

A&P Chapter 27 Fluid and Electrolyte Balance

Body Water Content

Total body water is about 40 Liters. Most of the body's water is in the Intracellular Fluid (25 L of 40 L), and the remaining is in the Extracellular Fluid (15 L of the 40 L). In the Extracellular Fluid there are two types of fluid...the Interstitial Fluid accounts for 12 Liters and the Plasma Volume accounts for 3 Liters.

TOTAL BODY WATER =	40 Liters
Intracellular fluid =	25 Liters (25% of body weight)
Extracellular fluid =	15 Liters (20% of body weight)
ISF =	12 Liters (80% of ECF)
Plasma =	3 Liters (20% of ECF)

The ICF and ECF are separated by membranes that provide selective permeability, so this allows the two fluid compartments to maintain different compositions.

Principal ions of the ECF:

Major cation is Na^+

Major anion is Cl^-

Buffer is HCO_3^-

--Salt is the most abundant and important ECF solute because it has such a huge affect on osmolarity.--

Principal ions of the ICF:

Major anion is PO_4^{3-}

Major cation is K^+

Another one is Mg^{2+}

--There are also an abundance of protein anions in the ICF. Proteins can bind to and release Hydrogen—

Ion balance is maintained primarily by the regulated reabsorption/secretion along renal tubules and collecting ducts. Note that the lungs are also involved in regulating H^+ by regulating CO_2 and this affects acid-base balance.

The role of proteins and non-electrolyte (fats) is that they provide oncotic pressure in the capillary, which pulls water into the capillary (inward directed force), and in the ICF they pull water out of the blood (outward directed force).

ECF Proteins: 90% of plasma mass, 60% in the Interstitial Fluid

ICF Proteins: 97% of plasma mass

Mixing of Body Fluids

There is continuous mixing within the ECF subcompartments... plasma, interstitial fluid, CSF, lymph, serous fluid, synovial fluid, etc... This is why imbalances in plasma volume and composition are representative of imbalances in the ECF as a whole.

Mixing between the ECF and ICF...most cell membranes are permeable to water, so there is continuous mixing of fluids. Note that the solutes do not diffuse. Even though the ionic composition of each compartment is different, the osmolarity remains the same due to osmosis. A change in the ECF osmolarity (caused primarily by NaCl), will cause fluid shifts between the ICF and ECF.

If ECF osmolarity drops, then the fluid will shift into the ICF until osmolarity equilibrates. This causes the cells of the ICF to swell, while BV decreases.

Because the ICF volume is about twice that of the ECF, then it can act as a water reservoir for short-term regulation of the ECF volume. For example, if the ECF becomes hypoosmotic, it can move a LOT of water into the ICF by putting a little bit into each cell. The ICF can handle this because it represents a small change in each cell.

4 Principles of Fluid and Electrolyte Regulation

1. Only the ECF is monitored...actually it's just the plasma (blood) that is monitored. This is what provides the stimulus for the negative feedback loops. Because of the selective permeability, this in turn regulates ICF volume and composition!
2. Nervous system receptors detect changes in pressure (and thus volume) and osmolarity. The receptors don't detect individual ion concentrations, but they do detect changes in osmolarity and pressure. The osmoreceptors are in the hypothalamus, and the baroreceptors are in the carotid sinus and aortic arch. There are two exceptions...the adrenocortical cells that secrete aldosterone are directly sensitive to Potassium. And the MD cells (of the JG apparatus) are sensitive to filtrate rate and osmolarity (TG feedback).
3. Water moves by osmosis, and this is always a passive process. Note that the active transport of ions causes the osmotic gradient in the first place.
4. Ion and fluid balance refers to matching ion/water gains with ion/water losses. This is primarily a matter of matching dietary gains with urinary excretion.

Hormones involved in regulation

ADH (Vasopressin) regulates osmolarity and thus BV, and thus MAP. This stimulus for ADH is HIGH OSMOLARITY, which occurs when MAP is low. The high osmolarity of the ECF stimulates the release of ADH, which enhances thirst and increases water reabsorption along the DCT/CD (by adjusting aquaporins on the luminal membrane), which conserves water while eliminating salt and this dilutes the ECF osmolarity. Other affects include raising BV/MAP and acting as a vasoconstrictor to increase TPR & MAP.

Aldosterone has to do with Na⁺ reabsorption. Low BV/MAP causes stimulation of the Renin-Ang II-Aldosterone pathway, which causes Aldosterone to increase. Aldosterone then inserts more Na⁺/K⁺ pumps at the DCT/CD, which increases Sodium reabsorption (and increases potassium secretion). This increases ICF osmolarity and water follows. This increases BV and MAP.

Natriuretic peptides (ANP/BNP) are released in response to stretch on atrial receptors (High BP). They inhibit SNS output and lower MAP. They have opposite effects of ADH and Aldosterone, which increases excretion of water and salt, which lowers BV and lowers MAP.

Fluid Balance

Water gains must equal water balance. This amounts to about 2.5 Liters per day.

Water gains: Metabolic formation of water molecules (300 ml/day)
 Consumption of food/beverage (2200 ml/day)

The hypothalamus is the thirst center. It is stimulated by osmoreceptors, which detect high ECF osmolarity. Other stimuli for the thirst center are Ang II and Baroreceptor input.

Water losses: Insensible water loss (lost at skin and lungs)
 Sensible water loss
 urine output of 500ml minimum daily
 feces, secretion of sweat.

Just a 2-3% increase on osmolarity stimulate ADH!

Causes of water imbalance

DEHYDRATION can occur via hemorrhage, severe burns, vomiting, diarrhea, profuse sweating, reduced intake, and diuretics. It may lead to hypovolemic shock.

Often, these water losses exceed loss of solutes, so the ECF osmolarity increases (usually resulting in hypernatremia). This causes a fluid shift out of the ICF which results in ICF and ECF that both have higher osmolarity and lower volumes than they would usually have. This may damage cells if it is severe and can lead to hypovolemic shock.

HYPOTONIC HYDRATION is caused by a large intake of pure water. It leads to low ECF osmolarity (hyponatremia) and inhibits the secretion of ADH, so you excrete a large volume of dilute urine. Excessive overhydration affects cellular function as the cells swell, and this can lead to CNS dysfunction called “water intoxication”

Electrolyte Balance

Electrolyte imbalances can make the cell hyper or hypo-excitabile, and this can be very dangerous, especially for the heart! Osmotic gradients, myocytes, contraction and cellular functions in general are also affected. The main electrolytes are Na^+ , K^+ and Ca^+ .

SODIUM IMBALANCE: Salts contribute to 95% of ECF osmolarity, so keeping Na^+ in balance is extremely important. The normal range for Na^+ in the ECF is about 140 mM. Na^+ salts such as NaCl and NaHCO_3 (sodium bicarbonate) account for 280 mOsm of the total blood osmolarity of 300 mOsm.

ECF sodium levels less than 130 mM is hyponatremia

ECF sodium levels greater than 150 mM is hypernatremia

By the time the filtrate reaches the DCT/CD, you have reabsorbed about 90% of the Na^+ and the remaining 10% is regulated by **Aldosterone** via negative feedback loops.

The primary stimulus for Aldosterone secretion is Ang-II (in response to low BV/MAP) via the Renin-AngII-Aldosterone pathway. The JG cells are stimulated via low filtrate flow/osmolarity and decreased stretch on the JF cells due to low MAP, they secrete renin and away you go!

Aldosterone increases
BV and MAP!

Another stimulus for Aldosterone is hyperkalemia, which the adrenocortical cells can detect directly. They secrete aldosterone in response!

Effects on the principal cells of the DCT/CD is that more Na^+/K^+ pumps are inserted as well as Na^+/K^+ channels. This causes more sodium to be reabsorbed and more potassium to be secreted. This increases ECF osmolarity and since water follows the salt, BV also goes up.

ADH responds to the ECF Na^+ imbalance due to resulting osmotic imbalance. It inserts water channels to increase water permeability along the DCT/CD and also enhances thirst! For example, if ECF osmolarity is high, then ADH will be secreted, which increases water reabsorption and thirst, which increases ECF volume and lowers ECF osmolarity.

Collective Regulation of low ECF volume results because ADH, Ang II and Aldosterone all respond by increasing water and salt reabsorption to increase BV and MAP. The renin pathway stimulates both ADH and Aldosterone! These hormones also inhibit ANP and stimulate the SNS.

Collective Regulation of high ECF volume is the work of ANP/BNP...they work by decreasing water and salt reabsorption to lower BV and MAP. They also inhibit ADH, Ang II and Aldosterone, SNS.

(will pick this up later with Potassium on page 6 of the outline)

pH and Acid balance

pH	Negative exponent of the hydrogen ion concentration
Neutral	pH of 7
Acidic	pH below 7
Alkaline	pH above 7 (also called alkaline)
Acid	A substance that dissociates to release hydrogen ions, decreasing pH
Base	A substance that dissociates to tie up hydrogen ions, raising pH
Buffer	A substance that tends to oppose changes in pH by removing or replacing hydrogen ions.

A STRONG ACID or BASE completely dissociates, while a WEAK ACID or BASE only partially dissociates (and the reaction is reversible).

Strong Acid example: Hydrochloric Acid

Strong Base example: Sodium Hydroxide

Types of Acids in the Body

VOLATILE ACIDS form gas in a solution. For example, Carbonic Acid forms the gas CO₂. Thus, PCO₂ is the most important contributor to free Hydrogen ions in the blood.

The complete reaction $\text{CO}_2 + \text{H}_2\text{O} \rightleftharpoons \text{H}_2\text{CO}_3 \rightleftharpoons \text{H}^+ + \text{HCO}_3^-$

FIXED ACIDS do not leave the solution as a gas, and they must be eliminated via the kidneys. Examples are sulfuric acid, phosphoric acid (metabolic products)

ORGANIC ACIDS originate from energy metabolism, an example is lactic acid. These normally don't accumulate except during intense exercise (lactic acid goes up) or during starvation (ketones go up and you get ketoacidosis).

Control of pH

The normal ECF pH is 7.4, plus or minus 0.5. The normal ICF pH is 7.0. If pH is out of range, then it is called acidemia or alkalemia (abnormal pH levels in the blood). This affects proteins and impairs cell functions which leads to organ dysfunction and failure. Acidemia leads to acidosis, which is the disease/physiological state. Alkalemia leads to the disease alkalosis. Acidosis is more common.

Long-term acid-base balance matches Hydrogen gains with losses. The gains come from metabolism, intestinal absorption...and the losses come from renal secretion (intercalated cells of the DCT/CD) and the lungs via CO₂. The long-term regulation takes hours to days. The short term response is to use chemical buffers!

Short-term chemical buffers are dissolved substances that stabilize pH by adding or removing Hydrogen from the solution. Note that buffers don't actually add or remove Hydrogen ions from the body...they don't correct an imbalance, they just help the body deal with it. The buffer systems usually consist of a weak acid and its dissociated anion (weak base). For example, a weak acid is H₂CO₃, and the weak base is HCO₃⁻.

Some major body fluid buffers are:

- Protein buffer systems, where AAs bind and release hydrogen
- Carbonic Acid-Bicarbonate buffer system (most important ECF buffer)
- Phosphate buffer system (important ICF and urine buffer)

Protein Buffer System

AAs contain carboxyl groups (COOH) that release Hydrogen, becoming COO^- if pH is high.

AAs contain base groups (NH_2) that accept Hydrogen, becoming NH_3^+ if pH is low.

Abundant ICF protein buffers resist changes in ECF pH by using H^+/K^+ antiporter that shifts Hydrogen into and out of the cells in exchange for K^+

- If pH is low, then Hydrogen is put in to the ICF, and Potassium into the ECF. This may cause an increase in ECF Potassium
- If pH is high, then it may lead to low ECF potassium

Carbonic Acid-Bicarbonate Buffer System

Carbonic Acid is the weak acid, and Bicarbonate is the weak base. The direction of the reaction depends on the concentrations of the reactants and products.

Three important limitations of this system:

1. You cannot prevent pH changes due to changes in concentration of its own weak acid. So, what this means is...carbonic acid cannot buffer itself. If you added carbonic acid to the solution, it would drive the reaction to the right, freeing up more Hydrogen and lowering pH.
2. It requires normal respiratory function. Carbonic acid levels need to be maintained by removing CO_2 via the lungs at the appropriate rate. Recall that high CO_2 leads to carbonic acid, which leads to high free hydrogen ions which is low pH. The reverse is also true.
3. Buffering capacity is limited by bicarbonate reserves. Without bicarbonate, then you cannot buffer a drop in pH...the reaction can go to the right, but not to the left. As hydrogen is continuously added to solution, more bicarb is used to bind the hydrogen and form carbonic acid. This will occur until all the available bicarb is used up. Normally, the bicarb reserves are large and there is also a lot of sodium bicarbonate (NaHCO_3), which dissociates into sodium and bicarbonate ion...and is primarily a buffer of the ICF. The kidneys can also add to the reserve by generating "new" bicarbonate. The level of bicarb reserve in the ECF is 24-28mEq/L.

Phosphate buffer system

This system has the same function as the bicarbonate system, but it is less abundant in the ECF. It is more important as an ICF and urine buffer. In this reaction, dihydrogen phosphate is the weak acid, and monohydrogen phosphate is the weak base. The ICF reserve is Na_2HPO_4

Acid-Base Balance

The respiratory and renal systems are responsible for maintaining acid-base balance and buffering capacity. The respiratory system compensates by removing hydrogen via the removal of CO_2 from the lungs. The renal system compensates by excreting hydrogen or bicarbonate, depending on the imbalance. Normally, you have a net gain of hydrogen, so hydrogen is excreted and bicarb is reabsorbed (and also produced by tubular cells).

Respiratory Compensation: Chemoreceptors are sensitive to arterial pH and PCO_2 , and they signal respiratory centers. This increases or decreases alveolar ventilation to regulate PCO_2 and pH accordingly. This is a fast response...about 1-3 minutes. It affects the Carbonic Acid-Bicarbonate Buffer System.

Renal Compensation:

1. Secretion of hydrogen at the PCT and intercalated cells of the DCT/CD. The cellular mechanisms involved include :
 - Hydrogen secretion via active luminal transport (pumps and cotransport)
 - Indirect bicarbonate reabsorption within tubular cells. Recall that bicarb can only be brought into the cell via CO_2
 - Basolateral cotransport???
2. Secreted hydrogen is buffered in the urine, because you cannot make a urine lower than a pH of 4. The urine buffers include filtered bicarbonate, phosphate and ammonia generated by the tubular cells.
3. Production of “new” bicarbonate at the DCT/CD. When bicarbonate is reabsorbed in exchange for a secreted hydrogen that binds to a filtrate/urine buffer other than bicarbonate, then it is not considered to be “replaced” by whatever is occurring in the filtrate. It is considered a NEW bicarbonate that is added to the ECF.
 - a. Things that the hydrogen can bind to in the filtrate that are NOT bicarbonate are the ammonia buffer and ammonia ion, and the phosphate buffer.
 - b. The ammonia buffer & ammonia ion involve glutamine metabolism. The glutamine breaks down into two bicarbonate ions and two ammonia (NH_4), and two hydrogen. The ammonia binds with the hydrogen either inside the cell or in the filtrate, thus classifying the bicarbonate that is reabsorbed as NEW.
 - c. The phosphate buffer involves the hydrogen leaving the cell and binding to monohydrogen phosphate in the filtrate. This reaction creates dihydrogen phosphate and it is excreted in the urine. The bicarbonate in the cell can now leave as NEW.
4. If plasma pH is low, then the kidneys up the reabsorption of filtered bicarbonate and production of “new” bicarbonate. When you gain a bicarbonate, you lose a hydrogen, which raises pH.
 - a. Respiratory and urinary response to acidosis: In acidosis you are using up the available bicarbonate, so the kidneys secrete more hydrogen, so it can bind to stuff other than carbonic acid, creating “new” bicarbonate. The

increased reserve of bicarbonate can bind to the free hydrogens, raising pH.

5. If plasma pH is high, then you will excrete bicarbonate because you don't want it to bind to the free hydrogen. You need the free hydrogen to lower pH. The secretion and excretion of bicarbonate is taken care of by TYPE B intercalated cells of the DCT/CD...the pumps/channels are on opposite membranes than in the Type A cells. The excretion of bicarbonate results in a new reabsorption of hydrogen and pH drops.

Acid-Base Disorders: Alkalosis and Acidosis

Normal arterial pH is 7.4 (7.35-7.45)

Normal arterial PCO₂ is 35-45 mmHg

Normal bicarbonate is 24-28 mEq/L

Respiratory acid-base disorders result from a mismatch between CO₂ production and removal via alveolar ventilation.

- Hypoventilation causes high PCO₂, which leads to high hydrogen and low pH
- Hyperventilation causes low PCO₂, which leads to low hydrogen and high pH

Respiratory problems are indicated by PCO₂ blood gas results.

- Respiratory acidosis is the most common disturbance. Renal compensation will show as high plasma bicarbonate. Caused by hypoventilation
- Respiratory alkalosis shows renal compensation when bicarbonate levels are low. Caused by hyperventilation

Metabolic acid-base disorders result from excess formation (inadequate removal) of organic/fixed acids or excessive gains/losses of bicarbonate in the ECF.

Metabolic problems are caused by anything other than high or low PCO₂

- Metabolic acidosis is the 2nd most common acid-base disturbance. Respiratory compensation shows as low plasma PCO₂. Caused by alcohol consumption, intense exercise, chronic diarrhea, ketosis
- Metabolic alkalosis shows respiratory compensation as high plasma PCO₂. It is caused by vomiting stomach contents, taking too many antacids, and constipation (the body absorbs too much bicarbonate).