OMG

- At first I thought I was going to have to refute "the paper"
- Then I got into it and thought:
  - I’m so confused
  - Then I learned a lot

HOPEFULLY I CAN LEARN YOU WHAT I LEARNED

---

**OBJECTIVES**

- Understand the basics of acid-base balance
- Know the common causes of neonatal metabolic acidosis
- Recognize the situations when sodium bicarbonate can be beneficial and when it cannot
- Recognize the potential risks of bicarbonate therapy in the neonate

---

**ACID-BASE PHYSIOLOGY**

- Oh yikes-Do we have to?
WHY

with these physiologic changes. It is hoped that a better understanding of the classical principles of acid-base chemistry will persuade the practitioner to view the administration of bicarbonate in its larger context and to recognize that bicarbonate therapy does considerably more than alter the parameters of the whole blood bicarbonate buffer system. Such awareness may lead to

HENDERSON-HASSELBACH EQUATION

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

- Every student’s nightmare
- Describes acid-base balance in bicarbonate buffer systems
- Illustrates the importance of the lungs
- Does not define all of the components of acid/base balance

BICARBONATE/CO₂ EQUILIBRIUM

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

- For every mole of proton (H⁺) neutralized by bicarbonate, an equimolar amount of carbon dioxide is formed
- Henderson- Hasselbach Equation:
  - pH depends on ratio of HCO₃⁻ and CO₂

Buffers and pKa

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

- For a buffer system, optimal buffering occurs when pH and pKa are within 1 unit of each other
  - pKa is the pH at which concentration of HCO₃⁻ and CO₂ are equal
- pKa of the bicarbonate buffer system is 6.1
  - Long way from our optimal pH of 7.4
  - All by itself it would be an ineffective buffer system
  - Works because of the efficiency of the lungs

The whole acid-base system

- Other buffers
  - Entire organism (body) is buffered by both bicarbonate and non-bicarbonate buffers
  - Non-bicarbonate buffers include hemoglobin, phosphates and proteins
- Multiple compartments
- Two major regulatory organs
  - Lungs and kidneys regulate ("compensate") for changes in buffer systems
**Determination of pH**

- Blood gas instrument measures pH and pCO₂ and estimates bicarbonate and base deficit from Henderson-Hasselbach
  - Total CO₂ on lytes accurately measures bicarbonate and carbonic acid
- Even if bicarbonate estimate is accurate, the base deficit can be wrong unless it is corrected for non-bicarbonate buffers
  - Most blood gas instruments do not correct for hemoglobin

**ACID-BASE COMPARTMENTS**

- Intravascular fluid compartment communicates with interstitial space which is about three times larger than intravascular space
  - Intravascular space is buffered by bicarbonate and Hemoglobin
  - Interstitial space buffered by bicarbonate
- Intracellular compartment is “equilibrium” with intravascular and interstitial compartments
  - Buffered by phosphates, proteins and bicarbonate

**CLINICAL PRACTICE**

- We track the success or failure of acid-base regulatory systems by measuring the difference between normal and prevailing buffers in whole blood (“base excess or deficit”)
- We are monitoring the quantitatively least important compartment
- We are using indirect measures to infer what is happening in intracellular space

---

**CLINICAL PRACTICE**

- What we really need to know is what is happening intracellularly:
  - Intramitochondrial acidosis alters energy production
  - Intracardiac acidosis alters cardiac function
  - Intra“brain” acidosis produces neonatologists
REST PERIOD

NEONATAL ACIDOSIS
- TWO TYPES (DUH!)
  - Respiratory
  - Metabolic

RESPIRATORY ACIDOSIS
- Most common cause of acidosis
- Deceptively complex—seems like a pure respiratory acidosis with increased pCO$_2$
  - CO$_2$ + H$_2$O $\rightarrow$ H$_2$CO$_3$ $\rightarrow$ H$^+$ and HCO$_3^-$
  - H$^+$ is buffered by hemoglobin
  - HCO$_3^-$ diffuses into interstitium and into cells
  - Results in low HCO$_3^-$ and a base deficit

Carbon dioxide titration curve
- Interstitial space is large in preterm infants
- Results in a large apparent base deficit even though the CO$_2$ has been buffered

NEONATAL METABOLIC ACIDOSIS
- Metabolic acidosis is a common finding in the NICU
- Intracellular acidosis can have adverse effects on cell function
  - Intracellular pH is often maintained despite extracellular acidosis
- Before treating, we should consider the underlying cause and whether treatment might make the problem worse

OH, YIKES
3 common mechanisms for neonatal metabolic acidosis
1. Loss of base from renal or GI routes
2. Intake of more acid than kidneys can excrete
3. Abnormal metabolism resulting in increased endogenous acids
   - Inorganic acids from rapid tissue catabolism
   - Organic acids from incomplete oxidation of fuels

ANION GAP
- Na – (Cl + CO₂)
- Normal: 0 because the body has to be neutral
- An acidosis is either:
  - Increased gap acidosis: implies presence of other “acids” (negative charges)
  - Nl gap acidosis: deficiency of bicarbonate with an increase in Cl

BICARBONATE LOSS
- Renal tubular acidosis or “diarrhea”
  - RTA - more common in premature infants
  - Short gut infants with malabsorption
- In both Bicarbonate is low
- Hyperchloremia is common,
- Anion gap is nl

ACID LOAD
- Often occurs with “net-acid” diet in the face of renal immaturity
  - Casein rich formulas
  - Excess amino acids in TPN
  - Surprise-amino acids are acids
- Anion gap is increased

ENDOGENOUS ACIDS
- Catabolic state of severely ill neonates
  - Increased inorganic acids (phosphates and nitrates)
- Hypoxemia or decreased tissue perfusion
  - Both result in inadequate cellular oxygenation
  - Mitochondria are unable to produce energy aerobically
  - Anaerobic metabolism produces organic acids including lactic acid
  - Increased Anion gap

LACTIC ACIDOSIS
- Lactic acid levels are increased when mitochondria are unable to convert lactate into CO₂, water and ATP
- Mitochondria that are not functioning properly (metabolic disease)
- Mitochondria that are deprived of O₂
  - Systemic Hypoperfusion of hypoxemia
METABOLIC ACIDOSIS FROM DECREASED OXYGEN DELIVERY

- Reduced oxygen delivery ultimately leads to acidosis in all compartments
- Source of acid is still unclear:
  - Lactic acid from anaerobic metabolism
  - Most of H ion liberated from the hydrolysis of ATP to ADP and iPhosphate
- Either way, metabolic acidosis parallels the reduction in energy stores

LACTIC ACIDOSIS

- Blood bicarbonate levels or pH do not correlate well with lactate levels
- Lactate levels correlate better with energy stores
- Elevated lactate levels are strongly associated with increased mortality in term and preterm infants

SO....who should we treat?

- Widely differing underlying causes of acidosis require different treatment approaches
  - Chronic Bicarb loss- may be reasonable to replace
  - Poor perfusion-addition of base won’t correct the problem
    - Administration of base my increase intracellular acidosis

ROLE OF BICARBONATE DURING CARDIAC ARREST

- Is there evidence for efficacy?
- Is there potential for harm?
- Is there anything about neonates?

Fair amount about adults and unfortunate animals

Cardiac Arrest and Bicarbonate

ANIMALS
- Bicarb corrected arterial metabolic acidosis but led to a decrease in intramyocardial pH
- Bicarb decreased coronary perfusion pressure
  - CPP: Systolic BP – R atrial pressure
- Bicarb decreased survival

Cardiac Arrest and Adults

- 1 RCT in adults after arrest: no benefit
- 19 retrospective trials
  - 11 identified no difference in outcomes
  - 8: mortality was worse
AHA 2005 Guidelines for CPR

- “lack of evidence that bicarbonate administration improves likelihood of successful defibrillation or

American Heart Association guidelines warn that arterial blood gas monitoring during cardiac arrest is not a reliable indicator of the severity of tissue hypoxemia, hypercarbia, or tissue acidosis, and they admonish us to recall that restoration of oxygen content with appropriate ventilation with oxygen, support of tissue perfusion and cardiac output with good chest compressions, and then rapid return of spontaneous circulation are the mainstays of acid-base balance restoration during cardiac arrest.”

Cardiac Arrest and Neonates

- 1 neonatal RCT (Lokesh, Resuscit., 2004)
- 55 asphyxiated infants who required ventilation at 5 minutes after birth
- 2 meq/kg of dilute bicarb
- No benefit in mortality rates or rates of abnormal neurological examines at discharge
- No long term follow up data

WHAT WILL I DO NOW?

- Honest to goodness bicarbonate loss: let’s replace it
- As part of a code or DR resuscitation: let’s not use it
- With RDS: let’s not give bicarbonate
- With shock or hypoxemia: let’s not use bicarbonate

References

- Lawn CJ, McGuire W: Base administration or fluid bolus for preventing morbidity and mortality in preterm infants with metabolic acidosis. Cochrane Database Syst Rev. 2005; April 18
POSSIBLE HARM
- Children and animals—bicarbonate exacerbates cardiac injury after hypoxemia
- Der Velden (2006): Increases in cerebral blood volume in infants who received H2CO3
  - Rapid infusion (IVP) was worse than slow (30 minutes)

IS METABOLIC ACIDOSIS BAD?
- Unclear to what extent arterial blood pH reflects intracellular pH
- Hard to distinguish between the effects of hypoxemia and acidosis
- Effects of acidosis on the heart
  - Decreases contractility
  - Decreases response to catechols
  - Increased pulmonary artery pressure
  - Decreased load tolerance of right ventricle