Acid Base Balance
Renal Regulations
Acid and Base Containing Food:

• To maintain health, the diet should consist of 60% alkaline forming foods and 40% acid forming foods.
• To restore health, the diet should consist of 80% alkaline forming foods and 20% acid forming foods.
• Generally, alkaline forming foods include: most fruits, green vegetables, peas, beans, lentils, spices, herbs, seasonings, seeds and nuts.
• Generally, acid forming foods include: meat, fish, poultry, eggs, grains, and legumes.
Citric Acid And Lactic Acid

Although both citric acid and lactic acid are acids. **BUT**

Citric acid leads to Alkalosis while Lactic acid leads to Acidosis due to metabolism.
Kidney plays a major role in acid-base regulation

1. Excretion of H⁺
2. Reclamation the bicarbonate ions present in the ultra-filtrate
3. Excretion of titrable acid
4. Excretion of ammonia
Acidosis: Clinical state where acids accumulate or bases are lost
Alkaosis: Clinical state where accumulation of base or loss of acids

\[
pH = pK_a + \log_{10} \frac{[\text{Bicarbonate}]}{[\text{Carbonic acid}]}
\]
**ACIDOSIS**

Regulated by Kidney
Metabolic component

\[ \text{pH} = \text{pKa} + \log_{10} \left[ \text{Bicarbonate} \right] \]

**Decreased Bicarbonate**
Decreases the ratio
Decreases pH

**METABOLIC ACIDOSIS**

**Metabolic acidosis** :- Primary alkali (bicarbonate) deficit
**ALKALOSIS**

Regulated by Kidney
Metabolic component

**Increased Bicarbonate**
Increases the ratio
Increases pH

**METABOLIC ALKALOSIS**

\[ pH = pK_a + \log_{10} \frac{[\text{Bicarbonate}]}{[\text{Carbonic acid}]} \]

Metabolic alkalosis :- Primary alkali (bicarbonate) excess
• BUFFER SYSTEM
  - Mainly bicarbonate buffer minimizes change in pH
  - $\text{HCO}_3^-$ concentration is decreased and ratio of $\text{HCO}_3^-/\text{H}_2\text{CO}_3$ less than 20/1

• RESPIRATORY MECHANISM
  - Increases rate and depth of respiration (Kussumauls breathing)
  - Elimination of carbonic acid as $\text{CO}_2$
  - Decrease in p$\text{CO}_2$ and consequently decrease in $\text{H}_2\text{CO}_3$
❖ RENAL compensation set in 2 to 4 days

▪ Increases excretion of acid and preserves the base by increased rate of Na- H exchange

▪ Increases ammonia formation and increased reabsorption of HCO₃⁻
Metabolic Alkalosis

**Causes:**

- **Loss of gastric juice along with H+ ions as in**
  - prolonged vomiting,
  - Nasogastric Suction

- **Therapeutic administration of large dose of alkali**
  - chronic intake of excess antacids
  - Intravenous administration of bicarbonate etc.
RESPIRATORY MECHANISM:
Increase in pH depresses the respiratory center, causes retention of CO$_2$ (pCO$_2$) which in turn increases the H$_2$CO$_3$.

RENAL MECHANISM:
- Kidney decreases H+ excretion
- Decreased reclamation of bicarbonate.
Renal Control of Acid-Base Balance

• The kidneys control acid-base balance by excreting either *acidic* or *basic* urine.
• Excreting acidic urine reduces the amount of acid in extracellular fluid.
• Excreting basic urine removes base from the extracellular fluid.
• The kidneys regulate extracellular fluid $H^+$ concentration through three fundamental mechanisms:

(1) Secretion of $H^+$

(2) Reabsorption of filtered HCO₃

(3) Production of new HCO₃
In acidosis, the kidneys do not excrete HCO₃⁻ into the urine but reabsorb all the filtered HCO₃⁻ and produce new HCO₃⁻ which is added back to the extracellular fluid.

This reduces the extracellular fluid H⁺ concentration back toward normal.
• **In alkalosis** the kidneys fail to reabsorb all the filtered HCO₃ thus increasing the excretion of HCO₃

• **Because HCO₃ normally buffers H⁺ in the extracellular fluid, this loss of HCO₃ is the same as adding H⁺ to the extracellular fluid.**

• **In alkalosis the removal of HCO₃ raises the extracellular fluid H⁺ concentration back towards normal**
Mechanism of Hydrogen ion secretion and Bicarbonate Reabsorption

Renal interstitial fluid

Tubular cells

Tubular lumen

Na⁺ + HCO₃⁻

Na⁺

H⁺

H₂CO₃

H₂CO₃ + H⁺

H₂CO₃

Carbonic anhydrase

H₂O + CO₂

CO₂

CO₂ + H₂O

ATP

K⁺

Na⁺
Primary Active Secretion of H\(^+\) in the Intercalated Cells of Late Distal and Collecting Tubules
Buffering of Secreted Hydrogen Ions by Filtered Phosphate
Excretion of Excess $H^+$ and Generation of New Bicarbonate by the Ammonia Buffer System
Buffering of hydrogen ion secretion by ammonia (NH$_3$) in the collecting tubules
Renal Correction of Acidosis-Increased Excretion of H\(^+\) and Addition of Bicarbonate to the ECF

- Acidosis decreases the ratio of Bicarbonate/Hydrogen ion in Renal Tubular Fluid
- As a result, there is excess H\(^+\) in the renal tubules, causing complete reabsorption of bicarbonate and still leaving additional H\(^+\) available to combine with the urinary buffers (phosphate and ammonia)
- Thus, in acidosis, the kidneys reabsorb all the filtered bicarbonate and contribute new bicarbonate through the formation of ammonium ions and titratable acid
Renal Correction of Alkalosis—Decreased Tubular Secretion of H\(^+\) and Increased Excretion of Bicarbonate

- Alkalosis increases the ratio of bicarbonate/hydrogen ion in renal tubular fluid
- The compensatory response to a primary reduction in PCO\(_2\) in respiratory alkalosis is a reduction in plasma concentration, caused by increased renal excretion of bicarbonate.
• In metabolic alkalosis, there is also an increase in plasma pH and decrease in H⁺ concentration

• The cause of metabolic alkalosis is a rise in the extracellular fluid bicarbonate concentration

• This is partly compensated for by a reduction in the respiration rate, which increases PCO₂ and helps return the extracellular fluid pH toward normal
• In addition, the increase in bicarbonate concentration in the extracellular fluid leads to an increase in the filtered load of bicarbonate which in turn causes an excess of bicarbonate over H\(^+\) secreted in the renal tubular fluid.

• The excess bicarbonate in the tubular fluid fails to be reabsorbed because there is no H\(^+\) to react with, and it is excreted in the urine.

• In metabolic alkalosis, the primary compensations are decreased ventilation, which raises P\(\text{CO}_2\), and increased renal excretion of bicarbonate which helps to compensate for the initial rise in extracellular fluid bicarbonate concentration.
• Acidosis is excessive blood acidity caused by an over abundance of acid in the blood or a loss of bicarbonate from the blood (metabolic acidosis), or by a buildup of carbon dioxide in the blood that results from poor lung function or slow breathing (respiratory acidosis).

Blood acidity increases when people ingest substances that contain or produce acid or when the lungs do not expel enough carbon dioxide.
Diabetic ketoacidosis; Starvation ketoacidosis; Lactic acidosis; Salicylate intoxication

Renal failure; Renal tubular acidosis type II

Severe diarrhoea; Renal tubular acidosis type I; Ureterosigmoidostomy replaced by chloride results in hyperchloremic acidosis
Metabolic Acidosis (Cont.)

- Metabolic balance before onset of acidosis pH 7.4
- Metabolic acidosis pH 7.1
- $\text{HCO}_3^-$ decreases because of excess presence of ketones, chloride, or organic ions
- Body’s compensation is hyperventilation “blow off” CO2
- Kidneys conserve $\text{HCO}_3^-$ and eliminate $\text{H}^+$ ions in acidic urine
- Therapy required to restore metabolic balance
Alkalosis

- Alkalosis is excessive blood alkalinity caused by an over abundance of bicarbonate in the blood or a loss of acid from the blood (metabolic alkalosis), or by a low level of carbon dioxide in the blood that results from rapid or deep breathing (respiratory alkalosis).
Metabolic Alkalosis

• **Metabolic alkalosis** is due to the gain of base or the loss of acid. The primary abnormality is an increased $\text{HCO}_3^-$

**Causes**

• Caused from an increase in bicarbonate in the blood because of ingestion of excess bicarbonate in the form of an antacid (Tums), eating excess fruits (vegetarian diets and fat diets), loss of acid from vomiting, or loss of potassium from diuretics.
Metabolic Alkalosis cont.

-Metabolic balance before onset of alkalosis
- pH = 7.4

  - metabolic alkalosis  pH = 7.7
  - HCO$_3^-$ increases because of loss of chloride ions or excess ingestion of NaHCO$_3$

- Body’s compensation
  - Breathing suppressed to hold CO$_2$
  - Kidneys conserve H$^+$ ions and eliminate HCO$_3^-$ in alkaline urine

- Therapy required to restore metabolic balance
Effects Of pH Change On Cells:

- Acidosis and alkalosis are not diseases but rather are the results of a wide variety of disorders.
- pH changes have dramatic effects on normal cell function:
  1. Changes in excitability of nerve and muscle cells.
  2. Influences enzyme activity.
  3. Influences K+ levels.
RESPONSES TO ACIDOSIS & ALKALOSIS

• Mechanisms protect the body against life-threatening changes in hydrogen ion concentration are
  1) Buffering Systems in Body Fluids
  2) Respiratory Responses
  3) Renal Responses
  4) Intracellular Shifts of Ions
• Buffer system: temporary solution
• ~Respiratory mechanism provide short time regulation
• ~Renal mechanism: permanent solution
Renal Regulation

• Only the kidneys can rid the body of acids generated by cellular metabolism (nonvolatile or fixed acids, (phosphoric, uric, and lactic acids and ketones) and prevent metabolic acidosis).

The kidney in response:

– **To Acidosis**
  – Retains bicarbonate ions and eliminates hydrogen ions

– **To Alkalosis**
  • Eliminates bicarbonate ions and retains hydrogen ions
• To maintain normal pH, the kidneys must perform 2 physiologic functions.

1. Reabsorb all the filtered HCO$_3$  
   A function principally of the proximal tubule.

2. To excrete the daily H$^+$ load:  
   A function of the collecting duct.
Chemical buffers can tie up excess acids or bases, but they cannot eliminate them from the body. The lungs can eliminate carbonic acid by eliminating carbon dioxide. The most important renal mechanisms for regulating acid-base balance are conserving (reabsorbing) or generating new bicarbonate ions and excreting bicarbonate ions.

Losing a bicarbonate ion is the same as gaining a hydrogen ion; reabsorbing a bicarbonate ion is the same as losing a hydrogen ion.
Reabsorption of Bicarbonate:

Plasma bicarbonate is freely filtered at the glomerulus. Carbonic acid formed in filtrate dissociates to release carbon dioxide and water. Carbon dioxide then diffuses into tubule cells, where it acts to trigger further hydrogen ion secretion. For each hydrogen ion secreted, a sodium ion and a bicarbonate ion are reabsorbed by the PCT cells. Secreted hydrogen ions form carbonic acid. Thus, bicarbonate disappears from filtrate at the same rate that it enters the peritubular capillary blood.
Reabsorption of Bicarbonate Ions

1. CO₂ combines with water within the tubule cell, forming H₂CO₃.

2. H₂CO₃ is quickly split, forming H⁺ and bicarbonate ion (HCO₃⁻).

3a. H⁺ is secreted into the filtrate.

3b. For each H⁺ secreted, a HCO₃⁻ enters the peritubular capillary blood either via symport with Na⁺ or via antiport with Cl⁻.

4. Secreted H⁺ combines with HCO₃⁻ in the filtrate, forming carbonic acid (H₂CO₃). HCO₃⁻ disappears from the filtrate at the same rate that HCO₃⁻ (formed within the tubule cell) enters the peritubular capillary blood.

5. The H₂CO₃ formed in the filtrate dissociates to release CO₂ and H₂O.

6. CO₂ diffuses into the tubule cell, where it triggers further H⁺ secretion.

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• Generating New Bicarbonate Ions:
• Two mechanisms carried out by tubule cells generate new bicarbonate ions
• Both involve renal excretion of acid via secretion and excretion of hydrogen ions or ammonium ions (NH4+).
Excretion Of Buffered H Ions:

Alpha intercalated cells of the renal tubules can synthesize new bicarbonate ions while excreting more hydrogen ions.
In response to acidosis hydrogen ions must be counteracted by generating new bicarbonate:

- Kidneys generate bicarbonate ions and add them to the blood.
- An equal amount of hydrogen ions are added to the urine.

**Dietary:** The excreted hydrogen ions must bind to buffers (phosphate buffer system) in the urine and excreted.

- Bicarbonate generated is then moved into the interstitial space via a cotransport system.
- Passively moved into the peritubular capillary blood.
Excretion Of Ammonium Ion:

- Ammonium ions are weak acids.
- This method uses ammonium ions produced by the metabolism of glutamine in PCT cells.
- Each glutamine metabolized produces two ammonium ions and two bicarbonate ions.
- Bicarbonate moves to the blood and ammonium ions are excreted in urine.
NH4+ Excretion

1. PCT cells metabolize glutamine to NH4+ and HCO3−.

2a. This weak acid NH4+ (ammonium) is secreted into the filtrate, taking the place of H+ on a Na+-H+ antiport carrier.

2b. For each NH4+ secreted, a bicarbonate ion (HCO3−) enters the peritubular capillary blood via a symport carrier.

3. The NH4+ is excreted in the urine.
• **Bicarbonate Ion Secretion**
• When the body is in alkalosis, tubular cells secrete bicarbonate ions and reclaim hydrogen ions and acidify the blood
• This mechanism is the opposite of bicarbonate ion reabsorption process
• The daily excretion in urine is 60 mEq/L of H+ excreted as ammonia.
Bicarbonate Ion Secretion

(b) Type B intercalated cells function in alkalosis. HCO₃⁻ and K⁺ are excreted; H⁺ is reabsorbed.

Lumen of collecting duct

Type B intercalated cell

Interstitial space

Blood

H₂O + CO₂

CA

HCO₃⁻

HCO₃⁻ + H⁺

ATP

H⁺

K⁺

[H⁺] low

Excreted in urine
Daily Reabsorption of HCO$_3^-$ By Kidneys:

• 85% HCO-3 reabsorption (H+ Secretion) occurs in PCT (proximal convoluted tubule)

• 10% HCO-3 reabsorption (H+ secretion) occurs in thick ascending LOH

• Approx. 5% reabsorption (H+ secretion) occurs in DCT & CT.

• For each HCO-3 reabsorbed, there must be one H+ ion excreted.
Figure 30–4. Reabsorption of bicarbonate in different segments of the renal tubule. The percentages of the filtered load of bicarbonate absorbed by the various tubular segments are shown as well as the number of milliequivalents reabsorbed per day under normal conditions.
# Excretion of $H^+$

- Occurs in proximal tubule

- CO$_2$ combines with H$_2$O to form H$_2$CO$_3$

- It dissociates to form HCO$_3^-$ and H$^+$

- H$^+$ is secreted in exchange for Na$^+$

- Net production of HCO$_3^-$ and net excretion of H$^+$

- Mechanism serves to increase the alkali reserve

\[
\begin{align*}
\text{Tubular cell} & : \\
HCO_3^- & \leftrightarrow HCO_3^- \\
H^+ & \uparrow H^+ \\
H_2O + CO_2 & \rightarrow H_2CO_3^- \\
Na^+ & \leftarrow Na^+ \\
\end{align*}
\]
$\text{H}_2\text{O} + \text{CO}_2 \rightarrow \text{H}_2\text{CO}_3^-$

$\text{H}_2\text{CO}_3^- \rightarrow \text{HCO}_3^- + \text{H}^+$

$\text{HCO}_3^- + \text{NH}_3 \rightarrow \text{NH}_4^+ + \text{H}_2\text{O}$

$\text{NH}_3$ transport into Tubular Lumen

$\text{NaH}_2\text{PO}_4^-$, $\text{Na}_2\text{HPO}_4^-$

Titrable acid
Anion Gap

In Extracellular fluid
Sum of anions = Sum of cations

- Electrical neutrality

<table>
<thead>
<tr>
<th>Measured cations</th>
<th>Measured anions</th>
<th>Unmeasured cation</th>
<th>Unmeasured anion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium</td>
<td>Chloride</td>
<td>Protein</td>
<td>Chloride</td>
</tr>
<tr>
<td>136 mEq/L</td>
<td>98 mEq/L</td>
<td>15 mEq/L</td>
<td>25 mEq/L</td>
</tr>
<tr>
<td>Potassium</td>
<td>Bicarbonate</td>
<td>Phosphate</td>
<td>Sulfate</td>
</tr>
<tr>
<td>4 mEq/L</td>
<td>25 mEq/L</td>
<td>2 mEq/L</td>
<td>5 mEq/L</td>
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<tr>
<td>Calcium</td>
<td>Organic acids</td>
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<td>1 mEq/L</td>
</tr>
<tr>
<td>4.5 mEq/L</td>
<td>Magnesium</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Magnesium</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.5 mEq/L</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

• Sodium (Na+) and Potassium (K+) together accounts for 95% of the cations

• Chloride and bicarbonate accounts for only 86% of the anions
• Unmeasured anions constitute the anion gap

• Calculated as difference between measured cations and measured anions. Anion Gap = (Na⁺ + K⁺) - (Cl⁻ + HCO⁻³)

• Normal is about 12

  e.g: mEq/L
  
  = (140 + 4) − (102 + 25)
  
  = 17
### Summary

<table>
<thead>
<tr>
<th></th>
<th>pH</th>
<th>H⁺</th>
<th>P(\text{CO}_2)</th>
<th>Bicarbonate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>7.4</td>
<td>40 mEq/L</td>
<td>40 mm Hg</td>
<td>24 mEq/L</td>
</tr>
</tbody>
</table>

- **Respiratory acidosis**: \(\downarrow\) \(\uparrow\) \(\uparrow\uparrow\) \(\uparrow\)
- **Respiratory alkalosis**: \(\uparrow\) \(\downarrow\) \(\downarrow\downarrow\) \(\downarrow\)
- **Metabolic acidosis**: \(\downarrow\) \(\uparrow\) \(\downarrow\) \(\downarrow\downarrow\)
- **Metabolic alkalosis**: \(\uparrow\) \(\downarrow\) \(\uparrow\) \(\uparrow\uparrow\)