ELECTROLYTE REVIEW

I. Definition

Electrolytes are molecules capable of a carrying an electric charge, an ion. Electrolytes are essential to maintaining the body's ability to function and maintain homeostasis.

Electrolyte function is based on maintaining proper concentrations of each ion, in its proper balance. This balance can change quickly and have severe consequences for a patient if this balance is not stabile.

The Chemistry laboratory plays a primary role in reporting the status of these in vivo systems.

II. Classification

1. Anion – carry a negative charge and move toward the anode.
   Examples: Chloride, Bicarbonate, Phosphate, Lactate
2. Cation – carry a positive charge and move toward the cathode.
   Examples: Sodium, Potassium, Calcium, Magnesium

III. Function

1. Maintaining volume and osmotic balance: Sodium, Chloride, Potassium
2. Keeping myocardial rhythm and proper heart contraction: Potassium, Magnesium, Calcium
3. Active transport of intra/extra-cellular fluids (ATPase ion Pumps): Magnesium
4. Acid/Base balance: Bicarbonate, Potassium, and Chloride
5. Blood Coagulation: Calcium, Magnesium
6. Neuromuscular excitability: Potassium, Calcium, Magnesium
7. Glucose Metabolism: Magnesium, Phosphorous

IV. Water & Volume Stability

Water Balance

Normal plasma contains 93% water, with the remaining balance containing lipids and proteins. The concentrations of electrolytes in cells and in plasma must be maintained. This processes is regulated by active and passive transport.

Active transport requires energy to move electrolytes across cell membranes. The ADPase-dependent ion pump utilizes magnesium during active transport.

Diffusion is the passive movement of electrolytes across a cell membrane due to brownian motion.

Regulation of Water

Osmosis is the flow of water across a semipermeable membrane such as a cell wall. Semipermealble membranes allow passage of some molecules and ions selectively into the cell and out of the cell.

Osmolality is the number of moles of particles per kilogram of water (the concentration of particles in a volume of water). It is clinically significant because its measurement indicates the level of water balance in the body (primarily regulated by sodium), mannitol toxicity, and renal ability.

If the water balance in vivo is low, the Osmolality will increase, initiating the secretion of ADH (antidiuretic hormone) from the hypothalamus to stimulate thirst and minimize renal water loss. This is the body's first mechanism used to maintain water balance in the body. The kidney's ability to form urine of greatly varying Osmolality also enables it to regulate solute concentration and hence the Osmolality of body fluids within narrow physiological limits, despite wide fluctuations in salt and water consumption.

Thirst is the first defense against hyperosmolality and hypernatremia.

Regulation of Blood Volume

Proper blood volume is essential to maintain blood pressure and ensure good distribution of elements to tissues and organs. Regulation of sodium and water are interrelated with blood volume. Volume depends on the integrated control of water and sodium balance by the water intake and output areas of the hypothalamus, the rennin-angiotensin-aldosterone system, atrial natriuretic factor, and renal function.

Hypothalamus: The portion of the brain beneath the thalamus and connected to the pituitary gland that secretes ADH to stimulate thirst and minimize renal water loss.

The Renin-Angiotensin-Aldosterone system responds to decreased blood volume, it is initiated by decreased renal blood flow and acts to increase retention of sodium and water by the renal tubules.

Atrial natriuretic factors (ANP, BNP, & CNP) are hormones secreted by the cardiac tissue in response to intravascular volume expansion to reduce blood pressure and plasma volume. Important in defending against salt-induced hypertension and congestive hear failure.

Laboratory Testing:

1. **Osmolality**: Measured in serum (Ref. Range: 275-295mOsmol/kg)
   or urine (Ref. Range: 300-900mOsmol/kg)

   Methodology: Freezing point depression, vapor pressure, manual calculation

   Osmolal Gap: The difference between the measured Osmolality and the calculated Osmolality. Indirectly indicates the presence of osmotically active substances other than sodium, urea, or glucose (ethanol, methanol, lactate).

Manual Formulas:

$$2\text{Na mmol/L} + \frac{\text{glucose mg/dL}}{20} + \frac{\text{BUN mg/dL}}{3}$$

-OR-

$$1.86\ \text{Na mmol/L} + \frac{\text{glucose mg/dL}}{18} + \frac{\text{BUN mg/dL}}{2.8} + 9$$

2. **BNP**: Measured in serum or plasma
   Methodology: Colorimetric, Electrochemilumineccence, Turbidmetric

V. Individual Electrolytes

1. **Sodium:** Most abundant cation in extracellular fluid (90%), for this reason it largely determines the Osmolality of the plasma and is integral in water balance and blood volume. Active transport through the ATPase-ion pump maintains the sodium concentration in the plasma by removing it from inside cells. Na+ levels are regulated primarily by water intake, water excretion, and blood volume.

   Clinical Significance: Sodium intake comes from food sources and reabsorption from the kidney. Sodium output is through GI tract, skin, and urine. Intake and output are closely regulated by active transport.

   Hypernatremia – An increase in sodium levels. Sodium intake exceeds sodium output. This condition can be due to cardiac failure, liver disease, renal disease, hyperaldosteronism, pregnancy. Increase in sodium is usually associated with edema.

Hyponatremia – A decrease in sodium levels. Sodium output exceeds sodium intake. Condition can be due to GI tract losses (vomiting, diarrhea), excessive sweating (fever), renal disease (decreased absorption), hypoaldostronism, diuretic therapy, DM.

Methodology: ISE (Ion Selective Electrode)

Reference Ranges:	Serum	135-145mmol/L
	Urine	40-220mmol/L

2. **Potassium:** The major intracellular cation in the body, 20% greater concentration inside cells than in plasma. Potassium regulates neuromuscular excitability (heart contraction), intracellular fluid volume, and hydrogen ion concentration. Excess potassium is excreted in urine in order to maintain proper intra- and extracellular levels.

Clinical Significance: Potassium ion concentration has a major effect on the contraction of cardiac muscles. Elevated K+ slows the heart rate. A decrease in the potassium increases myocardial excitability and causes arrhythmia. The heart may cease to contract in extreme cases of either hyper- or hypokalemia.

Hypokalemia - Low serum potassium. As the body loses K+, Na+ and H+ move into the cell. Hydrogen ion loss from the ECF causes alkalosis. Low levels are due to diuretics, insulin activity, decreased magnesium.

Hyperkalemia – High serum potassium. High levels are due to renal insufficiency, DM, metabolic acidosis.

Methodology: ISE
Proper specimen handling is a must.

Reference Ranges:	Serum/Plasma	3.4-5.0mmol/L
	Urine	25-125mmol/24hr

3. **Chloride**: Cl- is the major extracellular anion. Helps to maintain Osmolality, blood volume, and electric neutrality. Chloride ions shift secondary to Na+ or bicarbonate ions. Chloride ions are filtered and reabsorbed by the kidney with excess levels excreted in urine and sweat.

Chloride acts to maintain electric neutrality in two ways:

a. As the rate-limiting component in sodium reabsorption in the proximal tubules. Na+ is reabsorbed in conjunction with Cl- in order to maintain proper pH balance.

b. Chloride Shift: An exchange of Cl- in serum for HCO3-.

Carbon dioxide is generated by cellular metabolism of oxygen. CO_2 diffuses into the plasma and RBC. In the RBC, CO_2 forms carbonic acid (H_2CO_3), which splits into H+ and HCO_3^- (bicarbonate).

$$H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$$

Hemoglobin acts to buffer the Hydrogen ion concentration:

$$H_2CO_3 \rightleftharpoons HCO_3^- + H^+ \longrightarrow HHb^+ + O_2 \longrightarrow HbO_2$$

The HCO_3^- formed in the RBC, as a result of H+ uptake by the Hemoglobin (Hb), diffuses out of the RBC and into the plasma. To preserve the neutrality of the RBC, Cl- diffuses into the RBC from the plasma. As a result, venous blood has a lower concentration of Cl- than arterial blood. When CO_2 is expelled from the lungs, the Cl- shifts back to the plasma.

Hypochloremia: Low chloride levels. May occur with excessive loss of chloride from vomiting, diabetic ketoacidosis, aldosterone excess renal disease, and also metabolic alkalosis and compensated respiratory acidosis.

Hyperchloremia: High chloride levels. May occur with excessive loss of bicarbonate ion.

Methodology: ISE

Reference Ranges:		
	Plasma/Serum	98-106mmol/L
	Urine	110-250mmol/L

4. **Bicarbonate:** The second most abundant anion in the ECF. It is the major component of the buffering system in the blood and is derived from CO_2. Bicarbonate diffuses out of the RBC in exchange for chloride to maintain ionic charge neutrality. 85% of bicarbonate ion is reabsorbed by the kidney.

Metabolic acidosis leads to a *decrease* in bicarbonate ion when it combines with H+ to form CO_2, which is then exhaled from the lungs.

Metabolic alkalosis leads to an *increase* in bicarbonate ion, which is excreted from the kidney to correct pH.

Methodology: CO_2: ISE, Colorimetric
HCO_3^-: ISE

Reference Ranges:		
CO_2	Plasma/Serum	22-29mmol/L
HCO_3^-	Heparin Syringe (Arterial)	22-26mmol/L

5. **Magnesium:** Magnesium is an essential activator of >300 enzymes, including those involved in glycolysis, ion transport, muscle contraction. Magnesium is an essential component of chlorophyll and is similar in structure and function to the iron component of hemoglobin.

Magnesium is supplied through diet and reabsorbed through small intestine.

Relative distribution in the body:

Relative distribution in the body:	53%	Bone
	46%	Muscle, liver, heart
	1%	Blood, ECF

Circulating forms of Magnesium:	24%	Protein Bound
	10%	Complex Bound
	66%	Ionized Form

Hypomagnesemia usually results from decreased intake - malnutrition or increased loss - GI disorders, diuretics. In cardiac disorders low magnesium can cause a AMI.

Hypermagnesemia is usually due to medications or renal failure. Magnesium is used in the treatment of hypertension during pregnancy (preeclampsia) to reduce preterm labor.

Methodology: Atomic absorption spectrophotometry and Colorimetry
Proper specimen handling is a must.

Reference Ranges: Plasma/Serum 1.6-2.4 mg/dL

6. **Calcium**: Calcium is essential for myocardial contraction. Appropriate calcium concentrations promote good cardiac output and maintain adequate blood pressure. Maintaining normal ionized calcium in blood is critical during surgery and in critically ill patients.

Distribution:	99%	Bone
	1%	Blood, ECF

Circulating forms of Calcium:	45%	Free Calcium Ions
	40%	Bound to protein (albumin)
	15%	Bound to anions

In acute disorders, this distribution can change dramatically.

Regulated by three hormones that alter their secretion rate in response to ionized Ca+:

1. Parathyroid hormone (PTH) – In response to ***hypocalcemia***, PTH is secreted and affects the bone and kidney. In bone, PTH stimulates oseoclasts to break down bone and release calcium into the ECF. In the kidney, PTH conserves

calcium by increasing tubular reabsorption and stimulates renal production of active vitamin D.

2. Vitamin D – Increases calcium absorption in the intestine and enhances the effect of PTH on bone.

3. Calcitonin – Secreted in response to ***hypercalcemia***. Calcitonin lowers calcium by inhibiting the action of PTH and Vitamin D.

Calcium testing is also used to evaluate hyperparathyroidism, malignancy, renal disease, and pancreatitis.

Methodology: ISE (Ionized Calcium)
Atomic adsorption spectrophotometry and Colorimetric

Reference Ranges:	Plasma/Serum	8.7-10.2 mg/dL
	Urine	50-300 mg/day
	Ionized Calcium	4.6-5.3 mg/dL

7. **Phosphate**: Compounds containing phosphates are widely distributed in living cells, including DNA, RNA, ATP, co-enzymes. They also participate in many important biochemical processes including release of oxygen from hemoglobin. Phosphate is the predominant intracellular anion.

Regulated by dietary intake, intestinal absorption and renal excretion or reabsorption. Disturbances in any of these processes can alter phosphate concentration. The loss of kidney function also has a profound effect on phosphate levels. Parathyroid hormone (PTH) can lower phosphate concentration by increasing renal excretion.

Distribution: 80% Bone
20% Circulating & Intracellular

Circulation: Predominantly as organic phosphate
Small percent as inorganic phosphate

Hypophosphatemia: Primarily caused by a shift of phosphate into cells that can deplete phosphate in the blood. Once phosphate is inside the cell, it remains there to be used in the synthesis of phosphorylated compounds. This condition can be caused by infusion of dextrose solution, use of antacids that bind phosphate, or alcohol withdrawal.

Hyperphosphatemia: Usually due to increased intake but can also be due to increased cell breakdown from severe infection, intensive exercise, or neoplastic diseases.

Methodology: Photometric

Reference Ranges:	Serum/Plasma	2.7-4.5 mg/dL
	Urine	0.4-1.3 g/day

8. Lactate

Aerobic glycolysis produces pyruvate. Lactate is involved in anaerobic glucose metabolism in the absence of normal aerobic conditions. The conversion of pyruvate to lactate is activated when a deficiency of oxygen leads to excess NADH during glycolysis.

Clinical Importance:

Lactate is a by-product of anaerobic metabolism, so it is not specifically regulated. As oxygen decreases in the tissues, lactate concentration rises rapidly. This indicates tissue hypoxia (even earlier than pH levels). Therefore lactate is performed in the lab on a stat basis or POC.

Lactate is removed from the circulation by the liver by Gluconeogenesis.

Methodology: ISE, Enzymatic, Electronic Impedance

Reference Ranges:	Venous blood	0.5-2.2 mmol/L
	Arterial blood	0.5-1.6 mmol/L
	CSF	0.6-2.2 mmol/L

9. Anion Gap

Routine analysis of electrolytes generally involves Na+, K+, Cl-, & HCO3- (as CO2). The values obtained can be used to calculate the anion gap or the estimate of of unmeasured anions and cations.

Calculations: NA+ - (CL- + HCO3-)

- OR -

(NA+ + K+) - (Cl- + HCO3-)

Reference Range: 5-15 mmol/L