Chapter 15

Fluid and Acid-Base Balance

by Dr. Jay M. Templin
Fluid Balance

Water constitutes ~60% of body weight. All cells and tissues are surrounded by an aqueous environment. Most biochemical reactions inside the cell occur in the cytosol.
In the human organism, water is distributed between:

1) The intracellular fluid (~62%)

2) The extracellular fluid that consist of plasma (6.6%) and interstitial fluid (26.4%)
Fluid Balance

Fluid balance is maintained by regulating:

1) **Extracellular fluid volume. Effect on blood pressure**

2) **Osmolarity: measure of solutes dissolved in aqueous medium. Effect on cell volume**
Regulation of Extracellular Fluid Volume is Important for Regulation of Blood Pressure

Reduction in EC volume causes a fall in blood pressure

Short term regulation of blood pressure:
1) baroreceptor reflex, and
2) fluid shift between plasma and intestinal fluid

Long term regulation of blood pressure:
1) Control of Na⁺ ions filtration and reabsorption by the renin-angiotensin-aldosterone system
Baroreceptor Reflex

Parasympathetic stimulation → Heart → ↓ Heart rate → ↓ Cardiac output → ↓ Blood pressure

Sympathetic stimulation → Heart → ↑ Heart rate → ↑ Cardiac output → ↑ Blood pressure

Heart → Arterioles → ↑ Vasoconstriction → ↑ Stroke volume → ↑ Cardiac output → ↑ Blood pressure

Heart → Veins → ↑ Vasoconstriction → ↑ Venous return → ↑ Stroke volume → ↑ Cardiac output → ↑ Blood pressure

Total peripheral resistance → ↑ Blood pressure

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Fluid Shift Between Plasma and Interstitial Fluid

From arteriole

- $P_C$ (37)
- $\pi_p$ (25)

Interstitial fluid

- $P_{IF}$ (1)
- $\pi_{IF}$ (0)

To venule

- $P_C$ (17)
- $\pi_p$ (25)

11 mm Hg (ultrafiltration)

-9 mm Hg (reabsorption)

Initial lymphatic vessel

Blood capillary

(See next slide)
Na⁺ Control

1) Regulation of Na⁺ reabsorption in glomerulus by GFR
2) Regulation of Na⁺ reabsorption by the renin-angiotensin-aldosterone system
Juxtaglomerular Apparatus

Macula dense cells can detect changes in flow rate and release substances that alter capillary blood flow and Na\(^+\) filtration rate.
Regulation of GFR by Baroreceptor Reflex and Sympathetic Activity

Notice that sympathetic nerve activation reduce filtration coefficient (and GFR) by stimulating contraction of podocytes.
Renin-Angiotensin-Aldosterone Regulates Na⁺ Reabsorption

Aldosterone acting on distal/collecting tubules, drives the insertion of new Na⁺ channels and Na⁺/K⁺ ATPases in tubular cells.
Other Functions of the Renin-Angiotensin-Aldosterone System

- **Water conservation**
- **Arteriolar vasoconstriction**
- **Water/fluid intake**
Fluid Balance

Fluid balance is maintained by regulating:

1) Extracellular fluid volume. Effect on blood pressure

2) Osmolarity: measure of solutes dissolved in aqueous medium. Effect on cell volume: hypertonic and hypotonic extracellular fluid
Osmolarity-Induced Changes in Cell Volume

No net movement of water

Water tends to move in causing cell swelling

Water tends to move out of cell. Cell shrinking
Osmolarity can be regulated by:

1) Water intake (thirst)

2) Water output (in kidneys)
Vasopressin Release Controls Water Secretion and Osmolarity

Distal tubular cell

\[ \text{ATP} \]
\[ \text{Cyclic AMP} \]

Increases permeability of luminal membrane to \( \text{H}_2\text{O} \) by inserting new water channels
In the face of water deficit: vasopressin stimulates water movement out of distal/collecting tubules

Filtrate has concentration of 100 mosm/liter as it enters distal and collecting tubules.

Collecting tubule

Loop of Henle

Medulla

Cortex

Distal tubule

Concentration of urine may be up to 1,200 mosm/liter as it leaves collecting tubule.

= passive diffusion of H₂O

= active transport of NaCl

= portions of tubule impermeable to H₂O

* = permeability to H₂O increased by vasopressin
Figure 15.4

↓ ECF volume

↓ Arterial blood pressure

↑ Osmolarity

Hypothalamic osmoreceptors (dominant factor controlling thirst and vasopressin secretion)

↓ +

Hypothalamic neurons

↑ Thirst

↑ Vasopressin

Left atrial volume receptors (important only in large changes in plasma volume/arterial pressure)

↓ +

Arteriolar vasoconstriction

↑ H₂O intake

↑ H₂O permeability of distal and collecting tubules

↑ H₂O reabsorption

↓ Urine output

↓ Plasma osmolarity

↑ Plasma volume
Angiotensin II Regulates Thirst AND Water Intake

- NaCl / ECF volume / Arterial blood pressure
- Liver
- Kidney
- Lungs
- Adrenal cortex
- Kidney
- Renin
- Angiotensin converting enzyme
- Angiotensinogen
- Angiotensin
- Angiotensin II
- Aldosterone
- H₂O conserved
- Na⁺ (and Cl⁻) osmotically hold more H₂O in ECF
- Na⁺ (and Cl⁻) conserved
- Na⁺ reabsorption by kidney tubules (Cl⁻ reabsorption follows passively)
- Vasopressin
- Thirst
- Arteriolar vasoconstriction
- H₂O reabsorption by kidney tubules
- Fluid intake

Figure 14.19
Page 529
Slide 23
Vasopressing and Angiotensin Also Regulate Total Peripheral Resistance

Figure 10.14

Major factors affecting arteriolar radius

- Myogenic responses to stretch
- Heat, cold application (therapeutic use)
- Histamine release (involved with injuries and allergic responses)

Local (intrinsic) control

- Local metabolic changes in $O_2$, $CO_2$, other metabolites

Extrinsic control

- Sympathetic activity (exerts generalized vasoconstrictor effect)
- Vasopressin
- Angiotensin II
- Epinephrine and norepinephrine

Total peripheral resistance

- Arteriolar radius
- Blood viscosity

- Number of red blood cells
- Concentration of plasma proteins

Page 354
Slide 23
Acid-Base Balance
Regulation of free $H^+$ in body fluids

Substances that generate free $H^+$ in solution are called **acids**
Ex: $H_2CO_3$  $HCl$

Substances that accept free $H^+$ in solution are called **bases**
Ex: $HCO_3^-$  $NaOH$

**pH** is a number that allow us to quantify the amount of $H^+$ in solution:

$$pH = -\log \frac{1}{[H^+]}$$
Acids Release $H^+$ in Solution

Strong Acid versus Weak Acid

**Strong acids** undergo complete dissociation in solution.

**Weak acids** undergo incomplete dissociation in solution. At certain point, the amount of dissociated ions and whole molecule reach an equilibrium.

Concentration of each component in the reaction is regulated by the law of mass action.

http://www.chembio.uoguelph.ca/educmat/chm19104/chemtoons/chemtoons4.htm
pH Scale

Since pH is inversely proportional to the $H^+$ concentration, an acidic solution will have a low pH and a basic solution will have a high pH.

Notice that a pH = 7 is considered a neutral pH.

Pure water have a pH = 7.

Physiologically a pH = 7.45 is considered normal and correspond to the pH of blood.
pH Values For Some Substances and Body Fluids

- pH value
- Examples

0
- Gastric juice (stomach)
- Lemon juice
1
- Vinegar, beer, wine, soft drinks
- Sauerkraut
2
- Tomato juice
3
- Black coffee
- Rainwater
4
- Saliva
- Distilled water
- Human blood
5
- Seawater
- Baking soda, stomach antacids
6
- Milk of magnesia
7
- Household ammonia
8
- Oven cleaner
Physiological Changes Induced By H⁺ Fluctuations

Blood pH = 7.45
Acidosis pH < 7.35
Alkalosis pH > 7.45

Death may occur if 6.8 < Blood pH < 8

Decreased H⁺ (alkalosis) causes hyperexcitability of nervous system

Increased H⁺ (acidosis) disrupt enzymatic activity (disruption of hydrogen bonds)
Sources of $H^+$ in Human Body

**Carbonic acid formation**

$(H_2CO_3)$

**Inorganic acids produced during nutrients degradation**

(Phosphoric acid)

**Organic acids produced during cell metabolism**

(Lactic acid, Fatty acids)
How Does The Human Body Avoid Dramatic Changes in \([H^+]:\) Role of Chemical Buffers

Chemical buffers consist of weak acids that minimize pH changes when acids or bases are added.

Effect of law of mass action. Addition of a one component will shift equilibrium and partially compensate for changes in pH.

http://www.chembio.uoguelph.ca/educmat/chm19104/chemtoons/chemtoons5.htm
How Does The Human Body Avoid Dramatic Changes in $[H^+]$

Beside chemical buffers the human body try to regulate $[H^+]$ through regulation of:

- Respiration
- Renal function
Chemical Buffers in Human Body

Carbonic acid-bicarbonate buffer ($\text{H}_2\text{CO}_3/\text{HCO}_3^-$) is the most important system that controls blood pH.

- Protein Buffer
- Hemoglobin buffer
- Phosphate buffer
Carbonic Acid-Bicarbonate Buffer

Use to buffer extracellular fluid
Protein Buffer
Use to buffer intracellular fluid

1. Dissolved CO₂
2. CO₂ + Hb → HbCO₂
3. CO₂ + H₂O (ca) → H₂CO₃ → H⁺ + HCO₃⁻ (chloride shift)

From systemic circulation to pulmonary circulation:

- HbO₂ → O₂ + Hb
- Hb + H⁺ → HbH
- H₂O + CO₂ → H₂CO₃ → H⁺ + HCO₃⁻ (HCO₃⁻ in)

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Hemoglobin Buffer
Use to buffer $H^+$ generated from carbonic acid

$Hb + H^+ \leftrightarrow HHb$
Phosphate Buffer
Use to buffer urine and intracellular fluids

\[ \text{Na}_2\text{HPO}_4 + \text{H}^+ \leftrightarrow \text{NaH}_2\text{PO}_4 + \text{Na}^+ \]
(basic phosphate salt) \leftrightarrow (acid phosphate salt)
How Does The Human Body Avoid Dramatic Changes in $[H^+]$ Regulation of pH by Respiration
Effect of CO$_2$ on ventilation

↑ Arterial P$_{co_2}$

Brain ECF

↑ Brain ECF P$_{co_2}$

$\text{CO}_2 + \text{H}_2\text{O}$
$\text{H}_2\text{CO}_3$
$\downarrow \text{ca}$
$\text{H}^+ + \text{HCO}_3^-$

↑ Brain ECF H$^+$

Relieves

Peripheral chemoreceptors

Weakly +

Medullary respiratory center

↑ Ventilation

↓ Arterial P$_{co_2}$

Central chemoreceptors

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ca = Carbonic anhydrase
How Does The Human Body Avoid Dramatic Changes in \([H^+]\)?

Chemical buffers (can regulate plasma pH instantly)

Respiration (is involved in the minute-to-minute regulation of plasma pH)

Renal function (is involved in the long term regulation of pH-from hours to days)
Regulation of pH by Kidneys

The kidneys regulate body fluid pH by:

1) secreting H⁺
2) reabsorbing HCO₃⁻
Kidneys Regulate Body Fluid pH More Effectively Than the Lungs

(Lungs only regulate CO₂. Beside regulating HCO₃⁻, kidneys regulate H⁺ formed as a result of metabolic activity: lactic & fatty acids formation)
Kidneys Control pH by Adjusting:
1) H⁺ excretion
2) HCO₃⁻ filtration-reabsorption
3) NH₃ secretion
Kidneys Control pH by Adjusting:
1) $H^+$ excretion

Filtered $HPO_4^{2-}$ + $H^+$ → $H^+$ + $HCO_3^-

$HPO_4^{2-}$ → Excreted in urine

$H_2PO_4^-$ → $H_2CO_3$

$H_2CO_3$ + $ca$ → $H_2O + CO_2$

$H_2O + CO_2$ → Cellular metabolism

Peritubular capillary plasma → “New” $HCO_3^-$

$ca$ = Carbonic anhydrase
H⁺ excretion is influenced by:

1) [H⁺] in plasma
2) [CO₂] in plasma

The ability of the kidneys to regulate H⁺ and CO₂ independently allows regulation of free H⁺ produced as a result of respiratory and/or metabolic activity.
Kidneys Control pH by Adjusting:
2) $\text{HCO}_3^-$ filtration-reabsorption

ca = Carbonic anhydrase
Kidneys Control pH by Adjusting: 2) HCO₃⁻ filtration-reabsorption
Difference Between New and Reabsorbed HCO$_3^-$

Notice differential permeability of luminal and basolateral membrane of tubular cells to HCO$_3^-$
$\text{HCO}_3^-$ Excretion Depends on $[\text{H}^+]$
How Do the Kidneys Buffer Secreted H⁺?

1) Phosphate Buffer ($\text{Na}_2\text{HPO}_4$)

2) $\text{NH}_3$ secretion

$$\text{Na}_2\text{HPO}_4 + \text{H}^+ \leftrightarrow \text{NaH}_2\text{PO}_4 + \text{Na}^+$$
Why Is The Kidney Excreting \( \text{Na}_2\text{HPO}_4 \) Continuously? (Chapter 14, Pag. 532)

Carrier saturation limits transport of a substance in tubules- **tubular maximum**

If concentration of substance in tubules goes above **tubular maximum** excretion will take place- renal threshold

Kidneys regulate \( \text{Na}_2\text{HPO}_4 \) plasma levels
How Do the Kidneys Buffer Secreted H⁺?

1) Phosphate Buffer (Na₂HPO₄)
2) NH₃ secretion

\[ \text{NH}_3 + \text{H}^+ \leftrightarrow \text{NH}_4^+ \]

Notice:

- NH₃ is formed and released into the lumen by tubular cells
- NH₄⁺ is impermeable to luminal membranes
Acid-Base Imbalances Arise From:
1) Respiratory Disturbance
2) Metabolic Disturbance

Respiratory disturbance may cause:
- Respiratory acidosis (too much CO₂)
- Respiratory alkalosis (too little CO₂)

Metabolic disturbance may cause:
- Metabolic acidosis (too little HCO₃⁻)
- Metabolic alkalosis (too much HCO₃⁻)
Acid-Base Balance and the Henderson-Hasselbalch Equation

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

\[ \text{pH} = \text{pK} + \log \left( \frac{[\text{HCO}_3^-]}{[\text{CO}_2]} \right) \]

\[ \text{pH} = 7.45 \text{ (normal pH)} \]

\[ \text{pK is a constant, for H}_2\text{CO}_3 = 6.1 \]
\[ \frac{[\text{HCO}_3^-]}{[\text{CO}_2]} = 20/1 \text{ (normal)} \]

\[ [\text{HCO}_3^-] \text{ is regulated by the kidneys} \]
\[ [\text{CO}_2] \text{ is regulated by lungs} \]
## Respiratory Acidosis

<table>
<thead>
<tr>
<th>Respiratory Acidosis</th>
<th>Respiratory Alkalosis</th>
<th>Metabolic Acidosis</th>
<th>Metabolic Alkalosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Too much CO₂, hypoventilation</td>
<td>Too little CO₂, hyperventilation</td>
<td>Fall in HCO₃⁻</td>
<td>Increase in HCO₃⁻</td>
</tr>
<tr>
<td><strong>Cause:</strong> Lung disease  Depression of respiratory center  Respiratory motor dysfunction</td>
<td>Anxiety  Aspirin poisoning  High altitude</td>
<td>Diarrhea  Diabetes mellitus  Strenuous exercise  Real failure</td>
<td>Vomiting  Ingestion of alkaline compounds</td>
</tr>
<tr>
<td><strong>Compensation:</strong>  Chemical buffers  Kidneys (notice that damaged lungs cannot regulate CO₂)</td>
<td>Chemical buffers  Lungs  Kidneys</td>
<td>Chemical buffers  Lungs  Kidneys</td>
<td>Chemical buffers  Lungs  Kidneys</td>
</tr>
</tbody>
</table>
Aspirin Poisoning

http://www.emedicine.com/aaem/topic572.htm#section~signs_and_symptoms
http://www.gpnotebook.co.uk/cache/101056544.htm

High Altitude

Peripheral receptors sense a low $PO_2$ stimulating ventilation without regard for $PCO_2$

http://www.princeton.edu/~oa/safety/altitude.html
Diarrhea

$\text{HCO}_3^-$ from Digestive juices is loss

Diabetes Mellitus

Cells use fatty acids for energy production (transport of glucose into cells is impaired) resulting in the formation of ketonic acids