Acid-Base Balance and the Anion Gap

Electrical Neutrality
- Cations = Anions
- $\text{H}^+$ is special
- Bodily acids
  - Volatile = $\text{CO}_2$
  - Non-volatile
    - $\text{H}_2\text{PO}_4^-$
    - $\text{H}_2\text{CO}_3$
- Henderson-Hasselbalch
  $$\text{pH} = 6.1 + \log \frac{\text{HCO}_3^-}{\text{PaCO}_2 \times 0.0301}$$

CO$_2$ and H$_2$CO$_3$ Relationship
- Carbonic anhydrase
- Shuttles back and forth

$$\text{CO}_2 + \text{H}_2\text{O} \xrightleftharpoons[k_1]{k_{-1}} \text{H}_2\text{CO}_3$$

Measurement of pH and PaCO$_2$
- Arterial blood
- Through the lungs
- 7.35 – 7.45
- CNS respiratory control
  - PaCO$_2$
  - Secondarily $\text{H}_2\text{CO}_3$
- Renal contribution
  - Reabsorption of $\text{H}_2\text{CO}_3$
  - Titratable acid formation

So how do we maintain pH?
- PaCO$_2$ is maintained at about 40 mmHg
- CNS respiration rate
  - Blow off or retain CO$_2$
  - CO$_2$ production is not subject to regulation
  - Renal control is very important.

Renal Contribution
- Reabsorption of filtered $\text{H}_2\text{CO}_3$
  - This is recovery
  - Proximal tubule
  - You really didn’t mean to get rid of it.
- Formation of titratable acids
- Distal tubule
- Excretion of NH$_4^+$
- Distal tubule
The distal tubule story.

- Actual secretion of excess H⁺
- Distal tubular cell
- Formation of titratable acids
  - H₂PO₄⁻
- Excretion of NH₄⁺

This is what’s working for us

- Keep that bicarb
- Proximal tubule
  - 4000 mmol of H₂CO₃
  - 4000 mmol of H⁺
- What happens if you lose this bicarb?

Primary respiratory and metabolic disturbances

- One cause
- Compensation
- Respiratory
  - Acidosis
  - Alkalosis
- Metabolic
  - Acidosis
  - Alkalosis

If life were that simple.

- Mixed acid-base disorders
- Folks are entitled to more than one medical problem at a time.
- Even acidosis and alkalosis at the same time.
- What would their pH be?
- What will help
  - Anion gap
  - Bicarbonate gap
  - Chloride concentration

How to figure it out?

- Blood work
  - Arterial blood gases
  - Serum electrolytes
- Compare HCO₃⁻ for accuracy
- Calculate the anion gap (AG)
- Do some thinking, review
  - Causes of high AG acidosis
    - Ketosis
    - Lactic acidosis
    - Renal failure
    - Toxic exposure
  - Causes of non-gap acidosis
    - HCO₃⁻ loss from GI tract
    - Renal tubular acidosis
- Compare ΔAG and ΔHCO₃⁻
- Compare change in [Cl⁻] and [Na⁺]
- History and physical
  - Pulmonary
  - Vomiting?
  - Medications (diuretics)?
  - Sleep apnea

The Anion Gap

- Not really a gap, just the stuff we don’t normally measure.
- AG = Na⁺ - (Cl⁻ + HCO₃⁻)
  - Typically about 10 to 12 mmol
- Increased AG
  - Most often due to increased serum lactate or acetocetate.
  - Rarely due to a decrease in cations such as Ca²⁺, magnesium and/or K⁺
- Decreased AG
  - Increase in unmeasured cations
  - Addition of something new to the blood such as Li⁺
  - Reduction in a major plasma protein such as albumin (renal loss).
  - Hyperlipidemias and other less common causes.
Simple rules for simple, one cause, acid-base disturbances.

- Metabolic vs. respiratory?
  - Respiratory acidosis, PaCO₂ < 44
  - Metabolic acidosis, HCO₃⁻ < 22
  - Respiratory alkalosis, PaCO₂ > 36
  - Metabolic alkalosis, HCO₃⁻ > 26
- If primary change is:
  - HCO₃⁻, then the underlying cause is most likely metabolic
  - CO₂, the underlying cause is most likely respiratory

Metabolic Derangements

- Metabolic Acidosis with anion gap
- Increased endogenous acid production
  - lactate
  - ketoacidosis
  - accumulation of endogenous acids with renal failure
  - loss of HCO₃⁻, diarrhea
  - Metabolic, endogenous
- Metabolic acidosis with no ion gap
  - loss of HCO₃⁻, diarrhea
  - renal loss of HCO₃⁻, renal tubular acidosis
  - Carbolic anhydrase inhibition
- Metabolic alkalosis
  - vomiting
  - milk-alkali syndrome
  - K⁺ wasting as in with Conn’s syndrome
  - Loss of H⁺
  - Our compensate is respiratory
    - Renal CO₂

Respiratory Derangements

- Respiratory acidosis
  - CNS
  - Airway obstruction
  - Neuromuscular and faulty respiration
  - CO₂ is high and the reason is poor ventilation
  - Compensation must be to increase HCO₃⁻.
- Respiratory alkalosis
  - CO₂ is low
  - Pregnancy
  - Sepsis
  - Anxiety and physical pain leading to increased resp rate
  - Salicylates
  - Liver disease

Mixed Acid-Base Disorders

- HCO₃⁻ gap = delta AG - delta HCO₃⁻
  - This is also called the Delta gap.
  - Delta AG = patient’s AG - 12 mEq/L
  - Delta HCO₃⁻ = 27 mEq/L - patient’s HCO₃⁻
  - Just one acid-base abnormality, there should be a 1:1 correlation between the rise in the anion gap and a drop in the bicarbonate.
  - Example: if the AG goes up by 10, then the HCO₃⁻ should drop by 10.
  - Delta AG - delta HCO₃⁻ = 10 - 10 = 0
  - Just one acid-base problem here.
  - Variation of the bicarbonate gap from zero, either + or - means there is a mixed acid-base problem.

Renal Acidosis

- The renal tubules reabsorb HCO₃⁻ and secrete acid.
- Failure of either leads to renal tubular acidosis
- All forms of renal tubular acidosis are characterized by
  - Minimally elevated to normal ion gap
  - Hyperchloremia
  - Net retention of HCl (generally)
- Three basic patterns
  - Distal type (type 1 RTA)
  - Proximal type (type 2 RTA)
  - Type 3 RTA is absence of carbolic anhydrase
  - Hypoaldosteronism (type 4 RTA)

Case: 22 year-old man with vomiting, nausea and abdominal pain

- His blood pressure is low and he has tenting of the skin
- His electrolytes are
  - Na⁺ = 144
  - Cl⁻ = 95
  - K⁺ = 4.2
  - HCO₃⁻ = 14.
- AG = 35
- Delta AG = 23 (35 – 12)
- Delta HCO₃⁻ = 13 (27 – 14)
- HCO₃⁻ gap = +10 (also called Delta gap)
  - The high HCO₃⁻ gap indicates there are two conditions at work:
    - Metabolic acidosis from dehydration and poor tissue perfusion (lactacid acid accumulation).
    - Metabolic alkalosis from vomiting and loss of stomach acid.
A case of renal related acidosis

Amy is a 24-year-old mother of one who develops acute renal failure after a perforated ulcer gave her peritonitis and shock. Her labs are:

- **Na+**: 140 mEq/L
- **K+**: 4 mEq/L
- **Cl-**: 115 mEq/L
- **CO2**: 5 mEq/L
- **pH**: 7.12
- **PaCO2**: 13 mmHg
- **HCO3-**: 5 mEq/L

\[ \text{AG} = 21 = (140 - (\text{Cl} - + \text{CO}_2)) \]
\[ \Delta \text{AG} = 9 = (21 - 12) \]
\[ \Delta \text{HCO}_3^- = 23 = (27 - 4) \]

Delta (HCO3-) gap = ΔAG - ΔHCO3-

Her anion gap is up, but not off the chart.

The bicarbonate gap is off.

Renal Tubular Acidosis

- In other words, her HCO3- is significantly reduced at -14 mEq/L.
- That is 14 mEq/L lower than would be expected given her excess anion gap of 8.
- The fact that her CO2 is actually 5 mEq/L means there must be an additional reason for her acidosis.
- She has two renal related problems.
- Uremia from kidney failure causing the elevated AG.
- Tubular related problem of HC03- recovery and acid secretion, which leads to a non-ion gap acidosis with hyperchloremia.

Mixed Derangements

- Mixed acid-base disorders
- Folks are entitle to more than one medical problem at a time.
- Even acidosis and alkalosis at the same time.
- What would their pH be?
- What will help
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Renal Tubular Acidosis

<table>
<thead>
<tr>
<th>Type 1 RTA</th>
<th>Type 2 RTA</th>
<th>Type 4 RTA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary defect</td>
<td>Impaired distal acidification</td>
<td>Reduced proximal tubular bicarbonate reabsorption</td>
</tr>
<tr>
<td>Plasma bicarbonate</td>
<td>Variable, may be below 10 meq/l</td>
<td>Usually 15 to 20 meq/l</td>
</tr>
<tr>
<td>Urine pH</td>
<td>Greater than 5.3</td>
<td>Variable, greater than 5.3</td>
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<tr>
<td>Plasma potassium</td>
<td>Usually reduced but hyperkalemia from renal failure</td>
<td>Reduces, more severe by bicarbonate reabsorption enhanced by alkali therapy</td>
</tr>
</tbody>
</table>

Summing it up

- One cause
- Compensation
- Respiratory
  - Acidosis
  - Alkalosis
- Metabolic
  - Acidosis
  - Alkalosis

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- In this case, it’s a hyperchloremic metabolic acidosis, which is commonly seen with renal failure.
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