Pulmonary System (Chapter 28) — High-Yield Master Outline

1) Big Picture: What the Pulmonary System *Does*

Primary mission: exchange gases between environmental air and blood with minimal energy.

The 3 essential steps of gas exchange

1. **Ventilation** = moving air **in and out** of lungs.
2. **Diffusion** = moving gases **between alveoli and blood**.
3. **Perfusion** = moving blood **through pulmonary capillaries** to tissues (CV system drives this).

Clinical anchor: Problems with any step → impaired oxygenation/CO2 removal (hypoxemia and/or hypercapnia).

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2) Structures of the Pulmonary System (Know the Map)

A. Major components

- **Lungs** (Right: 3 lobes; Left: 2 lobes)
- **Upper airway** (nasopharynx/oropharynx/related structures)
- **Lower airway** (larynx → trachea → bronchi → bronchioles)
- **Gas-exchange units** (respiratory bronchioles → alveolar ducts → alveoli)
- **Pulmonary blood vessels + lymphatics**
- **Diaphragm + chest wall (thoracic cage)**
- **Pleura & pleural space**
- **Mediastinum** (space between lungs: heart, great vessels, esophagus)

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3) Pulmonary Defenses (Why lungs usually stay “clean”)

Goal: warm, humidify, trap, neutralize, and remove invaders before they reach alveoli.

Key defense mechanisms (high yield)

- **Upper respiratory mucosa / nasal hairs / turbinates:** trap particles + humidify/heat air.
- **Mucous blanket:** protective gel that traps pathogens/irritants.
- **Cilia:** move mucus upward toward pharynx (“mucociliary escalator”).
- **Cough + sneeze reflexes:** triggered by irritant receptors.
- **Surfactant:** helps immune defense in alveoli + dampens inflammation.
- **Macrophages (alveolar + interstitial):** phagocytosis + cytokines + antigen presentation.
- **Innate immune proteins:** lysozyme, lactoferrin, defensins, surfactant proteins A/D, IgA.

Clinical anchor: impaired cilia/mucus clearance → infections, chronic bronchitis, CF, etc.

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4) Conducting Airways (Air *Moves* Here, Not Gas Exchange)

A. Upper airway

- **Nasopharynx & oropharynx:** lined with **ciliated mucosa** → warms/humidifies/filters air.
- **Mouth breathing:** used if nose obstructed or high demand (exercise) but **less filtering/humidifying**.

B. Larynx (gateway + aspiration prevention)

- Contains:
    - **False vocal cords** (supraglottis)
    - **True vocal cords** with **glottis** between them
    - **Vestibule** above false cords
- **Swallow protection:** coordinated closure of cords + vestibule + epiglottis prevents aspiration.
- **Cartilage support:** prevents collapse during inspiration/swallowing.
- **Muscles:**
    - **Internal laryngeal muscles**: tension/length of cords; close during swallowing
    - **External muscles**: move larynx overall

C. Trachea → bronchi

- **Trachea:** C-shaped cartilage rings keep airway open.
- Splits at **carina** → right & left **main bronchi**
- Bronchi enter lungs at **hila** with blood & lymph vessels.

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5) Bronchial Wall (Know the Layers + Cells)

3 layers

1. **Epithelial (mucosal) lining**
2. **Submucosal layer (lamina propria)**
3. **Outer cartilaginous layer**

Key epithelial cells & what they do

- **Goblet cells:** secrete **mucins** (MUC5B, MUC5AC) → form mucus gel barrier.
- **Ciliated columnar cells:** beat mucus upward (clearance).
- **Club cells:** secrete immune molecules + protective surfactant-type proteins.
- **Basal cells:** regenerate new ciliated cells.
- **Neuroendocrine cells:** produce serotonin, dopamine, norepinephrine.

Lamina propria “high yield”

- **Smooth muscle:** increases as airways get smaller; greatest at **terminal bronchiole**.
- **Submucosal glands:** secrete mucins (notably MUC5B) → important in **CF** pathology.
- **Autonomic innervation**
    - **Parasympathetic (vagus): bronchoconstriction + ↑ secretions**
    - **Sympathetic: bronchodilation**
- **Clinical anchor:** asthma meds often **block parasympathetic** and/or **stimulate sympathetic (β-agonists)**.

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6) Gas-Exchange Airways (Where O2/CO2 Actually Swap)

A. Acinus (gas exchange region)

Conducting airways end →

- **Respiratory bronchioles**
- **Alveolar ducts**

- **Alveoli**
  Collectively called the **acinus**.

B. Alveoli essentials

- **~25 million at birth → ~300 million in adulthood**
- **Type I alveolar cells:** thin structure, prevent fluid leakage into alveoli.
- **Type II alveolar cells:** make **surfactant** + repair epithelium + help fluid/ion transport.
- **Surfactant proteins**
    - **SP-B & SP-C:** lower surface tension (keep alveoli open)
    - **SP-A & SP-D: collectins** → innate immune defense
- **Macrophages**
    - **Alveolar macrophages:** first-line defense in alveolar space
    - **Interstitial macrophages:** prevent spread into interstitium/capillaries
- **Pores of Kohn:** collateral ventilation between alveoli (helps even air distribution)

C. Alveolar-capillary membrane

- Ultra-thin interface where diffusion occurs.
- Thickening or fluid in interstitium → **impaired diffusion** → hypoxemia.

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7) Pulmonary vs Bronchial Circulation (Don’t Mix These Up)

Pulmonary circulation (gas exchange circulation)

- **Right heart → pulmonary artery → lungs → pulmonary veins → left heart**
- **Low pressure/low resistance** vs systemic.
- Functions: gas exchange, nutrient delivery, reservoir for LV, filter (clots/air/debris).

Bronchial circulation (systemic "support" circulation)

- Supplies **conducting airways**, large pulmonary vessels, lymph nodes, pleura.
- **Does NOT** do gas exchange.

Lymphatics

- Deep & superficial lymphatics remove fluid + macrophages; drain through mediastinal nodes.
- **Key role:** prevent pulmonary edema + support immunity.

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8) Control of Pulmonary Blood Flow (Key Reflex: Hypoxia = Constriction)

A. Vessel tone basics

- **Vasoconstriction** ↑ pulmonary artery pressure
- **Vasodilation** ↓ pulmonary artery pressure
- Controlled by local humoral factors + ANS input.

B. Hypoxic pulmonary vasoconstriction (HUGE test point)

- **Low PAO2 → pulmonary arteriolar constriction**
- Purpose: shunt blood away from poorly ventilated areas → improve V/Q matching.

- If widespread hypoxia → global constriction → **pulmonary hypertension**
- Chronic hypoxia → structural remodeling → permanent pulmonary HTN → **cor pulmonale (right HF)**.

C. Other vasoconstrictors/modulators

- **Acidemia** also constricts pulmonary arteries.
- Histamine, prostaglandins, serotonin, nitric oxide, bradykinin influence tone.

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9) Chest Wall + Pleura (Why Lungs Stay Expanded)

Chest wall

- Protection + provides muscles for ventilation (intercostals, accessory muscles, abdominal muscles).

Pleura basics

- **Visceral pleura:** covers lungs
- **Parietal pleura:** lines thoracic cavity
- **Pleural space:** thin fluid layer for lubrication
- **Normally negative pressure** (subatmospheric) helps keep lungs inflated.
- Air/fluid entry → loss of negative pressure → partial collapse (think pneumothorax/effusion).

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10) Ventilation (Mechanics + Key Numbers)

Ventilation vs respiration (common trap)

- **Ventilation:** air movement.
- **Respiration:** cellular O2/CO2 exchange during metabolism.

Minute ventilation

- **Minute volume ($\dot{V}$) = RR × VT**
- **Tidal volume (VT):** air per breath (~500 mL in quiet breathing)

Dead space ventilation (VD)

- Air that **doesn't participate** in gas exchange.
- **Anatomic dead space:** conducting airways
- **Alveolar dead space:** alveoli not perfused (ventilation without perfusion)

CO2 removal + acid-base tie

- Lungs remove CO2 (carbonic acid equivalent) to maintain **PaCO2 ~ 40 mm Hg**.
- Hypoventilation → **CO2 retention** → ↑ PaCO2 (respiratory acidosis tendency).
- **You can't judge ventilation adequacy by looking** → need **ABG or capnography**.

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11) Neurochemical Control of Breathing (Brainstem + Feedback)

Respiratory center (medulla + pons)

Adjusts RR + VT based on chemoreceptors and lung receptor feedback.

Key parts

- **DRG (dorsal respiratory group):** initiates inspiration; rhythm maintenance; responds to peripheral chemo + lung inputs.
- **VRG (ventral respiratory group):** modulates inspiration & expiration; contains **pre-Bötzinger complex** (rhythm generator).
    - **Opioids suppress VRG activity → ↓ RR** (classic opioid respiratory depression).
- **Pneumotaxic center (includes Kölliker-Fuse nucleus):** regulates inspiratory volume + switches inspiration → expiration.
- **Apneustic center (includes Bötzinger complex influence):** moderates/inhibits inspiration intensity.

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12) Lung Receptors (3 Types = Test Gold)

1. **Irritant receptors (C-fibers):**
    - Location: conducting airway epithelium
    - Trigger: dust, fumes, gases, particulates
    - Effects: **cough**, bronchoconstriction, ↑ ventilatory rate
2. **Stretch receptors (airway smooth muscle + chest wall):**
    - Sense lung inflation
    - Cause ↓ rate/volume when stimulated (**Hering-Breuer reflex**: important in newborns; in adults mainly at high VT)
    - Chest wall stretch receptor mismatch contributes to **dyspnea**
3. **J-receptors (juxtapulmonary capillary receptors):**

- Near alveolar capillaries/septa
- Trigger: ↑ pulmonary capillary pressure
- Effects: rapid shallow breathing, hypotension, bradycardia

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13) Chemoreceptors (Central vs Peripheral)

Central chemoreceptors

- Location: near respiratory center; sense **CSF pH** (indirectly reflects CO_2).
- ↑ CO_2 → crosses BBB → forms H^+ in CSF → ↓ pH → ↑ ventilation.
- In chronic hypercapnia (e.g., COPD): can **reset** and become less responsive; kidneys retain HCO_3^- which buffers CSF.

Peripheral chemoreceptors

- Location: carotid bodies & aortic bodies
- Primary sensitivity: **low PaO_2**
- Significant stimulation when **PaO_2 ~ 60 mm Hg or lower**
- Becomes dominant ventilatory drive when central receptors are reset.

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14) Mechanics of Breathing (3 Things Determine Work)

A. Muscles

- **Major inspiration:** diaphragm + external intercostals
- **Accessory inspiration:** sternocleidomastoid + scalenes (used with high demand or disease)
- **Expiration:** normally passive
- **Accessory expiration:** abdominal + internal intercostals (coughing, obstruction, high minute ventilation)

B. Alveolar surface tension + surfactant

- **Surface tension** tends to collapse alveoli.
- **Law of Laplace:** smaller radius (end-expiration) needs more pressure to inflate → collapse risk.
- **Surfactant (Type II cells)** reduces surface tension → prevents collapse, decreases work of breathing.
- Lack of surfactant → collapse + severe gas exchange issues (classic in preterm infants).

C. Elastic recoil + compliance

- **Elastic recoil:** lung returns to resting state → allows passive expiration.
- **Compliance:** “stretchiness” (volume change per pressure change)
    - **High compliance** = easy to inflate, poor recoil (e.g., emphysema)
    - **Low compliance** = stiff lungs (ARDS, pneumonia, pulmonary edema, fibrosis)

D. Airway resistance

- Depends on airway radius/length, gas properties.
- Biggest resistance normally: **nose** (then oropharynx/larynx).
- ANS effects:

    - Parasympathetic → bronchoconstriction
    - Sympathetic → bronchodilation
- Resistance increases with mucosal edema, mucus plugging, tumors, foreign bodies.
- **Diffuse ↑ resistance → ↑ work → hypercapnia risk.**
- **PFTs** quantify volumes and flows (FVC, FEV1 etc.).

E. Work of breathing

Rises when:

- ↓ lung compliance (pulmonary edema)
- ↓ chest wall compliance (obesity, spinal deformity)
- airway obstruction (asthma/COPD)
  → can cause ↑ O2 demand + fatigue → hypoventilation → hypercapnia.

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15) Gas Transport (4 steps for O2, reverse for CO2)

Oxygen transport (4 steps)

1. Ventilation
2. O2 diffusion alveoli → pulmonary capillary blood
3. Perfusion of systemic capillaries
4. O2 diffusion capillary → cells

CO2 transport (reverse)

Cells → systemic blood → pulmonary blood → alveoli → exhaled.

Key concept: any failure in steps → cellular hypoxia.

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16) Measuring Gas Pressures + A–a Gradient (High Yield)

Partial pressure

Pressure contributed by each gas in a mixture.

PAO2 depends on:

- Barometric pressure (PB)
- Water vapor pressure
- FiO2
- PaCO2 (ABG)

A–a gradient

- **(PAO2 calculated) − (PaO2 measured)**
- Estimates how well O2 moves alveoli → blood.
- Healthy young adult: **~5–10 mm Hg**.

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17) Ventilation/Perfusion ($\dot{V}/\dot{Q}$) Matching (Major cause of hypoxemia)

- Gravity makes **bases** of lungs:
    - more ventilated (more compliant alveoli)

    - more perfused (higher hydrostatic pressure)
- Not perfectly matched:
    - **Bases:** perfusion > ventilation
    - **Apices:** ventilation > perfusion
- **Normal V̇/Q̇ ≈ 0.8** (respiratory quotient)
- V/Q mismatch = **#1 cause of hypoxemia** in many lung diseases.

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18) Oxygen in Blood: PaO2 vs SaO2 (Don't Confuse)

- **PaO2:** dissolved O2 pressure in plasma (ABG).
- **SaO2:** % hemoglobin saturated (pulse ox).
- **~97% O2 binds hemoglobin**, ~3% dissolved in plasma.

Hemoglobin concentration matters

- Low Hgb → low O2 content even if PaO2 looks okay.

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19) Oxyhemoglobin Dissociation Curve (Right vs Left Shift)

Curve shows relation between PaO2 and SaO2.

Right shift = easier O2 release to tissues (↓ affinity)

Causes:

- **Acidosis (↓ pH)**
- **Hypercapnia (↑ PaCO2)**
- ↑ temperature
- ↑ 2,3-DPG
  Bohr effect: CO2/H+ cause right shift (enhances tissue unloading).

Left shift = tighter binding (↑ affinity)

Causes:

- alkalosis, hypocapnia
- ↓ temperature
- ↓ 2,3-DPG
  Clinical issue: holds O2 too tightly (less delivered to tissues).

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20) CO2 Transport (3 forms) + Haldane Effect

CO2 is ~20× more soluble than O2 → diffuses easily.

CO2 carried as:

1. dissolved in plasma
2. **bicarbonate (HCO3−)** (major)
3. carbamino compounds (bound to proteins/hemoglobin)

Haldane effect: deoxygenated hemoglobin carries more CO2 (tissues load CO2 better); oxygenation in lungs promotes CO2 unloading.

Pearl: diffusion defects often cause hypoxemia before hypercapnia because CO2 diffuses so well.

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21) Aging & Pulmonary System (Older Adult Must-Know)

- **Chest wall compliance** ↓ (stiffer ribs/joints) → ↑ work of breathing
- **Elastic recoil** ↓ → **lung compliance** ↑, **VC** ↓, **RV** ↑, TLC ~ unchanged
- **Peripheral airway support** ↓ + epithelial regeneration ↓ + distal airway fibrosis ↑
- **Gas exchange surface/perfusion** ↓ (capillary network diminishes), alveoli dilate/fibrose
- **PaO2 declines with age**; ventilatory response to hypoxia/hypercapnia ↓
- Estimation tip: **Max PaO2 ≈ 100 − (age × 0.3)** at sea level
- Fitness protects function; sedentary → more decline
- Lung immunity declines → ↑ infection risk

KEY TERMS (High-Yield Definitions)

Acinus: functional gas-exchange unit (respiratory bronchioles + alveolar ducts + alveoli).
Alveolar duct: passageway leading from respiratory bronchioles to alveolar sacs.
Alveolar ventilation (VA): fresh air reaching alveoli that participates in gas exchange.
Alveolar-capillary membrane (alveolocapillary membrane): thin diffusion barrier between alveoli and capillary blood.
Alveolus (alveoli): tiny air sac where gas exchange occurs.
Bohr effect: CO2/H+ shifts O2 dissociation curve (usually right) to enhance tissue unloading.
Bronchus (bronchi): large conducting airway branching from trachea into lungs.
Carina: tracheal bifurcation point into main bronchi; sensitive → cough reflex.
Central chemoreceptor: brainstem receptor sensing CSF pH changes driven by CO2.
Collectins: surfactant proteins (SP-A, SP-D) that bind pathogens and support innate immunity.
Compliance: ease of lung/chest wall expansion (ΔV/ΔP); inverse of stiffness.
Dead-space ventilation (VD): ventilated air not participating in gas exchange (anatomic + alveolar).

Elastic recoil: tendency of lungs/chest wall to return to resting volume after inspiration.
Fraction of inspired oxygen (FiO2): % O2 in inhaled air (room air ≈ 0.21).
Gas transport: delivery of O2 to tissues and removal of CO2 via ventilation, diffusion, perfusion.
Glottis: opening between true vocal cords.
Goblet cell: airway epithelial cell that secretes mucins to form mucus.
Haldane effect: oxygenation of blood in lungs promotes CO2 release; deoxygenation in tissues promotes CO2 uptake.
Hilum (hila): "root" of lung where bronchi, vessels, lymphatics enter/exit.
Hypoxic pulmonary vasoconstriction: low PAO2 triggers pulmonary arteriolar constriction to redirect blood.
Irritant receptor: airway receptor sensing noxious particles/gases → cough, bronchoconstriction.
J-receptor: receptor near pulmonary capillaries responding to ↑ capillary pressure → rapid shallow breathing.
Lamina propria: submucosal bronchial layer containing smooth muscle, glands, ANS fibers.
Larynx: airway structure between pharynx and trachea; protects airway, enables vocalization.
Mediastinum: thoracic space between lungs containing heart/great vessels/esophagus.
Minute volume (minute ventilation, $\dot{V}$): RR × VT (L/min).
Nasopharynx: upper airway behind nose; filters/warms/humidifies air.
Oropharynx: upper airway behind mouth; alternate route when nose obstructed.
Oxygen saturation (SaO2): % hemoglobin binding sites occupied by O2.
Oxyhemoglobin (HbO2): hemoglobin bound to oxygen.
Oxyhemoglobin dissociation curve: S-shaped relation between PaO2 and SaO2; shifts with pH/CO2/temp/2,3-DPG.
Partial pressure (P): pressure exerted by an individual gas in a mixture.
Peripheral chemoreceptor: carotid/aortic body receptors mainly sensing low PaO2.
Pleura (pleurae): serous membranes (visceral + parietal) around lungs/thorax.
Pleural space (pleural cavity): thin fluid-filled space between pleurae; normally negative pressure.
Respiratory bronchiole: first airway segment participating in gas exchange.
Respiratory center: medulla/pons network controlling RR and VT.
Stretch receptor: airway/chest wall receptors sensing lung inflation and ventilatory mechanics.
Surface tension: force at air-liquid interface tending to collapse alveoli.
Surfactant: lipoprotein from Type II cells lowering alveolar surface tension; prevents collapse; supports immunity.
Thoracic cavity: chest cavity containing lungs/mediastinum.
Tidal volume (VT): volume inhaled/exhaled per normal breath.
Trachea: cartilage-supported airway from larynx to bronchi.
Ventilation: movement of air into/out of lungs.
Ventilation-perfusion ratio ($\dot{V}/\dot{Q}$): relationship of airflow to blood flow; mismatch → hypoxemia.