Approach to the Patient with Acid-Base Problems

Maintenance of Normal pH

- normal pH = 7.40 --> [H+] = 40 neq / L
- $\text{H}_2\text{O} + \text{CO}_2 \leftrightarrow \text{H}_2\text{CO}_3 \leftrightarrow \text{H}^+ + \text{HCO}_3^-$
  - dietary breakdown of protein
  - (about 80 meq / d normally)
  - 13,000 to 20,000 mM CO2 produced per day

Henderson - Hasselbach Equation

- $\text{H}_2\text{O} + \text{CO}_2 \leftrightarrow \text{H}_2\text{CO}_3 \leftrightarrow \text{H}^+ + \text{HCO}_3^-$
  - is equivalent to:
  - $\text{pH} = 6.1 + \log \left( \frac{[\text{HCO}_3^-]}{[\text{H}_2\text{CO}_3]} \right)$
  - is equivalent to:
  - $\text{pH} = 6.1 + \log \left( \frac{[\text{HCO}_3^-]}{(.03 \times \text{pCO}_2)} \right)$
  - which can be approximated by the formula
\[ [H^+] = 24 \times pCO_2 / [HCO_3^-] \]

- Normally, \([H^+] = 40\) neq / L
- Normally, \(pCO_2 = 40\) mm Hg
- Normally, \([HCO_3^-] = 24\) meq / L

● Remember this formula !!!!!

\[ [H^+] = 24 \times pCO_2 / [HCO_3^-] \]

● This formula is easy to remember

\[ [H^+] = 24 \times pCO_2 / [HCO_3^-] \]

● This formula is easy to remember

● The constant is easy to remember (same as the usual [HCO3] level)
\[ [H^+] = 24 \times pCO_2 / [HCO_3^-] \]

- This formula is easy to remember
- The constant is easy to remember (same as the usual [HCO3] level
- And...most importantly →

This formula shows that it is the RATIO of CO2 and HCO3 which determines pH

\[ pCO_2 / [HCO_3^-] \]

- Getting from [H+] to pH (or back)
- Converting from [H+] to pH can be easy if you are a savant, if you carry a calculator, or if you take advantage of the fact that, over the range of physiologic pH, the relationship between [H+] and pH is almost linear
\[ [H^+] = 24 \times pCO_2 / [HCO_3^-] \]

- This formula is usable because, in the range of pH values we usually deal with, there is a nearly linear relationship between pH and \([H^+\]).

<table>
<thead>
<tr>
<th>pH</th>
<th>actual ([H^+])</th>
<th>estimated ([H^+])</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.10</td>
<td>79</td>
<td>70</td>
</tr>
<tr>
<td>7.20</td>
<td>63</td>
<td>60</td>
</tr>
<tr>
<td>7.30</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>7.50</td>
<td>32</td>
<td>30</td>
</tr>
</tbody>
</table>

Regulation of pH – 3 mechanisms

- Buffering
Regulation of pH – 3 mechanisms

- Buffering
- Respiratory regulation of pCO₂

Regulation of pH – 3 mechanisms

- Buffering
- Respiratory regulation of pCO₂
- Renal regulation of [H⁺] and [HCO₃⁻]

Regulation of pH – 3 mechanisms

Different Mechanisms

Different Speeds
Regulation of pH -- mechanisms

- **Buffering** -- OCCURS IMMEDIATELY
  - No semipermeable membranes to cross
  - No enzyme activation necessary
  - Everything needed is right at hand

- **Respiratory changes** OCCUR OVER HOURS
  - Brainstem response to pH
  - Delay in CSF pH changes

- **Renal changes** OCCUR MORE SLOWLY
  - Physiologic changes in renal H+ excretion
Buffering

- Extracellular
  - almost entirely through bicarbonate
    - it’s concentration is highest
    - small contribution from phosphate
  - \( \text{H}_2\text{O} + \text{CO}_2 \leftrightarrow \text{H}_2\text{CO}_3 \leftrightarrow \text{H}^+ + \text{HCO}_3^- \)

- Intracellular

Buffering

- Extracellular
- Intracellular
  - hemoglobin can directly buffer protons
  - \( \text{H}^+ \) entry into RBC matched by exit of Na\(^+\) and K\(^+\)
  - \text{relationship between pH and measured [H+]}
  - hemoglobin can directly buffer dissolved CO\(_2\)
  - intracellular conversion of CO\(_2\) (and H\(_2\)O) to
    \( \text{H}^+ \) and \( \text{HCO}_3^- \) \( \rightarrow \) generation of \( \text{HCO}_3^- \)
    - \( \text{H}^+ \) buffered by Hb; \( \text{HCO}_3^- \) exchanges for Cl\(^-\)

Respiratory regulation of pCO\(_2\)

- pCO\(_2\) is inversely proportional to
  - VENTILATION
- Ventilation increases in response to a drop in pH, and falls when pH rises
  - respiratory center in medulla
  - responds to pH “intermediate” between that of CSF and plasma
  - response is rapid (though not instantaneous)
  - response is more predictable for falls in pH than for increases
Renal Regulation of $[H^+]$ and $[HCO_3^-]$

A DUMB KIDNEY WILL USUALLY DO BETTER THAN A SMART DOCTOR

TWO MAJOR FUNCTIONS OF THE KIDNEY (regarding acid-base reg.)

- Reclamation of filtered bicarbonate
Renal Regulation of $[H^+]$ and $[HCO_3^-]$

**TWO MAJOR FUNCTIONS OF THE KIDNEY**

- Reclamation of filtered bicarbonate
  - a normal occurrence
  - 4000 meq / day in normal persons
  - by far the greatest use of secreted acid
- Excretion of Acid
  - titratable acidity
  - ammonium formation
  - free $H^+$ excretion
Renal Regulation of $[H^+]$ and $[HCO_3^-]$ Factors which effect renal acid excretion (bicarbonate reclamation) ACID EXCRETION IS STIMULATED BY:
- Acidemia
- Hypercapnea
- Volume depletion (?mediated by angiotensin II)
  - “Contraction alkalosis”
Renal Regulation of $[H^+]$ and $[HCO_3^-]$  
Factors which affect renal acid excretion (bicarbonate reclamation)  
ACID EXCRETION IS STIMULATED BY:  
- Acidemia  
- Hypercapnea  
- Volume depletion (mediated by angiotensin II)  
- Chloride depletion  
- Hypokalemia  
- Aldosterone

Renal Regulation of $[H^+]$ and $[HCO_3^-]$  
Factors which affect renal acid excretion (bicarbonate reclamation)  
ACID EXCRETION IS INHIBITED BY:  
- Alkalemia
Renal Regulation of [H+] and [HCO₃⁻]

Factors which affect renal acid excretion (bicarbonate reclamation)

ACID EXCRETION IS INHIBITED BY:
- Alkalemia
- Elevated [HCO₃⁻]
- Hypocapnea
- Hyperkalemia

Remember:

Compared to BUFFERING and RESPIRATORY adaptation, RENAL compensatory mechanisms take a bit longer.
Definitions

- Acidemia = pH below the normal of ~ 7.40
- Alkalemia = pH above the normal of ~ 7.40

Metabolic acidosis = loss of [HCO₃⁻] or addition of [H⁺]
Metabolic alkalosis = loss of [H⁺] or addition of [HCO₃⁻]

Respiratory acidosis = increase in pCO₂
Respiratory alkalosis = decrease in pCO₂
The ANION GAP

\[ \text{Na}^+ - \text{Cl}^- - \text{HCO}_3^- = 8-12 \text{ normally} \]
- mainly proteins, phosphates, and sulfates

In any patient with an acid-base disturbance, and especially in those with a metabolic acidosis, you should calculate the Anion Gap.

BRAINSTEM REFLEX
High Anion Gap Metabolic Acidosis

USUALLY FROM ADDITION OF ACID

- Ketoacidosis
  - DKA, Alcoholic KA, Starvation
- Lactic acidosis
  - Hypoperfusion; other causes
High Anion Gap Metabolic Acidosis

- Usually from addition of acid
  - Ketoacidosis
    - DKA, Alcoholic KA, Starvation
  - Lactic acidosis
    - Hypoperfusion; other causes
  - Ingestions
    - ASA, Ethylene glycol, methanol
  - Renal insufficiency
    - Inability to excrete acid

Normal Anion Gap Metabolic Acidosis

- Rise in chloride matches the decrease in HCO₃

Normal Anion Gap Metabolic Acidosis

- Renal disease
  - Proximal or distal RTA
  - Renal insufficiency (HCO₃⁻ loss)
  - Hypoaldosteronism / K⁺ sparing diuretics
Normal Anion Gap Metabolic Acidosis

- Renal Disease
  - proximal or distal RTA
  - renal insufficiency (HCO₃⁻ loss)
  - hypoaldosteronism / K⁺ sparing diuretics
- Loss of alkalai
  - diarrhea
  - ureterosigmoidostomy
- Ingestions
  - carbonic anhydrase inhibitors

Compensation

A “simple” acid-base disturbance is one with a primary problem (respiratory or metabolic, acidosis or alkalosis) leading to a compensation in the other arm.
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Primary metabolic problem – respiratory compensation

Primary respiratory problem – metabolic compensation

THREE THINGS TO REMEMBER
Compensation

THREE THINGS TO REMEMBER

1) Compensation is not immediate

2) Compensation is not complete

3) The pCO2 and HCO3 move in the same direction
Compensation - Rules

These formulas are EMPIRICALLY DERIVED from observation and measurement.

Respiratory Compensation for Metabolic Changes

- Metabolic acidosis
  - pCO₂ decreases by 1.2 x the drop in [HCO₃⁻]
- Metabolic alkalosis
  - pCO₂ increases by .7 x the rise in [HCO₃⁻]
  - less predictable than the comp. for acidosis

COMPENSATION IS USUALLY NOT COMPLETE

Metabolic Compensation for Respiratory Changes

- Respiratory Acidosis
  - ACUTE: [HCO₃⁻] increases by .1 x the rise in pCO₂
  - CHRONIC: [HCO₃⁻] increases by .35 x the rise in pCO₂
- Respiratory Alkalosis
  - ACUTE: [HCO₃⁻] decreases by .2 x the fall in pCO₂
  - CHRONIC: [HCO₃⁻] decreases by .5 x the fall in pCO₂

COMPENSATION IS USUALLY NOT COMPLETE
Approach to the Patient

- History and Physical Examination
  - In the majority of cases you should be able to predict, qualitatively, the type of disturbance

- Examples:
  - a patient with septic shock (hypoperfusion)
  - a patient with severe COPD
  - a patient with one day of worsening asthma

Is the patient ACIDEMIC or ALKALEMIC?

- What is the $[\text{HCO}_3^-]$?
  - elevated — metabolic alkalosis
  - decreased — metabolic acidosis

- What is the Anion Gap

- What is the $\text{pCO}_2$?
  - elevated — respiratory acidosis
  - decreased — respiratory alkalosis

- Is the degree of compensation what you expect?

Notation for Laboratory Values

<table>
<thead>
<tr>
<th>Na+</th>
<th>Cl-</th>
<th>BUN</th>
<th>Glu</th>
</tr>
</thead>
<tbody>
<tr>
<td>K+</td>
<td>$\text{HCO}_3^-$</td>
<td>Cr.</td>
<td></td>
</tr>
</tbody>
</table>

$\text{pH}$ / $\text{pCO}_2$ / $\text{pO}_2$ / base excess / $\text{FIO}_2$
Case 1 - History and Physical

The patient is a 73 year-old man admitted with profuse diarrhea. Stool culture later grows *Salmonella*. On admission his blood pressure is 100/60 mm Hg when lying. Upon sitting it drops to 70/40 mm Hg. Skin turgor is reduced.

What abnormalities would you expect based on this information??

*Salmonella* diarrhea -- Lab values

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>133</td>
<td>118</td>
<td></td>
</tr>
<tr>
<td>2.5</td>
<td>5</td>
<td></td>
</tr>
</tbody>
</table>

ABG on Room Air

7.11 / 16 / 96

\([H^+] = 77 \text{ neq/L}\)

Case 1) *Salmonella* diarrhea -- Answers

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<table>
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<td></td>
</tr>
</tbody>
</table>

The patient is profoundly acidemic. The very low bicarbonate clearly indicates that the acidosis is, at least in part, metabolic.

The anion gap is normal, pointing us in the direction of a limited number of possible causes.

The expected decrement in CO2 is \(-1.2 \times (25-5) = 1.2 \times 20 = 24\), and this is actually what we see in this case.

The potassium is low because of loss in the diarrheal fluid.
Case 2 -- History and Physical

A 26 year-old man with IDDM stopped taking his insulin because he was depressed. His family brought him to the emergency room the next day in a semi-comatose state.

On physical examination he was obtunded. His HR was 130, RR 24 and deep, BP 110/60 mm Hg.

What abnormalities would you predict??

IDDM without Insulin -- Predictions

- Lack of insulin --> KETOGENESIS and Hyperglycemia
- Obligate urination (osmotic diuresis) --> dehydration --> hypoperfusion --> inadequate oxygen delivery --> LACTIC ACIDOSOS
- Effect on K+
  - net loss of K b/o urination
  - possible high plasma K+ -- for what reason??

Diabetic -- Lab Values

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABG on RA</td>
<td>7.10 / 20 / 92</td>
</tr>
<tr>
<td>urine dipstick:</td>
<td>large ketones</td>
</tr>
<tr>
<td></td>
<td>140</td>
</tr>
<tr>
<td></td>
<td>105</td>
</tr>
<tr>
<td></td>
<td>51</td>
</tr>
<tr>
<td></td>
<td>470</td>
</tr>
<tr>
<td></td>
<td>4.8</td>
</tr>
<tr>
<td></td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>2.3</td>
</tr>
</tbody>
</table>
The patient is profoundly acidemic. The very low HCO3- is c/w a metabolic acidosis. The anion gap is 19 -- above normal. From our list, the two most obvious candidates for are DKA and LACTIC ACIDOSOS. The measured K+ is normal, though we strongly suspect that total body K+ is low. The respiratory response is a little bit less than predicted, perhaps b/o fatigue.

A young woman with a seizure disorder suffers a grand-mal seizure in the waiting room of the Emergency Department. She has been waiting to have a laceration evaluated. She is promptly brought to the treatment area. WHAT ABNORMALITIES WOULD YOU EXPECT TO SEE BASED ON THIS INFORMATION ???

Seizure Disorder -- Predictions

She might have difficulty with ventilation during her seizure, leading to hypercapnea and a respiratory acidosis.

The intense muscle activity might exceed her anaerobic threshold, leading to a lactic acidosis.
Seizure Victim -- Lab Values

ABG on RA: 7.14 / 45 / 86

140 98
4.0 17

Case 3) Seizure Victim -- Interpretation

The patient has a profound acidemia.

The cause of this problem is a COMBINATION of a high-anion-gap METABOLIC ACIDOSIS (AG = 25), and a moderate RESPIRATORY ACIDOSIS.

Case 4 -- History and Physical

- A 52 y/o man with longstanding COPD is admitted to the hospital with a lower extremity cellulitis. His COPD is clinically stable.

WHAT ABNORMALITIES MIGHT YOU EXPECT TO SEE ??
COPD -- Predictions

- We have no reason to expect the cellulitis to effect the patient’s pulmonary problem.
- COPD patients MAY have a chronic respiratory acidosis.
- A chronic respiratory acidosis will induce some metabolic compensation

COPD -- Lab Values

<table>
<thead>
<tr>
<th>ABG on RA: 7.34 / 60 / 60</th>
</tr>
</thead>
<tbody>
<tr>
<td>139</td>
</tr>
<tr>
<td>4.9</td>
</tr>
</tbody>
</table>

Case 4) COPD -- Interpretation

- The patient has a moderate acidemia. The bicarbonate is HIGH, and the anion gap is normal.
- The pCO2 is VERY HIGH, consistent with our prediction about a patient with COPD. THE PRIMARY DISTURBANCE IS PROBABLY RESPIRATORY
- The expected rise in HCO3- is: \( 35 \times (60-40) = 35 \times 20 = 7 \text{ meq/L} \)
The patient has a moderate acidemia. The bicarbonate is normal, as is the anion gap. The pCO2 is normal as well.

REMEMBER THE EQUATION:
$$[H^+] = 24 \times \frac{pCO_2}{[HCO_3^-]}$$

Plugging in the values from the case, we get:

\[
[H^+] = \sim 56 \text{ meq/L} \quad \text{our estimate}
\]
\[
\text{HCO}_3^- = 25 \text{ meq/L}
\]
\[
pCO_2 = 39 \text{ mm Hg}
\]
\[
56 = 24 \times \frac{39}{25}
\]

The numbers do not fit. Some piece of data is incorrect !!!!!!!
**Case 5 -- Interpretation**

<table>
<thead>
<tr>
<th>139</th>
<th>102</th>
<th>19</th>
<th>ABG on RA: 7.24 / 39 / 86</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.9</td>
<td>25</td>
<td>1.0</td>
<td>ABG on RA: 7.42 / 39 / 86</td>
</tr>
</tbody>
</table>

Perhaps someone in the lab wrote down the pH incorrectly.

If the pH were 7.42 instead of 7.24, the $[H^+]$ would be 38, and the equation would be an identity.

**ONE CAN USE THE FORMULA RELATING $[H^+]$, $[HCO_3^-]$, AND pCO2 TO CHECK FOR CONSISTENCY**

**Case 6 -- Lab Values**

<table>
<thead>
<tr>
<th>139</th>
<th>110</th>
<th>19</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.0</td>
<td>18</td>
<td>1.0</td>
</tr>
</tbody>
</table>

**ABG on RA: 7.36 / 33 / 95**

**WHAT IS THE ACID-BASE DISTURBANCE ?? WHAT MIGHT BE CAUSING IT ??**

**Case 6 -- Interpretation**

The pH is slightly low -- slightly acidemic
The $HCO_3^-$ is slightly low, c/w a metabolic acidosis
The anion gap is normal. One cause of a normal anion gap metabolic acidosis is a RENAL TUBULAR ACIDOSIS.
The hypokalemia is something commonly seen with RTA’s.
The respiratory compensation is appropriate.
WHAT IS THE ACID-BASE DISTURBANCE??
WHAT MIGHT BE CAUSING IT??

The pH is slightly alkalemic. The bicarbonate is low, c/w a metabolic acidosis. The pCO2 is also low, c/w a respiratory alkalosis. pH CHANGES USUALLY REFLECT THE PRIMARY PROBLEM, therefore: The changes are most c/w a primary resp. alkalosis with a metabolic compensation.

The expected compensation for a primary respiratory alkalosis is given by the formula:

- Respiratory Alkalosis
- ACUTE: [HCO3-] decreases by .2 x the fall in pCO2
- CHRONIC: [HCO3-] decreases by .5 x the fall in pCO2

The expected decrease in HCO3- is 5 meq/L.
Case 8 -- History and Physical

- A 54 y/o man with COPD is admitted with a two-day history of progressive shortness of breath and increasing sputum production.
- He is diffusely wheezing on examination, and his air movement is poor.
- His CXR shows a LLL pneumonia

Case 8 -- Labs

<p>| | | |</p>
<table>
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<th></th>
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<td>19</td>
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<tr>
<td>4.0</td>
<td>30</td>
<td>1.0</td>
</tr>
</tbody>
</table>

ABG on RA: 7.25 / 70 / 50

Case 8 -- Interpretation

The clinical scenario is c/w some degree of respiratory acidosis, either acute or chronic. The pH is acidemic, the pCO2 elevated, and the HCO3-elevated, c/w a compensated respiratory acidosis, BUT...

The degree of compensation is NOT what we would expect. The most likely explanation is a baseline chronic respiratory acidosis with a superimposed worsening resp. acidosis.
Case 9 -- History

- A 63 y/o man with insulin-requiring diabetes mellitus but a history of poor compliance with his diet and treatment is brought to the emergency room after passing out.
- His finger-stick glucose in the field was 40

Case 9 -- Labs

<table>
<thead>
<tr>
<th>132</th>
<th>117</th>
<th>43</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.2</td>
<td>9</td>
<td>3.3</td>
</tr>
</tbody>
</table>

ABG on RA: 7.23 / 28 / 107

Case 9 -- Interpretation

He has a normal-anion-gap metabolic acidosis. The predicted respiratory compensation would result in a pCO2 of 20.8 mm Hg, so there is a second process involved. Clinically, this could be either a decrease in his respiratory drive due to his altered state of consciousness, or an acute-on-chronic metabolic acidosis, without enough time for further compensation.
Case 10 - History and Physical

The patient is a middle aged man with arthritis of his knee. He was referred to Loyola. Medications include HCTZ and Furosemide, for ankle edema. In his clinic visit, he was noted to be tachycardic. He was otherwise asymptomatic.

In the ER, they were concerned about the possibility of PE.

<table>
<thead>
<tr>
<th>Tachycardic OA pt. -- Lab values</th>
</tr>
</thead>
<tbody>
<tr>
<td>142</td>
</tr>
<tr>
<td>2.5</td>
</tr>
</tbody>
</table>

ABG on Room Air
7.66 / 24 / 116
BUN 39
Creatinine 1.3

<table>
<thead>
<tr>
<th>Tachycardic OA pt. -- Answers</th>
</tr>
</thead>
<tbody>
<tr>
<td>142</td>
</tr>
<tr>
<td>2.5</td>
</tr>
</tbody>
</table>

ABG on Room Air
7.66 / 24 / 116
BUN 39
Creatinine 1.3

He has a “contraction alkalosis” with hypokalemia, from the diuretic.
ABG on Room Air
7.66 / 24 / 116
He has a “contraction alkalosis” with hypokalemia, from the diuretic. He was told to “breathe deeply” before they drew his ABG, because it would hurt.