Three Different Mechanisms that Act in the Following Order:

- 1st Day-to-Day Production/Consumption and Acquisition/Loss of Acids/Bases (in general there is a constant production of acid)
  - Acids: CO_2 from Complete Aerobic Respiration of Glucose, Ketoacids/Lactate from Incomplete Aerobic Respiration of Glucose, Sulfuric and Phosphoric Acids from Metabolism of Amino Acids, et al
  - Bases: HCO_3^- loss into Stool, et al
- 2nd Disturbances in pH are acutely reversed with buffers
  - Extracellular Buffers: CO_2 (CO_2 is an acid b/c the direction of this buffer is more to the right) $CO_2 + H_2O$ ⇔>>> H_2CO_3 ⇔>>> $HCO_3^- + H^+$
  - Intracellular Buffers: Proteins like Hb (Protein is an acid b/c the direction of this buffer is more to the right) Protein-H ⇔>>> H^+ + $Protein^-$
- 3rd The lung/kidney returns the acid/base disturbance back to normal (in general there is a constant removal of acid)
  - Lung: Regulates the Expiration of pCO_2 (ACID)
  - Kidney: Regulates the Reclamation (not exactly reabsorption b/c the molecule is technically different, usually 99% reclamed) of filtered HCO_3^- (BASE) via Carbonic Anhydrase and Na^+/H^+ Antiporter System at PCT AND Regulates the of secretion of H^+ (ACID) via K^+/H^+ antiporter at CD via binding to Ammonia produced by PCT and filtered SO_4/PO_4/Creatinine System forming Ammonium/H_2SO_4/H_3PO_4/H-Creatinine in CD lumen
    - NB In RF nothing is filtered and when it is there is a combination of all RTAs where you can't reclame HCO_3^- or secrete H^+ therefore metabolic acidosis

Henderson-Hasselbach Equation

$$pH = pKa + \log \frac{[HCO_3^-]}{(0.3P_aCO_2)} = 6.1 + \log \frac{24}{0.3(40)} = 7.40$$

(Punch in the numbers to see if the ABG/BMP is accurate)

<u>Assessing Acid-Base Status</u>

There are three different approaches to acid-base:

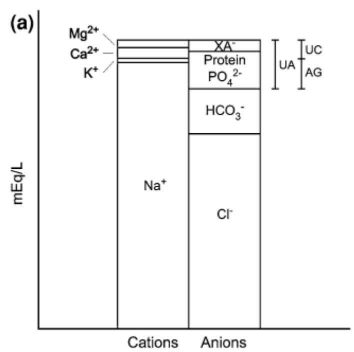
- Boston (approach below)
- Stewart (used by Intensivists/Anesthesiologist which looks at unusual parameters like SID)
- Copenhagen (used by Surgeons/Anesthesiologists which looks at Base Excess)

- (1) Look at pH
  - Acidemic (<7.35) vs Alkalemic (>7.45)
  - NB If pH is w/in normal limits this is not to say that everything is normal and that there are no acid-base disorders going on. There could be two simultaneous primary opposite disorders of different systems (metabolic and respiratory) or two metabolic disorders that cancel each other out. Hence look at (2)
- (2) Look at $[HCO_3^-]$ from venous blood BMP and pCO_2 from ABG to determine which one is causing the pH disturbance b/c one should reflect the pH and the other should reflect a compensation
  - $[HCO_3^-]$ = 22-26 mmol/L, Met Alkalosis: ↑ $[HCO_3^-]$ vs Met Acidosis: ↓ $[HCO_3^-]$
  - pCO_2 = 35-45 mm of Hg, Resp Acidosis: ↑ pCO_2 vs Resp Alkalosis: ↓ pCO_2
  - NB If each is in a different direction then two simultaneous primary same disorders (primary metabolic acidosis/alkalosis and primary respiratory acidosis/alkalosis) are occurring such that in the end there is a double disturbance
  - NB If both are w/in normal limits this is not to say that everything is normal and that there are no acid-base disorders going on rather there could be two simultaneous primary opposite disorders of the same system (metabolic only b/c you can't have both resp acidosis and resp alkalosis) that cancel each other out
- (3) Calculate what the other parameter should be after compensation kicks in using the following equations:

Primary Disturbance	**Secondary Compensation Calculation**	**Time**
Metabolic Acidosis	For every 1 ↓ in $[HCO_3^-]$ there is a 1.25 ↓ in pCO_2 (pCO_2 should be last two digits of pH)	<1d
Metabolic Alkalosis	For every 1 ↑ in $[HCO_3^-]$ there is a 0.75 ↑ in pCO_2	<2d
Acute Respiratory Acidosis	For every 1 ↑ in pCO_2 there is a 0.1 ↑ in $[HCO_3^-]$	Min-Hrs
Chronic Respiratory Acidosis	For every 1 ↑ in pCO_2 there is a 0.3 ↑ in $[HCO_3^-]$	Days
Acute Respiratory Alkalosis	For every 1 ↓ in pCO_2 there is a 0.2 ↓ in $[HCO_3^-]$	Min-Hrs
Chronic Respiratory Alkalosis	For every 1 ↓ in pCO_2 there is a 0.5 ↓ in $[HCO_3^-]$	Days

  - NB Compensation is NEVER perfect i.e. they never bring pH back to normal hence that is how you know that you have an acid/base disturbance
- (4) Compare expected calculated compensation with the measured value
  - Normal Compensation (you have one primary problem with a normal compensation)
  - Over Compensation (you have another primary problem opposite to the first primary problem and in this scenario many times the pH is normal but $[HCO_3^-]$ and pCO_2 are not normal)
    - Primary Metabolic Acidosis + Primary Respiratory Alkalosis
    - Primary Metabolic Alkalosis + Primary Respiratory Acidosis
  - Under Compensation (you have another primary problem contributing to the first primary problem)

        - Primary Metabolic Acidosis + Primary Respiratory Acidosis
        - Primary Metabolic Alkalosis + Primary Respiratory Alkalosis
- (5) Other useful calculations depending on disturbance
    - (A) If MAc then calculate serum AG = $[Na^+] - ([Cl^-] + [HCO_3^-])$ = measured cations (MC) – measured anions (MA) ~ unmeasured anions (UA) – unmeasured cations (UC)
        - High AG (>12mEq/L)
            - increase in an unmeasured anion (**increase in endogenous (Lactate/Ketones/Other) or exogenous (Ingestants) organic non-Cl anion acids, hyperPO4, hyperalbuminemia**) resulting in an increase in a measured cation (Na)
            - decrease in a unmeasured cation (**hypoCa, hypoMg, hypoK**) resulting in a decrease in a measured anion (Cl, HCO_3)
        - Normal AG (~8mEq/L)
        - Low AG (<4mEq/L)
            - increase in an unmeasured cation (**hyperCa, hyperMg, hyperK**) resulting in an increase in a measured anion (Cl, HCO_3)
            - decrease in an unmeasured anion (**decrease in endogenous (rare) organic non-Cl anion acids, hypoPO4**, **hypoalbuminemia** therefore always correct AG for albumin: $AG_{corrected}$ = AG + ¼[4 – albumin]) resulting in a decrease in a measured cation (Na)



    - (B) If AGMAc then Calculate "delta+delta" = $\Delta AG + \Delta HCO_3^-$ = determines if an additional metabolic acid-base disturbance exists (for every 1mEq of non-Cl acid added to circulation a 1mEq of HCO_3^- should be removed from circulation, if not 1:1 then some additional disturbance is accounting for the difference)
        - 0 = only an AGMA exists
        - + (less bicarb is being added) = AGMA + metabolic alkalosis
        - – (more bicarb is being removed) = AGMA + non-AGMA
    - Other: Actual Base Excess Calculated (ABE_C) if you take a pt and make their pCO2 40mm Hg the amount of acid/base you have to add to make their pH 7.4 is there ABE_C
        - – = add base
        - + = add acid

	Decreased Ventilation	Increased Ventilation
Brainstem	• Drug Induced (Opiates, Anesthetics, other sedatives) • Oxygen administration in acute hypercapnia • Central Sleep Apnea • Lesions (Tumors, Infarcts, Trauma) • Metabolic (hypoTH)	• Any Primary CNS Process • Hypoxia • Pain/Anxiety (catecholamines) • Sepsis (cytokines) • Pregnancy (progesterone) • Liver Disease (nitrogenous toxins like NH3) • Medication (salicylates) • Metabolic (hyperTH)
NM	• Myopathy, NM Jxn Disease, Peripheral Nerve Dz, Radiculopathy/Plexopathy, Myelopathy (refer) esp Phrenic Nerve Paralysis from cardiac surgery, GBS, MG, damage to above C3-5 from trauma "3,4,5 keeps the diaphragm alive", • HypoPO4, HypoK • Pickwickian Syndrome (obesity induced hypoventilation)	• Seizure?
Lung	• Parenchyma (pneumonia, pulm edema, restrictive lung dz, et al) • Airway (obstructive lung dz, laryngobronchospasm, OSA, foreign body, et al) • Pleura (pneumothorax, pleural effusion, fibrosis, et al) • Thoracic Cage (obesity, pregnancy, ascites,	• Pulmonary Embolus • Pneumonia • Pulmonary Edema • Restrictive Lung Disease

	kyphoscoliosis, ankylosing spondylitis)	

	Respiratory Acidosis	Respiratory Alkalosis
Etiology	• Where is the problem? Brainstem/NM/Lung (refer above)	
S/S	• CNS (AMS, HAs, Irritability, Anxiety, Insomnia, Asterixis, Somnolence) • CV (Arrhythmias)	• CNS (AMS, Paresthesia esp Perioral Numbness (2/2 cerebral vasoconstriction due to low CO_2)) • CV (Arrhythmias)
Tx	• Treat Underlying Cause • Pulmonary Toilet • Mechanical Ventilation (you want to decrease pCO2 gradually b/c if rapid then neurologic problems including seizures/death)	• Treat Underlying Cause • Breath into a Paper Bag which contains Increasing Amounts of CO_2 which decreases diffusion gradient for CO_2 from venous blood to air thus decreasing alkalosis (this doesn't slow down your breathing just prevent too low CO_2) • Oxygen if hypoxic b/c can suppress resp drive

Metabolic Acidosis

- S/S
  - CNS (AMS)
  - Pulm (Compensatory Hyperventilation w/ Kussmual Hyperventilation aka deep and fast)
  - CV (Arrhythmias/CHF/Vasodilation)
  - Metabolic (Bone Breakdown and Protein Catabolism)
- Tx
  - correct underlying cause and specific treatments below
  - MV if fatigued
  - RRT if severe
  - keep pH<7.2 and HCO_3<8 w/ acute IV $NaHCO_3$ or chronic PO $NaHCO_3$ (NB tastes bad and causes belching so some use KCitrate, Italian Briasci Soda 1drink TID, Baking Soda 1/2tsp TID)

<u>AGMAc</u>

- **Lactic Acid**
  - L-LA
    - Type A (less oxidation of pyruvate and thus more conversion of pyruvate to lactate)
      - decreased oxygenation (cardiopulmonary failure w/ ischemia especially of bowel/limb, profound anemia, etc)
      - increased oxygen consumption (post-ictal, post-exertional, catechol excess, tumor, etc)
      - defect in oxygen utilization (1° **salicylate**, CO, CN, linezolid, NRTIs, metformin, tylenol, nitrates, etc)
        - Salicylates (early on there is a primary (seen usually in children) respiratory alkalosis 2/2 stimulation of CNS resp center followed by a primary (seen usually in adults) AG metabolic acidosis 2/2 lactic acid))
    - Type B (nl oxidation but there is failure of the liver to metabolize the small amount of lactate that is normally produced everyday 2/2 liver dz, renal dz, DM, cancer, salicylates, alcohols, iron, isoniazide, inborn errors of metabolism)
  - D-LA (short bowel syndrome results in metabolism of glucose by colonic bacteria to D-lactate which is absorbed into blood but not measured by standard lactate assays b/c normally in the human body D-LA is never produced therefore if suspected then specifically order a D-Lactate)
- **Ingestant Acid** (Osmolar Gap (OG) = (measured osmoles) – (2Na + Glu/18 + BUN/2.8)
  - OG > 15 therefore Toxic Alcohol Ingestion (check "Volatile Acid Panel" in urine, formic/carboxylic/oxalic acid in serum, calcium oxalate in urine, fluorascene (component of antifreeze) in urine/clothes w/ woods lamp, Tx: (1) saturate/inhibit alcohol dehgydrogenase w/ EtOH/Fomepizole, (3) Dialysis, (2) **F**olic Acid enhances metabolism of **F**ormic Acid in Methanol vs Thiamine/Pyridoxine/Mg enhances metabolism of Oxalic Acid in Ethylene Glycol)
    - **Methanol** (aka Wood Alcohol, Windshield Wiper Fluid, Paint Thinner) → **Formic Acid** → + "drunk", "snow storm" visual field changes, ab Sx (pain, N/V, pancreatitis)
    - **Ethyl Alcohol** (Regular Alcohol) → Aldehyde → **Carboxylic Acid** → ++ "drunk"
    - **Ethylene Glycol** (Antifreeze) → **Oxalic Acid** → +++ "drunk", precipitates w/ calcium (calcium oxalate) in kidneys causing renal failure, in heart/lung causing cardiopulmonary failure, and in other vital organs, hypocalcemia
    - NB Isopropanol (Rubbing Alcohol) → Acetone (not an acid) → ++++ "drunk", gastritis, asphyxia (BUT NO AGMA, included here b/c one of the three toxic alcohols)
  - OG < 10 therefore Medication Overdose
    - **Propylene Glycol** found in many drugs that are given IV like benzos, dilantin, abx, et al (converted to **Pyruvic Acid**)
    - **Acetaminophen** (glutathione depletion resulting in accumulation of **5-Oxoproline**)
- **Chronic Kidney Failure**
- **Keto Acid** (when there is low glucose in cells b/c of poor intake or low insulin, the liver converts FFAs into aceto-acetate (AcAc, measure in urine/plasma) and beta-hydroxy-butyrurate (B-OHB, cannot be measured) (NB AcAc + NADH ↔ B-OHB + NAD) where they are used as oxidative fuel by other organs esp heart/CNS)

- **Diabetic** KA (reduced cellular glucose intake) 3AcAc:1B-OHB
- **Starvation** KA (reduced oral glucose intake) 8AcAc:1B-OHB

<u>Non-AGMAc</u>

- GI Gain HCl/Equivalent (NH4-Cl, Lysine-Cl, Arginine-Cl) where H then binds HCO3 and is converted into water therefore increase in Cl and decrease in HCO3 hence nl AG
  - **Ingesting/Injecting** (TPN)
- GI Lose NaBicarb/Equivalent (Na-Lactate, Na-Citrate, Na-Acetate, Na-Butyrate) where there is an increase in Na and HCO3 hence nl AG
  - **Loss of Colon Contents** (Diarrhea, Fistulas, High Output Ostomies, Uretero-Intestinal Diversion aka Ileal Conduit (urine is diverted into the colon where it leads to increased GI reabsorption of chloride and GI secretion of bicarb))
- Impaired Kidney
  - **Acute Kidney Failure** (impaired acid filtering)
  - **RTAs** (impaired tubular function)
- Other
  - **Post Chronic Hypercapnea** (similar to hypocapnea below)
  - **Expansion Acidosis aka Volume Expansion aka Dilutional** (from rapid infusion of bicarb free IVF which has neutral pH of 7.0 hence in body it is "acidic")
- NB UAG reflects Urine NH4 but very inaccurate

Renal Tubular Acidosis (RTAs) "241"				
	Type II Proximal RTA		**Type IV Distal RTA (most common)**	**Type I Very Distal RTA**
Etiology For All: Idiopathic, Primary Congenital, s/p Renal Transplant, Tubulo-interstitial Dz	• Secondary Congenital (Fanconi's, Medullary Cystic Dz, Cystinosis, Tyrosinemia, Hereditary Fructose Intolerance, Galactosemia, Von Gierke's, Wilson's, Glycogen Storage Dz, Lowe Syndrome, etc) • Meds (Acetazolamide, Heavy Metals, Ifosfamide, Toluene, Streptozotocin, etc) • Paraprotein (Multiple Myeloma, Amyloidosis, etc) • Other (High PTH, Cancer, Nephrotic Syndrome, PNH, Congenital Heart Dz, etc)		(refer to potassium for low mineralocorticoid states)	• Secondary Congenital (Wilson's, Medullary Sponge Kidney, SCD, Fabry's, etc) • Meds (Amphotericin, Toluene, Analgesics, etc) • Autoimmune (Sjogren's, etc) • Other (Hypercalcuria, Cirrhosis, OP, etc)
Defect	Inability to reabsorb HCO_3^- at PCT		Defective ENaC at CD Principle Cells therefore decreased K+ secretion and thus H+ excretion	Defective K^+/H^+ Antiporter at CD Alpha-Intercalated Cells therefore decreased H+ excretion
Serum pH Serum HCO_3 Serum K	Moderate Acidosis Very Low HCO_3 (10-16) Low K (b/c Na goes w/ HCO3 to CD)		Mild Acidosis Low HCO_3 (16-22) High K	Severe Acidosis Very Very Low HCO_3 (<10) Low K
Urine pH $FeHCO_3$	<5.3 >15%		<5.3 <3%	>5.3 <3%
Treatment	You can't just give HCO_3 b/c the kidney will just rapidly excrete it out as its plasma levels increase above threshold therefore quite hard to treat as you must use more sophisticated approaches specifically you must volume contract with thiazide diuretics so that the kidney holds on to Na proximally and in turn reclames HCO_3, also replete K		Easy to Tx just give HCO_3/Aldo and decrease K	Easy to Tx just give HCO_3 and replete K NB Pt is usually asymptomatic until presenting w/ • Hypercalciuria (not sure if it is the cause or result of Type 1 RTA) and thus causing Nephrolithiasis and Medullary Calcifications aka Nephrocalcinosis • Hearing Problems • Cerebral Calcifications • Osteopetrosis

Metabolic Alkalosis

- S/S (much less well tolerated than metabolic acidosis)
  - CNS (AMS)
  - Pulm (Compensatory Hypoventilation)
  - CV (Arrhythmias/CHF/Vasoconstriction)

- Metabolic (hypoK/Ca/Mg/PO_4, shift in the oxyhemoglobin curve to the left such that Hgb is less willing to release oxygen to tissues, increased activity of intracellular enzymes requiring more ATP and thus more O_2)

- Tx
  - correct underlying cause and specific treatments below
  - MV if too much respiratory depression
  - RRT if severe
  - NS (if chloride sensitive) vs Aldactone/Diamox (if chloride resistant)
  - HCl
- Normally the kidneys have a large capacity to filter HCO_3 therefore for metabolic alkalosis to occur two events must occur: (1) There must be increased HCO_3 GENERATION and (2) the kidney must be impaired in its ability to handle the increased HCO_3 generation resulting in a MAINTAINED metabolic alkalosis (normally causes metabolic acidosis b/c normally there are more acids than bases that are filtered… but if a pt has increased HCO_3 production above in the presence of renal failure then metabolic alkalosis will occur)
  - GI Gain NaBicarb/Equivalent (Na-Lactate, Na-Citrate, Na-Acetate, Na-Butyrate)
    - **Ingest/Injecting** (baking soda, Milk-Alkali Syndrome ($CaCO_3$ supplements), IVF w/ bicarb, blood w/ citrate, TPN w/ acetate/glutamate, etc)
  - GI Loss HCl (NH4-Cl, Lysine-Cl, Arginine-Cl)
    - **Loss of Stomach Contents** (when pts are actively gastric suctioned, vomiting, etc large amounts of acid are removed and in addition there is volume depletion, hypokalemia, and loss of chloride into stomach which stimulates bicarb reclamation), Tx: H2B/PPI
  - Impaired Kidney
    - **Opposite RTA-2** (Volume Contraction, etc results in proximal absorption of Na and thus loss of H and thus reclamation of HCO3)
    - **Opposite RTA-4** (HyperAldo State, Increased Distal Delivery of Na as in chronic loop/thiazide diuretic use, etc)
    - **Opposite RTA-1** (Hypokalemia, etc)
  - Other
    - **Post Chronic Hypocapnea** (after long standing resp acidosis the kidneys have time to compensate by retaining HCO_3^-, when the resp disorder is acutely corrected as with mechanical ventilation the kidneys still retain HCO_3^- therefore you will have a transient alkalosis)
    - **Contraction Alkalosis aka Volume Depletion** (when a pt is on diuretics they are losing HCO_3^- poor fluid therefore when the blood "contracts" it contracts around a fixed amount of HCO_3^- resulting in an increase in [ ]) it is like pulling out neutral water which has a pH of 7.0 and in body that is considered "acidotic", in addition proximal tubule will absorb Na to absorb more volume but in doing so HCO_3 is absorbed and there is also stimulation of renin which leads to aldo and loss of H+ distally)
- NB diuretic use causes all of the "Opposite RTA" problems and "Contraction Alkalosis"
- NB GI Loss (volume contracted) VS GI Gain + Post Chronic Hypocapnea (non-volume contracted) hence assess volume status b/c some respond to fluids and others don't and since fluids are so easy to give why not just start there, instead of looking at FeNa to estimate volume status (as you would in other situations) you shouldn't in metabolic alklalosis b/c Na is altered and pulled into urine by HCO_3 spill over, hence you can look at Urine [Cl] or even FeUrea
  - Low Urine [Cl] <20mEq/L = volume contracted states = responds to fluids = Saline Responsive
  - High Urine [Cl] >20mEq/L = non-volume contracted states = does not respond to fluids = Saline Resistant