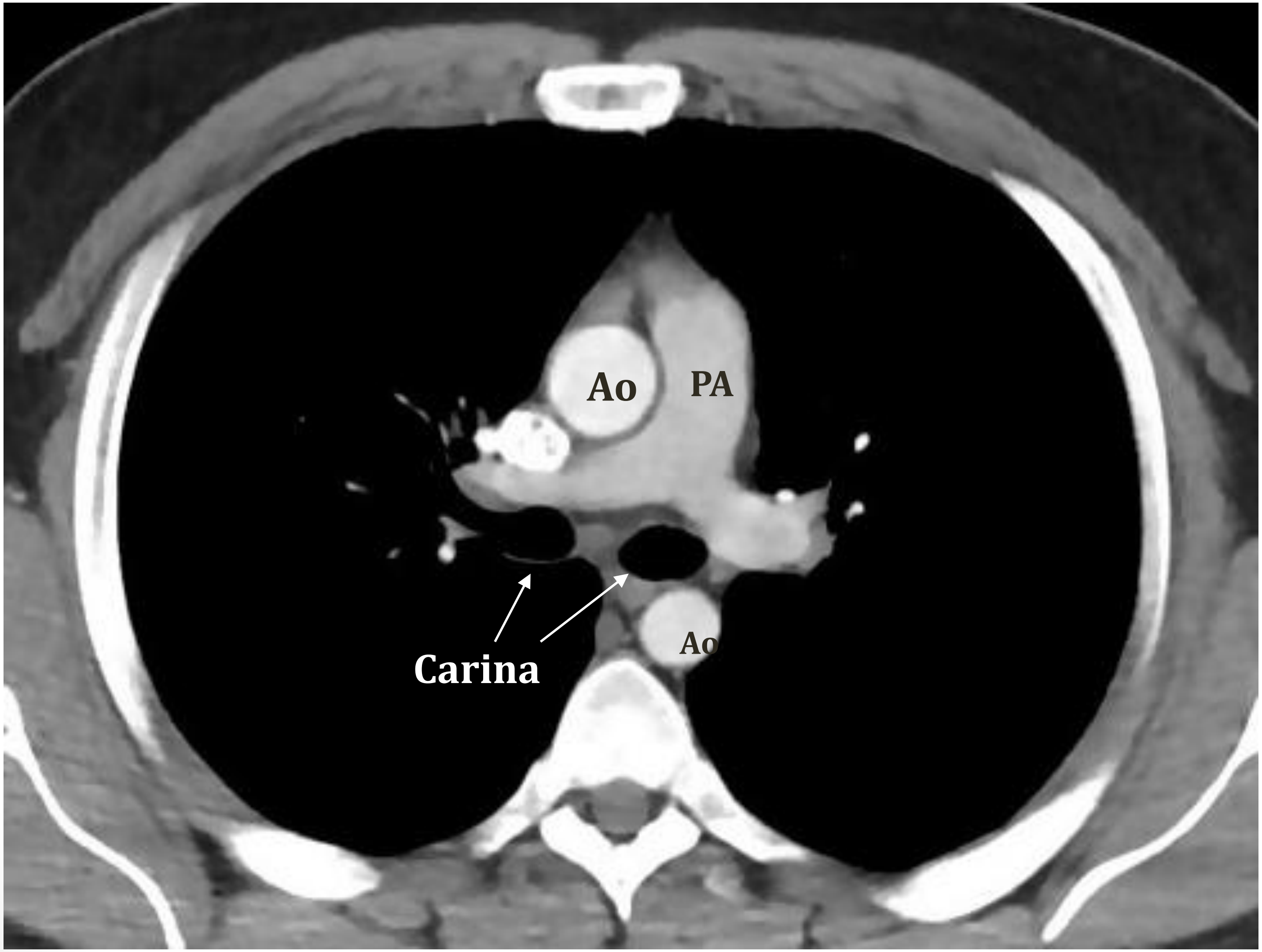
Mediastinal Anatomy



Mediastinal Structures

- Mediastinum: space between lungs
- Divided into 3 anatomical compartments
  - Anterior
  - Middle
  - Posterior
- Differential diagnosis of mass varies by compartment

Mediastinal Compartments

Mediastinal Structures

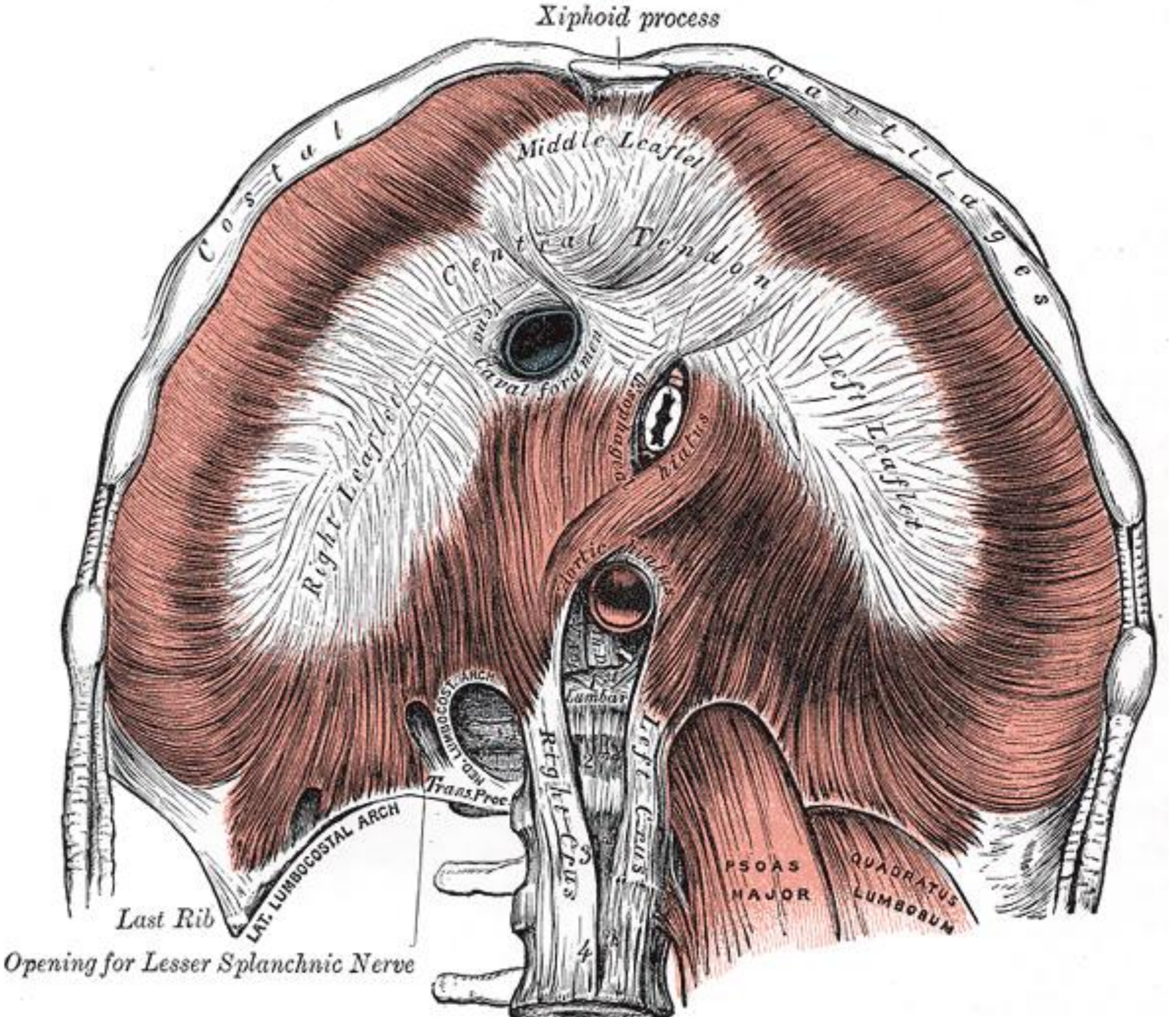
Compartment	Major Structures	Masses
Anterior	Thymus, internal mammary arteries, lymph nodes	Thyroid, Thymic neoplasm, Teratoma, Lymphoma
Middle	Pericardium, heart, aorta, airway and esophagus	Lymphadenopathy: lymphoma, sarcoid, or metastatic lung cancer
Posterior	Spine, nerves and spinal ganglia	Neurogenic tumors: schwannoma, neuroblastoma

Anterior Mediastinal Masses

Terrible Ts

- **Thymic masses**
  - Half of anterior masses derive from thymus
  - Thymoma: associated with myasthenia gravis
- Teratoma or **germ cell tumors** in adults
  - Mediastinum: most common location extra nodal GCT
  - Teratomas, seminomas
- Terrible **lymphomas**
- **Thyroid** growths
  - Enlarged or ectopic thyroid tissue may present as mass
  - Usually connected to thyroid gland

Diaphragm


Xiphoid process
Costal Cartilages
Middle Leaflet
Central Tendon
Caval foramen
Œsophageal hiatus
Right Leaflet
Left Leaflet
Aortic hiatus
Lumbar
Right Crus
Left Crus
MED. LUMBOCOST. ARCH
Trans.Proc.
LAT. LUMBOCOSTAL ARCH
Last Rib
Opening for Lesser Splanchnic Nerve
PSOAS MAJOR
QUADRATUS LUMBORUM

Diaphragm

- Caval opening
  - T8
  - Inferior vena cava
- Esophageal hiatus
  - T10
  - Esophagus, Vagus nerve
- Aortic hiatus
  - T12
  - Aorta, thoracic duct, azygous vein

Diaphragm

- Innervated by **C3, C4, C5 (phrenic nerve)**
- Diaphragm irritation → “referred” shoulder pain
  - Classic example: gallbladder disease
  - Also lower lung masses
  - Irritation can cause dyspnea and hiccups
- Cut nerve → diaphragm elevation, dyspnea
  - “Paradoxical movement” → Moves up with inspiration
  - Can see on fluoroscopy (“sniff test”)

Muscles of Quiet Respiration

- Diaphragm → inspiration
- Exhalation is passive with normal ("quiet") breathing

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Exercise Breathing

- Inspiration (neck)
  - Scalenes – raise ribs
  - Sternocleidomastoids – raise sternum
- Exhalation (abdomen)
  - Rectus muscle
  - Internal/external obliques
  - Transverse abdominis
  - Internal intercostals
- Use of accessory muscles in respiratory distress

Pulmonary Physiology

Jason Ryan, MD, MPH

Lung Volumes

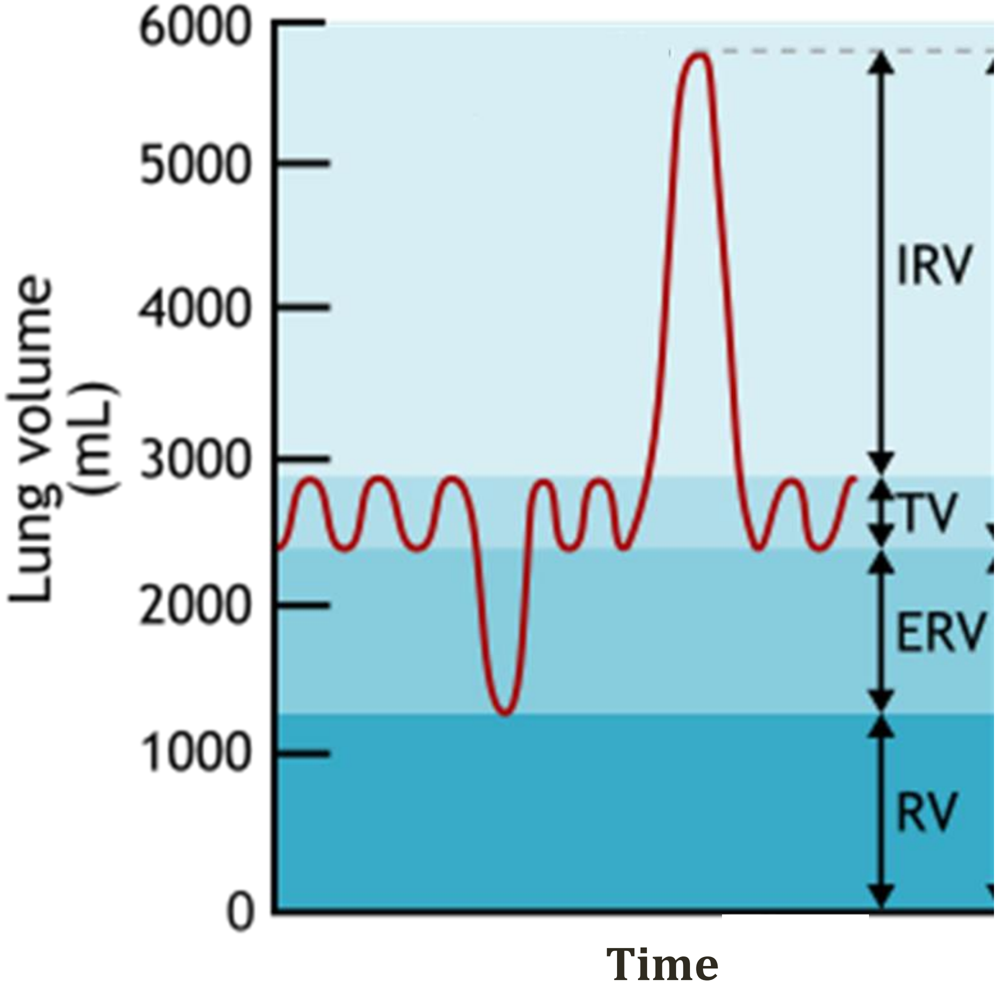


Image courtesy of Michal Komorniczak, Medical Illustrations

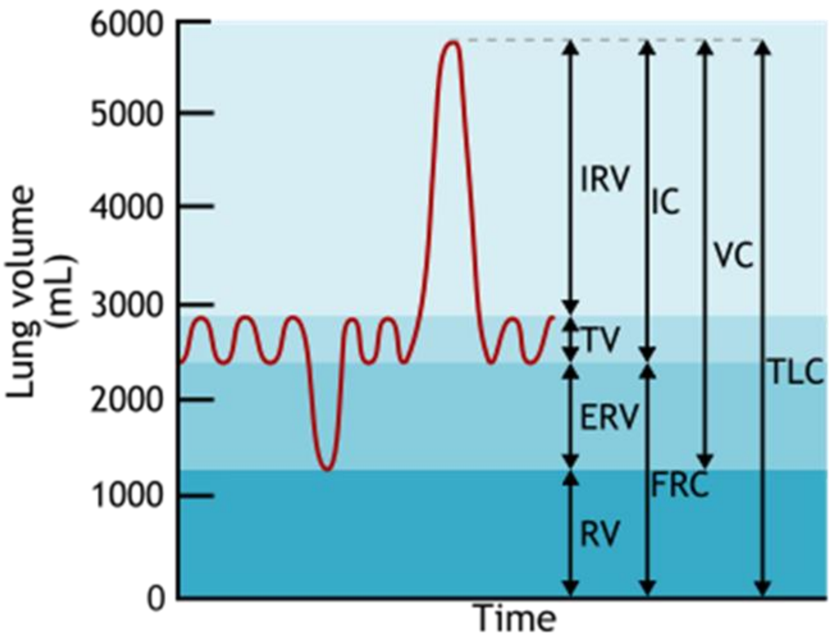
Lung Volumes

- Tidal volume (TV)
  - In/out air with each quiet breath
- Expiratory reserve volume (ERV)
  - Extra air pushed out with force beyond TV
  - RV remains in lungs
- Inspiratory reserve volume (IRV)
  - Extra air can be drawn in with force beyond TV
  - Lungs filled to capacity
- Residual volume (RV)
  - Air that can't be blown out no matter how hard you try

Lung Capacities

Capacity = sum of two volumes

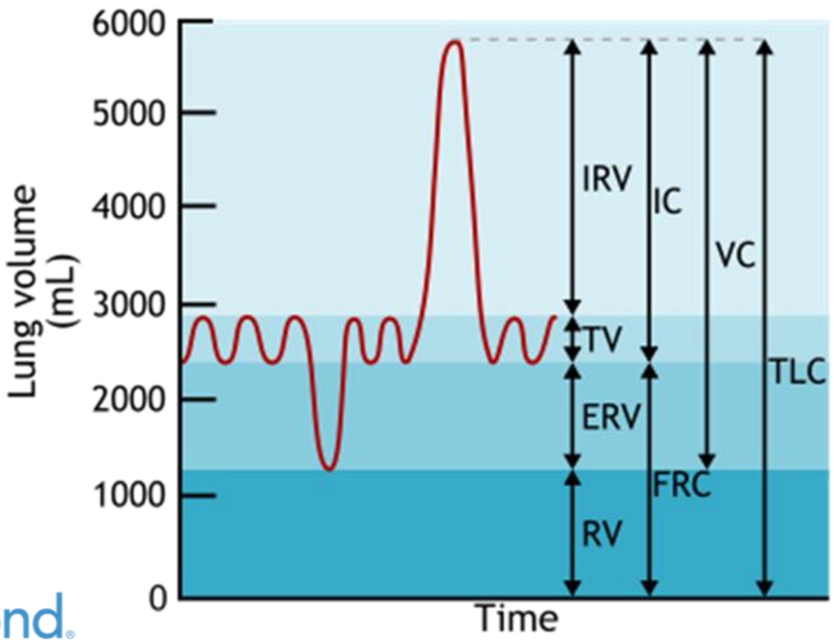
- Total lung capacity
  - Sum of all volumes
  - RV + ERV+ IRV + TV
- Inspiratory capacity
  - Most air you can inspire
  - TV + IRV
- Vital capacity
  - Most you can exhale
  - TV + IRV + ERV



Lung Capacities

Capacity = sum of two volumes

- **Functional Residual Capacity**
  - Residual volume after quiet expiration
  - RV + ERV
  - Volume when system is relaxed
  - Equilibrium: chest wall pulling out = lungs pulling in

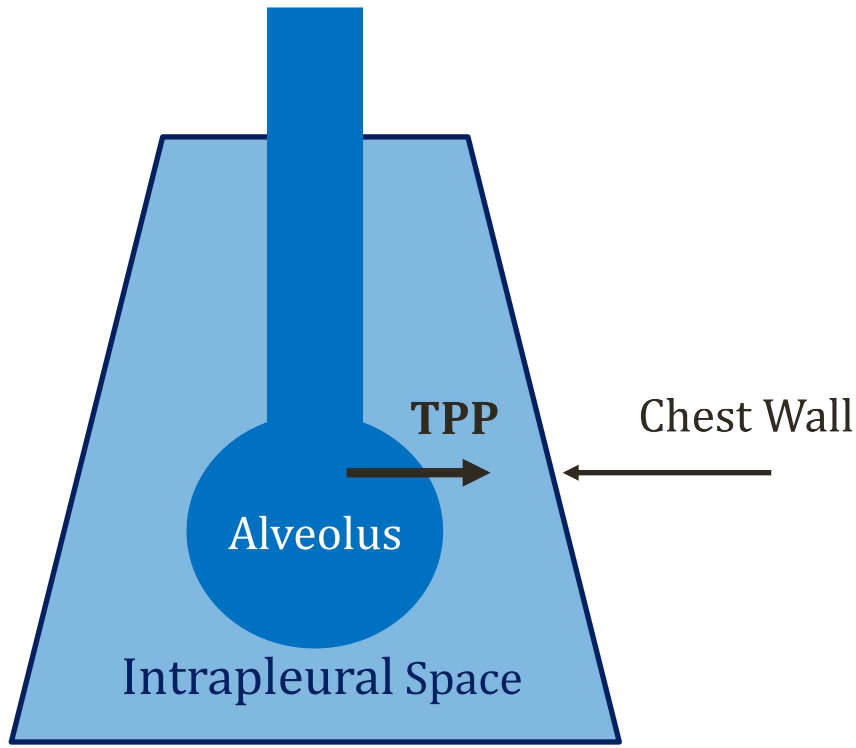


Lung Pressures

- Atmospheric pressure = 760 mmHg = 0 mmHg
- Alveolar pressure = pressure within alveoli
- Intrapleural pressure = pressure in pleural space
- **Transpulmonary pressure**
  - Alveolar pressure –intrapleural pressure
  - Pressure across walls of alveoli
  - Necessary to keep alveoli open

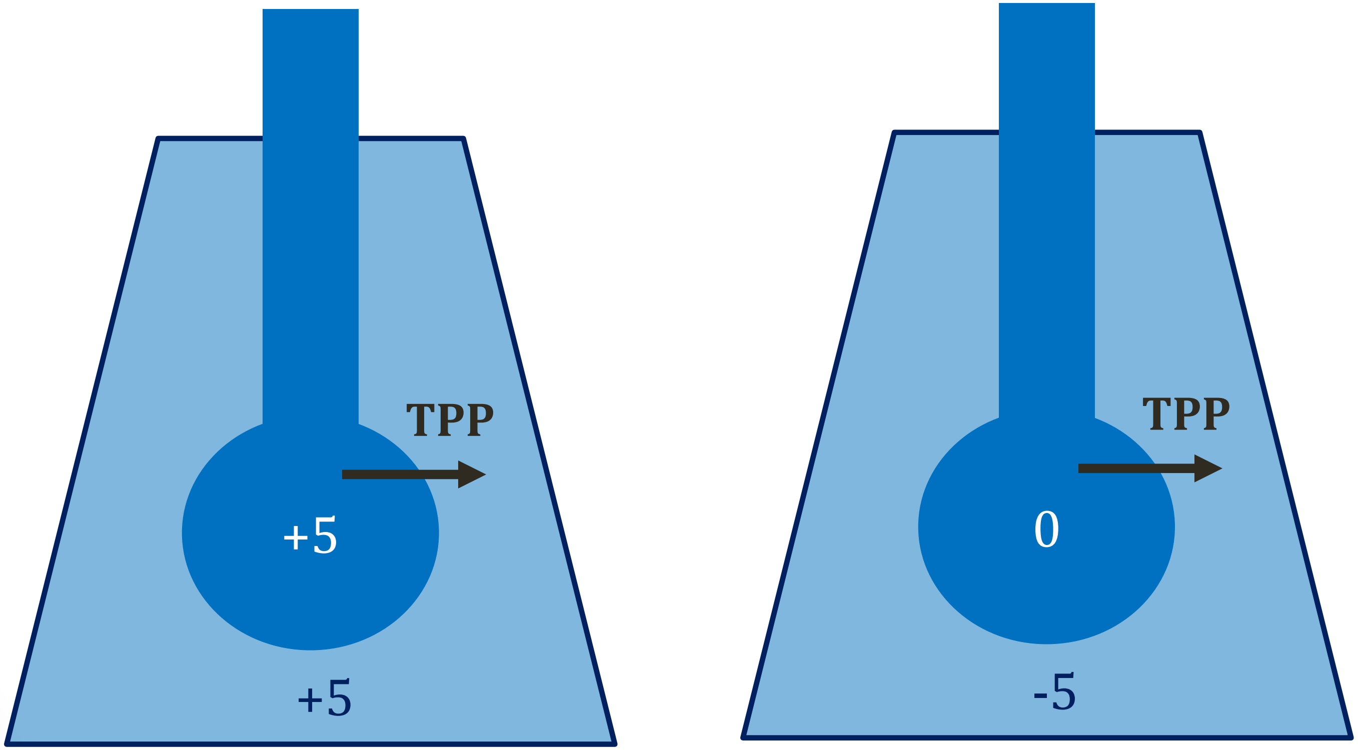
Transpulmonary Pressure

- Alveolar Pressure – Intrapleural Pressure



Transpulmonary Pressure

- Alveolar Pressure – Intrapleural Pressure



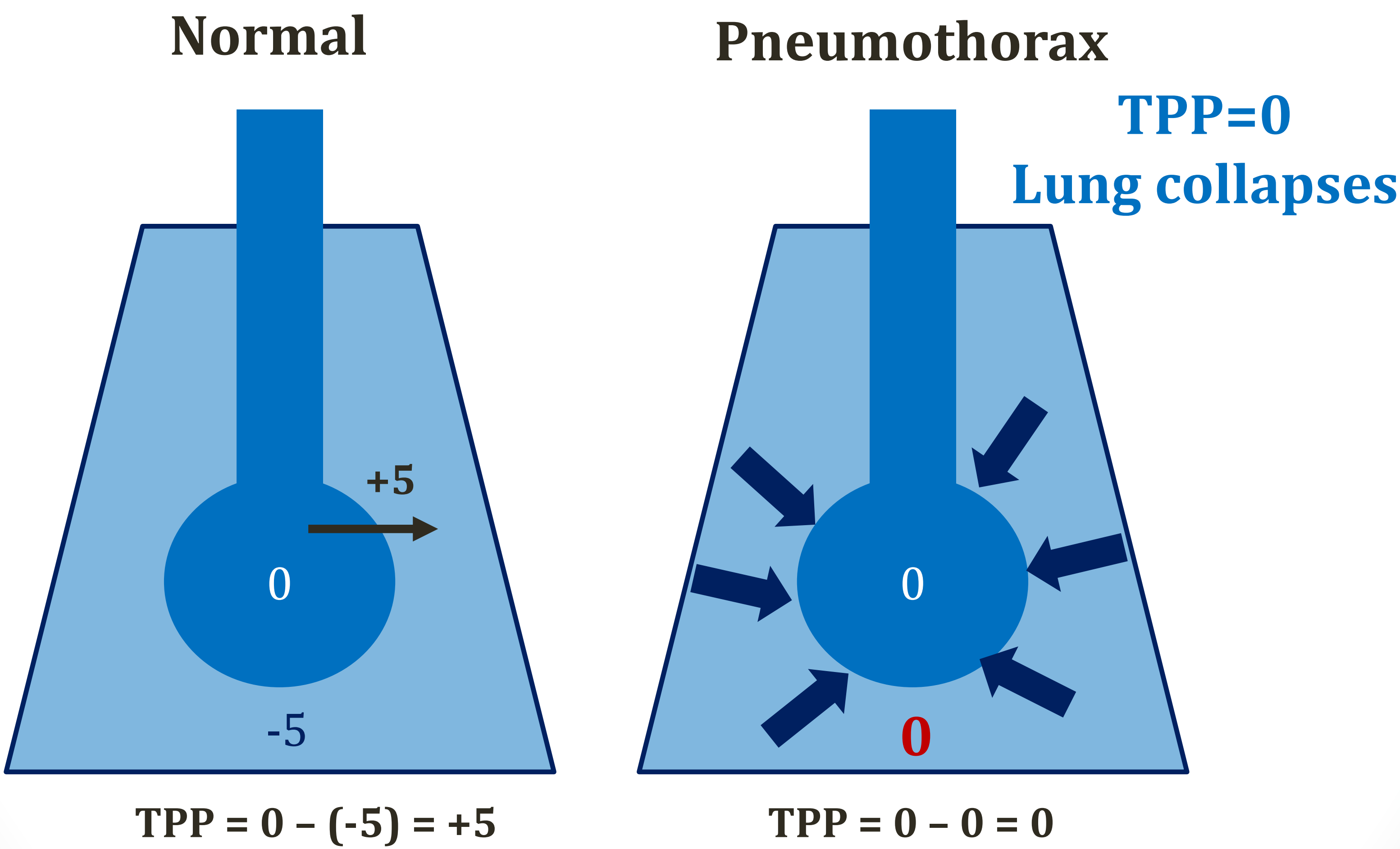
TPP = 5 – 5 = 0

TPP = 0 – (-5) = +5

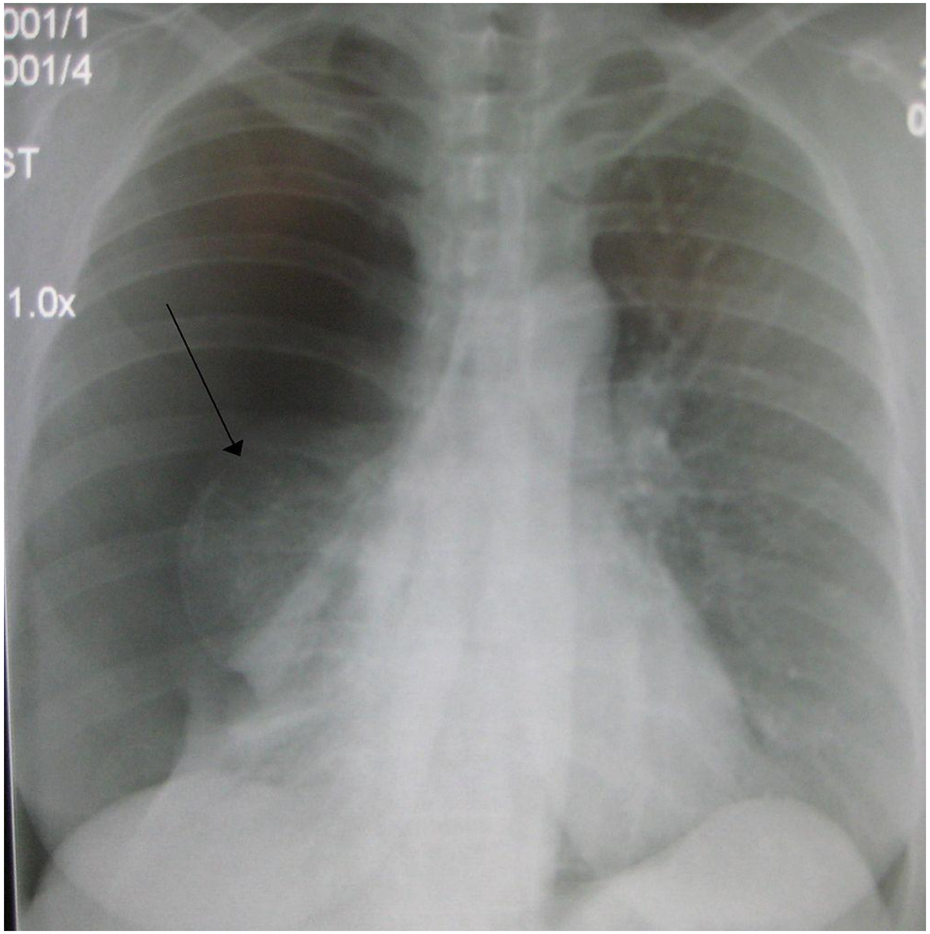
Intrapleural Pressure

- **Negative** during normal quiet breathing
- Alveoli and lungs tend to **collapse**
  - Pull inward/recoil
  - Need outward force to keep walls open
- Chest wall tends to **expand**
  - Spring outward
  - Creates negative pressure in pleural space
- Negative pressure "sucks" alveoli open

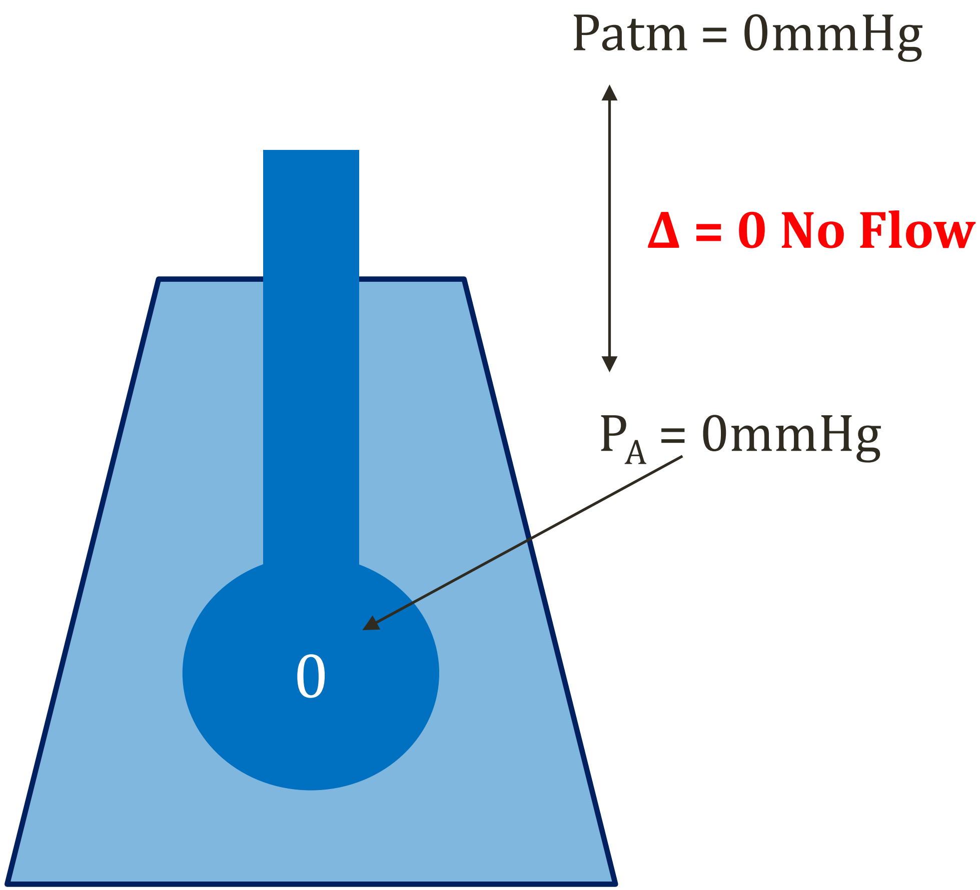
Pneumothorax



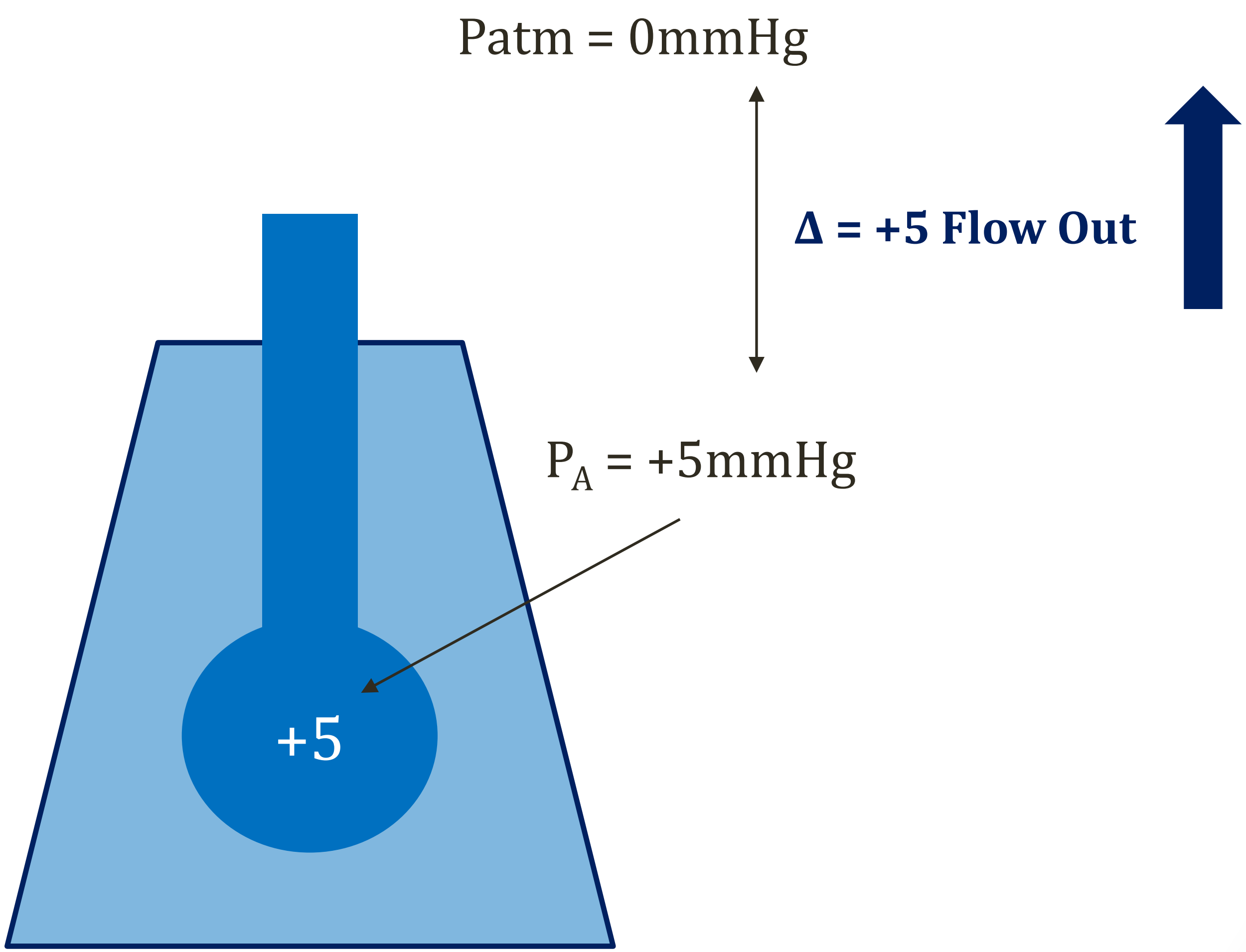
Pneumothorax



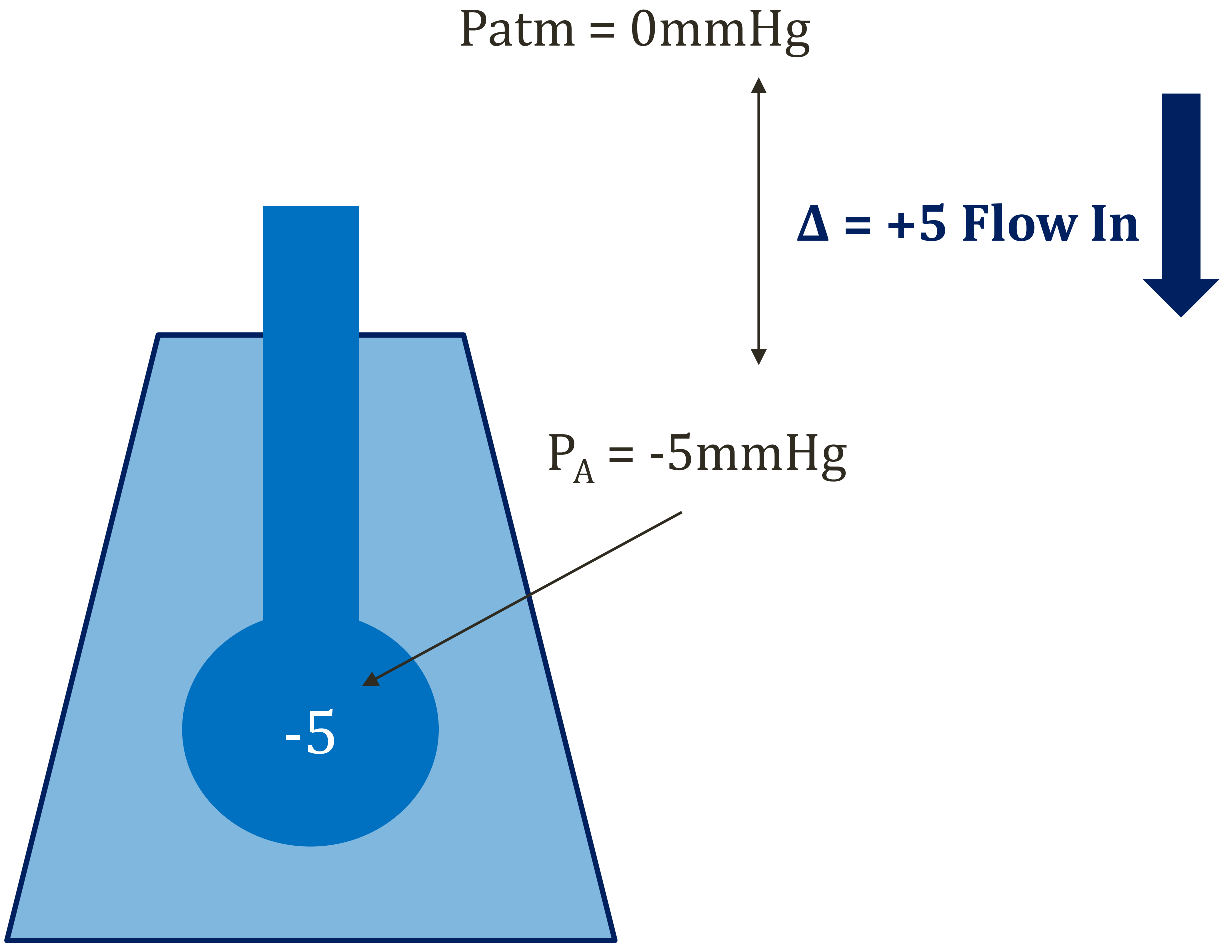
Pressures and Air Flow



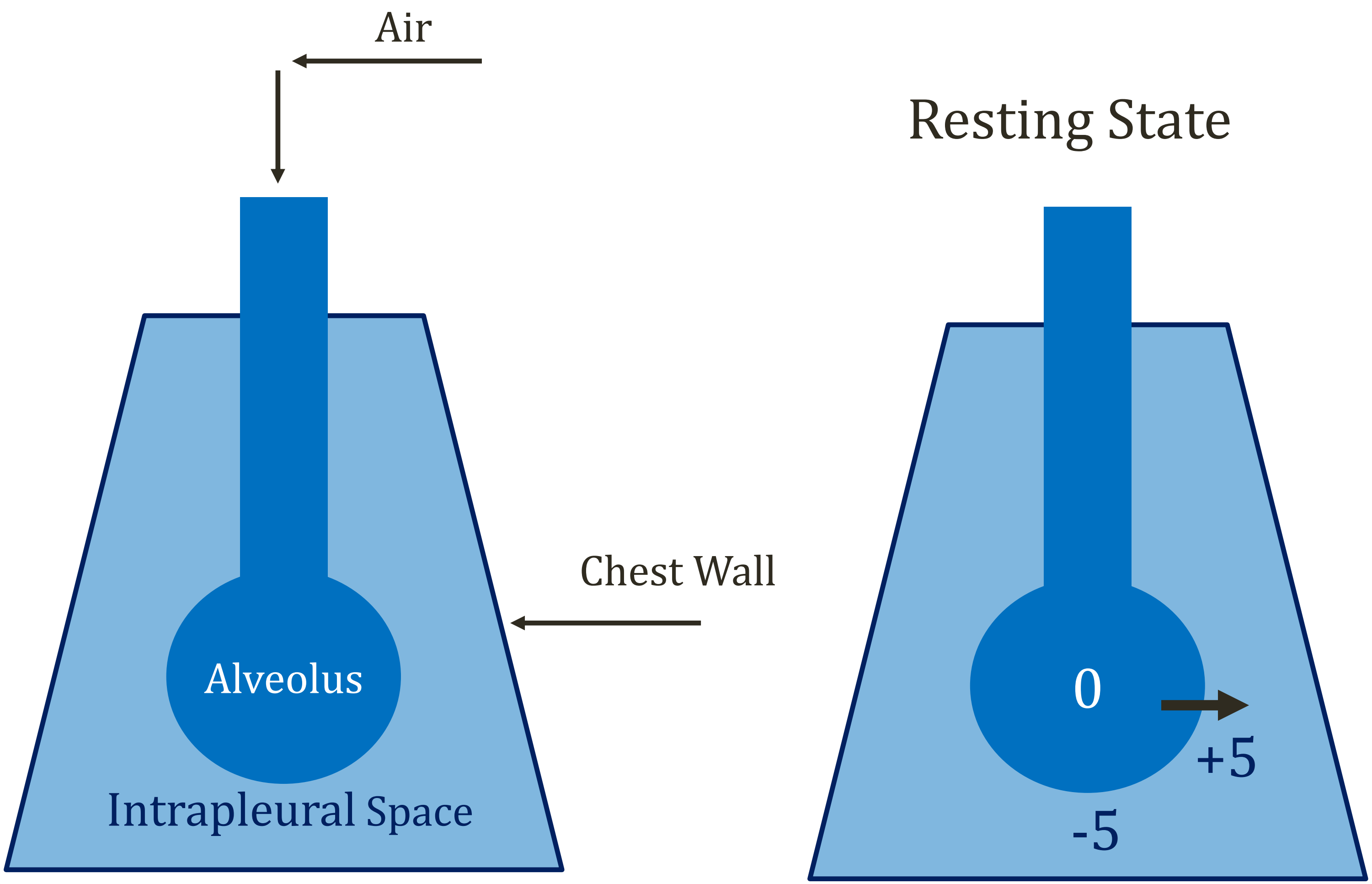
Pressures and Air Flow



Pressures and Air Flow



Lung Pressures

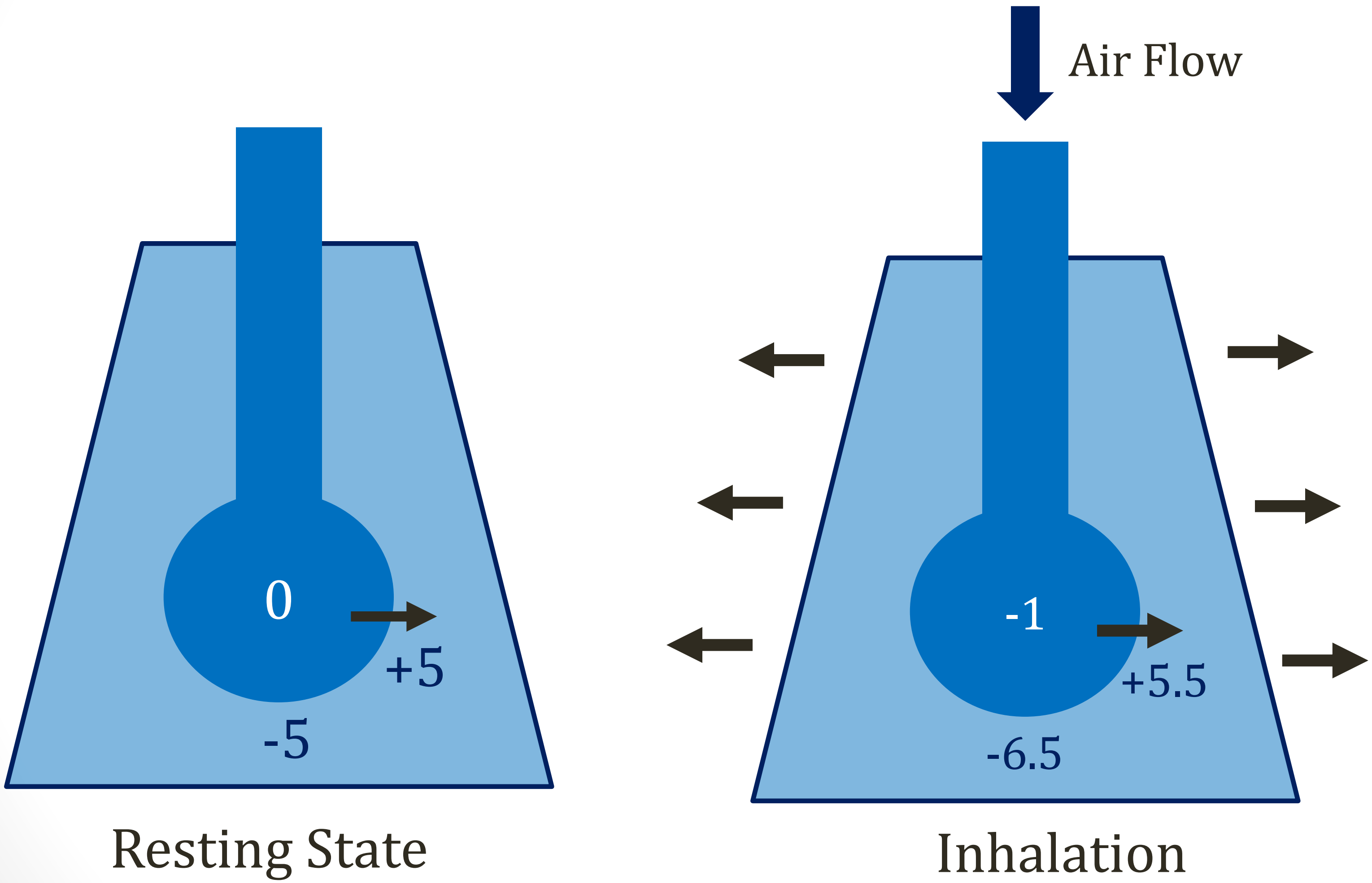


Air Flow and Pressure Changes

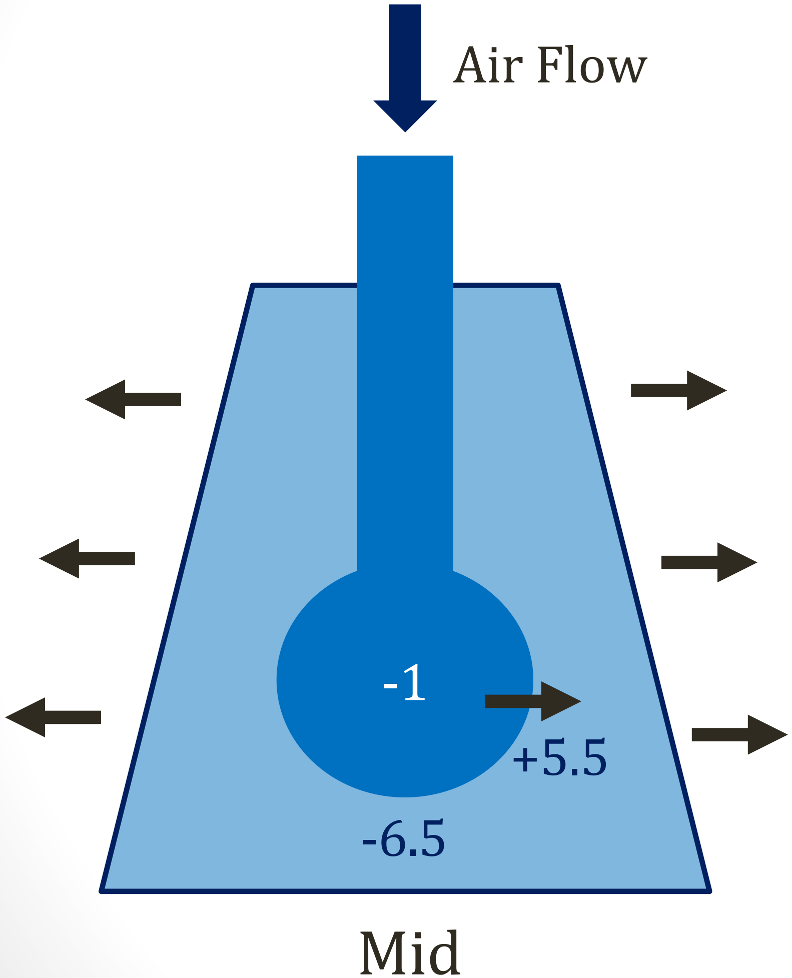
Quiet Breathing

- Inhalation
  - Intrapleural pressure becomes **more negative**
  - Alveolar pressure becomes negative
  - Air flow into lungs
- Exhalation
  - Intrapleural pressure becomes **less negative**
  - Alveolar pressure becomes positive
  - Air flow out of lungs

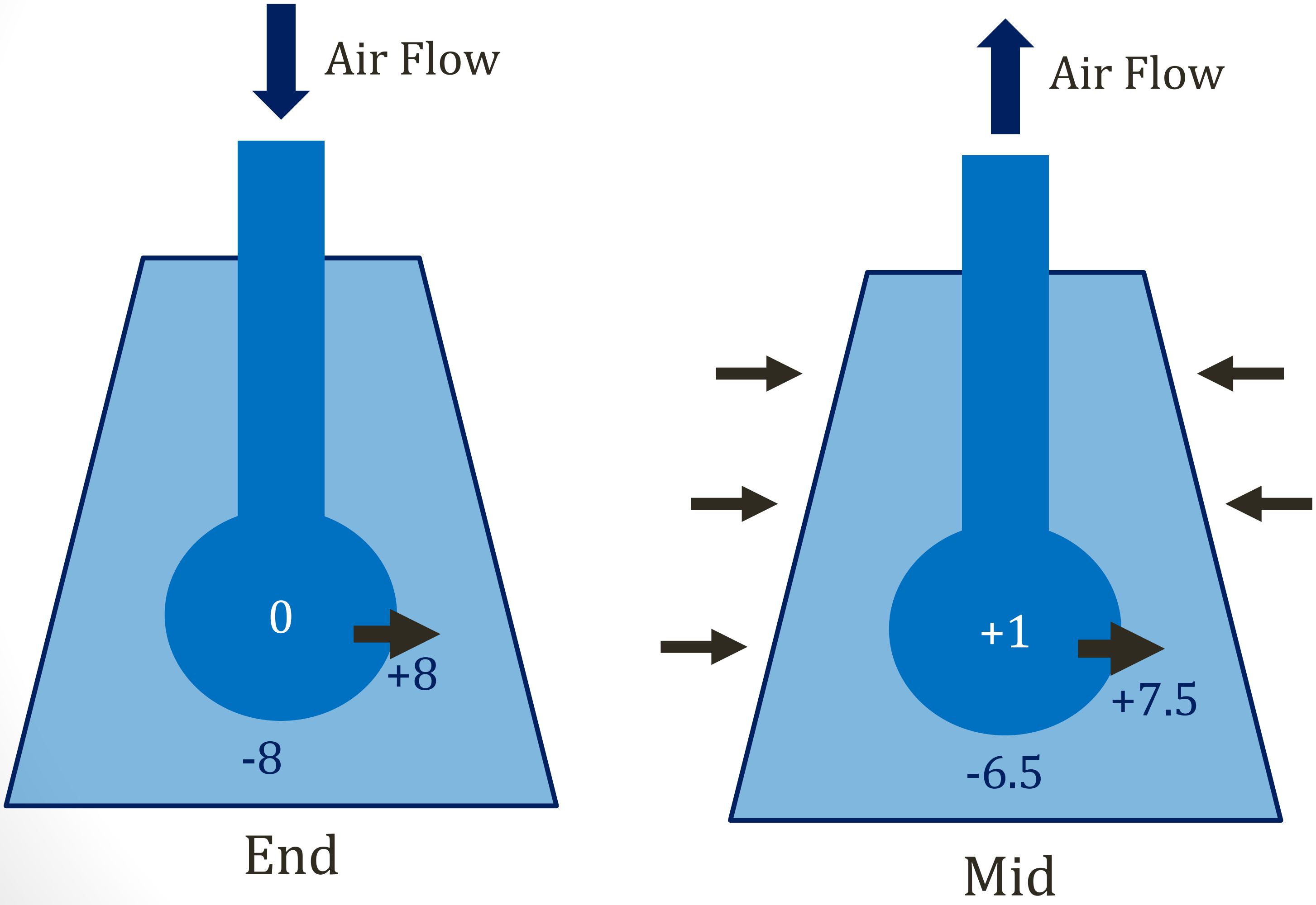
Inhalation



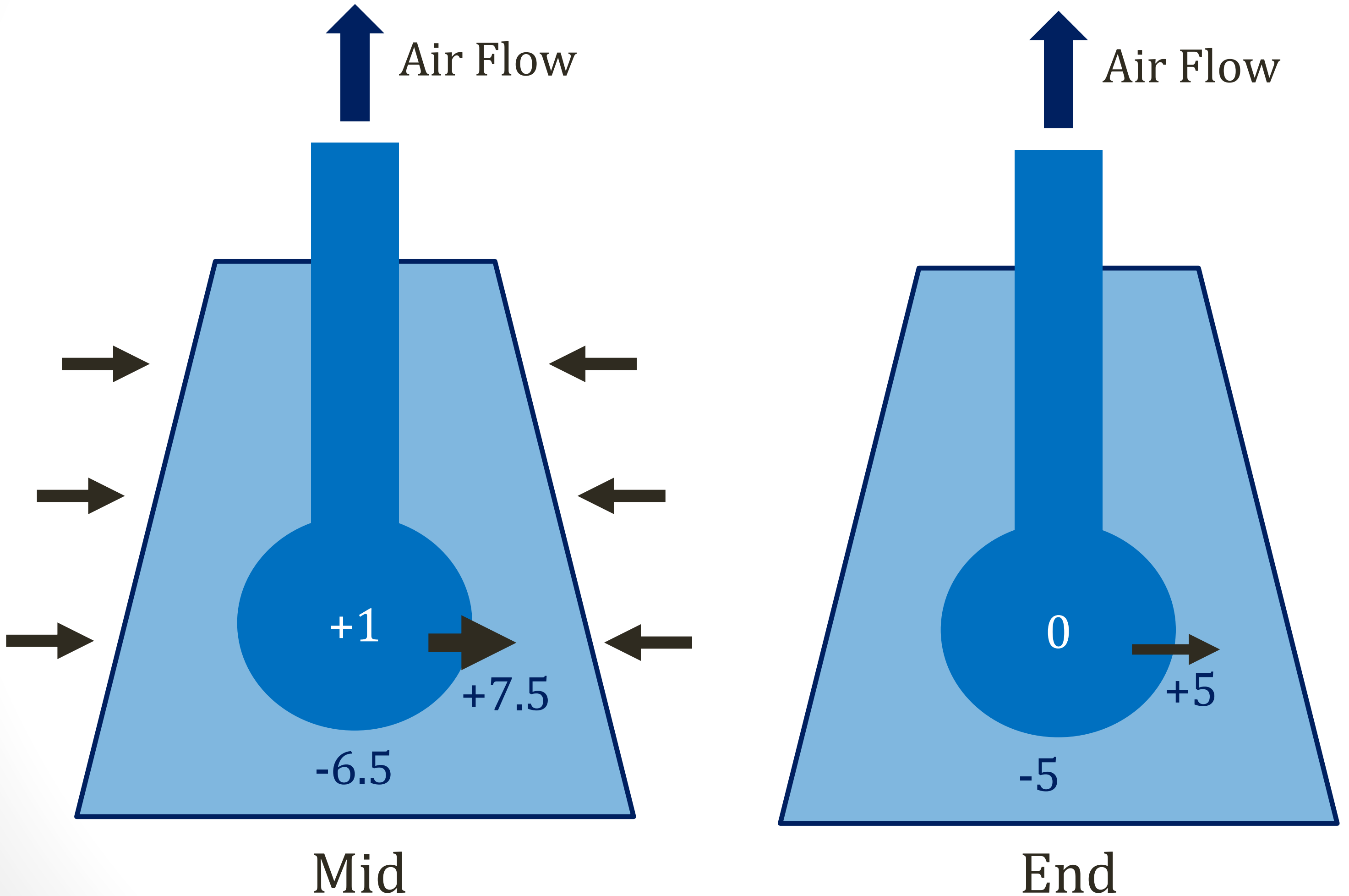
Inhalation



Exhalation

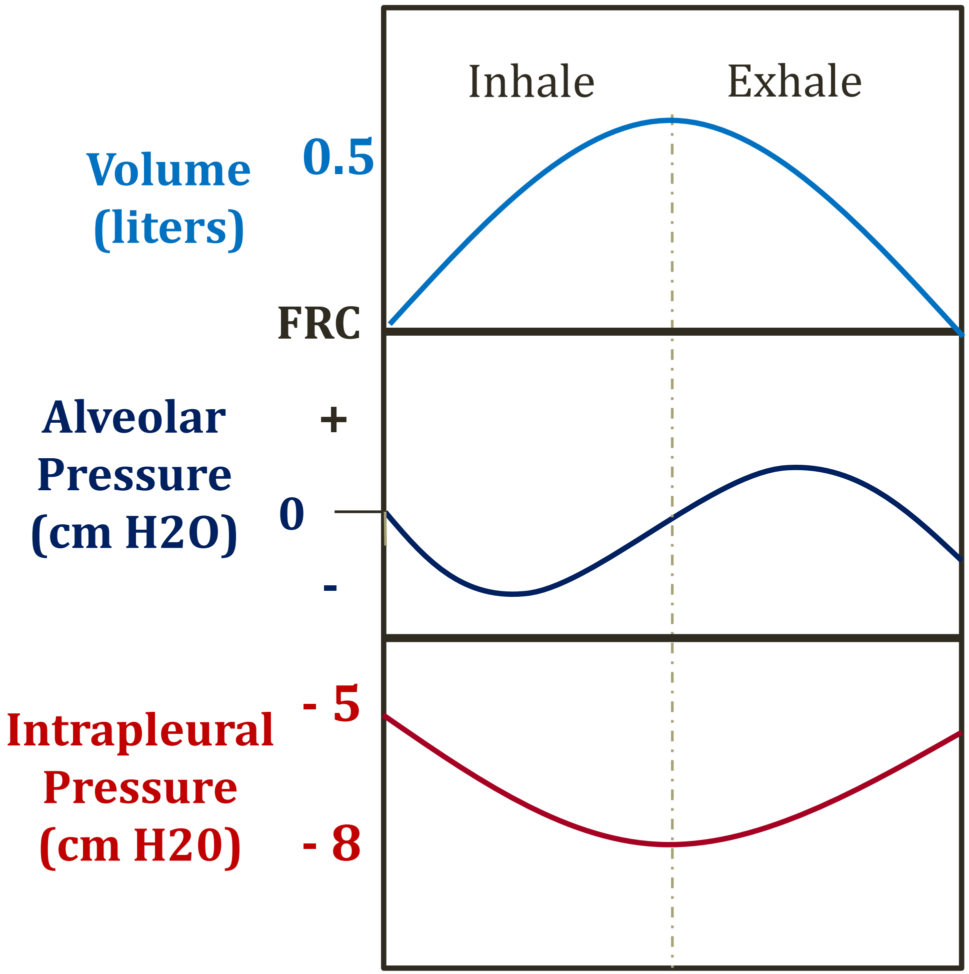


Exhalation

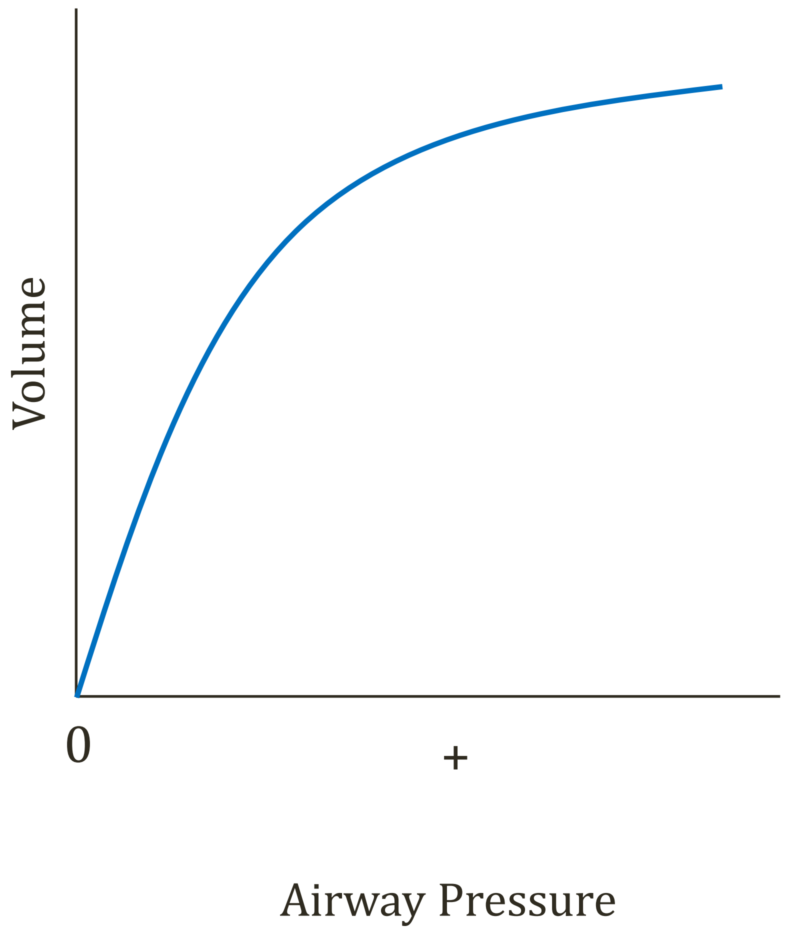


Alveoli and Pleural Pressures

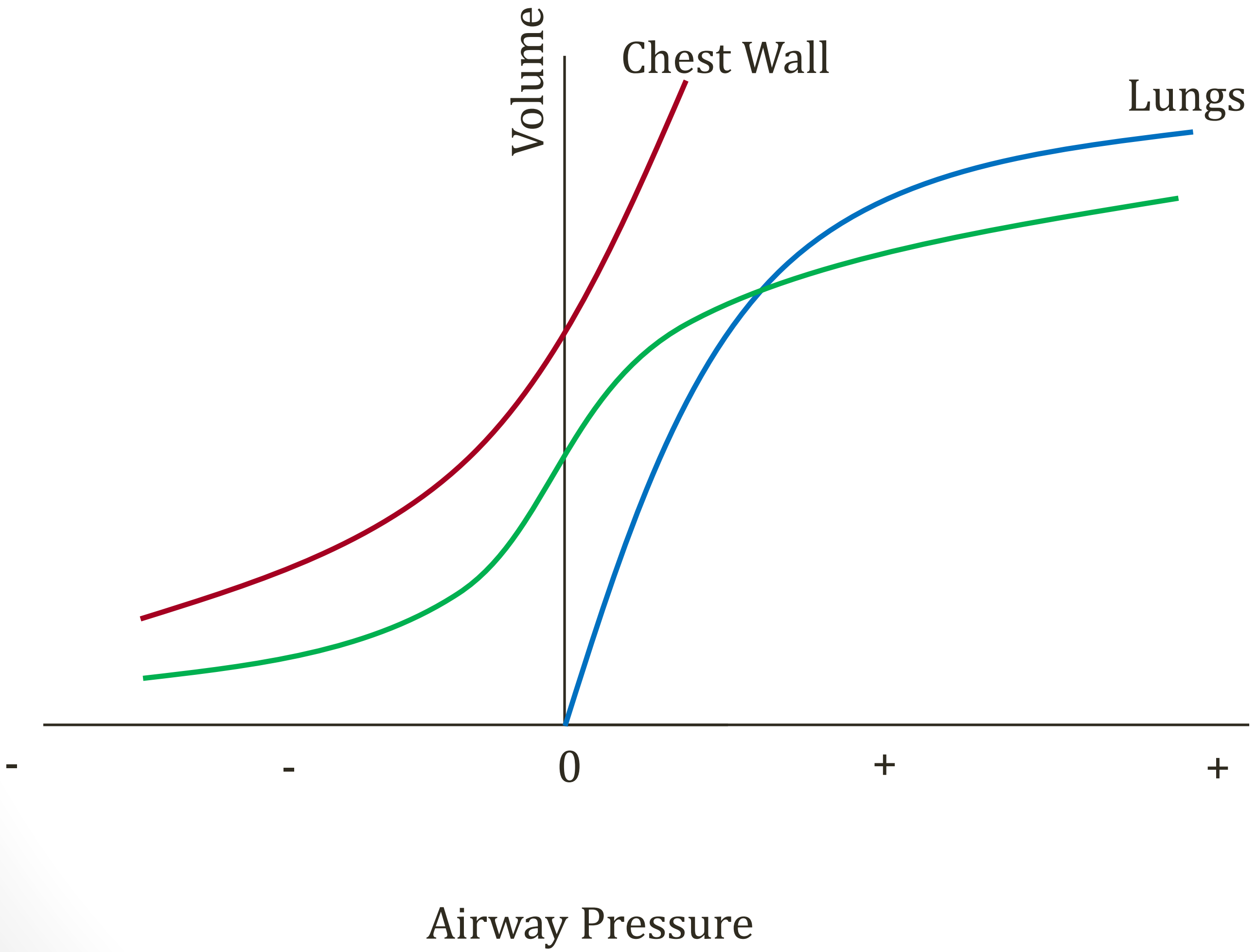
Quiet (tidal) breathing



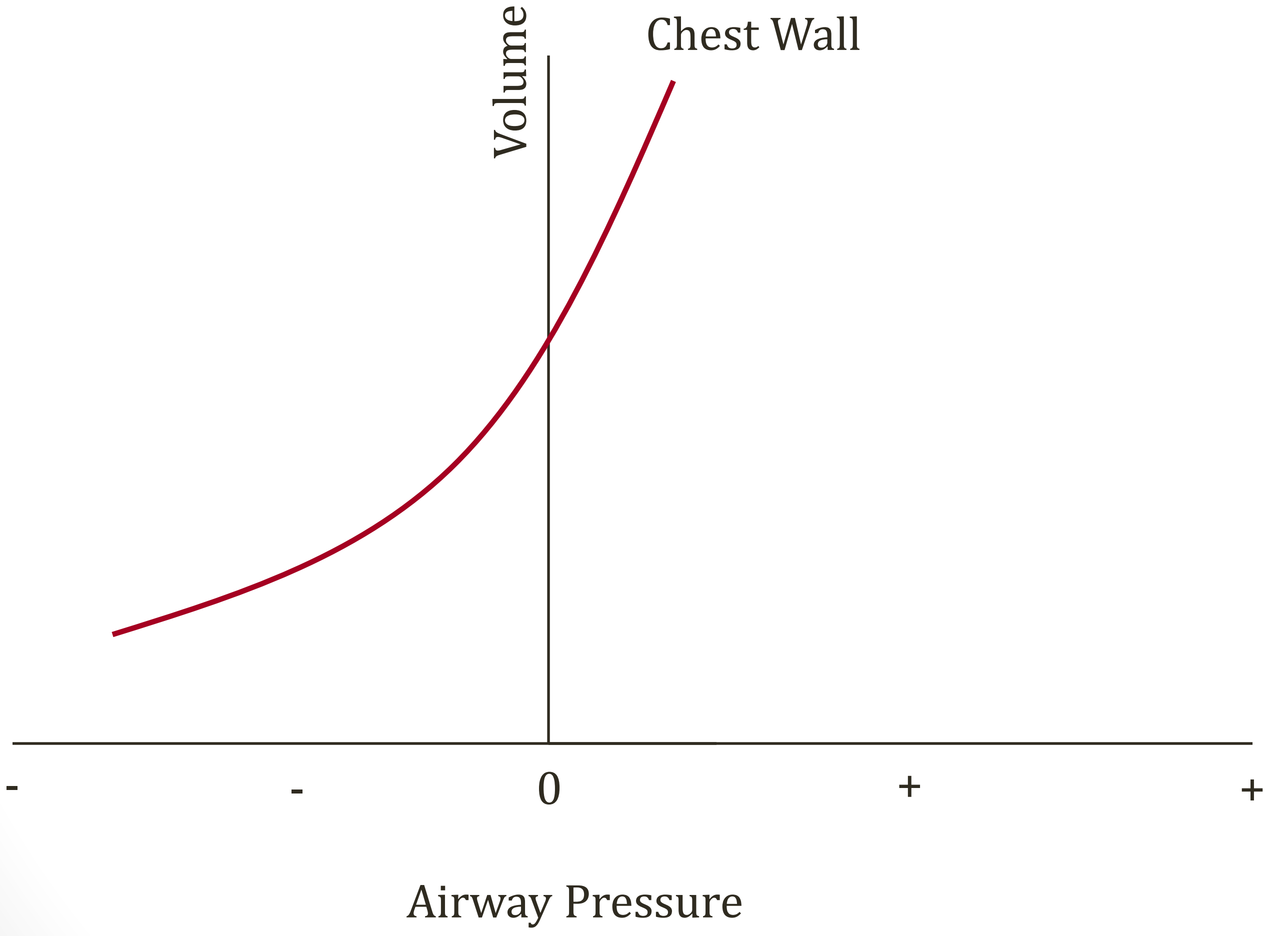
Lung Volumes and Pressures



Chest Volumes and Pressures



Chest Volumes and Pressures



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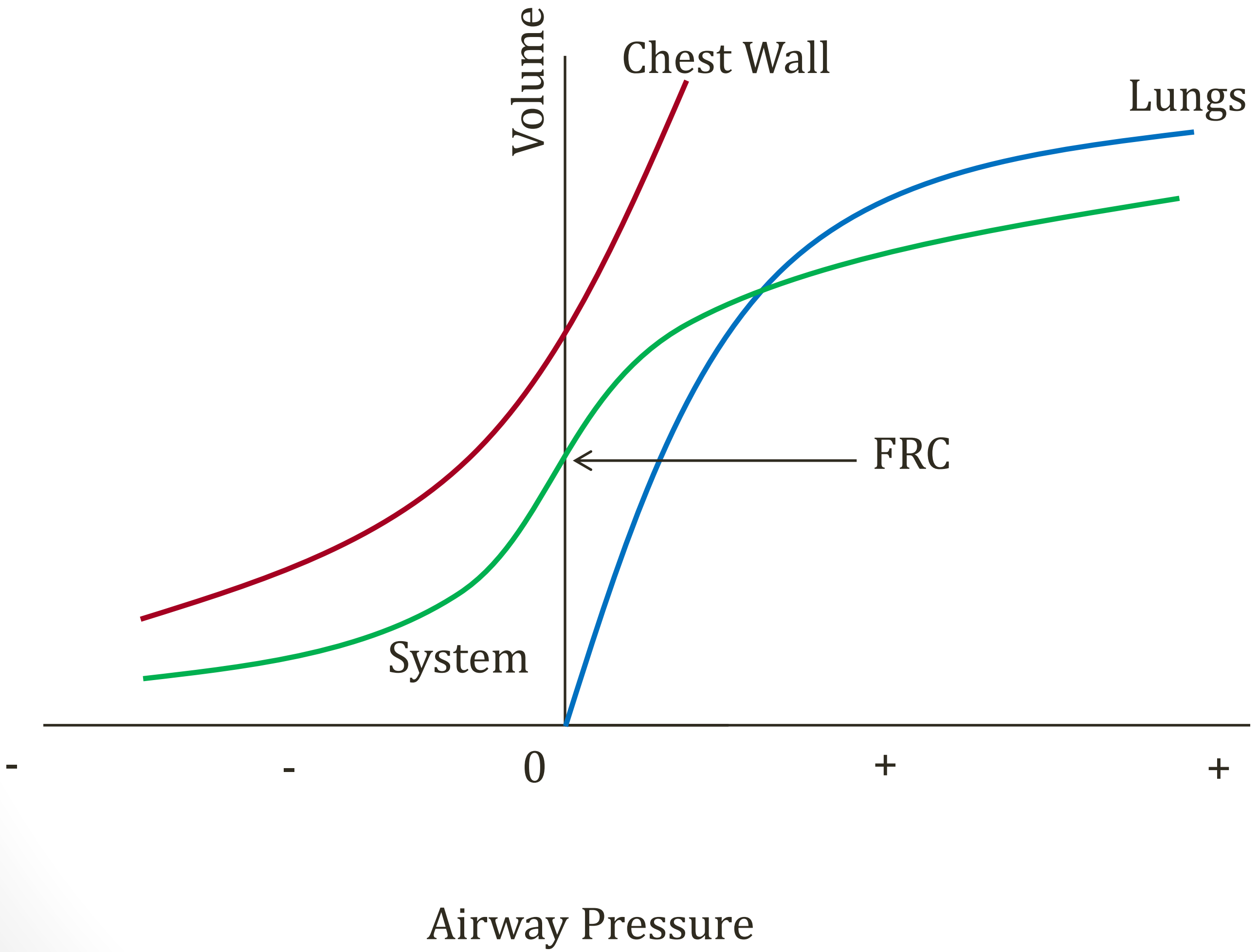
Chest Volumes and Pressures



Functional residual capacity

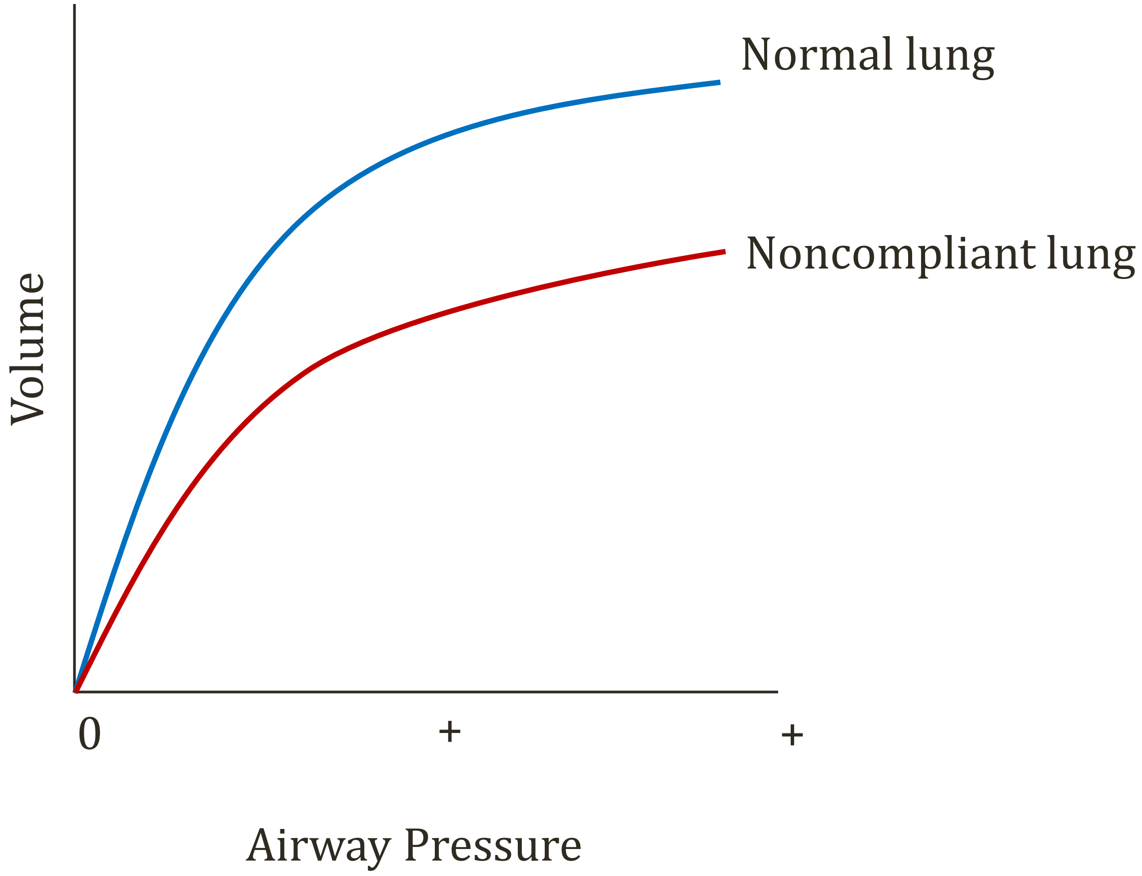
- Lung in = chest out
- Volume where lungs rest after quiet exhalation
- Pressure inside system is zero
  - No ↑/↓ pressure from push/pull of lungs or chest wall
  - Pressure = atmospheric pressure

Lung Compliance

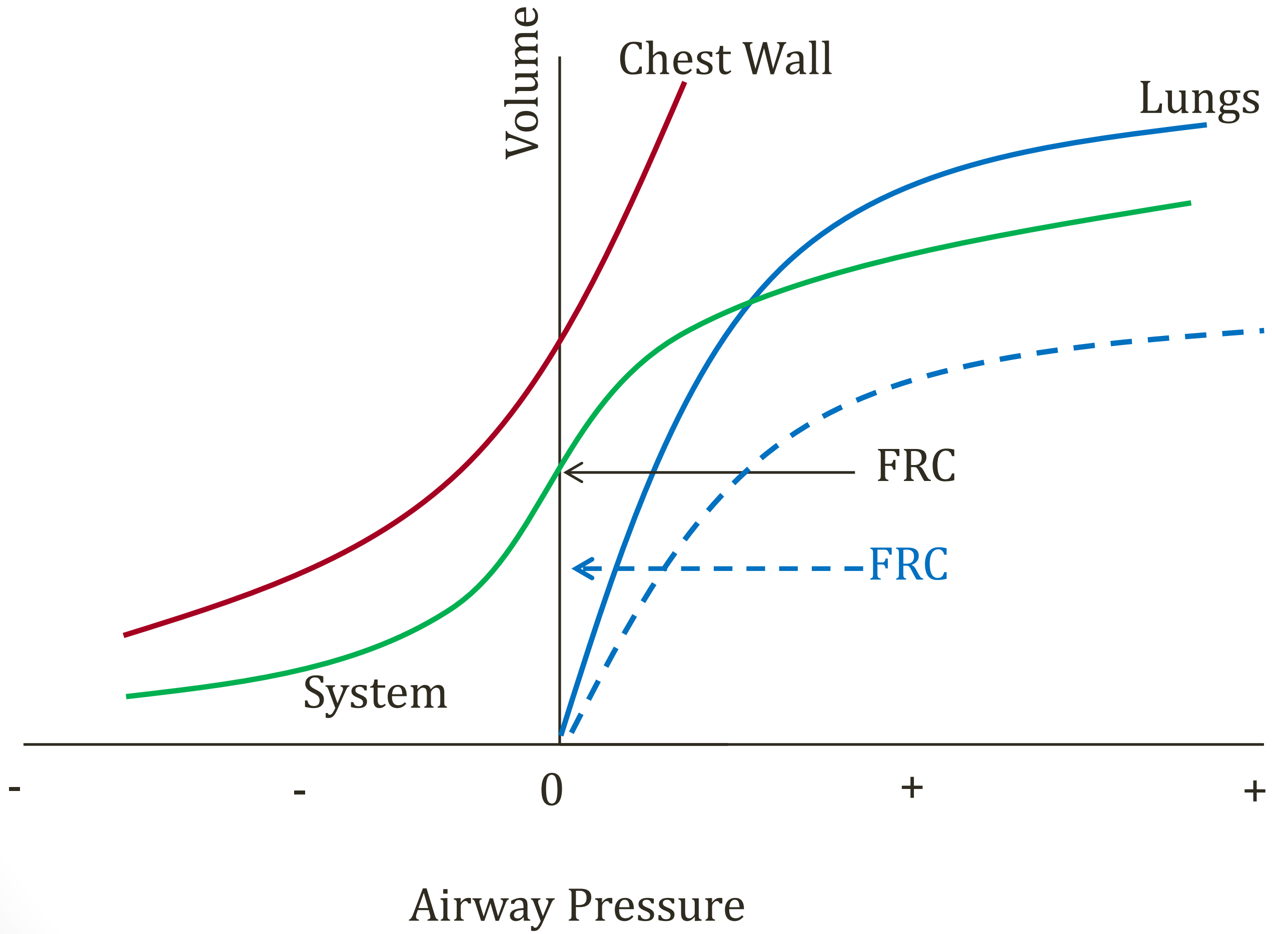
- For given pressure how much volume changes
- Compliant lung
  - Small amount of diaphragm effort
  - Generates small pressure change across lungs
  - Large volume change
  - Easy to move air in/out
- Non-compliant lung
  - Large amount diaphragm effort
  - Big pressure change across lung
  - Small volume change (lungs stiff)
  - Hard to move air in/out

$$C = \frac{\Delta V}{\Delta P}$$

Lung Compliance

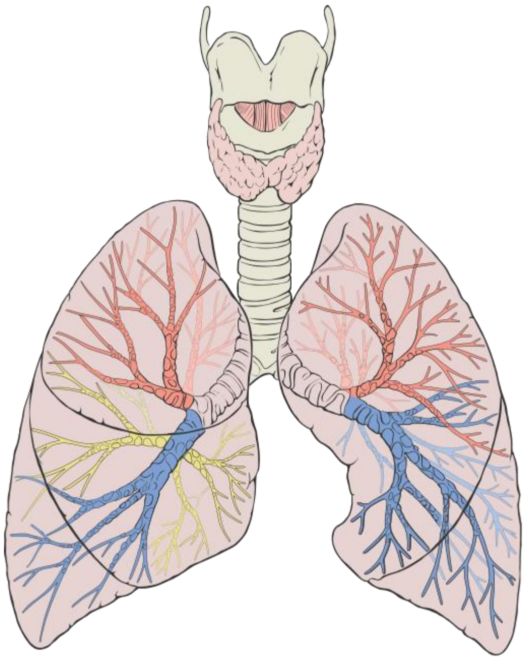


Chest Volumes and Pressures



Lung Compliance

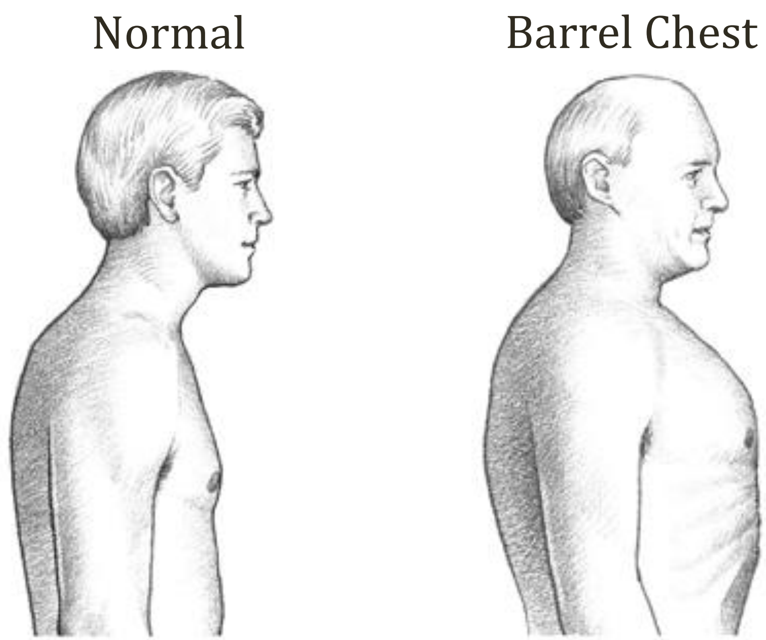
- **Decreased (↓ FRC)**
  - Pneumonia
  - Pulmonary edema
  - Pulmonary fibrosis
- **Increased (↑ FRC)**
  - Emphysema (floppy lungs)
  - Aging
  - Surfactant



Patrick Lynch/Wikipedia

Barrel Chest

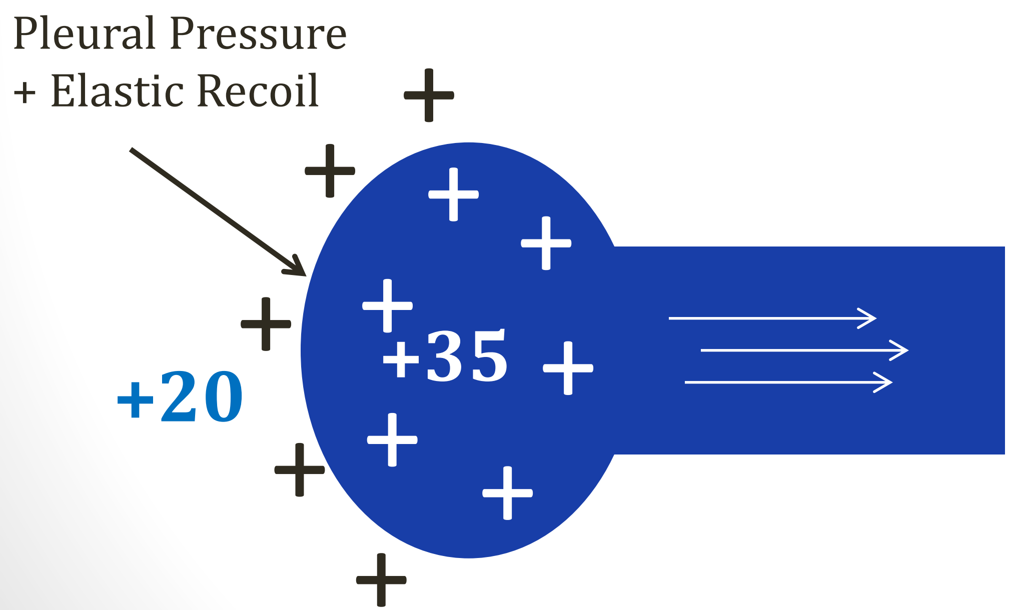
- Seen in patients with **emphysema**
- Increased lung compliance
- Increased FRC → larger volumes in chest



Quora/Public Domain

Forced Exhalation

- Pleural pressure becomes **positive**
- Compresses airway
- Pressure on alveoli → positive pressure in airway
- Pushes air out → air flows from airways



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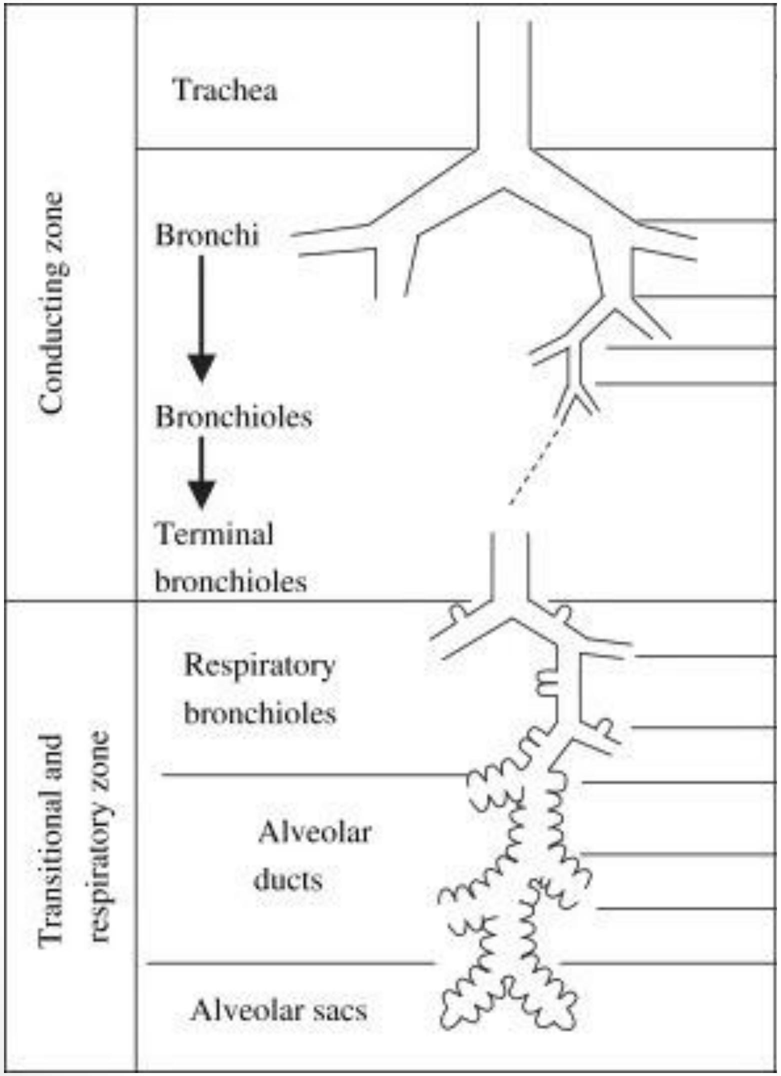
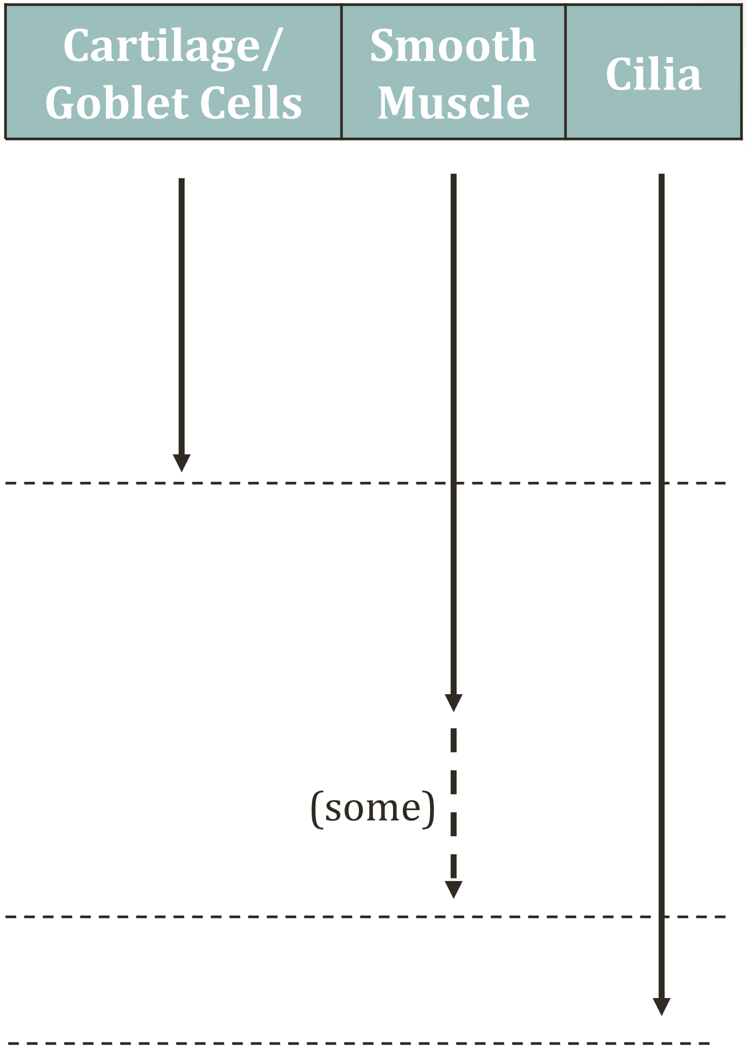
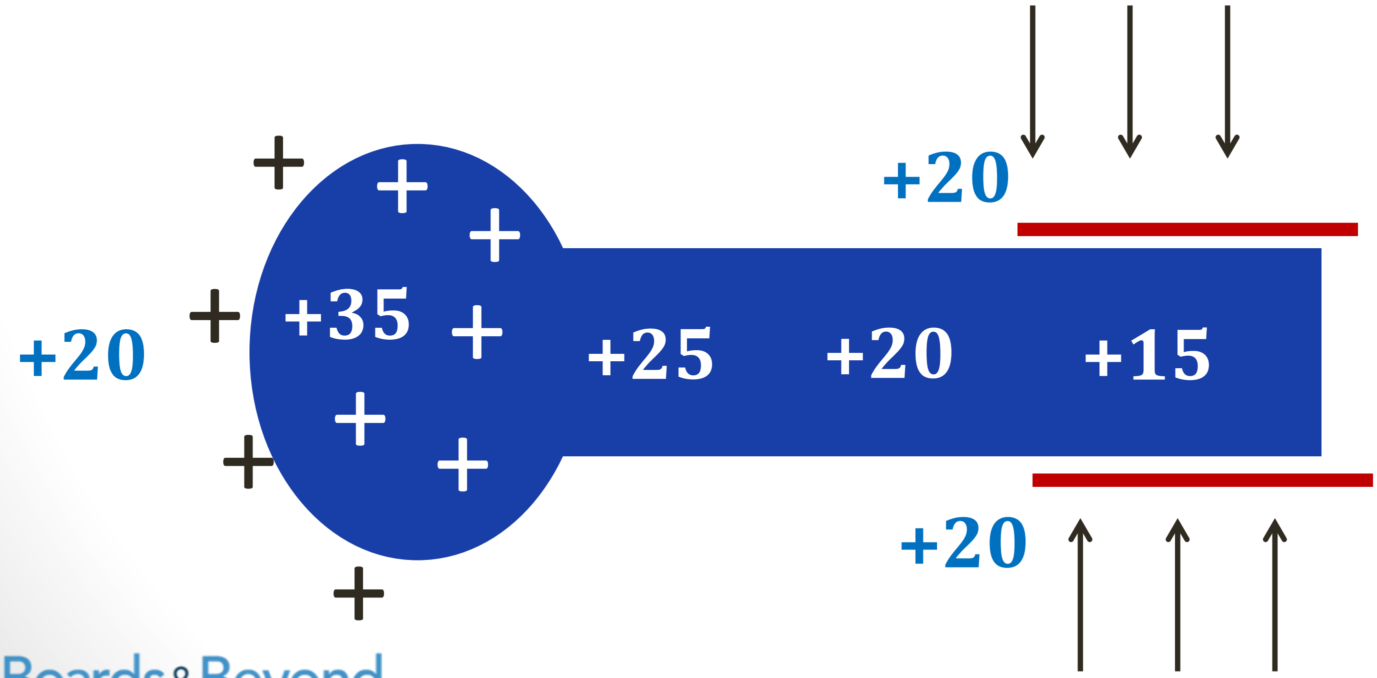
Zones


Conducting zone
Trachea
Bronchi
Bronchioles
Terminal bronchioles
Transitional and respiratory zone
Respiratory bronchioles
Alveolar ducts
Alveolar sacs


Cartilage/ Goblet Cells
Smooth Muscle
Cilia
(some)

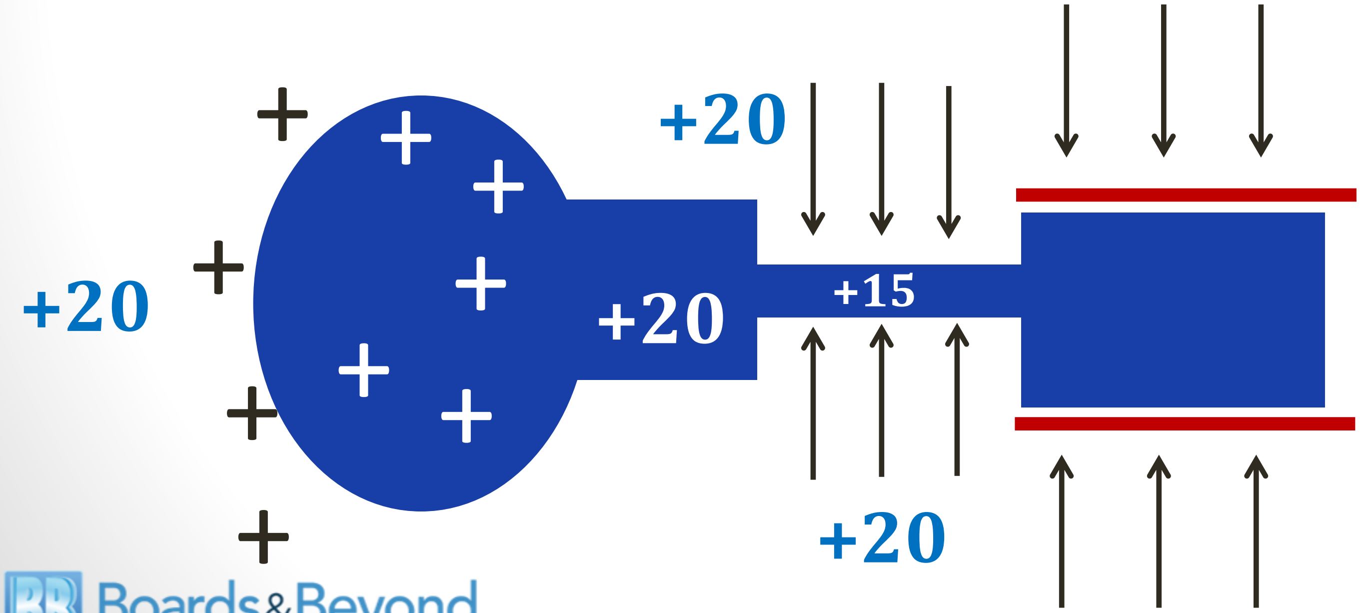
Equal Pressure Point

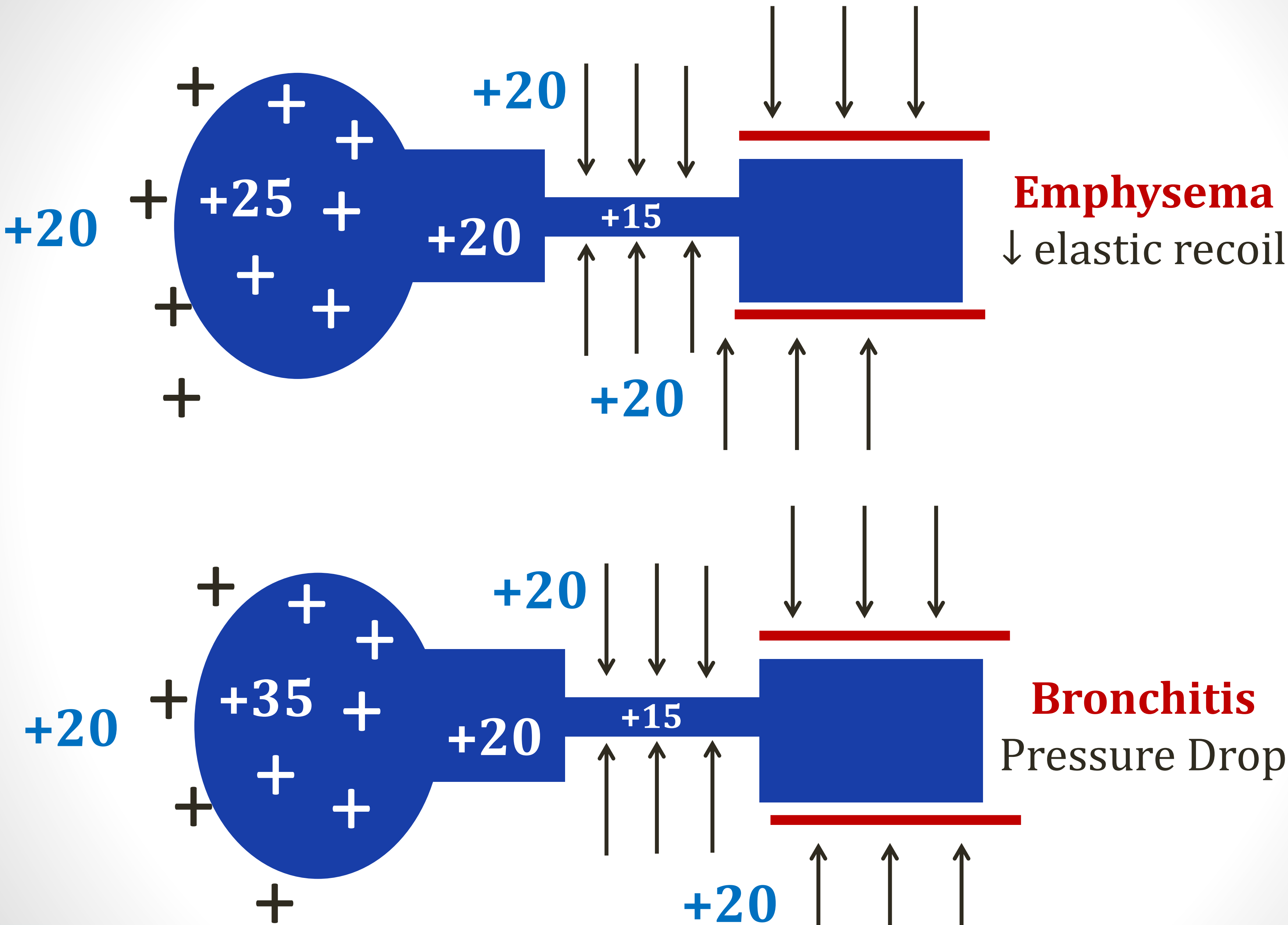
- Pleural pressure = airway pressure
- Beyond this point airway collapses
- In healthy lungs: EPP occurs in **cartilaginous** airways
- Prevents airway collapse



Equal Pressure Point

- In disease: EPP **moves toward alveoli**
  - Obstruction (bronchitis): more pressure drop
  - Emphysema: loss of elastic recoil
- Can be reached in thin-walled bronchioles
- Result: Collapse, obstruction to airflow, air trapping





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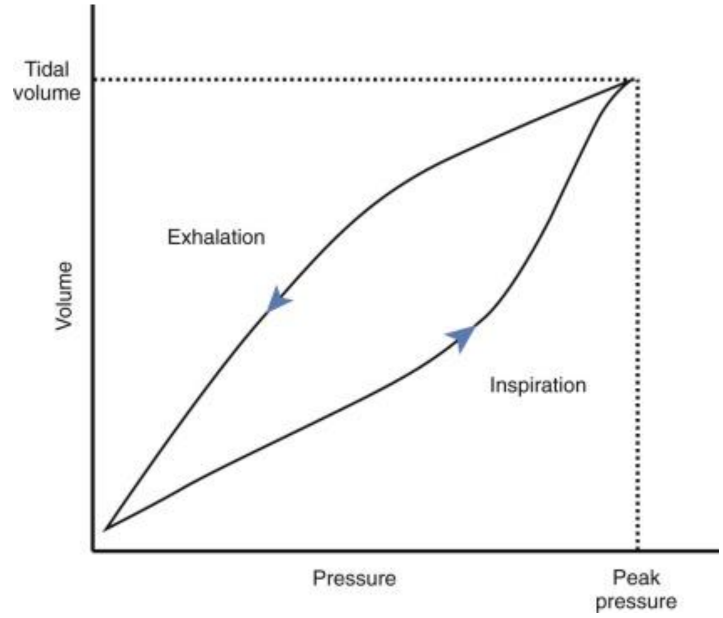
COPD

Chronic Obstructive Pulmonary Disease

- **Slow exhalation**
  - Prevents large rise in pleural pressure
  - Forceful exhalation would ↑↑ intrapleural pressure
- **Pursed lips**
  - Increases airway (alveolar) pressure
  - Prevents collapse

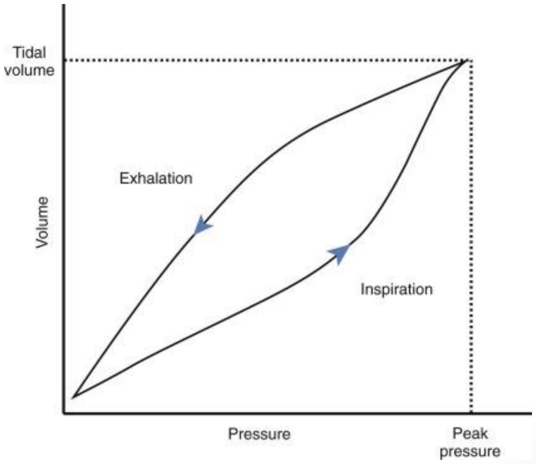
Hysteresis

- Hysteresis = dependence of property on its history
- Different PV curves for inhalation and exhalation
- Slope PV curve = compliance
- Different compliance despite same lung structures



Hysteresis

- PV hysteresis caused by **surface tension**
- Inspiration begins with smallest volume
  - Molecules close together
  - **Strongest surface tension**
- Expiration begins at high lung volumes
  - Intermolecular forces low

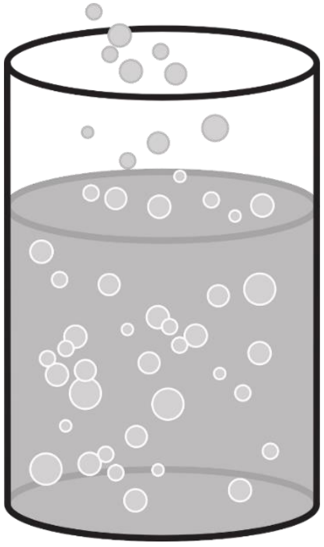


Hemoglobin

Jason Ryan, MD, MPH

Oxygen Transport

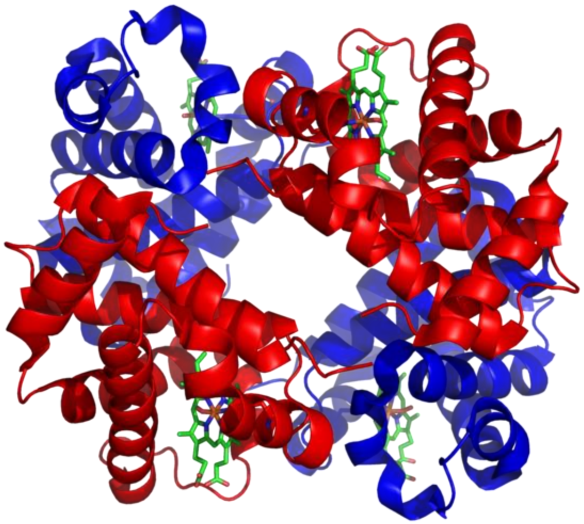
- **Dissolved O_2**
  - Determined by Henry's law
  - Pa_{O2} x solubility = dissolved O_2
  - Very small amount (2%) total blood O_2
- **Bound to hemoglobin (98%)**



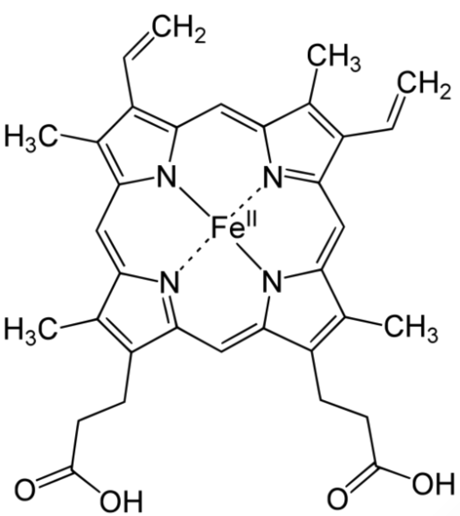
Public Domain

Hemoglobin

- Globin chains
  - Proteins
  - Alpha (α)
  - Beta (β)
  - Gamma (γ)
  - Delta (δ)
  - 4 chains in 2 pairs
- Heme
  - Molecule (non-peptide)
  - Contains iron (Fe)
  - Porphyrin ring
  - Oxygen binds iron



Richard Wheeler and Zephyris

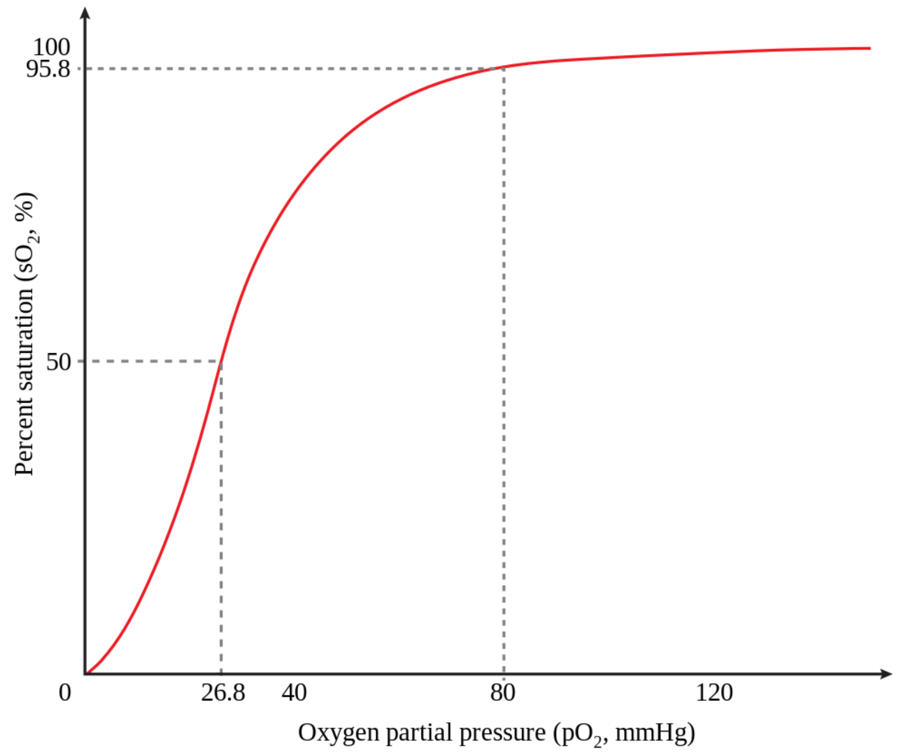


Hemoglobin Types

- **Hemoglobin A**
  - Adult type
  - Most common type found (95%)
  - $\alpha 2\ \beta 2$
- **Hemoglobin A2**
  - Adult type
  - Less common type (2-3%)
  - $\alpha 2\ \delta 2$
- **Hemoglobin F**
  - Fetal type
  - $\alpha 2\ \gamma 2$

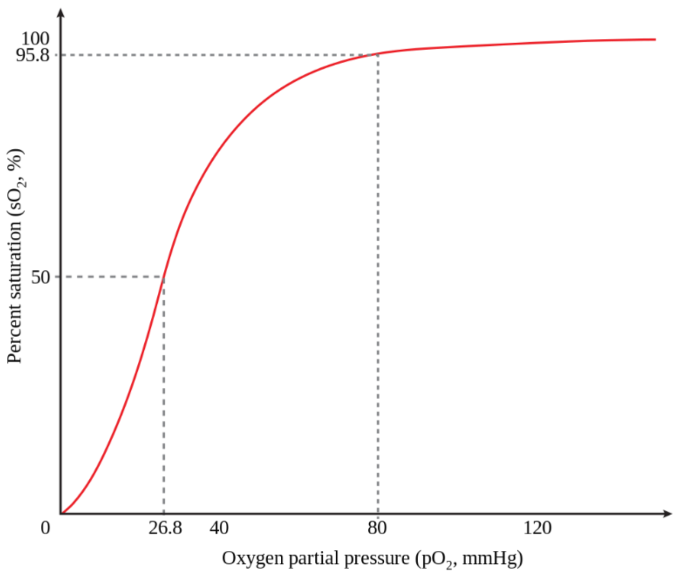
O2-Hgb Dissociation Curves

- Y axis: percentage of hemoglobin bound to oxygen
- X-axis: partial pressure of oxygen (Pa_{O2})



Oxygen-Hgb Binding

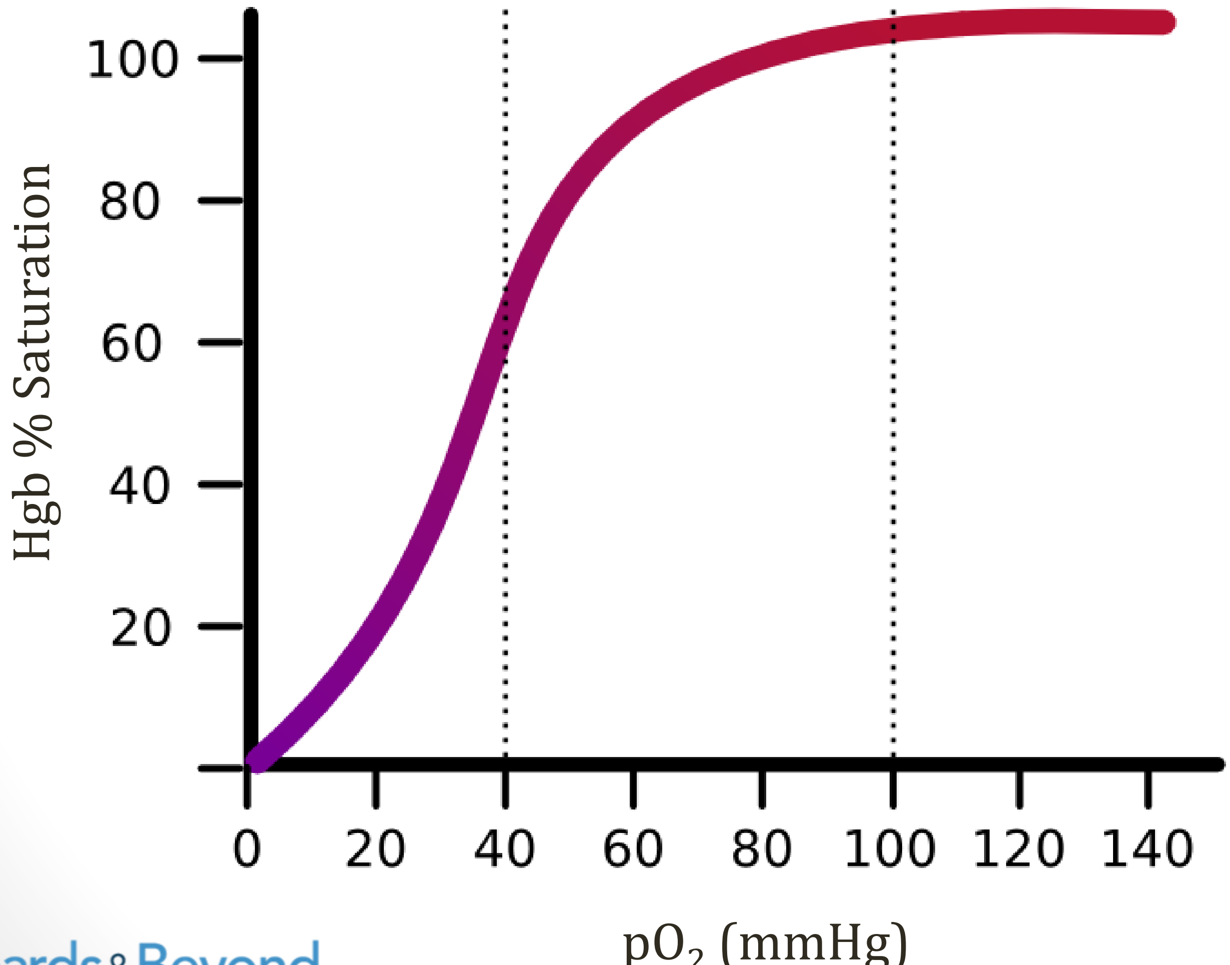
- Four heme groups do not simultaneous oxygenate
- First O_2 molecule INCREASES affinity for 2nd molecule
  - Second O_2 molecule INCREASES affinity for 3rd molecule
  - Third O_2 molecule INCREASES affinity for 4th molecule
  - Affinity last O_2 = _300 times_ affinity for first O_2
- **Positive cooperativity**
- Makes curve S shaped



Allosteric Proteins

- Allosteric = “other site”
- Binding at one site influenced by other sites
- Usually multi-subunit proteins
- Hemoglobin is an allosteric structure
- O_2 cooperativity is a **positive** allosteric effect

O2-Hgb Dissociation Curves

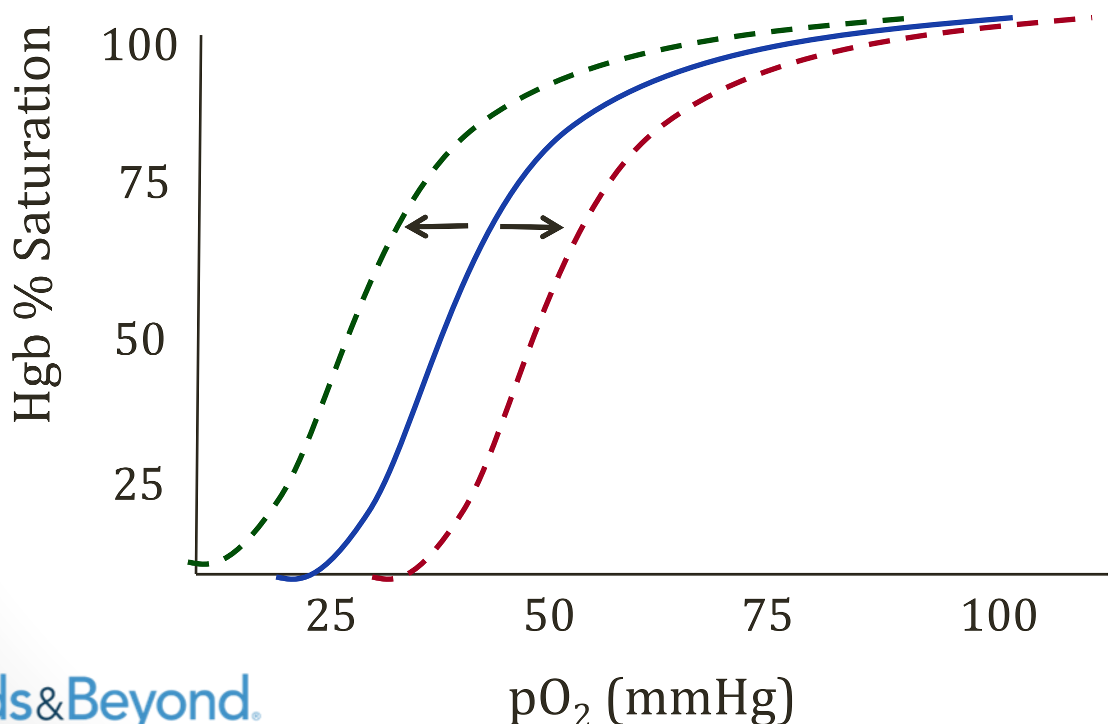


Hemoglobin Forms

- Globin chains can assume two formations
- **Taut form (T)**
  - Tends to release O_2
  - Favored form in tissues
  - Allows more release of O_2
- **Relaxed form (R)**
  - Holds on to O_2
  - Favored form in lungs
  - Allows more binding of O_2

Shifts in O_2-Hgb Curves

- Affinity of Hgb for O_2 can change – not fixed
- Hgb modified by environment within RBCs
- Dissociation curve shifts may occur to right or left



Rightward Shift

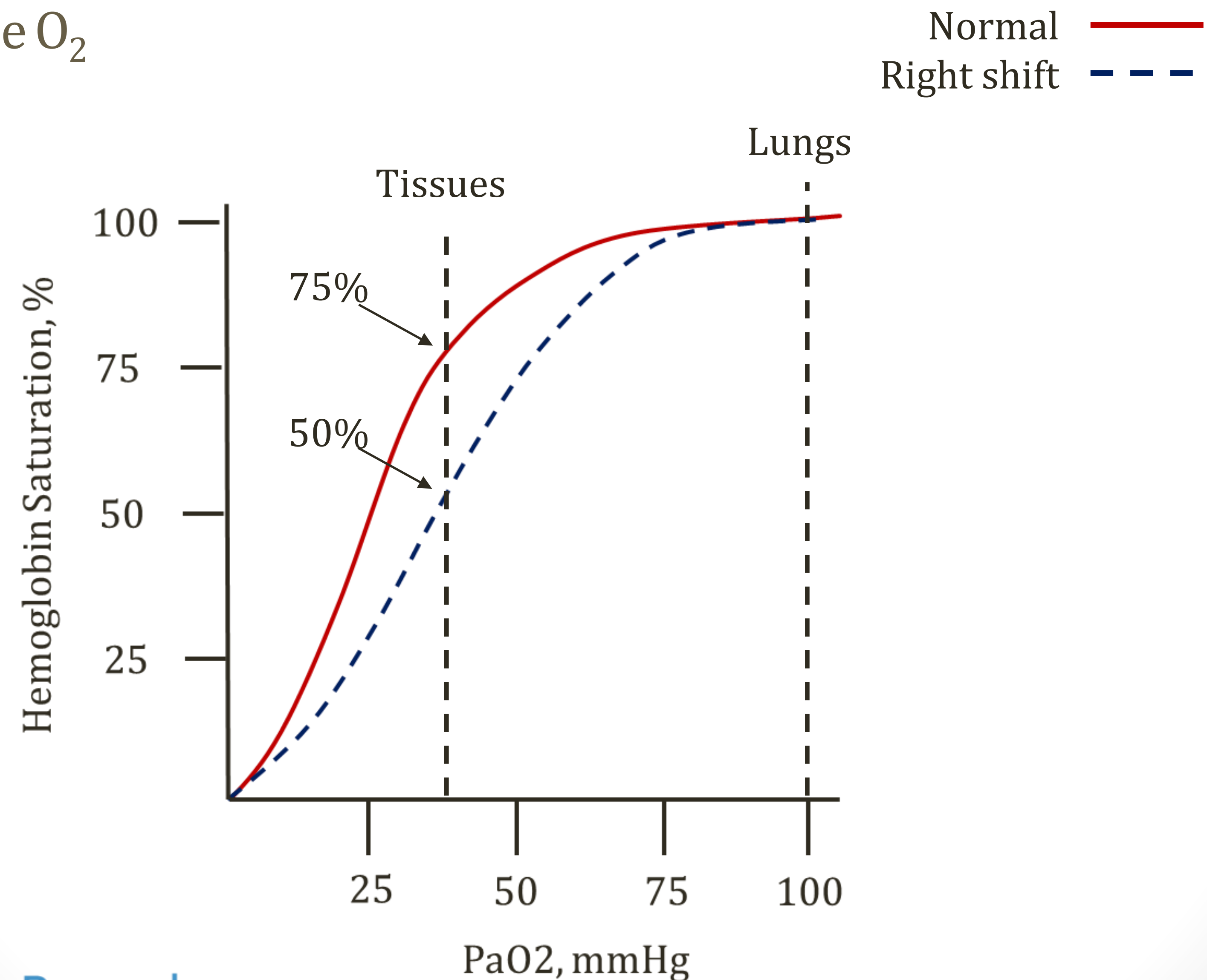
	Lungs PaO2	Lungs %Sat	Tissues PaO2	Tissues %Sat
Normal	100	100	40	**75%**
Right Shift	100	100	40	**50%**

Normal: 100% → 75% **Δ 25%**

Right shift: 100% → 50% **Δ 50%**

Right Curve Shifts

Release O_2

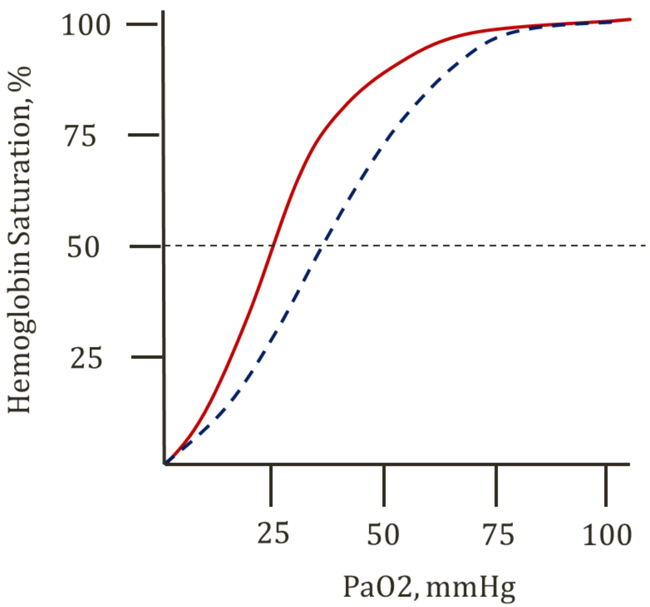


Right Curve Shifts

Release O_2

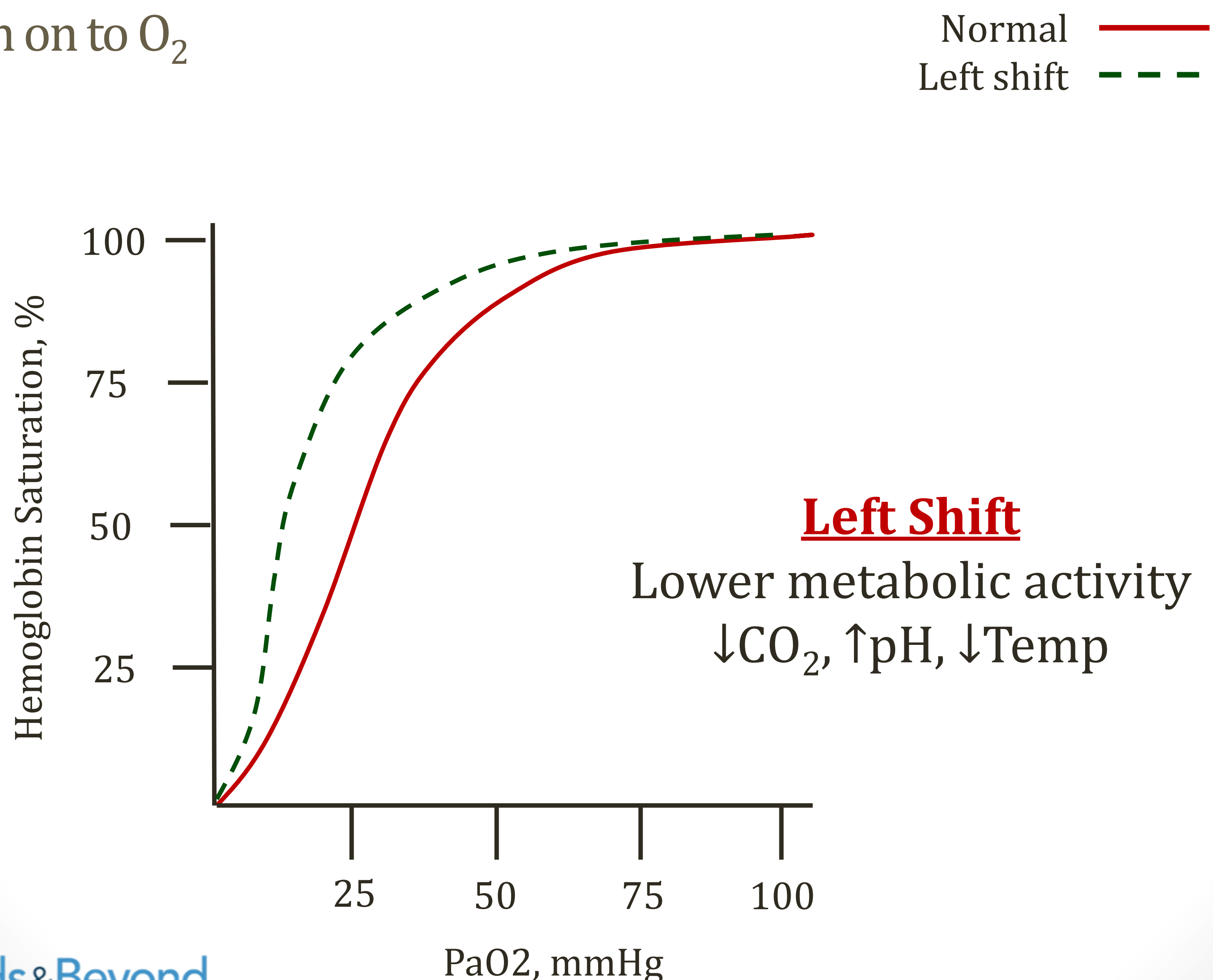
- Favors **taut form**
- Causes of **r**ight shifts
  - **R**ising Metabolic Activity
  - ↑CO_2
  - ↓pH
  - ↑Temp
- Increases P50

Release O_2
i
g
h
Taut



Left Curve Shifts

Latch on to O_2



Left Shift

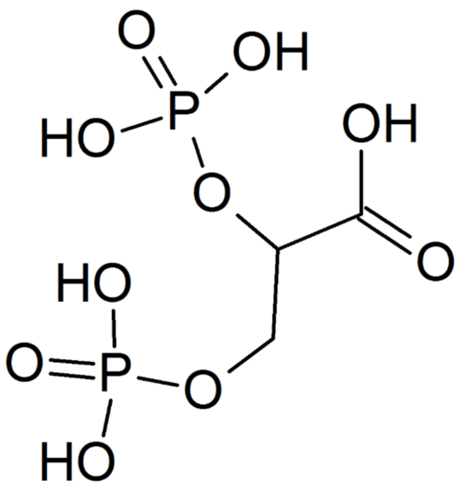
Lower metabolic activity

↓CO_2, ↑pH, ↓Temp

2,3-Bisphosphoglycerate

2,3 BPG

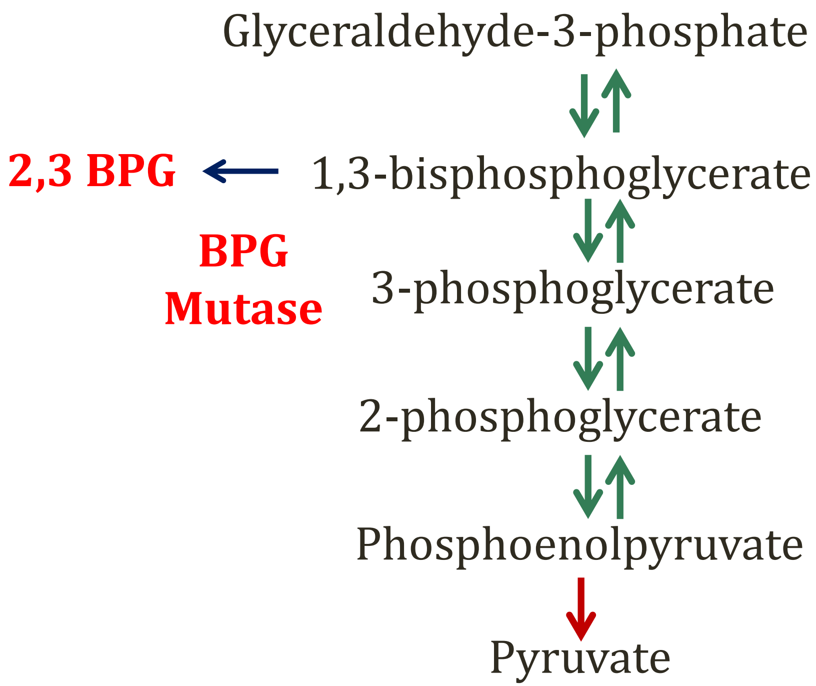
- Found in RBCs
- Promotes O_2 release from hemoglobin
- *Negative* allosteric effector
- Increasing levels:
  - Decrease oxygen affinity of hemoglobin
  - Increase delivery oxygen to tissues



2,3-Bisphosphoglycerate

2,3 Bisphosphoglycerate

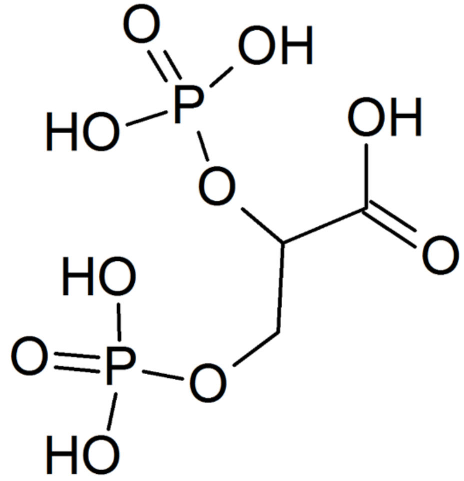
- Created from diverted 1,3 BPG (glycolysis)
- **Sacrifices ATP** from glycolysis



2,3-Bisphosphoglycerate

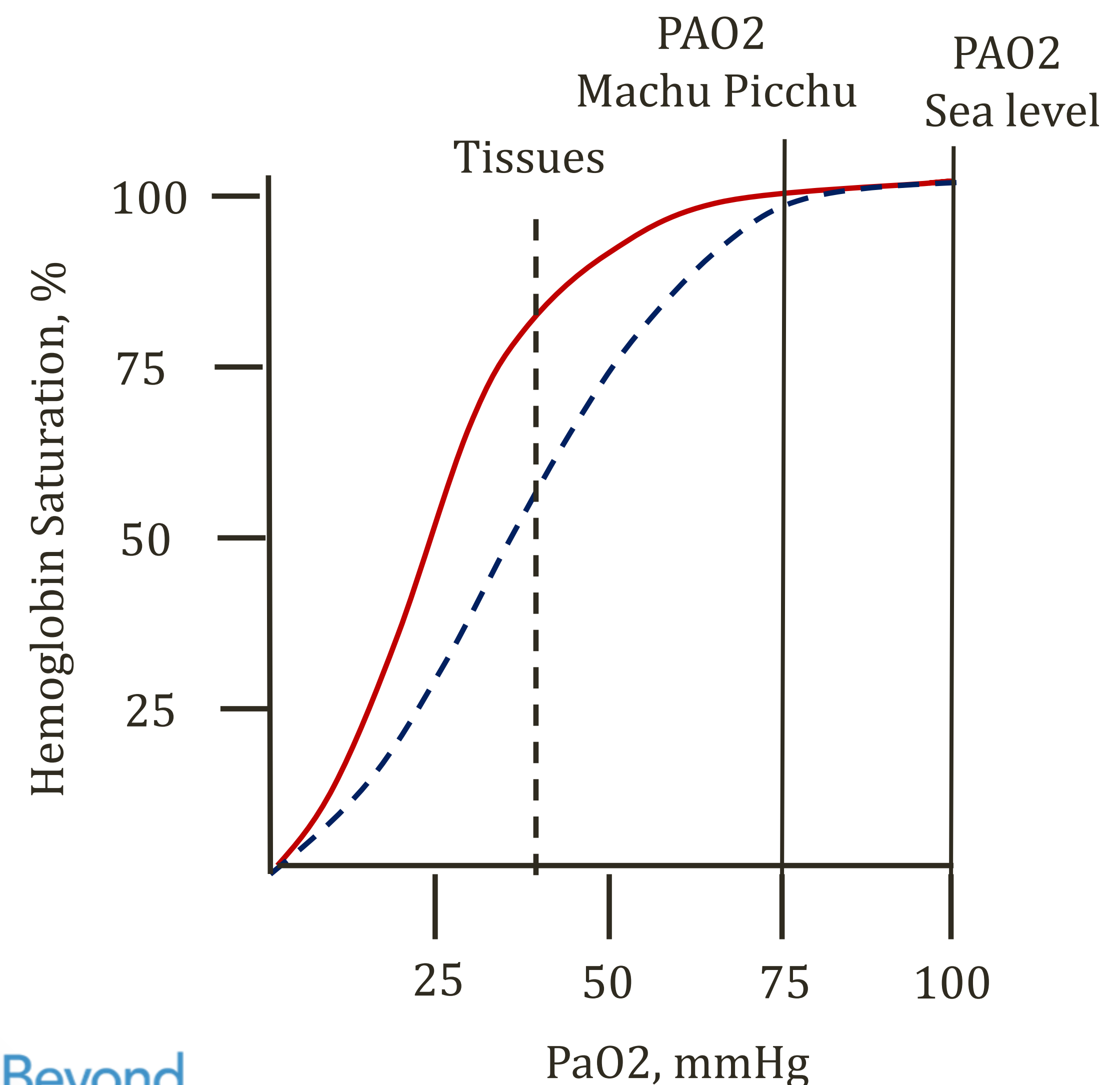
2,3 BPG

- ↑ BPG with **chronic hypoxia**
  - COPD
  - High altitude
  - Chronic anemia



2,3-Bisphosphoglycerate

High Altitude



Fetal Hemoglobin

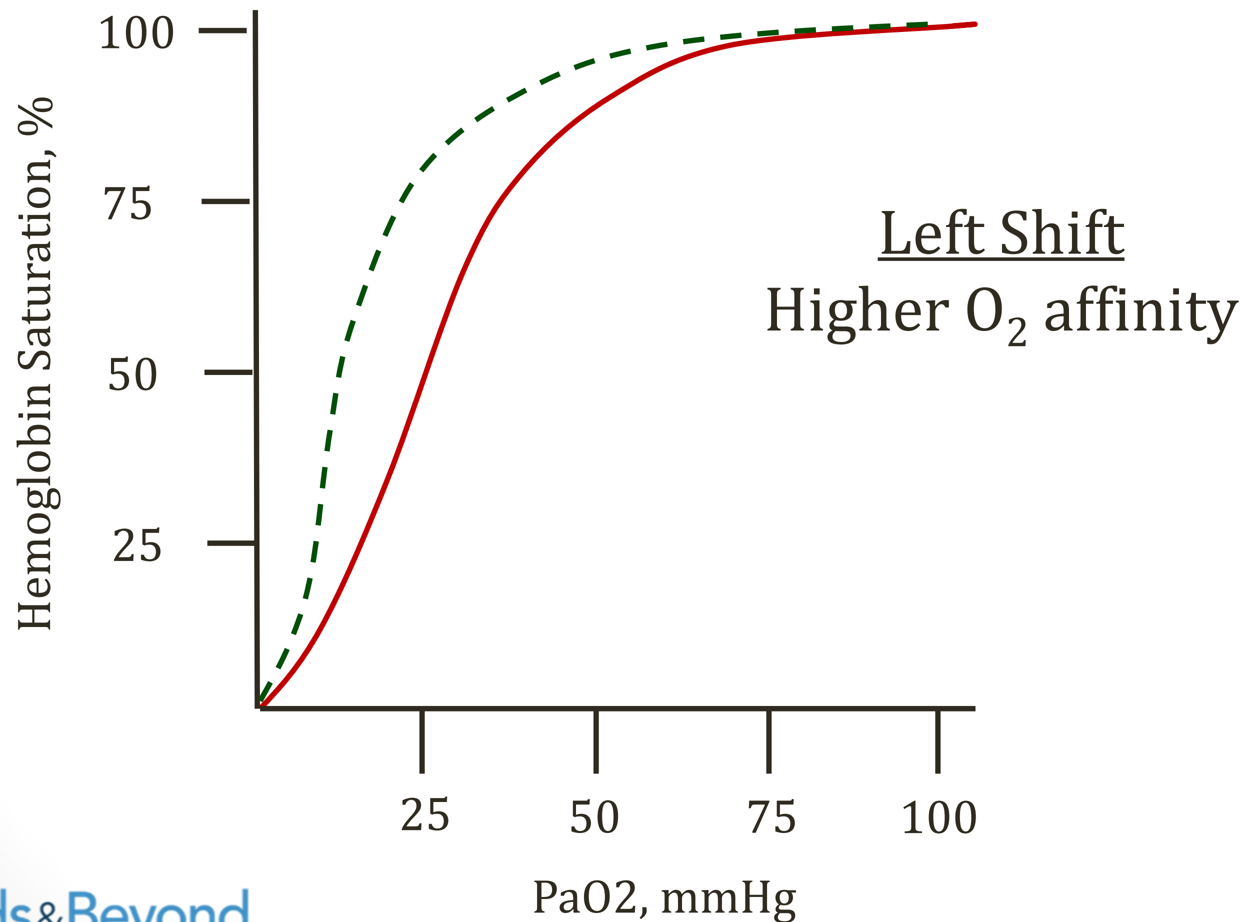
HgbF (α2γ2)

- After 8 weeks HgbF is predominant Hgb
  - Up to 90% fetal hemoglobin
  - Levels fall in weeks/months after birth
  - In adult HgbF <1% total hemoglobin
- Higher O_2 affinity than HgbA
  - Necessary because fetal pO2 = 40mmHg

Wikipedia/Public Domain

Fetal Hemoglobin

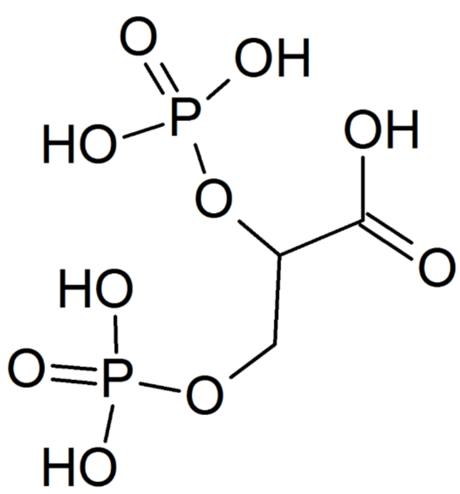
HgbF (α2γ2)



Fetal Hemoglobin

HgbF (α2γ2)

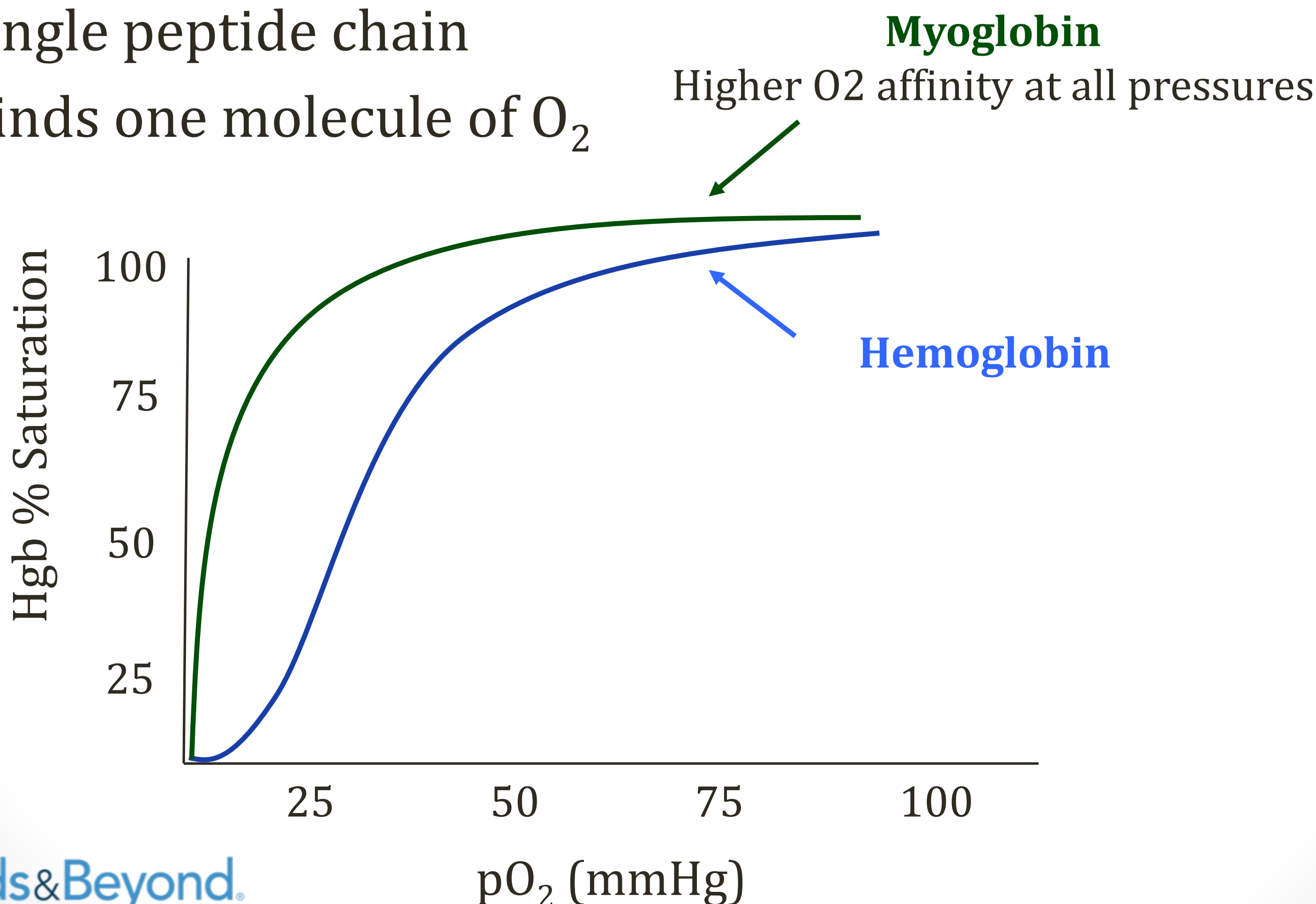
- Left shift caused by altered **2,3 BPG binding**
  - 2,3-BPG binds γ chains poorly (binds β chains avidly)
  - Less 2,3-BPG binding → O_2 affinity increases (left shift)



2,3-Bisphosphoglycerate

Myoglobin

- Found in skeletal muscle and heart
- Single peptide chain
- Binds one molecule of O_2

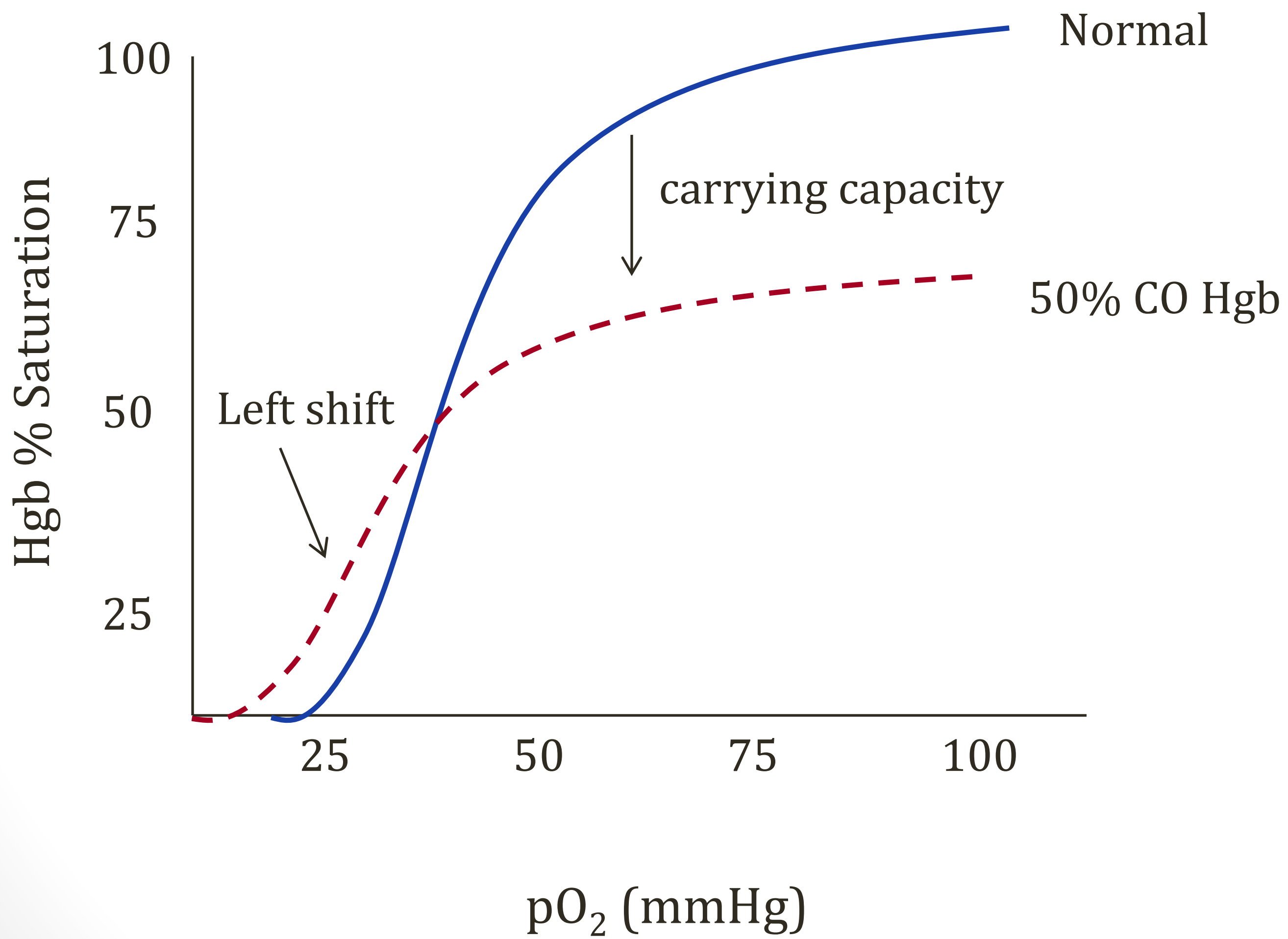


Carbon Monoxide

- Binds to iron in heme 240x the affinity of O_2
- Forms **carboxyhemoglobin** (HbCO)
- Blocks O_2 binding sites (less O_2 can be absorbed)
- "Functional anemia"
- Other binding sites cannot offload O_2
  - Allosteric modification of hemoglobin
  - Shifts dissociation curve left

$$:C\equiv O:$$

Carbon Monoxide



Carbon Monoxide Poisoning

- Nonspecific symptoms
- Headache most common
- Malaise, nausea, dizziness
- Classic (but rare) sign: **cherry red lips**
  - Carboxyhemoglobin is red
  - Do not see blue lips (cyanosis)

Carbon Monoxide Poisoning

- Standard pulse oximetry normal
  - Cannot differentiate carboxyhemoglobin/oxyhemoglobin
- Diagnosis: **carboxyhemoglobin level**
  - Normal <3%
  - Smokers 10-15%
  - >15% suggest poisoning
- Treatment: **oxygen**

Methemoglobinemia

- Most iron in hemoglobin normally reduced (Fe^{2+})
- Small amount oxidizes iron: Fe^{3+}
  - Called **methemoglobin**
  - Cannot bind O_2
- Excess methemoglobin: hypoxia

$$Fe^{3+}$$

Methemoglobinemia

- Acquired methemoglobinemia from **drugs**
  - Local anesthetics (benzocaine)
  - Nitric oxide
  - Dapsone
- Treatment: **methylene blue**
  - Reducing agent
  - $Fe^{3+} \rightarrow Fe^{2+}$

Clinical Scenario

- Endoscopy patient
- **Benzocaine** spray used for throat analgesia
- Post procedure shortness of breath
- "Chocolate brown blood"
- O_2 sat (pulse oximetry) = variable (80s-90s)
- Oxygen does not improve shortness of breath
- P_{aO2} (blood gas) = normal
- Diagnosis: ↑ methemoglobin level
- Other example:
  - Premature babies given **NO** for pulmonary vasodilation

Pulmonary Circulation

Jason Ryan, MD, MPH

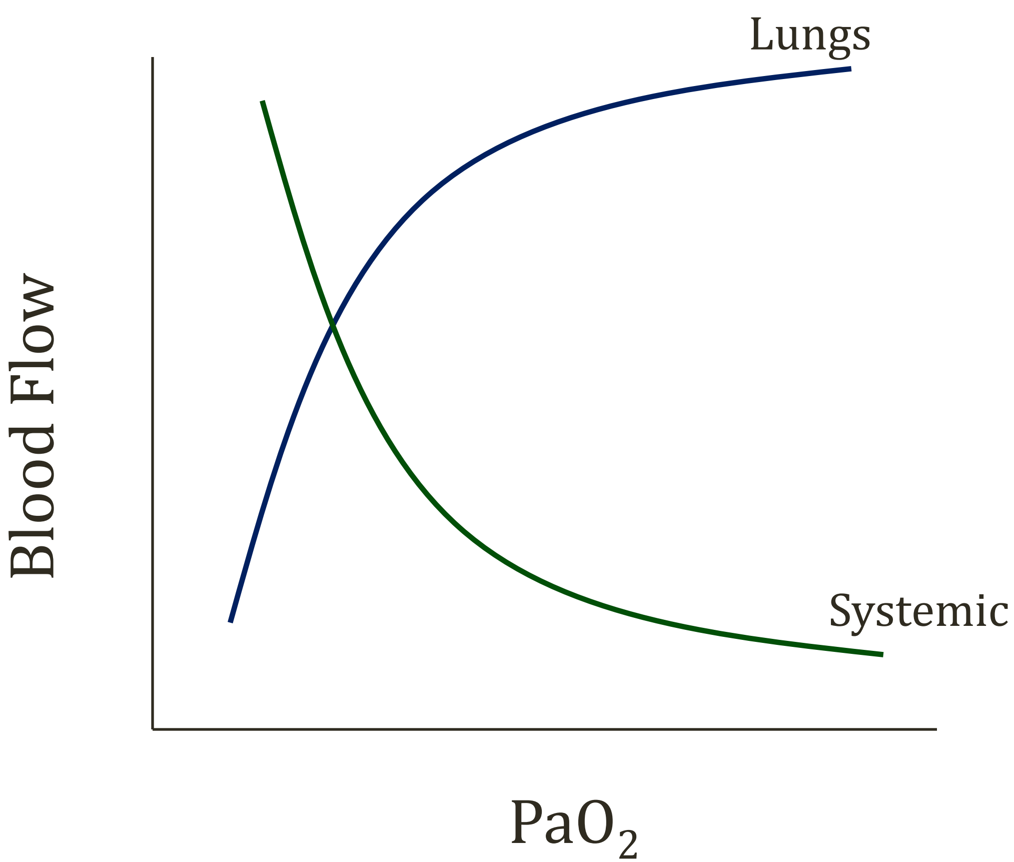
Pulmonary Circulation

- Low pressure system
  - Systemic: 120/80
  - Pulmonary artery: 24/12
- Walls of pulmonary artery very thin
  - Little smooth muscle
  - Low resistance to flow
  - Very distensible (compliant)

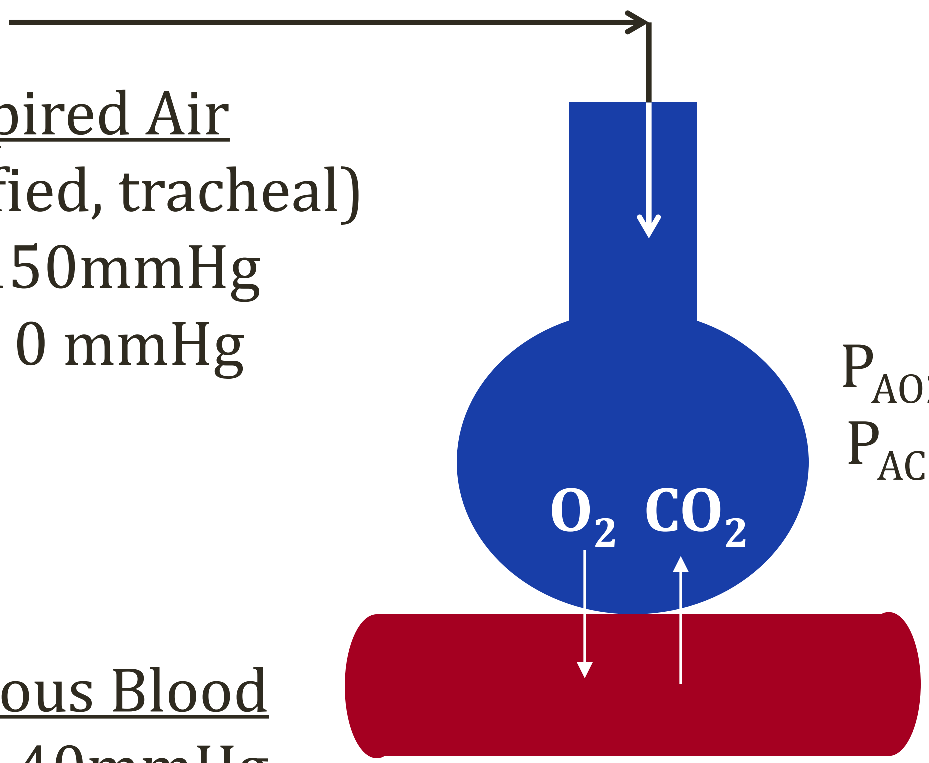
Blood Oxygen Content

- Systemic circulation
  - ↓ O_2 level (PaO_2) leads to vasodilation (↑blood flow)
- Pulmonary circulation
  - ↓ O_2 level (PaO_2) leads to **vasoconstriction** (↓blood flow)
  - "Hypoxic vasoconstriction"
  - Shunts blood away from poorly ventilated areas
  - More blood to well ventilated areas
- Key for fetal circulation
  - Low O_2 constricts pulmonary arteries in womb
  - At birth, arteries receive O_2 and dilate

Blood O_2 Content



Gas Exchange



Inspired Air
(humidified, tracheal)
P_{O2} 150mmHg
P_{CO2} 0 mmHg

Alveoli
P_{AO2} 100 mmHg
P_{ACO2} 40 mmHg

Venous Blood
P_{vO2} 40mmHg
P_{vCO2} 46mmHg

Arterial Blood
P_{aO2} 90mmHg
P_{aCO2} 40mmHg

Gas Exchange

- Gasses classified by limiting factor for gas transfer
- **Perfusion limited**
  - Gas transport limited by perfusion (blood flow)
  - More blood flow → more uptake of gas
- **Diffusion limited**
  - Gas transport limited by *diffusion*

Venous blood

↓

Delivered to lung (perfusion)

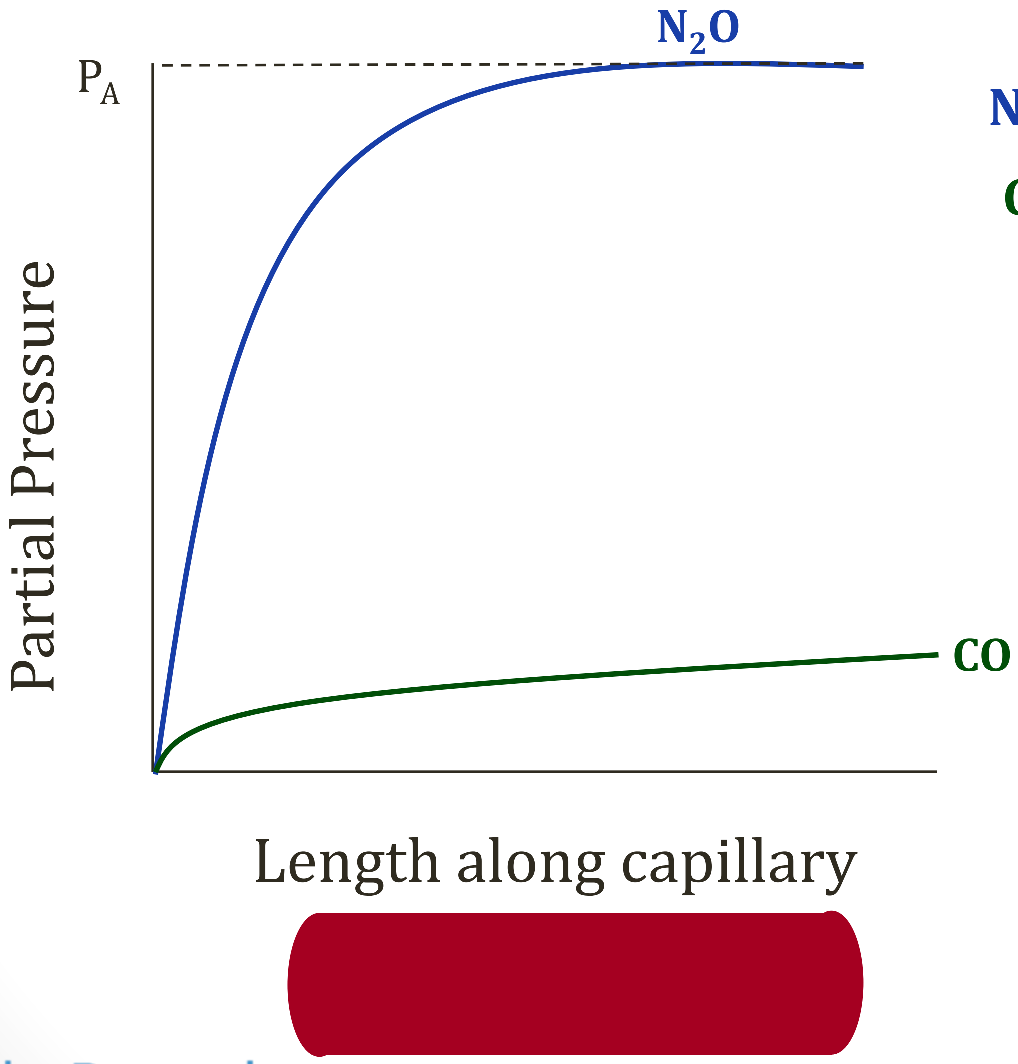
↓

Gas diffusion

↓

Equilibrium with alveoli

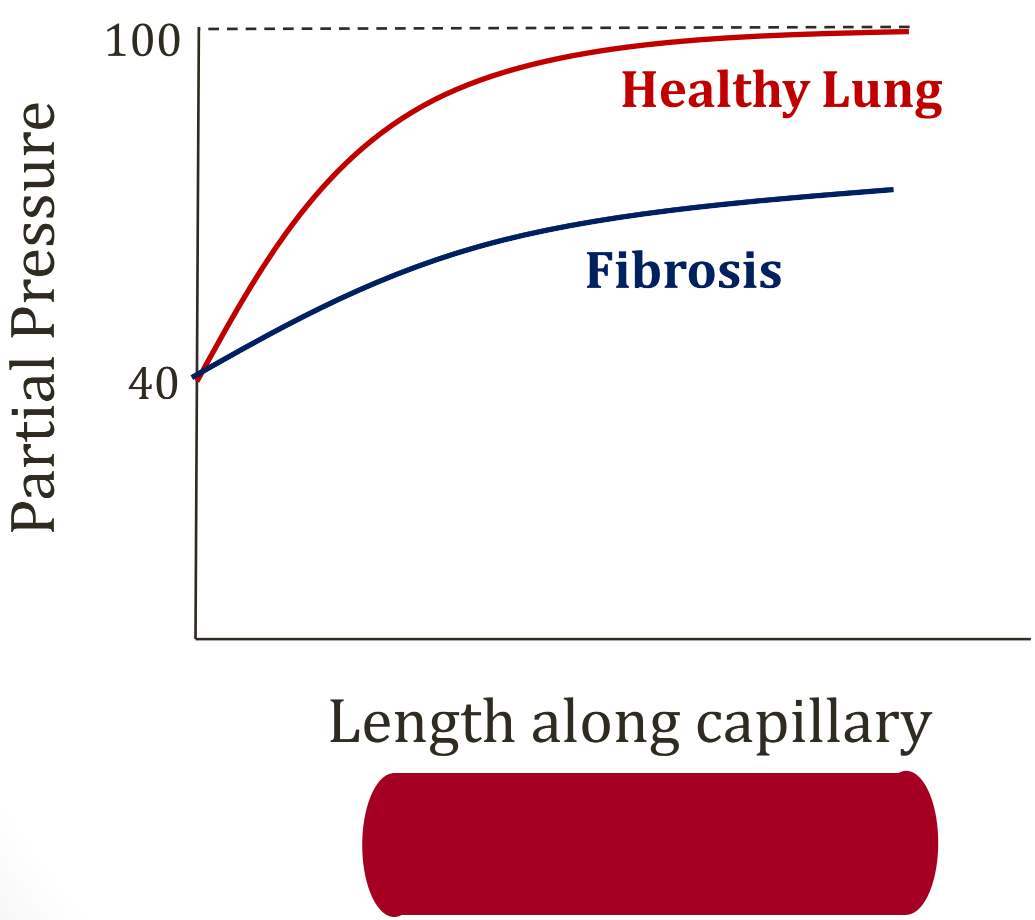
Gas Exchange



N_2O: Perfusion limited

CO: Diffusion limited

Gas Exchange: Oxygen

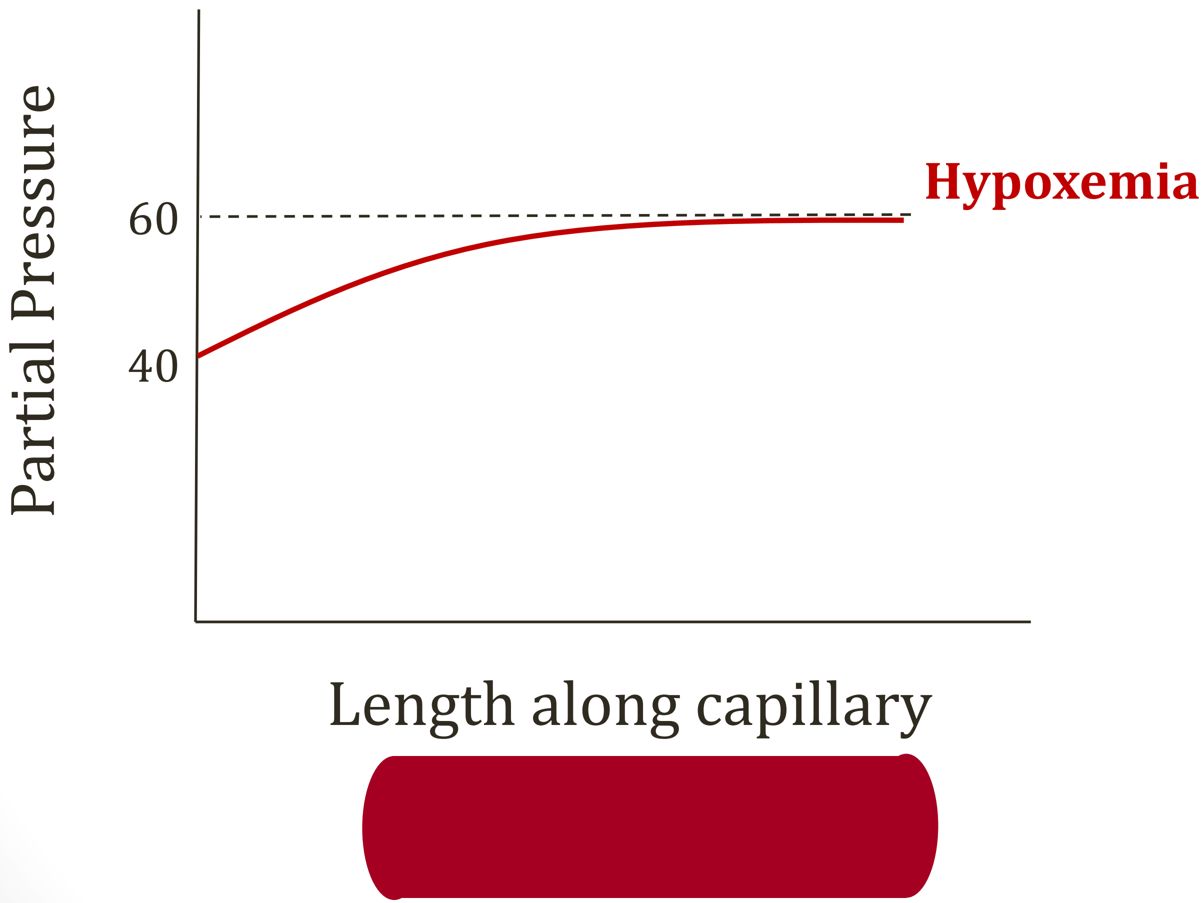


Normal
Perfusion limited

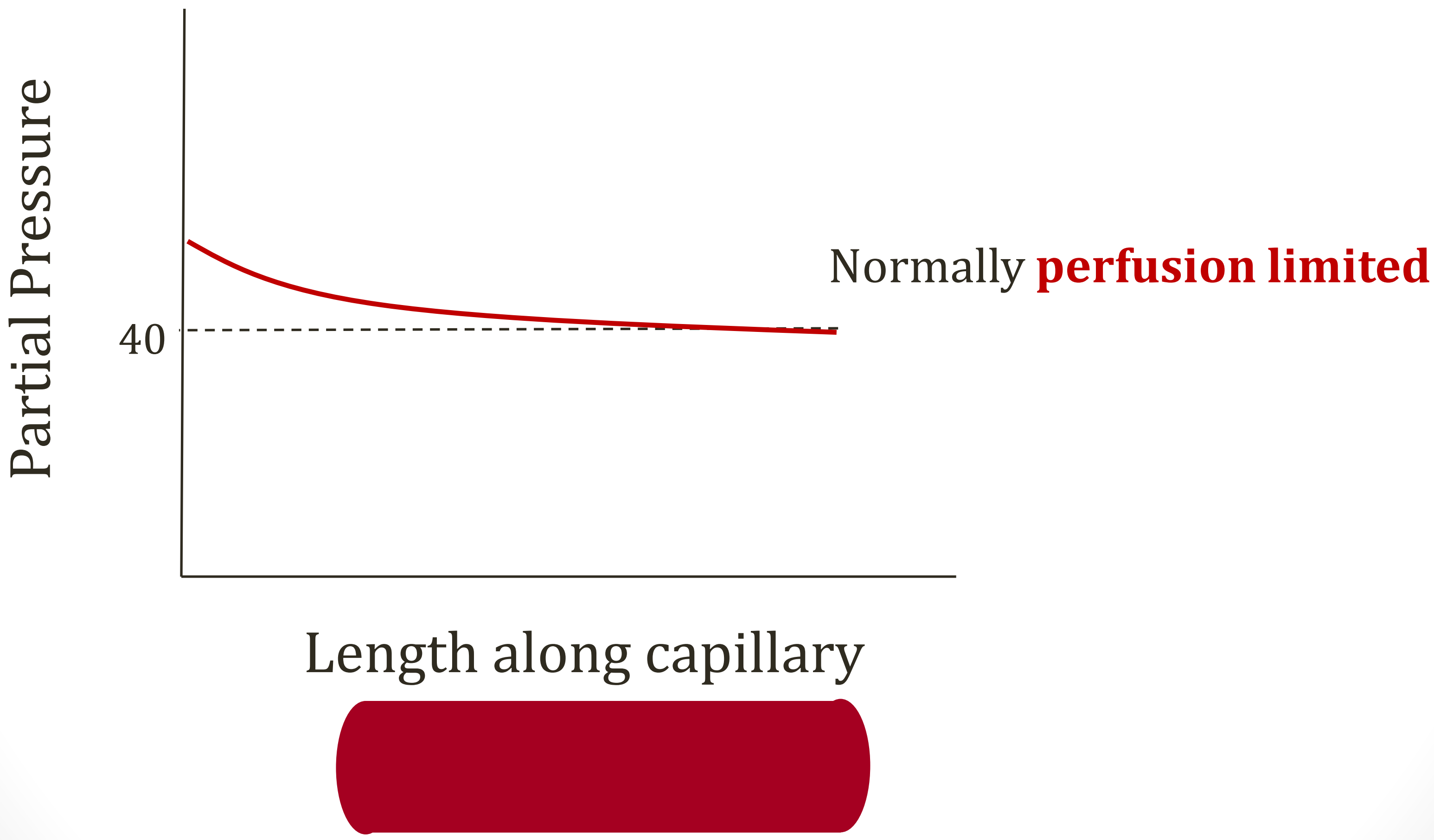
Disease
Diffusion limited

Gas Exchange: Oxygen

High Altitude



Gas Exchange: Carbon Dioxide



DLCO

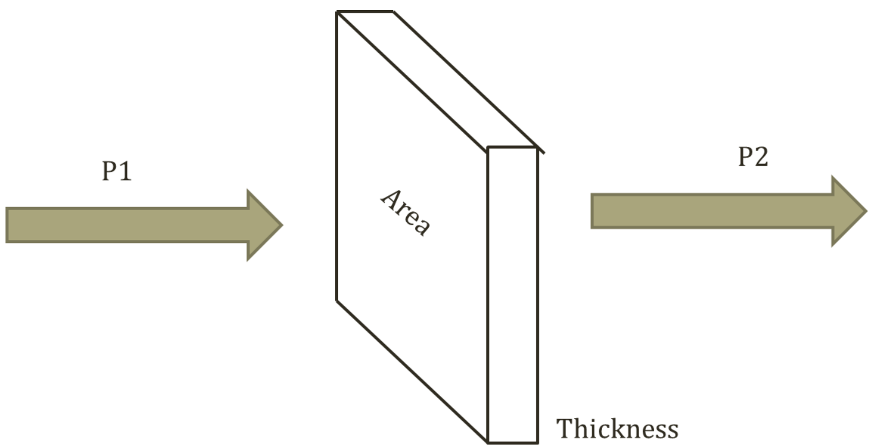
Diffusing capacity of carbon monoxide

- Measures ability of lungs to transfer gas
- Patient inhales small amount (not dangerous) CO
- CO uptake is **diffusion limited**
  - Amount taken up ≈ diffusion capacity of lungs
- Machine measures CO exhaled
- Normal = 75 – 140 % predicted
- Severe disease <40% predicted

Low DLCO Disorders

$$V_{gas} = \frac{Area \;\; * D \;\; * (P1 - P2)}{Thickness}$$

- **Emphysema**
  - Destruction of alveoli
  - Decreased surface area
- **Fibrosis or pulmonary edema**
  - Diffusion distance (thickness) increases



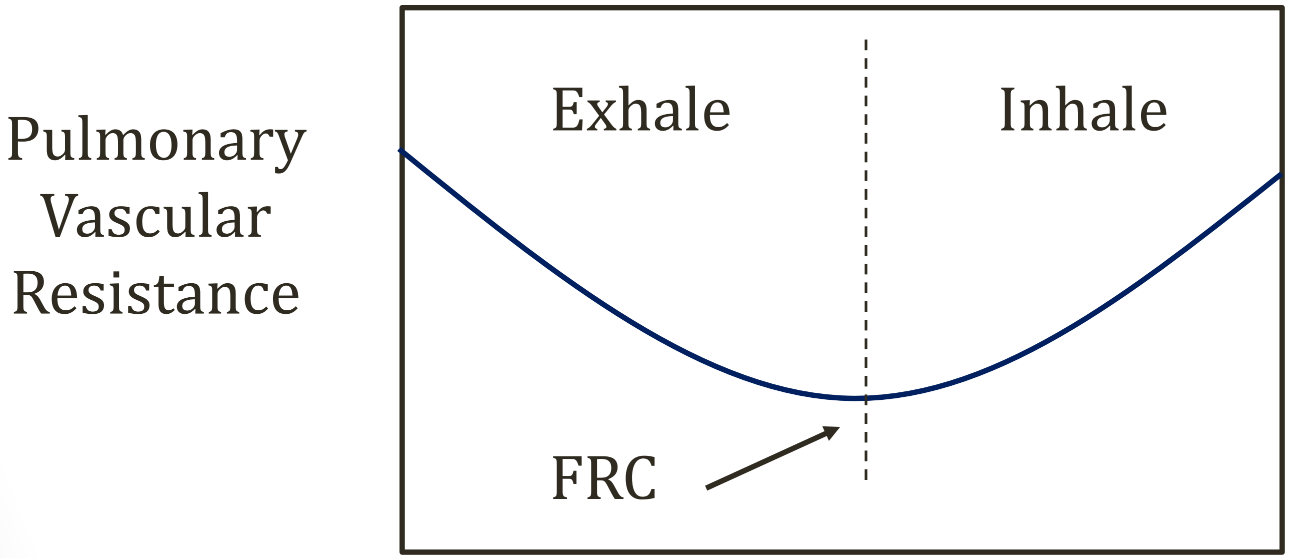
Resistance to Blood Flow

Pulmonary Vascular Resistance

- Two vessels types:
  - Alveolar: capillaries
  - Extra-alveolar: arteries and veins
- Increased lung volumes:
  - Crushes alveolar vessels → high resistance
  - Pulls extra-alveolar vessels open

Pulmonary Vascular Resistance

Resistance to blood flow

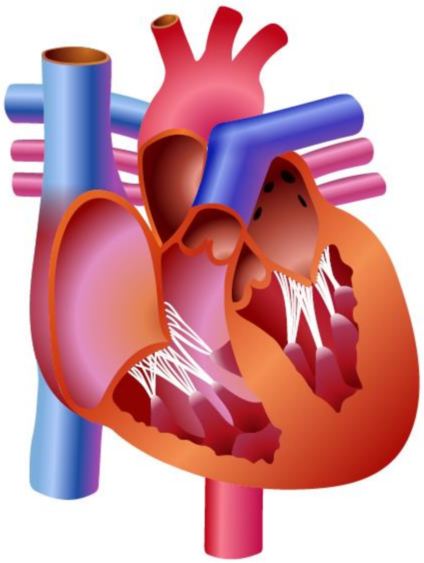


Pulmonary Hypertension

- Normal PA pressure
  - 24/12
  - Mean 10-14mmHg
- **Pulmonary hypertension**
  - Mean pressure >25mmHg
- **Loud P2** = pulmonary hypertension
  - "Accentuated" or "loud" second heart sound
  - Left upper sternal border

Pulmonary Hypertension

- Main symptom is dyspnea
- Untreated can lead to **"cor pulmonale"**
  - Chronic high pressure in right ventricle
  - Right ventricle hypertrophies
  - Eventually dilates and fails
  - Jugular venous distension
  - Lower extremity edema
  - Hepatomegaly
- Death from heart failure or arrhythmia

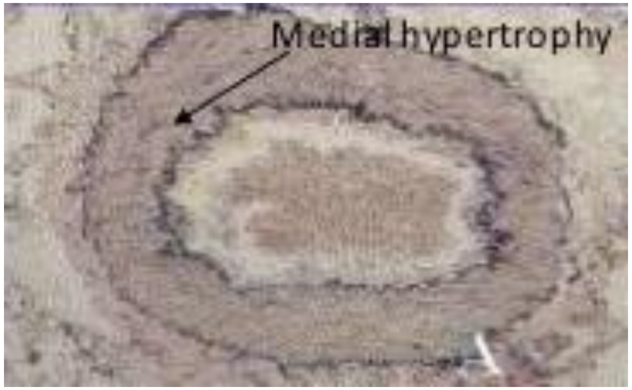


Pulmonary Hypertension

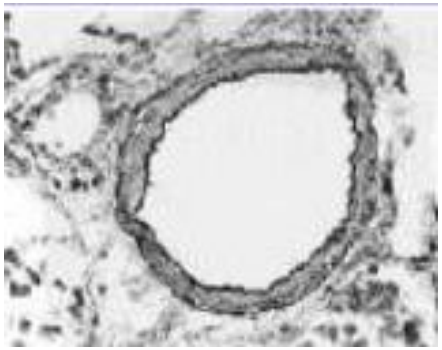
- Gold standard diagnosis: **right heart catheterization**
- Non-invasive diagnosis by **echocardiography**
  - Estimate PA pressure
  - Visualize right heart structures

Pulmonary Hypertension

- **Arteriosclerosis**
  - Thickening of arterial walls
- Proliferation smooth muscle cells
  - Thickening media
  - Narrowing of the lumen



Medial Hypertrophy



Normal

Pulmonary Hypertension

High PVR
"Pulmonary Arterial HTN"
Primary or Secondary

↓

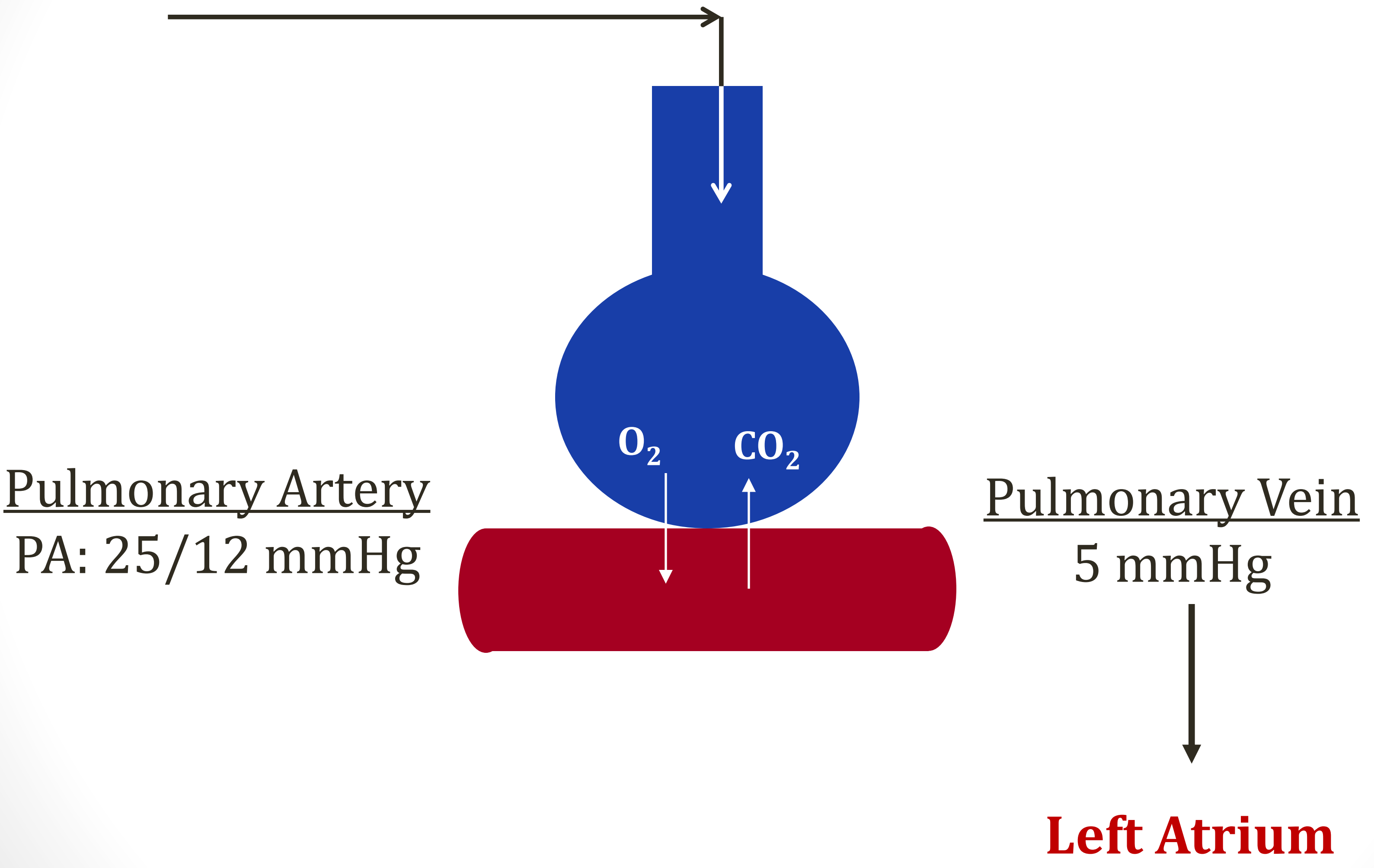
$$P_{PA} = CO * PVR + P_{LA}$$

↑

High LA Pressure
Most common cause PHTN
"Pulmonary Venous HTN"
Heart Failure
Valve Disease

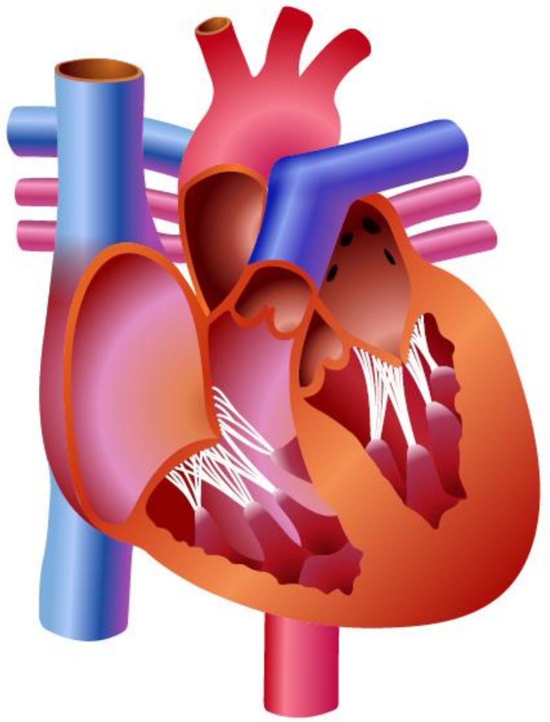
Left Heart Disease

Pulmonary *Venous* Hypertension



Left Heart Disease

- Most common cause of pulmonary hypertension
- "Pulmonary *venous* hypertension"
- Any cause of **high left atrial pressure**
  - Heart failure
  - Mitral stenosis
  - Mitral regurgitation



High PVR

Pulmonary *Arterial* Hypertension

- **Hypoxemia** → vasoconstriction
  - COPD, other chronic lung diseases
  - Sleep apnea or high altitude (chronic hypoxia)
- **Chronic pulmonary emboli**
  - Decreased **area** for blood flow

PAH

Pulmonary Arterial Hypertension

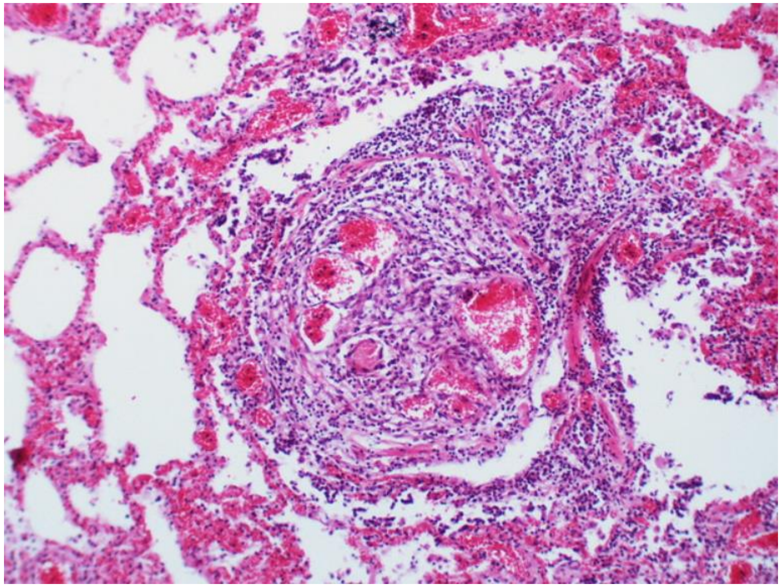
- High pulmonary vascular resistance
- No chronic lung disease or thrombosis
- Key associations:
  - **Connective tissue disease (scleroderma)**
  - Human immunodeficiency virus
  - Congenital heart disease (shunts)
  - Schistosomiasis
  - Drugs (amphetamines, cocaine)

Idiopathic PAH

- Rare disease
- Classically affects young women
- **High pulmonary vascular resistance**
- Increased activity vasoconstrictors
  - Endothelin
- Decreased activity vasodilators
  - Nitric oxide

Plexiform Lesions

- Unique to idiopathic PAH
- Endothelial proliferation forms **multiple lumens**
- Small arteries branch points from medium arteries



Yale Rosen/Flikr

BMPR2 gene mutations

- Bone morphogenetic protein receptor type II
  - Inhibits smooth muscle proliferation
  - Mutations → abnormal growth (endothelium, smooth muscle)
- Up to 25% of idiopathic cases
- Up to 80% **familial cases**

PAH Treatments

- All lower PVR
- Epoprostenol: Prostacyclin (IV)
  - PGI_2
  - Potent vasodilator
- Bosentan:
  - Antagonist endothelin-1 receptors (PO)
- Sildenafil:
  - Inhibits PDE-5 in smooth muscle of lungs (PO)

Ventilation & Perfusion

Jason Ryan, MD, MPH

Ventilation

- Ventilation = volume x frequency (respiratory rate)
  - 500cc per breath x 20 breaths per minute
  - 10,000cc/min
- **Alveolar ventilation** = useful for gas exchange
- **Dead space ventilation** = wasted ventilation

Pixabay/Public Domain

Dead Space

- Filled with air but no gas exchange
- **Anatomic dead space**
  - Volume of conducting portions of respiratory tract
  - Nose, trachea
- **Physiologic dead space**
  - Anatomic PLUS volume of alveoli that don't exchange gas
  - Includes functional dead space
  - Insufficient perfusion
  - Apex is largest contributor
- Physiologic dead space increases many diseases

Measuring Dead Space

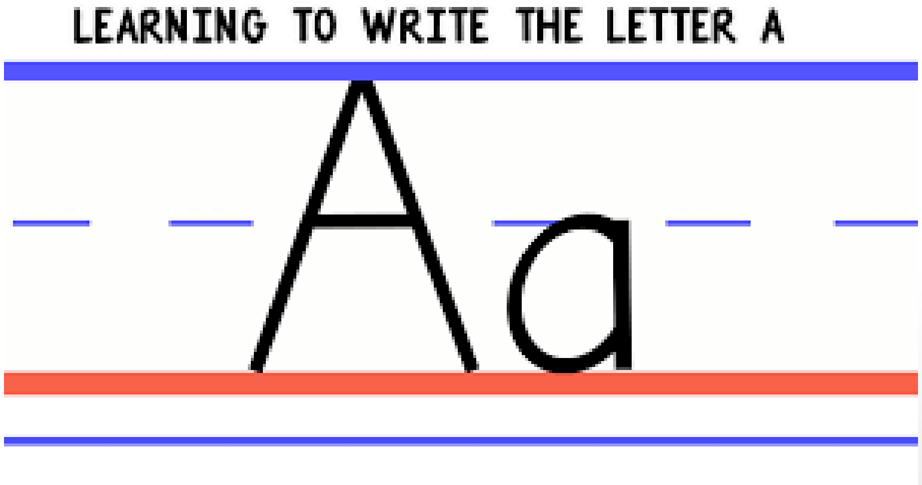
- **Bohr's method**
- Physiologic dead space (V_d) from:
  - Tidal volume (V_t)
  - $PeCO_2$ (exhaled air)
  - $PaCO_2$ (blood gas)

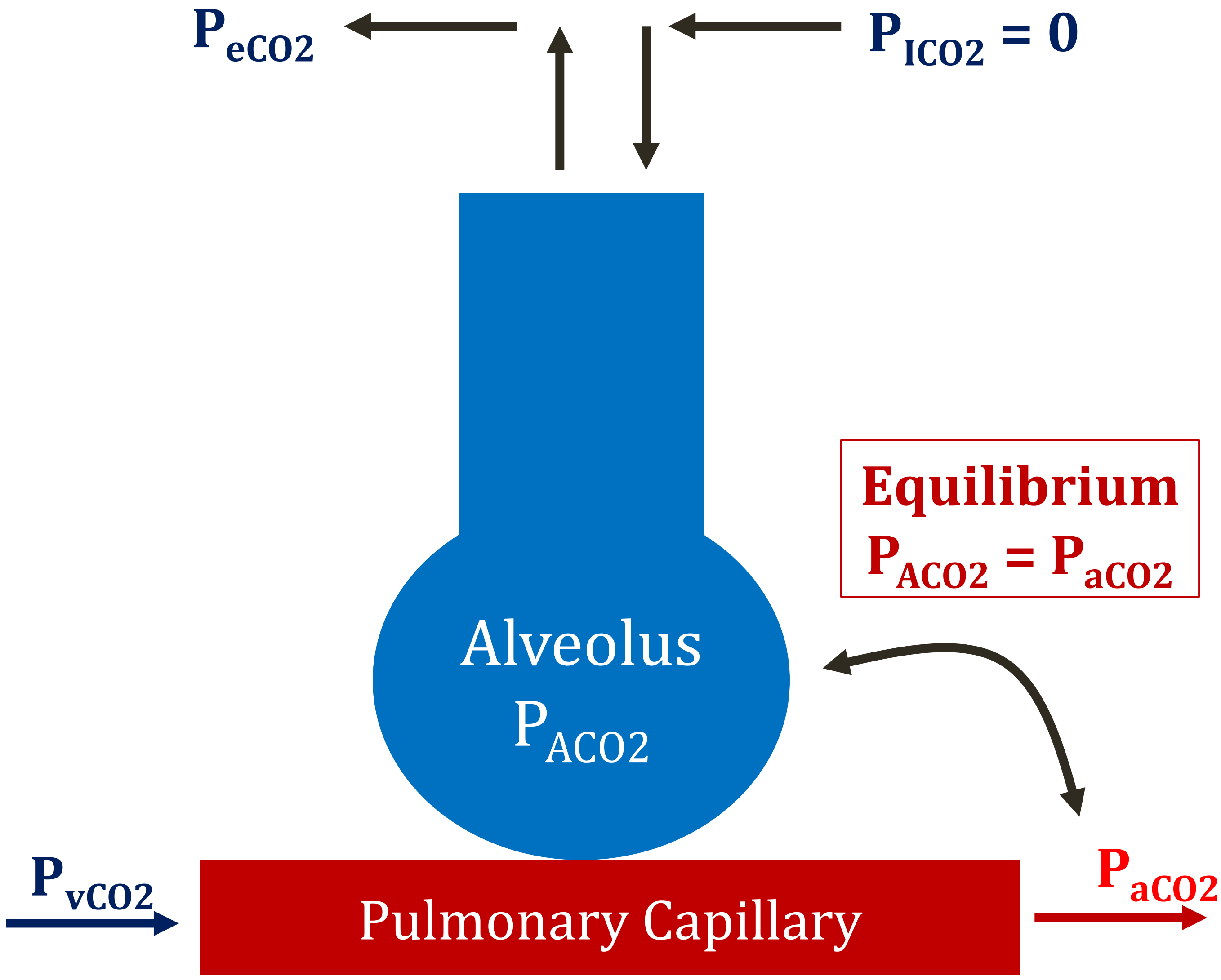
$$\frac{V_d}{V_t} = \frac{P_aCO2 - P_eCO2}{P_aCO2}$$

Nomenclature

- P_A = alveolar pressure
  - P_{AO2} = alveolar O_2
  - P_{ACO2} = alveolar CO_2
- P_a = arterial pressure
  - P_{aO2} = arterial O_2
  - P_{aCO2} = arterial CO_2
- P_v = venous pressure
- P_e = expired pressure

A = alveolar
a = arterial





P_{eCO2}
$P_{ICO2} = 0$
Equilibrium
$P_{ACO2} = P_{aCO2}$
Alveolus
P_{ACO2}
P_{vCO2}
Pulmonary Capillary
P_{aCO2}

Bohr Equation

$$\frac{V_d}{V_t} = \frac{P_aCO2 - P_eCO2}{P_aCO2}$$

Zero Dead Space

$$\frac{V_d}{V_t} = \frac{P_aCO2 - P_eCO2}{P_aCO2}$$

$$0 = \frac{P_aCO2 - P_eCO2}{P_aCO2}$$

$$0 = P_aCO2 - P_eCO2$$

$$P_eCO2 = P_aCO2$$

↓ dead space → P_eCO2 approaches P_aCO2

More gas exchange

Less retained CO2

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100% Dead Space

$$\frac{V_d}{V_t} = \frac{P_aCO2 - P_eCO2}{P_aCO2}$$

$$1 = \frac{P_aCO2 - P_eCO2}{P_aCO2}$$

$$P_aCO2 = P_aCO2 - P_eCO2$$

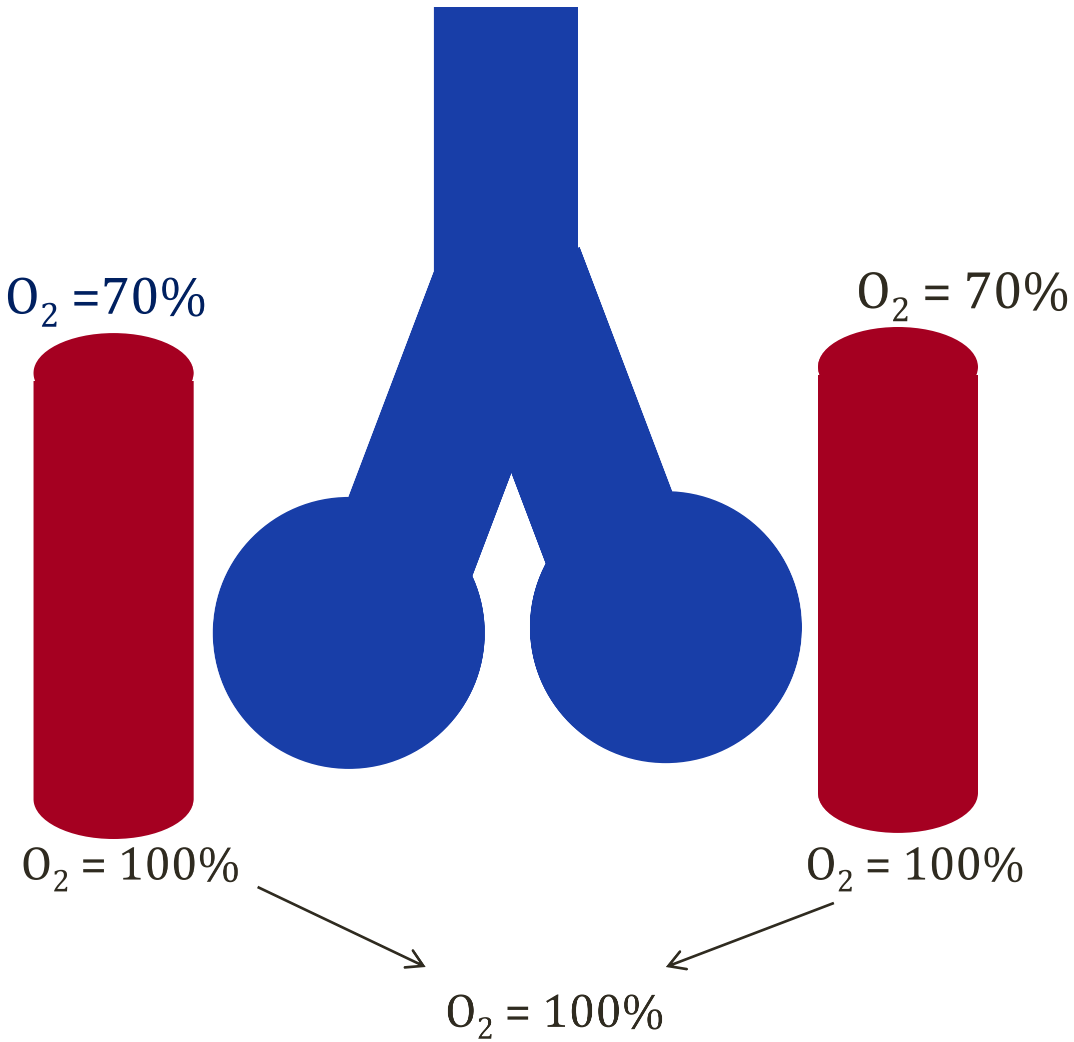
$$P_eCO2 = 0$$

↑ dead space → P_eCO2 approaches zero

Less gas exchange

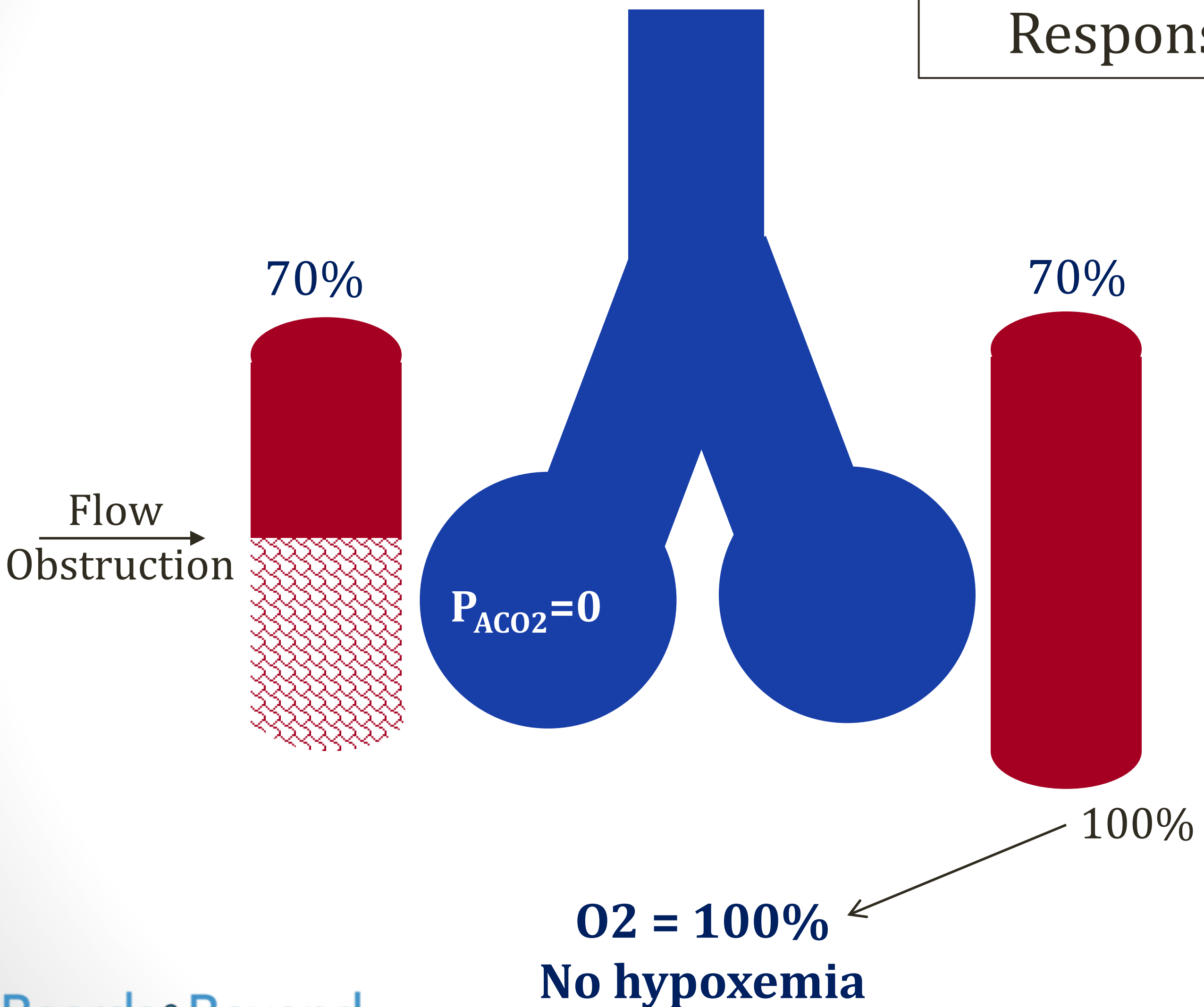
More retained CO2

Dead Space



Dead Space

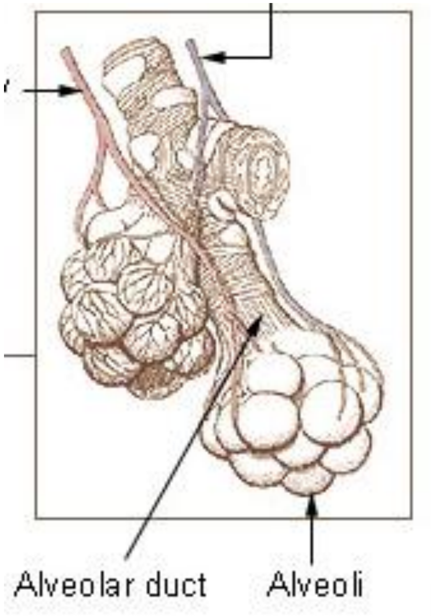
Main problem: ↑ CO_2
Hypercapnia
Response: ↑ RR



Alveolar Ventilation Equation

Predicts Alveolar CO2

- Total ventilation (TV) = volume/min
  - **Volume in slightly > volume out due to O_2 uptake
  - Sometimes called minute ventilation
- **Alveolar ventilation**
  - TV minus "dead space"
- Example: 500cc per minute
  - 150cc fills dead space
  - Only 350cc available for gas exchange



Elevated Carbon Dioxide

- Hypercapnia
- Hypercarbia
- Causes acidosis
- Physiologic response: **↑ respiratory rate**
  - Increased alveolar ventilation

Alveolar Ventilation Equation

Predicts Alveolar CO2

- V_A = *alveolar* ventilation
- V_{CO2} = rate of CO2 production
- P_{ACO2} = alveolar PCO2
- Vt = total ventilation
- V_{ds} = dead space ventilation
- K = constant

Three Major Causes of ↑ CO_2

↑ CO2 production
↓V_A (hypoventilation)
↑V_{ds} (dead space)

$$P_{ACO2} = \frac{V_{CO2} * K}{V_A} \qquad P_{ACO2} = \frac{V_{CO2} * K}{V_T - V_{ds}}$$

Alveolar Gas Equation

Predicts Alveolar O2

- P_{AO2} = alveolar O2
- P_{IO2} = inspired O2
- P_{ACO2} alveolar CO2
- R = respiratory exchange ratio
  - CO_2 production/O_2 consumption
  - Varies with diet, metabolic state

$$P_{AO2} = P_{IO2} - \frac{P_{ACO2}}{R}$$

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Alveolar Gas Equation

Predicts Alveolar O2

P_{ACO2}	P_{IO2}	P_{AO2}
40	150	100
50	150	88
60	150	75
70	150	63
80	150	50

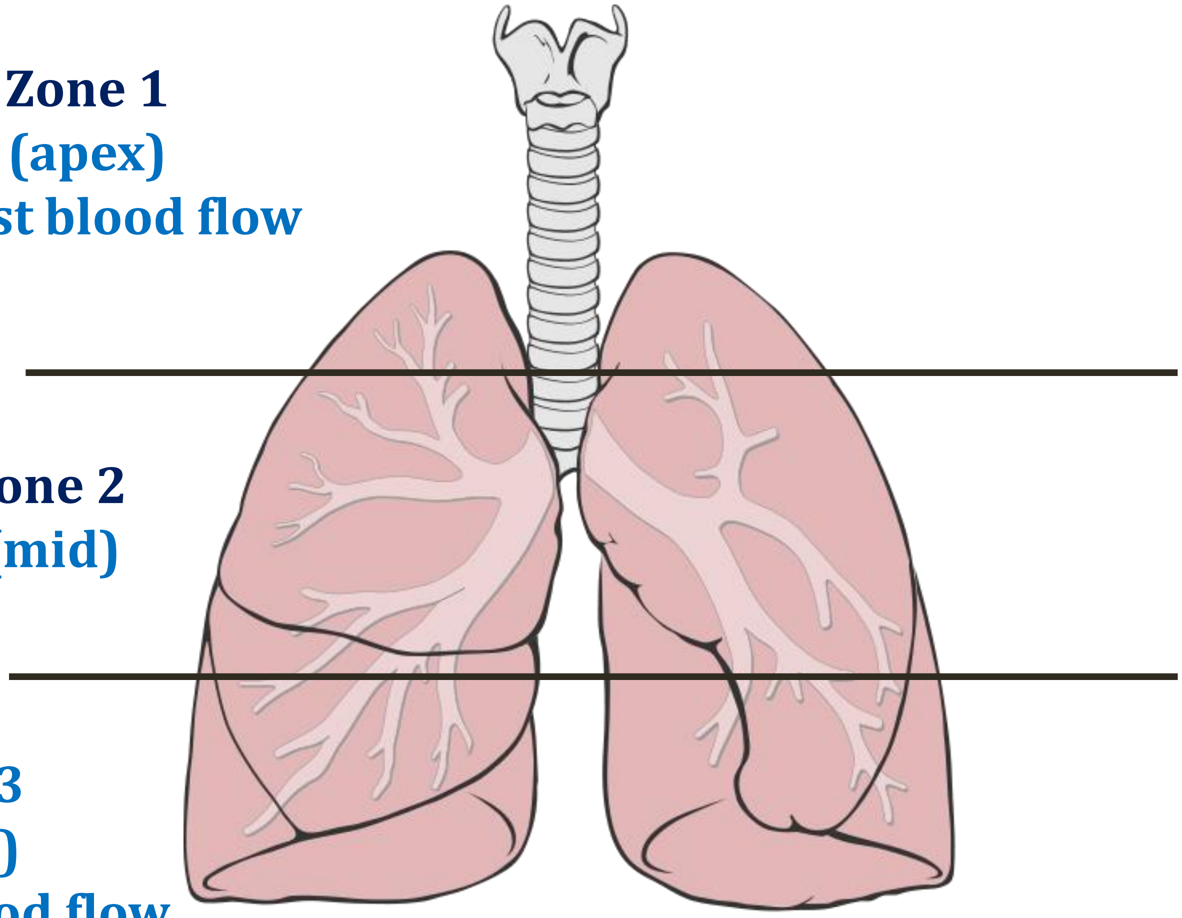
$$P_{AO2} = P_{IO2} - \frac{P_{ACO2}}{R}$$

Lung Perfusion

- Upright position: Blood flow distribution is **uneven**
  - Caused by **gravity**
  - Apex: Lowest blood flow
  - Base: Highest blood flow
- Lung divided into **3 zones** to describe perfusion

Lung Perfusion

Zone 1
(apex)
Lowest blood flow

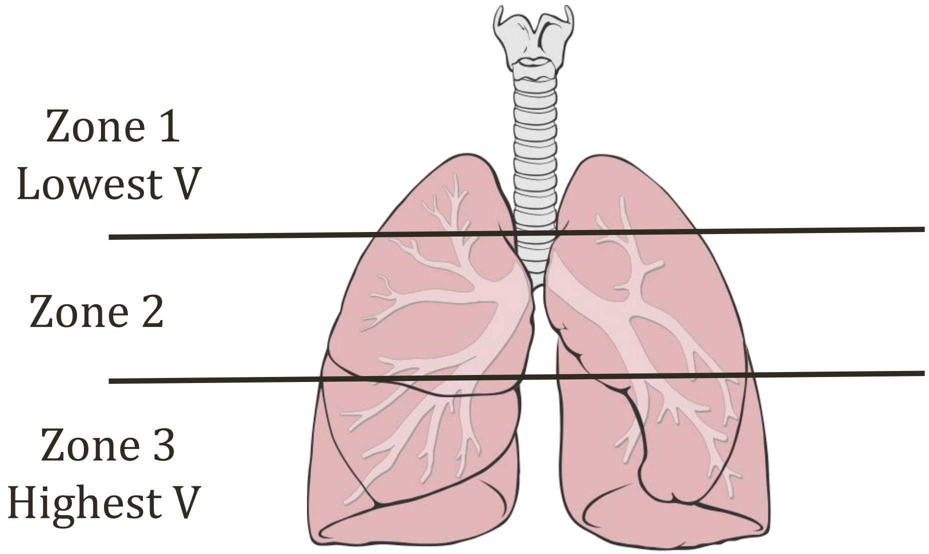


Zone 2
(mid)

Zone 3
(base)
Highest blood flow

Lung Ventilation

- Ventilation highest zone 3, lowest zone 1
  - Also caused by gravity
  - Upper lung compresses base → pushes air out
  - More room for filling of base with next breath
  - Variations smaller (L/min) than blood flow



Ventilation-Perfusion Ratio

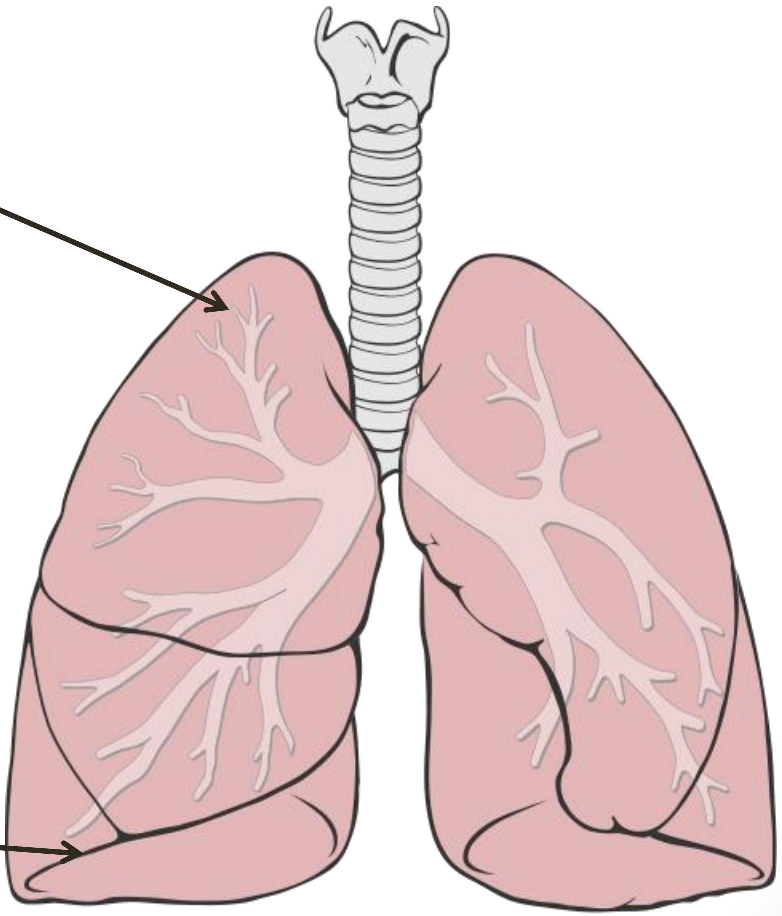
- V/Q ratio: alveolar ventilation/pulmonary blood flow
  - Matching critical for gas exchange
  - Under-ventilated or under-perfused alveoli inefficient
- **Normal V/Q ratio = 0.8**
  - Alveolar ventilation (L/min)/pulmonary blood flow (L/min)
  - Yields normal P_{aO2} (90 mmHg) and P_{aCO2} (40 mm Hg)

Ventilation-Perfusion Ratio

<u>Apex</u>
Lowest Blood Flow
Lowest Ventilation
Highest V/Q
Wasted V

$\frac{\downarrow V}{\downarrow\downarrow Q}$

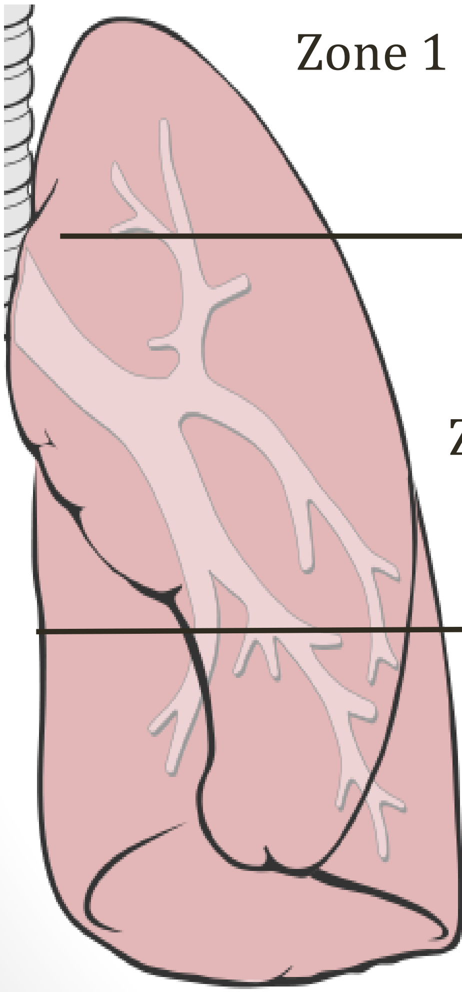
Both decrease bottom to top
Blood flow decreases more
V/Q ratio changes



<u>Base</u>
Most Blood Flow
Most Ventilation
Lowest V/Q
Wasted Q

$\frac{\uparrow V}{\uparrow\uparrow Q}$

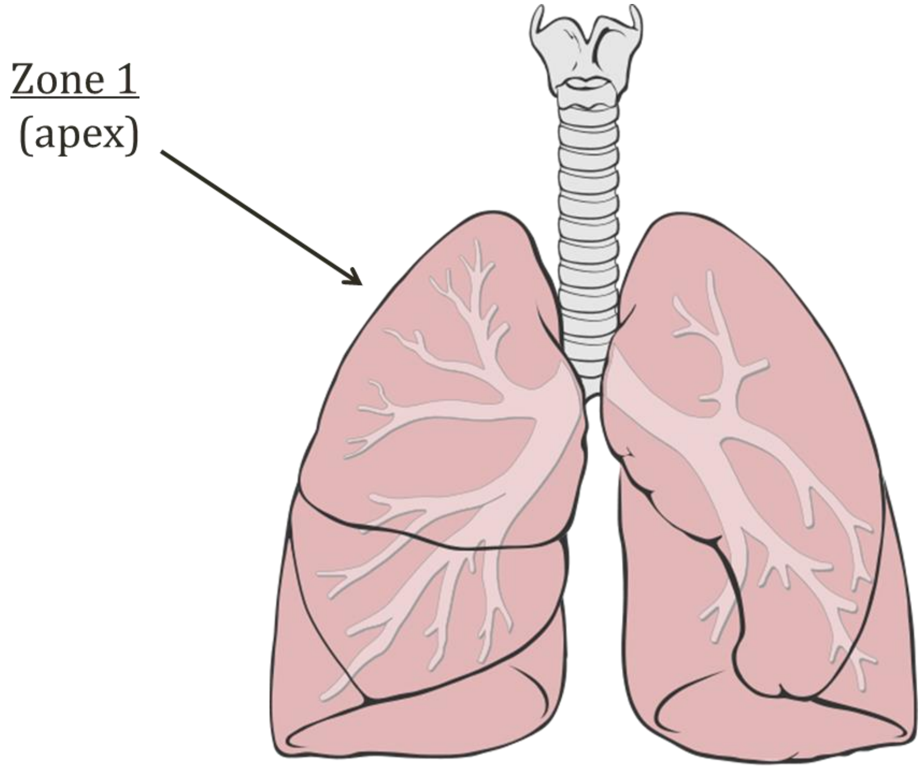
Ventilation-Perfusion Ratio



	V	Q	V/Q	P_{aO2}	P_{aCO2}
Zone 1	↓	↓	↑ **(3.0)**	130	30
Zone 2					
Zone 3	↑	↑	↓ **(0.6)**	90	42

Zone 1

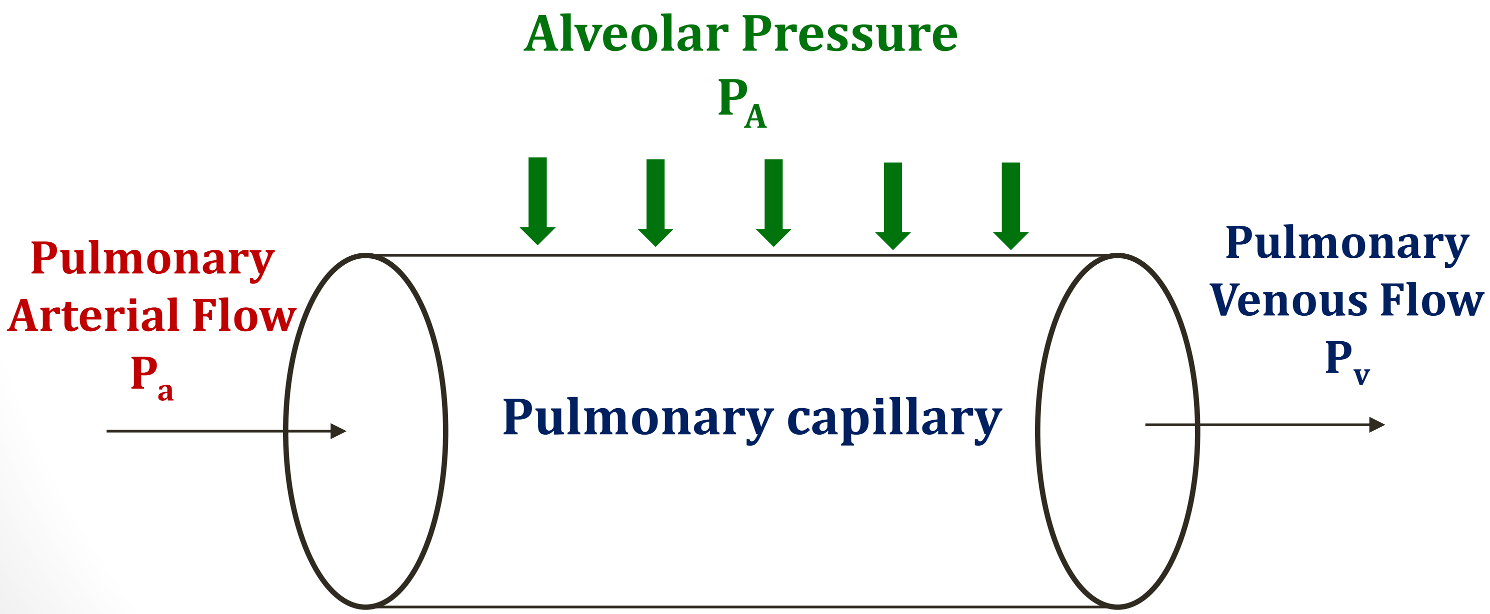
- Lowest blood flow
- Lowest ventilation
- Highest V/Q ratio
- Highest P_{aO2}
- Lowest P_{aCO2}



Tuberculosis

Pulmonary Blood Flow

- Normally, A-V pressure difference drives blood flow
- In lungs, alveolar pressure may determine blood flow
- High alveolar pressure → no blood flow → dead space



Pulmonary Blood Flow

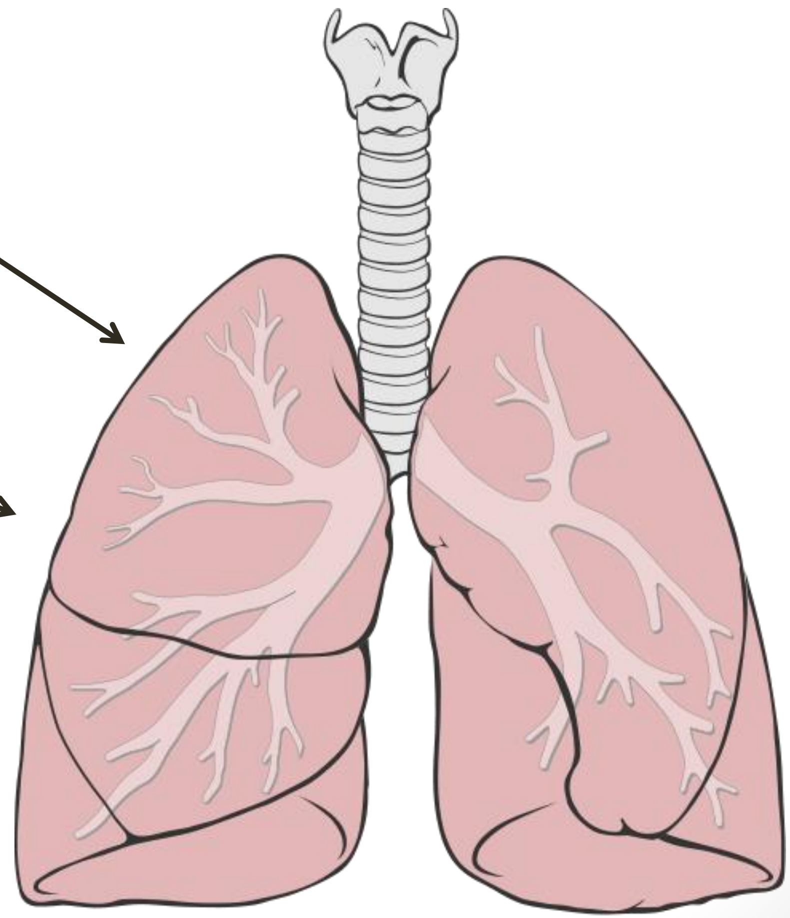
Pressures
P_A Alveolar
P_a Arterial
P_v Venous

- P_A constant
- At base, P_a and P_v highest
- At apex, P_a and P_v lowest

Zone 1 (Apex)
$P_A \geq P_a > P_v$
Minimal flow

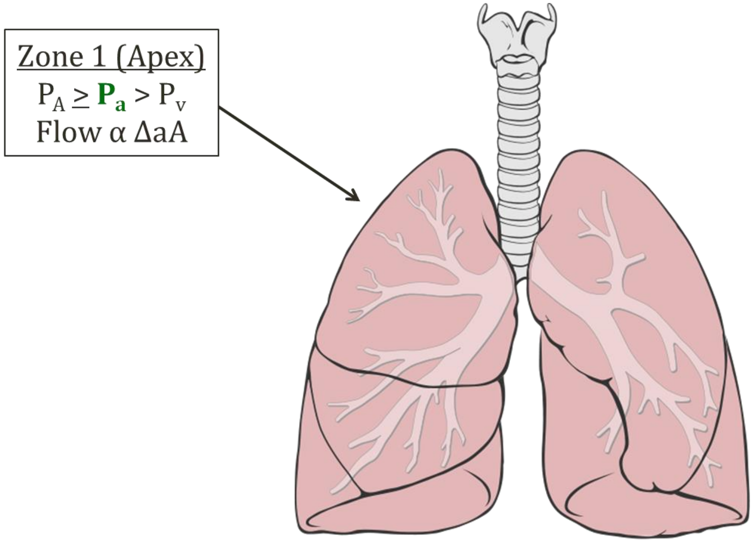
Zone 2 (Mid)
$P_a > P_A > P_v$

Zone 3 (Base)
$P_a > P_v > P_A$
Highest flow



Zone 1

- Lung apex: $P_A \geq P_a > P_v$
- Slight fall in P_a → **capillary compression**
  - Hemorrhage/shock
- Zone 1 becomes **dead space**
  - Ventilation without perfusion



Exercise

- Increased O_2 demand
- Ventilation rate increases
- Increased cardiac output
- **V/Q ratio approaches 1**
  - More blood flow
  - More ventilation
  - ↑ ventilation > ↑blood flow
  - Becomes more even in zones

William Warby/Flikr

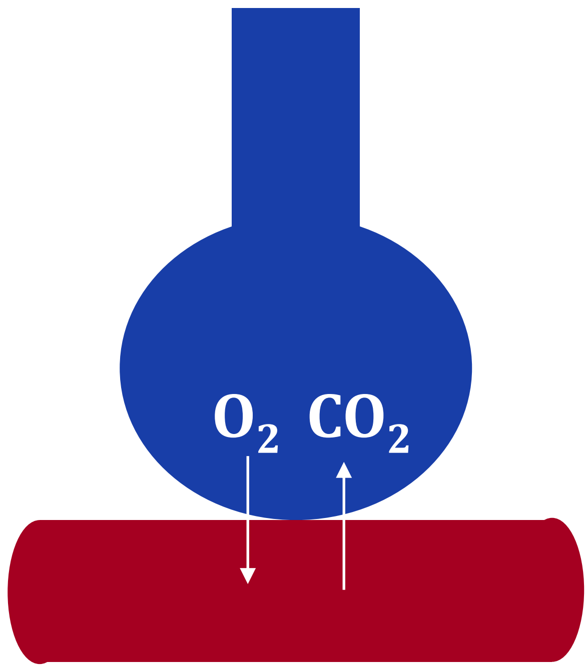
Exercise

- No change in mean P_{aO2} and P_{aCO2}
- Increased venous CO_2 (P_{VCO2})
- Decreased venous O_2 (P_{VO2})

<u>Venous Blood</u>

P_{vO2} 40mmHg

P_{vCO2} 46mmHg



<u>Arterial Blood</u>

P_{aO2} 90mmHg

P_{aCO2} 40mmHg

Hypoxia

Jason Ryan, MD, MPH

Oxygen delivery to tissues

- Oxygen delivery to tissues depends on:
  - Cardiac output
  - O_2 content of blood
- For proper O_2 delivery need:
  - Normal cardiac output
  - Normal O_2 content

What determines O_2 content?

- O_2 binding capacity
  - How much O_2 blood can hold
  - Determined by hemoglobin
- Hemoglobin saturation
  - % Hemoglobin molecules saturated
- Dissolved O_2
  - O_2 directly dissolved in blood

PaO_2

- Partial pressure oxygen in blood
- Obtained from an arterial blood gas
- Reflects amount of O_2 dissolved in blood
- Normal: >80mmHg

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Pulse Oximetry

- Measures Hgb-O_2 saturation of blood
- Related to PaO_2
- Uses light and a photodetector

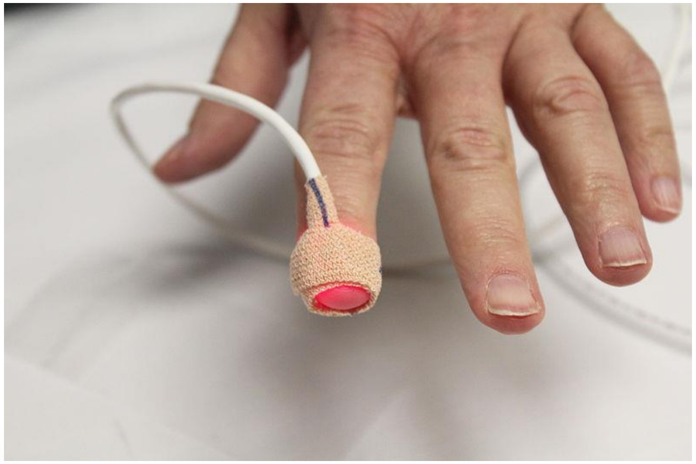
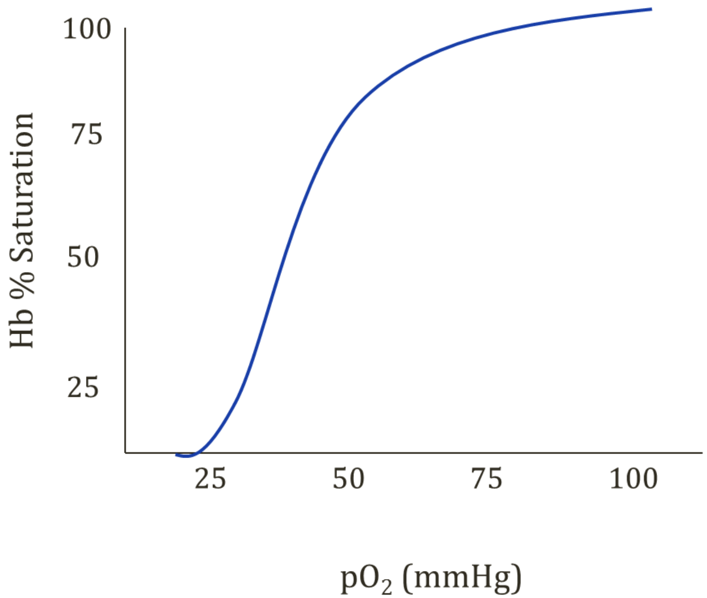


Image courtesy of Quinn Dombrowski



Oxygen Content

O_2 Content = (O_2 Binding Capacity) * (% Sat) + (Dissolved O_2)
(ml O_2/dl)

↑ (1.39 * Hgb)

↑ 0.003 P_{aO2}

- **Normal O2 content requires:**
  - Presence of hemoglobin
  - Sufficient saturation of hemoglobin
  - Normal P_{aO2}

Hypoxemia, Hypoxia, Ischemia

- Hypoxemia: low oxygen content of blood
- Hypoxia: low O_2 delivery to tissues
- Ischemia: loss of blood flow

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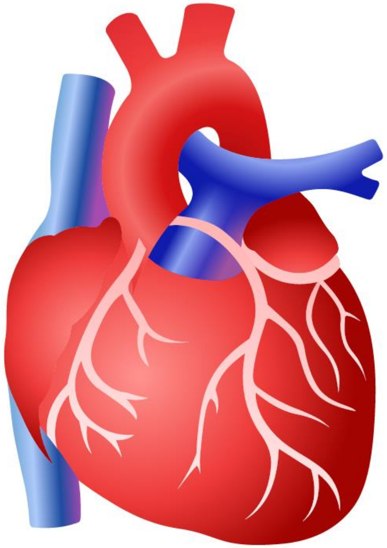
Hypoxemia, Hypoxia, Ischemia

- Low Hgb-O_2 sat or low PaO_2 = hypoxemia
- Hypoxemia → hypoxia
- Can have hypoxia ***without hypoxemia***

Common Hypoxia Causes
Hypoxemia Heart Failure Anemia Carbon Monoxide

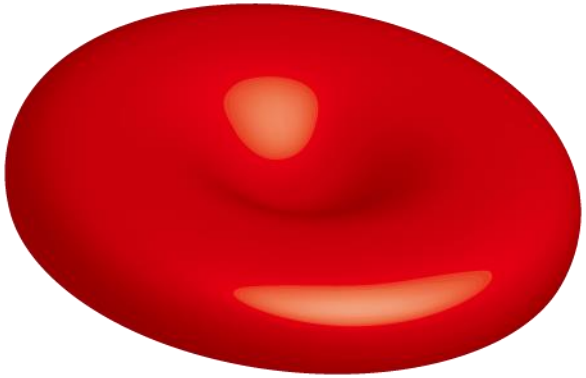
Heart Failure

- **↓ cardiac output**
- ↓ blood flow to tissues → hypoxia
- O_2 content of blood may be normal
- PaO_2 and Hgb-O_2 sat may be normal



Anemia

- Oxygenation of blood by lungs is normal
- **Oxygen carrying capacity** of blood reduced
- Low O_2 content of blood
- PaO_2 and Hgb-O_2 sat normal



Databese Center for Life Science (DBCLS)

Carbon Monoxide

- Binds to iron in heme 240x the affinity of oxygen
- Blocks O_2 binding sites: **"functional anemia"**
- Alveolar O_2 (P_{AO2}) usually normal
  - Amount of CO gas required for poisoning usually small
- Normal P_{AO2} → Normal P_{aO2}
  - ↓ O_2 binding to Hb despite normal P_aO_2

Carbon Monoxide

- Low Hgb-O_2 sat (CO blocking O_2 binding sites)
- Pulse oximeter shows normal (100%) O_2 sat
  - Can't distinguish Hb bound to CO from that bound to O_2
- O_2 content of blood reduced

Normal PaO2
Low O_2 % sat (reality)
Normal O_2 % sat (detector)
Hypoxia

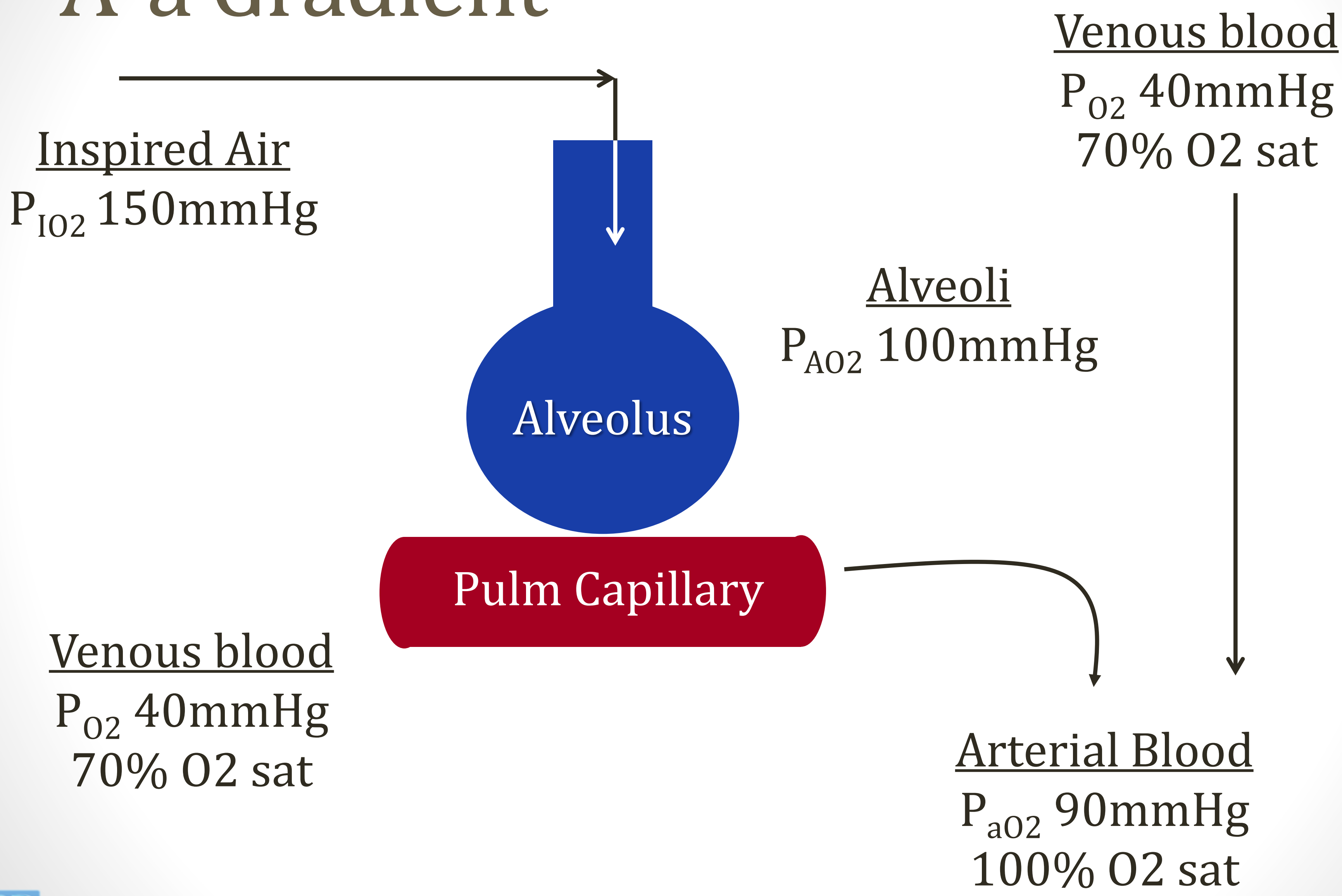
Causes of Hypoxia

	O2 Content	PaO2	% Sat
Hypoxemia	↓	↓	↓
Heart Failure	Normal	Normal	Normal
Anemia	↓	Normal	Normal
Carbon Monoxide	↓	Normal	↓*

Hypoxemia

- Indicates defect oxygenating blood
- Causes categorized by **A-a gradient**
  - Alveolar O_2 (P_{AO2})– Arterial O_2 (P_{aO2})
  - P_{AO2} from alveolar gas equation
  - P_{aO2} from blood gas

A-a Gradient



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Alveolar Gas Equation

$$P_{AO2} = P_{IO2} - \frac{P_{aCO2}}{R} = 150 - \frac{P_{aCO2}}{0.8}$$

A-a Gradient

- Difference between alveolar (A) and arterial (a) O_2
- Helpful for evaluating hypoxemia
- Step 1: Measure $P_{aO2,}$ P_{aCO2}
- Step 2: Determine P_{AO2} from gas equation
- Step 3: A-a gradient = $P_{AO2} - P_{aO2}$
- Normal 10-15mmHg
  - Shunting from **thebesian** and **bronchial veins**

Normal A-a Gradient

- **Low alveolar oxygen content (P_{AO2})**
- **Decreased oxygen content of air**
  - High altitude
  - P_{IO2} sea level = 150 mmHg
  - P_{IO2} high altitude ~ 100 mmHg

$$P_{AO2} = P_{IO2} - \frac{P_{aCO2}}{R} = 150 - \frac{P_{aCO2}}{0.8}$$

- **Hypoventilation**
  - Reduced respiratory rate
  - Reduced tidal volume
  - Causes increase P_{ACO2} → decreased P_{AO2}
  - Narcotics, neuromuscular weakness, obesity

Normal A-a Gradient

- **Improves with oxygen**

$$P_{AO2} = P_{IO2} - \frac{P_{aCO2}}{R} = 150 - \frac{P_{aCO2}}{0.8}$$

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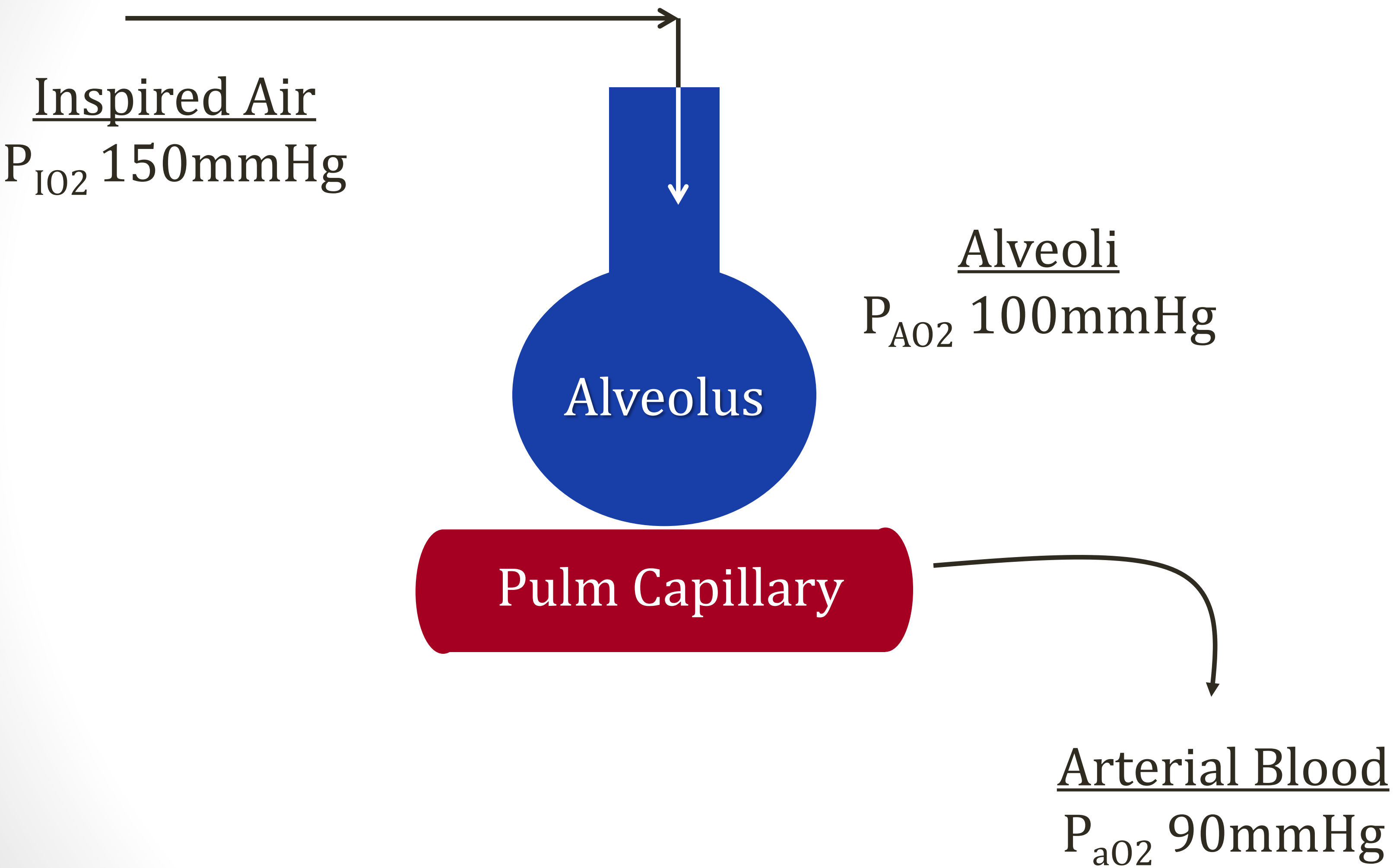
A-a Gradient


Inspired Air
P_{IO2} 150mmHg
Alveolus
Alveoli
P_{AO2} 100mmHg
Pulm Capillary
Arterial Blood
P_{aO2} 90mmHg

Alveolar Gas Equation

Hypoventilation
High CO2

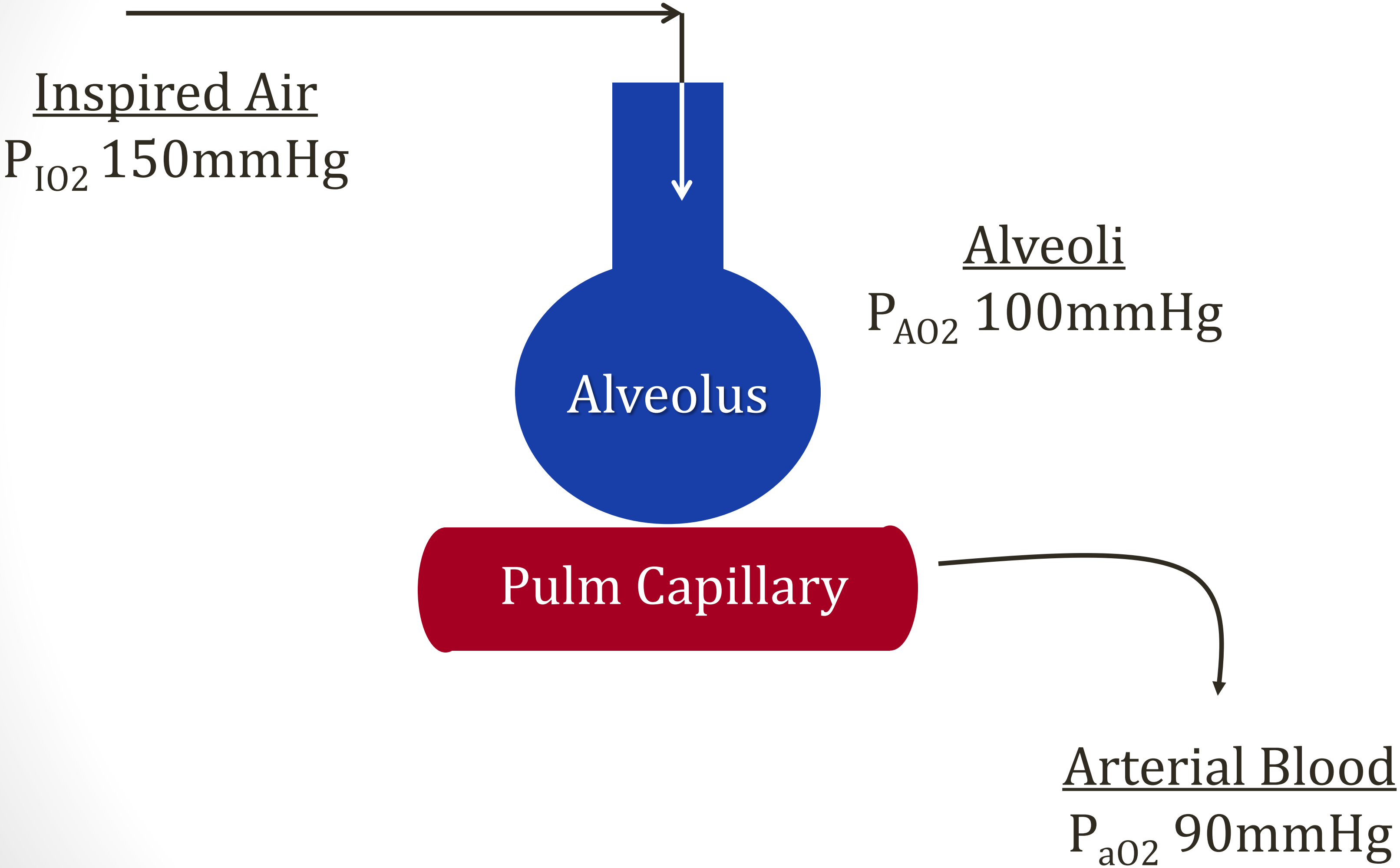
$$P_{AO2} = P_{IO2} - \frac{P_{aCO2}}{R} = 150 - \frac{P_{aCO2}}{0.8}$$

Low O2
Inspired Air

Increased A-a Gradient

- No problem with alveolar oxygen content (P_{AO2})
- **Low arterial oxygen content (P_{aO2})**
- Most primary lung diseases: high A-a gradient
  - Pneumonia, pulmonary edema, etc.
- Three basic mechanisms create the high A-a gradient
  - Diffusion defects
  - Shunt
  - V/Q Mismatch

A-a Gradient


Inspired Air
P_{IO2} 150mmHg
Alveoli
P_{AO2} 100mmHg
Alveolus
Pulm Capillary
Arterial Blood
P_{aO2} 90mmHg

Diffusion

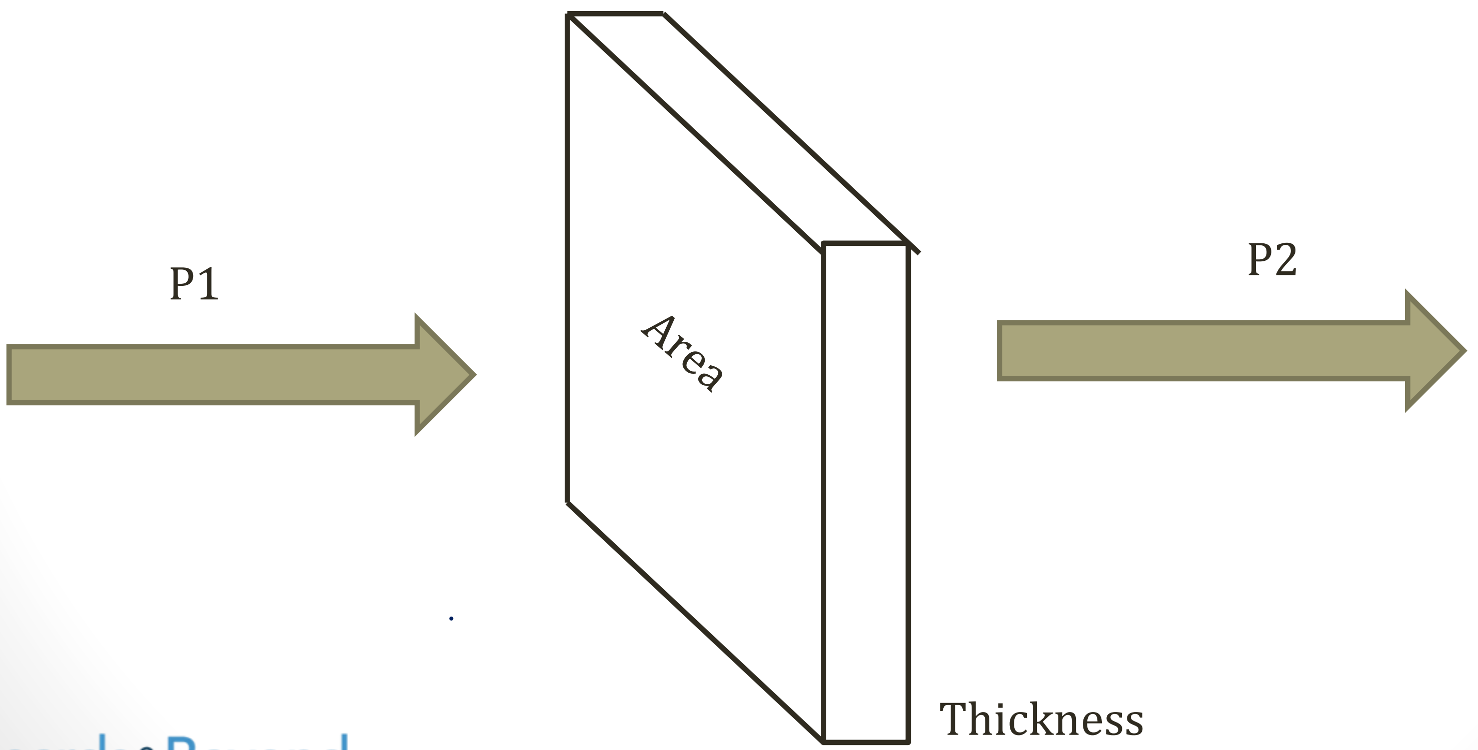
- Gases must diffuse from air to blood
- Rate of diffusion depends on:
  - Pressure difference (air-blood)
  - Area of alveoli for diffusion
  - Thickness of alveolar tissue

Diffusion

(diff. coefficient)

$$V_{gas} = \frac{\text{Area} * D * (P1 - P2)}{\text{Thickness}}$$

(vol/time)



Diffusion Limitation

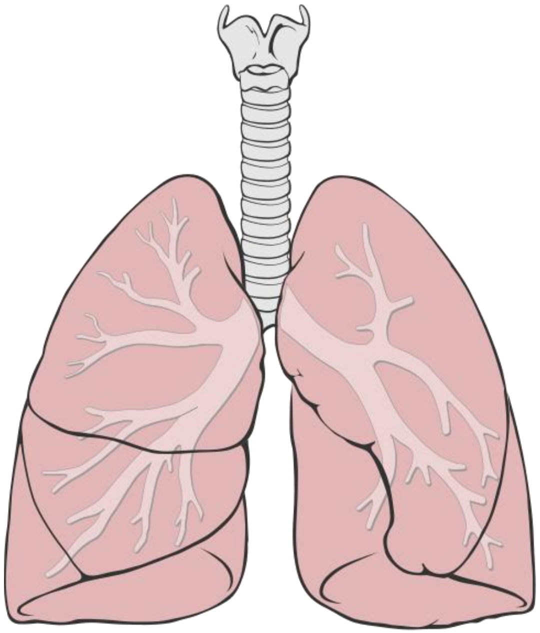
$$Vgas = \frac{Area * D * (P1 - P2)}{Thickness}$$

(vol/time)

- Surface area of alveoli falls in **emphysema**
- Diffusion distance (thickness) rises in:
  - **Pulmonary fibrosis**
  - **Pulmonary edema**
- Both lead to decreased diffusion → hypoxemia

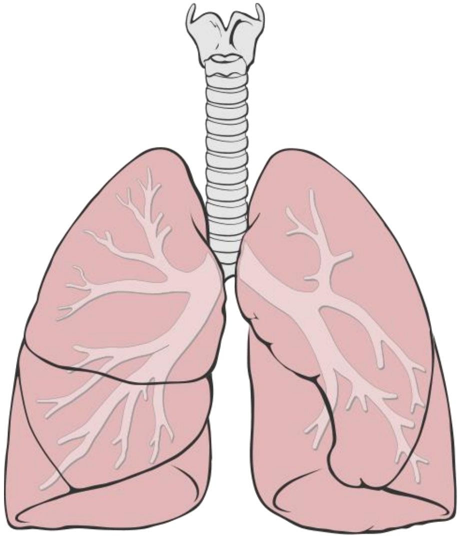
Ventilation-Perfusion Ratio

- V/Q ratio: alveolar ventilation/pulmonary blood flow
  - Matching critical for gas exchange
  - Unventilated or unperfused alveoli inefficient

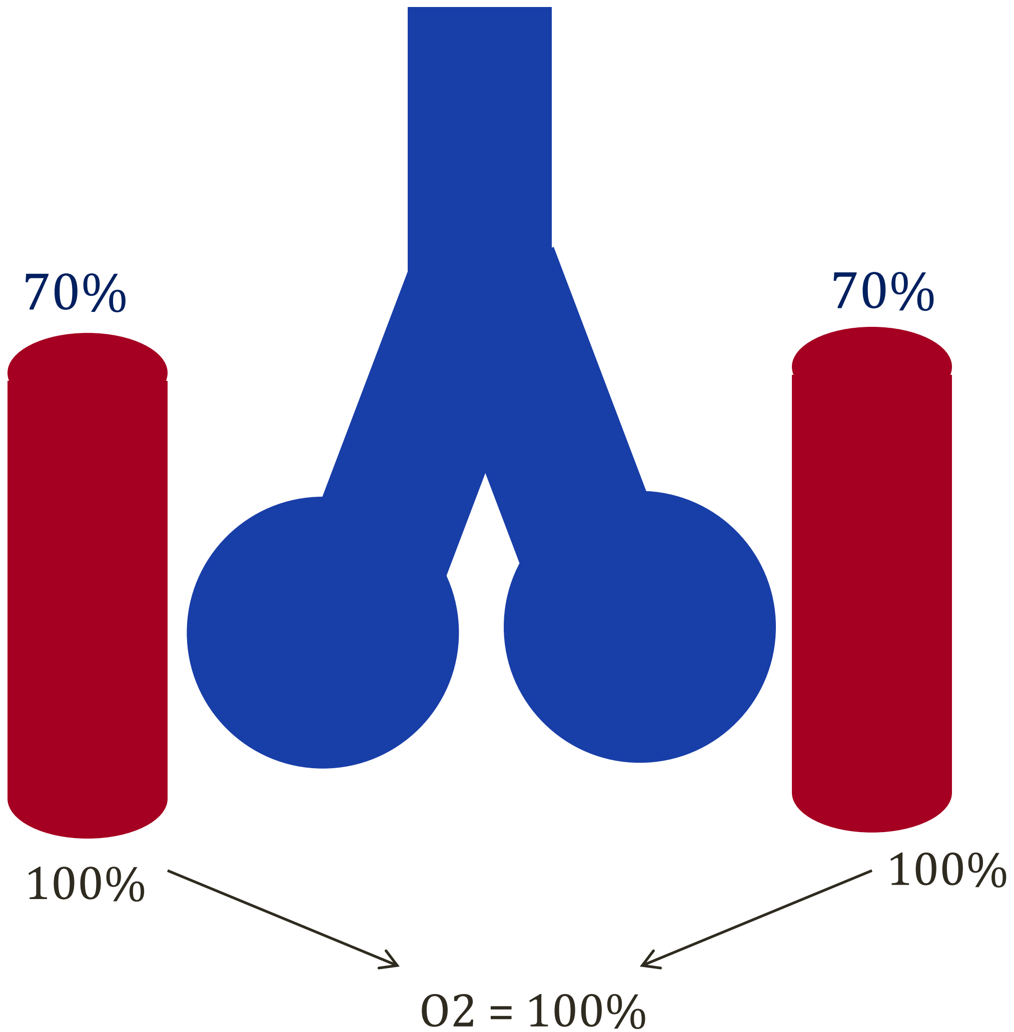


Shunting

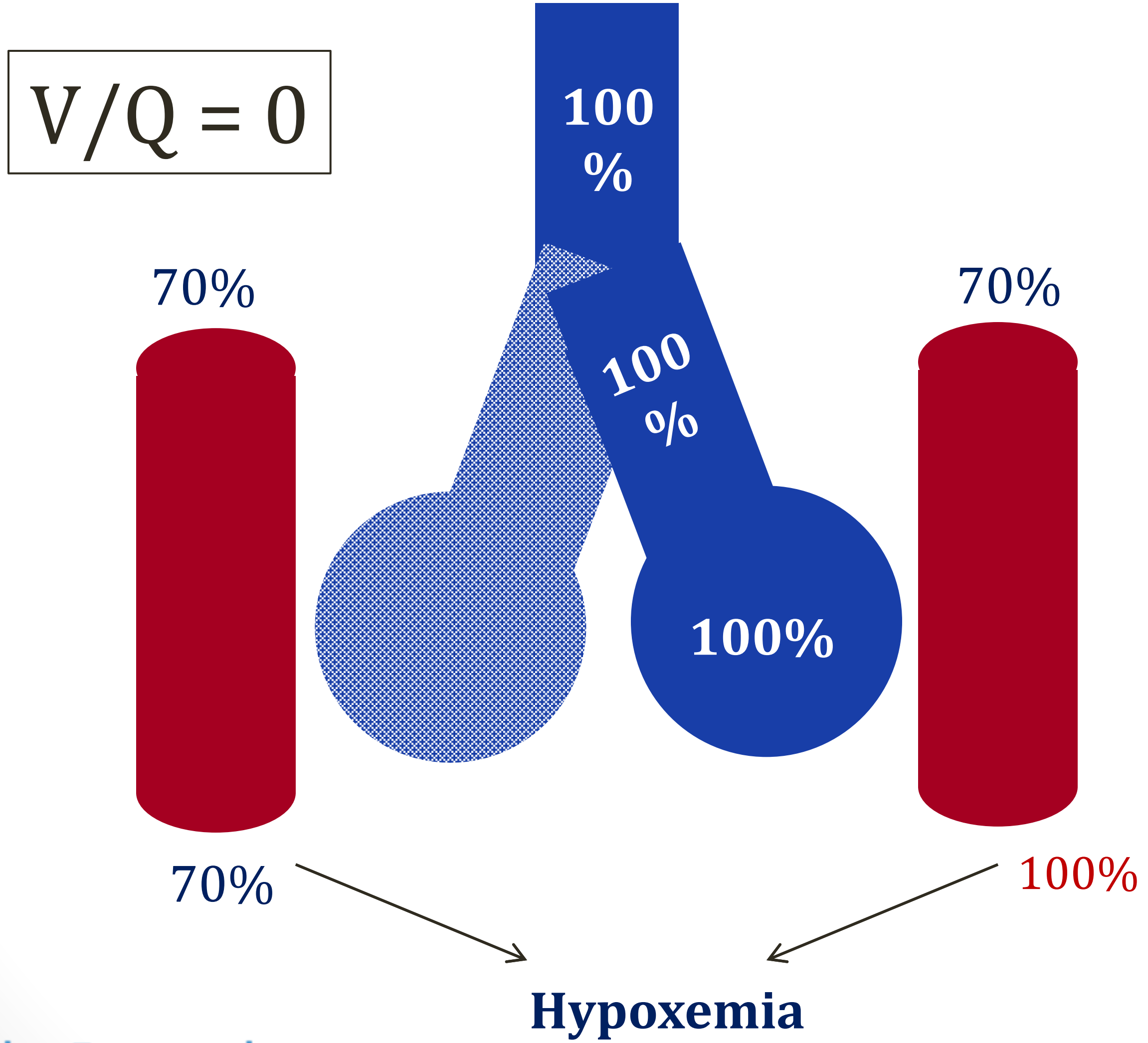
- No V
- Extreme reduction in V/Q
- **V/Q = 0**
- Venous blood to arterial system without oxygenation
- Causes **hypoxemia**



Shunting



Shunting

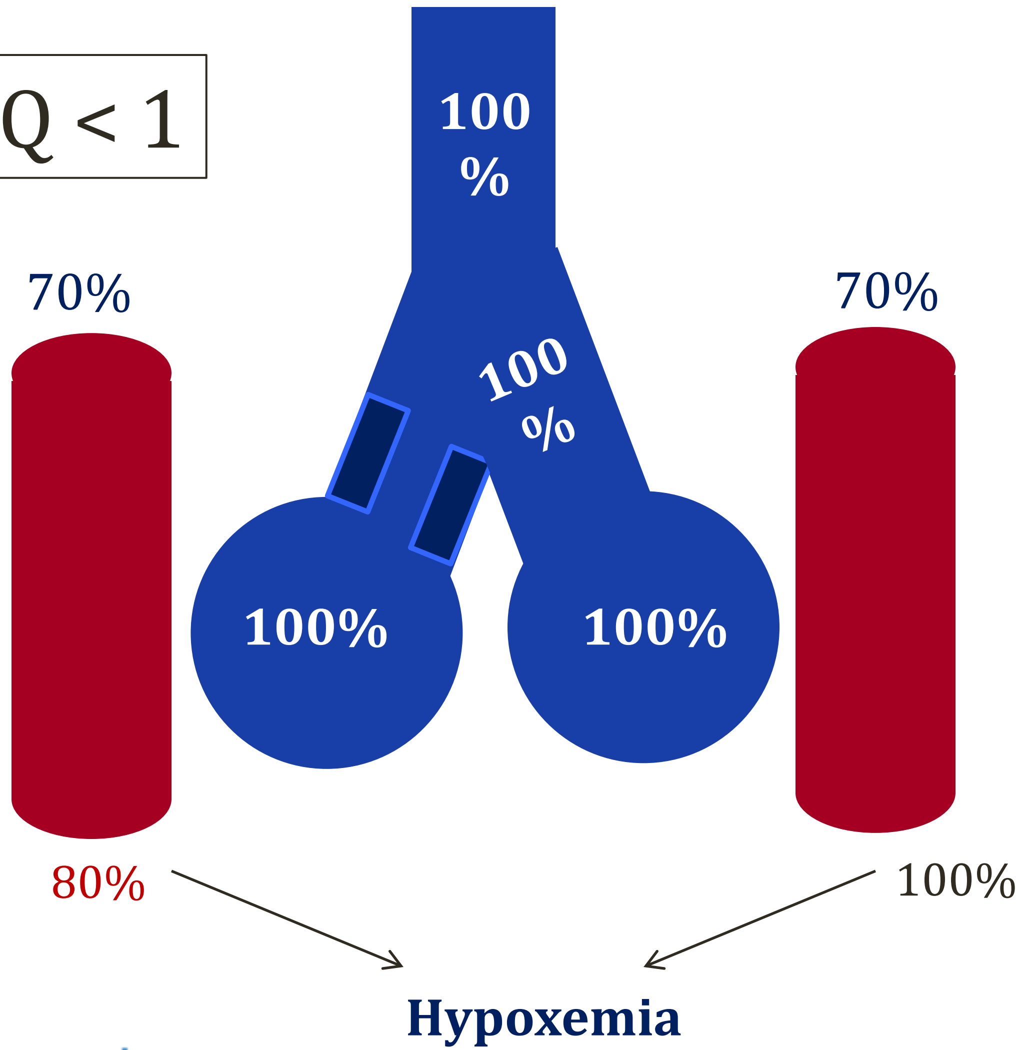


V/Q Mismatch

- V/Q <1
  - **Reduced ventilation** relative to perfusion
  - Perfusion wasted
  - Blood going where not enough O_2 present
  - Extreme version V/Q = 0 is shunt
- Hypoxemia with increased A-a gradient
- **Improves with oxygen**

V-Q Mismatch

V/Q < 1



Carbon Dioxide

- Causes of hypercapnia
  - Hypoventilation
  - Increased dead space
  - Increased CO_2 production
- Hypoxemia with high A-a gradient: **no ↑ CO_2**

Mechanisms of Hypoxemia

High A-a gradient

	PaO2	PaCO2	PaO2 using 100% O2
Diffusion Limitation	↓	--	↑
Shunt V/Q = 0	↓	--	No change
V/Q Mismatch	↓	--	↑

Mechanisms of Hypoxemia

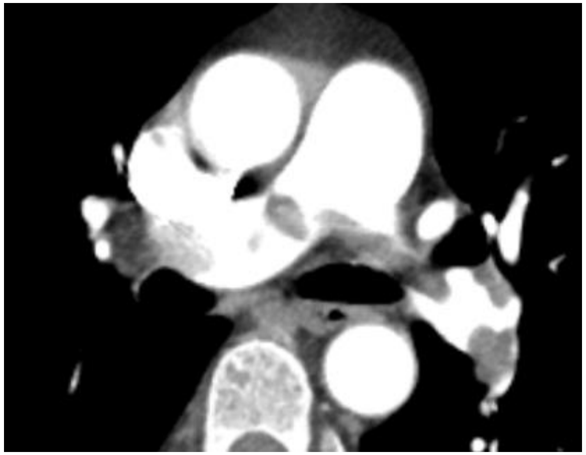
	PaO2	PAO2	A-a difference
Normal A-a Gradient	↓	↓	10-15
High A-a Gradient	↓	--	Increased

Mechanisms by Disease

- Most diseases (COPD, PNA, pulm edema) have hypoxemia from multiple mechanisms
  - PNA may cause V/Q mismatch or shunt
- Some examples worth knowing
  - Intra-cardiac shunt: pure shunt mechanism
  - Inhale a peanut: V/Q = 0 (also pure shunt)
  - Pulmonary Embolism

Pulmonary Embolism

- Obstructed blood flow
- **↑ dead space**
- Hypoxemia does occur in many patients
- **V/Q mismatch**
  - Blood flow forced through open vessels
  - Increased Q (working vessels)
  - Same V
  - Decreased V/Q (mismatch)

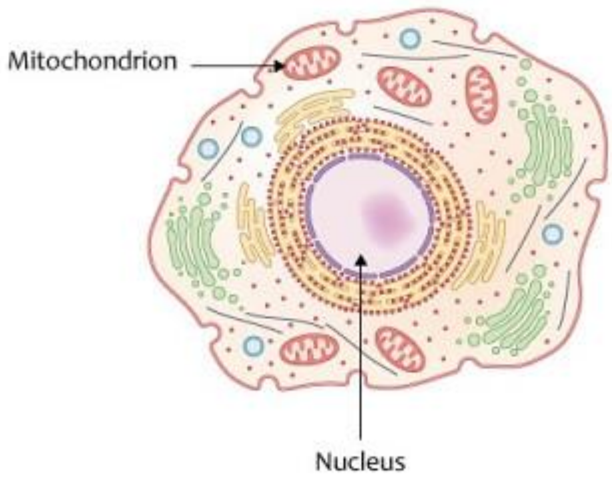


Carbon Dioxide

Jason Ryan, MD, MPH

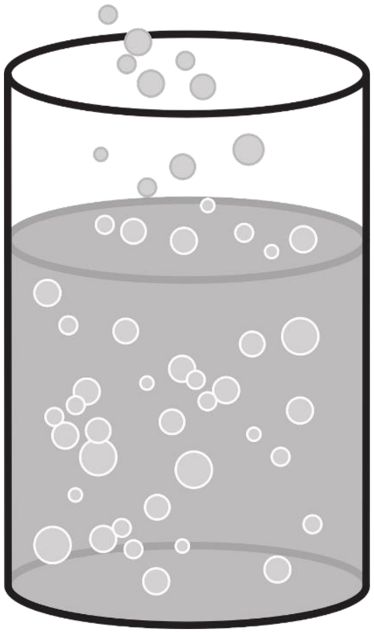
Carbon Dioxide

- Produced by **cellular metabolism**
- Transported to lungs via <u>three</u> mechanisms
  - Dissolved (5%)
  - Bound to hemoglobin (3%)
  - Bicarbonate (>90%)



Dissolved CO2

- Determined by **Henry's law**
- Pa_{CO2} x solubility = dissolved CO_2
- Very small amount (5%) total blood CO_2



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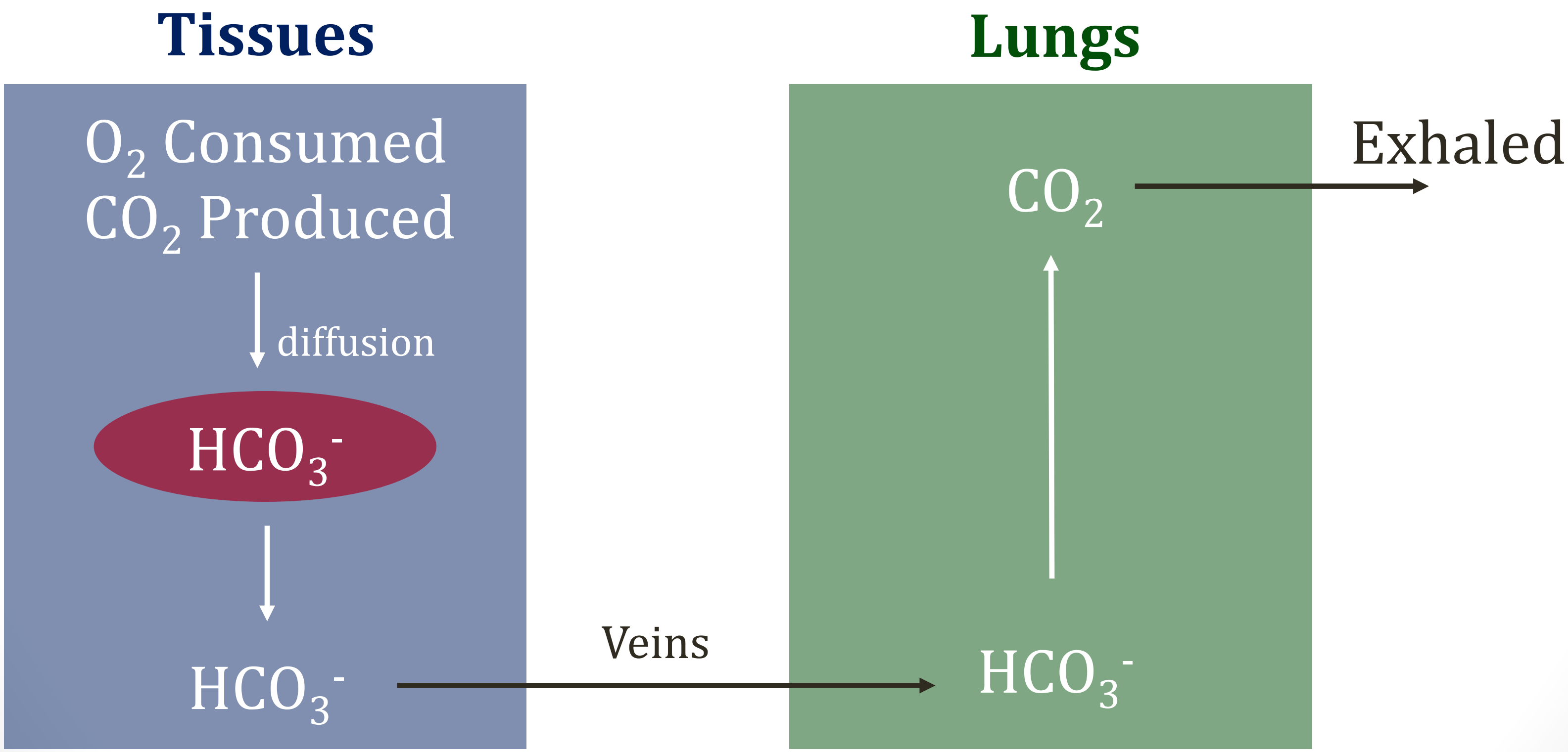
Bicarbonate

- Most (>90%) CO_2 exists as bicarbonate
- Carrier form of CO_2
- Red cells contain large amounts **carbonic anhydrase**
- Converts CO_2 to HCO_3^-

$$CO_2 + H_2O \Leftrightarrow H_2CO_3 \Leftrightarrow \mathbf{HCO_3^-} + H^+$$

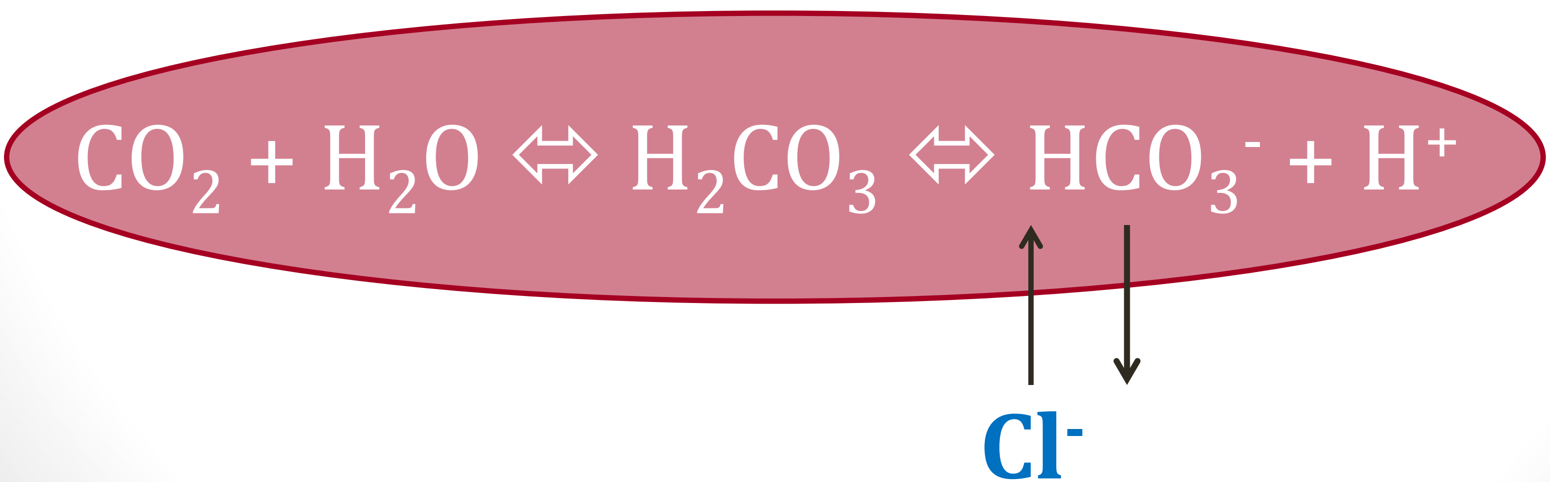
Bicarbonate

$$CO_2 + H_2O \Leftrightarrow H_2CO_3 \Leftrightarrow \mathbf{HCO_3^-} + H^+$$



RBC Bicarbonate Transport

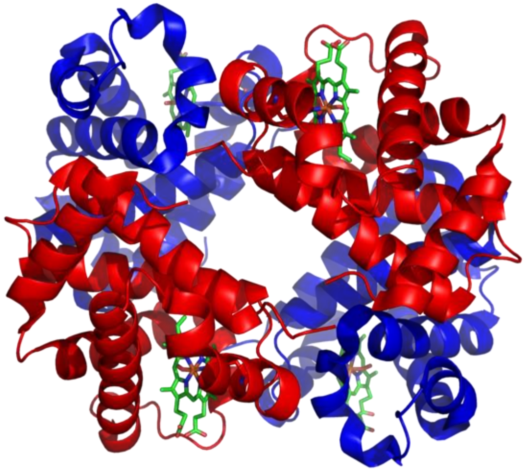
- HCO_3^- inside RBCs leaves cell to plasma
  - H+ remains in red cells
- **Chloride (Cl^-)** enters cell
  - Maintains electrical neutrality
  - "Chloride shift"
- RBCs have high Cl^- content in venous blood



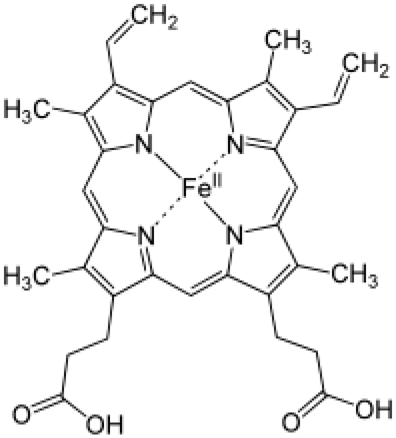
RBC Buffering H^+

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

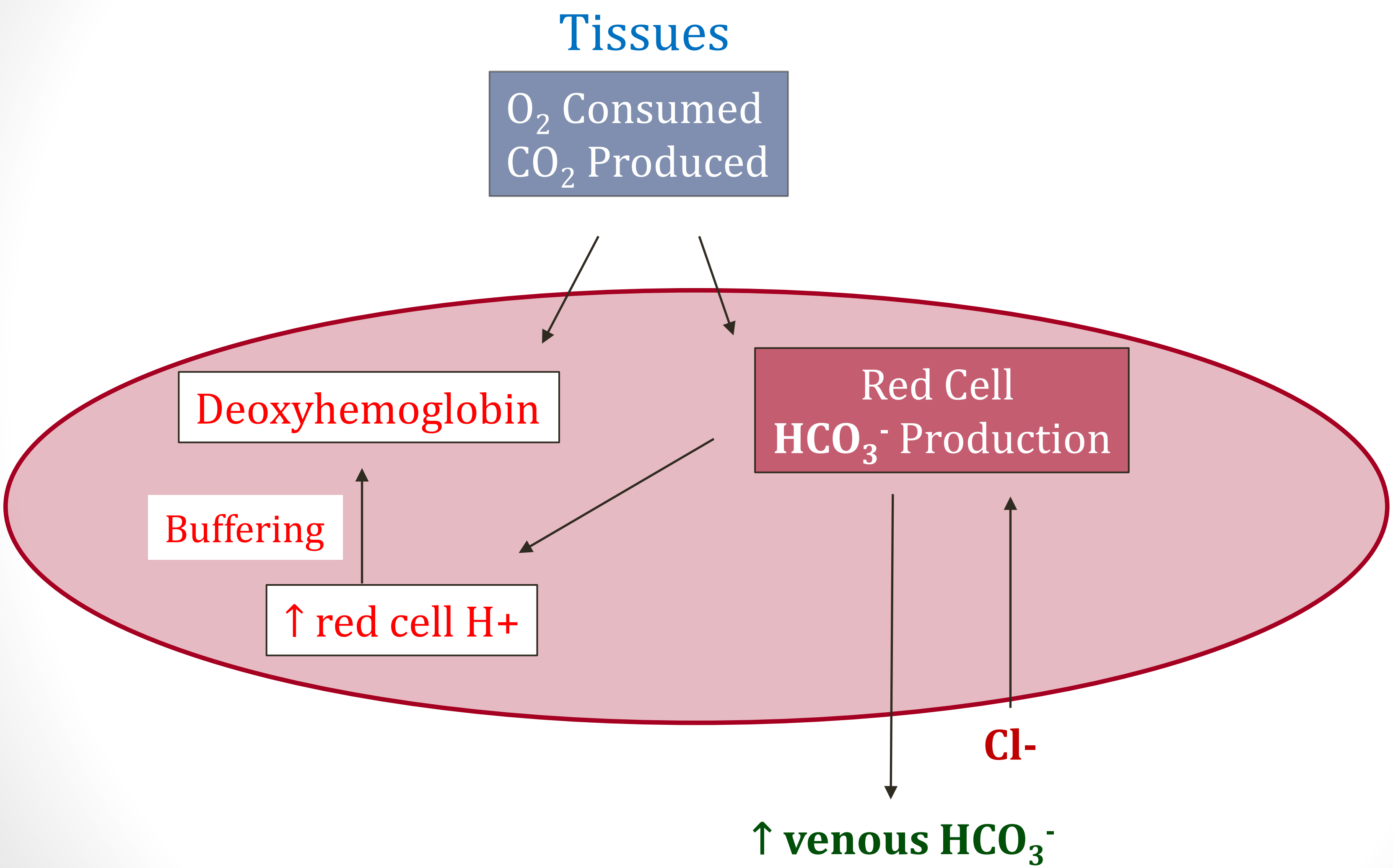
- H^+ produced when bicarbonate generated
  - Could cause dangerous fall in pH
- **Deoxyhemoglobin** buffers (absorbs) H^+ in red cells
  - ↑ deoxyhemoglobin in RBCs when ↑ CO_2
- Prevents H^+ from reducing pH



Richard Wheeler and Zephyris

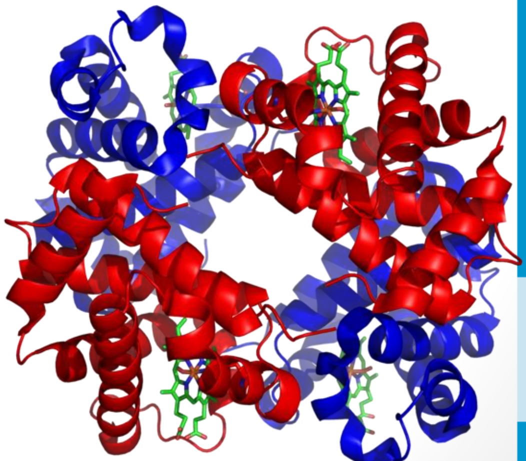


Bicarbonate



Carbaminohemoglobin

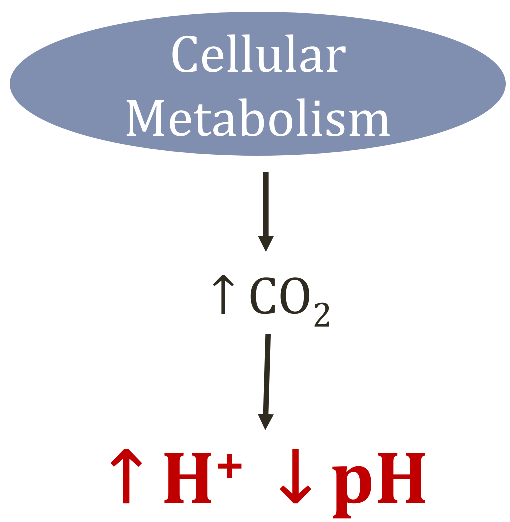
- Hemoglobin bound to CO_2
  - Binds at different site from O_2
- CO_2 binding alters affinity for oxygen
  - More CO_2 → More O_2 release
  - CO_2 decreases affinity for oxygen



Richard Wheeler and Zephyris

Bohr Effect

- CO_2 produced by metabolism → generates **H^+** in RBCs
  - $CO_2 + H_2O \Leftrightarrow H_2CO_3 \Leftrightarrow HCO_3^- + H^+$
- H^+ and low pH are ***indicators of metabolism***
- H^+ and low pH trigger **release of O_2** by hemoglobin



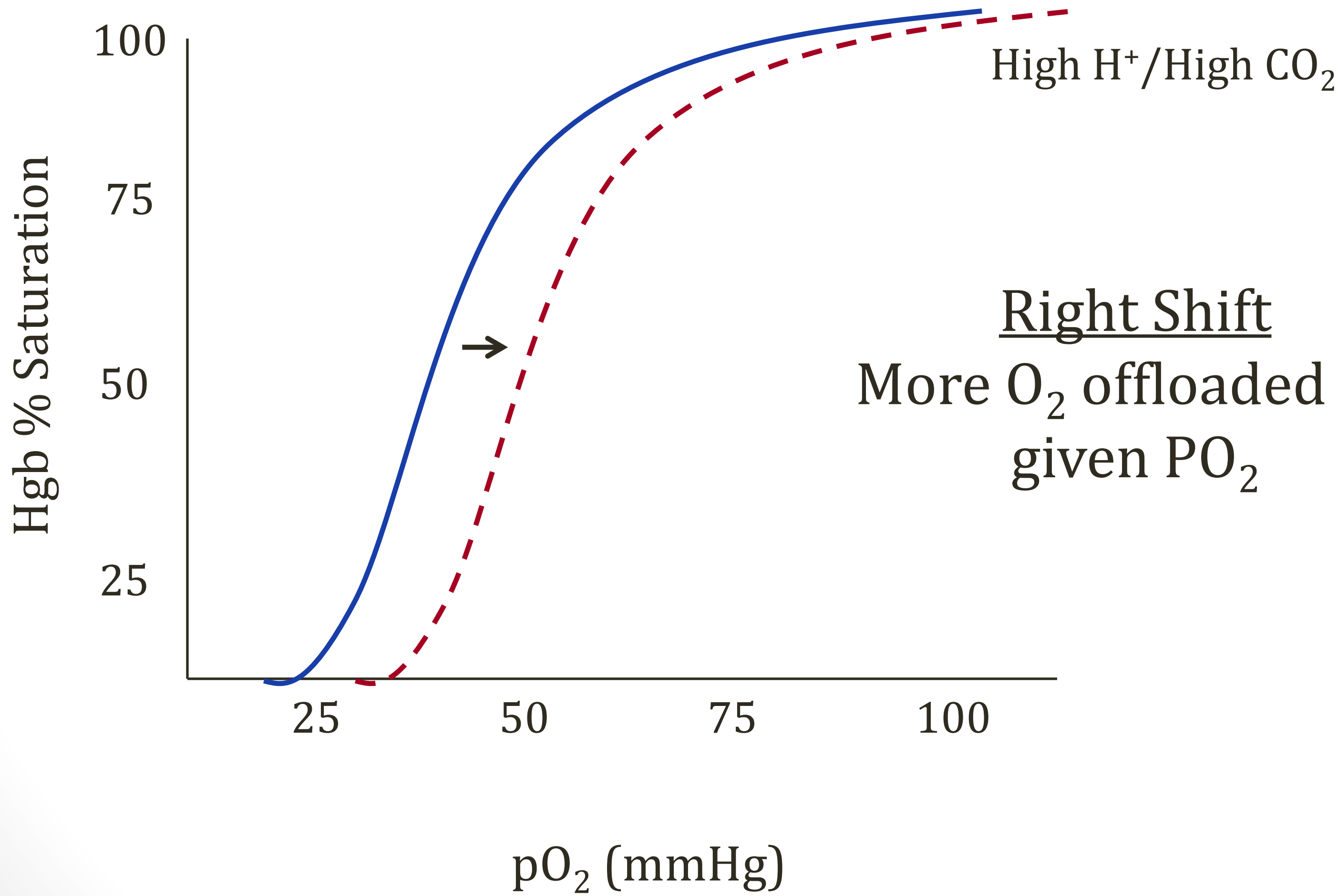
Bohr Effect

- Deoxyhemoglobin has high affinity for H^+
- H^+ binds hemoglobin in low O_2/high CO_2 areas
- Converts Hgb to "taut form" which releases O_2
  - Shifts O_2 curve to right
- Hemoglobin **releases more oxygen**

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

Bohr Effect ← Hgb

Bohr Effect

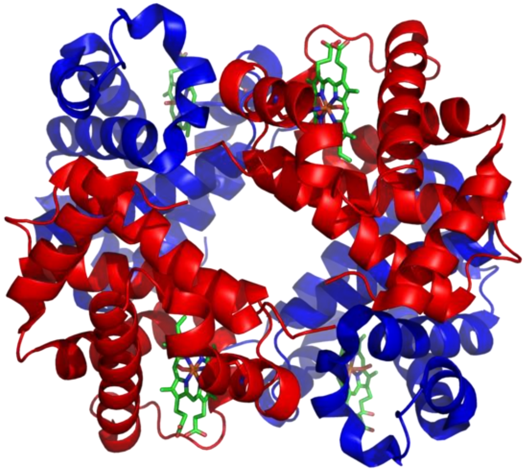


<u>Right Shift</u>

More O_2 offloaded for given PO_2

Haldane Effect

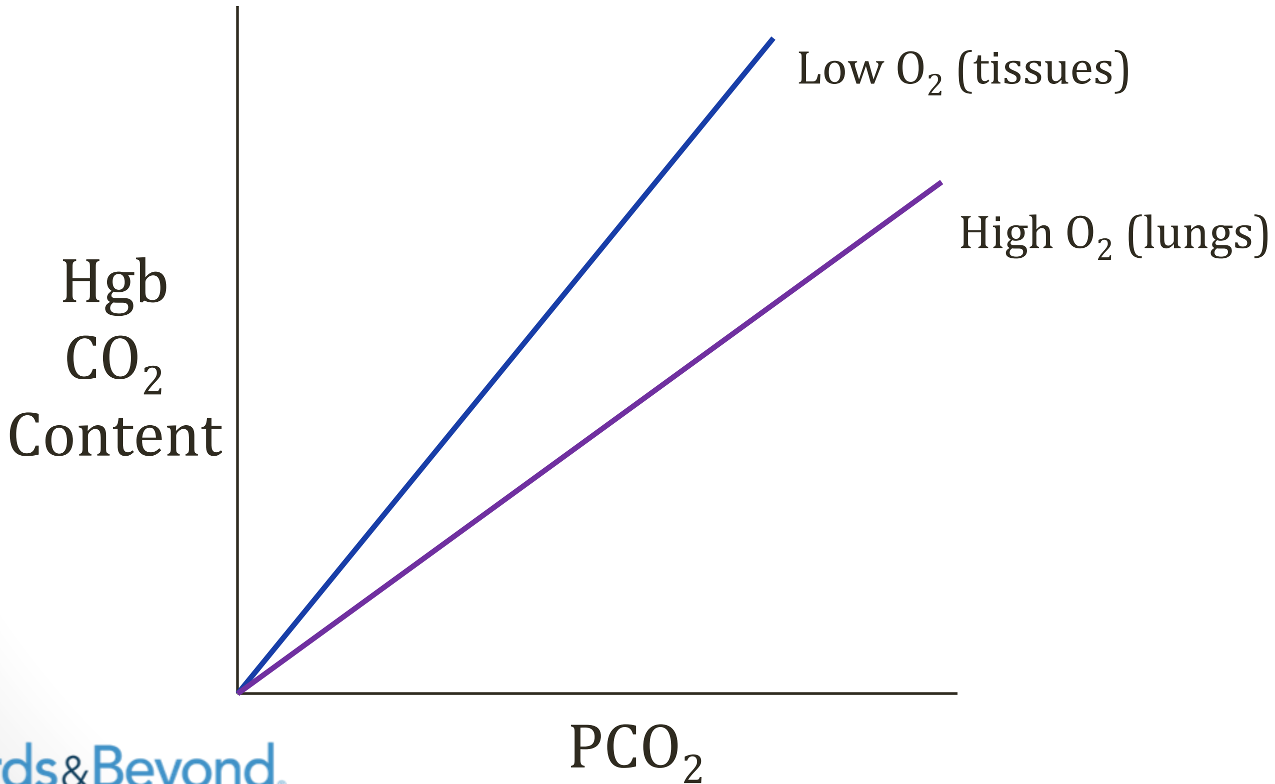
- O_2 binding alters **affinity for CO_2**
  - Low O_2 environment Hgb binds more CO_2
  - High O_2 environment Hgb binds *less* CO_2



Richard Wheeler and Zephyris

Haldane Effect

- Deoxyhemoglobin binds more CO_2
  - Allows more CO_2 loading with O_2 consumption
  - Allows more CO_2 unloading with high O_2



Tissues versus Lungs

Tissues

- Low O_2 (consumption)
- High CO_2 (metabolism)
- High H^+
- Low pH
- Favors O_2 unloading
  - Bohr Effect
- Favors CO_2 loading
  - Haldane Effect

Lungs

- High O_2 (air)
- Low CO_2 (exhalation)
- Low H^+
- High pH
- Favors O_2 loading
  - Bohr Effect
- Favors CO_2 unloading
  - Haldane Effect

CO_2 Transport

	Lungs/Arteries	Tissues/Veins
P_{O2}	100	↓
P_{CO2}	40	↑
HCO_3^-	24	↑
pH	7.4	↓
Deoxyhemoglobin	↓	↑
Red cell Cl^-	↓	↑
Dissolved CO2	↓	↑
Carbaminohemoglobin	↓	↑

High Altitude

- Lower atmospheric pressure
- Lower pO_2
- Hypoxia → hyperventilation
- ↓pCO_2 → respiratory alkalosis (pH rises)
- After 24-48hrs, kidneys will excrete HCO_3^-
- pH will fall back toward normal

pH ↑
pO_2 ↓
pCO_2 ↓
HCO_3^- ↓

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Exercise

- ↑ O_2 consumption
- ↑ CO_2 production
- ↑ Ventilation

William Warby/Flikr

Exercise

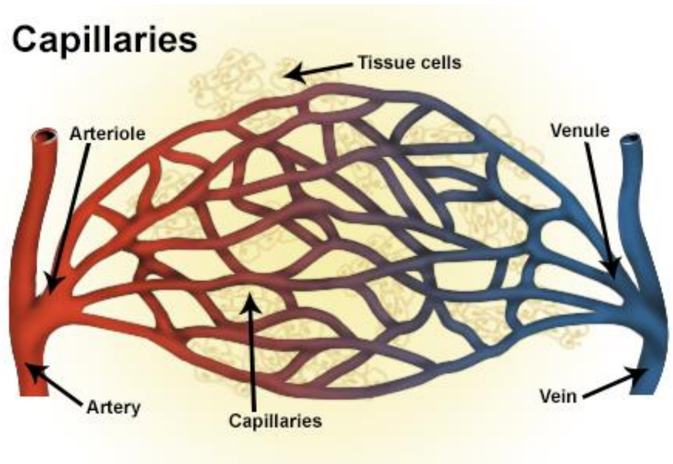
- More CO_2 produced by muscles
- CO_2 levels in *venous* blood rise
- More O_2 consumed by muscles
- O_2 levels in *venous* blood fall

William Warby/Flikr

Exercise

- ↑ ventilation and blood flow
- Normal PaO_2 and $PaCO_2$ despite metabolic changes

<u>Veins</u>: O2 falls, CO2 rises
<u>Arteries</u>: O2 and CO2 normal



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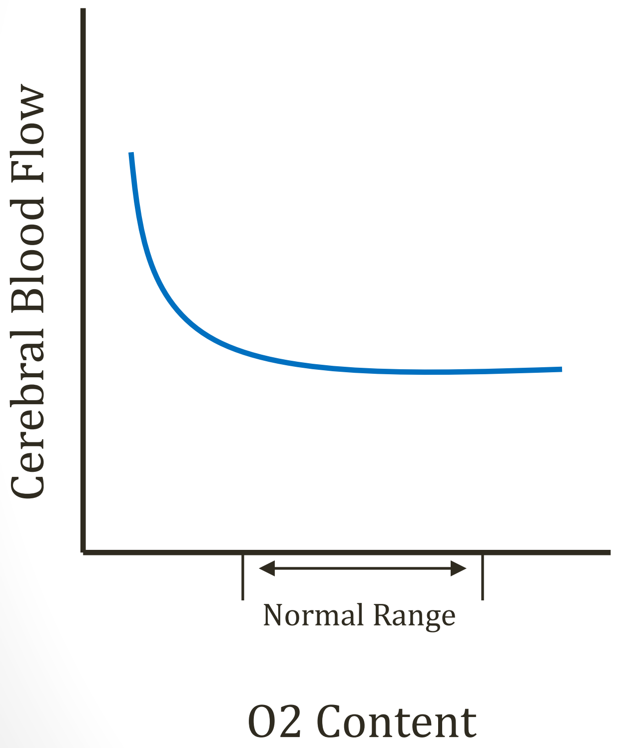
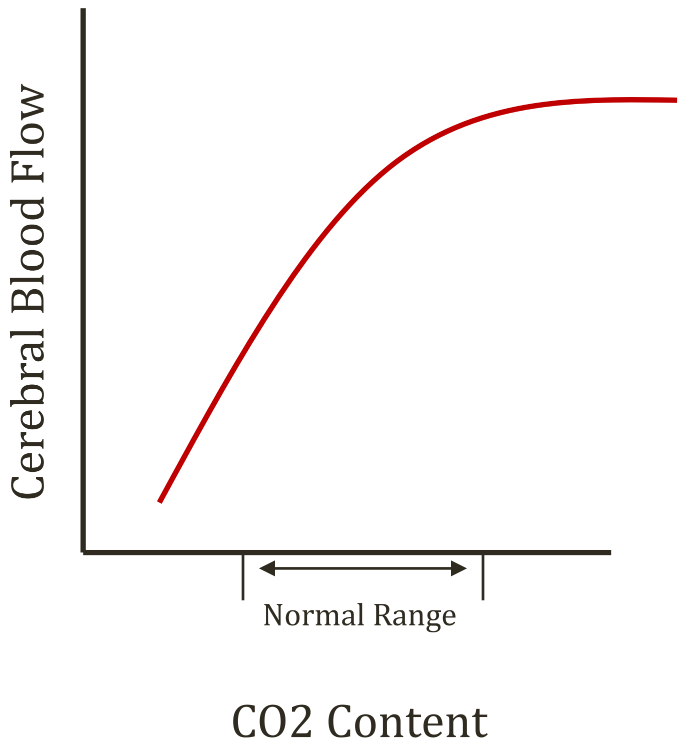
Cerebral Blood Flow





Panic Attacks

- Hyperventilation
- Low CO_2
- Hypocapnia → cerebral vasoconstriction
- CNS symptoms (dizziness, blurred vision)

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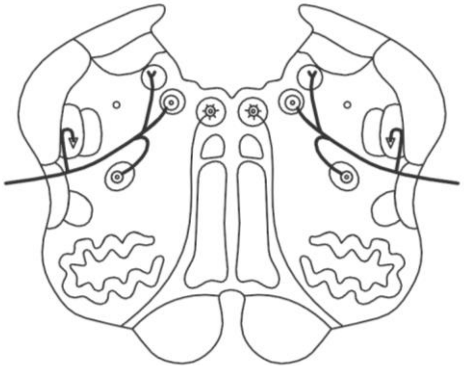
CO_2 and Breathing Control

- $PaCO_2$ is the major stimulus for breathing
- Central chemoreceptors in **medulla** most important
- Peripheral chemoreceptors: carotid and aortic bodies
  - Sense CO_2 but more sensitive to O_2
- High Pa_{CO2} → increased respiratory rate
- Low Pa_{CO2} → decreased respiratory rate



Medulla

CO_2 and Breathing Control

- COPD patients: chronic retention of CO_2
  - Lose sensitivity to CO_2
  - Oxygen becomes major breathing stimulus
- Excess oxygen therapy given → hypoventilation
- Theory: response to CO_2 blunted
  - Respiratory depression with high O_2
- New data indicates more complex
  - Haldane effect

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CO_2 and Breathing Control

- CO_2 level useful to determine **ventilation status**
  - High CO_2 : hypoventilation
  - Low CO_2 : hyperventilation
- Clinical scenario:
  - Patient with pneumonia
  - O_2 applied via nasal cannula
  - O_2 level 95%
  - Blood gas: $PaCO_2$ = 60mmHg (high)

CO_2 and Breathing Control

- Clinical scenario
  - Patient with neuromuscular disease (ALS)
  - O_2 saturation on O_2 95%
  - Blood gas: $PaCO_2$ = 60 (high)
  - Respiratory muscles failing
- Symptoms of hypercapnia (high CO_2)
  - Lethargy
  - Confusion
  - Agitation

Lung Physical Exam

Jason Ryan, MD, MPH

Lung Exam

- Percussion
  - Finger against thorax → tap
- Auscultation
  - Stethoscope thorax
  - Upper, mid, lower lung fields
- Special techniques
  - Fremitus
  - Pectoriloquy

Percussion

- Normal sounds = resonant
- Abnormal: dull or hyperresonant
- Dull
  - Pleural effusion
  - Consolidation (pneumonia)
- Hyperresonant → air trapped
  - Pneumothorax
  - Emphysema

Lung Auscultation

- Normal breath sounds are vesicular
- Most all pathologic lung processes result in decreased lung sounds over affected area

Adventitious Lung Sounds

- Rales
- Wheezes
- Rhonchi
- Bronchial breath sounds
- Stridor

Rales

- Also called crackles
- Small airways "pop" open after collapse
- Early inspiratory, late inspiratory or expiratory
- Classic causes
  - Pulmonary edema (bases)
  - Pneumonia
  - Interstitial fibrosis

Wheezes

- Air flows through narrowed bronchi
- Usually expiratory or inspiratory/expiratory
- Classic cause is asthma
- Other causes:
  - Heart failure (cardiac asthma)
  - Chronic bronchitis
  - Obstruction (tumor; localized wheeze)

Rhonchi

- Secretions in large airways
- Coarse breath sounds
- Classic cause is COPD

Bronchial Breath Sounds

- High pitched lung sounds
- Like flow through tube
- Longer expiratory phase than normal
- Seen in pneumonia with consolidation

Stridor

- Wheeze that is almost entirely inspiratory
- Usually loudest over neck
- Indicates partial obstruction of larynx or trachea
- Some classic causes
  - Laryngotracheitis (croup)
  - Epiglottitis (Hib in children)
  - Retropharyngeal abscess
  - Diphtheria

Pectoriloquy

- Sounds over chest through stethoscope
- Bronchophony
  - Voice sounds are louder and clearer
- Whispered pectoriloquy
  - Whispered "99-99-99"
  - Should be muffled
  - Abnormal if clear
- Egophony: "Eeeeee" sounds like "Aaaay"
- All indicated fluid in lungs: Effusion, consolidation

Fremitus

- Place hands on patients back
- Patient says "ninety-nine"
- Vibrations travel through airways to back
- Varies with density of lung tissue
- Only common condition with increased fremitus is lobar pneumonia
- Decreased in most other processes
  - Pleural effusion
  - Pneumothorax
  - Atelectasis

Nail Clubbing

- Associated with many pulmonary diseases
- Bronchiectasis
- Cystic Fibrosis
- Lung tumors
- Pulmonary fibrosis
- Also cyanotic congenital heart disease

Image courtesy of James Heilman, MD

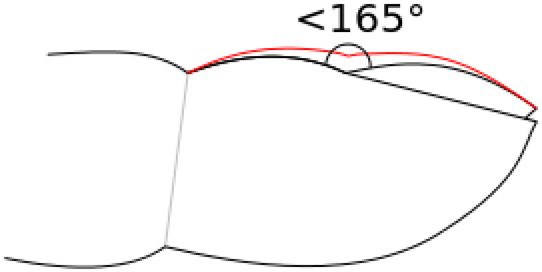


Image courtesy of Jfdwolff

Pulmonary Function Tests

Jason Ryan, MD, MPH

Dyspnea

- Many, many causes
- Deconditioning
- Cardiac causes
- Anemia
- Pulmonary causes

Pulmonary Dyspnea

- Obstruction
  - Can't get air out of lungs
  - Air trapped
  - Poor oxygenation
- Restriction
  - Can't get air into lungs
  - Poor oxygenation

Pulmonary Function Testing

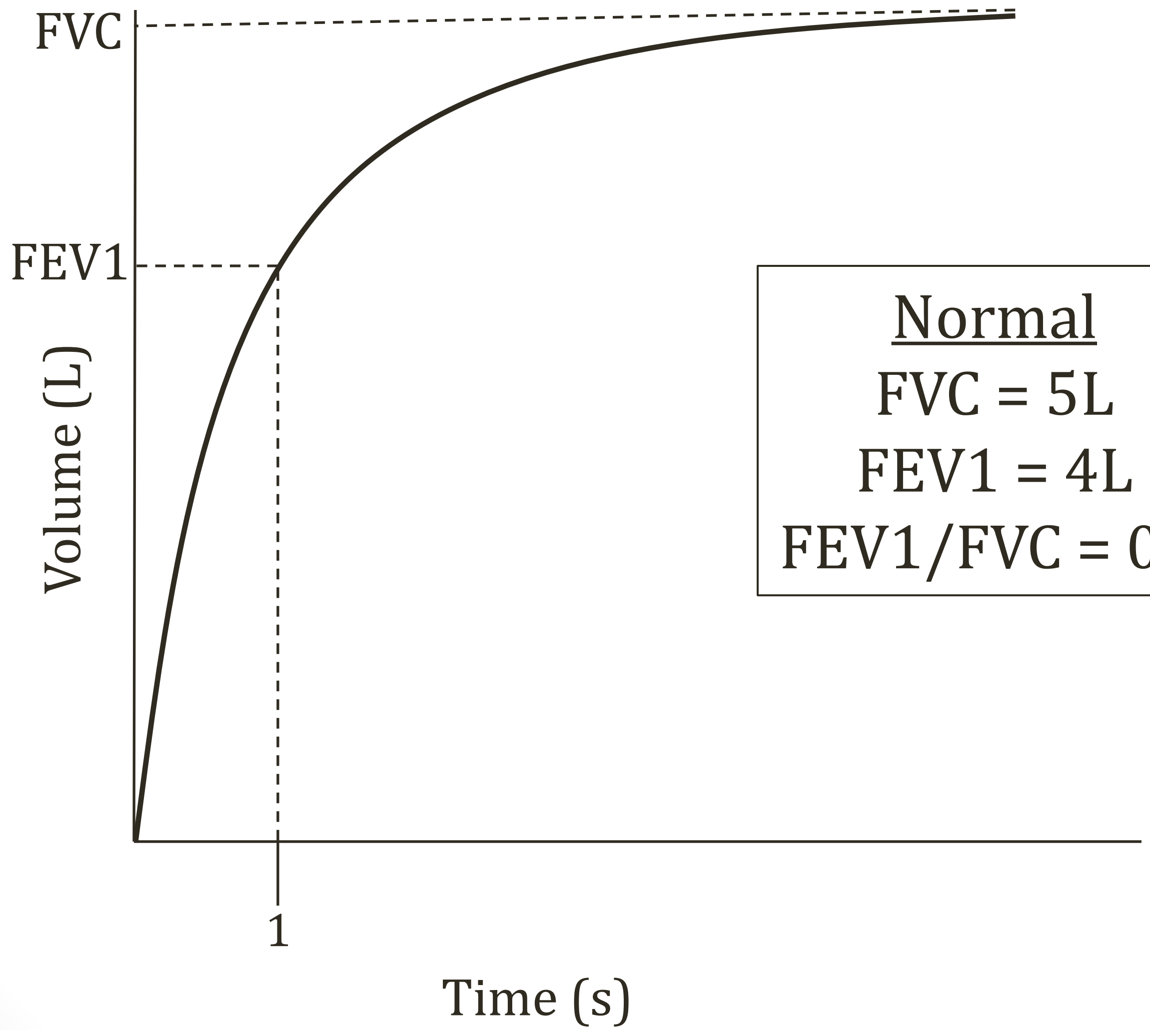
- Determining flows, volumes in lung
- Helps determine cause of dyspnea
  - Sometimes unclear from history, exam, x-ray, etc.
- Helps determine disease severity/progression
  - Many diseases monitored by PFTs
  - COPD, Pulmonary Fibrosis

Spirometry

- Method for assessing pulmonary function
  - Pulmonary function tests (PFTs)
- Patient blows into machine
- Volume of air measured over time

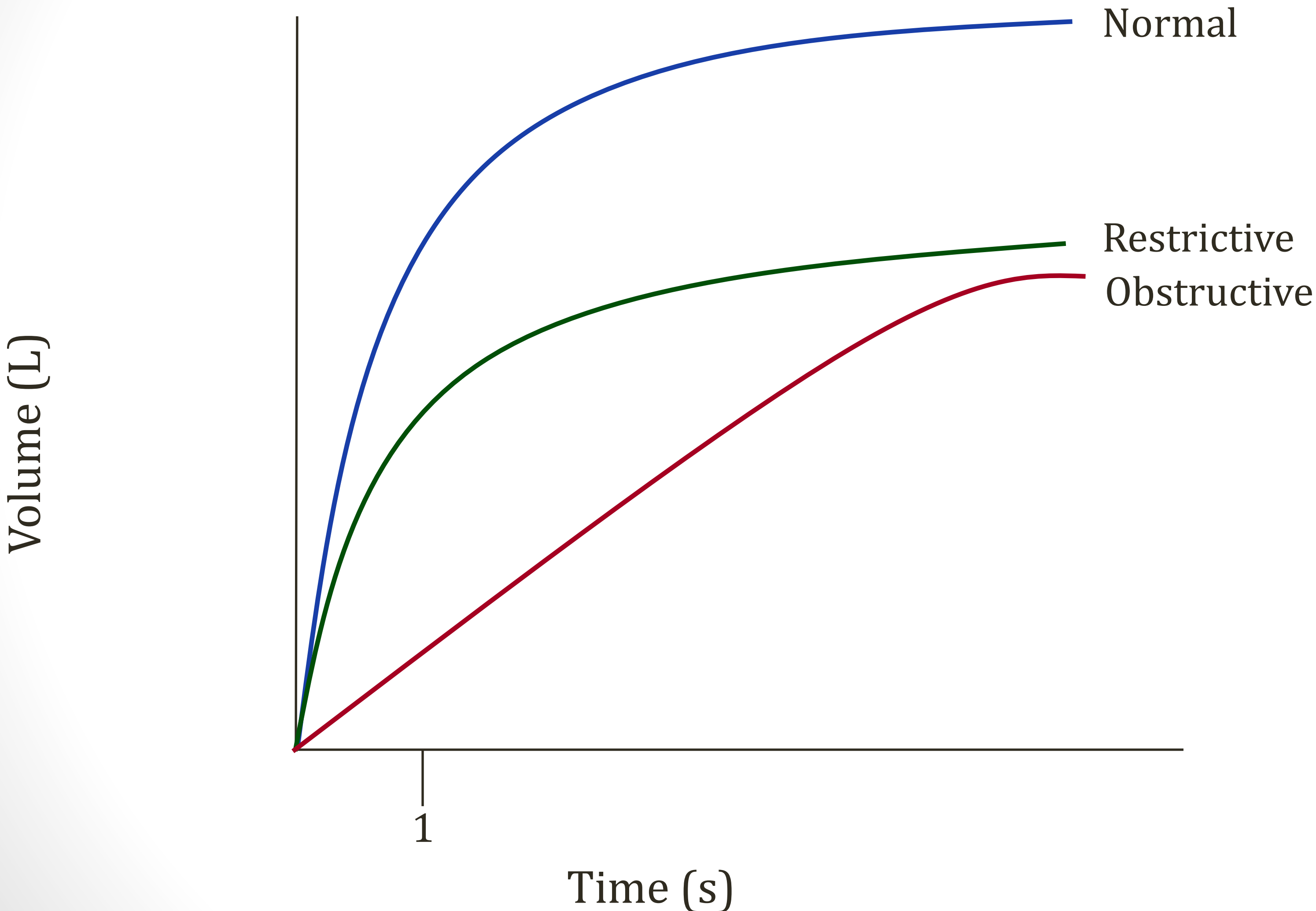
Image courtesy of Jmarchn

Spirometry

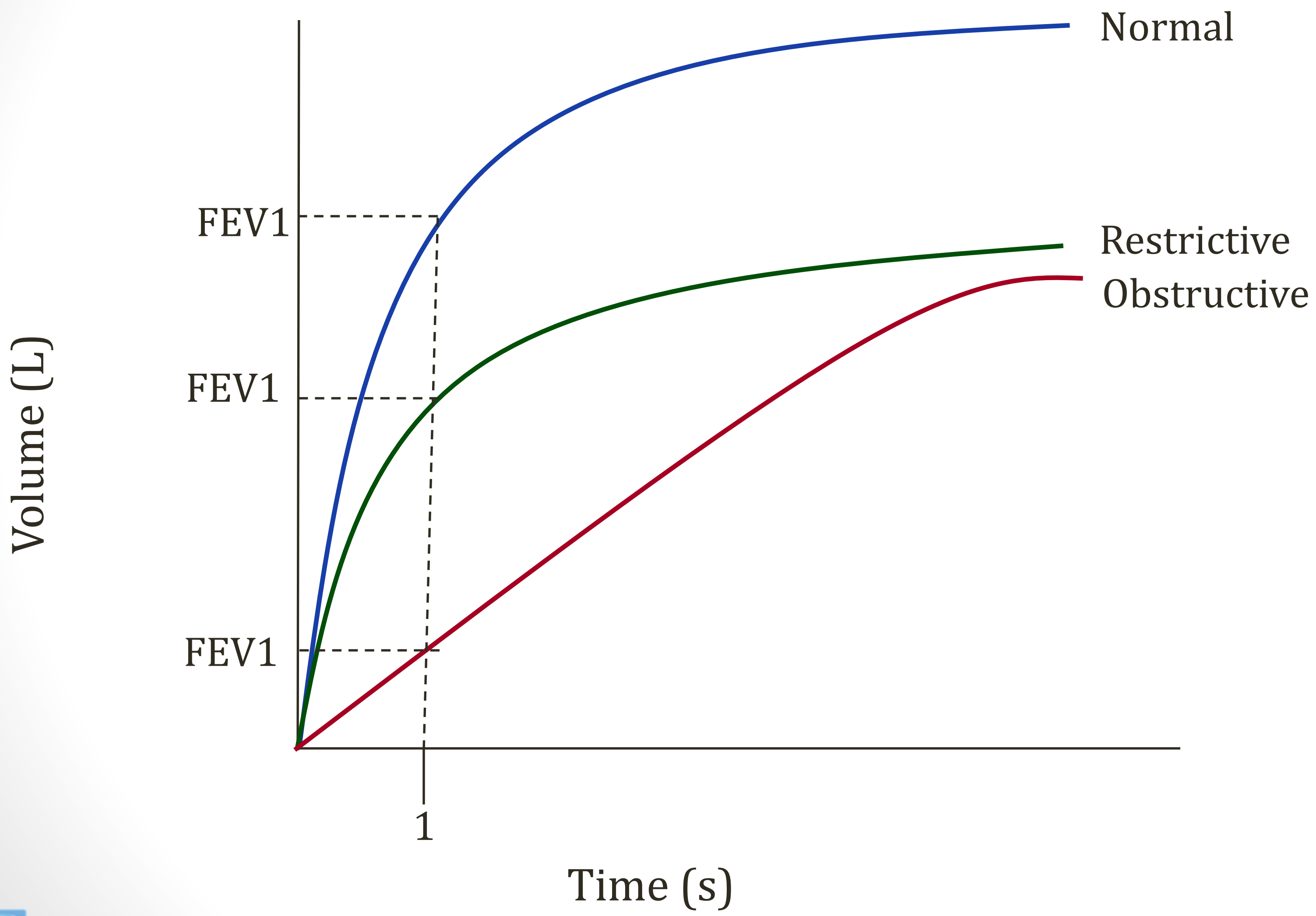


Normal
FVC = 5L
FEV1 = 4L
FEV1/FVC = 0.8

Spirometry

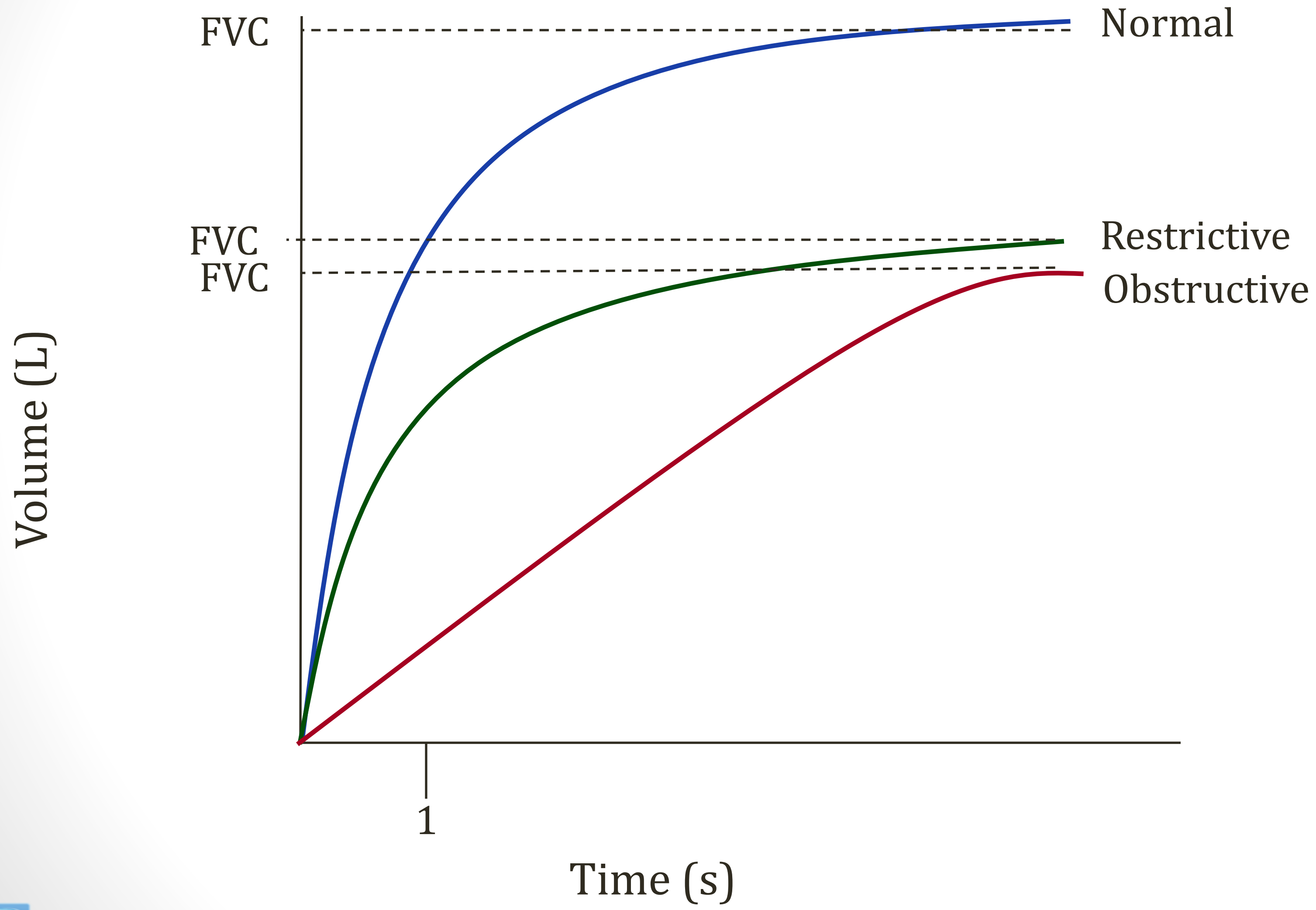


Spirometry



Normal
Restrictive
Obstructive
FEV1
FEV1
FEV1
Volume (L)
1
Time (s)

Spirometry


FVC
Normal
FVC
Restrictive
FVC
Obstructive
Volume (L)
1
Time (s)

Summary

- FEV1 and FVC fall in both obstructive and restrictive diseases
- FEV1 falls MORE than FVC in obstructive

	FEV1	FVC	FEV1/FVC
Obstructive	↓↓	↓	↓
Restrictive	↓	↓	>80%

Volumes

- Spirometry can measure
  - VC (FVC)
  - IRV
  - ERV
- Cannot measure
  - RV
  - FRC
- Residual volume rarely measured clinically
- Requires special techniques

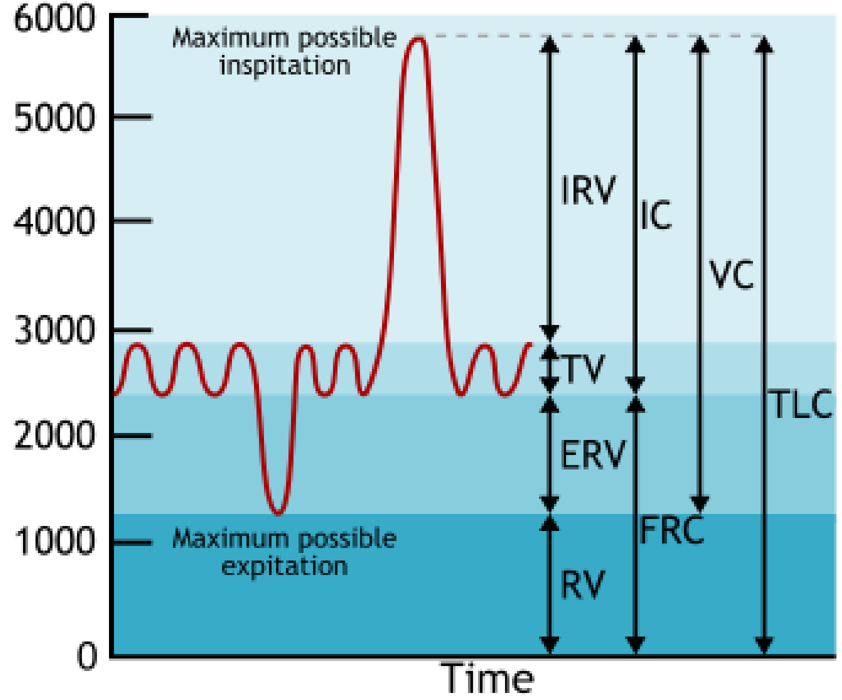
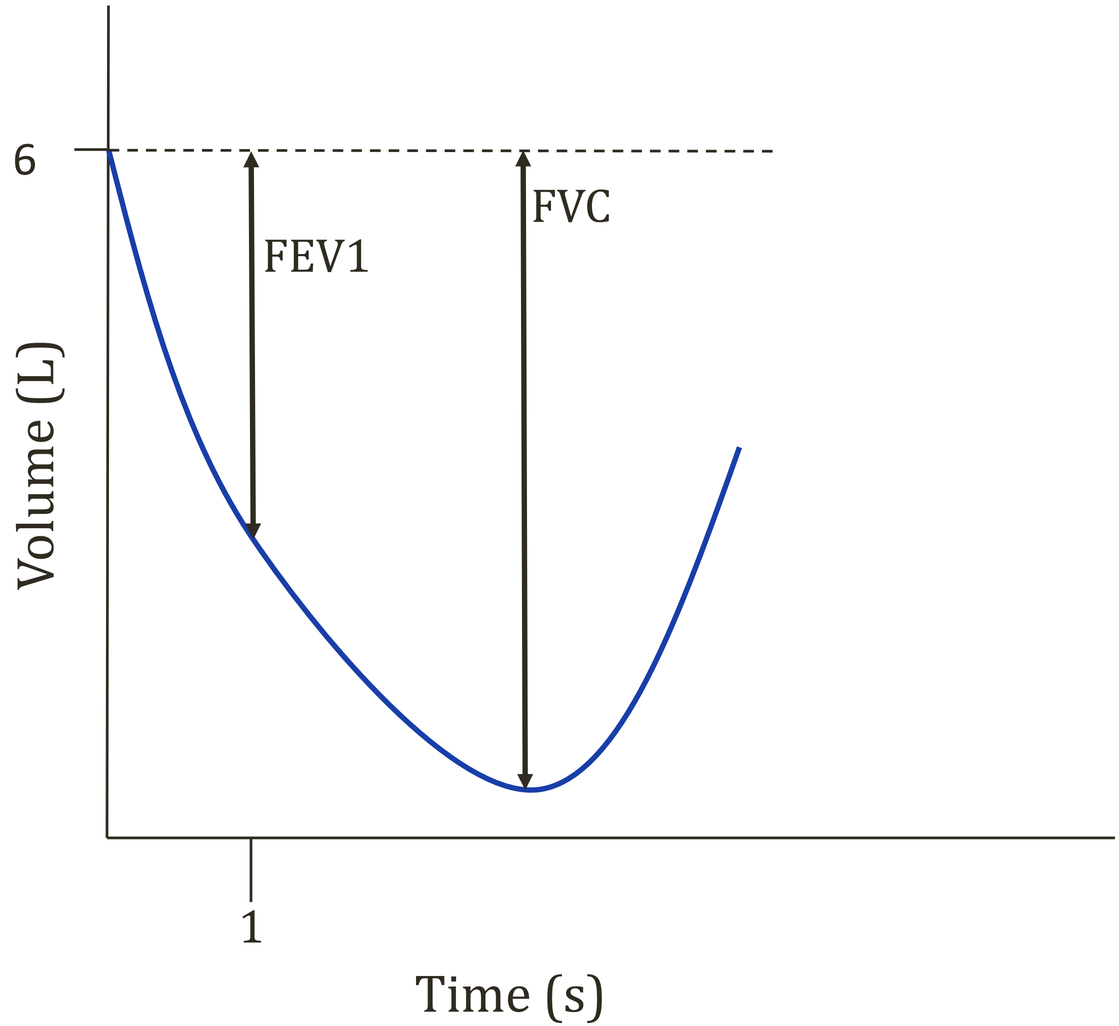
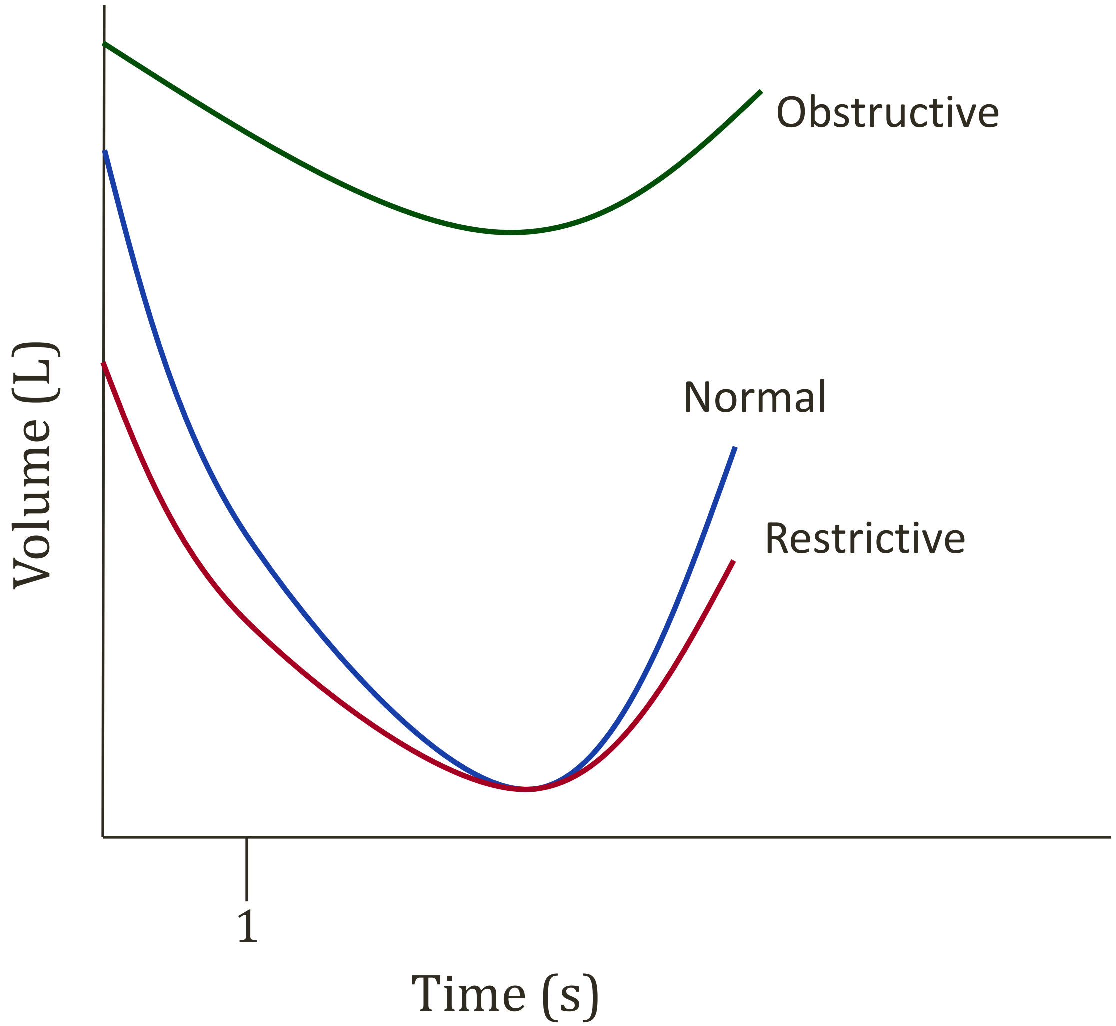


Image courtesy of Michal Komorniczak, Medical Illustrations

Spirometry with Volumes



Spirometry with Volumes



Flow Volume Loop

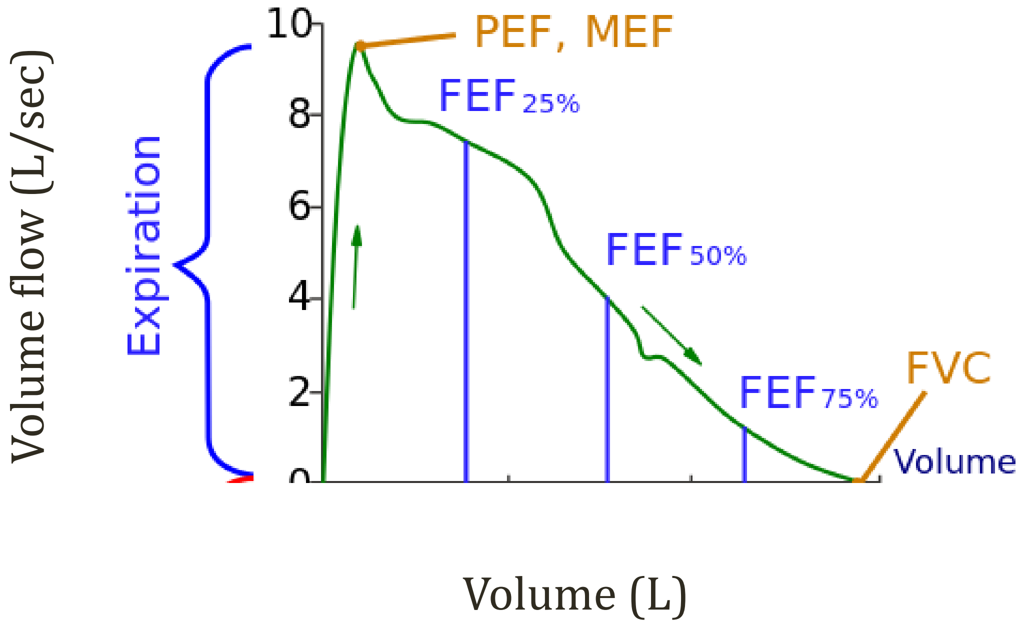


Image courtesy of SPhotographer

Flow Volume Loop

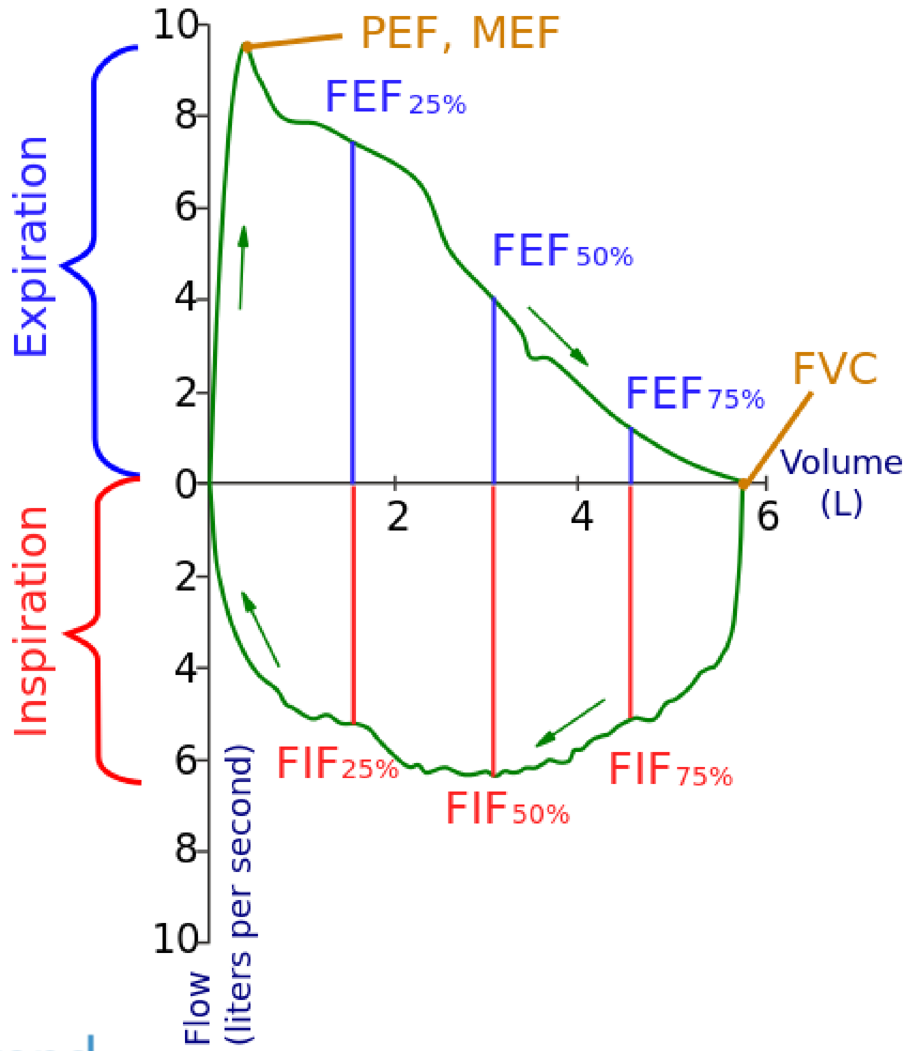


Image courtesy of SPhotographer

Flow Volume Loops

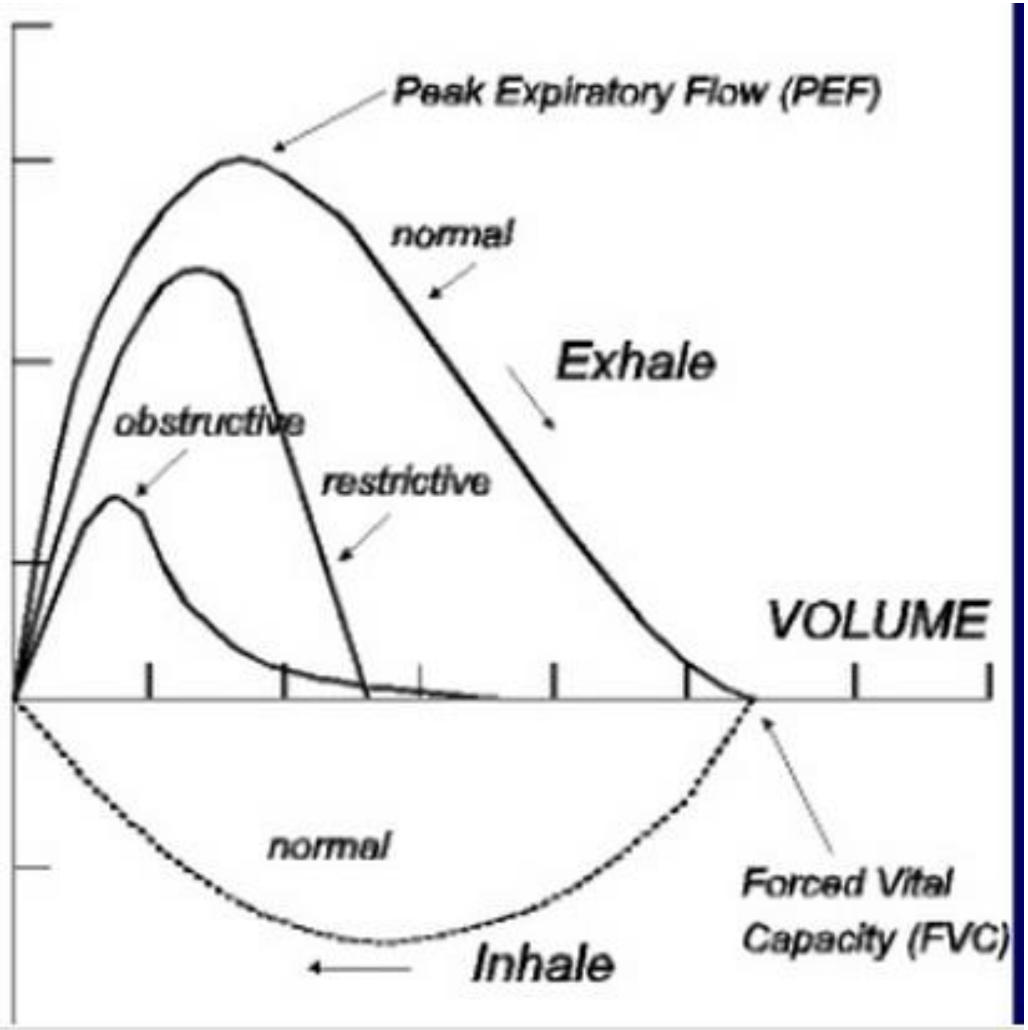


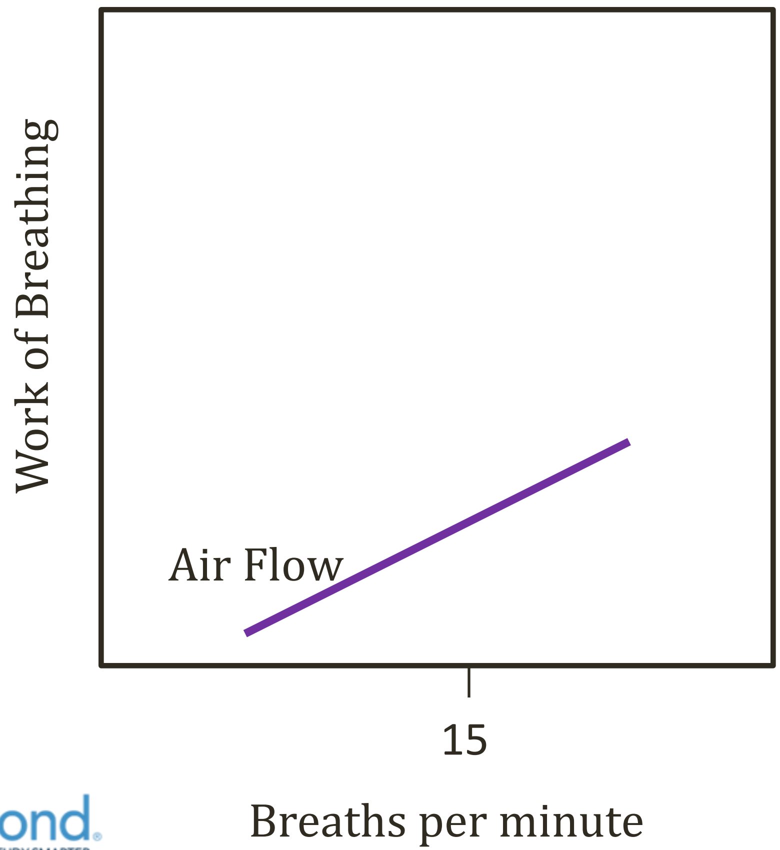
Image courtesy of Yaser Ammar,

Work of Breathing

- Work proportional to resistance

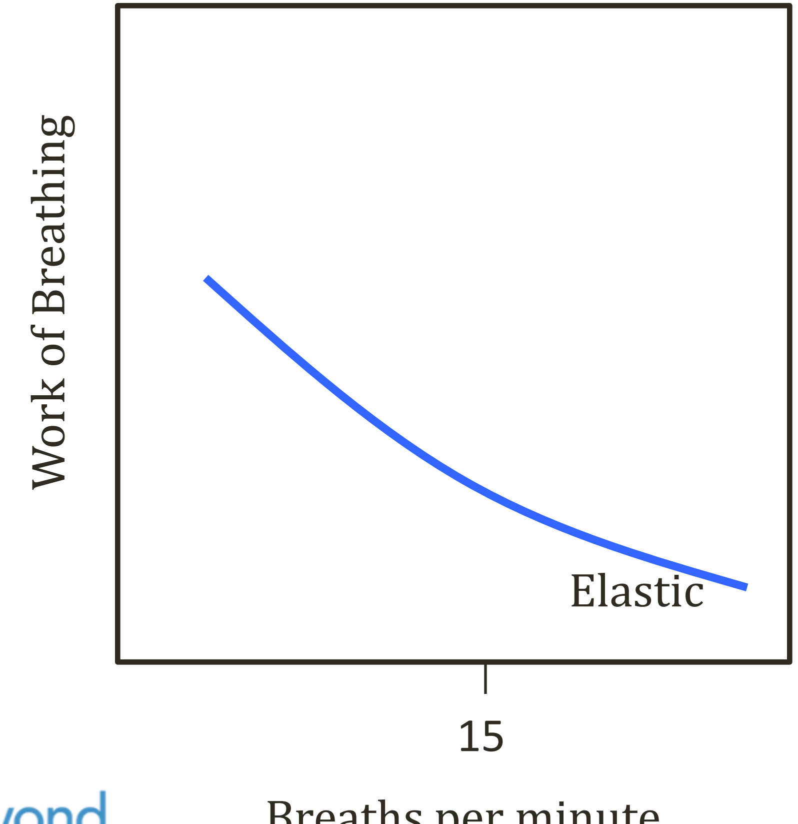
Work of Breathing

- Airflow resistance: Slower you breathe, less resistance



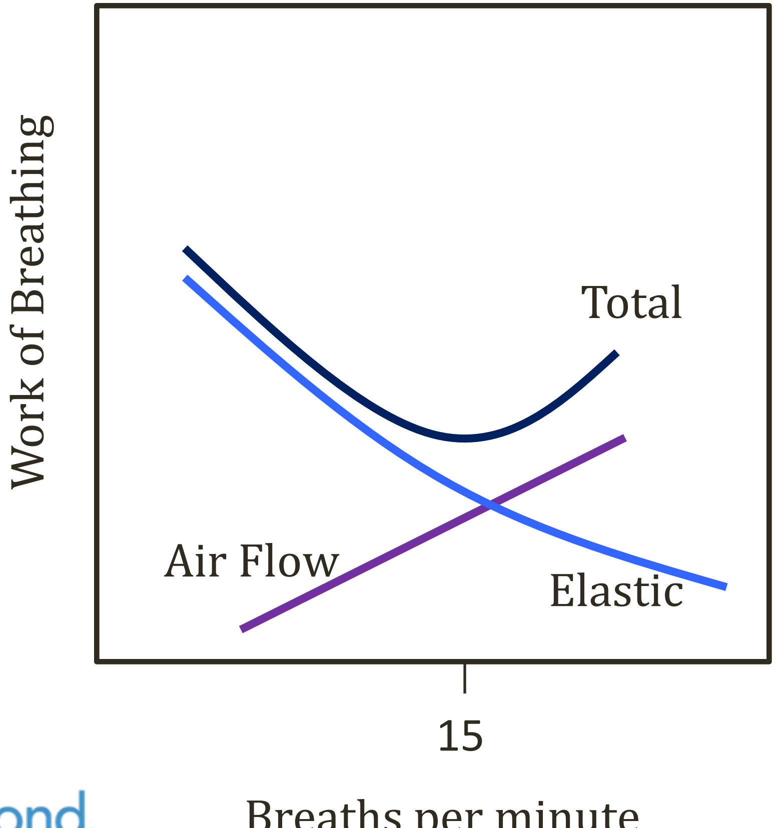
Work of Breathing

- Elastic resistance: Faster you breathe, less resistance



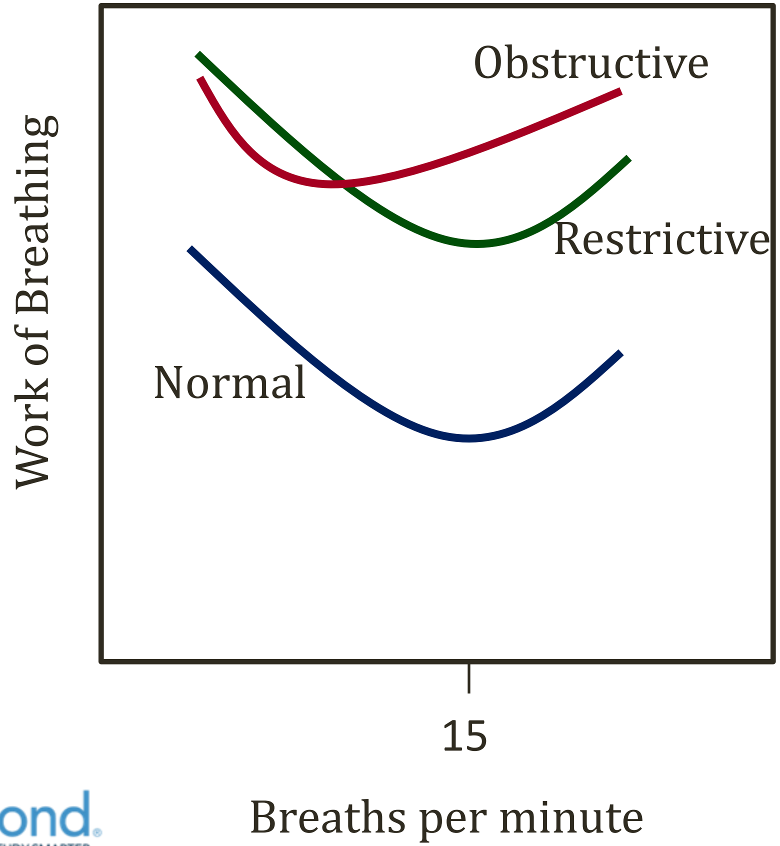
Work of Breathing

- Slower you breathe, less airflow resistance
- Faster you breathe, less elastic resistance



Work of Breathing

- Increases in obstructive and restrictive disease
- Different patterns



Obstructive Lung Disease

Jason Ryan, MD, MPH

Obstructive Lung Diseases

- Key points: Air trapping, slow flow out, less air out
- Reduced FEV1 (slow flow out)
- Reduced FVC (less air out)
- Reduced FEV1/FVC (hallmark)

Residual & Total Lung Volume

- Both go up in obstructive disease
  - From air trapping
- Both fall in restrictive disease
  - Less air fills the lungs due to restriction

Obstructive Lung Diseases

- Chronic bronchitis
- Emphysema
- Asthma
- Bronchiectasis

Chronic Bronchitis

- Chronic cough
- Productive of sputum
- At least 3 months over two years
- No other cause of cough present
- Strongly associated with smoking

Chronic Bronchitis

- Hypertrophy of mucous secreting glands
- Reid Index
  - Thickness of glands/total wall
  - >50% in chronic bronchitis
- Lungs can plug with mucous "mucous plugging"
- Increased risk of infection

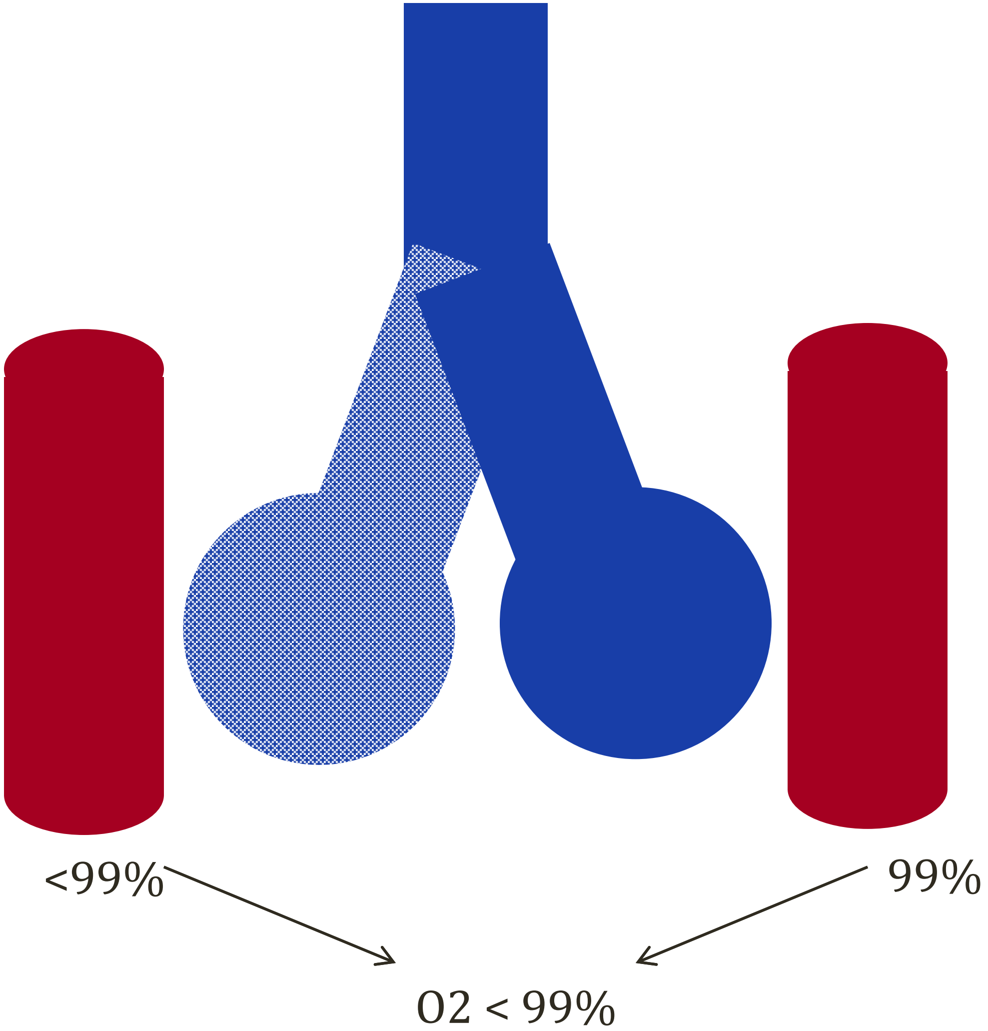
Chronic Bronchitis

- Poor ventilation of lungs
- Increased CO_2
- Decreased O_2
- Hypoxic vasoconstriction
- Pulmonary hypertension
- Right heart failure (cor pulmonale)

Chronic Bronchitis

- Cough
- Wheezing
- Crackles
- Dyspnea
- Cyanosis (shunting)

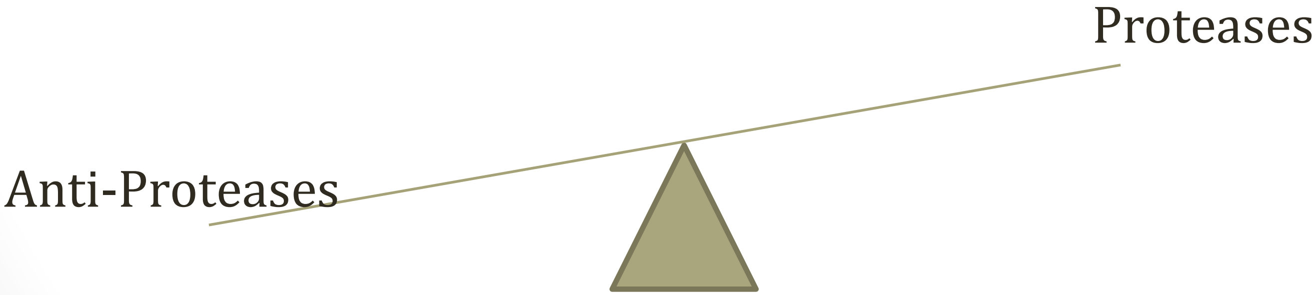
Shunting



Boards&Beyond STUDY SMARTER

Emphysema

- Smokers
  - Too many proteases created
  - Overwhelm anti-proteases
  - Upper lung damage
- α1 anti-trypsin deficiency
  - Ineffective anti-proteases
  - Lower lobe damage



Emphysema

- Destruction of alveoli
  - Smoke activates macrophages
  - Recruitment of neutrophils
  - Release of proteases
- Loss of elastic recoil
- Small airways collapse on exhalation
- Air "trapped" in lungs

Emphysema

- Dyspnea
- Cough (less sputum than chronic bronchitis)
- Hyperventilation
- Weight loss
- Cor pulmonale
- Barrel Chest

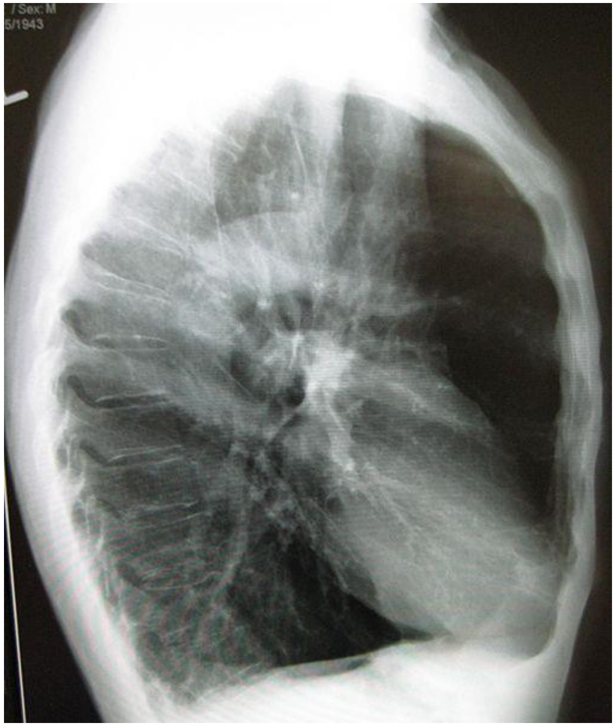
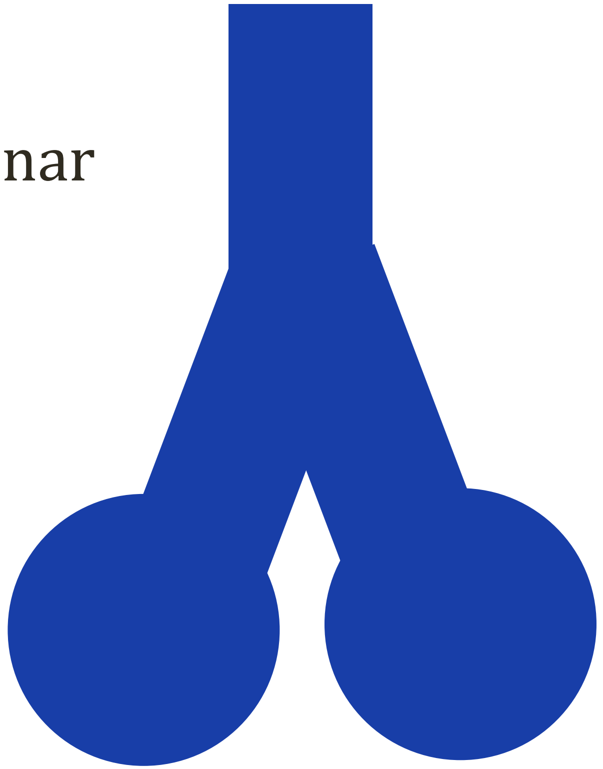


Image courtesy of James Heilman, MD

Acinus

- Acinus = bronchiole + alveoli
- Smokers = centriacinar damage
- α1 anti-trypsin deficiency = panacinar



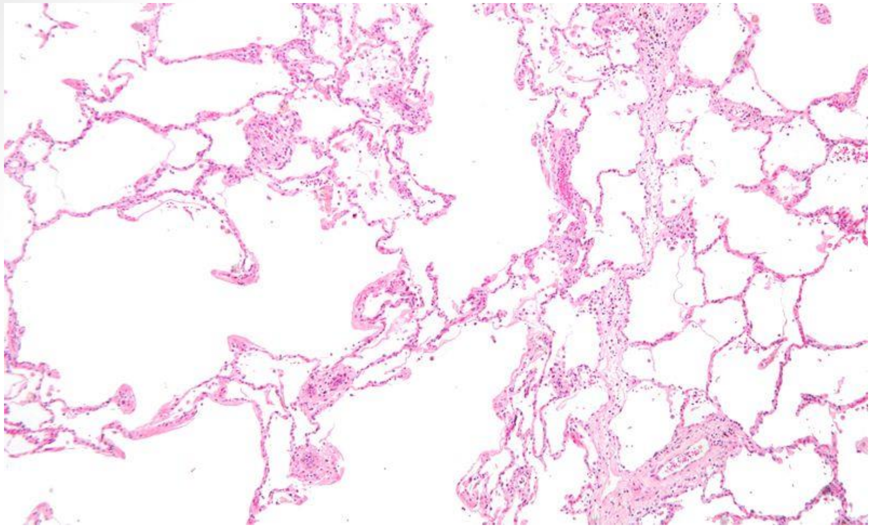


Image courtesy of Nephron

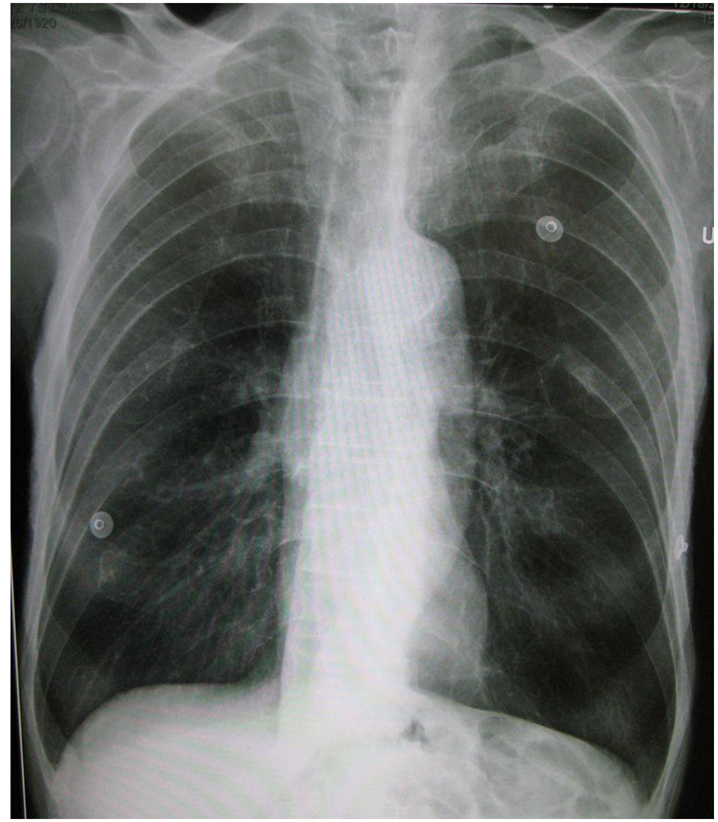
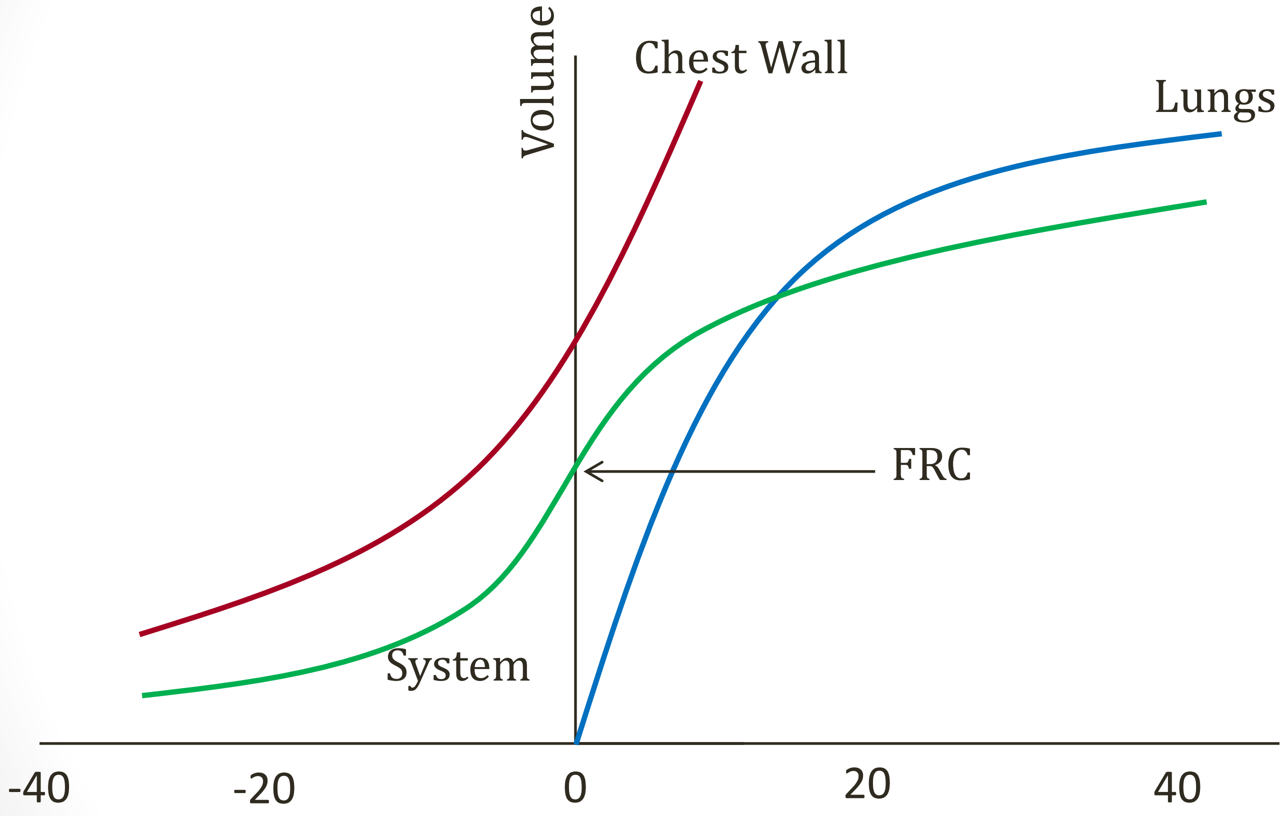


Image courtesy of James Heilman, MD

Chest Volumes and Pressures



Blue Bloater – Pink Puffer

- Chronic Bronchitis – Blue Bloater
  - Cyanosis from **shunting** (blue)
  - Air trapping (bloated)
- Emphysema – Pink Puffer
  - Loss of alveoli
  - Loss of surface area for O2 absorption (**dead space**)
  - Hyperventilation to compensate (puffer)
  - Initially this maintains O2 level (pink)

COPD

- Chronic Obstructive Pulmonary Disease
- Includes chronic bronchitis, emphysema, asthma
- Many similar symptoms (cough, dyspnea, wheezing)
- Many similar treatments

α1 Anti-trypsin Deficiency

- Inherited (autosomal co-dominant)
- Decreased or dysfunctional AAT
- AAT balances naturally occurring proteases
- Elastase found in neutrophils & alveolar macrophages

α1 Anti-trypsin Deficiency

- Lung
  - Panacinar emphysema
  - Imbalance between neutrophil elastase (destroys elastin) and elastase inhibitor AAT (protects elastin)
  - Lower lung damage
- Liver cirrhosis
  - Abnormal α1 builds up in liver
  - Only occurs in phenotypes with pathologic polymerization of AAT in endoplasmic reticulum of hepatocytes
  - Some patients have severe AAT deficiency but no intra-hepatocytic accumulation

α1 Anti-trypsin Deficiency

- Classic case
  - Typical COPD symptoms: cough, sputum, wheeze
  - Younger patient (40s)
  - Imaging: emphysematous changes most prominent at bases
  - Obstructive PFTs
- Question often asks about panacinar involvement
- These patients should NEVER smoke
  - Stimulates neutrophil elastase production

Asthma

- Reversible bronchoconstriction
- Usually due to allergic stimulus
  - Type I hypersensitivity reaction
- Airways are HYPERresponsive
- Common in children
- Associated with other allergic (atopic) conditions
  - Rhinitis, eczema
  - May have family history of allergic reactions

Asthma Triggers

- URI
- Allergens (animal dander, dust mites, mold, pollens)
- Stress
- Exercise
- Cold
- Aspirin

AERD

Aspirin Exacerbated Respiratory Disease

- Asthma, chronic rhinosinusitis, nasal polyposis
  - Chronic asthma/rhinosinusitis symptoms
  - Acute exacerbations after ingestion aspirin or NSAIDs
- Dysregulation of arachidonic acid metabolism
- Overproduction leukotrienes
- Treatment: Leukotriene receptor antagonists
  - Montelukast, Zafirlukast

Asthma Symptoms

- Episodic symptoms
- Dyspnea, wheezing, cough
- Hypoxia during episodes
- Decreased I/E ratio
- Reduced peak flow
- Mucous plugging (airway obstruction/shunt)
- Death: Status asthmaticus

Asthma Diagnosis

- Usually classic history/physical exam
- Methacholine challenge
  - Muscarinic agonist
  - Causes bronchoconstriction
  - Administer increasing amounts of nebulized drug
  - Spirometry after each dose
  - Look for dose at which FEV1 falls significantly
  - If dose is low → positive test

Asthma Pathology

- Recurrent episodes
- Smooth muscle hypertrophy
- Inflammation

Asthma Pathology

- Classic sputum findings
  - Curschmann's spirals
  - Charcot-Leyden crystals

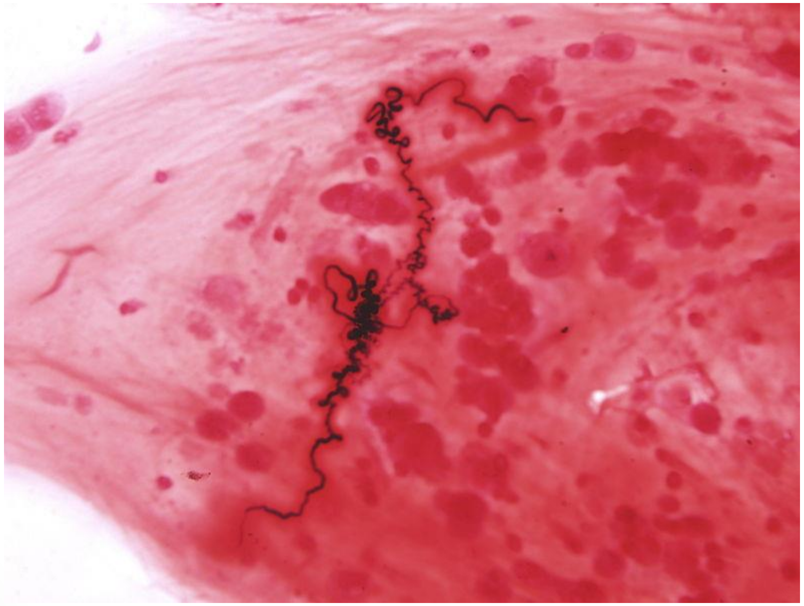


Image courtesy of Jmh649

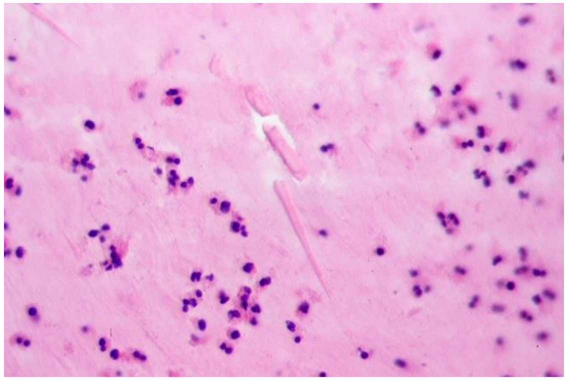


Image courtesy of Patho

Pulsus Paradoxus

- Most frequent non-cardiac causes are asthma/COPD

Bronchiectasis

- Result of chronic, recurrent airway inflammation
- Airways become permanently dilated
- Obstruction
  - Large airways dilated
  - Small/medium airways thickened bronchial walls

Bronchiectasis

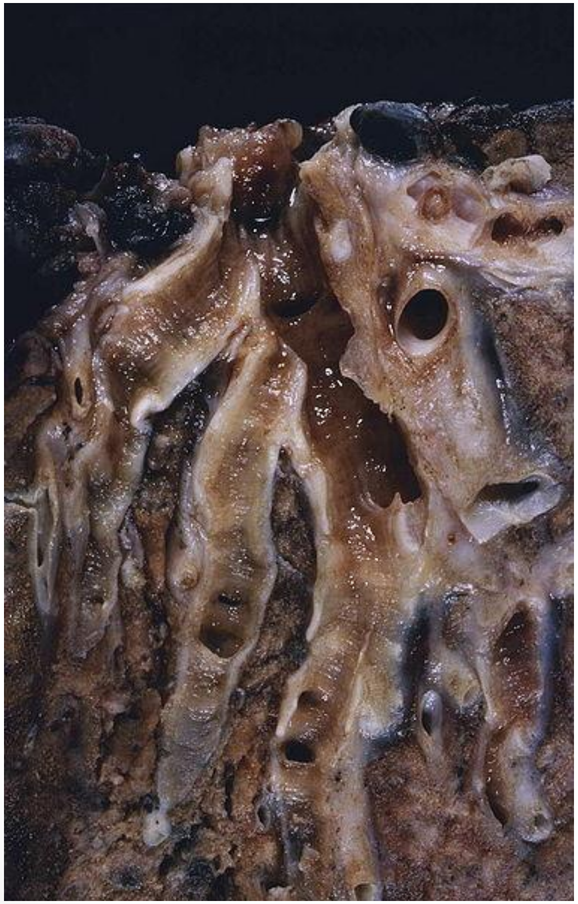


Image courtesy of Yale Rosen

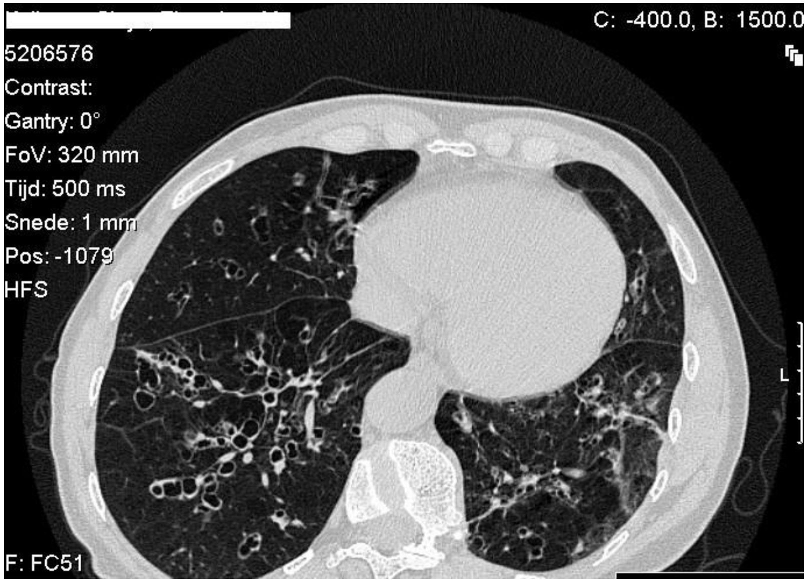


Image courtesy of Laura Fregonese, Jan Stolk

Bronchiectasis Symptoms

- Recurrent infections
- Cough, excessive sputum (foul smelling)
- Hemoptysis
- Cor pulmonale
- Amyloidosis

Bronchiectasis Etiologies

- Obstruction (tumor)
- Smoking
- Cystic fibrosis
- Kartagener's syndrome
- Allergic bronchopulmonary aspergillosis

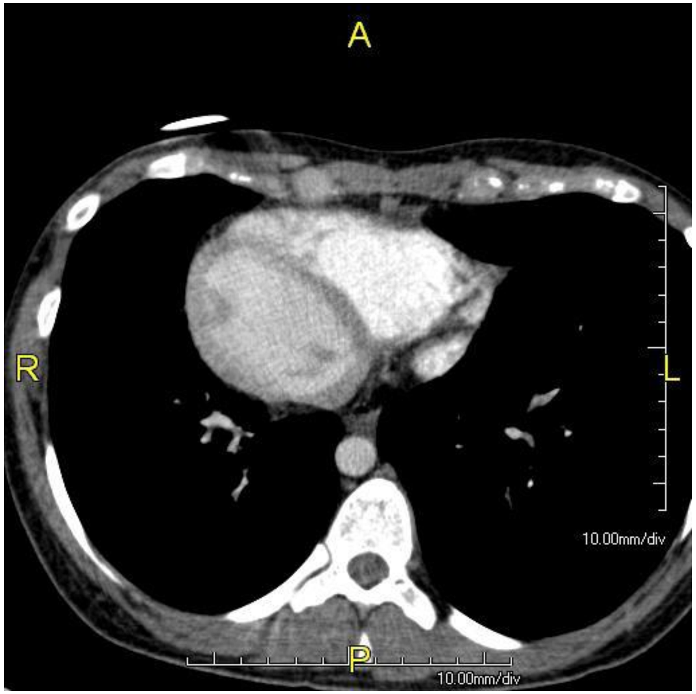
Primary Ciliary Dyskinesia

Immotile-cilia syndrome

- Cilia unable to beat, beat normally, or absent
- Inherited (autosomal recessive)
- Gene mutations dynein structure/formation
- Dynein = motor protein creates movement

Kartagener's syndrome

- Chronic sinusitis
- Bronchiectasis (chronic cough, recurrent infections)
- Male infertility
- Situs inversus



Kartagener's syndrome

- Classic case:
  - Child
  - Recurrent sinus/ear infections
  - Chronic cough
  - Bronchiectasis on chest CT
  - Obstruction on PFTs
  - Situs inversus
- Question often asks about dynein protein

ABPA

Allergic bronchopulmonary aspergillosis

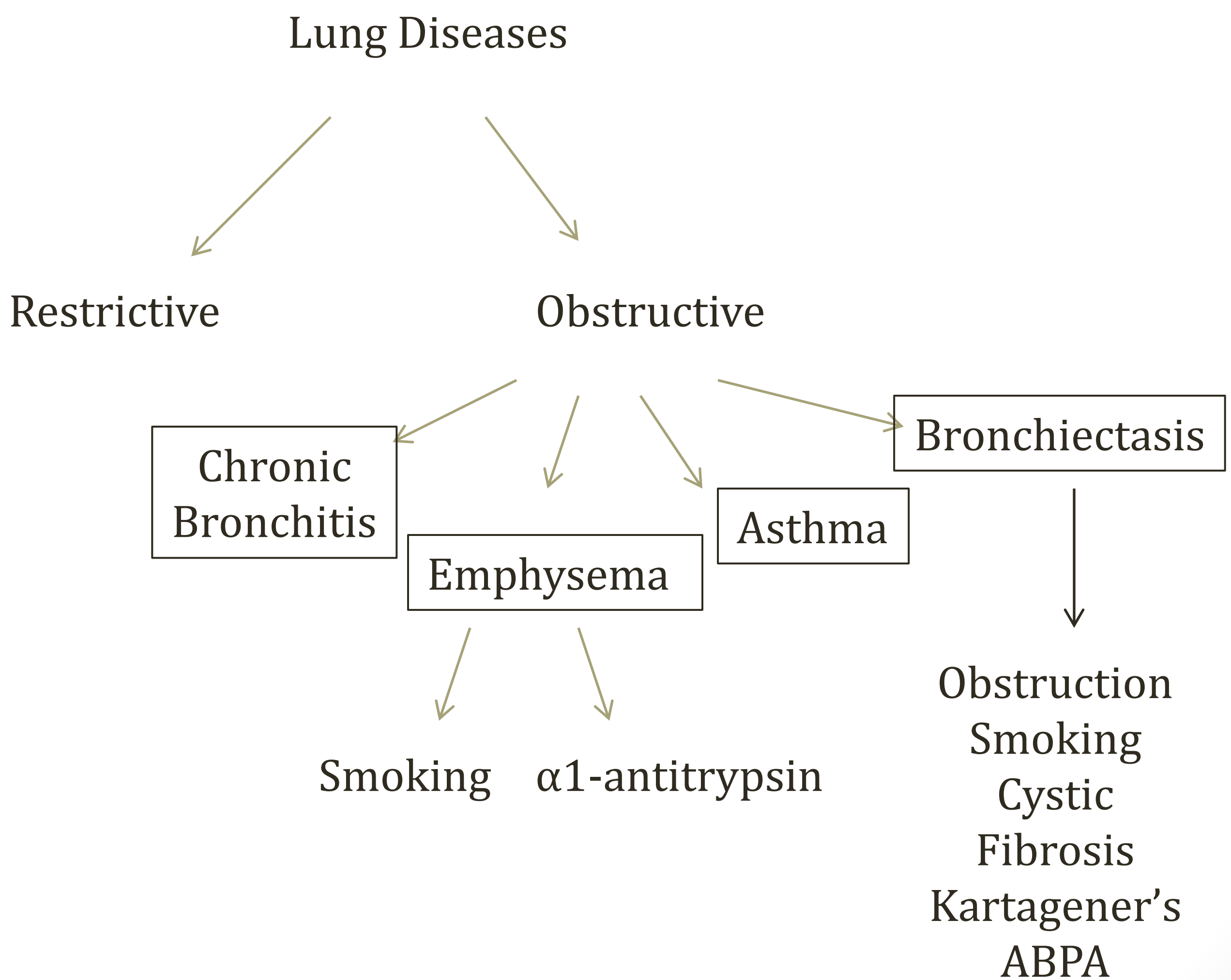
- Hypersensitivity (allergic) reaction to aspergillus
- Lungs become colonized with Aspergillus fumigatus
  - Low virulence fungus
  - Only infects immunocompromised or debilitated lungs
- Occurs predominantly in asthma and CF patients
- ABPA patients:
  - Increases Th2 CD4+ cells
  - Synthesis interleukins
  - Eosinophilia
  - IgE antibody production

ABPA

Allergic bronchopulmonary aspergillosis

- Classic case
  - Asthma or CF patient
  - Recurrent episodes cough, fever, malaise
  - Brownish mucus plugs, hemoptysis
  - Peripheral blood eosinophilia
  - High IgE level
  - Bronchiectasis on imaging
  - PFTs with obstruction
- Diagnosis: Skin testing aspergillosis
- Treatment: Steroids

Summary


Lung Diseases
Restrictive
Obstructive
Chronic Bronchitis
Emphysema
Asthma
Bronchiectasis
Smoking
α1-antitrypsin
Obstruction
Smoking
Cystic Fibrosis
Kartagener's
ABPA

Restrictive Lung Disease

Jason Ryan, MD, MPH

Restrictive Lung Diseases

- Key points: Can't get air in → less air out
- Reduced FVC (less air in/out)
- Reduced FEV1 (less air in/out)
- Normal (>80%) FEV1/FVC (hallmark)

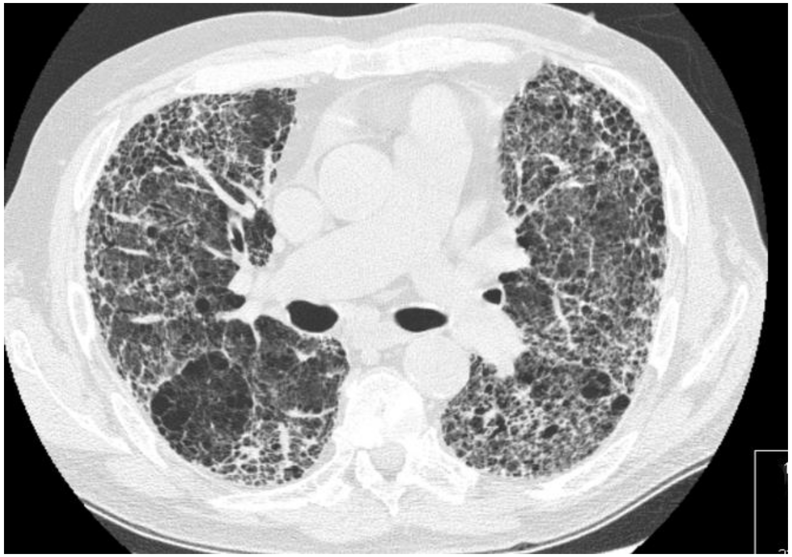
Causes

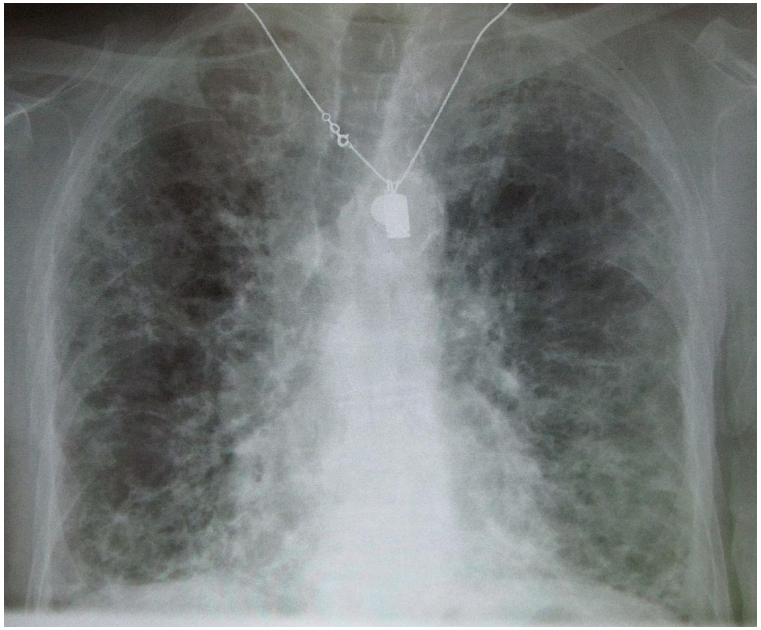
- #1: Poor breathing mechanics
- #2: Interstitial lung diseases

Poor Breathing Mechanics

- Not a primary pulmonary issue
- Under-ventilation of lungs
- Alveoli working: A-a gradient normal
- Neuromuscular
  - ALS, Polio, myasthenia gravis
- Structural
  - Scoliosis
  - Morbid obesity

Interstitial Lung Disease





Bilateral, diffuse pattern
Small, irregular opacities (reticulonodular)
"Honeycomb" lung appearance.

Image courtesy of Drriad

Image courtesy of James Heilman, MD

DLCO

Diffusing capacity in lung of carbon monoxide

- DLCO separates cases restrictive disease
- Restriction with normal DLCO
  - Extra-pulmonary cause: obesity
- Restriction with low DLCO
  - Interstitial lung disease

DLCO

- DLCO = diffusing capacity of carbon monoxide
- Measures ability of lungs to transfer gas to RBCs
- Patient inhales small amount (not dangerous) CO
- CO uptake is diffusion limited
  - Amount taken up ≈ diffusion function lungs
- Machine measures CO exhaled
- Normal = 75 – 140% predicted
- Severe disease <40% predicted

Low DLCO Conditions

- Interstitial lung disease
- Emphysema
- Abnormal vasculature
  - Pulmonary hypertension
  - Pulmonary embolism
- Prior lung resection
- Anemia
  - Corrects when adjusted for Hb level

Interstitial Diseases

- "Diffuse parenchymal lung diseases"
- Large group of disorders
- Similar clinical, radiographic, physiologic, or pathologic manifestations

Interstitial Diseases

- Idiopathic pulmonary fibrosis
- Systemic diseases with interstitial lung features
  - Scleroderma
  - Rheumatoid arthritis
  - Goodpasture's
  - Wegener's
  - Sarcoidosis
- Pneumoconiosis
- Drug toxicity (amiodarone, methotrexate)
- Hypersensitivity pneumonitis

Idiopathic pulmonary fibrosis

- Most common type: Idiopathic interstitial pneumonia
- Slow onset dyspnea
- Typically affects adults over the age of 40

Pneumoconiosis

Occupational lung diseases

- Coal miner's lung
- Silicosis
- Asbestosis

Coal miner's lung

- Inhalation of coal dust particles
- CXR or Chest CT:
  - Small, rounded, nodular opacities
  - Preference for the upper lobes

Silicosis

- Inhalation of silica in quartz, granite, or sandstone
- Most widespread pneumoconiosis in US
- Foundries (metal production facilities)
- Sandblasting (abrasive blasting)
- Mines

Silicosis

- Macrophages react to silica
- Inflammation → fibroblasts → collagen
- High prevalence of TB
  - Impaired macrophage killing
- High prevalence of bronchogenic carcinoma

Silicosis

- Affects upper lobes
- Eggshell calcifications of lymph nodes

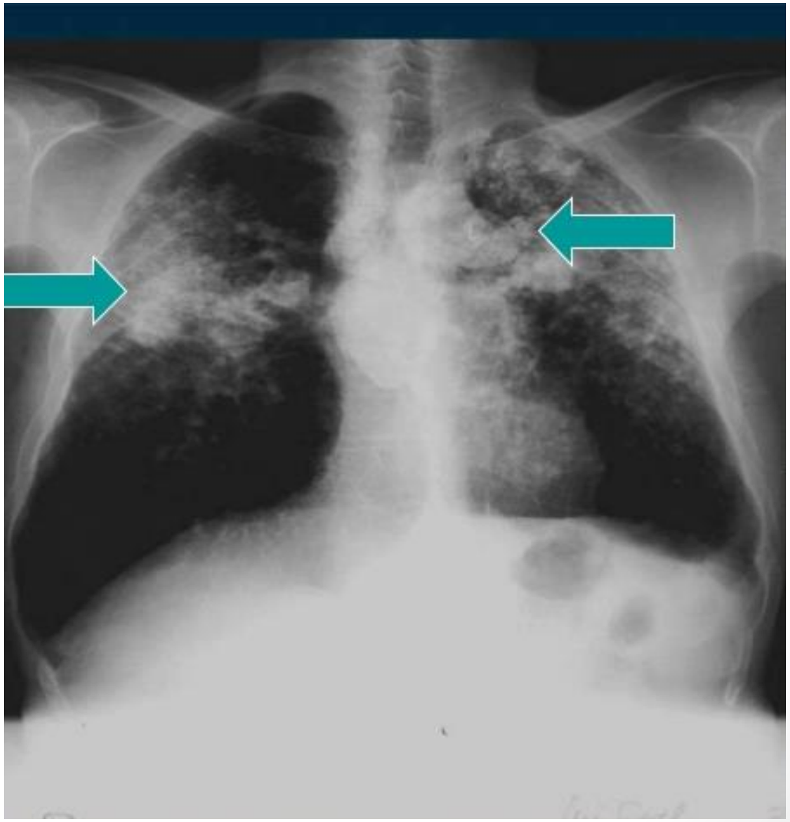


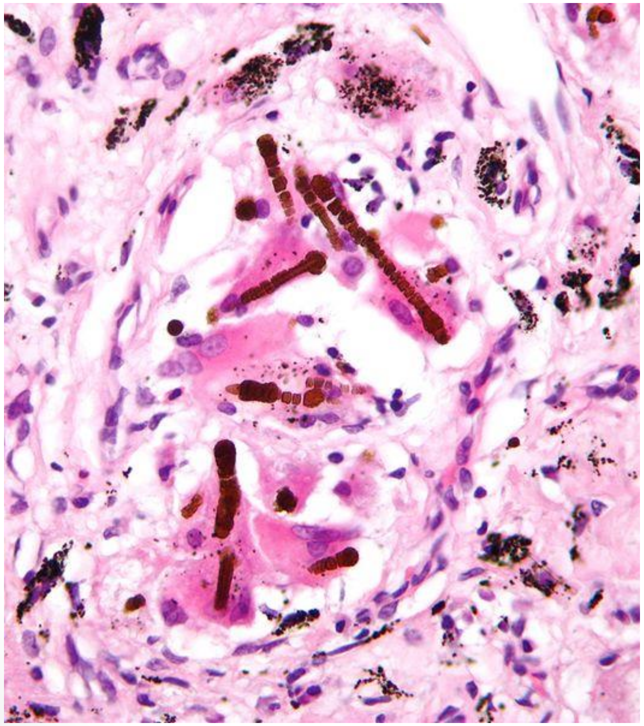
Image courtesy of Dr. Lucas Pedro Pablo Burchard Señoret

Asbestosis

- Inhalation of asbestos fibers
- Shipbuilding, roofing, plumbing
- Classically affects lower lobes
- Three clinical problems:
  - Interstitial lung disease (asbestosis)
  - Pleural plaques
  - Lung cancer

Asbestosis

- CXR: Calcified pleural plaques pathognomonic
- Path: Asbestos bodies (ferruginous body)
  - Asbestos fibers surrounded by a coating of iron and protein



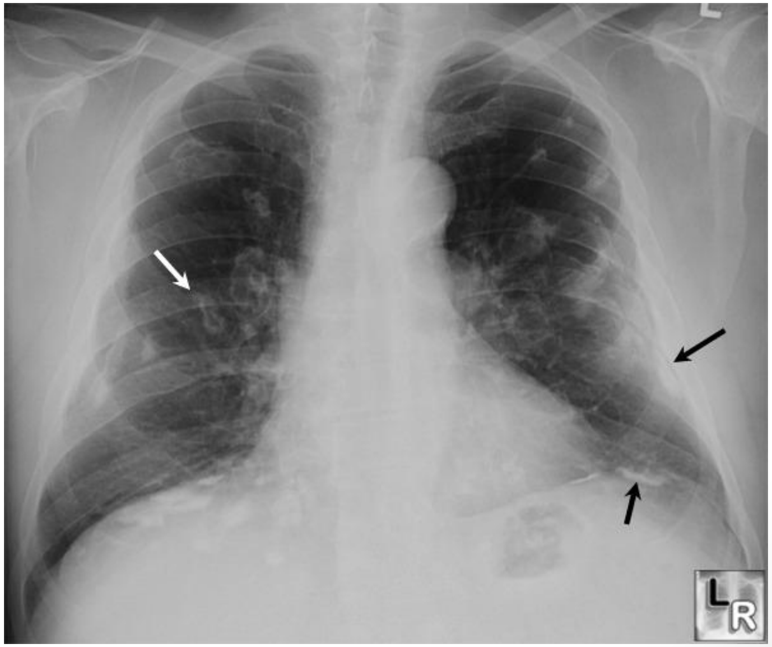


Image courtesy of Nephron

Image courtesy of www.learningradiology.com

Asbestosis

- Bronchogenic carcinoma
- Mesothelioma
  - Asbestos is the only known risk factor for mesothelioma
  - Occurs decades after exposure
  - Pleural thickening and pleural effusion
  - Slow onset symptoms (dyspnea, cough, chest pain)
  - Poor prognosis

Drug toxicity

- Bleomycin
- Busulfan
- Amiodarone
- Methotrexate

Hypersensitivity pneumonitis

- Hypersensitivity reaction to environmental antigen
  - Agricultural dusts
  - Microorganisms (fungal, bacterial, or protozoa)
  - Chemicals
- Mixed type III/IV hypersensitivity
- Classic case is a farmer's lung
  - Moldy hay, grain exposure
- Also common in bird/poultry handlers
  - Waste from birds → dried, finely dispersed dust

Hypersensitivity pneumonitis

- Classic case
  - Farmer or bird handler
  - Cough, dyspnea, chest tightness
  - Diffuse crackles
- Diagnosis (challenging):
  - Bronchoalveolar lavage
  - Inhalation challenge
  - Lung biopsy
- Treatment:
  - Avoid exposure
  - Steroids

Treatment of COPD & Asthma

Jason Ryan, MD, MPH

COPD and Asthma Drugs

- Short-acting bronchodilators
  - Albuterol
  - Ipratropium
- Long-acting bronchodilators
  - Salmeterol, Formoterol
  - Tiotropium
- Steroids

β2 Agonists

- Activate adenylate cyclase → ↑cAMP
- Relax bronchiole smooth muscle
- Short acting: Albuterol
  - Nebulizer or inhaler
  - Use during acute attacks (prn)
- Long acting: Salmeterol, Formoterol
  - Not used as monotherapy (always with ICS)
- Systemic side effects (rare)
  - Tremor, arrhythmia

Muscarinic Antagonists

- Vagal nerve → Ach → Bronchoconstriction
- MA drugs block M receptors smooth muscle
- Prevents bronchoconstriction

Muscarinic Antagonists

- Short acting: Ipratropium
- Long acting: Tiotropium

Steroids

- Inhaled: Beclomethasone, Fluticasone, Budesonide
- Oral: Prednisone
- IV: Methylprednisolone (Solumedrol)

Steroids

- Inhibit synthesis of cytokines
- Bind to glucocorticoid receptor (GR)
- Many, many immunosuppressive effects
- ↓ expression many interleukins, IFN-γ, TNF-α, GM-CSF
- Inactivation NF-KB
  - Transcription factor
  - Induces production of TNF-α

Steroids

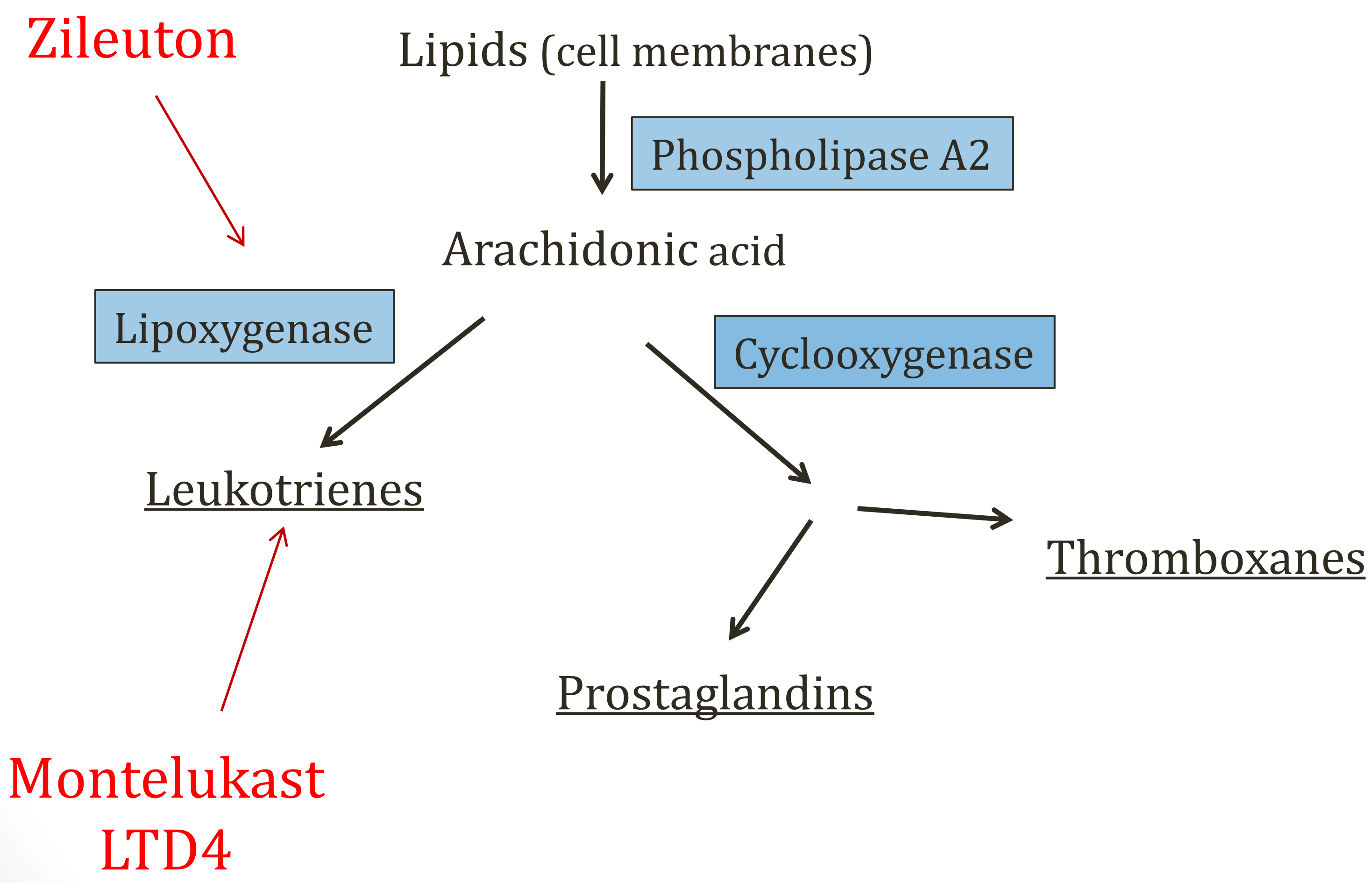
- Common side effect is oral candidiasis ("thrush")
- Patients instructed to rinse after inhalation

Image courtesy of James Heilman, MD

Special Asthma Drugs

- Leukotriene receptor antagonists (PO)
  - Montelukast (Singulair)
  - Useful in aspirin sensitive asthma
- Zileuton (PO)
  - 5-lipoxygenase inhibitors
  - Blocks conversion of arachidonic acid to leukotrienes

Eicosanoids



Special Asthma Drugs

- Omalizumab (SQ injection)
  - IgG monoclonal antibody
  - Inhibits IgE binding to IgE receptor on mast cells & basophils
- Cromolyn (inhaler/nebulizer)
  - Inhibits mast cell degranulation
  - Blocks release of histamine, leukotrienes

Theophylline

- Methylxanthines
- Multiple, complex mechanisms
- Bronchodilation
  - Likely through inhibition PDE
  - Less hydrolysis (breakdown) cAMP
  - ↑cAMP
- Also down-regulates inflammatory cell functions

Theophylline

- Narrow therapeutic index
- Levels must be monitored
- Dose must be titrated
- Goal is a peak serum concentration 10 to20mg/L

Theophylline

- Metabolized by P450
- Many drug-drug interactions
- Common culprits:
  - Cimetidine
  - Ciprofloxacin
  - Erythromycin
  - Clarithromycin
  - Verapamil

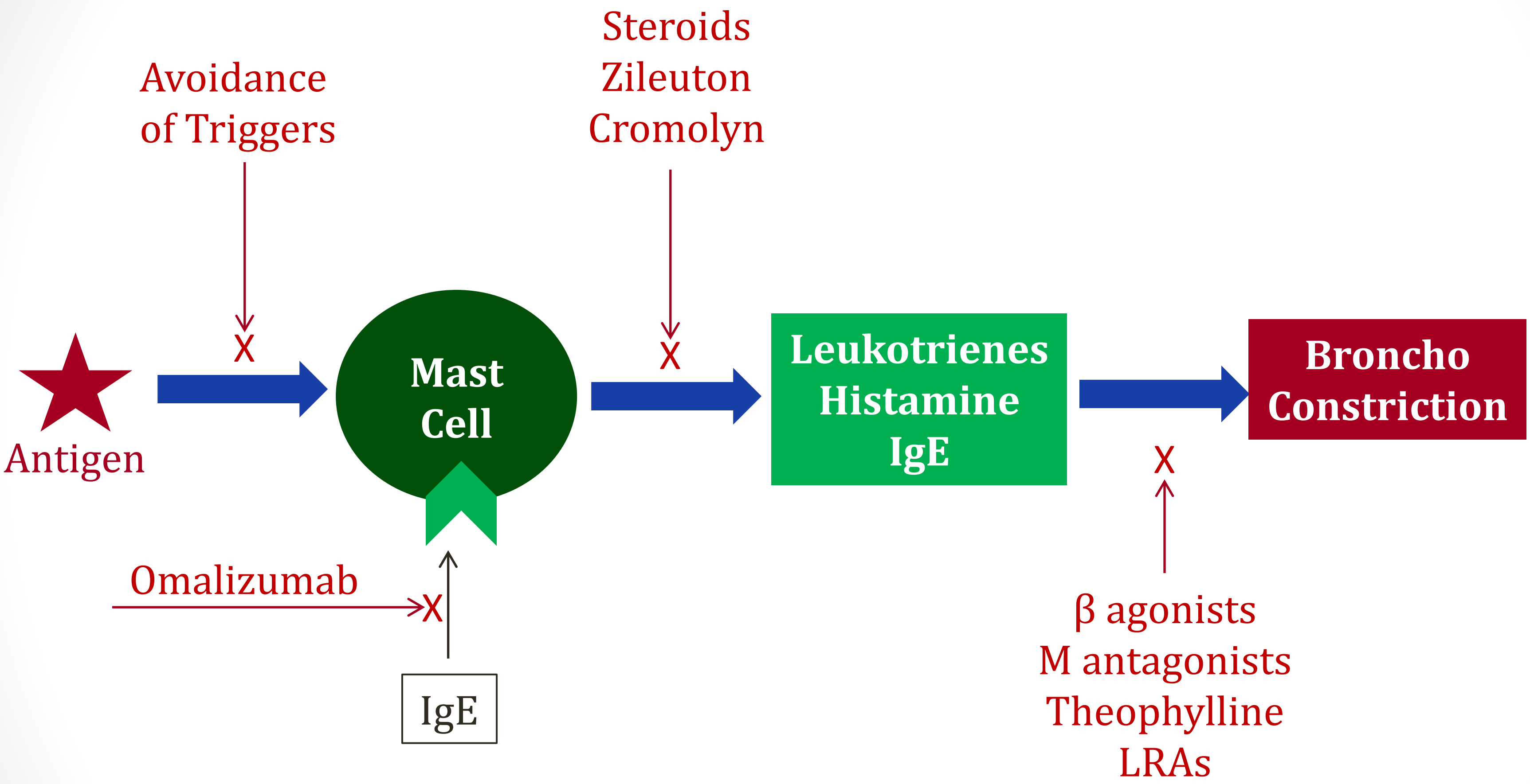
Theophylline

- GI toxicity
  - Nausea, vomiting
- Neurotoxicity
  - Seizures
- Overdose scenario: Nausea, vomiting, seizures

Theophylline

- Cardiotoxicity
  - Blocks adenosine receptors
  - Increased heart rate
  - Arrhythmias (atrial tachycardia, atrial flutter)
  - Cause of death in overdose/poisoning
- Key clinical scenario
  - Patient on theophylline for asthma/COPD
  - SVT
  - Adenosine fails to slow heart rate

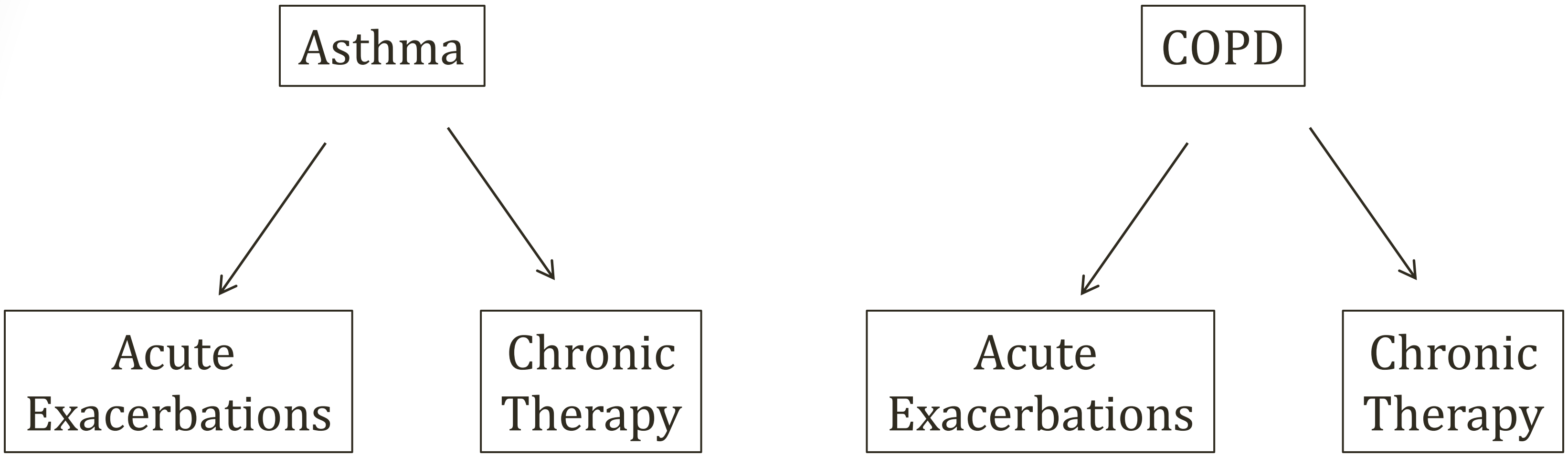
Asthma


Steroids
Zileuton
Cromolyn
Avoidance
of Triggers
Antigen
Mast
Cell
Leukotrienes
Histamine
IgE
Broncho
Constriction
Omalizumab
IgE
β agonists
M antagonists
Theophylline
LRAs

Special COPD Drugs

- Theophylline
- Roflumilast (PO)
  - Phosphodiesterase-4 (PDE-4) inhibitor
  - Decreases inflammation
  - May relax airway smooth muscle

Treatment Asthma & COPD



COPD: Acute Exacerbations

- Oxygen
- Nebulized albuterol +/- ipratropium (Combivent)
- IV or oral corticosteroids
  - Prednisone 60mg daily
  - Methylprednisolone 80mg IV q8hrs
- Antibiotics (severe, hospitalized patients)
  - Fluoroquinolones
  - Amoxicillin/clavulanate

GOLD Criteria

Global Initiative for Chronic Obstructive Lung Disease

Stage	Symptoms	FEV1
Gold 1	Mild	FEV1 >80%
Gold 2	Moderate	FEV1 50-79%
Gold 3	Severe	FEV1 30-49%
Gold 4	Very Severe	FEV1 <30%

COPD: Chronic Therapy

Mild FEV1 > 80%	Moderate FEV1 50-79%	Severe FEV1 30-49%	Very Severe FEV1 <30%
As needed short acting bronchodilator			
	Add long-acting bronchodilator		
		Add ICS	
			Oxygen/ Surgery

Refractory Disease
Theophylline
Roflumilast

COPD: Chronic Therapy

- Oxygen
  - Associated with increased survival
  - PaO2 < 55mmHG or O2 sat <88%
- Pulmonary rehabilitation
  - Improves exercise capacity, quality of life
  - Decrease dyspnea
- Vaccinations
- Smoking cessation

Asthma: Acute Exacerbations

- Oxygen
- Nebulized albuterol
- IV or oral corticosteroids
  - Prednisone 60mg daily
  - Methylprednisolone 80mg IV q8hrs
- Rarely used:
  - Ipratropium
  - IV Magnesium sulfate

Asthma: Chronic Therapy

Step 1	Step 2	Step 3	Step 4	Step 5	Step 6
SABA as needed	Add Low dose ICS	Medium ICS or Low ICS + LABA	Medium ICS + LABA	High ICS + LABA	High ICS + LABA + Oral Steroids

LTRA, Zileuton, Theophylline, Omalizumab (add-on options for Steps 2–6)

Surgical Treatment

- For advanced “end-staged” COPD
- Lung volume reduction surgery/Bullectomy
  - Remove diseased lung tissue
  - Allow healthy lung tissue more room to expand
- Lung transplant

Pneumonia

Jason Ryan, MD, MPH

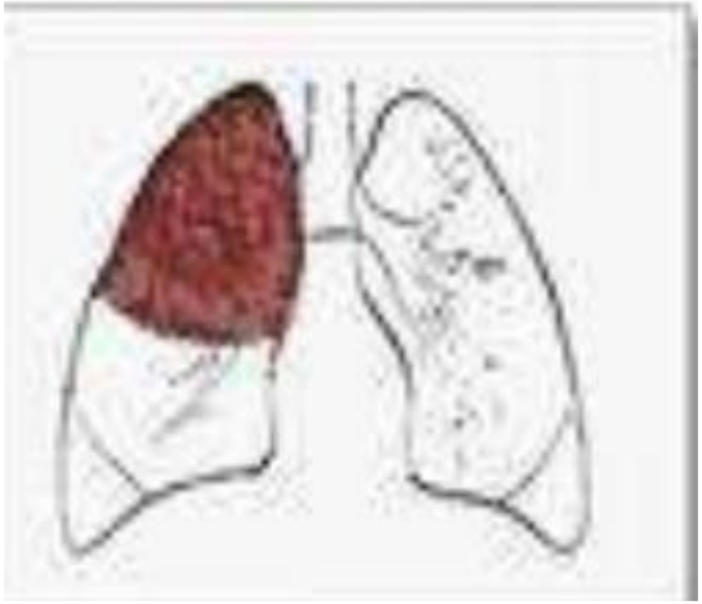
Pneumonia

- Infection of the lungs
- Three patterns
  - Lobar
  - Bronchopneumonia
  - Interstitial (atypical)

Lobar Pneumonia

- Classic form of pneumonia (*S. pneumoniae*)
- Bacteria acquired in nasopharynx
- Aerosolized to alveolus
- Enter alveolar type II cells
- Pneumococci multiply in alveolus
- Invade alveolar epithelium
- Pass from one alveolus to next (pores of Cohn)
- Inflammation/consolidation of lobes
- Can involve entire lung

Lobar Pneumonia



Images courtesy of Vijit Agrawal

Four Lobar Stages

- #1: Congestion (1st 24 hours)
  - Alveolar capillaries dilate
  - Exudate of bacteria develops
- #2: Red hepatization (2-3days)
  - Exudate of RBCs, neutrophils, fibrin
  - “Fresh" exudate: RBCs/WBCs intact
  - Pneumococci alive
  - Lobes look red

Four Lobar Stages

- #3: Gray hepatization (4-6days)
  - Gray, firm lobe
  - Exudate with neutrophils/fibrin
  - RBCs disintegrate
  - Dying pneumococci
- #4: Resolution
  - Return to normal (little scarring)
  - Enzymes digests exudate
  - Type II pneumocyte key for regeneration

Bronchopneumonia

- *Patchy* inflammation of multiple lobules
- Primary involvement airways and surrounding interstitium
- *Staphylococcus aureus*

Image courtesy of drahmed142010

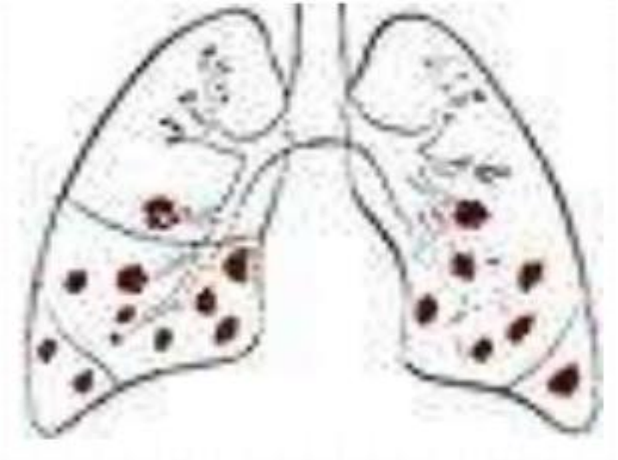


Image courtesy of Vijit Agrawal

Interstitial Pneumonia

- Inflammatory infiltrate of alveolar walls only
- More indolent course
- Viruses
- Legionella pneumophila
- Mycoplasma pneumoniae
- Chlamydophila pneumoniae

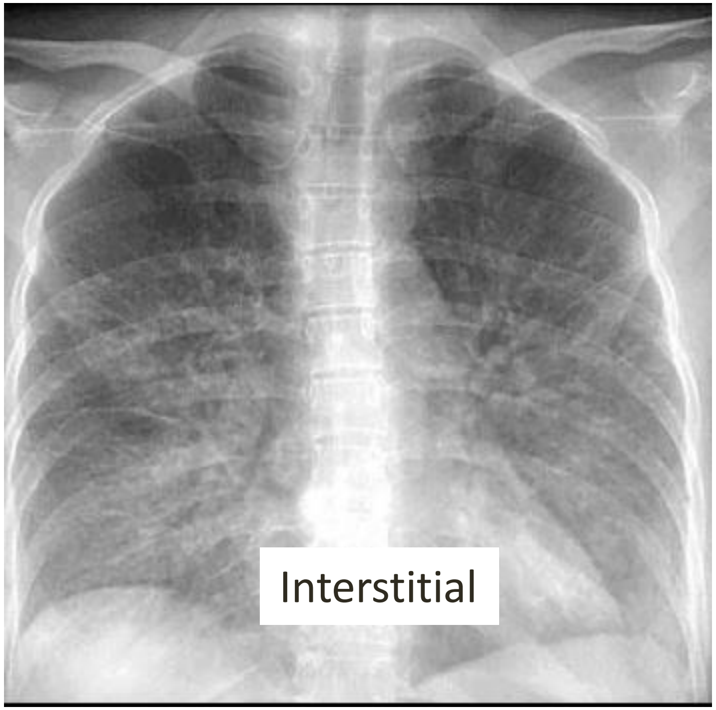
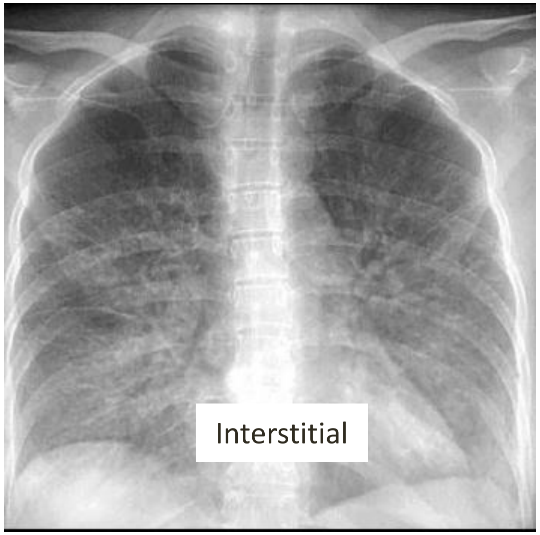


Image courtesy of drahmed142010

Atypical Pneumonia

- Pneumonia caused by:
  - Legionella pneumophila
  - Mycoplasma pneumoniae
  - Chlamydophila pneumoniae
- Usually milder than strep pneumonia
- Respiratory distress rare
- Interstitial infiltrates on CXR
- “Walking pneumonia”



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Causes of Pneumonia

Children

Neonates <4weeks	Children 4wk-18yr
Group B Strep E. Coli	Viruses (RSV) Mycoplasma Chlamydia Pneumoniae Streptococcus Pneumoniae

Causes of Pneumonia

Adults

- S. pneumoniae – most common
- Haemophilus influenzae
- Mycoplasma pneumoniae
- C. pneumoniae
- Legionella

Causes of Pneumonia

Adults

- Gram-negative rods
  - Klebsiella, E. Coli, Pseudomonas
  - Uncommon unless severe PNA
  - Often isolated in hospitalized patients
- S. Aureus (postinfluenza pneumonia)
- Anaerobes (aspiration PNA; lung abscess)
- Viruses
  - Influenza
  - RSV (children)

Signs/Symptoms

- High Fever
- Cough
- Sputum production
- Elevated WBC
- Pleuritic chest pain

Diagnosis

- Usually:
  - History
  - Physical exam
  - X-ray (sometimes CT scan)
- Rarely
  - Sputum culture
  - Bronchoalveolar lavage

Clinical Classes of Pneumonia

- Community acquired
  - Usually S. Pneumoniae, H. Influenza, S. Aureus
  - Sometimes Mycoplasma, Chlamydia, Legionella (atypicals)
- Nosocomial
  - Bad bugs
  - Often gram negatives (Pseudomonas, Klebsiella, E. Coli)
  - Hospital Acquired
  - Ventilator-associated pneumonia (VAP)
  - Healthcare-associated pneumonia (HCAP; nursing homes)

Community Acquired PNA

Uncomplicated

- No co-morbidities
- No recent antibiotic use
- Low community rates resistance
- Azithromycin, Clarithromycin, or Doxycycline
- Three to five day course
    - Patient should be afebrile 48-72 hrs and clinically stable

Community Acquired PNA

Complicated

- COPD, CKD, Diabetes, CHF, Alcoholism
- Recent antibiotic use
- Fluoroquinolone (levofloxacin)
- Amoxicillin plus azithromycin

Nosocomial PNA

- Lots of resistance to antibiotics
- Gram negative rods
  - E. coli, Klebsiella, Enterobacter, Pseudomonas, Acinetobacter
- Staph Aureus including MRSA
- Often cover for pseudomonas, MRSA
- Sometimes multi-drug combinations
- Cefepime or Ceftazidime
- Imipenem or Meropenem
- Piperacillin-tazobactam (Zosyn)

Complications

- Sepsis
- Respiratory failure
- Lung abscesses
- Pleural effusion
- ARDS

ARDS

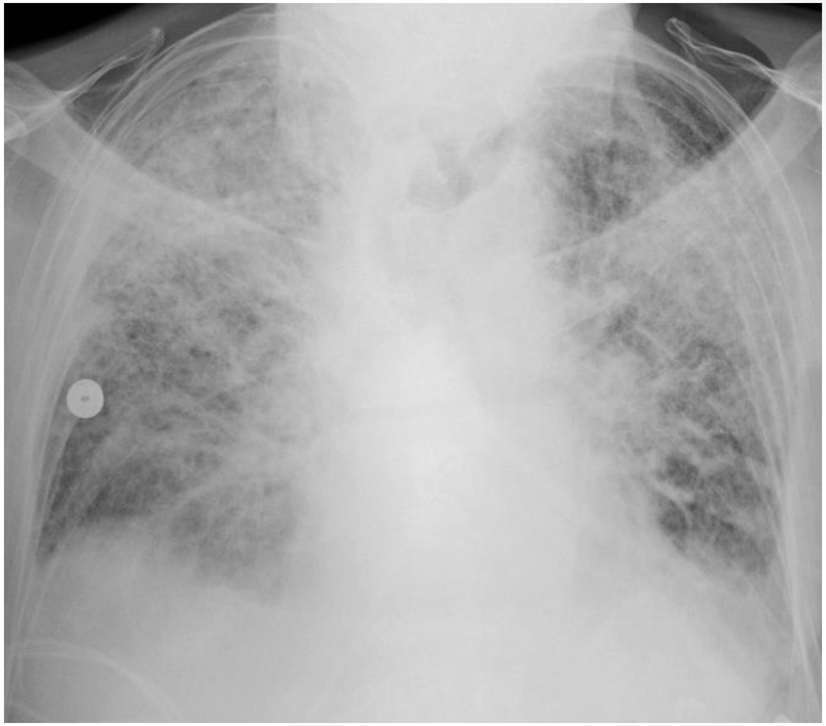
Acute Respiratory Distress Syndrome

- Triggered by various lung injuries
- Injury → release of pro-inflammatory cytokines
  - TNF, interleukins
- Cytokines recruit neutrophils to lungs
- Neutrophils release toxic mediators
  - Reactive oxygen species, proteases
- Damage to capillary endothelium and alveolar epithelium
- Protein escapes from vascular space
- Fluid pours into the interstitium

ARDS

Triggers

- Sepsis (most common)
- Infection (PNA)
- Aspiration
- Trauma
- Acute pancreatitis
- Transfusion-related acute lung injury (TRALI)



Looks like pulmonary edema but PCPW is normal

Image courtesy of James Heilman, MD

ARDS

Treatment

- Mechanical ventilation
- Low tidal volume
- Supportive care (fluids, nutrition)
- VAP pneumonia is serious complication

Legionella

- First identified at American Legion convention
- Infection from inhalation of aerosolized bacteria
  - Not airborne
- Outbreaks at hotels with contaminated water
- Can cause nosocomial pneumonia in nursing homes

Legionella

Symptoms

- Initially mild pneumonia symptoms
  - Fever; mild, slightly productive cough
- Can progress to severe pneumonia
- GI symptoms
  - Watery diarrhea, nausea, vomiting, and abdominal pain
- Hyponatremia ($Na<130$ meq/L) common
  - Can occur in any PNA but more common Legionella

Legionella

Diagnosis

- Special culture requirements
  - Does not gram stain well
- Buffered charcoal yeast extract agar (BCYE)
- Iron and cysteine added for growth
- Supplemented with antibiotics and silver dyes
  - Antimicrobials prevent overgrowth by competing organisms
  - Dyes give distinctive color to Legionella
- Urinary antigen test
  - Rapid test available in minutes
  - Does not test for all Legionella types

Legionella

Diagnosis

- Classic Case
  - Mild cough
  - Watery diarrhea
  - Confusion (low Na)
  - Negative bacteria on gram stain
- Diagnose with urinary antigen test
- Treatment: Fluoroquinolone or Azithromycin

Pontiac Fever

- Mild form of Legionella infection
- Fever, malaise, chills, fatigue, and headache
- No respiratory complaints
- Chest radiograph usually normal

Mycoplasma Pneumonia

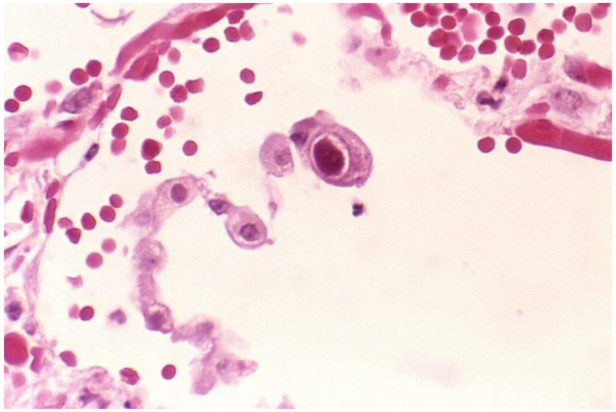
- Atypical pneumonia
- Can't see on gram stain (no cell wall)
- Classically causes outbreaks in young adults
  - College dorm residents
  - Military recruits
- CXR looks worse than symptoms
- Can cause autoimmune hemolytic anemia
  - IgM antibody → RBC antigen
  - "Cold" hemolytic anemia
- Stevens-Johnson syndrome

Influenza Virus

- Atypical pneumonia
- Influenza A or B viruses
- Fever, headache, myalgia, and malaise
- Nonproductive cough, sore throat, runny nose
- Major complication is secondary pneumonia
  - Strep pneumoniae, Staph aureus, H. influenzae
  - Worsening symptoms after initial improvement
  - Cause of death

CMV

- Pneumonia in transplant patients on immunosuppressive drugs
- "Owl eye" intranuclear inclusions



RSV

Respiratory Syncytial Virus

- Viral respiratory infection in infants
- Often seasonal outbreaks (Nov – April)
- Most common cause lower respiratory tract illness in children
  - Bronchiolitis, pneumonia, acute respiratory failure
- Often starts as upper airway infection
  - Runny nose
- Few days later, lower tract symptoms
  - Wheezing often present

RSV

Respiratory Syncytial Virus

- Treatment: Ribavirin
  - Inhibits synthesis of guanine nucleotides
- Prevention: Palivizumab
  - Monoclonal antibody against F protein
  - RSV contains surface F (fusion) protein
  - Causes respiratory epithelial cell fusion
  - Used in pre-term infants (high risk RSV)
  - Sometimes congenital heart disease

RSV

Respiratory Syncytial Virus

- Classic case
  - Young child (often <2yo)
  - Fever, runny nose
  - Few days later, cough, wheezing

Aspiration Pneumonia

- Aspiration of microorganisms
- Bugs from oral cavity and nasopharynx to lungs
- Risk factors:
  - Reduced consciousness (anesthesia)
  - Seizures
  - Alcoholics
  - Dysphagia from neuromuscular weakness
- Classic patients:
  - Debilitated nursing home patient
  - Alcoholic

Aspiration Pneumonia

- Klebsiella
- Staph Aureus
- Anaerobic bacteria
  - Peptostreptococcus
  - Fusobacterium
  - Prevotella
  - Bacteroides
- Clindamycin first-line therapy

Klebsiella Pneumonia

- Can cause lobar pneumonia
- Often from aspiration
- Marked inflammation/necrosis
- Thick, mucoid and blood-tinged sputum
- "Currant jelly"

Lung Abscess

- Contained, fluid-filled space in lungs
  - "Air fluid level" on imaging
- Usually a consequence of aspiration
- Rarely due to bronchial obstruction from cancer
- Predominantly anaerobes
  - Peptostreptococcus
  - Prevotella
  - Bacteroides
  - Fusobacterium
- Sometimes S. Aureus, Klebsiella
- Treatment: Clindamycin

PCP

Pneumocystis jirovecii

- Diffuse interstitial pneumonia
- Requires immunocompromise
  - Classically HIV
  - AIDS-defining illness
- Yeast → inhaled
  - Usually no symptoms if immune system intact

PCP

Pneumocystis jirovecii

- Diagnosed by microscopy
  - Sputum sample or BAL
- Staining required → cannot be cultured
- Special stains used
  - Silver stains often used

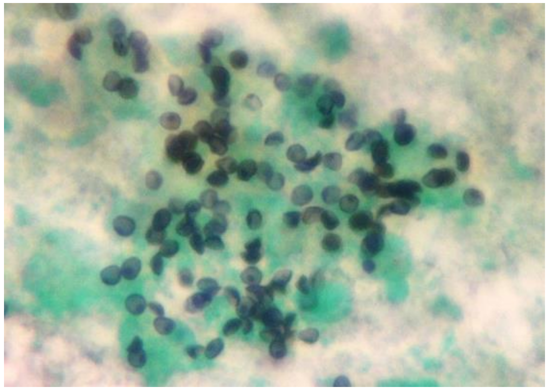


Image courtesy of Yale Rosen

PCP

Pneumocystis jirovecii

- Treatments
  - TMP-SMX (first line)
  - Dapsone
  - Pentamidine
- Prophylaxis
  - TMP-SMX when CD4 <200cells/microL
  - High dose steroid or other immunosuppressant

Pleural Disease

Jason Ryan, MD, MPH

What are the pleura?

- Two layers of tissue surrounding lungs
  - Visceral pleura – attached to lung
  - Parietal pleura – attached to chest wall
- Pleural space/cavity – between layers
- Pleural lined by mesothelial cells
- Secrete small amount pleural fluid for lubrication

Pneumothorax

- Air in pleural space
- Two types to know about
  - Spontaneous
  - Tension

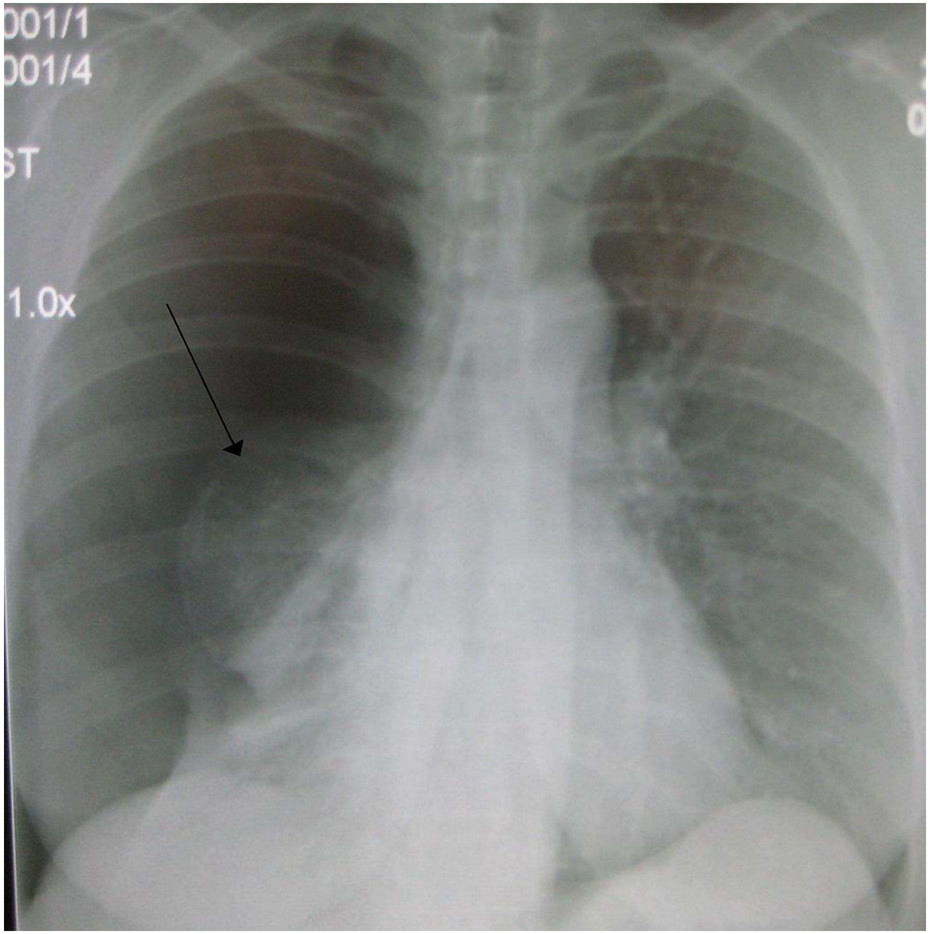
Spontaneous PTX

- Primary
  - Rupture of subpleural bleb
  - Common in tall, thin young males
- Secondary
  - Older patients with underlying pulmonary disease
  - COPD

Spontaneous PTX

- Sudden onset dyspnea
- Sometimes pleuritic chest pain
- CXR for diagnosis

Pneumothorax



Pneumothorax

Treatment

- 100% Oxygen
  - Displaces nitrogen from capillary blood
  - ↑gradient for nitrogen reabsorption from pleural space
- Chest tube
  - Larger pneumothoraces (>15% lung volume)

Tension PTX

- Usually from trauma
- Air enters pleural space but cannot leave
- Medical emergency
- Emergent thoracentesis/chest tube placement
- Trachea deviates AWAY from affected side

Pleural Effusion

- Accumulation of fluid in pleural space

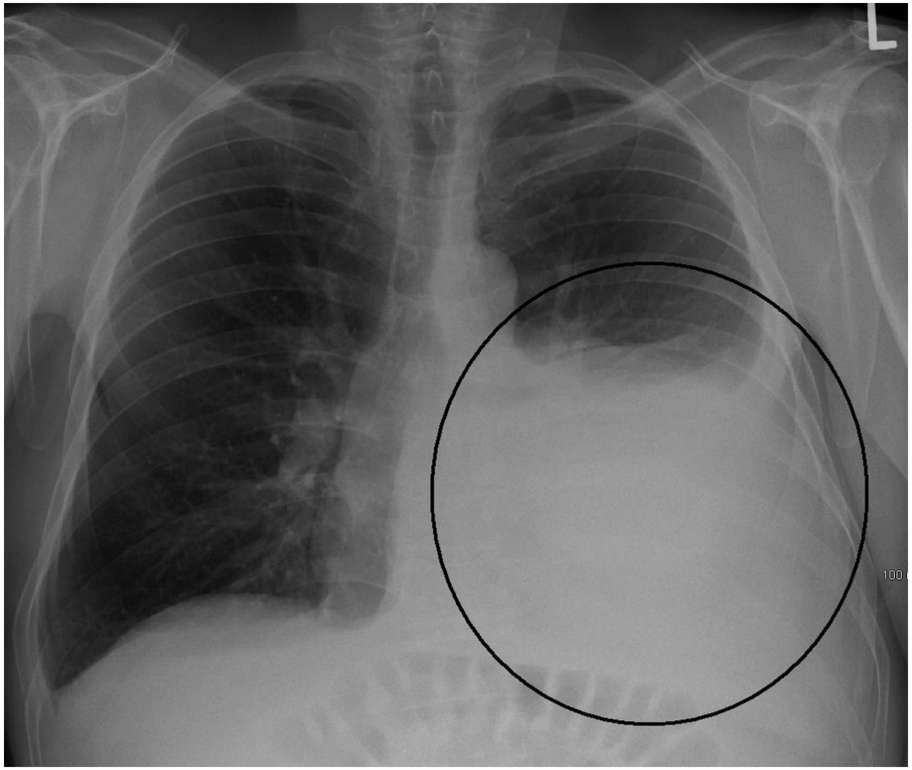


Image courtesy of James Heilman, MD

Pleural Effusion

- Three general etiologies
  - Transudative
  - Exudative
  - Lymphatic

Transudative Effusion

- Something driving fluid into pleural space
- Most commonly due to CHF (High pressure)
- Other causes:
  - Nephrotic syndrome (low protein)
  - Cirrhosis (low albumin)
- Mostly fluid in effusion
- Very little protein in effusion
- Usually treat for underlying cause (no drainage)

Exudative Effusion

- Fluid leaking into pleural space
  - High vascular permeability
- Many causes
- Malignancy
- Pneumonia
- More protein in pleural fluid vs. transudative
- Usually requires drainage

Transudate vs. Exudate

- Thoracentesis to obtain fluid sample
- Test for protein, LDH
- Light's Criteria – Exudate if:
  - Pleural protein/serum protein greater than 0.5
  - Pleural LDH/serum LDH greater than 0.6
  - Pleural LDH greater than 2/3 upper limits normal LDH

Lymphatic Effusions

"Chylothorax"

- Lymphatic fluid effusion
- From thoracic duct obstruction/injury
- Malignancy most common cause
- Trauma (usually surgical)
- Milky-appearing fluid
- Very high triglycerides
  - TG usually > 110 mg/dL

Other Effusions

- Hemothorax
  - High Hct in fluid
- Empyema
  - Infected pleural fluid
  - Pus, putrid odor, positive culture
- Malignant effusion
  - Positive cytology

Mesothelioma

- Pleural tumor
- Asbestos is only known risk factor
  - Decades after exposure
- Imaging: Pleural thickening and pleural effusion
- Slow onset symptoms (dyspnea, cough, chest pain)
- Poor prognosis
  - Median survival 4 to 13 months untreated
  - 6 to 18 months treated with chemo

Lung Cancer

Jason Ryan, MD, MPH

Common Cancers

- Breast
- Prostate
- Lung (most deadly)
- Colorectal

Lung Cancer Risk Factors

- Cigarette smoking
  - Polycyclic Aromatic Hydrocarbons (PAHs)
- Radiation Therapy
  - Hodgkin's and breast cancer survivors
- Environmental toxins
  - Asbestos
  - Radon

Symptoms

- Usually advanced at presentation
- Cough, dyspnea, rarely hemoptysis
- Usually leads to chest imaging

Diagnosis

- Pulmonary nodule
- “Coin lesion”
- Compare with prior
- Biopsy for diagnosis

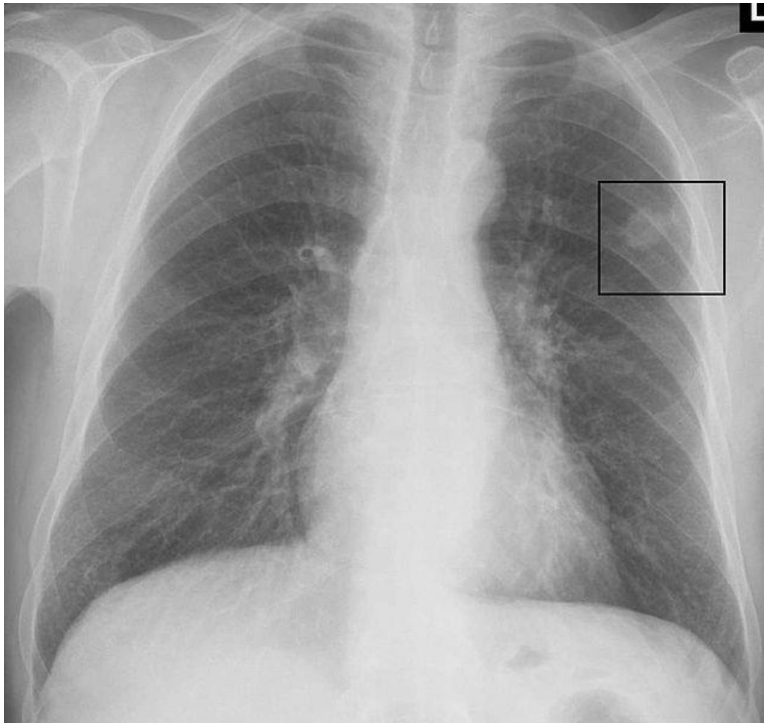


Image courtesy of Lange123

Benign Pulmonary Nodules

- Granulomas (80% benign nodules)
- Hamartomas
  - Lung tissue and cartilage (with scattered calcification)

Granulomas

- Fungi
  - Histoplasmosis (patient from Midwest, Miss/Ohio river valley)
  - Coccidioidomycosis (southwest, California)
- Mycobacteria
  - Usually tuberculosis

Lung Cancers

- Small cell (15%)
  - Fast growing; Early mets
  - Non amenable to surgical resection
  - Smokers
  - Treated with chemo
  - Poor prognosis
- Non-small cell (Most Common: 85%)
  - Can sometimes be resected
  - Better prognosis
  - Smokers and non-smokers

Small Cell Cancer

- Poorly differentiated small cells
- Classic in male smokers
- Neuroendocrine tumor
- Central tumor

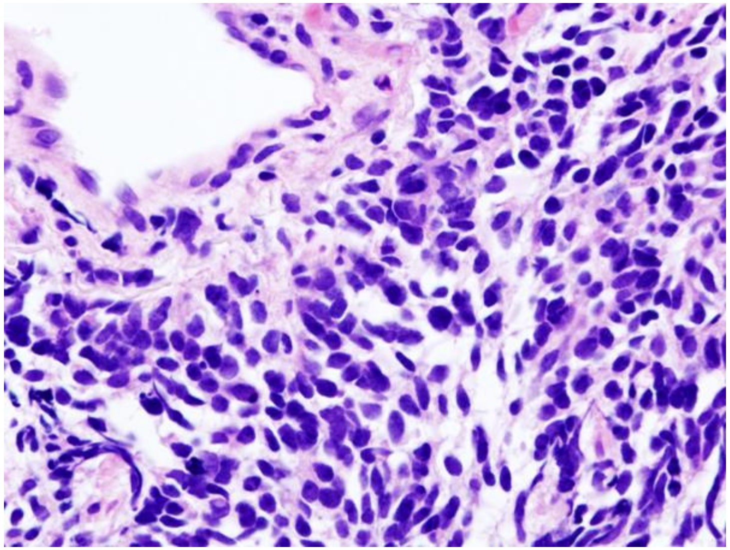


Image courtesy of Wikipedia

Small Cell Cancer

Paraneoplastic Syndromes

- ACTH
  - Cushing syndrome
  - Progressive obesity
  - Hyperglycemia
- ADH
  - SIADH
  - Hyponatremia (confusion)
- Antibodies
  - Antibodies against pre-synaptic Ca channels in neurons
  - Block release of acetylcholine
  - Lambert-Eaton syndrome
  - Main symptom is weakness

Non-Small Cell Cancers

- Squamous Cell Carcinoma
- Adenocarcinoma
- Large cell carcinoma
- Bronchioloalveolar Carcinoma
- Carcinoid tumor

Squamous Cell Carcinoma

- Hilar mass arising from bronchus
- Key pathology
  - Keratin production ("pearls") by tumor cells
  - Intercellular desmosomes ("intercellular bridges")
- Male smokers
- Can produce PTHrP
  - Hypercalcemia
  - Stones, bones, groans, psychiatric overtones
  - Bone and abdominal pain, confusion

Adenocarcinoma

- Glandular tumor
- Most common lung cancer: nonsmokers/females
- Peripheral

Large Cell Carcinoma

- Poorly differentiated
  - Lacks glandular or squamous differentiation
  - Lacks small cells
- Smokers cancer
- Central or peripheral
- Poor prognosis

Bronchioloalveolar Carcinoma

- Subtype of adenocarcinoma
- Many similar features to adeno:
  - Nonsmokers, Peripheral
- Mucinous type: Derived from goblet cells
- Nonmucinous: Clara cells or type II pneumocytes
- Looks like PNA on CXR
  - Lobar consolidation
- Excellent prognosis
  - Surgery, radiotherapy, sometimes adjuvant chemotherapy

Carcinoid tumor

- Neuroendocrine
- Well-differentiated cells
- Chromogranin positive
- Non-smokers
- Rarely causes carcinoid syndrome
  - Secretion of serotonin
  - Flushing, diarrhea

Complications

- Pleural effusions
  - Tap fluid, send for cytology
- Phrenic nerve compression
  - Diaphragm paralysis
  - Dyspnea
  - Hemidiaphragm elevated on CXR
  - Sniff test
- Recurrent laryngeal nerve compression
  - Hoarseness

SVC Syndrome

- Obstruction of blood flow through SVC
- Can be caused by compression from tumor
  - Lung Masses: NSCLC, SCLC
  - Mediastinal Masses: Lymphoma
- Other causes include thrombosis
  - Indwelling catheters, pacemaker wires
- Facial swelling or head fullness
- Arm swelling
- Can cause increased ICP
  - Headaches, confusion, coma
  - Cranial artery rupture

SVC Syndrome

- Usually diagnosed CXR or CT Chest
- Various treatment options:
  - Anticoagulation for thrombus
  - Steroids (lymphoma)
  - Chemo/Radiation
  - Endovascular stenting

Pancoast Tumor

- Carcinoma at apex of lung
- Involve superior sulcus
  - Groove formed by subclavian vessels
- Arm edema affected side
- Shoulder pain radiating toward axilla/scapula
- Arm paresthesias, weakness
- Can compress sympathetic nerves
- Horner's syndrome
  - Miosis
  - Ptosis
  - Anhidrosis

Image courtesy of Jmarchn

Metastasis from Lung Cancer

- Adrenals
  - Usually found on imaging without symptoms
- Brain
  - Headache, neuro deficits, seizures
- Bone
  - Pathologic fractures
- Liver
  - Hepatomegaly, jaundice

Metastasis to Lung

- More common than primary lung tumors
- Most commonly from breast or colon cancer
- Usually multiple lesions on imaging

Sleep Apnea

Jason Ryan, MD, MPH

Sleep Apnea

- Apnea = cessation of breathing
- Sleep apnea = cessation of breathing during sleep
- Usually >10 seconds
- Multiple episodes per night are typical

Sleep Apnea Symptoms

- Unrestful sleep
- Daytime somnolence
- Loud snoring

Sleep Apnea Types

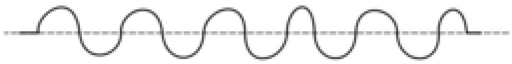
- Central sleep apnea
  - No effort to breathe
- Obstructive sleep apnea
  - Decreased air flow despite effort to breathe

Central Sleep Apnea

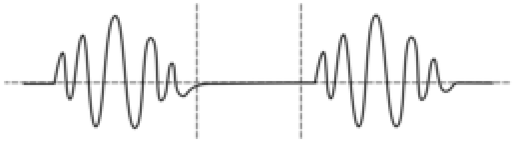
- Patients with marginal ventilation when awake
  - Hypoventilate when awake
  - Fall asleep → apnea periods
  - Central nervous system disease (encephalitis)
  - Neuromuscular diseases (polio, ALS)
  - Severe kyphoscoliosis
  - Narcotics

Central Sleep Apnea

- Cheyne-Stokes breathing
  - Cyclic breathing
  - Delayed detection/response to changes in $PaCO_2$
  - Common in heart failure and stroke patients



Normal Breathing



Cheyne-Stokes

Images courtesy of Aleksa Lukic

Obstructive Sleep Apnea

- Recurrent soft tissue collapse in the pharynx
- Strongest risk factor is obesity

Sleep Apnea Complications

- HTN
- Pulmonary HTN
- Arrhythmias
- Sudden death

Erythropoiesis

- Chronic hypoxia
- EPO release

Sleep Apnea Diagnosis

- Polysomnography
- "Sleep study"
- Patient sleeps in monitored setting
- EEG, eye movements
- O2 level, HR, respiratory rate
- Number of apnea episodes recorded

Sleep Apnea Treatments

- Weight loss
  - Takes time; not best option for exhausted patients
- CPAP
  - First line for symptomatic patients
- Upper airway surgery
  - Severe disease

CPAP

Image courtesy of Aslam Calicut

Cystic Fibrosis

Jason Ryan, MD, MPH

Cystic Fibrosis

- Inherited genetic disease
  - Autosomal recessive pattern
  - Both parents must be carriers
- Results in thick, sticky mucus in lungs/GI tract
- Common cause chronic lung disease in children

CFTR

Cystic Fibrosis Transmembrane Regulator

- CFTR protein is abnormal in CF
- CFTR gene encodes for the abnormal protein

CFTR

Cystic Fibrosis Transmembrane Regulator

- ATP ion transporter
- Epithelial Cell Functions
  - Pumps Cl^- out of epithelial cells
  - Against concentration gradient (uses ATP)
  - Creates a membrane potential that draws out Na/H2O
  - Hydrates mucosal surfaces (lungs, GI tract)
- Sweat gland functions
  - Removes NaCl from sweat (makes sweat hypotonic)
  - CF patients have high NaCl in sweat

CFTR Mutations

- Many mutations identified
- Most common mutation: delta F508
  - Deletion of 3 DNA bases
  - Codes for 508th AA acid: phenylalanine
- Most common consequence: abnormal processing
  - Abnormal protein folding
  - Prevents protein trafficking to correct cellular location

CF Pathophysiology

- Thick mucous in lungs
  - Recurrent pulmonary infections (Pseudomonas, S. Aureus)
  - Chronic bronchitis
  - Bronchiectasis
- Thick mucous in GI tract
  - Impaired flow of bile and pancreatic secretions
  - Malabsorption especially fats
  - Loss of fat soluble vitamins (A, D, E, K)
  - Steatorrhea

CF Presentation

- Usually diagnosed <2yo
- Respiratory disease (45%)
- Failure to thrive (28%)
- Meconium ileus (20%)

CF Lung Disease

- Productive cough
- Hyperinflation of lungs on CXR
- Obstructive pattern
- Later disease
  - Chronic bronchitis
  - Bronchiectasis
- Acute exacerbations
- Pseudomonas aeruginosa: major pathogen in CF

Pancreatic insufficiency

- Chronic pancreatitis
- CF-related diabetes
- Fat malabsorption
- Steatorrhea:
  - Frequent stools
  - Foul-smelling stools
  - Oily or greasy
  - Stools may float

Pancreatic insufficiency

- Deficiencies of fat-soluble vitamins: A, D, E, and K
- Vitamin K: coagulopathy
- Vitamin D: rickets
- Vitamin A: Night blindness
- Vitamin E: Ataxia, hemolysis

Meconium ileus

- Meconium
  - Meconium: first stool of newborn
  - Very thick and sticky
- Meconium ileus = bowel obstruction
  - Meconium too thick/sticky
  - Meconium plug forms
- Abdominal distension
- Vomiting
- Air fluid levels of X-ray
- Failure to pass meconium

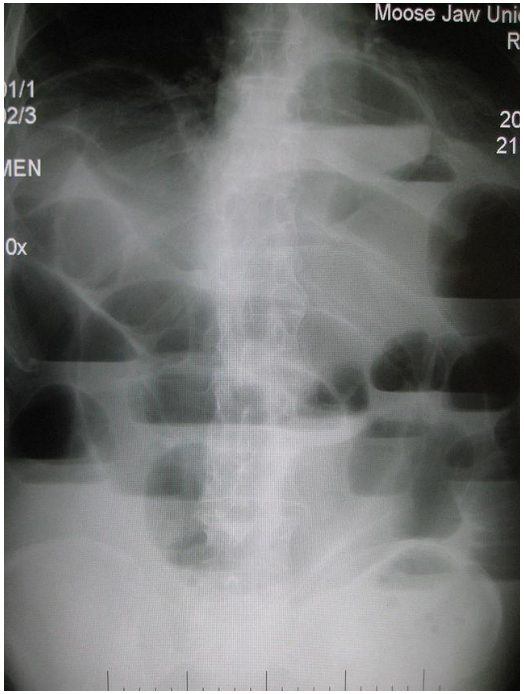


Image courtesy of James Heilman, MD

Other symptoms

- Biliary disease
  - Bile duct obstruction
  - Pale or clay colored stool
  - Elevation of LFTs
  - Hepatomegaly
  - Cirrhosis
  - Gallstones

Other symptoms

- Infertility
  - 95 percent males with CF are infertile
  - Absent vas deferens
  - Problem is sperm transport not spermatogenesis
  - Can have children with assisted techniques

Other symptoms

- Digital clubbing
- Nasal polyps

Image courtesy of James Heilman, MD

Diagnosis

- Sweat chloride test
- Pilocarpine iontophoresis
- Pilocarpine gauze placed on skin
- Electrode placed over gauze
- Small electrical current drives pilocarpine into skin
- Sweating occurs
- Sweat collected on filter paper
- Chloride content analyzed
- High chloride level suggests CF
- DNA testing done if sweat test abnormal

Diagnosis

- Rare CF patients have negative sweat test
  - Usually have milder disease
  - Often recurrent pulmonary and sinus infections
- If symptoms highly suggestive, can test nasal transepithelial potential difference
  - Measure nasal voltage
  - CF patients: more negative voltage
  - Due to abnormal sodium processing

Treatment

- Promote clearance of airway secretions
  - Inhaled DNase (dornase alfa)
  - Inhaled saline
  - N-acetylcysteine
- Ivacaftor (tablets)
  - Increased chloride ion flux
  - Only for patients with G551D mutation
- Exacerbations are treated with antibiotics
- Lung transplantation

Other Treatments

- Pancreatic enzyme replacement
- Vitamins (A, D, E, K)
- Vaccinations

Prognosis

- Average life span ~ 37 years
- Death from lung complications

Screening

- Prenatal
  - Test for 23 most common CF mutations in US
  - Often test mother first and stop if negative
- Newborn
  - ↑ blood levels immunoreactive trypsinogen (IRT)
  - Blood test → if positive → sweat test

Tuberculosis

Jason Ryan, MD, MPH

Tuberculosis

- Ancient disease: Found in mummies!
- Old name: Consumption
- Tubercle = round nodule
- Tuberculosis = multiple round nodules

Mycobacterium tuberculosis

- Obligate aerobes
  - Prefer lungs
  - Reactivation disease prefers upper lobes
- Facultative intracellular pathogens
  - Infect macrophages

Culture of TB

- Difficult to culture
  - Special media used
  - Lowenstein-Jensen agar
- Slow growing
- Does not stain well with Gram stain
- This is due to mycolic acids in cell wall
  - Also fatty acids and complex lipids

Acid Fast

- Cell walls impermeable to many dyes
- Stain with very concentrated dyes plus heat
  - Lipid soluble; contain phenols
- Once stained, plate rinsed with acid decolorizer
  - "Acid fast stain"
- TB resists decolorization with acid solvents
- Some other bacteria (Nocardia) also do this

Virulence Factors

- Trehalose dimycolate ("cord factor")
  - Helps evade immune response
  - Causes granuloma formation
  - Triggers cytokine release
- Sulfatides
  - Glycolipids
  - Inhibits fusion of phagosomes/lysosomes
- Catalase-peroxidase
  - Resists host cell oxidation

Spread of TB

- Spreads through the air
- Active TB patient's cough, sneeze, etc.
- Inhaled by uninfected person
- Can spread rapidly in crowded areas

Exposure to TB

- Most patients will not develop active disease
  - Infection can clear or remain "latent"
- Small proportion patients develop active disease

Primary TB

Clinical Picture

- Mainly a disease of childhood or chemo patients
  - Ineffective immune response
- Gradual onset: weeks
- Fever
- Cough
- Pleuritic chest pain
- Fatigue, arthralgias

Primary TB
Pathophysiology

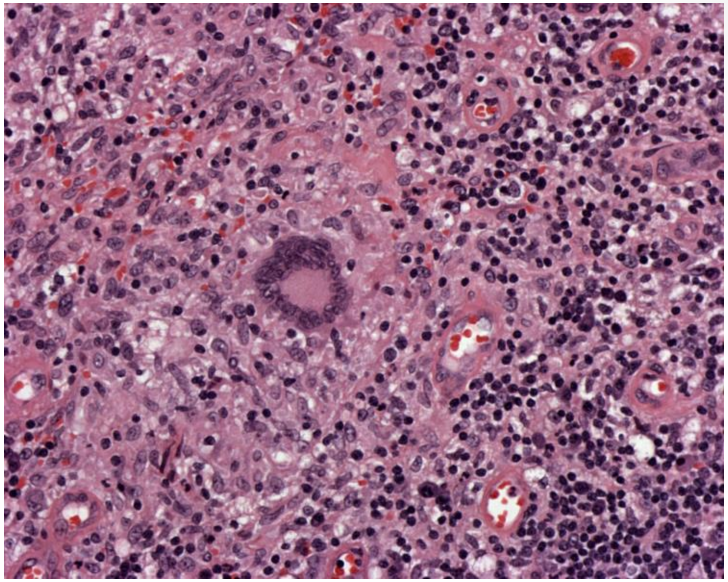
- First week
  - TB infects macrophages
  - Phagocytosed
  - Intracellular bacterial proliferation

Primary TB

Pathophysiology

- Two to four weeks
  - Cell-mediated immune system controls TB
  - TH1 response
  - Activation of CD4+ T cells
  - Interferon-γ secreted
  - Activated macrophages and cytotoxic T lymphocytes

Granulomas



- Granulomatous inflammation
- Caseating necrosis
- Macrophages transform to :
  - Epithelioid cells
  - Langhans giant cells
- Fibroblasts activated → collagen
- T-cell mediated delayed type hypersensitivity reaction
  - Type IV hypersensitivity reaction

Hilar Lymphadenopathy

- CXR often normal
- Classic finding is hilar lymphadenopathy
- Occur as early as 1 week after infection
- Resolve slowly over months to years

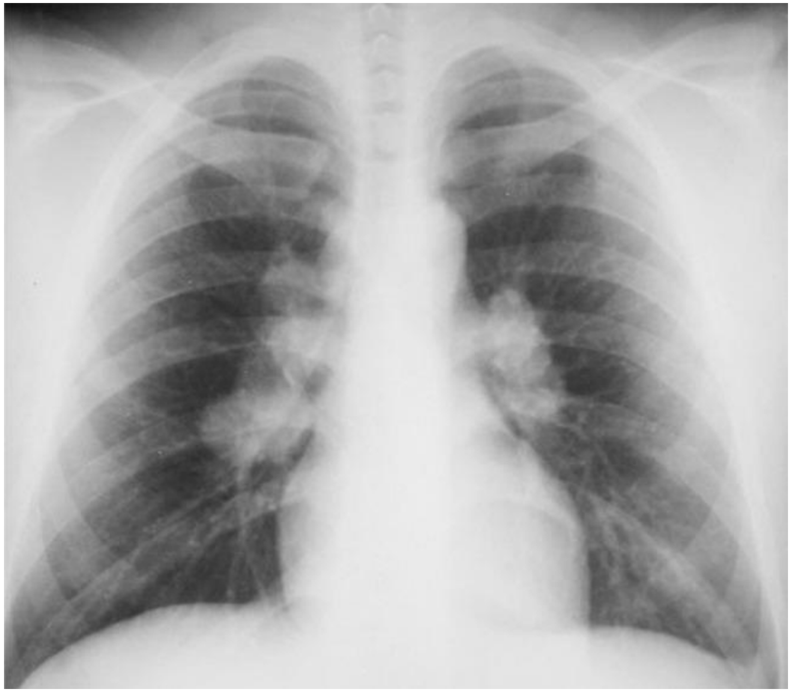
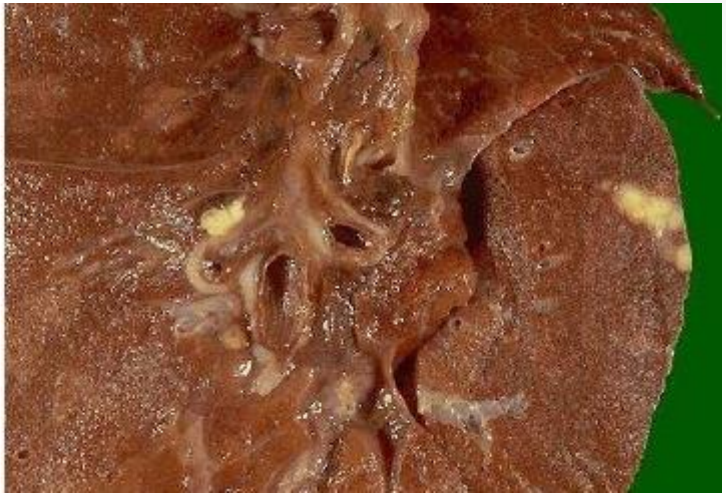


Image provided by www.learningradiology.com, courtesy of Dr. William Herring, MD, FACR. Used with permission.

Ghon Foci

- Ghon foci form
  - Granulomas
  - Subpleural
  - Mid to lower lungs
- Ghon foci plus lymph node is Ghon complex
- Calcified Ghon complex is a Ranke complex



Images courtesy of kaziomer

Primary TB Resolution

- Most (90%) patients control infection
  - Disease heals leaving fibrosis
  - Sometimes completely clears
  - Usually enters latent phase ("walled off")
  - Immunity develops
  - PPD positive
- Rare (10%) patients have expanded illness
  - Miliary dissemination
  - More common with HIV, CKD, DM (impaired immunity)

Miliary TB

- Hematogenous spread of TB
- Progressive primary infection or reactivation
- Nearly any organ system can be involved
  - Bones
  - Liver
  - CNS (meningitis)
  - Heart (pericarditis)
  - Skin

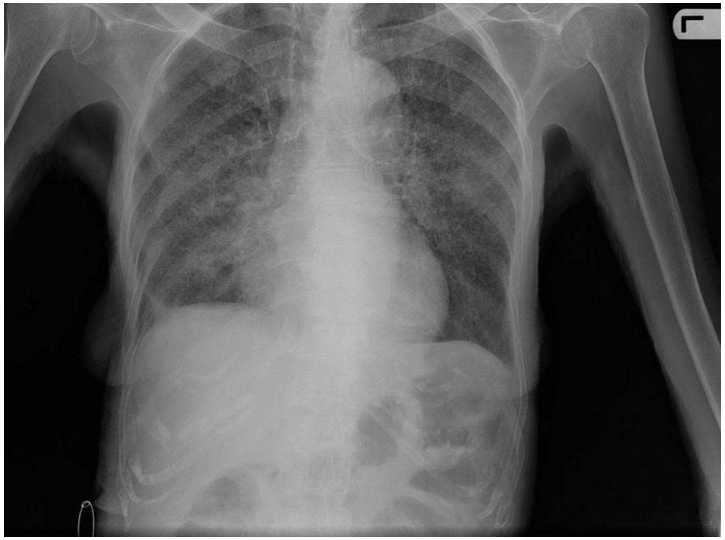
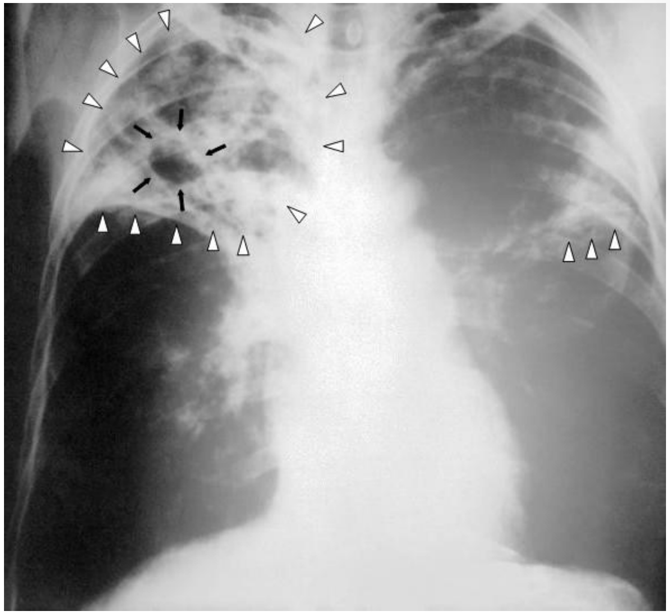


Image courtesy of Yale Rosen

Miliary TB

- Pott's disease
  - Spine infection (osteomyelitis)
  - Back pain, fever, night sweats, weight loss
- Constrictive pericarditis

Reactivation TB



- Reactivation of dormant TB
- Cough, weight loss, fatigue
- Fever
- Night sweats
- Chest pain
- Often cavitation (caseous and liquefactive necrosis)
- Hemoptysis (erode pulmonary vasculature)
- CXR classically shows upper lobe lesions

Reactivation TB

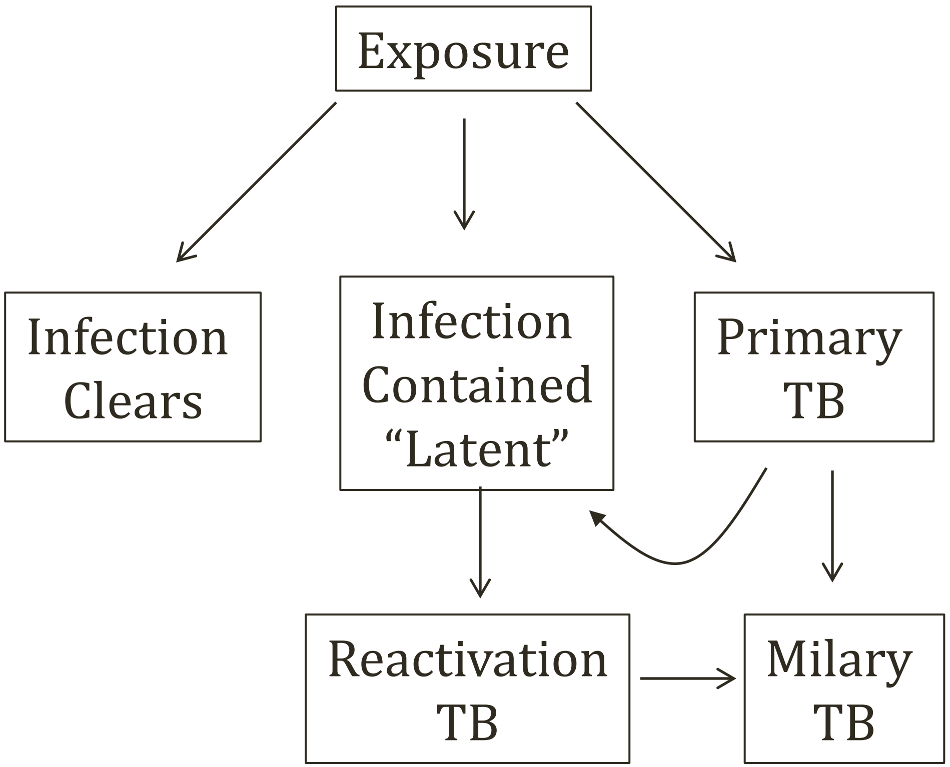
- Can occur when immune compromise develops
- HIV infection
- TNF-α inhibitors
  - Used in autoimmune diseases
  - Etanercept, Infliximab
- Diabetes

Aspergilloma

<u>Aspergillus</u>
ABPA
Invasive Aspergillus
Aspergilloma

- Fungus ball
- Caused by Aspergillus fumigatus
- Non-invasive form of aspergillosis
- Grows in pre-formed cavities
- Pulmonary TB is most common association
- Often asymptomatic
- Can cause hemoptysis
- Diagnosis: Imaging plus sputum culture
- Treatment: Observation vs. surgery

TB Infection Summary



Diagnosis of Active TB

- Usual method: 3 sputum samples
  - Usually about 8hrs apart
  - Spontaneous or induced
  - Induced: Inhalation of aerosolized saline by nebulizer
- Acid-fast smear and culture

Diagnosis of Active TB

- Not necessary to hospitalize just for TB suspicion
- Outpatients: Remain at home, avoid visitors, mask
- Inpatients: Respiratory isolation
  - Private room
  - Negative air pressure
  - Persons entering must wear a respirator
  - Tight seal over the nose and mouth

Diagnosis of Latent TB

- Identification of latent TB crucial to infection control
- Diagnosis: Tuberculin skin testing (TST)
- SC injection purified protein derivative (PPD)
  - 5 tuberculin units (0.1 mL)
- Wait 48 hours
- Measure diameter of induration (not erythema)

PPD Testing

Induration	Interpretation
<5mm	Negative
>5mm	Positive if HIV, Immunosuppressed
>10mm	High risk individuals*
>15mm	Healthy patients >4yo with low likelihood of TB

* Silicosis, CKD, DM, IV drug users, homeless, prison employees, others

PPD Testing

- False negatives can occur
- Immunosuppressive drugs
  - Corticosteroids
  - TNF-α inhibitors
- Immunocompromised
  - HIV
  - CKD
  - Malnutrition
- Diseased lymph system
  - Sarcoidosis
  - Some lymphomas or leukemias

BCG Vaccine

- Bacille Calmette-Guérin
- Live strain of *Mycobacterium bovis*
- More effective in patients with no TB exposure
  - About 80% effective in children
  - Less effective in adults
- Used in children in areas with high prevalence of TB
- Creates false positive PPD

Treatment of Positive PPD

- Most patients with latent TB will not develop disease
- Small proportion may reactivate
- Prophylaxis lowers risk
- Commonly isoniazid (INH) for 9 months
- Further PPD testing not indicated
  - Will remain positive for life

Treatment of Active TB

- Requires multi-drug regimens
- Typical regimen:
  - Isoniazid
  - Rifampin
  - Pyrazinamide
  - Ethambutol
  - Sometimes streptomycin
- Sometimes direct observation therapy (DOT)
- Risk of Multi-drug resistant (MDR) TB

Isoniazid

- Blocks synthesis of mycolic acids
- Bacteria lose their acid fastness
- katG-encoded catalase-peroxidase
  - Converts INH to active form
  - Mutations lead to INH resistance
  - Monotherapy produces resistance

Isoniazid

- Neurotoxic
  - Neuropathy, ataxia, and paresthesia
  - Competes with B6 as co-factor neurotransmitter synthesis
  - Pyridoxine (B6) co-administered
  - Limits neurotoxicity
- Hepatotoxic (check LFTs)
  - Probably related to metabolites of INH
- Drug-induced lupus

Rifampin

- Inhibit bacterial DNA-dependent RNA polymerase
- Blocks RNA synthesis
- Main side effects are liver, GI
  - Increased LFTs
  - GI upset: nausea, cramps, diarrhea
- Red/orange discoloration fluids (not dangerous)
  - Urine
  - Saliva
  - Sweat, tears
  - CSF

Rifampin

Other uses

- Leprosy
- Meningococcal prophylaxis
- Chemoprophylaxis in contacts of children HiB

Pyrazinamide

- Mechanism unknown
  - Converted to pyrazinoic acid (PZA)
  - May be more active in acidic environment inside macrophages
- Hepatotoxic
  - Can raise LFTs
- Competes with uric acid for excretion in kidneys
  - Can raise uric acid levels
  - Hyperuricemia
  - Gout exacerbations

Ethambutol

- Inhibits arabinosyl transferase
  - Polymerizes arabinose for mycobacteria cell walls
- Key side effect: optic neuropathy
  - Red-green color blindness
  - Difficulty discriminating red and green hues
  - Loss of visual acuity
  - Reversible

Streptomycin

- Older, aminoglycoside drug
- Inhibits bacterial 30S ribosomal subunit
  - Prevents protein synthesis
- Lots of resistance
  - Mutations of genes for ribosomal proteins

Tuberculosis Key Points

- Mycolic acid cell walls → acid fast
- Infects macrophages (intracellular)
- Delayed type hypersensitivity reaction
- Hilar lymphadenopathy; Ghon complex
- Reactivation in upper lobes (immunosuppressed)
- Latent infection diagnosed with PPD
- Treat latent disease with INH
- Treat active disease with multidrug regimen

Sarcoidosis

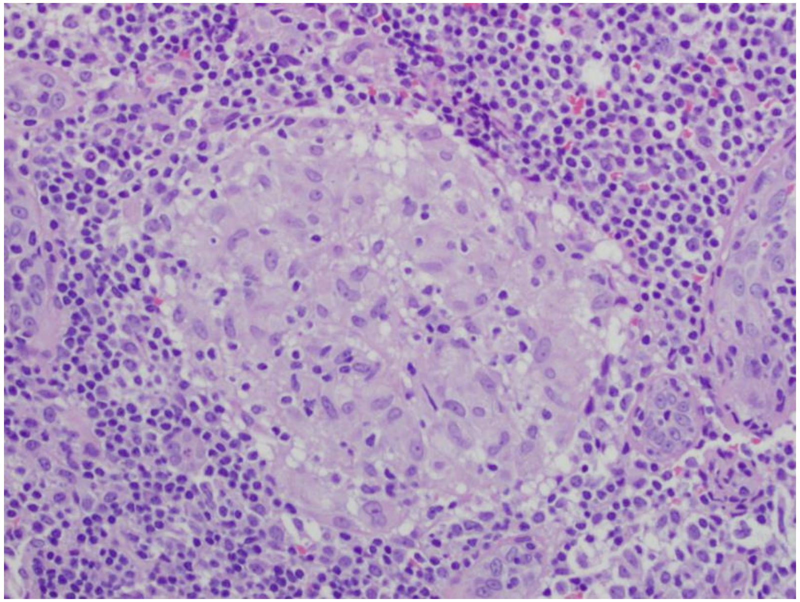
Jason Ryan, MD, MPH

Sarcoidosis

- Granulomatous disease
  - Granulomas form many places in the body
- Immune-mediated
  - Immune cells play major role
- Unknown cause

Sarcoidosis

- Hallmark is widespread non-caseating granulomas
- Tightly packed central area of macrophages, epithelioid cells, multinucleated giant cells
- Surrounded by lymphocytes, monocytes, mast cells, fibroblasts



Pathology

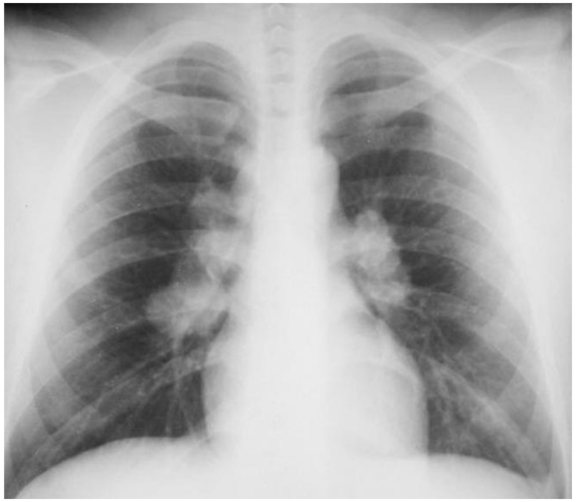
- Cell mediated immune process
- Accumulation of TH1 CD4+ helper T cells
  - High CD4:CD8 ratio
- Secrete IL-2 and interferon-γ
- IL-2 stimulates TH1 proliferation
- IFN-γ activates macrophages
- Ultimately leads to granuloma formation
- Key players: CD4 T cells, IL-2, IFN- γ

Organ Involvement

- Lungs (most common)
- Skin
- Eye
- Heart
  - Conduction disease (heart block)
  - Cardiomyopathy
- Many other systems rarely involved
  - Renal: Renal failure
  - CNS: Neurosarcoid, Bells Palsy, Motor loss
- Any system can be involved

Lung Involvement

- Classic finding is hilar lymphadenopathy
- Classic symptom is cough, dyspnea
- Can cause infiltrates
- Can cause pulmonary fibrosis



Skin Involvement

- Many lesions possible
  - Plaques, maculopapules, subcutaneous nodules
- Classic lesion is erythema nodosum
  - Inflammation of fat cells under skin
  - Tender red nodules
  - Usually on both shins

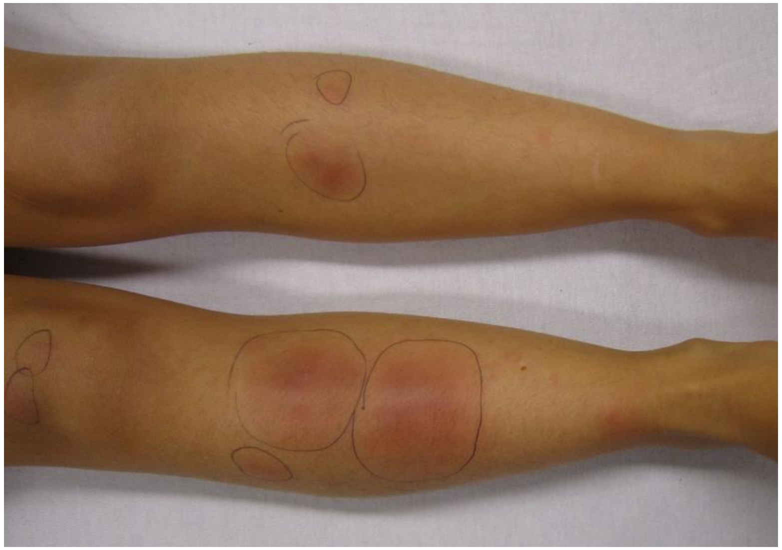
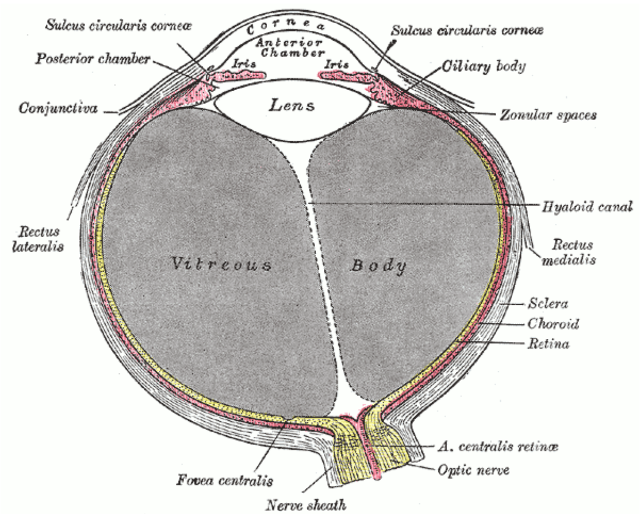


Image courtesy of James Heilman, MD

Eye Involvement: Uveitis

- Can involve many parts of eye
- Classic is uveitis
- Uvea:
  - Iris, ciliary body, choroid
- Uveitis Types
  - Anterior (iris, ciliary)
  - Posterior (choroid)
- Often mild symptoms
  - Dry eye, blurry vision
- Often detected on routine exam



Other Sarcoidosis Features

- Hypercalcemia
  - Elevated 1-α hydroxylase activity in alveolar macrophages
  - Increased vitamin D levels (calcitriol)
- High ACE levels
  - Non-specific finding
  - Elevated in many lung diseases

$$\text{25-OH Vitamin D} \xrightarrow{1\alpha\text{ - hydroxylase}} \text{1,25-OH}_2\text{ Vitamin D}$$

Classic Presentation

- African American female
- Hilar lymphadenopathy
- Cough, dyspnea
- Often asymptomatic, detected on routine chest x-ray

Treatment

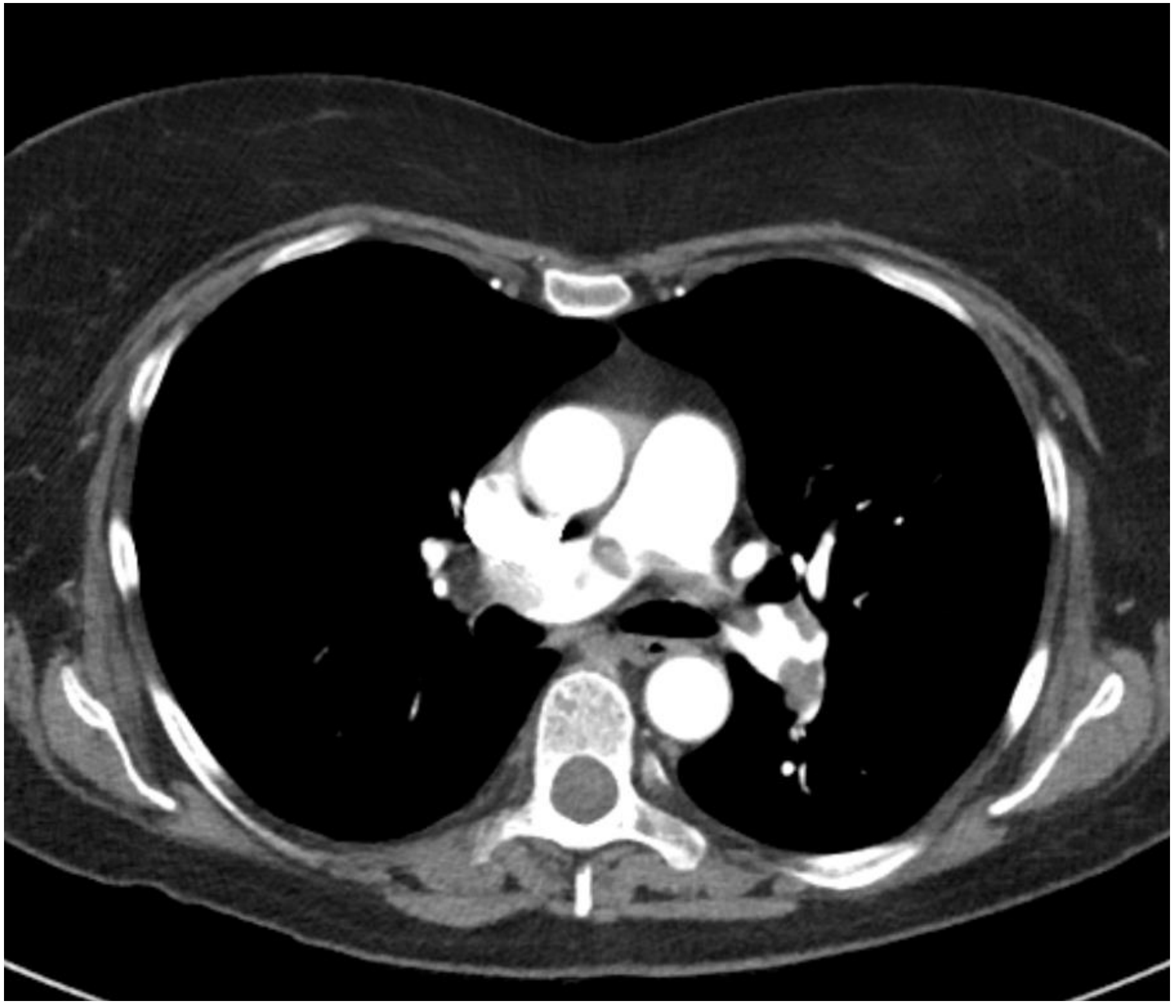
- Steroids
- Other immunosuppressants
  - Methotrexate
  - Azathioprine
  - Mycophenolate

Pulmonary Embolism

Jason Ryan, MD, MPH

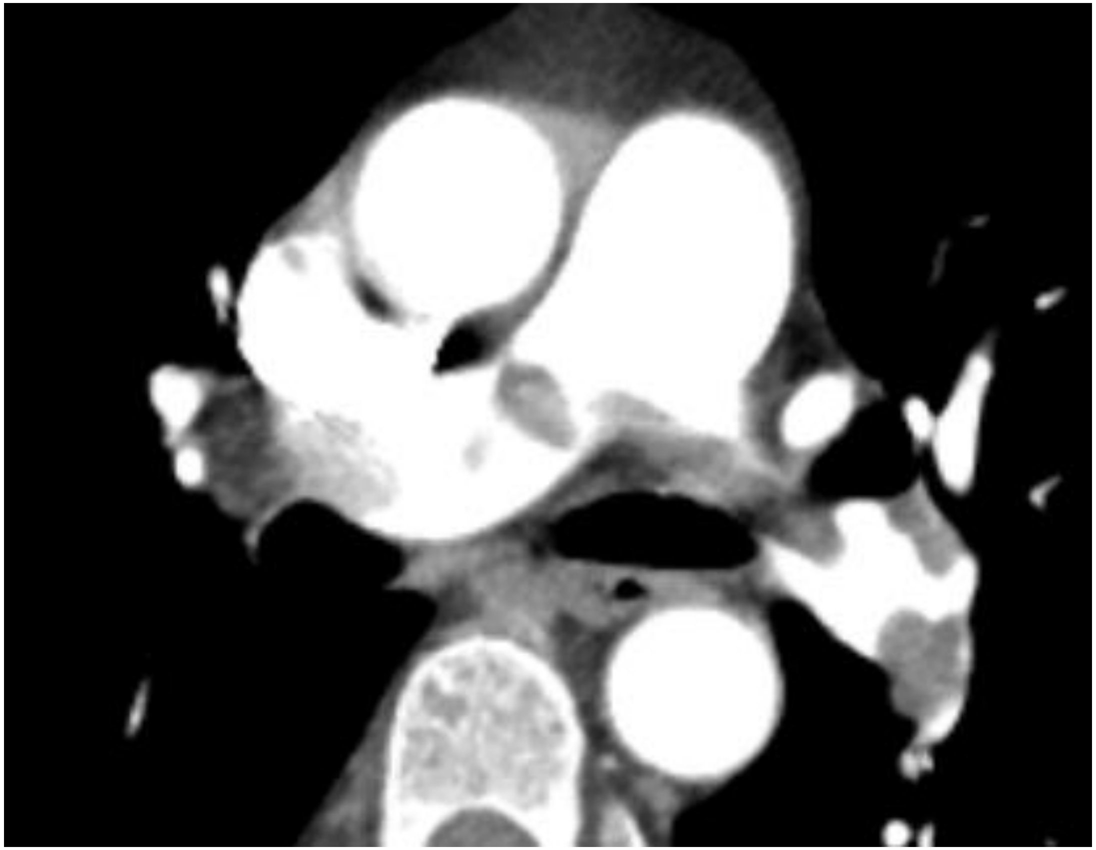
Pulmonary Embolism

CT Angiogram



Pulmonary Embolism

CT Angiogram



Pulmonary Embolism

- Thrombus in pulmonary artery
- Rarely formed in heart or pulmonary vasculature
- Majority come from **femoral vein or deep leg veins**
- Travels to lung via IVC → RA → RV

Pulmonary Embolism

- Can be “unprovoked”
- Often secondary to a **hypercoagulable state**
  - Secondary: Malignancy, surgery, etc.
  - Primary: Protein C/S deficiency, ATIII deficiency, etc.

Pulmonary Embolism

- **Chest pain**
  - Classic presentation is pleuritic
- **Respiratory distress**
  - Dyspnea
  - Hypoxemia
  - Tachypnea
- Massive PE can cause **sudden death**
  - Obstruction to flow through pulmonary arteries
- Small, chronic emboli: **pulmonary hypertension**

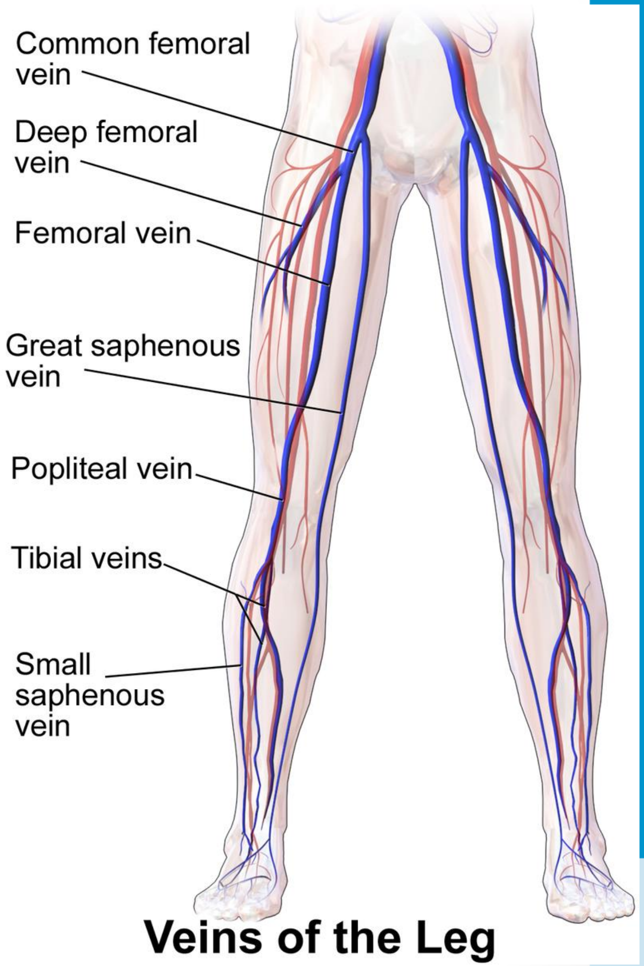
Pulmonary Embolism

Ventilation-Perfusion

- Dead space
  - Ventilation without perfusion
- **V/Q mismatch**
- Hyperventilation
- Blood gas findings variable
- Classic findings: **low PaO_2 and low PCO_2**

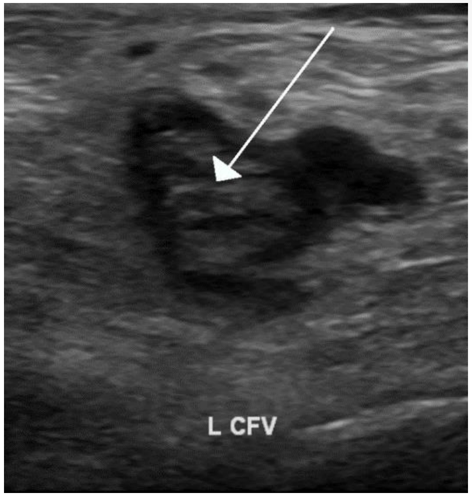
Deep Vein Thrombosis

- Thrombus within a deep vein
- Usually occurs in calf or thigh
- Commonly femoral/popliteal veins
- Can extend or "grow"
- Precedes pulmonary embolism
- Often 2° hypercoagulable state



Bruce Blaus/Wikipedia

Deep Vein Thrombosis



James Heilman, MD

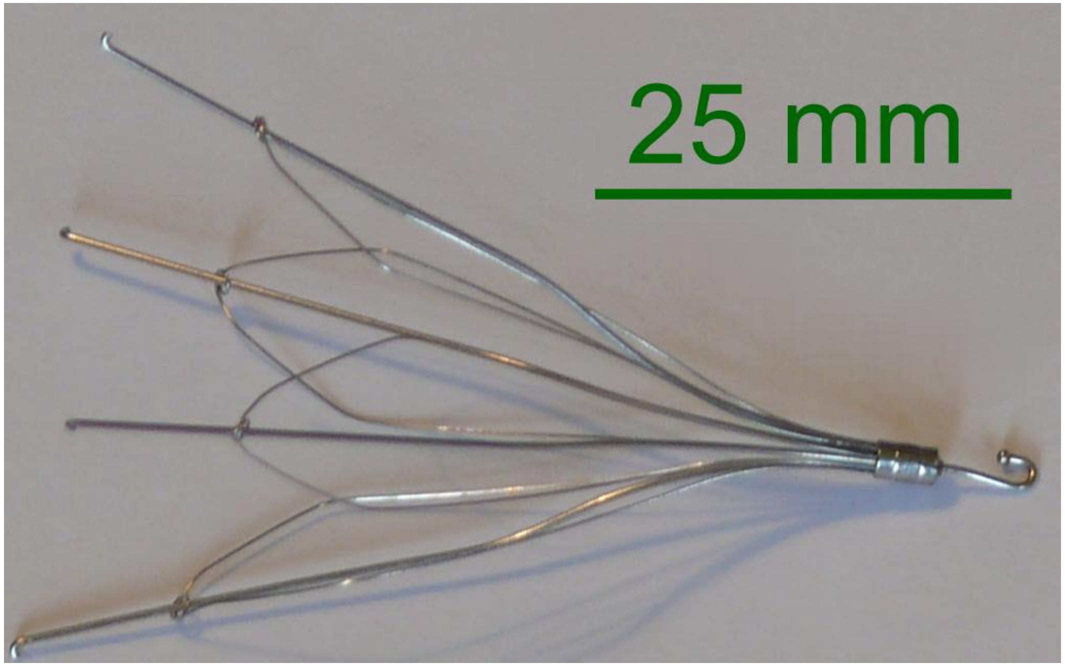
- Often asymptomatic until PE
- Calf pain
- Palpable cord (thrombosed vein)
- Unilateral edema
- Warmth, tenderness, erythema
- Homan's sign: calf pain with dorsiflexion of foot
- Diagnosis: **Lower extremity ultrasound**

Deep Vein Thrombosis

- Similar treatment to PE
  - "DVT/PE"
  - "Venous thromboembolism" (VTE)
- Prevention important in **hospitalized patients**
  - Hypercoagulable
  - Immobility, stasis of blood, inflammation
- **Prophylaxis**: SQ heparin, LMWH

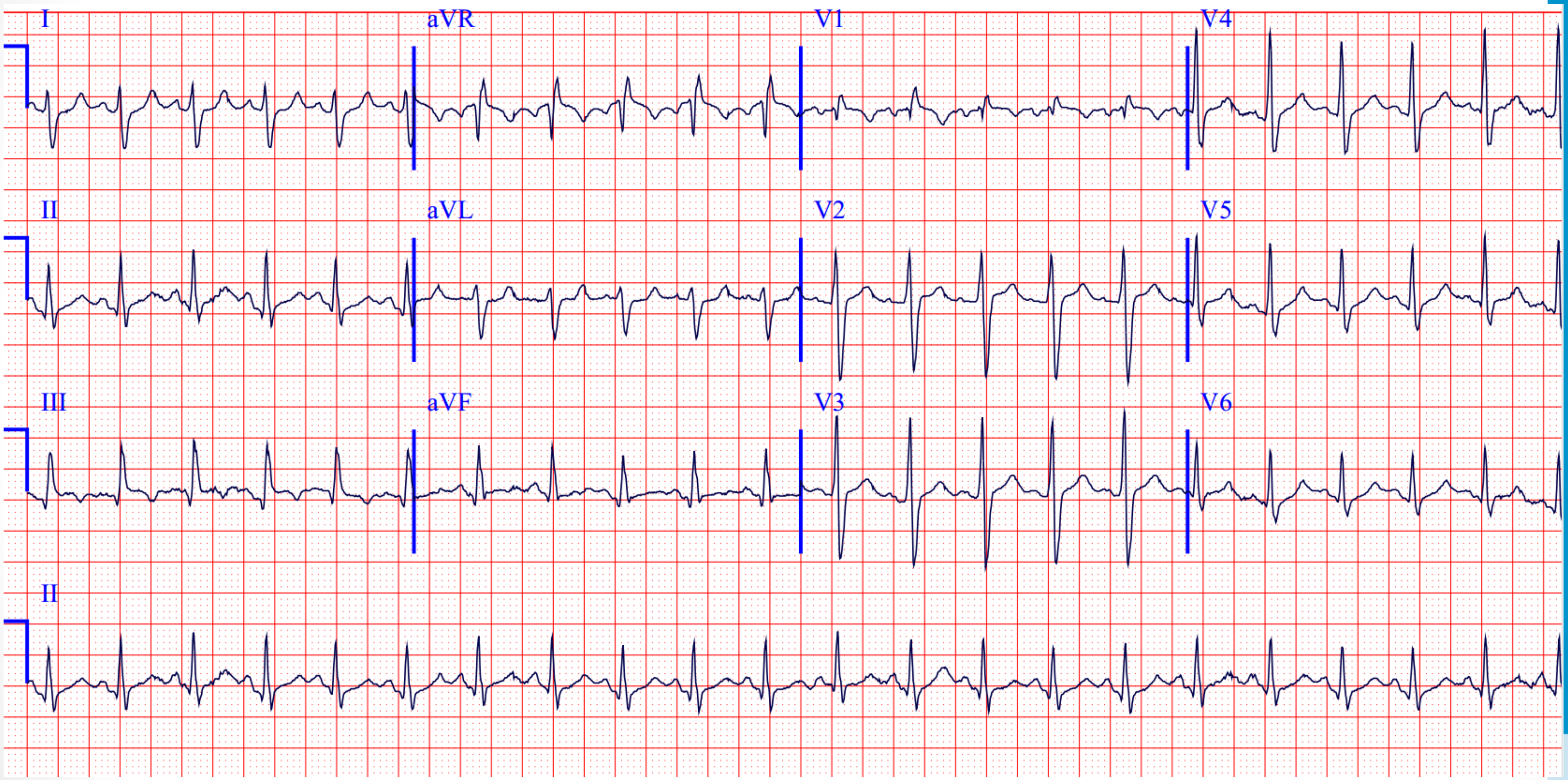
IVC Filter

- Used in high-risk DVT patients
- Placed to prevent pulmonary embolism

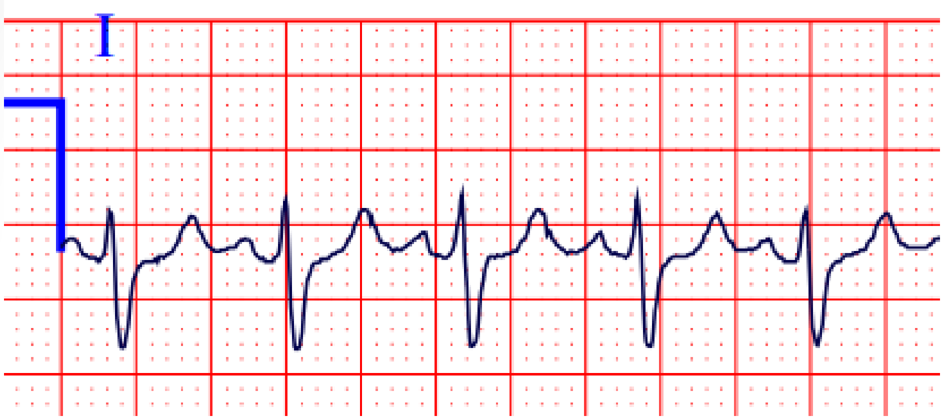


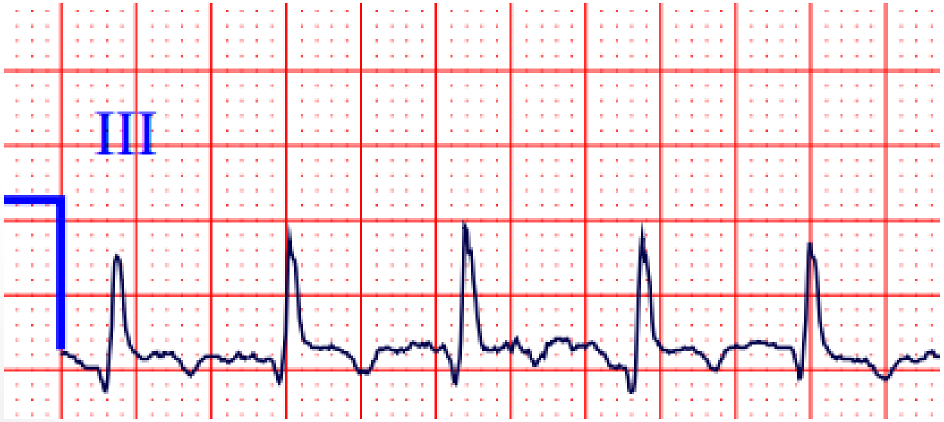
BozMo/Wikipedia

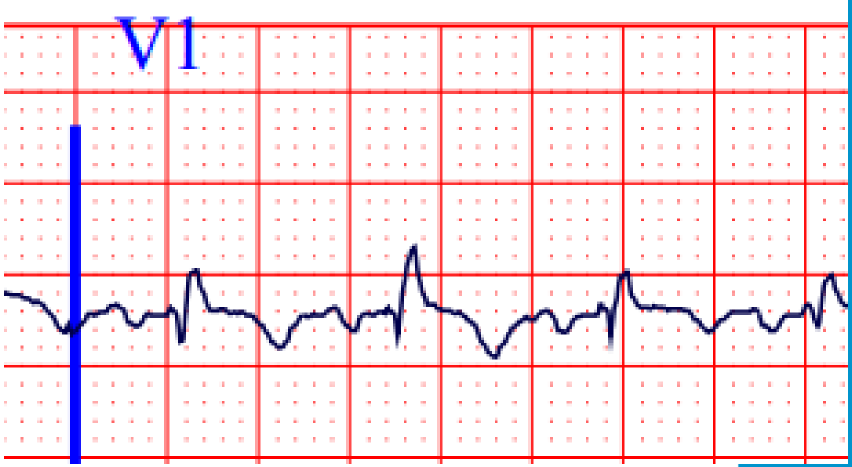
S1Q3T3



S1Q3T3







Wells Score

Active cancer	1
Immobilization of the lower extremities	1
Recently bedridden	1
Localized tenderness	1
Leg swelling	1
One leg swollen > other	1
Pitting edema	1
Superficial veins visible	1
Alternative diagnosis likely	-2

Score >=3 High Probability
1-2 Mod Probability
0 Low Probability

D-dimer

- Degradation product of fibrin
- Sensitive but not specific (unidirectional)
  - Levels elevated in DVT/PE
  - Levels also elevated in many, many other conditions
- Useful when normal in setting of low-mod Wells score

Pulmonary Embolism

Diagnosis

- CT angiogram
- VQ Scan

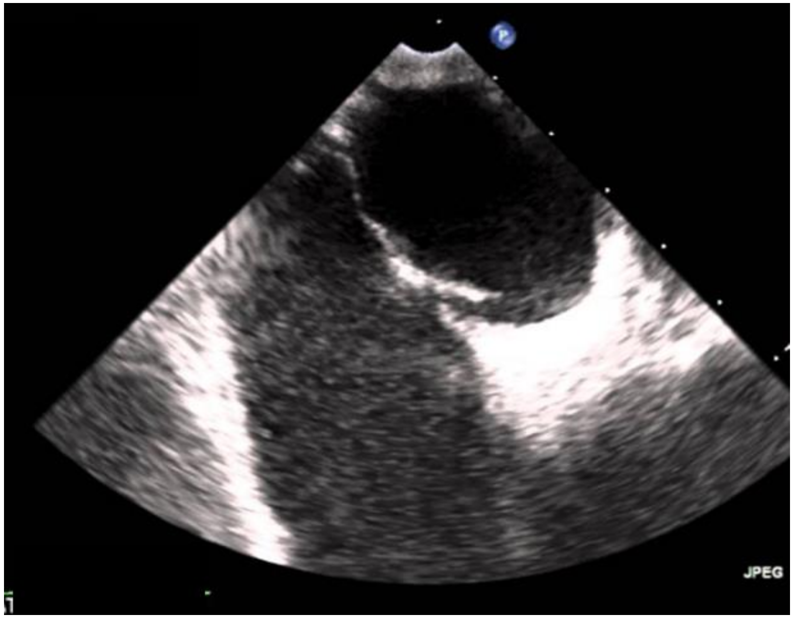
Westgate EJ, FitzGerald GA
Pulmonary Embolism in a Woman Taking Oral Contraceptives and Valdecoxib.
PLoS Medicine Vol. 2, No. 7, e197. doi:10.1371/journal.pmed.0020197

Treatment DVT/PE

- Initial treatment with heparin or LMWH
- Transition to warfarin (oral)
- Massive PE: thrombolysis (tPA)

Patent Foramen Ovale

- Found in ~25% adults
- Failure of foramen ovale to close after birth
- Can allow venous clot to reach arterial system (brain)
- Rarely causes **stroke** in patients with DVT/PE



Fat Embolism

- Often occurs after a **long bone facture**
- Fat may cross lungs → small artery infarctions
- Fat embolism syndrome: pulmonary, neuro, skin

Hellerhoff /Wikipedia

Fat Embolism

- **Lung**
  - Dyspnea, hypoxemia
  - Diffuse capillary leak (ARDS)
  - Often requires mechanical ventilation
- Neurological
  - Usually **confusion**
  - May develop focal deficits
- **Petechiae**

James Heilman, MD/Wikipedia

Amniotic Fluid Embolism

- During labor or shortly after
- Amniotic fluid, fetal cells, fetal debris enter maternal circulation
- Inflammatory reaction
- Often fatal

Wikipedia/Public Domain

Amniotic Fluid Embolism

- Phase I
  - Pulmonary artery vasospasm → pulmonary hypertension
  - Right heart failure
  - Hypoxia
  - Myocardial capillary damage → left heart failure
  - Pulmonary capillary damage → ARDS
  - Acute respiratory distress syndrome
- Key features: **respiratory distress, ↓O_2, hypotension**

Amniotic Fluid Embolism

- Phase II (hemorrhagic phase)
  - Massive hemorrhage
  - DIC
- Key feature: **bleeding**
- **Seizures** also often occur

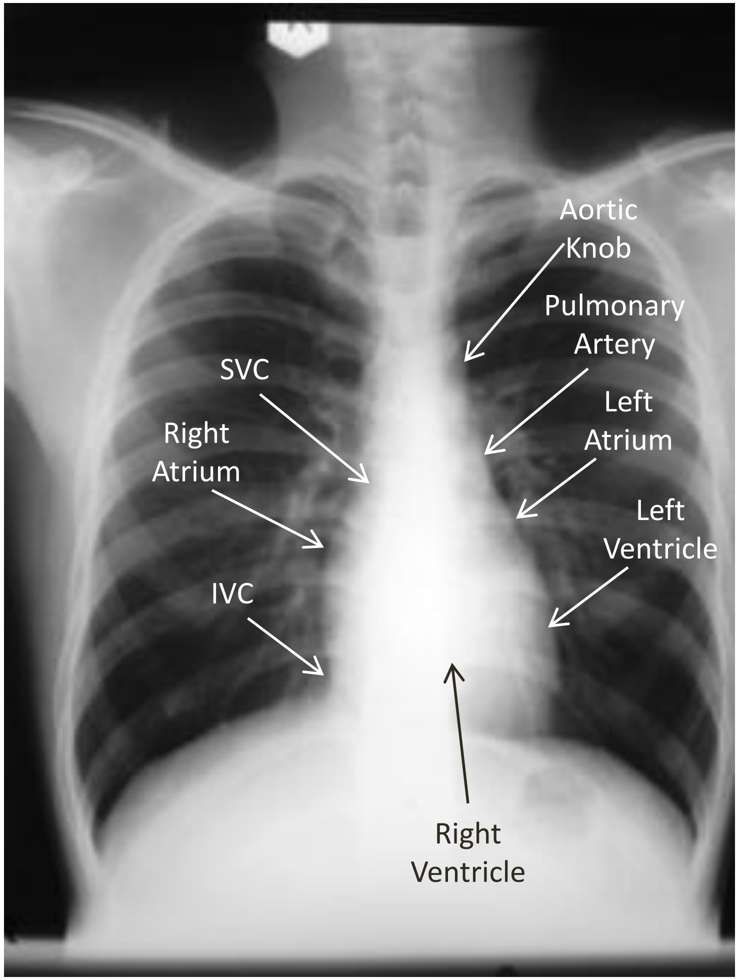
Chest X-rays

Jason Ryan, MD, MPH

Chest X-ray

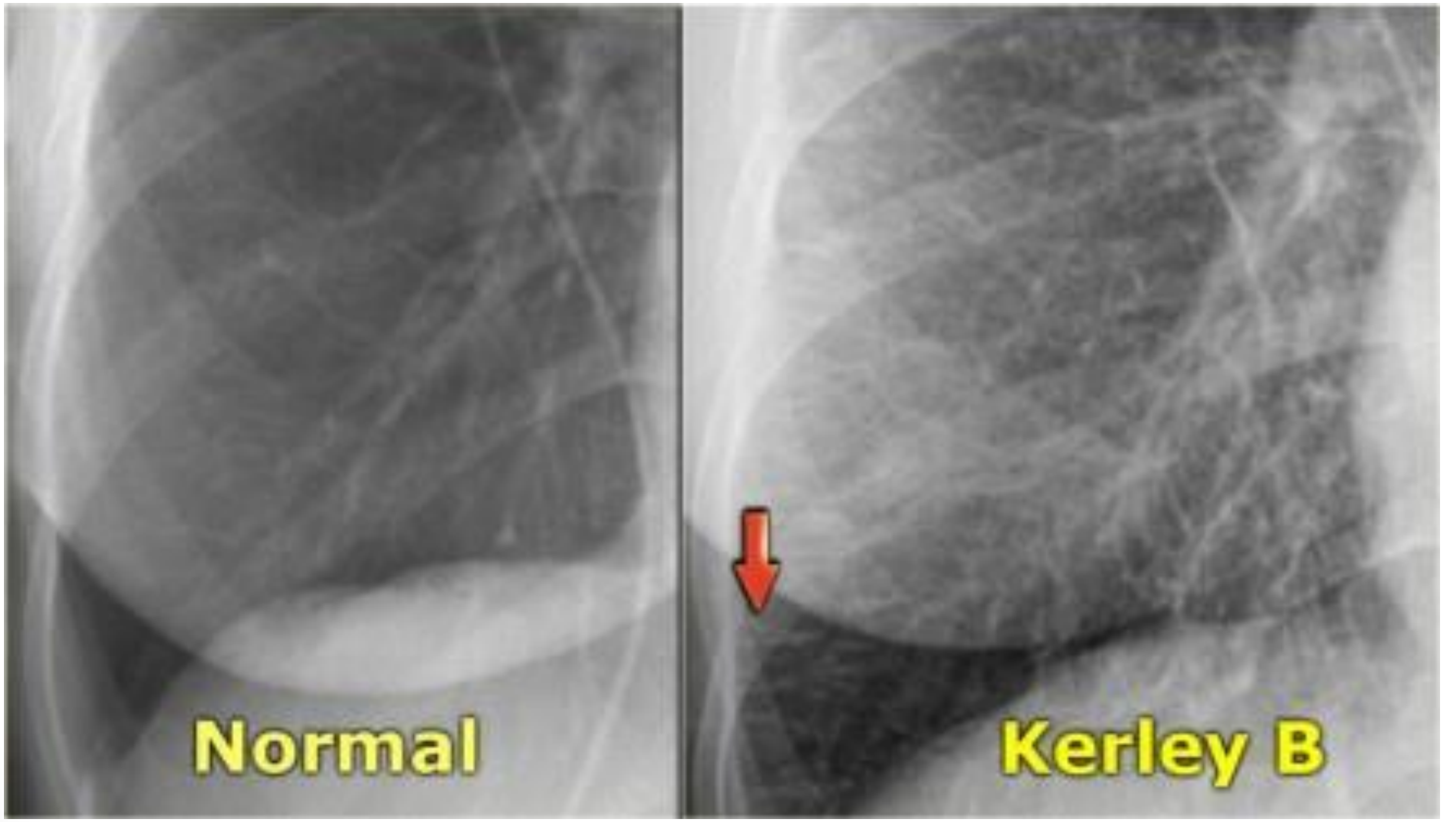
- Difficult to see different structures
- Many, many normal variants
- Many, many pathologic findings
- Reasonable goals:
  - Basic chest anatomy
  - Classic examples of pathology

Chest Anatomy



Pulmonary Edema

Pulmonary Edema



Boards&Beyond STUDY SMARTER

Image courtesy of Radiology Assistant

Pleural Effusion

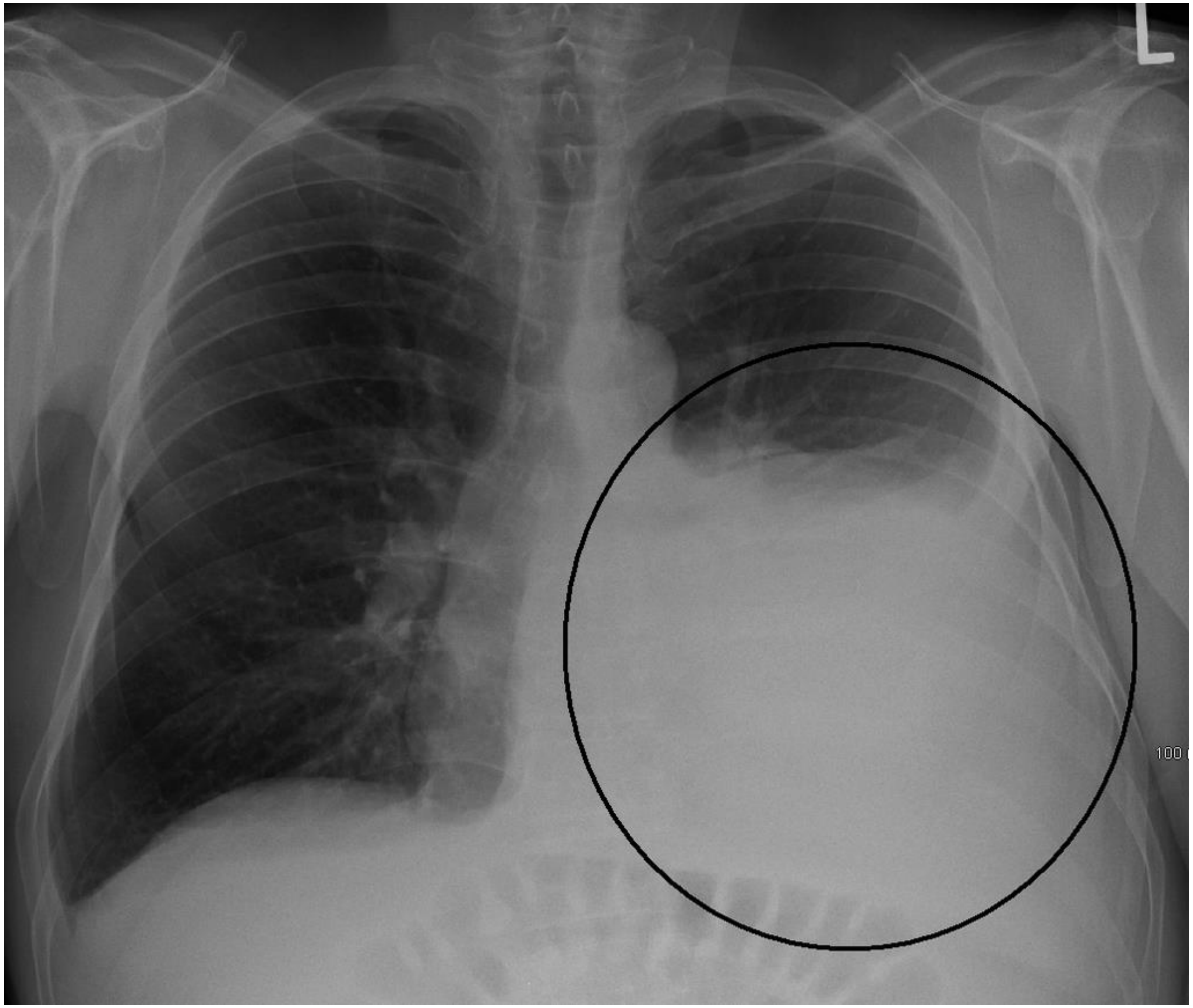
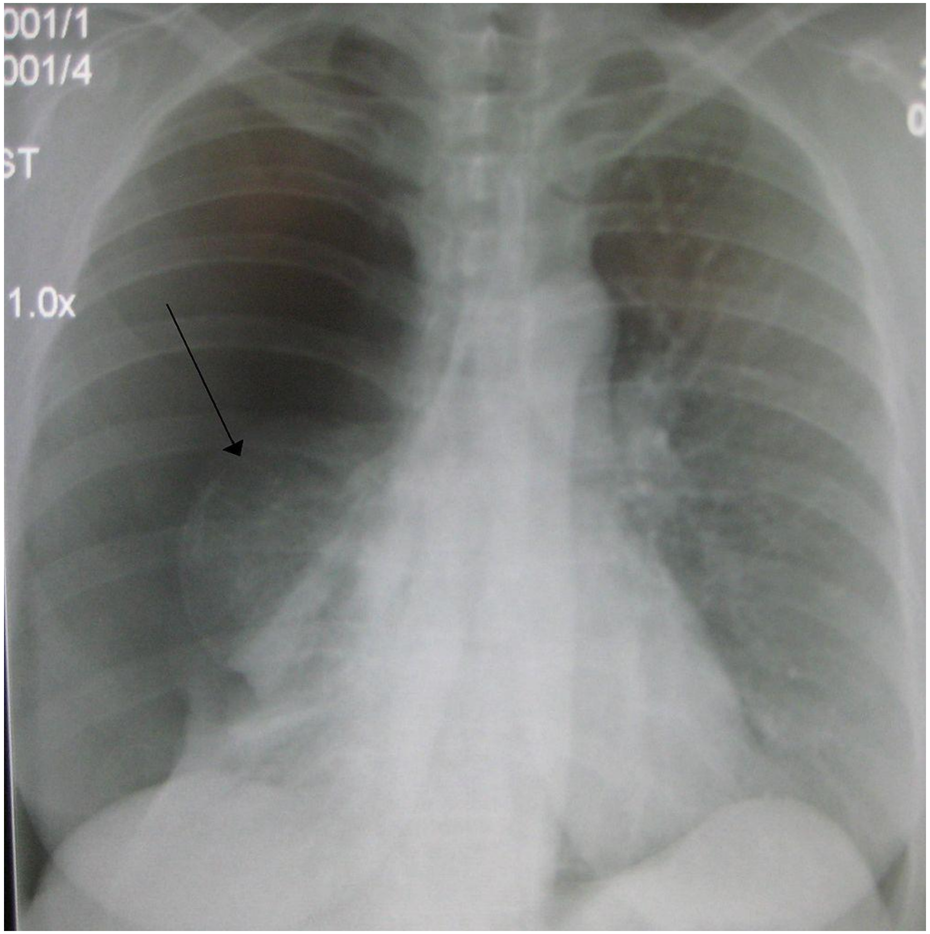


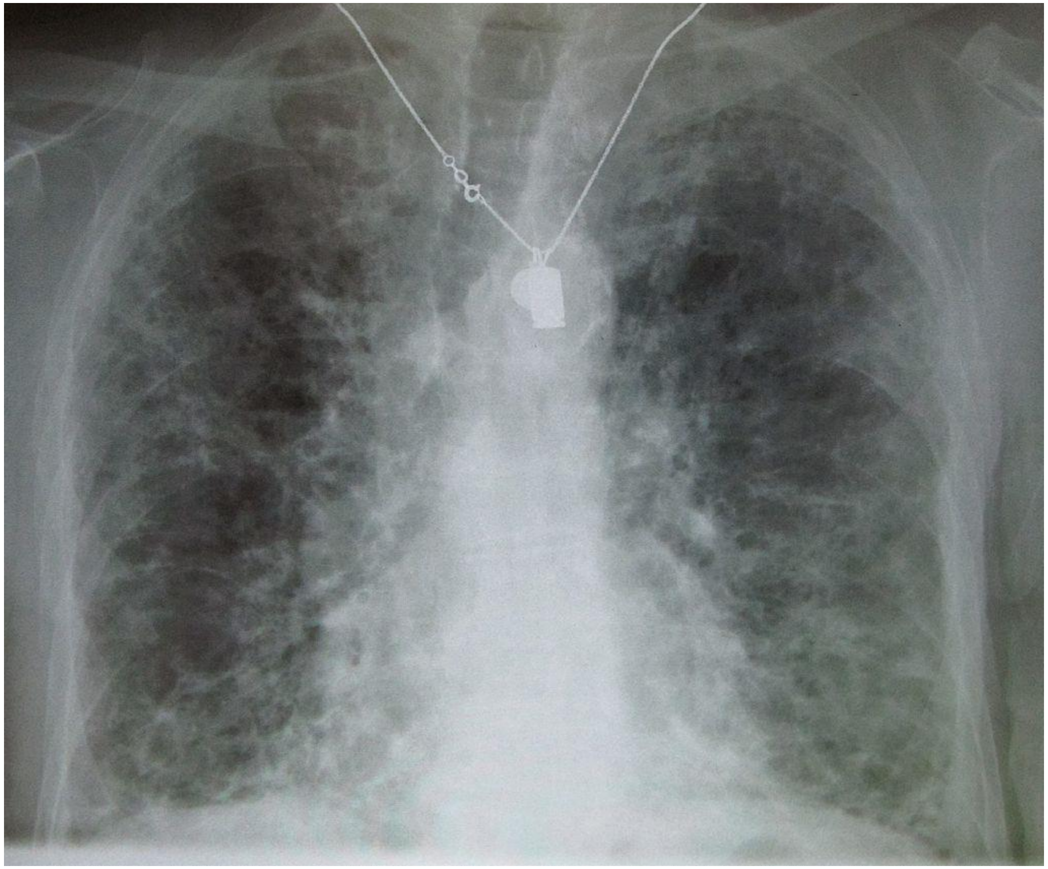
Image courtesy of James Heilman, MD

Pneumothorax

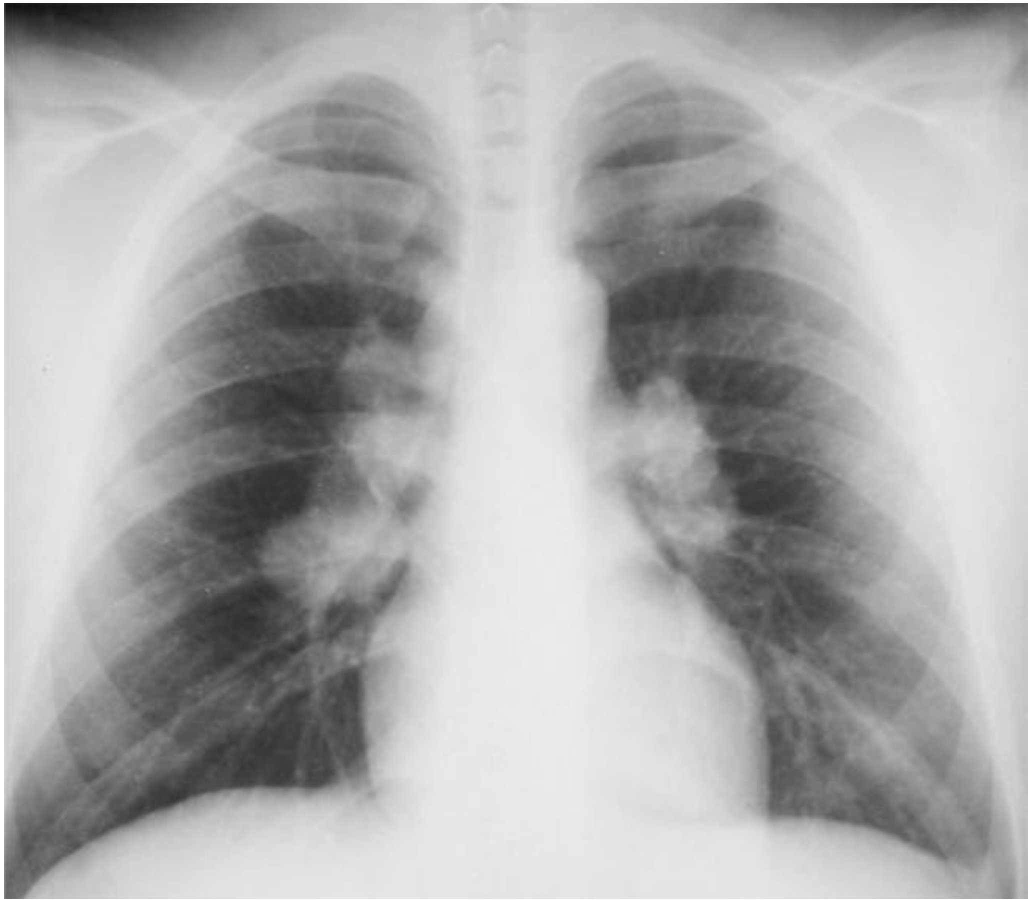


Lobar Pneumonia

Interstitial Fibrosis



Hilar Lymphadenopathy



Pulmonary Nodule

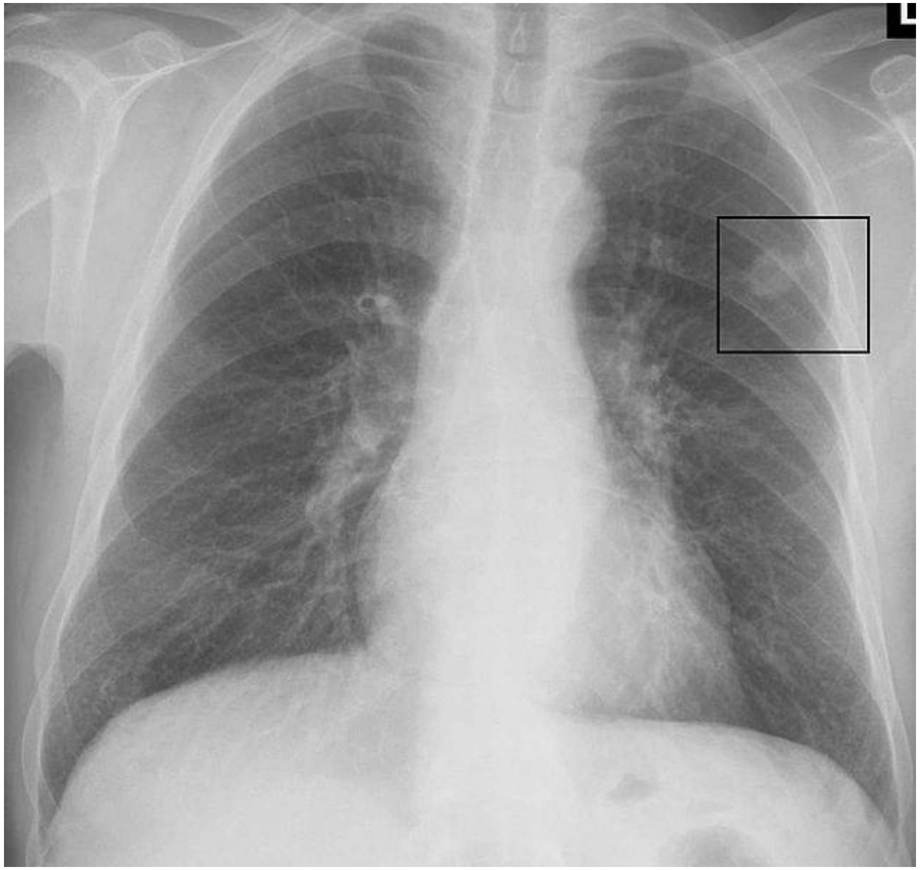


Image courtesy of Lange123