Zuku Review FlashNotes™

Acid/Base "Basics"

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

Changes in acid/base (A/B) status affect virtually <u>everything</u>.

→ Physiologic chemical reactions are **pH dependent**

→ Most chemical reactions occur correctly *only* over a **<u>specific range</u>** 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

Acids – low pH - reds;
Bases – high pH - blues;
Normal pH – green;

Image adapted from BordercollieX

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

Use of square brackets ' [X] ' means 'the concentration of ' X

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.

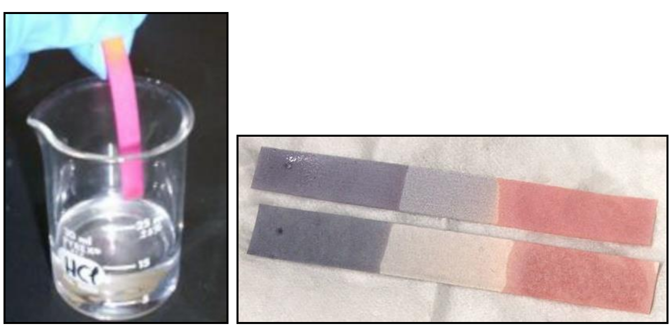
- **Buffer – a compound that can accept OR donate a proton (H^+)**;

  Important to minimize pH changes in solutions/tissues;

  Buffers are usually weak acids with their corresponding salts.

	reversibly			
HA	⇆	**H^+**	**+**	**A^-**
	dissociates into	an acid	and	a base

  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.



Acid turns litmus paper pink/red; base stays or turns blue;

Images courtesy Walkerma, and Chemicalinterest

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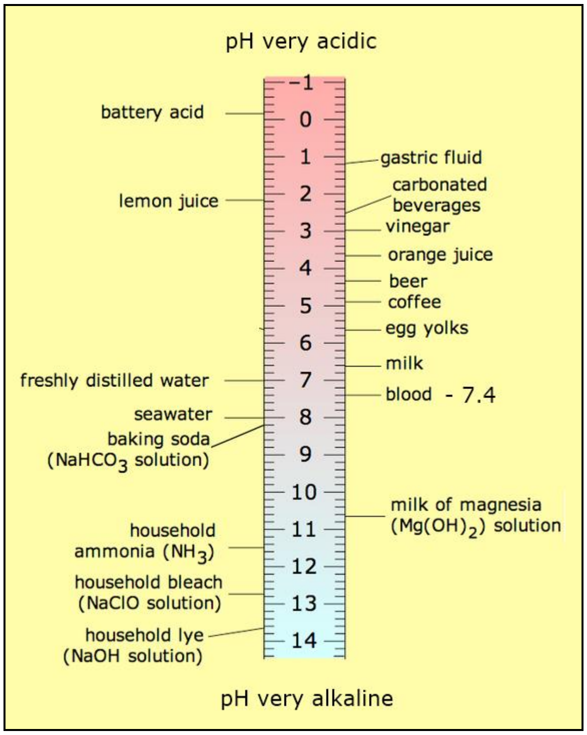
Acid/Base “Basics”

- **Buffers** (continued)
  - TWO categories of buffers
    - **Bicarbonate (HCO_3^-)**
      - 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 (4×10^{-8} Eq/L)



Common acids/bases on the pH scale

Image courtesy [Slower]

Note: electrolytes are measured in milliequivalents/L, a MILLION times greater than H+

- **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

pH	[H+]
0	10000000
1	1000000
2	100000
3	10000
4	1000
5	100
6	10
7	1
8	0.1
9	0.01
10	0.001
11	0.0001
12	0.00001
13	0.000001
14	0.0000001

Acid/Base "Basics"

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

Immediate

- **Physiochemical buffering** - develops immediately
  - Balance of cations/anions always maintained
  - Occurs intra- and extra-cellularly
  - Bicarbonate ion - HCO_3
  - Proteins, especially hemoglobin, albumin
  - Phosphates

Very Fast

- **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_2CO_3) formed when combined with water.
    - Called a 'volatile' acid because it is removed via the lungs.

Slower

- **Metabolic compensation**
  - Elimination or retention of H^+/HCO_3^- by the kidney
  - Begins within hours, 2-5 days to complete

$$\mathbf{HCO_3^- + H^+ \leftrightarrows H_2CO_3} \text{ **(carbonic acid)**}$$

$$\mathbf{H_2CO_3 \leftrightarrows H_2O + \uparrow CO_2}$$

- **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)

Acid/Base "Basics"

- **Anion Gap (AG) –** continued

Measured cations	**"Unmeasured" cations**	**Measured anions**	**"Unmeasured" anions (LOTS)**
(MC)	(UC)	(MA)	(UA)
• Sodium (Na^+)	Gamma globulins	• Bicarbonate	• Albumin, other plasma proteins
• Potassium (K^+)	Ionized Calcium (Ca^{2+})	• Chloride (Cl^-)	• Organic acids
	Ionized Magnesium (Mg^{2+})		Lactate, sulfate, ketones, phosphates
			• Toxins
	UC only rarely affect AG		Ethylene glycol, salicylate, methanol, etc
			• Some drugs
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 **un**measured components.
When there are changes in **un**measured ions, the anion gap will $\uparrow$ or $\downarrow$ accordingly.

(MC + UC) = (MA + UA), rearrange to (MC – MA) = (UA – UC) add components,

$$(Na^+ + K^+ + UC^+) = (Cl^- + HCO_3^- + UA^-) = (Na^+ + K^+) - (Cl^- + HCO_3^-) = (UA - UC)$$

The difference (gap) between the groups = AG

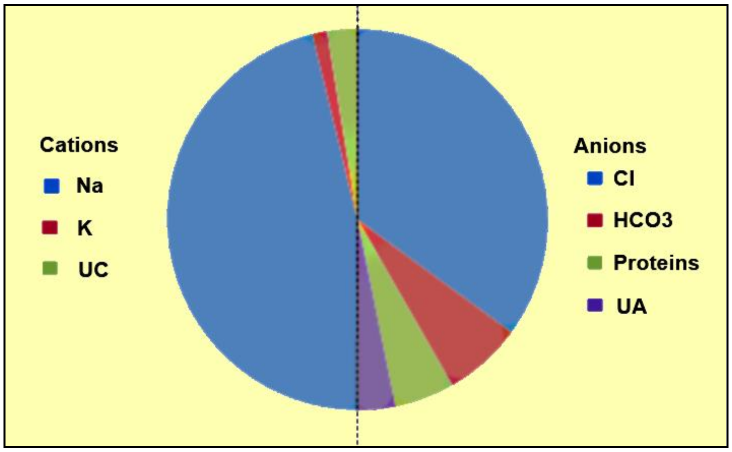
$$\mathbf{(Na^+ + K^+) - (Cl^- + HCO_3^-) = (UA - UC) = \text{Anion Gap}}$$

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

BUT it also reflects the difference between the **un**measured cations/anions.

A high anion gap is the most common change, usually due to $\uparrow$ UA; A high AG is usually a metabolic acidosis. The chart above shows that there are many **un**measured anions.

Increased AG	**Decreased AG**
$\uparrow$ Organic acids (UA)	
Alkalemia	Acidemia
• $\downarrow$ H^+ bound to protein	• $\uparrow$ H^+ bound to protein
Dehydration	Hemodilution
Hyperalbuminemia	Hypoalbuminemia
Some drugs – eg Na salts	$\uparrow$ UC
• Na penicillin	• Hyperglobulinemia
False $\uparrow$ - loss of HCO_3	▪ Plasma cell myeloma
• Delayed analysis	▪ Other neoplasia
• Overdilution of sample	▪ Chronic infection
	• Hypercalcemia



Acid/Base "Basics"

- **<u>Traditional</u> 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_2CO_3) and bicarbonate (HCO_3) as follows:

  pH = pKa + log [Base]/[Acid], or pH = pKa + log $[HCO_3^-]/H_2CO_3$;

  since H_2CO_3 = 0.03 X pCO_2 and the pKa is 6.1,

  pH = 6.1 + log $[HCO_3]/(0.03 \times pCO_2)$

  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.

- **<u>Non-traditional</u> approach to A/B status –** also called **"strong ion theory"**
  - A "physiochemical" concept of A/B balance derived from complicated forumulae 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 completed 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

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- **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 (%)
    - **pCO_2** – partial pressure of carbon dioxide
    - **pO_2 -** partial pressure of oxygen
    - **CO_2** and **O_2** are the main ‘blood gases’; nitrogen & other gases also preseny

- **Carbon dioxide** (**CO_2** 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** (**HCO_3** , 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:

$$\mathbf{HCO_3^- + H^+ \leftrightarrows \underbrace{H_2CO_3}_{\text{(carbonic acid)}} \leftrightarrows H_2O + \uparrow CO_2}$$

KNOW THIS EQUATION !

- **Total carbon dioxide** (**TCO_2** , mEq/L)
    - A calculated measure of the *metabolic* component
    - $TCO_2 = [HCO_3^-]$ + the CO_2 dissolved in plasma ($0.03 \times pCO_2$)
    - Commonly measured by routine chemistry analyzers on serum or plasma.
    - pCO_2 rarely contributes more than 1-2 mmHg to TCO2
    - Used in place of HCO_3 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

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Normal Values:

- Dogs and cats tend toward **acidemia**
  - See postprandial alkalemia
  - as HCO_3 ↑s 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

	Dog	Cat	Horse	Cow
pH	7.31-7.42	7.24-7.40	7.32-7.44	7.35-7.50
pCO_2 mmHg	29-42	29-42	36-46	35-44
pO_2 mmHg	85-95	85-95	94	92
HCO_3 mEq/L	17-24	17-24	24-30	20-30
TCO_2 mEq/L	14-26	13-21	22-33	22-34
BE mEq/L	-2 to +2	-2 to +2	0 to +5	0 to +5

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

Brachycephalic breeds (even healthy patients) may have chronic respiratory acidosis.

Anatomy limits ventilation; should see a compensatory metabolic alkalosis

Some clinical signs are specific to pH, but most are non-specific (tachypnea w/acidemia) -

usually the signs of underlying dz predominate

Images and Links worth a look:

The pH Scale and 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

DiBartola SP, ed. 2012. Fluid, Electrolyte, and Acid Base Disorders in SA Practice, 4th ed. Elsevier, St Louis, MO. Chapters 9 -13, pp. 231-329.

Latimer KS. 2011. Duncan and Prasse's Veterinary Laboratory Medicine Clinical Pathology, 5th ed., John S. Wiley & Sons, West Sussex, UK. Chapter 5, pp. 145-171.

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