CLINICAL LABORATORY TESTING:
BLOOD CHEMISTRY & CBC ANALYSIS
FROM A FUNCTIONAL MEDICINE PERSPECTIVE

Part 4 of 8
Electrolytes, Minerals, and Acid-Base

Dr. Wayne Sodano, DC, DABCI, DACBN, CIHP, BCTN
Director of Clinical Support & Education, Evexia Diagnostics, Inc.
Electrolytes, Minerals, and Acid-Base

Laboratory tests for evaluation of disorders of renal, water, electrolyte, and acid-base are the most common procedures performed in clinical chemistry laboratories (The Metabolic Panel)

Proper interpretation of laboratory tests of renal, electrolyte, and acid-base disorders requires an understanding of the physiology and pathophysiology of these systems
Minerals such as magnesium, calcium, and phosphate are frequently discussed in the context of the endocrine system because of the effects of vitamin D, and parathyroid hormone on the regulation of these minerals.

Acid-Base: The maintenance of normal body pH is required for the normal functioning of the organs.
Accumulation of Acid Substances in the Body

When the body’s internal environment becomes acidified, deleterious effects on the biochemical systems of the body can ensue:

- reduced enzyme activity
- mineral loss and demineralization of the bone
- inflammation and tissue irritability due to the corrosive nature of acids

– all of which lead to illness.
# Electrolytes and Serum Anion Gap

Anion gap = (Na +K) – (Cl + HCO3) or Na – (Cl + HCO3)

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Age</th>
<th>Reference Range</th>
<th>Optimal Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium (Na⁺)</td>
<td>Adult</td>
<td>136 – 142 mEq/L</td>
<td>Same</td>
</tr>
<tr>
<td>Potassium (K⁺)</td>
<td>Adult</td>
<td>3.8 – 5.0 mEq/L</td>
<td>4 – 4.6</td>
</tr>
<tr>
<td>Chloride (Cl⁻)</td>
<td>Adult</td>
<td>95 – 103 mEq/L</td>
<td>99 - 103</td>
</tr>
<tr>
<td>Carbon dioxide as bicarbonate</td>
<td>Adult</td>
<td>23 – 30 mEq/L</td>
<td>26 - 31</td>
</tr>
<tr>
<td>Anion Gap</td>
<td>Adult</td>
<td>10 – 20 mEq/L</td>
<td>8 – 12 mmol/L</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(K⁺ used)</td>
<td>(K⁺ not used)</td>
</tr>
</tbody>
</table>
Normal volumes and composition of electrolytes in various body fluid compartments are essential for maintenance of life.

The body fluid: the extracellular fluid compartment and the intracellular fluid compartment. Each compartment normally contains a different amount of the same electrolytes.
Normal Volume of Body Fluid Distribution (73 kg male)

<table>
<thead>
<tr>
<th>Fluid Type</th>
<th>Volume</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intracellular Volume</strong></td>
<td>24 liter</td>
<td>(60%)</td>
</tr>
<tr>
<td>(normally, more fluid is in the cells)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total Extracellular Volume</strong></td>
<td>16 liters</td>
<td>(40%)</td>
</tr>
<tr>
<td><strong>Extracellular (interstitial)</strong></td>
<td>11.2 liters</td>
<td>(28%)</td>
</tr>
<tr>
<td><strong>Extracellular (plasma)</strong></td>
<td>3.2 liters</td>
<td>(8%)</td>
</tr>
<tr>
<td><strong>Extracellular (*transcellular)</strong></td>
<td>1.6 liters</td>
<td>(4%)</td>
</tr>
</tbody>
</table>

* Transcellular fluid: lumen of GI; fluids in the CNS; eye fluid; serous fluid
## Electrolyte Concentrations in Extracellular and Intracellular Fluids

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Plasma (mEq/L)</th>
<th>Interstitial (mEq/L)</th>
<th>Intracellular Water (mEq/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na⁺</td>
<td>140</td>
<td>145.3</td>
<td>13</td>
</tr>
<tr>
<td>K⁺</td>
<td>4.5</td>
<td>4.7</td>
<td>140</td>
</tr>
<tr>
<td>Ca²⁺</td>
<td>5.0</td>
<td>2.8</td>
<td>1 x 10⁻⁷</td>
</tr>
<tr>
<td>Mg²⁺</td>
<td>1.7</td>
<td>1.0</td>
<td>7.0</td>
</tr>
<tr>
<td>Cl⁻</td>
<td>104</td>
<td>114.7</td>
<td>3</td>
</tr>
<tr>
<td>HCO₃⁻</td>
<td>24</td>
<td>26.5</td>
<td>10</td>
</tr>
<tr>
<td>Bicarbonate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SO₄²⁻</td>
<td>1.0</td>
<td>1.2</td>
<td>107</td>
</tr>
<tr>
<td>Sulfate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phosphorus</td>
<td>2.1</td>
<td>2.3</td>
<td>107</td>
</tr>
<tr>
<td>Protein</td>
<td>1.5</td>
<td>8</td>
<td>40</td>
</tr>
<tr>
<td>Organic anions</td>
<td>5</td>
<td>5.6</td>
<td>10</td>
</tr>
</tbody>
</table>
Disturbances in Water Balance and Electrolyte Balance = Disease and Dysfunction

One of the major causes of an aberrant fluid distribution in the body is significant body burden of endogenous (metabolic waste) and exogenous (environmental toxins) toxins.

A toxic body burden leads to a reduction in intracellular fluid volume and an increase in extracellular fluid volume. This is the body’s attempt to dilute the toxins that have accumulated in the interstitial space.
Reduced Intracellular Fluid Volume

Many illnesses may be a function of the body’s attempt to manage the increased amount of toxics that have accumulated and/or sequestered in the body.

A reduced intracellular fluid volume leads to cellular dysfunction and an increase in extracellular fluid volume leads to edema, inflammation, nervous tissue irritation, and an overall disturbance in interstitial...
Sodium: major cation in the extracellular fluid

- regulating water balance in the body
- maintaining electrical potential
- nerve transmission
- pH balance
- osmotic pressure
Sodium Regulation

Sodium balance is regulated by many factors such as aldosterone (produced by the adrenal glands), atrial natriuretic hormone/peptide (right atrium of the heart) and antidiuretic hormone (posterior pituitary gland).
Sodium and Water Regulation Receptors
Osmoreceptors and Baroreceptors

**Baroreceptors** are located in the carotid sinus, aortic arch, cardiac atria, hypothalamus, and the kidneys

**Osmoreceptors** are located in the hypothalamus, which when stimulated; cause the release of antidiuretic hormone, natriuretic peptides (atrial natriuretic peptide and brain natriuretic peptide) and the renin-angiotensin-aldosterone system
Increased Sodium (hypernatremia): Increased sodium intake, dehydration, Cushing syndrome and adrenal hyperfunction (decrease sodium loss), diuretics, excessive body water loss (e.g. gastrointestinal loss, excessive sweat, and diabetes insipidus), toxic body burden.

Decreased Sodium (hyponatremia): decrease sodium intake, increased sodium loss (Addison disease, diarrhea, vomiting, chronic renal insufficiency) underactive adrenal or thyroid gland

Changes in serum sodium most often reflect changes in water balance, rather than sodium balance
Potassium: Major intracellular cation

- Regulates muscle and nerve excitability and is an important electrolyte for cardiac function
- Controls intracellular volume
- Contributes to protein synthesis, enzymatic reactions, and carbohydrate metabolism

In acidic states, potassium tends to shift to the extracellular fluid causing an increase in serum potassium. The opposite is true in the alkaline state.
Increased serum potassium: excessive dietary intake, acidosis, dehydration, infection hemolysis, renal disease, low insulin, potassium sparing diuretics, NSAIDs, adrenal hypofunction, and dehydration

Decreased serum potassium: decreased dietary intake, licorice ingestion, alkalosis, diuretics, adrenal hyperfunction, corticosteroids and folic acid deficiency
Chloride: Major Extracellular Anion

Maintain electrical neutrality mostly as a salt with sodium

Primarily a passive physiological role: balances out the positive charges in the extracellular fluid and, by passively following sodium, helps to maintain extracellular osmolality

**Increased serum chloride:** adrenal hyperfunction, Cushing syndrome, metabolic acidosis, and dehydration

**Decreased serum chloride:** metabolic alkalosis, adrenal hypofunction, Addison disease diuretic therapy, vomiting, and diarrhea
Carbon Dioxide

Total carbon dioxide: (CO2) in solution or bound to proteins, bicarbonate (HCO3-), carbonate (CO32-), and carbonic acid (H2CO3).

In practice, **80 – 90% is present as bicarbonate**, and is a general guide to the body’s buffering capacity. Essentially, CO2 is primarily used as a rough guide for acid-base balance.

\[
\text{CO}_2 + \text{H}_2\text{O} \leftrightarrow \text{H}_2\text{CO}_3 \leftrightarrow \text{HCO}_3^- + \text{H}^+
\]

**Increased carbon dioxide**: severe vomiting, **metabolic alkalosis**, COPD, renal disorders, and alcoholism

**Decreased carbon dioxide**: **metabolic acidosis**, dehydration, diabetic ketoacidosis, chronic diarrhea, malabsorption syndrome, and starvation
Increased acidosis: increase in hydrogen ion concentration and decreased HCO3 concentration

**Anion Gap = Na+ - (Cl- + HCO3-) or (Na+ + K+) - (Cl- + HCO3-) Used to determine metabolic acidosis**

**Na + unmeasured cations = Cl + HCO3 + unmeasured anions**

<table>
<thead>
<tr>
<th>Major unmeasured cations</th>
<th>Major unmeasured anions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium</td>
<td>Plasma proteins (albumin)</td>
</tr>
<tr>
<td>Magnesium</td>
<td>Sulphate</td>
</tr>
<tr>
<td>Potassium</td>
<td>Phosphates</td>
</tr>
<tr>
<td>Gamma globulins</td>
<td>Lactate</td>
</tr>
<tr>
<td></td>
<td>Other organic anions</td>
</tr>
</tbody>
</table>
Although the term gap implies that there is a gap between cation and anion concentrations, the concentration of total cations in the serum is exactly equal to the concentration of total anions.

\[
AG = Na^+ - (Cl^- + HCO_3^-)
\]
The two slides must balance.
Increased Anion Gap: thiamine deficiency (Thiamine deficiency has been associated with metabolic acidosis.)

Nearly all metabolic acidosis results from reduction in bicarbonate content of the body.

Causes of metabolic acidosis include renal acidosis and extra-renal acidosis (e.g. gastrointestinal loss of bicarbonate, organic acidosis such as lactic acidosis, diabetic ketoacidosis, starvation, alcoholic ketoacidosis, acids precursors or toxins such as salicylate and acetaminophen)

Decreased Anion Gap: multiple myeloma, lithium toxicity
## Serum Calcium, Phosphorous, Magnesium and RBC Magnesium

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Age</th>
<th>Reference Range</th>
<th>Optimal Range</th>
</tr>
</thead>
</table>
| Total Calcium (bound and unbound)| Adult  | 9.2 – 10.5 mg/dL         | 9.4 – 10 mg/dL
                              |        | 2.35 – 2.5 mmol/L        | 2.35 – 2.5 mmol/L           |
| Calcium, Ionized                 | Adult  | 4.6 – 5.3 mg/dL          |                            |
| Phosphorous (P) Phosphate (PO₄)  | Adult  | 2.3 – 4.7 mg/dL          | 3.4 – 4.0 mg/dL
                              |        |                          | 1.10 – 1.30 mmol/L          |
| Serum Magnesium                  | Adult  | 1.6 – 2.4 mg/dL          | .82 – 1.23 mmol/L           |
                              |        | 1.3 – 2.1 mEq/L          | 2.0 – 3.0 mg/dL            |
| RBC-Mg                           | Adult  | 4.2 – 6.8 mg/dL          | 4.2 – 6.8 mg/dL
                              |        | 3.6 - 5.6 mEq/L          | 1.72 – 2.8 mmol/L          |
Serum Calcium

Serum calcium three forms:

- **Protein-bound calcium** - about 41%;

- **Ionized calcium - free fraction** - about 50% - which is diffusible through the capillary membrane;

- **Calcium complexed to anions**, such as citrate, phosphate, and bicarbonate - about 9% - which is not non-ionized is diffusible through the capillary membrane.

The ionic form of calcium is the physiologically active form, which is involved with bone formation and the functioning of the heart and nervous system.
Calcium’s actions include:

• neuronal excitation
• hormonal secretion (pancreatic insulin release and gastric hydrogen secretion)
• blood coagulation
• neurotransmitter release
• innate immunity
• muscle tone of smooth muscle cells of the vasculature, airways, uterus, gastrointestinal tract, and urinary bladder
Standard laboratory tests typically measure total serum calcium (bound and unbound/free), and do not report on ionized calcium unless ordered.

The measure total calcium value is affected by total protein concentration, particularly albumin.

Low albumin levels frequently correspond to low calcium levels, albumin testing should be included with serum calcium measurements since ionized calcium may be increased.

In general, low serum albumin (e.g. nephrotic syndrome, compromised liver function) will cause a drop in total serum calcium level.

**Corrected** $\text{Ca} = [0.8 \times (\text{normal albumin} - \text{patient's albumin})] + \text{serum Ca level}$. 
Increased Total Serum Calcium (hypercalcemia): Malignant tumors and hyperparathyroidism (the most common cause), osteomalacia associated with malabsorption, drugs (e.g. diuretics, estrogens, androgens, progestins, tamoxifen, and thyroid medication), renal disease, vitamin D and vitamin A intoxication, sarcoidosis (vitamin D effect produced by granulomatous infection)

Decreased Total Serum Calcium (hypocalcemia): low serum proteins (most common cause) malabsorption, hypoparathyroidism, gross vitamin D deficiency, low magnesium, and dietary deficiency
Phosphate is a major intracellular anion that is involved in the metabolism of proteins, lipids, and carbohydrates, and is a major component in phospholipid membranes, nucleic acids, nicotinamide diphosphate (an enzyme cofactor), cyclic adenine and guanine (second messengers), and phosphoproteins.

Phosphate also acts as an acid-base buffer and is involved in the production of ATP.
Serum Phosphorous (Phosphate)

Phosphate absorption is diminished when large amounts of calcium or aluminum (e.g. aluminum containing antacids) are present in the intestine due to the formation of insoluble phosphate compounds.

Phosphorus levels are determined by calcium metabolism, parathyroid hormone, vitamin D, renal excretion and intestinal absorption.

**Increased Phosphorous (hyperphosphatemia):** renal disease (decreased renal excretion – most common cause), vitamin D toxicity, sarcoidosis, bone metastasis, acidosis, and hypoparathyroidism

**Decreased Phosphorous (hypophosphatemia):** hypercalcemia, chronic antacid ingestion, alcoholism, vitamin D deficiency, and alkalosis
Serum Magnesium

Magnesium is involved in more than 300 - 350 essential metabolic reactions.

Required for energy production (ATP), numerous steps for the synthesis of nucleic acids and protein synthesis, and carbohydrate and lipid metabolism.

The Δ-6 desaturase enzyme required in the metabolism of fatty acids depends on magnesium.

Key cofactor in both methylation and sulfur amino acid metabolism, and involved in the production of glutathione (important antioxidant) and S-adenosylmethionine
Magnesium depletion is commonly associated with both type 1 and type 2 diabetes mellitus. Between 25 and 38% of people with diabetes have been found to have hypomagnesemia.”

Since only 1 to 2% of magnesium is present in the extracellular fluid, a better index of whole-body magnesium nutriture is assessing the intracellular content in red blood cells.

**Increased Magnesium (hypermagnesemia):** renal insufficiency (decreased excretion), ingestion of magnesium-containing antacids, and Addison disease

**Decreased Magnesium (hypomagnesemia):** malabsorption, malnutrition, alcoholism, and loop diuretics,
FHR shows LOW LEVELS OF MAGNESIUM

The Functional Health Report highlights out-of-range analytes and then provides a summary of possible health conditions related to the results in multiple summary areas like, Health Improvement Plan, Functional Index Report and Clinical Dysfunctions Report.

Here is an example of the summary, from a report with Low Magnesium levels, provided in the Health Improvement Plan section of the FHR.

The majority of magnesium is found inside the cell so measuring magnesium levels in the serum may not be the best way to assess for magnesium deficiency. That being said, an increased serum magnesium is associated with kidney dysfunction and thyroid hypofunction. A decreased magnesium is a common finding with muscle cramps.
Acid-Base and Acid-Base Disorders: Bicarbonate and CO2 Buffer System

Maintaining normal pH (i.e. acid-base balance) in the body is necessary for normal organ function.

The main organs involved in regulating and maintaining this balance are the lungs - CO2 excretion - and the kidneys - regulation of blood concentration of bicarbonate.

Bicarbonate and CO2 are considered the main buffers of the body, and their ratio is used to determine pH.
Acid-base physiology centers around maintaining the narrow range of the blood pH, which a pH of 7.38 to 7.44.

Deviations of blood pH, either above or below the set range, are termed alkalosis and acidosis, respectively.

Both alkalosis and acidosis can be categorized further in respiratory and metabolic components.
<table>
<thead>
<tr>
<th>Condition</th>
<th>pH</th>
<th>Analyte</th>
<th>Causes</th>
</tr>
</thead>
</table>
| Metabolic Acidosis  | ↓  | ↓HCO₃⁻      | Renal Acidosis: reduction in acid excretion  
Extra-renal acidosis: increase in net acid production  
• GI loss of bicarbonate  
• Organic acidosis – lactic acidosis (e.g. bowel dysbiosis)  
ketoacidosis (e.g. diabetes)  
• Ingestion of acid precursors/toxins – salicylate, acetaminophen |
| Metabolic Alkalosis | ↑  | ↑HCO₃⁻      | Loss of HCl from stomach – vomiting  
Ingestion of bicarbonate  
Increased renal excretion of acid – diuretic therapy, potassium depletion, secondary hypoparathyroidism |
| Respiratory Acidosis| ↓  | ↑CO₂        | Lung disease  
• COPD  
• Advanced interstitial lung disease  
Thoracic deformity or airway obstruction  
Diseases of respiratory muscle and nerves  
Depression of respiratory center |
| Respiratory Alkalosis| ↑  | ↓CO₂        | Pneumonia  
Pulmonary fibrosis  
Pulmonary congestion  
CNS lesions  
Drugs: salicylate, progesterone |
Monitoring Urinary pH
Ask the Doctor

A **FREE** service available to all Evexia clients, accessed via your Evexia Clinician Portal. Dr. Wayne Sodano, will **review test results, clinical conditions, further test recommendations or answer any other questions you may have via email.** In addition our clients have the option of scheduling either a **telephone or video conference for a fee.**
Dr. Wayne L. Sodano
DC, DABCI, DACBN, CFMP, CIHP, BCTN

Next lesson: Part 5 of 8
Clinical Approach to Anemia