Because our bodies are essentially a mass of cells full of chemicals →

**Changes in acid/base (A/B) status affect virtually everything.**

→ Physiologic chemical reactions are **pH dependent**
→ Most chemical reactions occur correctly **only** over a **specific range** of pH.
  - Outside this range, essential activity occurs too slowly or not at all,
  - Cells and tissues are damaged or dysfunctional
  - Secondary to changes that occur at an abnormal pH.
→ For example
  - Acidosis impairs cardiac contractility, affects blood flow to vital organs
  - Alkalosis inhibits the release of oxygen to tissues and may cause neurologic signs, weakness, muscle twitching and more

**FIRST, KNOW THE VOCABULARY:**

- **Acid** – a substance that gives up/donates a proton (hydrogen ion, H⁺)
  - Acidosis – the process that causes an excess of acid
  - Acidemia – pH of extracellular fluid is lower than normal, < 7.4
- **Base** – a substance that accepts/binds a proton (hydrogen ion, H⁺)
  - Alkalosis – the process that causes an excess of base
  - Alkalemia – pH of extracellular fluid is higher than normal, > 7.4

*Patients with alkalosis/acidosis are not necessarily alkalemic/acidotic, respectively; w/ mixed A/B disorders, the pH may be normal even though an A/B abnormality exists.*

- **Buffer** – a compound that can accept OR donate a proton (H⁺);

  Important to minimize pH changes in solutions/tissues;
  Buffers are usually weak acids with their corresponding salts.

  When a strong acid is added to a solution, its protons are donated to/accepted by the weak acid, forming a salt, and limiting the change in pH.
Buffers (continued)

- **TWO categories of buffers**

  - **Bicarbonate (HCO₃⁻)**
    - Major extracellular buffer
    - Used most often in A/B evaluation
  
  - **Everything else** (non-bicarbonate buffers)
    - Intracellular and extracellular effects
    - Proteins – albumin, hemoglobin, etc
    - Phosphates - organic/inorganic

- **All buffers shift in same direction as pH**
- **pH and [H+] inversely related**
  - Measurement of only one buffer needed
  - …to evaluate metabolic side of A/B

- **[H+]**
  - Direct H+ measurement difficult* (nanoequivalents/L)
  - therefore, we use **pH**
  - [H+] constantly produced - metabolism of carbohydrates, fats, proteins, phospholipids
  - **pH and [H+] inversely related**
    - Affects activity of proteins, cell membranes, enzymes
    - Most commonly measure H+ in the blood
    - Body fluids, effusions, tissues can also be used
    - Range = 16 - 160 mEq/L; at 7.4 = 40 Eq/L (4 X 10⁻⁸ Eq/L)

- **pH = an approximate measure of the concentration of hydrogen ion [H+]**
  - **pH = the negative log (base 10) of [H+]**
  - **pH and [H+] inversely related**
  - **3 Mechanisms**
    - Higher [H+] = lower pH, vice versa
    - **Exponential relationship**
  
- Reflects net activity of all chemical processes
- Reveals balance between acids and bases
- **Normal pH ~ 7.4** for most all animal species
- Compensatory mechanisms to maintain 7.4

---

**Common acids/bases on the pH scale**

*Image courtesy Slower*

*Note: electrolytes are measured in milliequivalents/L, a MILLION times greater than H+*
Zuku Review FlashNotes™

Acid/Base “Basics”

- **Compensation**
  - Response to maintain homeostasis keep a pH ~ 7.4

- **3 Mechanisms**

  - **Physiochemical buffering** - develops immediately
    - Balance of cations/anions always maintained
    - Occurs intra- and extra-cellularly
    - Bicarbonate ion - HCO$_3^-$
    - Proteins, especially hemoglobin, albumin
    - Phosphates

  - **Respiratory compensation** – elimination or retention of CO$_2$
    - Seen w/in minutes, complete - minutes to hours
    - CO$_2$ *functions* as an acid
      - Carbonic acid (H$_2$CO$_3$) formed when combined with water.
      - Called a ‘volatile’ acid because it is removed via the lungs.

  - **Metabolic compensation**
    - Elimination or retention of H$^+/\text{HCO}_3^-$ by the kidney
    - Begins within hours, 2-5 days to complete

- **Anion Gap (AG)** – A calculation/estimate of the difference between cations/anions in serum/plasma

  - Used to evaluate A/B balance, to categorize/identify metabolic acidoses.
  - Uses the amount of cations (+ charged ions) and anions (- charged ions) present
  - Based on electroneutrality ➔ total cations must = anions, but a “gap” exists between the concentration of commonly measured +/- ions- only measured ions used in the calculation
  - “Unmeasured ions” = exist in amounts too small to affect the AG (Ca, Mg), or they are not commonly measured (sulfates, ketones, etc)
- **Anion Gap (AG)** – continued

<table>
<thead>
<tr>
<th>Measured cations</th>
<th>“Unmeasured” cations</th>
<th>Measured anions</th>
<th>“Unmeasured” anions (LOTS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(MC)</td>
<td>(UC)</td>
<td>(MA)</td>
<td>(UA)</td>
</tr>
<tr>
<td>Sodium (Na⁺)</td>
<td>Gamma globulins</td>
<td>Bicarbonate</td>
<td>Albumin, other plasma proteins</td>
</tr>
<tr>
<td>Potassium (K⁺)</td>
<td>Ionized Calcium (Ca²⁺)</td>
<td>Chloride (Cl⁻)</td>
<td>Organic acids</td>
</tr>
<tr>
<td></td>
<td>Ionized Magnesium (Mg²⁺)</td>
<td></td>
<td>Lactate, sulfate, ketones, phosphates</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Toxins</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Ethylene glycol, salicylate, methanol, etc</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Some drugs</td>
</tr>
</tbody>
</table>

**Note:** Many formerly “Unmeasured Cations” & “Unmeasured Anions” are measurable these days, eg. Dogs have 157 mEq/L each of cations & anions, Cats have 167, see DiBartola, p 243

**What (the heck) is anion gap anyway?**

There is always a “gap” between measured ions, because sodium, [Na] is greater all other measured ions. This “gap” will be balanced by the unmeasured components.

When there are changes in unmeasured ions, the anion gap will ↑ or ↓ accordingly.

\[
(MC + UC) = (MA + UA), \text{ rearrange to } (MC - MA) = (UA - UC) \text{ add components,}
\]

\[
(Na^+ + K^+ + UC^+) = (Cl^- + HCO_3^- + UA^-) = (Na^+ + K^+) - (Cl^- + HCO_3^-) = (UA - UC)
\]

The difference (gap) between the groups = AG

\[
(Na^+ + K^+) - (Cl^- + HCO_3^-) = (UA - UC) = \text{ Anion Gap}
\]

Anion gap is the difference between components of the measured ions,

**But it also reflects the difference between the unmeasured cations/anions.**

A high anion gap is the most common change, usually due to ↑ UA; A high AG is usually a metabolic acidosis. The chart above shows that there are many unmeasured anions.
**Traditional approach to A/B status**  
Uses the **Henderson-Hasselbalch equation** to determine the metabolic component of A/B status.

Derived using the law of mass action and the equilibrium relationship between carbonic acid (H$_2$CO$_3$) and bicarbonate (HCO$_3^-$) as follows:

\[
\text{pH} = \text{pKa} + \log \left( \frac{[\text{Base}]}{[\text{Acid}]} \right), \quad \text{or} \quad \text{pH} = \text{pKa} + \log \left( \frac{[\text{HCO}_3^-]}{\text{H}_2\text{CO}_3} \right) \\
\text{since } \text{H}_2\text{CO}_3 = 0.03 \times \text{pCO}_2 \text{ and the pKa is 6.1,} \\
\text{pH} = 6.1 + \log \left( \frac{[\text{HCO}_3^-]}{(0.03 \times \text{pCO}_2)} \right)
\]

Plug in measured pH and carbon dioxide, solve for bicarbonate.

pH is relative to the ratio of HCO$_3^-$ (base) to CO$_2$ (acid); HCO$_3$/CO$_2$ is normally approximately 20:1.

**Non-traditional approach to A/B status** – also called “**strong ion theory**”

- **A “physiochemical”** concept of A/B balance derived from complicated formulae that determine variables affecting [H$^+$].
- **Basic concept:** A/B status determined by conc. of CO2, proteins & anion/cation balance.
- **Based on 3 physical laws**
  - Electroneutrality always maintained
  - Equilibrium equations of incompletely dissociated solutes are satisfied
  - Conservation of mass
- **3 Independent** variables - can be affected by external sources
  - 1. pCO2
  - 2. $A_{TOT}$ - total concentration of weak acids – proteins and phosphates
  - 3. ‘**Strong ion’ difference** (SID) – balance between strong cations/anions
    - ‘Strong ions’ are almost completely dissociated in body fluids at normal pH
    - Cations - Na, K, Ca, Mg
    - Na most important - high concentration affects SID
    - Anions – Cl and the Unmeasured anions (UA) – lactate, ketones, sulfates, etc
    - NOT HCO$_3^-$
    - Similar to pH: ↑SID = alkalosis, ↓SID = acidosis
    - SID – basic calculation is Na-Cl (but there is a lot more to it than this!)

- **1 Dependent** variable - altered by internal changes only = Bicarbonate
  - Strong ion theory identifies pH changes caused by hypo/hyperproteinemia – via $A_{TOT}$
  - Some believe strong ion theory is a more correct approach to evaluation
  - More calculations required than w/ traditional method– simplified versions have been derived
  - Requires different equations for the different species – see references

---

Strong ions – complete dissociation at body pH; normal and abnormal  
Weak ions – incomplete dissociation at body pH; these are buffers  
SID is similar to AG
Partial pressure – the pressure exerted by one compound contained in a mixture; Usually refers to gases; denoted by the lowercase letter “p” before the name; Units = millimeters of mercury (mmHg) in the United States; kPa, kilopascals, in Europe; may also see a percent (%)

- pCO₂ – partial pressure of carbon dioxide
- pO₂ - partial pressure of oxygen
- CO₂ and O₂ are the main ‘blood gases‘; nitrogen & other gases also present

Carbon dioxide (CO₂ mmHg) –
- End product of metabolism
- The ‘respiratory’ component of A/B balance in both approaches to A/B
- A volatile acid - exhaled by the lungs
  - receptors in brain (respiratory center) and great vessels
  - pH changes stimulate/suppress ventilation
- Can be converted to bicarbonate. See equilibrium equation below.

Bicarbonate ion (HCO₃⁻, mEq/L)
- The metabolic component of A/B balance
- The major chemical buffer in the body
- Regulated by the kidneys, indirectly by the lungs
- Calculated via the Henderson-Hasselbalch equation
- See Traditional Approach to A/B above.

Bicarbonate exists in equilibrium with carbonic acid and carbon dioxide:

\[
\text{HCO}_3^- + \text{H}^+ \rightleftharpoons \text{H}_2\text{CO}_3 \rightleftharpoons \text{H}_2\text{O} + \uparrow\text{CO}_2
\]  
(carbonic acid)

Total carbon dioxide (TCO₂, mEq/L)
- A calculated measure of the metabolic component
- \(\text{TCO}_2 = [\text{HCO}_3^-] + \text{the CO}_2 \text{ dissolved in plasma}\ \times \ p\text{CO}_2\)
- Commonly measured by routine chemistry analyzers on serum or plasma.
- pCO₂ rarely contributes more than 1-2 mmHg to TCO2
- Used in place of HCO₃⁻ when necessary

Base excess (BE, mEq/L)
- = the net amount of base present;
- “Base deficit” (BD) = net amount of acid present
- Most clinicians use ‘negative BE” (-BE) when an excess of acid is present
- Negative base excess = amount of additional acid or base needed to bring pH back to 7.4
Normal Values:

- **Dogs and cats tend toward acidemia**
  - See postprandial alkalemia
  - as $\text{HCO}_3^-$ to balance gastric acid secretion

- **Herbivores tend toward alkalosis** – diet related
  - Acidemia in cows prior to parturition
  - Dietary changes alter the anion/cation balance
  - Promotes calcium mobilization to prevent milk fever

<table>
<thead>
<tr>
<th></th>
<th>Dog</th>
<th>Cat</th>
<th>Horse</th>
<th>Cow</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.31-7.42</td>
<td>7.24-7.40</td>
<td>7.32-7.44</td>
<td>7.35-7.50</td>
</tr>
<tr>
<td>$\text{pCO}_2$ mmHg</td>
<td>29-42</td>
<td>29-42</td>
<td>36-46</td>
<td>35-44</td>
</tr>
<tr>
<td>$\text{pO}_2$ mmHg</td>
<td>85-95</td>
<td>85-95</td>
<td>94</td>
<td>92</td>
</tr>
<tr>
<td>$\text{HCO}_3^-$ mEq/L</td>
<td>17-24</td>
<td>17-24</td>
<td>24-30</td>
<td>20-30</td>
</tr>
<tr>
<td>$\text{TCO}_2$ mEq/L</td>
<td>14-26</td>
<td>13-21</td>
<td>22-33</td>
<td>22-34</td>
</tr>
<tr>
<td>BE mEq/L</td>
<td>-2 to +2</td>
<td>-2 to +2</td>
<td>0 to +5</td>
<td>0 to +5</td>
</tr>
</tbody>
</table>

*These values are taken from DiBartola and Latimer references; Be sure to use ranges from lab where tests are performed*

Images and Links worth a look:

- **The pH Scale and $\text{H}^+$** (Very) Basic chemistry of acid base
- **Cornell University** Clinical Chemistry basics, Acid/base, Mixed acid base, Bicarbonate and Anion Gap
- **University of Pennsylvania** Clin Path case studies
- **Tufts University** “Strong Ion” theory of Acid Base

**References:** Unless otherwise noted, images are courtesy of Dr. JG Adams

