Acid-base Balance by the Lungs and Kidneys

**Acid:** Any chemical that releases hydrogen ions (H\(^+\)) into a solution
- Strong acids release almost all of their hydrogen ions into water.
- Phosphoric acid, hydrochloric acid
- Tastes sour

**Base** – any chemical that accepts H\(^+\)
- Strong bases, like hydroxide ion (OH\(^-\)), has a strong tendency to bind H\(^+\)
- Weak bases, like bicarbonate ion (HCO\(_3^-\)) bind less available H\(^+\)
- Tastes bitter, feels slippery

**pH** = potential Hydrogen
- A measure of hydrogen ion concentration
- Acids
  - High hydrogen ion concentrations
  - Low pH
- Bases
  - Low hydrogen ion concentrations
  - High pH
- The pH Scale
  - There is a **10-fold** difference in hydrogen ion concentration between solutions that differ by one pH unit.
  - Solution with pH 4 has **ten times** as many hydrogen ions as a solution with pH 5

**Salts**
- Neither acids nor bases
- Neutral
- Usually formed when acids and bases react
  \[ \text{H}^+\text{Cl}^- + \text{Na}^+\text{OH}^- \rightarrow \text{Na}^+\text{Cl}^- + \text{H}^+\text{OH}^- \]
  - Hydrochloric acid + Sodium hydroxide → Sodium chloride + Water

**Acid-Base Balance**
- 7.35 to 7.45 is the normal pH range of blood and tissue fluid
- Very narrow range of neutral pH is acceptable!
  - acidosis – blood pH lower than 7.35
  - alkalosis – blood pH higher than 7.45
- One of most important aspects of homeostasis
- metabolism depends on enzymes, and enzymes are sensitive to pH
- slight deviation from normal pH can
  - shut down entire metabolic pathways
  - alter the structure and function of macromolecules
- Challenges to acid-base balance:
- Your body is constantly producing acid
  - lactic acids from anaerobic fermentation
  - phosphoric acid from nucleic acid catabolism
  - fatty acids and ketones from fat catabolism
  - carbonic acid from carbon dioxide
- **Acidosis:** Body fluids become too acidic
  - Causes
    - Build-up of CO\(_2\) (emphysema)
    - Increased production of organic acids such as lactic acid and ketone bodies (alcoholism, diabetes)
    - Ingestion of acidic drugs (ie aspirin)
    - Loss of bases (chronic diarrhea due to intestinal problems or laxative overuse)
    - Diet?
- **Alkalosis**: Body fluids become too basic
  - Hyperventilation
  - Overuse of bicarbonates (antacids)
  - Loss of stomach acid (chronic vomiting, overuse of acid reflux drugs)
  - Long-term drinking of alkaline water

**Buffers**
- Buffer – any mechanism that resists changes in pH
- Convert strong acids or bases to weak ones
- Keep pH level

**Chemical buffers**
- Substance that binds H\(^+\) and removes it from solution as its concentration begins to rise, or releases H\(^+\) into solution as its concentration falls
- Restores normal pH in fractions of a second
- Three major chemical buffers: bicarbonate, phosphate, and protein systems

**Bicarbonate Buffer System**
- Bicarbonate buffer system – a solution of carbonic acid and bicarbonate ions.
- Goes either way to make H\(^+\) or get rid of it
  - \(\text{CO}_2 + \text{H}_2\text{O} \leftrightarrow \text{H}_2\text{CO}_3 \leftrightarrow \text{HCO}_3^- + \text{H}^+\)
- Functions best in lungs and kidneys to constantly remove \(\text{CO}_2\)
- To lower pH, kidneys excrete \(\text{HCO}_3^-\)
- To raise pH, kidneys excrete \(\text{H}^+\) and lungs excrete \(\text{CO}_2\)

**Phosphate Buffer System**
- Phosphate buffer system – a solution of \(\text{HPO}_4^{2-}\) and \(\text{H}_2\text{PO}_4^-\)
- \(\text{H}_2\text{PO}_4^- \leftrightarrow \text{HPO}_4^{2-} + \text{H}^+\)
- Reaction can go either way
- As in the bicarbonate system, reactions that proceed to the right liberating H\(^+\) (decreasing pH), and those to the left increase pH
- Most important in kidneys

**Protein Buffer System**
- Proteins are more concentrated than bicarbonate or phosphate systems, especially in the ICF
- Protein buffer system accounts for ~ 3/4 of all chemical buffering in the body fluids
- Protein buffering ability is due to certain side groups of their amino acid residues
- Carboxyl (\(-\text{COOH}\)) side groups which releases H\(^+\) when pH too high
- Amino (\(-\text{NH}_2\)) side groups bind H\(^+\) when pH gets too low

**Physiological Buffers**
- The respiratory and urinary systems also act as buffers
- **Urinary system**: strong but slow
  - Buffers greatest quantity of acid or base
  - Takes several hours to days to exert its effect
- **Respiratory system**: fast but weak
  - Buffers within minutes
  - But cannot alter pH as much as urinary system
  - Kidneys compensate for pH imbalances of respiratory origin
  - Respiratory system compensates for pH imbalances of metabolic origin
- In a nutshell...
  - Acidosis stimulates breathing, and alkalosis inhibits breathing
  - Kidneys change pH by the amount of H\(^+\) secreted into urine
Respiration

Word has three meanings:
1. Breathing
2. Exchange of gases between the air and blood, and between blood and the tissue fluid
3. Use of oxygen in cellular metabolism

- The respiratory system consists of a system of tubes that delivers air to the lungs
- Oxygen diffuses into the blood, and carbon dioxide diffuses out (Remember the RBCs?)
- Principal Organs of Respiratory System:
  - nose
  - pharynx
  - larynx
  - trachea
  - lungs
  - bronchi
  - alveoli

Conducting division of the respiratory system
- Passages for airflow only
- No gas exchange
- Nostrils → major bronchioles

Respiratory division of the respiratory system
- Alveoli and other gas exchange regions

Lungs
- Lungs are crowded by adjacent organs,
- Don’t fill entire ribcage
- Not symmetrical
- Right lung
  - shorter than left because the liver rises higher on the right
  - 3 lobes
- Left lung
  - taller and narrower because the heart tilts toward the left and occupies more space on this side
  - indentation – cardiac impression
  - 2 lobes

Trachea and Primary Bronchi
- Bronchial tree – branching system of air tubes in each lung
- from main bronchus to 65,000 terminal bronchioles

- Cells progressively shorter and epithelium thinner
- Lots of lymphatic tissue positioned to intercept inhaled pathogens
- Large amount of elastic connective tissue
- contributes to the recoil that expels air from lungs
- Smooth muscle contracts or relaxes to constrict or dilate the airway, regulating air flow

Primary bronchi—forks off from trachea
- Right is slightly wider and more vertical than left
- Inhaled foreign objects lodge right bronchus more often than in left
- Left is slightly narrower and more horizontal than the right

Secondary bronchi
- 3 forks on right, one for each lobe of the right lung
- 2 forks on left, one to each lobe of the left lung
Tertiary bronchi -
- 10 on right, and 8 on left
- Each ventilates a functionally independent unit of lung tissue

Bronchioles
- No cartilage
- 1 mm or less in diameter
- One bronchiole ventilates one pulmonary lobule
- Each divides into 50 - 80 terminal bronchioles
- final branches
- 0.5 mm or less in diameter
- each terminal bronchiole gives off two or more smaller respiratory bronchioles
- Respiratory bronchioles: the tiniest branches
- Divide into 2-10 alveolar ducts
- End in alveolar sacs – grape-like clusters of alveoli arrayed around a central space called the atrium

Alveoli (air sacs)
- An alveolus is a pouch 0.2-0.5 mm in diameter
- 150 million alveoli in each lung, providing about 70 m² of surface for gas exchange
- Thin cells on surface allow rapid gas diffusion between alveolus and blood
- Cells inside repair alveolus and secrete pulmonary surfactant to coat alveoli and smallest bronchioles
  - Soap is an example of a surfactant
  - Without surfactant, walls of alveolus would stick together like wet paper
  - Surfactant makes them slippery
- Each alveolus is surrounded by basket of blood capillaries
  - supplied by pulmonary arteries and veins
  - Gas exchange (O2 for CO2) takes place with the blood inside these capillaries
- Respiratory membrane – the barrier between air inside alveolus and blood
  - Consists of:
    - Cells of alveolus
    - Cells of blood capillary
    - Their shared basement membrane
    - Covered with thin film of water
- Important to prevent fluid from accumulating in alveoli!
  - Blood capillaries absorb excess liquid
  - Lungs have a more extensive lymphatic drainage than any other organ
  - Low capillary blood pressure also prevents the rupture of the delicate respiratory membrane
- Alveolar macrophages (dust cells)
  - Most numerous of all cells in the lung
  - Wander lumen and connective tissue between alveoli
  - Keep alveoli free from debris by phagocytizing dust particles
  - Also blood and bacteria
  - 100 million dust cells die every day as they ride up the mucociliary escalator to be swallowed and digested with their load of debris

Air Breathed into Alveoli
- Composition of outside air
  - 78.6 % nitrogen, 20.9% oxygen, 0.04% carbon dioxide, 0 – 4% water vapor depending on temperature and humidity, and minor gases argon, neon, helium, methane and ozone
  - Imagine the volume of air in a typical classroom (30 x 30 x10 ft)
  - (Also assume we separated all the gases.)
    - Oxygen would cover the room to about 2 feet deep.
Nitrogen would fill almost to the ceiling.
Argon gas would fill a one inch layer over the whole room.
The remaining gases fill the last one inch.
Carbon dioxide has about the same volume of one student.
Neon is 1.5 gallons.
Helium would fill a one liter bottle.
Methane gas would fill someone's 1/2 liter bottle.
Krypton would fill a 12 oz soda can.
Hydrogen would fill about half of a 12 oz soda can.
And xenon gas would have the volume of a pencil's eraser.

Once inside an alveolus, air
  - Has 10xs more water moisture because of contact with mucous membranes
  - Has less O₂ and more CO₂ (Mixes with left-over air from last breath)
  - 130 xs CO₂

Alveolar Gas Exchange
- Back-and-forth traffic of O₂ and CO₂ across respiratory membrane
- Air inside contacts a film of water covering wall of alveolus
  - For O₂ to get into blood it must dissolve in this water, then pass through respiratory membrane
  - For CO₂ to leave the blood it must pass the other way
  - Diffuse out of the water film into the alveolar air
- Each gas diffuses down its own concentration gradient until the partial pressure of each gas in the air is equal to its partial pressure in water
- One gas does not influence the diffusion of another
- CO₂ does not affect O₂: each does its own thing by diffusing from where there is a lot to where there is a little until both sides are equal
- The more O₂ in alveolar air, the more O₂ goes into the blood
- Since blood arriving at an alveolus has more CO₂ than air, it releases CO₂ into the air inside
- At the alveolus, the blood is said to unload CO₂ and load O₂
  - Involves erythrocytes
  - 0.25 sec necessary to reach equilibrium

Factors Affecting Gas Exchange
1. Amount of oxygen in atmosphere
   - Changing the amount of O₂ in outside air can cause more or less oxygen to enter blood
2. Membrane thickness - only 0.5 μm thick
   - Left ventricular failure, pneumonia cause thickening of respiratory membrane
   - Farther to travel between blood and air
   - Cannot equilibrate fast enough to keep up with blood flow
3. Membrane surface area – each lung has 100 ml blood in alveolar capillaries, spread thinly over 70 m²
   - Emphysema, lung cancer, and tuberculosis decrease surface area for gas exchange
   - Lead to low concentration of oxygen

Gas transport - carrying gases from the alveoli to the body and vice versa
- Oxygen transport
  - 98.5% bound to hemoglobin
  - 1.5% dissolved in plasma
- Carbon dioxide transport
  - 70% as bicarbonate ion
  - 23% bound to hemoglobin
  - 7% dissolved in plasma
Hemoglobin – molecule specialized for oxygen transport

- four protein (globin) portions
- each with a heme group which binds one \( O_2 \) to the ferrous ion (\( Fe^{2+} \))
- **one hemoglobin molecule can carry up to 4 \( O_2 \)**

Carbon Dioxide Transport

Carbon dioxide transported in three forms

- 90% of \( CO_2 \) combines with water to form carbonic acid
  - \( CO_2 + H_2O \rightarrow H_2CO_3 \rightarrow HCO_3^- + H^+ \)
  - then dissociates into bicarbonate and hydrogen ions
- 5% binds to the amino groups of plasma proteins and hemoglobin
  - **carbon dioxide does not compete with oxygen**
  - they bind to different moieties on the hemoglobin molecule
  - **hemoglobin can transport \( O_2 \) and \( CO_2 \) simultaneously**
- 5% is carried in the blood as dissolved gas

Systemic Gas Exchange Between capillaries and tissues throughout body:

**\( CO_2 \) loading**

- \( CO_2 \) diffuses **into** the blood, reacts with water
  - \( CO_2 + H_2O \rightarrow H_2CO_3 \rightarrow HCO_3^- + H^+ \)
- \( H^+ \) binds to hemoglobin

**\( O_2 \) unloading**

- \( H^+ \) binding to hemoglobin reduces its affinity for \( O_2 \)
- makes hemoglobin release oxygen

Voluntary control of breathing provided by motor cortex

Limits to voluntary control

- Breaking point – when \( CO_2 \) levels rise to a point when automatic controls override one’s will
- >6 minutes risk brain damage
- David Blaine 17 min 4 sec
- But what stimulates your brain to want to breathe?
  - It’s NOT lack of oxygen! It’s too many H+ ions! Means blood is too acidic
  - Too many H+ ions (acidity) in CSF and brain tissue signals the brain to override whatever you are doing and make you BREATHE
  - Rate and depth of breathing adjust to maintain levels of:
    - \( pH \) 7.35 - 7.45 (neutral)
    - \( PCO_2 \) 40 mm Hg
    - \( PO_2 \) 95 mm Hg

Brainstem respiratory centers receive input from chemoreceptors that monitor the composition of blood and CSF (remember from circulatory system?)

H+ ions in CSF and tissue fluid of brain arise mainly from \( CO_2 \) diffusing into them and generating H+ through carbonic acid rxn

thus high \( CO_2 \) level from holding your breath causes acidity

Breathing adjusted to maintain certain \( pH \) and \( CO_2 \) concentration; **indirectly keeps \( O_2 \) at 97%**

**Effects of Hydrogen Ions**

**Hyperventilation is a corrective homeostatic response to acidosis**

“blowing off ” \( CO_2 \) faster than the body produces it

pushes reaction to the left

\( CO_2 \) (expired) + \( H_2O \leftarrow H_2CO_3 \leftarrow HCO_3^- + \downarrow H^+ \)

reduces \( H^+ \) (reduces acid) raises blood \( pH \) towards normal
Hypoventilation is corrective homeostatic response to alkalosis
allows CO₂ to accumulate in the body fluids faster than we exhale it
shifts reaction to the right
\[ \text{CO}_2 + \text{H}_2\text{O} \rightarrow \text{H}_2\text{CO}_3 \rightarrow \text{HCO}_3^- + \text{H}^+ \]
raising the H⁺ concentration, lowering pH to normal

Carbon Dioxide has only indirect effects on respiration through pH as seen previously
Respiration and Exercise
- When brain sends motor commands to the muscles
- also sends this information to the respiratory centers
- they increase pulmonary ventilation in anticipation of the needs of exercising muscles
- increase breathing because they are informed that the muscles have been told to move or are actually moving, not because of increased need for oxygen!

Oxygen Concentration
Little effect on respiration!
Exceptions: emphysema, pneumonia, several days at high altitude

Urinary System

Kidneys regulate:
- Blood volume and pressure
  - eliminating or conserving water
  - secretes enzyme, renin, which activates hormonal mechanisms that control blood pressure and electrolyte balance
- Erythrocyte count
  - secretes the hormone erythropoietin
- Blood pH
  - CO₂ levels
- Electrolyte and acid base balance

Urinary system consists of 6 organs: 2 kidneys, 2 ureters, urinary bladder, and urethra

What happens if your kidneys don’t work?
http://www.youtube.com/watch?v=cIp2OLPiosE

Kidneys
- size of bar of bath soap
- receives renal nerves, blood vessels, lymphatics, and ureter
- lie against posterior abdominal wall
- right kidney slightly lower due to large right lobe of liver
- rib 12 crosses the middle of the left kidney
- drop about 3 cm when go from lying down to standing up

Gross Anatomy of Kidney: cortex, medulla, calyx, pyramid, sinus, column
Nephron: 1.2 million nephrons per kidney
Urine Formation
kidneys convert blood plasma to urine in three stages, happens in each nephron

1. Filtration
   Blood plasma is filtered in renal corpuscle

2. Reabsorption and secretion
   Substances removed or added by tubular cells
   Keep beneficial compounds, remove wastes

3. Water conservation
   Water returned to blood
   Urine concentrated in collecting duct (one duct per several nephrons)

Sodium Chloride
- Sodium reabsorption into blood is the key to everything else
- creates an osmotic and electrical gradient that drives the reabsorption of water and other solutes
- most abundant cation in filtrate
- creates steep concentration gradient that favors its diffusion into the epithelial cells
- Other electrolytes reabsorbed (Potassium, magnesium, phosphate, etc.)

Tubular Secretion
- tubular secretion —renal tubule extracts chemicals from capillary blood and secretes them into tubular fluid
- two purposes:
  - waste removal
    - urea, uric acid, bile acids, ammonia, catecholamines, prostaglandins and a little creatinine are secreted into the tubule
    - clears blood of pollutants, morphine, penicillin, aspirin, and other drugs
  - acid-base balance
    - secretion of hydrogen and bicarbonate ions help regulate the pH of the body fluids
- Water Reabsorption
  - kidneys reduce 180 L of glomerular filtrate to 1 or 2 liters of urine each day
  - Keeps us from urinating 45 gallons per day!
  - after water and solutes leave surface of the tubular epithelium, they are reabsorbed by capillaries

- Collecting Duct Concentrates Urine
  - as urine passes through the increasingly salty medulla, water leaves by osmosis concentrating urine
  - collecting duct (CD) begins in the cortex where it receives tubular fluid from several nephrons

Renal Control of pH
- kidneys can neutralize more acid or base than either the respiratory system or chemical buffers
- renal tubules secrete H⁺ into the tubular fluid
- most binds to bicarbonate, ammonia, and phosphate buffers
- bound and free H⁺ are excreted in the urine actually expelling H⁺ from the body
- other buffer systems only reduce its concentration by binding it to other chemicals