ACID-BASE PHYSIOLOGY & ANESTHESIA

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Introductions

- ***Abnormal acid-base changes are a result of a disease process. They are not the disease.***
- Abnormal acid base disorder predicts the outcome of the case but often is not a direct cause of the mortality, but rather is an epiphenomenon.
- Disorders of acid base balance result from disorders of primary regulating organs (lungs or kidneys etc), exogenous drugs or fluids that change the ability to maintain normal acid base balance.
- An acid is a hydrogen ion or proton donor, and a substance which causes a rise in H^+ concentration on being added to water.
- A base is a hydrogen ion or proton acceptor, and a substance which causes a rise in OH^- concentration when added to water.
- Strength of acids or bases refers to their ability to donate and accept H^+ ions respectively.
- When hydrochloric acid is dissolved in water all or almost all of the H in the acid is released as H^+.
- When lactic acid is dissolved in water a considerable quantity remains as lactic acid molecules.
- Lactic acid is, therefore, said to be a weaker acid than hydrochloric acid, but the lactate ion possess a stronger conjugate base than hydrochlorate.
- The stronger the acid, the weaker its conjugate base, that is, the less ability of the base to accept H^+, therefore termed, 'strong acid'
- Carbonic acid ionizes less than lactic acid and so is weaker than lactic acid, therefore termed, 'weak acid'.
- Thus lactic acid might be referred to as weak when considered in relation to hydrochloric acid but strong when compared to carbonic acid.
- Weak and strong in relation to acids and bases are thus relative terms.
- A buffer solution is one in which the pH changes less when an acid or base is added than would have occurred in a non-buffer solution.
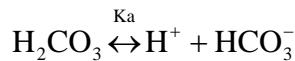
Importance of acid-base balance

- The hydrogen ion (H^+) concentration must be precisely maintained within a narrow physiological range
- Hydrogen ion concentration is most commonly expressed as pH (= negative logarithm of the H^+ concentration)
- Small changes of pH from normal can produce marked changes in enzyme activity & chemical reactions within the body
- Acidosis - CNS depression, coma (if severely acidotic, i.e., pH <7.0)
- Alkalosis - CNS excitability, tetany, seizures

H^+ (nmol/l)	pH
100	7
80	7.1
63	7.2
50	7.3
44	7.36
40	7.4
36	7.44
32	7.5
25	7.6
20	7.7

- The table on the right doesn't allow you to mentally calculate every pH and $[H^+]$ value but the 4 basic pairs which are useful and easy to memorize are:
  - pH 7.4 is 40 nM
  - pH 7.1 is 80 nM
  - *pH 7.36 is 44 nM*
  - *pH 7.44 is 36 nM*
  - The last two values above are the normal range of pH values which is easy to remember because the relationship between the $[H^+]$ and the decimal part of the pH (ie the normal range of 7.*36* to 7.*44* is a $[H^+]$ range of *44* to *36* nmol.
  - Now you can work out that a pH of 7.06 has a $[H^+]$ value of 88nm as this is double that at 7.36 (i.e. 44nM) - and so on.
- Normal pH:
  - arterial blood: 7.35 - 7.45
  - venous blood, interstitial fluid: 7.35
  - intracellular: 6.0-7.4 (average 7.0)

Henderson-Hesselbach Equation

- The pH resulting from the solution of CO_2 in blood and the consequent dissociation of carbonic acid is given by the Henderson-Hesslebach Equation.

$$H_2CO_3 \overset{Ka}{\leftrightarrow} H^+ + HCO_3^-$$

- The law of mass conservation gives the dissociation constant of carbonic acid as K_a

$$K_a \propto \frac{(H^+) \times (HCO_3^-)}{H_2CO_3}$$

- Now, since the concentration of carbonic acid is proportional to the concentration to the concentration of dissolved carbon dioxide, we can change to

$$K_a = \frac{(H^+) \times (HCO_3^-)}{CO_2}$$

- Take log,

$$\log K_a = \log(H^+) + \log\left(\frac{HCO_3^-}{CO_2}\right)$$

- Whence,

$$-\log(H^+) = -\log(K_a) + \log\left(\frac{HCO_3^-}{CO_2}\right)$$

- Since pH is negative logarithm of H^+,

$$pH = pK_a + \log\left(\frac{HCO_3^-}{CO_2}\right)$$

- According to Henry's law, replace CO_2 with PCO_2 x 0.03

$$pH = pK_a + \log\left(\frac{HCO_3^-}{PCO_2 \times 0.03}\right)$$

- The value of pK_a is 6.1, and the normal HCO_3^- and PCO_2 are 24 mmol/L and 40 mmHg, respectively. Substitute these,

$$pH = 6.1 + \log\left(\frac{24}{40 \times 0.03}\right)$$
$$= 6.1 + \log 20$$
$$= 6.1 + 1.3$$
$$= 7.4$$

Regulation of pH

- Buffer systems - very rapid (seconds), incomplete
- Respiratory responses - rapid (minutes), incomplete
- Renal responses - slow (hours to days), complete

Buffer Systems

- Bicarbonate, phosphate and protein buffering systems are the three major buffering systems.
- The bicarbonate system is primarily extracellular and the fastest to respond to pH imbalance, but it has less total capacity than intracellular system.
- Intracellular buffering occurs through the phosphate and protein systems.
- Intracellular buffering has a very large capacity, about 75 % of the body chemical buffering.

Bicarbonate buffer system
- Primary extracellular buffer system (>50% of extracellular buffering)
- Accurate assessment - readily calculated from PCO_2 and pH using available blood gas machines
- Consists of carbonic acid (weak acid) and bicarbonate
- Carbonic acid dissociates into carbon dioxide and water
$$\textbf{H}_2\textbf{O} + \textbf{CO}_2 \leftrightarrow \textbf{H}_2\textbf{CO}_3 \leftrightarrow \textbf{H}^+ + \textbf{HCO}_3^-$$
- CO_2 regulated by the lungs - rapidly
- HCO_3^- is regulated by the kidneys - slowly
- Not powerful
- pKa = 6.1

Protein buffer system
- Most powerful
- 75 % of all intracellular buffering
- Hemoglobin
  - important extracellular buffer due to large concentration of hemoglobin in blood
  - buffering capacity varies with oxygenation
  - reduced hemoglobin is a weaker acid than oxyhemoglobin
  - dissociation of oxyhemoglobin results in more base available to combine w/ H^+
- Plasma protein
  - acid buffer

- o important intracellular buffer system
- Phosphate buffer system
  - o $H_2PO_4^-$ and HPO_4^{2-}
  - o important renal buffering system
  - o extracellular concentration, 1/12 that of bicarbonate
  - o pKa = 6.8
  - o phosphate is concentrated in the renal tubules

Respiratory Responses

- Occurs within minutes of alteration in pH due to stimulation/depression of respiratory centers in the CNS
- H^+ acts directly on respiratory center in Medulla Oblongata
- Alveolar ventilation increases/decreases in response to changes in CO2
- Alveolar ventilation is inversely proportional to P_aCO_2
  - o 2 x ventilation: pH 7.4 to 7.63
  - o 1/4 ventilation: pH 7.4 to 7.0
- Incomplete response because as the change in alveolar ventilation brings pH back towards normal, the stimulus responsible for the change in ventilation decreases

Renal Responses

- The kidneys regulate pH by either acidification or alkalinization of the urine
- Complex response that occurs primarily in the proximal renal tubules
- With acidosis, rate of H^+ secretion exceeds HCO_3^- filtration
- With alkalosis, rate of HCO_3^- filtration exceeds H^+ secretion
- Occurs over hours/days, and is capable of nearly complete restoration of acid/base balance

Anion Gap (AG)

- A useful tool to assess mixed acid-base disorders
- Traditionally it has been used to detect lactic acidosis, ketoacidosis and the presence of certain poisons (ethylene glycol etc.)
- The derivation of the anion gap is usually comes from the relationship of preservation of charges of anions and cations.
- The plasma is actually electrically neutral, and total cations equal total anions.
- $[Na^+] + [K^+] + [UC^+] = [Cl^-] + [HCO_3^-] + [UA^-]$ (as body maintains electroneutrality)
- Rearranged, $[UA^-] - [UC^+] = ([Na^+] + [K^+]) - ([Cl^-] + [HCO_3^-])$
- Since, in clinical sense, $[UC^+]$ are negligible the anion gap is basically $[UA^-]$, unmeasured anions
- AG= $[UA^-] = ([Na^+] + [K^+]) - ([Cl^-] + [HCO_3^-])$
- $[UA^-]$ consist of $[protein^-]$, phosphates, sulfates, beta hydroxybutyrate, acetoacetate, and citrate
- Therefore, from the above equation, the gap is calculated difference between the sum of serum sodium and potassium and the sum of serum chloride and bicarbonate.
- Anion gas is usually measured in venous blood with HCO_3^- estimated as total CO_2.
- Usually an increase in AG implies accumulation of organic acids in the body, and suggest the presence of lactic acidosis, ketosis, sepsis, poisoning or renal failure.
- Normal is approximately 14, and ranges from 12– 16 mEq/L

- Commonly, the AG remains normal in an acidosis that is due to simple HCO_3^- loss (as in diarrhea and certain renal diseases) because, as a general principle, [Cl^-] increases to meet the drop in HCO_3^- anions, thereby maintaining anionic balance.
- When an acid load is present, HCO_3^- titrates acid and anion gap increases, creating a condition known as 'anion gap metabolic acidosis'.

Major Acid Base Disorders and Compensatory Mechanism

Primary Disorder	Primary Disturbance	Primary Compensation
Respiratory Acidosis	$\uparrow PCO_2$	$\uparrow HCO_3^-$
Respiratory Alkalosis	$\downarrow PCO_2$	$\downarrow HCO_3^-$
Metabolic Acidosis	$\downarrow HCO_3^-$	$\downarrow PCO_2$ (hyperventilation)
Metabolic Alkalosis	$\uparrow HCO_3^-$	$\uparrow PCO_2$ (hypoventilation)

- The primary compensation (acute compensation) is generally achieved most rapidly through respiratory control of CO_2.
- Ultimately the renal system excretes acid or bicarbonate (chronic compensation) to reach the final response to the disturbance
- Mixed disorders are common

Blood Gas Evaluation

What do we get from a blood gas machine?

- pH - measured
- PCO_2 - measured
- PO_2 - measured
- HCO_3^- - calculated (via Henderson Hesselbalch equation)
- Base excess (deficit) - calculated
- Hemoglobin oxygen saturation - calculated
- Gases (carbon dioxide & oxygen) are reported as partial pressures, commonly in unit of mmHg (US), or KPa (International); 1 KPa = 7.5 mmHg (torr)

Blood Gas Sampling

- Arterial vs. venous
- Venous samples are adequate for metabolic function if the respiratory function is near normal
- Venous samples are of limited value in evaluating respiratory components

Preservation of Sample

- Heparinize syringe (5 units of heparin/l ml of blood)
- Eliminate air bubbles from the sample
- Cap the needle with rubber stopper
- If greater than 10 minute delay to the machine, place sample in an ice water bath. Will preserve samples for up to 10 hours

Sites for Arterial Samples

- Dog: dorso pedal, femoral, anterior tibial, lingual
- Cat: femoral, dorso pedal
- Horse: facial, mandibular, lateral metatarsal, posterior auricular, carotid
- Cow: coccygeal, posterior auricular
- Pig: coccygeal, posterior auricular

Normal Values

	Arterial	Venous
pH	7.35-7.45	7.35
PCO_2	35-45 mmHg	45 mmHg
PO_2	90-100 mmHg	40 mmHg
HCO_3^-	24 mEq/L	24 mEq/L

Interpretation

1st step:	What is the pH?	<7.35	acidemia
		>7.45	alkalemia
2nd step:	What is the P_aCO_2?	>45	respiratory acidosis
		<35	respiratory alkalosis
3rd step:	What is the HCO_3^-?	<24*	metabolic acidosis
		>25*	metabolic alkalosis

*If PaCO2 is normal

- When the pH is low (i.e., more acidotic)
  - A low (or normal) PCO_2 points to a primary metabolic acidosis
  - A high PCO_2 points to a primary respiratory acidosis
- When the pH is high (i.e., more alkalotic)
  - A high (or normal) PCO_2 points to a primary metabolic alkalosis
  - A low PCO_2 points to a primary respiratory alkalosis
- Simply stated,
  - If pH and PCO_2 change in the same direction, the primary disorder is metabolic
  - If pH and PCO_2 change in the opposite direction, the primary disorder is respiratory

Alterations in the HCO_3^- due to P_aCO_2

- Acute change:
  - if P_aCO_2 increases by 10, the HCO_3^- is expected to increase by 1 mEq
  - if P_aCO_2 decreases by 10, the HCO_3^- is expected to decrease by 2 mEq
- Chronic change:
  - if P_aCO_2 increases by 10, the HCO_3^- is expected to increase by 3 - 4 mEq
  - if P_aCO_2 decreases by 10, the HCO_3^- is expected to decrease by 4 - 6 mEq

Bicarbonate Replacement

- Metabolic acidosis is the most frequent acid base abnormality observed in the critically ill, with the most likely underlying disturbance as 'lactic acidosis' (Bihari 1986, Mizock 1987).
- Although sodium bicarbonate has been advocated the drug of choice in treating metabolic acidosis by many critical care clinicians, there is no consensus concerning the use of sodium bicarbonate in the treatment of life-threatening acidosis.
- The American Heart Association removed routine use of sodium bicarbonate as part of Advanced Cardiac Life Support (ACLS) protocol related to the treatment of cardiac arrest in 90's, indicating little use or potential deterioration of clinical outcome regarding the drug therapy for CPR.
- The use of sodium bicarbonate in the treatment of metabolic acidosis has been very controversial and will probably remain so for a long time.
- The risks of overzealous bicarbonate therapy include
    - paradoxical cerebral acidosis (through increased production of CO_2)
    - hypernatremia
    - hyperosmolality
    - iatrogenic metabolic alkalosis
- If you have a mixed respiratory/metabolic acidosis, important to address the respiratory acidosis first, before treating the metabolic acidosis
- Bicarbonate therapy is not usually recommended unless $pH < 7.1$ or HCO_3^- deficit is greater than 10 meq/L.
- 8.4% $NaHCO_3$ = 1 meq/ml
- 1 gm of baking soda (e.g. Arm & Hammer) = 12 mEq of $NaHCO_3$
- Formula for Bicarbonate replacement based on 'Base deficit'
    - **Base deficit = BW (Kg) x 0.3 $\times$ (desired – observed bicarbonate, HCO_3^-)**
    - 0.3 assumes 30% of BW is extracellular fluid.
    - It is recommended that 25 % of the calculated dose to be given over 10 to 15 minutes, and the remaining to be given following subsequent evaluation of acid base status to the initial therapy.

Oxydynamics

P_aO_2 vs. O_2 Content

- PO_2 = partial pressure of oxygen in plasma
- O_2 content = ml of O_2/100 ml of blood
- Hb: 1 gm of saturated Hb carries 1.34 ml of O_2
- Plasma: 0.3 ml of O_2 dissolved/100 mmHg O_2 tension/100 ml blood
- Calculation of O_2 content (O_2CT)

$$O_2CT = Hb + plasma = 1.34 \text{ x Hb x Saturation } + PaO_2 \text{ x } 0.003$$

  - Example 1: What is O_2CT if $P_aO_2 = 100$ and Hb = 10?

$$(1.34 \times 10 \times 1.0) + (100 \times 0.003) = 13.7 \text{ mg } O_2/100 \text{ ml blood}$$

  - Example 2: What is the O_2CT if $P_aO_2 = 400$ and Hb = 10?

$$(1.34 \times 10 \times 1.0) + (400 \times 0.003) = 14.6 \text{ mg } O_2/100 \text{ ml blood}$$

- Can you demonstrate the importance of giving 100% oxygen to a very anemic animal (Hb = 4) vs. a normal animal (Hb = 15)? What percentage increase in oxygen content would occur in each if a P_aO_2 of 500 was achieved from 100?

  - Hb 4
    - $(4 \times 1.34) + (500 \times 0.003) = 6.86$ mg/dl (vs. 5.66 mg/dl at PaO_2 100)
    - 6.86/5.66= **21 % increase**
  - Hb 15
    - $(15 \times 1.34) + (500 \times 0.003) = 21.6$ mg/dl (vs. 20.4 mg/dl at PaO_2 100)
    - 21.6/20.4 = **6 % increase**
  - It is apparent, even in anemic condition, increasing fraction of oxygen still helps although primary therapeutic goal must be to 'elevate the Hb concentration' quickly.

Examples

- In each of the following problems, ask the following questions in this order:
  - Is the patient acidotic or alkalotic? Remember, the body never overcompensates!
  - Is there a respiratory component to the blood gas disturbance?
    (Is the $P_aCO_2 < 35$ or > 45?)
  - Is there a metabolic component to the blood gas disturbance?
    (Is the $HCO_3^- < 24$ or > 26?
  - Remember, HCO_3^- must be adjusted for P_aCO_2 changes.
    - 12 mmHg P_aCO_2, 6 meq/L equal to change of 0.1 (pH)

PCO_2	pH	HCO_3^-
12 mmHg	0.1	6 mEq/L

  - Acute Respiratory Alteration
    - $PCO_2 = 52$, pH = 7.3.
    - $PCO_2 = 28$, pH = 7.5.
  - Metabolic Alteration
    - $PCO_2 = 52$, pH = 7.5.
    - $PCO_2 = 28$, pH = 7.3.
  - Mixed
    - $PCO_2 = 52$, pH = 7.2.
    - $PCO_2 = 28$, pH = 7.6.

Horse on the surgery table

pH = 7.2
$P_aCO_2 = 76$
$HCO_3^- = 30$
$P_aO_2 = 300$

  - What is the acid base status?
    - Acidemia or alkalemia?
    - Is there a respiratory component?
    - Is there a metabolic disturbance?
  - Why is the P_aO_2 300?

30 Kg German Shepherd on surgery table with volvulus of intestine

pH = 7.1
$P_aCO_2 = 70$
$HCO_3^- = 21$

  - Same as above
    - Same as above

- ¤ Same as above
- ¤ Same as above
  - o What is the HCO_3^- deficit? (expected - actual = deficit)
  - o How much HCO_3^- should be given?

500 Kg horse standing, kicking, bouncing in the stocks with colic signs

pH = 7.2
P_aCO_2 = 20
HCO_3^- = 15

- o Same as above
  - ¤ Same as above
  - ¤ Same as above
  - ¤ Same as above
- o What is the HCO_3^- deficit?
- o What would happen if we gave this animal 50 gms of $NaHCO_3$?
  (1 gm = 12 mEq/L)

Normal cat, awake when sample taken

pH = 7.5
P_aCO_2 = 20
HCO_3^- = 20

- o Why would a cat have this type of blood gas picture?