I. FUNCTIONAL ANATOMY OF THE RESPIRATORY SYSTEM

A. Introduction

- body needs oxygen for cellular respiration:

\[ \text{O}_2 + \text{glucose} \rightarrow \text{ATP} + \text{CO}_2 + \text{H}_2\text{O} \]

* \( \text{CO}_2 \) is an acid.
* \( \text{O}_2 \) is not very soluble in water.


* at same time, some structures are there to:

1. Warm air in order to conserve water
2. Immunity
3. Make sure food doesn't get into respiratory tract.

- due to cellular metabolism, can't last long w/out oxygen gas--& energy needs of cells.

*also, cellular metabolism produces \( \text{CO}_2 = \text{a gas} \)

*body needs an organ system that can bring in and get rid of these 2 gasses = GAS EXCHANGE.

- RESPIRATION -this process. 4 steps:

1. PULMONARY VENTILATION -move air in/out of the lungs (or, more specifically, the ALVEOLI [ = air sacs of the lungs; see later] ).
2. EXTERNAL RESPIRATION - = gas exchange between air & blood.
3. TRANSPORT OF RESPIRATORY GASES -dissolve gases in blood; cardiovascular system carries them to where they need to go.
4. INTERNAL RESPIRATION -gas exchange between blood & cells, so they can do cellular respiration.
B. Functional Anatomy
-2 major subdivisions:

-CONDUCTING ZONE -(nose -----> brachioles). Cleanse, filter, warm & moisten incoming air.

-RESPIRATORY ZONE -(bronchioles -----> alveoli; all = microscopic structures). Gas exchange.

1. Upper Respiratory Tract. The conducting zone. Will be done in lab. For class, be familiar with the following terms:

a. The nose. Only external visible portion. Includes the vestibule, vibrissae, external nares (nostrils), nasal septum, root, bridge, apex

   * lateral walls have CONCHAE: increase surface area & turbulence of air (arm air to conserve moisture).


c. Olfactory & respiratory mucosae. Olfactory receptors take smell to brain through cribriform plate, enter olfactory bulbs. Respiratory mucosae wet sticky = traps foreign particles.

d. Paranasal sinuses. Lighten skull, produce mucous.

   **Sinusitis**: inflamed mucosae of the sinuses. Allergy or autoimmune.  
   **Sinus infection**: infection of sinuses, may lead to more serious problems if it moves into meninges, brain, spinal cord, etc...
e. Pharynx: muscular passageway. Subdivided:
  * nasopharynx w/ opening of auditory tube, pharyngeal tonsil
  * oropharynx w/ palatine & lingual tonsil
  * laryngopharynx w/ entranceway into larynx & esophagus

f. Larynx. Voice box. Contains structures to:
  (1) stop food & beverages from entering (epiglottis) &
  (2) voice production (vocal fold).
  * gag reflex: closes epiglottis
  * cleft palate: incomplete fusion of bones. Opening dangerous as food, beverage can now enter respiratory tract.
ii) Trachea & the Lower Respiratory Tract

**Gas exchange.**

- Trachea divides into the rest of the RESPIRATORY TREE

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**TERMINAL BRONCHIOLES**

- .05 mm in diameter.

**ALVEOLI** - structures where gas exchange w/ blood occurs.

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**-tracheal wall composed of 3 tissue layers:**

1. **Mucosae** - goblet cells in pseudostratified epithelium. CILIA help propel mucus. Smoking destroys cilia = "SMOKER'S COUGH" = only way to propel mucus w/ dust.

2. **Submucosae** - seromucosal glands (serus = produces lysosome) produce mucus sheets.
3. Adventitia - connective tissue w/ C-shaped rings of hyaline cartilage (tracheal cartilage).

*everything past terminal bronchioles - RESPIRATORY ZONE = gas exchange.

*HEIMLICH MANEUVER - use air in lungs to propel out trapped object.

-Trachea and Respiratory tree:

terminal bronchioles ----> respiratory bronchioles --------> alveolar ducts, which dead-end in the blind sacs called alveoli.

*alveoli = small, circular = increased surface area!

- lung occupies most of thoracic cavity. Heart in middle mediastenum. Know apex, base and lobes of the lung.
2. Alveoli - respiratory zone anatomy

*alveolar wall = single layer of squamosal epithelium = diffusion surface w/ capillary wall (also simple squamosal epith.). These 2 walls are fused together to form the RESPIRATORY MEMBRANE = the membrane over which gasses must diffuse.

This membrane = composed of 2 kinds of cells:

1. TYPE I CELLS -"air-blood barrier" - form diffusions surface.

2. TYPE II CELLS -cuboidal cells; secrete water + lubricant called SURFACTANT.

*also have DUST CELLS (= alveolar macrophages) that pick up dust particles, are picked up by ciliary current, passed to larynx and swallowed, where dust & bacteria are destroyed in the stomach.
iv) Blood Supply & Pleura

-BLOOD FLOW: heart -----> pulmonary arteries -----> pulmonary arterioles -----> pulmonary capillaries (gas exchange with alveoli) -----> pulmonary venules -----> pulmonary veins -----> heart.

-PULMONARY PLEURA -surround organs w/ fluid filled sac; 2 layers:

1. PARIETAL PLEURA -attaches to thoracic wall + mediastinum. This attachment is very strong, and will become important later.

2. VISCERAL PLEURA -space between the 2 layers = PLEURAL CAVITY, and is filled w/ fluid.

*PLEURISY -inflammation of pleura. Can be due to BOTH a drying-out of the pleura (= increased friction) OR an increase in liquid in the pleura (puts pressure on the lungs & restricts breathing).

*another function of pleura = COMPARTMENTALIZE thoracic cavity into 3 separate units (2 lateral pleural cavities & one central mediastinum). This way, infection in one area doesn't necessarily spread to rest.
II. RESPIRATORY PHYSIOLOGY

A) Mechanisms of Breathing

- Pulmonary ventilation: moving air in and out; "breathing"

Two phases:
Inhalation or Inspiration- flow of air into lung
Exhalation or Expiration- air leaving lung

- Pressure differences in the thoracic cavity:

\[-\text{INTRAPULMONARY PRESSURE} = P(\text{alveoli})\text{ rises and falls during cycle, but ALWAYS equals outside pressure.}\]

\[-\text{INTRAPLEURAL PRESSURE} \text{ pressure in pleural cavity; DOES NOT change with cycle, stays constant; always 4 mmHg LESS than } P(\text{atm}). \text{ Accomplishes this by sticking to the thoracic and mediastinal walls AND being filled with liquid, allowing it to have a lower pressure than it normally would.}\]

* pressure in pleural space is always NEGATIVE ( = “less”) to pulmonary pressure (pressure in lung), preventing LUNG COLLAPSE
1. Inhalation:
- Diaphragm and intercostal muscles contract
- The size of the thoracic cavity increases
- External air is pulled into the lungs due to an increase in intrapulmonary volume

2. Exhalation:
- Largely a passive process which depends on natural lung elasticity
- As muscles relax, air is pushed out of the lungs
- Forced expiration can occur mostly by contracting internal intercostal muscles to depress the rib cage

*Anything I do to break this bond between wall & parietal pleura, thereby lowering or rising the intrapleural pressure = LUNG COLLAPSE (ATELECTASIS).

**PNEUMOTHORAX - air pocket in the interpleural space.

- Nonrespiratory Air Movements

- Can be caused by reflexes or voluntary actions

- Examples:
  * Cough and sneeze - clears lungs of debris
  * Laughing
  * Crying
  * Yawn
*Hiccup

- FORCED (DEEP) INSPIRATION & EXPIRATION -ACTIVE process.
  *forced expiration: compress muscles of abdominal wall.
  *forced inspiration: sternocleidomastoid + pectoralis minor.

- Respiratory Volumes and Capacities

a. Normal breathing moves about 500 ml of air with each breath (tidal volume [TV])

Many factors that affect respiratory capacity
- A person's size
- Sex
- Age
- Physical condition
b. Residual volume of air - after exhalation, about 1200 ml of air remains in the lungs

c. Inspiratory reserve volume (IRV)
   Amount of air that can be taken in forcibly over the tidal volume
   Usually between 2100 and 3200 ml

d. Expiratory reserve volume (ERV)
   -Amount of air that can be forcibly exhaled
   -Approximately 1200 ml

e. Residual volume
   -Air remaining in lung after expiration
   -About 1200 ml

f. Vital capacity
   -The total amount of exchangeable air
   -Vital capacity = TV + IRV + ERV

g. Dead space volume
   -Air that remains in conducting zone and never reaches alveoli
   -About 150 ml

h. Functional volume
   -Air that actually reaches the respiratory zone
   -Usually about 350 ml

- Respiratory sounds: heard with stethoscope against back.
  
  Bronchial sounds—produced by air rushing through trachea and bronchi

  Vesicular breathing sounds—soft sounds of air filling alveoli
B) External Respiration, Gas Transport, and Internal Respiration

-IN GENERAL: we maintain PP gradients for \( \text{O}_2 \) and \( \text{CO}_2 \) in order to keep things flowing the way we want them to flow!

* at the lungs, we want \( \text{O}_2 \) to move into the blood stream so we can transport it to the tissues, and \( \text{CO}_2 \) to move out of blood into alveoli so it can be expired.

Oxygen **loaded** into the blood

The alveoli always have more oxygen than the blood

Oxygen moves by diffusion towards the area of lower concentration

Pulmonary capillary blood gains oxygen

Carbon dioxide **unloaded** out of the blood

Blood returning from tissues has higher concentrations of carbon dioxide than air in the alveoli

Pulmonary capillary blood gives up carbon dioxide to be exhaled

Blood leaving the lungs is oxygen-rich and carbon dioxide-poor

* at the tissues, we want \( \text{O}_2 \) to move out of the blood stream (into the tissues) and \( \text{CO}_2 \) to move out of tissues and into the blood, so it can be transported to lungs and expired.
-NOTE: all movement of RESPIRATORY GASES = diffusion! NEVER pump!

-QUESTION: how are these gradients maintained? Why doesn't the system go to equilibrium, thereby stopping the flow of respiratory gases?

1. Blood is ALWAYS CIRCULATING - remember, I told you in the Blood Vessel chapter that it was important for blood flow to never stop--now you know why. If it does, diffusion stops, CO₂ builds up in the cells, and they die. First to die are brain cells, because CO₂ is an acid (lowers pH; see later).

2. New, oxygenated air is always being brought into the alveoli through inspiration, maintaining a PP gradient. If you want to see how long it takes for diffusion to stop if new air isn't brought in, see how long you can hold your breath!
3. Both CO$_2$ and O$_2$ are attached to a carrier molecule (red blood cell) as soon as they enter the blood plasma. Therefore, they are no longer CO$_2$ and O$_2$, which maintains the gradient.

4. CO$_2$ is immediately converted to bicarbonate (see later). Therefore, it is no longer CO$_2$, and the gradient is maintained.

-NOTE ONE OTHER THING: the system depends on diffusion, which is why the RESPIRATORY MEMBRANE must be so thin. Anything that lowers the membrane's diffusion capability damages the system, and lets CO2 build up.

*PNEUMONIA -tissue becomes edematous & takes in more fluid ---> lower diffusion, patient poisons himself.

*EMPHYSEMA -walls between adjacent alveoli break down, causing alveoli to fuse together. Larger alveoli = less surface area; eventually, not enough to maintain diffusion rates of CO2. Patient poisons himself.
1) Transport of Oxygen

-oxygen is carried to the cells for their use. Therefore, blood plasma must be able to carry it DESPITE THE FACT THAT IT IS NOT VERY SOLUBLE IN WATER! To combat this, we attach it to a carrier molecule in the RBC -HEMOGLOBIN (Hb)

-Also, we must not only be able to carry it, by the system has to have a way of letting it go once it has arrive at the tissues that need oxygen for cellular respiration

"ASSOCIATION & DISSOCIATION" or "LOADING & UNLOADING" of O₂

-SO, in order to deal with these 2 requirements, oxygen is transported in the plasma in 2 ways:

1. Directly dissolve in plasma - only 1.5%
2. Attached to hemoglobin - 98%

-hemoglobin = 4 polypeptide chains, each with an iron-containing bonding group (= the HEME group).
*iron - easily OXIDIZED (picks up an O₂) in the following reaction:

\[
Fe + O₂ \rightarrow FeO₂
\]
- Some variables can speed up/slow down the movement of O2, assuring that metabolically active tissues receive it while those that are not working don’t receive it!

1. Active tissues have a higher gradient for O2 into themselves, so it moves in faster via diffusion.

2. Any hormone or chemical that increase metabolic activity increase movement of O2 into the tissue from blood.
3. Ph. Metabolic tissues make acid. Blood adapted to release O2 if there is a low pH.
4. CO2. Same as above, but with CO2. “Bohr Effect”.
- HYPOXIA - any impairment to O₂ delivery at the cells.
  * Cyanotic ("blue skin") - first sign. Look @ mucosae & nail beds.
  * Anemic Hypoxia - low # RBC, or abnormal Hb.
  * Ischemic Hypoxia - blocked circulation
  * Histoxic Hypoxia - cells are unable to use O₂, despite the fact that delivery is normal. Usually caused by METABOLIC TOXINS (CYANIDE, etc.).
  * Hypoxemic Hypoxia - reduced arterial P O₂; caused by a pulmonary disease or breathing air with low concentration of O₂ = DROWNING.
  * Carbon Monoxide (CO) Poisoning - Hb has a 200 X greater affinity for CO than O₂; soon, all heme groups are occupied by CO.

2) Transport of CO₂ in the Bloodstream

- Active cells produce 200 ml / minute. If it builds up near the cells, cells die because they can't make more ATP.

  * Difference from O₂ : VERY soluble in water!

- How transported? 3 ways:

  (i) Dissolved in plasma --- 7 - 10%. Very little CO₂ transported this way, although more soluble than O₂.

  [Graph showing CO₂ transport in blood]

  * For the majority of CO₂, it diffuses into the RBC, where one of the next 2 things happens:
(ii) Chemically bound to hemoglobin to form CARBAMINOHEMOGLOBIN. 10 - 20%

*THAT'S RIGHT---Hb can carry CO2, also!!!! However, CO2 not carried on the HEME group; rather, it attaches to the amino acid chain of the polypeptide = DOES NOT COMPETE WITH O2!!!!

(iii) transported as the BICARBONATE ION in the plasma --MAJORITY (60 - 70%)

*NOTE: CO2 is an acid (hydrogen donor), and therefore it's presence causes the release of oxygen (the Bohr Effect); this assures that oxygen is released near tissues that are metabolically active and are producing high levels of CO2.
*ALSO NOTE: this is a BUFFER SYSTEM, which is any series of reactions that protects against a sudden change in pH (up or down). If the system becomes acidic, the reaction goes to the left, CO2 is generated, which can be expelled at the lungs. If the system becomes too basic, hydrogen ions are "eaten up", causing the reaction to go to the right, and when make more carbonic acid, which neutralizes the base.

**BLOOD pH MUST STAY BETWEEN 7.4 and 7.34, or brain tissue dies!

ACCUMULATION OF CO₂ = ACIDOSIS
DEPLETION OF CO₂ = ALKALOSIS

C) Control of Respiration

1. Neural Regulation: Setting the basic Rhythm
   - Activity of respiratory muscles is transmitted to the brain by the phrenic and intercostal nerves
   - Neural centers that control rate and depth are located in the medulla
   - The pons appears to smooth out respiratory rate
   - Normal respiratory rate (eupnea) is 12-15 respirations per minute
   - Hyperpnea is increased respiratory rate often due to extra oxygen needs

2. Factors Influencing Respiratory Rate and Depth

   (i) Physical factors
      - Increased body temperature
      - Exercise
      - Talking
      - Coughing
      - Volition (conscious control)
      - Emotional factors
(ii) Chemical factors
-Carbon dioxide levels
  *Level of carbon dioxide in the blood is the main regulatory chemical for respiration
  *Increased carbon dioxide increases respiration
  *Changes in carbon dioxide act directly on the medulla oblongata

-Oxygen levels
  *Changes in oxygen concentration in the blood are detected by chemoreceptors in the aorta and carotid artery
  *Information is sent to the medulla oblongata
D) RESPIRATORY DISORDERS

1. Chronic Obstructive Pulmonary Disease (COPD)
   - Exemplified by chronic bronchitis and emphysema
   - Major causes of death and disability in the United States
   - Features of these diseases
     - Patients almost always have a history of smoking
     - Labored breathing (dyspnea) becomes progressively more severe
     - Coughing and frequent pulmonary infections are common
   - Most victims retain carbon dioxide, are hypoxic and have respiratory acidosis
   - Those infected will ultimately develop respiratory failure

   a. Emphysema
      - Alveoli enlarge as adjacent chambers break through
      - Chronic inflammation promotes lung fibrosis
      - Airways collapse during expiration
      - Patients use a large amount of energy to exhale
      - Overinflation of the lungs leads to a permanently expanded barrel chest
      - Cyanosis appears late in the disease

   b. Chronic Bronchitis
      - Mucosa of the lower respiratory passages becomes severely inflamed
      - Mucus production increases
      - Pooled mucus impairs ventilation and gas exchange
      - Risk of lung infection increases
      - Pneumonia is common
      - Hypoxia and cyanosis occur early

2. Lung Cancer
   - Accounts for 1/3 of all cancer deaths in the United States
   - Increased incidence associated with smoking
   - Three common types
   - Squamous cell carcinoma
   - Adenocarcinoma
   - Small cell carcinoma
3. Sudden Infant Death Syndrome (SIDS)
   - Apparently healthy infant stops breathing and dies during sleep
   - Some cases are thought to be a problem of the neural respiratory control center
   - One third of cases appear to be due to heart rhythm abnormalities

4. Asthma
   - Chronic inflamed hypersensitive bronchiole passages
   - Response to irritants with dyspnea, coughing, and wheezing