Approach to the Patient with Acid-Base Problems

Outline and Objectives

1. Understand basic physiology of acid-base balance
   - Maintenance of normal pH
   - Relevant organs and mechanisms for maintaining pH and dealing with changes of pH
2. Develop an approach to acid base problems (from numbers to diagnosis)
   - Definition of terms (acidosis, alkalemia, anion gap, compensation, etc)
   - Calculations for compensation for single, double and triple acid base disorders
3. Develop an approach to patients with acid base problems (from clinical scenario to diagnosis)
   - Learn to predict the type and approximate severity of a patient's acid base disturbance based on clinical findings (without an ABG)
4. Practice Cases

Background and Physiology

Maintenance of Normal pH

The ratio of pCO2 to bicarb determines pH

[H+] = 24 x pCO2 / [HCO3-]

Kidneys and Lungs maintain the balance between pCO_2 and HCO_3^-

$H_2O + CO_2 \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$

kidneys

Lungs

Normal Values

pH	=	7.4
pCO_2	=	40 mmHg
$[HCO_3^-]$	=	24 meq / L

3 mechanisms for regulation of pH

Buffering

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

Respiratory regulation of pCO_2

- OCCURS OVER HOURS
- Brainstem response to pH
- Delay in CSF pH changes

Renal regulation of $[H^+]$ and $[HCO_3^-]$

- OCCUR MORE SLOWLY (Hours to Days)
- Physiologic changes in renal H+ excretion

3 mechanisms for regulation of pH - Buffering

Extracellular buffering

- almost entirely through bicarbonate
  - $H_2O + CO_2$ <--> H_2CO_3 <--> $H^+ + HCO_3^-$
- small contribution from phosphate

Intracellular buffering

- hemoglobin molecule can buffer protons and dissolved CO_2
  - Dissolved CO2 enters the cell and is buffered as this equation proceeds to the right

    $H_2O + CO_2$ <--> H_2CO_3 <--> $H^+ + HCO_3^-$
    - This generates HCO_3^- and H^+
    - HCO_3^- exchanges out of the cell for Cl^- to maintain electrical neutrality
    - H^+ is bound by hemoglobin molecules in the RBC to prevent acidification of the blood
  - H^+ entry into RBC matched by exit of Na^+ and K^+
    - Clinical Pearl: remember this relationship between pH and measured [K+]: As pH drops, K+ increases

3 mechanisms for regulation of pH – respiratory regulation of pCO_2

Key Point: pCO_2 is inversely proportional to VENTILATION (we breathe out CO_2)

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 – meaning ventilation responds more predictably to acidosis than alkalosis

3 mechanisms for regulation of pH - renal regulation of [H^+] and [HCO_3^-]

Reclamation of filtered bicarbonate (proximal tubule)

- ~ 4000 meq / day in normal persons is filtered at the glomerulus
- 85-90% of filtered bicarbonate is reabsorbed in the proximal tubules
- H^+ secreted into the tubular lumen is used to reabsorb bicarbonate from the lumen into the blood stream
- This process also causes secretion of NH_4^+ ions into the tubular lumen, to then be removed in the medulla

Excretion of Acid (distal tubule)

- Also called titratable acidity (excretion of protons with urinary buffers by the distal tubule)
- Urinary buffers:
  - Ammonium excretion (formed in distal tubule or transferred across the medulla)
  - free H^+ excretion via fixed acids (acid anion [creatinine, phosphate, urate] and associated H^+)

3 mechanisms for regulation of pH - renal regulation of [H^+] and [HCO_3^-]

Factors which effect renal acid excretion (bicarbonate reclamation)

ACID EXCRETION IS <u>STIMULATED</u> BY:

- Acidemia
- Hypercapnia
- Volume depletion
- Chloride depletion
- Aldosterone
- Hypokalemia

3 mechanisms for regulation of pH - renal regulation of [H^+] and [HCO_3^-]

Factors which effect renal acid excretion (bicarbonate reclamation)

ACID EXCRETION IS <u>INHIBITED</u> BY:

- Alkalemia
- Elevated [HCO_3^-]
- Hypocapnia
- Hyperkalemia

3 mechanisms for regulation of pH - renal regulation of [H^+] and [HCO_3^-]

Compared to BUFFERING and RESPIRATORY compensation,

RENAL compensatory mechanisms take a bit longer.

Approach to Acid Base Problems

Definitions

Acidemia = pH below the normal of ~ 7.40 (7.35)

Alkalemia = pH above the normal of ~ 7.40 (7.45)

Metabolic acidosis = loss of [HCO_3^-] or addition of [H^+]

- (Acidosis and a low HCO_3^-)

Metabolic alkalosis = loss of [H^+] or addition of [HCO_3^-]

- (Alkalosis and a high HCO_3^-)

Respiratory acidosis = increase in pCO_2

- (Acidosis and a high pCO_2)

Respiratory alkalosis = decrease in pCO_2

- (Alkalosis and a low pCO_2)

The ANION GAP

Anion gap is made up of the (typically) unmeasured anions in blood

- mainly proteins, phosphates, and sulfates

The anion gap is calculated using the commonly measured anions (Cl^- and $HCO3^-$)

- Normal value is 10-12
- AG = Na^+ - [Cl^- + $HCO3^-$]

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

- A “brainstem reflex” for physicians – you must calculate this every time

If AG is present, you should also calculate the delta-delta ratio

- (Actual anion gap – normal anion gap) / (normal bicarb – actual bicarb)

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

MUDPILES (CAT)

Methanol

Uremia

Diabetic ketoacidosis, starvation ketoacidosis

Paraldehyde, propylene glycol

Iron, Isoniazid, ingestions

Lactic Acid (shock, hypoperfusion, metformin)

Ethylene glycol, ethanol (alcohol ketoacidosis)

Salicylate

Carbon monoxide, cyanide

Aminoglycosides

Toluene (glue sniffing), Teophylline

Normal Anion Gap Metabolic Acidosis (hyperchloremic metabolic acidosis)

- Renal Disease
  - proximal or distal RTA
  - renal insufficiency (HCO_3^- loss)
  - hypoaldosteronism / K^+ sparing diuretics
- Loss of alkali
  - diarrhea
  - ureterosigmoidostomy
- Ingestions
  - carbonic anhydrase inhibitors

USED CAR(P)

Uretero-sigmoid diversion

Saline administration (NaCl)

Endocrinopathies (Addison's, Prim hyperparathyroid)

Diarrhea

Carbonic anhydrase inhibitors

Alimentation (TPN, etc)

Renal Tubular Acidosis

Pancreatic fistulas

Compensation

Compensation is when an acid-base disturbance with a primary problem (respiratory or metabolic, acidosis or alkalosis) leads to changes in the other arm that returns pH to (near) normal.

Primary metabolic problem → respiratory compensation

Primary respiratory problem → metabolic compensation

Three things to remember:

1) Compensation is not immediate

1) Compensation is not complete

1) The pCO_2 and HCO_3 move in the same direction (rule of thumb)

Compensation

Single disorders:

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

Double Disorders:

Detectable by the absence of compensation for the primary disorder (or an abnormal delta ratio)

Triple Disorders:

Detectable by the absence of compensation for the primary disorder and an abnormal delta ratio

Respiratory Compensation Rules

Respiratory Compensation for Metabolic Changes:

compare the expected pCO_2 to the measured pCO_2

- Metabolic acidosis
  - pCO_2 decreases by 1.2 x the drop in $[HCO_3^-]$
    - Expected $\Delta pCO_2 = 1.2 * \Delta [HCO_3^-]$
- Metabolic acidosis (Winter's Formula)
  - Expected $pCO_2 = (1.5 * [\text{serum } HCO_3^-]) + (8 +/- 2)$

Respiratory Compensation for Metabolic Changes:

compare the expected pCO_2 to the measured pCO_2

- Metabolic alkalosis
  - pCO_2 increases by .7 x the rise in $[HCO_3^-]$
    - Expected $\Delta pCO_2 = 0.7 * \Delta [HCO_3^-]$
  - less predictable than the comp. for acidosis

Metabolic Compensation Rules

Metabolic Compensation for Respiratory Changes:

compare the *expected* HCO_3 to the *measured* HCO_3

- Respiratory Acidosis
  - ACUTE: $[HCO_3^-]$ increases by .1 x the rise in pCO_2
    - Expected $\Delta HCO_3 = (0.1 * \Delta pCO_2)$
  - CHRONIC: $[HCO_3^-]$ increases by .35 x the rise in pCO_2
    - Expected $\Delta HCO_3 = (0.35 * \Delta pCO_2)$
- Respiratory Alkalosis
  - ACUTE: $[HCO_3^-]$ decreases by .2 x the fall in pCO_2
    - Expected $\Delta HCO_3 = 0.2 * \Delta pCO_2$
  - CHRONIC : $[HCO_3^-]$ decreases by .5 x the fall in pCO_2
    - Expected $\Delta HCO_3 = 0.5 * \Delta pCO_2$

Metabolic Compensation for Respiratory Changes:

compare the *expected* pH to the *measured* pH

- Respiratory Acidosis
  - ACUTE:
    - Expected $\Delta pH = 0.08 * [(\text{measured } pCO_2 - 40) / 10]$
  - CHRONIC:
    - Expected $\Delta pH = 0.03 * [(\text{measured } pCO_2 - 40) / 10]$
- Respiratory Alkalosis
  - ACUTE:
    - Expected $\Delta pH = 0.08 * [(40 - \text{measured } pCO_2) / 10]$
  - CHRONIC : $[HCO_3^-]$ decreases by .5 x the fall in pCO_2
    - Expected $\Delta pH = 0.03 * [(40 - \text{measured } pCO_2) / 10]$

Compensation rules – triple disorders

Delta Ratio (aka the delta-delta):

- asks the question “Do the anion gap and bicarbonate change the same amount?”
- When AG is elevated, calculate delta-delta to determine the ratio of the change in anion gap to change in bicarbonate

$$\frac{\text{Delta AG}}{\text{Delta HCO3}} \quad \frac{\text{(Measured AG – 12)}}{\text{(24 – measured } HCO_3\text{)}}$$

Compensation rules – triple disorders

Delta Ratio Interpretation:

Pure disorders	Mixed disorders
< 0.4 due to a pure NAGMA	**0.4 – 0.8 due to a mixed NAGMA + AGMA**
0.8 – 2.0 due to a pure AGMA	>2.0 due to a mixed AGMA + metabolic alkalosis* this is uncommon

Rules of thumb:

- If the ratio is near **half (1:2)** or near **double (2:1)**, then there is a third disorder
- If the ratio is near zero or near one, then there is only a double disorder.
  - Near zero - the anion gap changed much less than bicarb changed - implies a pure NAGMA
  - Near one - they changed about the same - implies a pure AGMA

Putting it all together with a stepwise approach

1. Is this an acidosis or alkalosis?
2. Is the primary disturbance respiratory or metabolic?
3. What is the anion gap?
4. If AG is elevated, what is the delta-delta?
5. Is the degree of compensation what you expect for the primary disturbance?
6. What is the overall acid-base disturbance?

Approach to the patient with acid base disturbances

Approach to the Patient

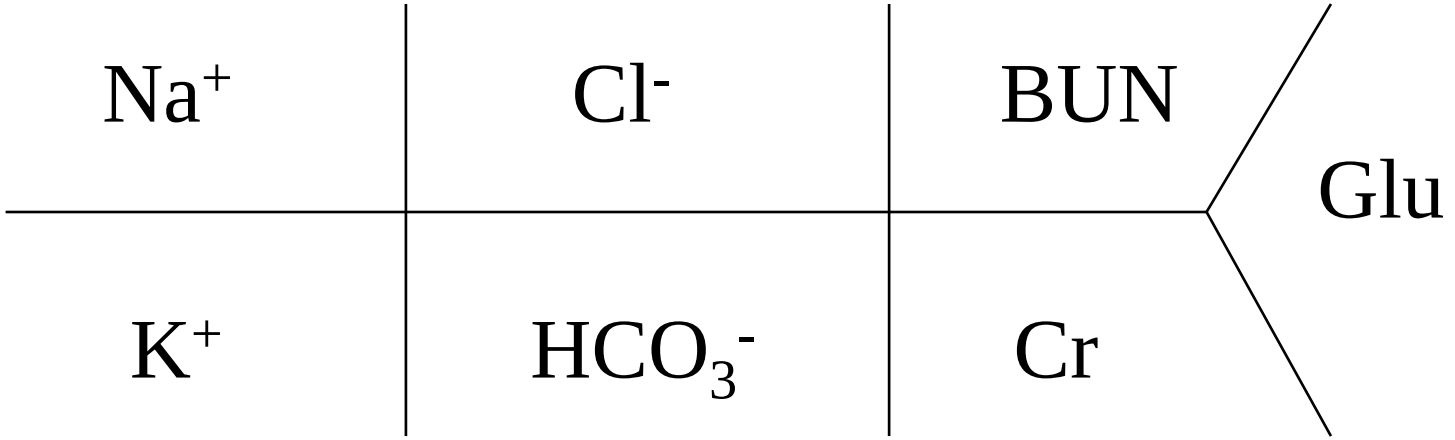
History and Physical Examination

- 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 chronic severe COPD
- a patient with one day of worsening asthma
- a patient with new, severe acute kidney injury

Notation for Laboratory Values



pH / pCO_2 / pO_2 / HCO_3^- [aka Base Excess]

Example

Example 1 -- History and Physical

A 26 year-old man with Type 1 diabetes mellitus stopped taking his insulin because of severe depression. His family brought him to the emergency room the following 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 acid-base abnormalities would you predict based on this history?

Metabolic acidosis, specifically DKA

What clues do we get from the physical examination?

Kussmaul respirations

Obtunded mental status secondary to acidosis and respiratory depression

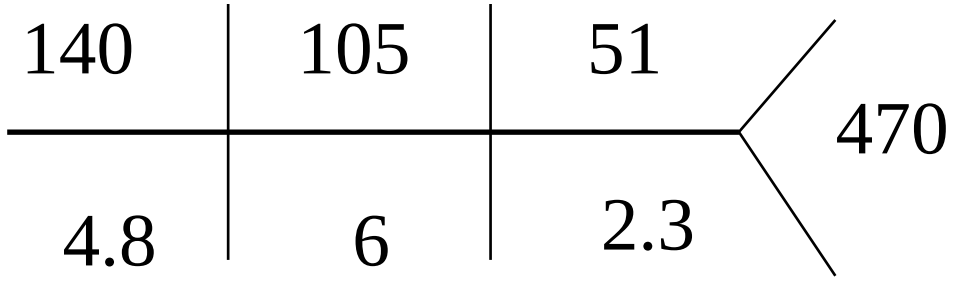
Example 1 -- Pathophysiology

IDDM without insulin

- Lack of insulin --> KETOGENESIS and hyperglycemia
- Obligate urination (osmotic diuresis) -->

  dehydration --> hypoperfusion --> inadequate oxygen delivery --> LACTIC ACIDOSIS
- Effect on K^+
  - net loss of total body K^+ 2/2 urination
  - possible high plasma K^+ despite this
    - *-- for what reason??*

Example 1 -- Lab Values



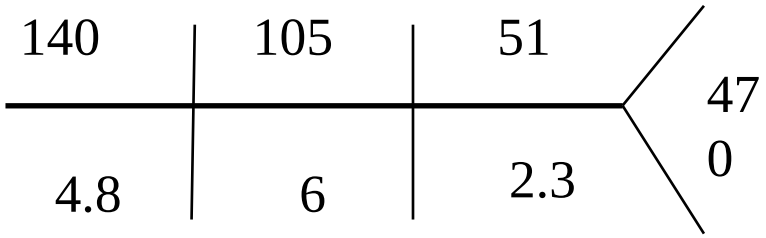
ABG on RA: 7.10 / 20 / 92

urine dipstick: large ketones

Example 1 – Stepwise Interpretation

1. Is this an acidosis or alkalosis?
2. Is the primary disturbance respiratory or metabolic?
3. What is the anion gap?
4. If AG is elevated, what is the delta-delta?
5. Is the degree of compensation what you expect for the primary disturbance?
6. What is the overall acid-base disturbance?

Example 1 -- Answers



ABG on RA:

7.10 / 20 / 92

1. Is this an acidosis or alkalosis?
   Acidosis, pH 7.10

2. Is the primary disturbance respiratory or metabolic?
   Metabolic, with very low HCO_3^-

3. What is the anion gap?
   AG = 140 – (105 + 6) = 29, elevated

4. If AG is elevated, what is the delta-delta?
   $\Delta\Delta = \Delta AG / \Delta HCO_3^- = (29 - 12) / (24 - 6) = 17 / 18 = 0.94$

   Interpretation: $\Delta\Delta$ 0.8 – 2.0 → pure AGMA

5. primary Is the degree of compensation what you expect for the disturbance?

   Expected $\Delta pCO_2 = 1.2 * \Delta [HCO_3^-] = 1.2 * (24 - 6) = 21.6$
   Measured Δ pCO2 = 40 -20 = 20

   *Expected pCO_2 = (1.5 * [serum HCO3-]) + (8 +/- 2)*
   *Expected pCO_2 =(1.5 * 6) + 8 = 17*
   Measured pCO_2 = 20 = 20

   Measured Δ pCO2 (20) and measured pCO_2 (20) are slightly higher than the predicted (21.6 or 17 respectively), perhaps from respiratory fatigue

6. What is the overall acid-base disturbance?

   Pure AGMA from DKA (and maybe AKI)

Cases in Small Groups

Cheat Sheet

Respiratory Compensation for Metabolic Changes:

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