ACID-BASE BALANCE

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- Close regulation of pH is necessary for cellular enzymes and other metabolic processes, which function optimally at the normal pH.
- Chronic, mild derangements in acid-base status may interfere with normal growth and development,
- Acute, severe changes in pH can be fatal.
- Control of acid-base balance depends on the kidneys, the lungs, and intracellular and extracellular buffers.

Henderson-Hasselbach equation

- pH = pK + log (HCO3/H2CO3)

pK = 6.1 for H2CO3

Normal ratio of HCO3/H2CO3

= 20/1

Log 20 = 1.3

Normal pH =6.7 + 1.3 =7.4

Physiological Buffers

- Bicarbonate
- Non-bicarbonate

Bicarbonate buffer system

- Based on the relationship between carbon dioxide (CO_2) and bicarbonate (HCO_3^-):

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

Non-bicarbonate buffers

- Protein buffers
- Phosphate
- Bone

- **Protein buffers –**
  extracellular proteins - mostly albumin and intracellular proteins -including hemoglobin.
- **Phosphate buffers**:
  Phosphate can bind up to 3 hydrogen molecules, so it can exist as PO_4^{3-}, HPO_4^{2-}, or H_2PO_4. However, at a physiologic pH, most phosphate exists as either HPO_4^{2-} or $H_2PO_4^{1-}$. $H_2PO_4^{1-}$ is an acid, and HPO_4^{2-} is its conjugate base:
  $H_2PO_4^{1-} \leftrightarrow H^+ + HPO_4^{2-}$

- **Bone** is an important buffer.
- Bone is basic—it is composed of compounds such as sodium bicarbonate and calcium carbonate—and thus, dissolution of bone releases base.
- This can buffer an acid load, although at the expense of bone density, if this occurs over an extended period.
- In contrast, bone formation, by consuming base, helps to buffer excess base.

NORMAL ACID-BASE BALANCE

- The **lungs** and kidneys maintain a normal acid-base balance.
- Carbon dioxide generated during normal metabolism is a weak acid.
- The lungs prevent an increase in the partial pressure of CO_2(Pco_2) in the blood by excreting the CO_2that the body produces.
- CO_2production varies depending on the body's metabolic needs, increasing with physical activity.
- The rapid pulmonary response to changes in the CO_2concentration occurs via central sensing of the $Pco_2$and a subsequent increase or decrease in ventilation to maintain a normal Pco_2(35–45 mm Hg).
- An increase in ventilation decreases the Pco_2, and a decrease in ventilation increases the Pco_2.

- The **kidneys** excrete endogenous acid.
- The kidneys regulate the serum bicarbonate concentration by modifying acid excretion in the urine. This requires a 2-step process.
- First, the renal tubules resorb the bicarbonate that is filtered at the glomerulus.
- Second, there is tubular secretion of hydrogen ions.
- The urinary excretion of hydrogen ions generates bicarbonate that neutralizes endogenous acid production

Normal ABG values

- pH 7.35 – 7.45
- pCO2 35 – 45 mm Hg
- pO2 50 – 70 mm Hg
- HCO3 20 – 24 meq/L
- BE ± 5

Terminology

- Acidosis pH < 7.3
- Alkalosis pH > 7.5
- Hypercapnia paCO2 > 50 mmHg
- Hypocapnia paCO2 < 30 mmHg
- Hypoxia pO2 < 50 mm Hg
- Hyperoxia pO2 > 70 mm Hg

- The **plasma anion gap** is useful for evaluating patients with a metabolic acidosis.
- Anion gap = $[Na^+] - [Cl^-] - [HCO_3^-]$
- A normal anion gap is 4–11.
- The anion gap is the difference between the measured cation (sodium) and the measured anions (chloride + bicarbonate).
- The anion gap is also the difference between the unmeasured cations (potassium, magnesium, calcium) and the unmeasured anions (albumin, phosphate, urate, sulfate).
- An increased anion gap occurs when there is an increase in unmeasured anions.

Calculated values

- Buffer Base (BB)
  48-50 mmol/L
  Hb(25%),HCO3(50%),Proteins(25%)
- Base Excess(ABE , SBE)
  ± 5 mmol/L

Simple disorder

Disorder	pH	pCO2	HCO3
Metabolic acidosis	↓	↓	↓
Metabolic alkalosis	↑	↑	↑
Resp. acidosis	↓	↑	↑
Resp. alkalosis	↑	↓	↓

Compensatory mechanisms

- Respiratory
  Renal effect on bicarbonate
- Metabolic
  Respiratory effect on CO2

Metabolic Acidosis

There are many causes of a metabolic acidosis which occur via 3 basic mechanisms:

- Loss of bicarbonate from the body
- Impaired ability to excrete acid by the kidney
- Addition of acid to the body (exogenous or endogenous)

Causes of Metabolic Acidosis

- ***NORMAL ANION GAP***
  - Diarrhea
  - Renal tubular acidosis (RTA)
  - Distal (type I) RTA (MIM 179800/602722/267300)[*]
  - Proximal (type II) RTA (MIM 604278)[†]
  - Hyperkalemic (type IV) RTA (MIM 201910/264350/177735/145260)[‡]
  - Urinary tract diversions
  - Posthypocapnia
  - Ammonium chloride intake

- ***INCREASED ANION GAP***
  - Lactic acidosis
    - Tissue hypoxia (shock, hypoxemia, severe anemia)
    - Liver failure
    - Malignancy
    - Intestinal bacterial overgrowth
    - Inborn errors of metabolism
    - Medications (nucleoside analogues, metformin)

- Ketoacidosis
  - Diabetic
  - Starvation
  - Alcoholic
- Kidney failure
- Poisoning
  - Ethelene glycol
  - Methanol
  - Salicylate
  - Paraldehyde
  - Toluene
- Inborn errors of metabolism

Causes of Metabolic Alkalosis

- ***CHLORIDE RESPONSIVE (URINARY CHLORIDE < 15 mEq/L)***
  - Gastric losses (emesis or nasogastric suction)
  - Diuretics (loop or thiazide)
  - Chloride-losing diarrhea (MIM 214700)
  - Chloride-deficient formula
  - Cystic fibrosis (MIM 219700)
  - Post-hypercapnia

CHLORIDE RESISTANT (URINARY CHLORIDE > 20 mEq/L)

- High blood pressure
  - Adrenal adenoma or hyperplasia
  - Glucocorticoid-remedial aldosteronism (MIM 103900)
  - 17α-hydroxylase deficiency (MIM 202110)
  - Renovascular diseaseRenin-secreting tumor
  - 11β-hydroxylase deficiency (MIM 202010)
  - Cushing syndrome
  - 11β-hydroxysteroid dehydrogenase deficiency (MIM 218030)
  - Licorice ingestion
  - Liddle syndrome (MIM 177200)
- Normal blood pressure
  - Gitelman syndrome (MIM 263800)
  - Bartter syndrome (MIM 602023/607364/602522/241200/601678)
  - Autosomal dominant hypoparathyroidism (MIM 146200)
  - Base administration

Causes of respiratory alkalosis

- **HYPOXEMIA OR TISSUE HYPOXIA**
  - Pneumonia
  - Pulmonary edema
  - Cyanotic heart disease
  - Congestive heart failure
  - Asthma
  - Severe anemia
  - High altitude
  - Laryngospasm
  - Aspiration
  - Carbon monoxide poisoning
  - Pulmonary embolism
  - Interstitial lung disease
  - Hypotension

- **LUNG RECEPTOR STIMULATION**
  - Pneumonia
  - Pulmonary edema
  - Asthma
  - Pulmonary embolism
  - Hemothorax
  - Pneumothorax
  - Respiratory distress syndrome (adult or infant)

- **CENTRAL STIMULATION**
  - Central nervous system disease
    - Subarachnoid hemorrhage
    - Encephalitis or meningitis
    - Trauma
    - Brain tumor
    - Stroke
  - Fever
  - Pain
  - Anxiety (panic attack)
  - Psychogenic hyperventilation or anxiety
  - Liver failure
  - Sepsis
  - Pregnancy
  - Medications
    - Salicylate intoxication
    - Theophylline
    - Progesterone
    - Exogenous catecholamines
    - Caffeine
  - Mechanical ventilation
  - Hyperammonemia
  - Extracorporeal membrane oxygenation or hemodialysis

Causes of respiratory acidosis

- **CENTRAL NERVOUS SYSTEM DEPRESSION**
  - Encephalitis
  - Head trauma
  - Brain tumor
  - Central sleep apnea
  - Primary pulmonary hypoventilation (Ondine curse)
  - Stroke
  - Hypoxic brain damage
  - Obesity-hypoventilation (Pickwickian syndrome)
  - Increased intracranial pressure
  - Medications
    - Narcotic
    - Barbiturates
    - Anesthesia
    - Benzodiazepines
    - Propofol
    - Alcohols

DISORDERS OF THE SPINAL CORD, PERIPHERAL NERVES, OR NEUROMUSCULAR JUNCTION

- Diaphragmatic paralysis
- Guillain-Barré syndrome
- Poliomyelitis
- Spinal muscular atrophies
- Tick paralysis
- Botulism
- Myasthenia
- Multiple sclerosis
- Spinal cord injury
- Medications
  - Vecuronium
  - Aminoglycosides
  - Organophosphates (pesticides)

RESPIRATORY MUSCLE WEAKNESS

- Muscular dystrophy
- Hypothyroidism
- Malnutrition
- Hypokalemia
- Hypophosphatemia
- Medications
- Succinylcholine
- Corticosteroids

- **PULMONARY DISEASE**
  - Pneumonia
  - Pneumothorax
  - Asthma
  - Bronchiolitis
  - Pulmonary edema
  - Pulmonary hemorrhage
  - Adult respiratory distress syndrome
  - Respiratory distress syndrome, neonatal
  - Cystic fibrosis
  - Bronchopulmonary dysplasia
  - Hypoplastic lungs
  - Meconium aspiration
  - Pulmonary thromboembolus
  - Interstitial fibrosis

- **UPPER AIRWAY DISEASE**
  - Aspiration
  - Laryngospasm
  - Angioedema
  - Obstructive sleep apnea
  - Tonsillar hypertrophy
  - Vocal cord paralysis
  - Extrinsic tumor
  - Extrinsic or intrinsic hemangioma
- **MISCELLANEOUS**
  - Flail chest
  - Cardiac arrest
  - Kyphoscoliosis
  - Decreased diaphragmatic movement due to ascites or peritoneal dialysis