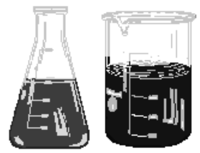
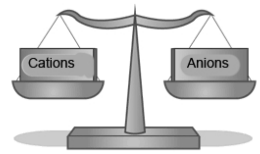
Acid-Base Balance and the Anion Gap



Electrical Neutrality

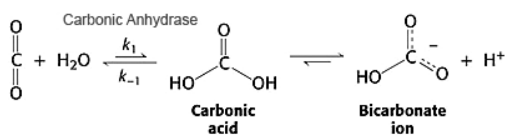
- Cations = Anions
- H^+ is special
- Bodily acids
  - Volatile = CO_2
  - Non-volatile
    - $H_2PO_4^-$
    - H_2CO_3
- Henderson-Hasselbalch



$$pH = 6.1 + \log \frac{HCO_3^-}{Pa_{CO_2} \times 0.0301}$$

CO_2 and H_2CO_3 Relationship

- Carbonic anhydrase
- Shuttles back and forth



Measurement of pH and $PaCO_2$

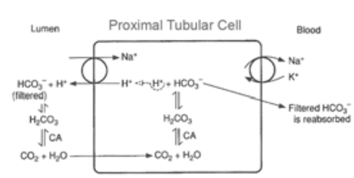
- Arterial blood
- Through the lungs
- 7.35 – 7.45
- CNS respiratory control
  - $PaCO_2$
  - Secondarily H_2CO_3
- Renal contribution
  - Reabsorption of H_2CO_3
  - Titratable acid formation

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.

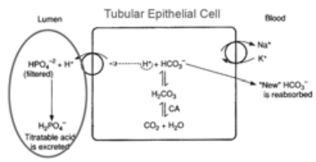
Renal Contribution

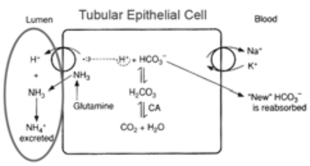
- Reabsorption of filtered H_2CO_3
  - This is recovery
  - Proximal tubule
  - You really didn't mean to get rid of it.
- Formation of titratable acids
  - Distal tubule
- Excretion of NH_4^+
  - Distal tubule



The distal tubule story.

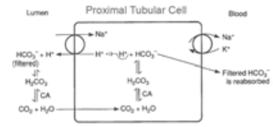
- Actual secretion of excess H^+
- Distal tubular cell
- Formation of titratable acids
  - $H_2PO_4^-$
- Excretion of NH_4^+

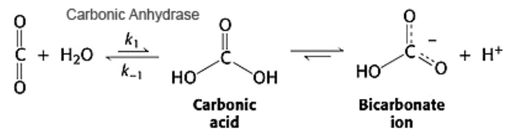




This is what's working for us

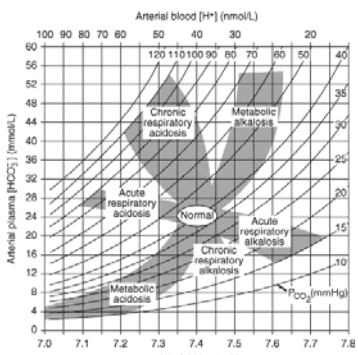
- Keep that bicarb
- Proximal tubule
  - 4000 mmol of H_2CO_3
  - 4000 mmol of H^+
- What happens if you lose this bicarb?





Primary respiratory and metabolic disturbances

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



If life were that simple.

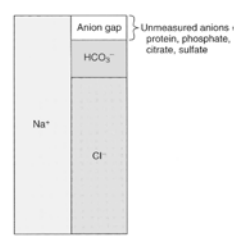
- Mixed acid-base disorders
- Folks are entitle to more than one medical problem at a time.
- Even acidosis and alkalosis at the same time.
  - What would their pH be?
- What will help
  - Anion gap
  - Bicarbonate gap
  - Chloride concentration

How to figure it out?

- Blood work
  - Arterial blood gases
  - Serum electrolytes
- Compare HCO_3^- for accuracy
- Calculate the anion gap (AG)
- Do some thinking, review
  - Causes of high AG acidosis
    - Ketoacidosis
    - Lactic acidosis
    - Renal failure
    - Toxic exposure
  - Causes of non-gap acidosis
    - HCO_3^- loss from GI tact
    - Renal tubular acidosis
- Compare ΔAG and $\Delta\ HCO_3^-$
- Compare change in [Cl^-] and [Na^+]
- History and physical
  - Pulmonary
  - Vomiting?
  - Medications (diuretics)?
  - Sleeping meds

The Anion Gap

- Not really a gap, just the stuff we don't normally measure.
- $AG = Na^+ - (Cl^- + HCO_3^-)$, typically about 10 to 12 mmol
- Increased AG
  - Most often due to increased serum lactate or acetoacetate.
  - Rarely due to a decrease in cations such as Ca^{+2}, 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.

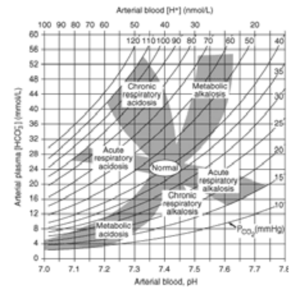


Simple rules for simple, one cause, acid-base disturbances.

- Metabolic vs. respiratory?
  - Respiratory acidosis, $PaCO_2$ is > 44
  - Metabolic acidosis, HCO_3^- is < 22
  - Respiratory alkalosis, $PaCO_2$ is < 36
  - Metabolic alkalosis, HCO_3^- is > 26
- If primary change is:
  - HCO_3^-, then the underlying cause is most likely metabolic
  - CO_2, the underlying cause is most likely respiratory

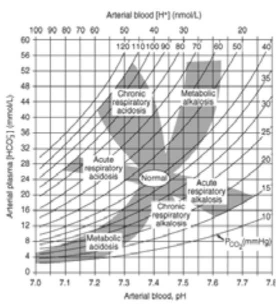
Metabolic Derangements

- Metabolic Acidosis with anion gap
  - Increased endogenous acid production
    - lactate
    - ketoacidosis
  - accumulation of endogenous acids with renal failure
    - loss of HCO_3^-, diarrhea
    - Methanol, antifreeze
- Metabolic acidosis with no ion gap
  - loss of HCO_3^-, diarrhea
  - renal loss of HCO_3^-, renal tubular acidosis
  - Carbonic anhydrase inhibition
- Metabolic alkalosis
  - vomiting
  - milk-alkali syndrome
  - K^+ wasting as in with Conn's syndrome
  - Loss of H^+
  - Our compensate is respiratory
    - Retain CO_2



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 HCO_3^-
- Respiratory alkalosis
  - CO_2 is low
  - Pregnancy
  - Sepsis
  - Anxiety and physical pain leading to increased resp rate
  - Salicylates
  - Liver disease



Mixed Acid-Base Disorders

- HCO_3^- gap = *delta AG - delta* HCO_3^-
  - This is also called the *Delta gap*.
  - *Delta AG =* patient's AG - 12 mEq/L
  - *Delta* HCO_3^- = 27 mEq/L - patient's HCO_3^-
- 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 HCO_3^- should drop by 10.
  - *Delta AG - delta* HCO_3^- *=* 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.*

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
  - HCO_3^- =14.
- AG = 35
- *Delta AG* = 23 (35 – 12)
- *Delta* HCO_3^- = 13 (27 – 14)
- HCO_3^- gap = +10 (also called Delta gap)
- The high HCO_3^- gap indicates there are two conditions at work.
  - Metabolic acidosis from dehydration and poor tissue perfusion (lactatic acid accumulation).
  - Metabolic alkalosis from vomiting and loss of stomach acid.

Renal Acidosis

- The renal tubules reabsorb HCO_3^- 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 carbonic anhydrase
  - Hypoalderstonism (type 4 RTA)

Renal Tubular Acidosis

	Type 1 RTA	Type 2 RTA	Type 4 RTA
Primary defect	Impaired distal acidification	Reduced proximal bicarbonate reabsorption	Decreased aldosterone secretion or effect
Plasma bicarbonate	Variable, may be below 10 meq/L	Usually 12 to 20 meq/L	Greater than 17 meq/L
Urine pH	Greater than 5.3	Variable, greater than 5.3 if above bicarbonate reabsorptive threshold	Usually less than 5.3
Plasma potassium	Usually reduced but hyperkalemic forms exist; hypokalemia largely corrects with alkali therapy	Reduced, made worse by bicarbonaturia induced by alkali therapy	Increased

A case of renal related acidosis

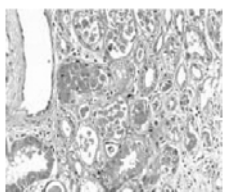
- Amy is a 24 year-old mother of one who develops acute renal failure after a perforated ulcer gave her peritonitis and shock. Her labs are:
  - Na^+ 140 mEq/L,
  - K^+ 4 mEq/L,
  - Cl^- 115 mEq/L,
  - CO_2 5 mEq/L,
  - pH = 7.12,
  - $PaCO_2$ 13 mmHg,
  - HCO_3^- 4 mEq/L.
- AG = 21 = (140 – (Cl^- + CO_2)
- *Delta AG* = 9 = (21-12)
- *Delta* HCO_3^- = 23 = (27-4)
- *Delta* (HCO_3^-) gap = -14 = *delta AG – delta* HCO_3^-

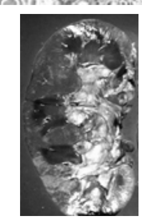
Her anion gap is up, but not off the chart.

The bicarbonate gap is off.

Renal Tubular Acidosis

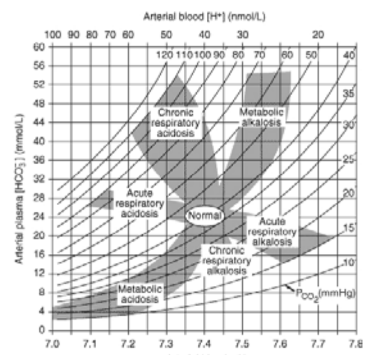
- In other words, her HCO_3^- is significantly reduced at -14 mEq/L.
  - That is 14 mEq/L lower than would be expected given her excess anion gap of 8
- Were this a simple 'one cause' acidosis, the acid causing her drop in pH should have lowered her CO_2 to only about 19 mEq/L.
- The fact that her CO_2 is actually 5 mEq/L means there must an additional reason for her acidosis.
- In this case, it's a hyperchloremic metabolic acidosis, which is commonly seen with renal failure.
- She has two renal related problems.
  - Uremia from kidney failure causing the elevated AG.
  - Tubular related problem of HCO_3^- recovery and acid secretion, which leads to a non-ion gap acidosis with hyperchloremia.





Summing it up

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



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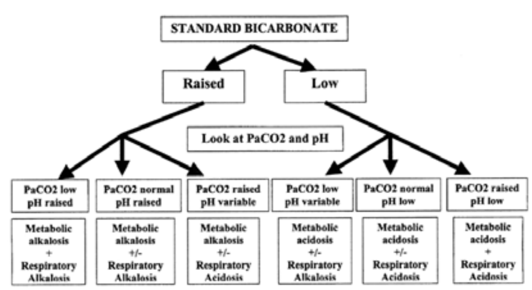

The End