“All I Need is the Air That I Breathe”
Review of Pulmonary Anatomy and Physiology

Eric Olson, MD
Associate Professor of Medicine
College of Medicine
Mayo Clinic

2016 Big Sky Pulmonary Conference
Disclosures

• None
Overview: Anatomy

250 million L of air partake in respiration over a lifetime!
Upper Airway Anatomy

* Tonsil locations

Hard palate

Epiglottis

Vocal fold

Tongue

Nasal turbinate

Soft palate

Uvula

Nasopharynx

Velopharynx

Oropharynx

Hypopharynx

Esophagus
Coronal section

- Falx cerebri
- Brain
- Nasal cavities
- Nasal septum
- Middle nasal concha
- Middle nasal meatus
- Maxillary sinus
- Inferior nasal meatus
- Inferior nasal concha
- Hard palate
- Oral cavity
- Genioglossus muscle
- Mylohyoid muscle
- Geniohyoid muscle
- Olfactory bulbs
- Frontal sinus
- Orbital fat
- Ethmoidal cells
- Opening of maxillary sinus
- Intra-orbital
- Zygomatic
- Alveolar
- Recess of maxillary sinus
- Buccinator muscle
- Alveolar process of maxilla
- Body of tongue
- Sublingual gland
- Mandible (body)
- Anterior belly of digastric muscle

Nasal polyps

Sinusitis

Septal deviation

https://www.clinicalkey.com/
Grading of Tongue-Palate Relationship, Palatine Tonsil Size

Stridor: Sign of Vocal Cord Dysfunction
Airway Tree: 23 Generations

Conducting airways
- bronchi ➔ terminal bronchiole
- lead air to the site of exchange

Respiratory airways
- respiratory bronchiole ➔ alveoli
- site of gas exchange

https://www.clinicalkey.com/
Lining of Conducting Airways

Microscopic view

Cilia beat in coordinated fashion causing mouthward movement of mucous and trapped inhaled particles
Asthma: Airway Wall Findings

Normal Bronchiole

Bronchiolar Smooth Muscle Thickening
Asthma: Airway Wall Findings (cont)

- Goblet Cell Hyperplasia
- Thickened Basement Membrane
- Eosinophils
Bronchiectasis
Bronchiectasis
Pulmonary acinus

Terminal bronchiole

Respiratory bronchioles

Alveoli

https://www.clinicalkey.com/
Centrilobular (smoking-related) Emphysema
Pulmonary Lobule; Contain 3-6 acini
Acinus: Lung derived from a terminal bronchiole

- Pulmonary artery
- Terminal bronchioles
- Interlobular septa
- Lymphatics; veins

Pulmonary acinus
Clinical Application: Causes of Interlobular Septal Thickening

Congestive heart failure (smooth septal thickening)

Normal

Lymphangitic spread of malignancy (beaded septal thickening)
Alveolar-Capillary Interface

Microscopic view

- Pneumocytes
- Capillary
- Alveolus
Alveolar-Capillary Interface

Schematic view
ARDS
2 Blood Supplies: Bronchial and Pulmonary

Airway bleeding source

Alveolar bleeding source

Aird WC. Circ Res 2007;100:174
Special Properties of Pulmonary Circulation: Hypoxic Vasoconstriction; Recruitment

Hypoxic vasoconstriction

Recruitment
Pulmonary Lymphatic System
Thoracic Lung Node Stations

Clinical application: Lymph node involvement important determinant in lung cancer treatment
Interim Summary

- Air travels 23 airway generations
- Examples of airways disease
  - Larynx: stridor
  - Conducting bronchi: asthma, bronchiectasis
  - Bronchioles: COPD
- Site of gas exchange: alveolus
  - Impressive area for gas exchange
- 2 arterial supplies to the lung
  - Bronchial: airways
  - Pulmonary: alveoli; capable of hypoxic vasoconstriction, recruitment during exercise
- Lymphatics: filtering system
  - Critical in lung cancer staging
Overview: Physiology
Central Control

O₂, CO₂ Exchange

Ventilation
Central Respiratory Control

Central Pacemaker

VRG (I, E)
DRG (I)
Pontine
"Wakefulness drive to breathe"
Response to $\uparrow \text{CO}_2$

- Ventilation $\uparrow$ 2 to 3 L/min for every 1mmHg $\uparrow \text{PCO}_2$
- Lower the PO$_2$, the brisker the response
- With chronic hypercapnia, ventilatory drive arising from central chemosensors will be lower
Response to $\downarrow \text{O}_2$

- Markedly increases when $\text{PAO}_2 < 50$-$60$
- Response to hypoxia augmented by $\uparrow \text{PACO}_2$
Sleep: Loss of Wakefulness Drive

- Sleep
- Central Pacemaker

"Wakefulness Drive"
Physiologic Changes in Breathing During Sleep

• Controller of ventilation: $CO_2$

• Respiratory rate: $\leftrightarrow$

• Tidal volume: $\downarrow$

• Upper airway muscles: $\downarrow$

• Ventilation: $\downarrow$ (10-15%)

• $PCO_2$: $\uparrow$ (3-7 mm Hg)

• $SpO_2$: $\downarrow$ (1-3%)
Physiologic Changes in Breathing: NREM vs REM

<table>
<thead>
<tr>
<th></th>
<th>NREM</th>
<th>REM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tidal volume</td>
<td>Regular</td>
<td>Irregular</td>
</tr>
<tr>
<td>Resp rate</td>
<td>Regular</td>
<td>Irregular</td>
</tr>
<tr>
<td>CO$_2$ responsiveness</td>
<td>↔ or ↓</td>
<td>↓</td>
</tr>
<tr>
<td>O$_2$ responsiveness</td>
<td>↔ or ↓</td>
<td>↓</td>
</tr>
<tr>
<td>Accessory muscles</td>
<td>Normal</td>
<td>Paralyzed</td>
</tr>
</tbody>
</table>
Upper Airway Muscles and Sleep

Tensor palatini (stiffens palate)

Awake vs. NREM

Tensor Palatini EMG:

↓ Tonic activity

Genioglossus (protrudes tongue)

↓ Negative pressure reflex

Changes in upper airway during sleep leaves an anatomically challenged pharynx vulnerable to collapse
Clinical Application:
Loss of Accessory Muscle Input in Stage R results in deeper desaturations in COPD, ALS
Sleep and Asthma

- Circadian drop in airway caliber at night
  - More dramatic in asthmatics
  - More deaths from asthma per hour at night than by day
- Nocturnal symptoms signal suboptimal control
- Mechanism unclear, but contributor may be ↑ parasympathetic bronchoconstrictor input to airways

“Morning dipper” per peak flows
Interim Summary

- Pacemaker for breathing located in the brainstem; composed of multiple neuronal groups

- Pacemaker responds to multiple inputs

- During sleep:
  - $PCO_2$ is the main ventilatory determinant
  - ↓ ventilation:
    - Loss of “wakefulness drive to breathe”
    - ↓ chemo responsiveness
    - ↑ upper airway resistance
Interim Summary (cont)

• During REM sleep:
  • Diaphragm function intact; marked reduction in intercostal muscle activity

• Ventilatory responses to chemical stimuli most blunted

• Clinical significance of these changes:
  • Desaturations most severe in patients with lung disease during REM

• Airways narrow during; exaggerated in asthma
Central Control

O₂, CO₂ Exchange

Ventilation
Inhalation

Collapsing forces (negative pressure +/- anatomic barriers) > distending forces (pharyngeal muscles)
Clinical Application
Diaphragm Paralysis

Symptoms: Dyspnea; orthopnea
Signs: Intolerance of supine positioning; thoracoabdominal paradox
Determinants of Inspiratory Volume

- Central drive
- Neuromuscular transmission
- Strength of inspiratory muscles
- Respiratory system compliance
- Airways resistance

Work of breathing
Compliance

- $\Delta$ Volume/ $\Delta$ Pressure
- ↑ compliance = ↑ distensibility
- Influenced by volume

[Images of a child blowing up balloons to illustrate low and high compliance.]
Respiratory System Compliance: Lung & Chest Wall Components

Compliance influence by lung volume:
↑ lung volume → ↓ compliance
Compliance curve of the normal upright lung
Conditions of ↓ Chest Wall Compliance

Scoliosis

Obesity
Conditions of ↓ Lung Compliance

Pulmonary fibrosis

Pleural disease
Airway Resistance

↑ tube radius → ↓ resistance

Medium-sized bronchi provide most resistance

Airway resistance inversely influence by lung volume: ↑ lung volume → ↓ resistance
Condition of \( \uparrow \) Airway Resistance: COPD

Subdivisions of Ventilation

Alveolar Ventilation = Total ventilation – Dead space ventilation

Anatomic dead space

Alveolar dead space

Dead space ventilation

Amount of ventilation devoted to gas exchange

Alveolar ventilation \( (V_A) \)
Normal Lung Ventilation

- Tidal volume: 500 mL
- Frequency: 15 breaths/min
- Total ventilation: 7500 mL/min
- Anatomic dead space: 150 mL
- Dead space ventilation: 2250 mL/min
- Alveolar gas: 3000 mL
- Alveolar ventilation: 5250 mL/min
- Pulmonary blood flow: 5000 mL/min

Ventilation Governs $\text{PCO}_2$

- $\text{PCO}_2 = \frac{\text{VCO}_2}{\text{VA}}$
  - $\text{CO}_2$ production
  - $\text{alveolar ventilation}$

- $\uparrow\text{PCO}_2 = \downarrow\text{alveolar ventilation}$
  - $\downarrow$ tidal volume and/or
  - $\uparrow$ dead space

Hypoventilation results if $\uparrow\text{RR}$ not sufficient to augment $\text{VA}$
Causes of Hypercapnia (high $PCO_2$)

- “Won’t breathe”
  - ↓ Central drive (drugs; hypothyroidism)
- “Can’t breathe”
  - ↓ Neuromuscular transmission (spinal cord injury)
  - ↓ Strength of inspiratory muscles (ALS)
  - ↓ Respiratory system compliance (pneumonia)
  - ↑ Airways resistance (asthma exacerbation)

*Bi-level PAP may enhance alveolar ventilation and thus overcome causes of hypoventilation*
Clinical Application
Symptoms and Signs of Hypoventilation

- Nonspecific, insidious; accentuated by coexistent hypoxia
- Dyspnea not uniformly present!
- CNS effects
  - Altered mentation
  - Sleep disruption
  - Hypersomnolence
  - Headache
- Pulmonary hypertension
  - Dependent edema
  - Orthopnea
  - Cor pulmonale
- Cyanosis
- Elevated serum bicarbonate
Clinical Application
Evaluation for Cause(s) of Hypoventilation

- ABG: confirmatory test
- Physical exam: emphasis on thoracic, neuro systems
- Pulmonary function tests (maximal respiratory pressures)
- CXR
- Bloods: Thyroid; Ca++; Mg++; PO$_4$; CK; aldolase; Hgb
- Diaphragm studies
- CNS imaging
- PSG

Martin TJ, Sanders MH. Sleep 1995; 18:617
Exhalation

Lung Volumes and Capacities

- Tidal volume
- Residual volume
- Functional residual capacity
- Vital capacity
- Total lung capacity

↓ with obesity, sleep
Obstructive Lung Disease

- Slower exhalation time
- Tidal volume
- Residual volume
- Functional residual capacity
- Total lung capacity
Restrictive Lung Diseases

- Tidal volume
- Residual volume
- Functional residual capacity
- Vital capacity
- Total lung capacity
Interim Summary

- Main inspiratory muscle is diaphragm

- Thoracoabdominal paradox and orthopnea (shortness of breath when supine) → diaphragmatic dysfunction

- Alveolar ventilation: balance between inspiratory load and neuromuscular competence

- $\uparrow$PCO$_2$ = inadequate alveolar ventilation for metabolic demand
  - Causes:
    - “Won’t breathe:” impaired central drive
    - “Can’t breathe:” Dysfunction of breathing apparatus
## Summary of PFT Interpretation

<table>
<thead>
<tr>
<th></th>
<th>TLC</th>
<th>FEV1</th>
<th>FVC</th>
<th>FEV1/FVC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Obstruction</strong></td>
<td>↑</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td><strong>Restriction</strong></td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>NL or ↑</td>
</tr>
</tbody>
</table>
Central Control

O₂, CO₂ Exchange

Ventilation
Pulmonary Gas Exchange

Alveolus

**Diffusion**

Normal

O\(_2\)   CO\(_2\)

Capillary

Terminology

V = Ventilation
Q = Perfusion

Alveolar-capillary membrane = 0.3 uM

Equilibration < 0.20 sec
Diffusion

Flow depends on:
- Concentration difference
- Area available for diffusion
- Thickness of membrane
Arterial Oxygen Transport

O₂ carried on hemoglobin in red blood cells

Alveolus

Normal

Capillary

O₂ carried on hemoglobin in red blood cells

©2015 MFMER | slide-72
Measurements of Oxygen

- **PaO$_2$**
  - Pressure exerted by O$_2$ in blood
  - Measured by arterial blood gas

- **SpO$_2$**
  - % total hemoglobin bound with O$_2$
  - Measured by pulse oximetry
Oxyhemoglobin Dissociation Curve
Physiologic Mechanisms of Hypoxemia: V/Q Mismatch

- Example:
  - Asthma
  - COPD

- Treatment:
  - Bronchodilators
  - Steroids
Physiologic Mechanisms of Hypoxemia: V/Q Mismatch

- Example:
  - Obesity
- Treatment
  - Weight loss

Impairment of “V” due to collapse of alveoli
Mechanisms of Hypoxemia: Hypoventilation

- Examples:
  - “Can’t Breathe” (dysfunction of respiratory apparatus)
    - ALS
  - “Won’t Breathe” (depressed respiratory drive)
    - Opioids

- Treatment
  - Bilevel PAP ± O₂
  - Remove respiratory depressants
Mechanisms of Hypoxemia: Shunt

- Examples:
  - Intracardiac
    - Septal defect in heart
  - Intrapulmonary
    - AVM
    - Hepatopulmonary syndrome

- Treatment
  - Close the defect

Blood bypasses alveoli; cannot load $O_2$
Mechanisms of Hypoxemia: Diffusion Limitation

- Example:
  - Pulmonary fibrosis

- Treatment
  - Treat underlying disorder
  - O₂

Blood leaving alveolus fails to reach equilibrium with alveolar gas
Mechanisms of Hypoxemia: Low Inspired Oxygen

- Example:
  - High altitude

- Treatment
  - Descent
  - O₂
Clinical Application: Differentiating Causes of Hypoxemia

- Clinical scenario
- Calculate A-a gradient
- Assess response to oxygen
Clinical Application: 
**Alveolar-arterial ("A-a") Gradient**

- Measure of how well the lungs are oxygenating the blood independent of alveolar ventilation

- $P_{aO_2}$: must be calculated; $PaO_2$ measured by ABG

- $P_{aO_2} = (P_B - P_{H2O})(F_iO_2) - P_{ACO_2}/R$
  
  $= (P_B - P_{H2O})(F_iO_2) - P_{ACO_2}/R$
  
  $=(760-47)(.21) - 40/0.8$
  
  $=150 - 50$
  
  $=100$ mm Hg

- $A-a$ gradient $= P_{aO_2} - PaO_2$
  
  $= 100 - 90$
  
  $= 10$
# Summary of Mechanisms of Hypoxemia

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Clinical scenario</th>
<th>A-a gradient</th>
<th>O₂ responsiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low FiO₂</td>
<td>↑ altitude; w/o usual O₂</td>
<td>Normal</td>
<td>Yes</td>
</tr>
<tr>
<td>Hypoventilation</td>
<td>↑ PCO₂</td>
<td>Normal</td>
<td>Yes</td>
</tr>
<tr>
<td>Diffusion Limitation</td>
<td>Abnormal lung imaging</td>
<td>Increased</td>
<td>Yes</td>
</tr>
<tr>
<td>Shunt</td>
<td></td>
<td>Increased</td>
<td>No</td>
</tr>
<tr>
<td>V/Q Mismatch</td>
<td>Most common</td>
<td>Increased</td>
<td>Yes</td>
</tr>
</tbody>
</table>
**CO₂ Transport**

In lung, HCO₃⁻ converted back to CO₂ and exhaled

A. CO₂ dissolved in blood: 10%
B. CO₂ attached to hemoglobin: 30%
C. Bicarbonate: 60%

\[
\text{CO}_2 + \text{H}_2\text{O} \leftrightarrow \text{H}_2\text{CO}_3 \leftrightarrow \text{H}^+ + \text{HCO}_3^- 
\]

Carbonic anhydrase
Clinical Question

- Why does the depth of desaturation vary between disordered breathing events?
Interim Summary

• Alveolus is site of gas exchange

• \( \text{O}_2, \text{CO}_2 \) cross alveolar-capillary interface via diffusion
  • Partial pressure gradient drives the process

• Vast majority of oxygen carried in the blood by hemoglobin

• The S-shaped hemoglobin dissociation curve:
  • Physiologically advantageous
  • Governs relationship between \( \text{SpO}_2 \) and \( \text{PaO}_2 \)
    • \( \text{SpO}_2 \text{ 90\%} = \text{PaO}_2 \text{ 60 mm Hg} \)
Interim Summary (cont)

- Mechanisms of hypoxemia
  - V/Q mismatch (most common)
  - Shunt (unresponsive to supplemental $O_2$)
  - Hypoventilation ($\uparrow$PCO$_2$)
  - Diffusion impairment (abnl lung exam, imaging)
  - Low inspired oxygen

- CO$_2$ primarily transported as HCO$_3^-$
Effects of Obesity on the Respiratory System

• ↑ O₂ consumption and CO₂ production

• ↓ ventilatory response to hypoxia and hypercapnia

• ↓ Functional residual capacity
  • ↓ Respiratory system compliance
  • ↑ upper and lower airways resistance
  • ↑ V/Q mismatching
  • ↓ lung O₂ stores (deeper desats with apneas/hypopneas)
Lung $O_2$ stores = Lung volume $\times P_{A}O_2$

“Before I came here I was confused about this subject. Having listened to your lecture I am still confused. But on a higher level”

Enrico Fermi
Thank you for your attention!

Please e-mail if questions

- olson.eric@mayo.edu