CLINICAL LABORATORY TESTING:

BLOOD CHEMISTRY & CBC ANALYSIS

FROM A FUNCTIONAL MEDICINE PERSPECTIVE

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

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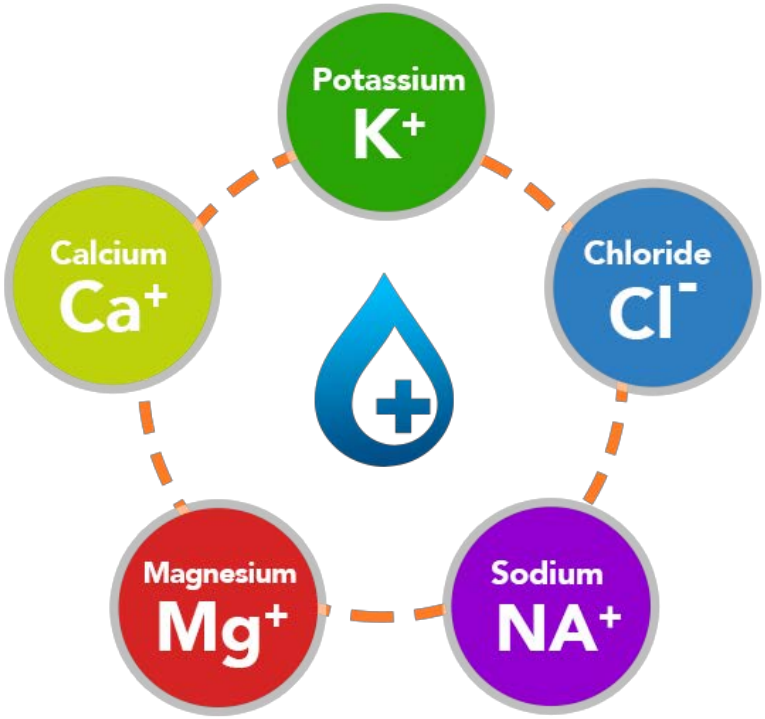
EVEXIA DIAGNOSTICS™

8 PART SERIES

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



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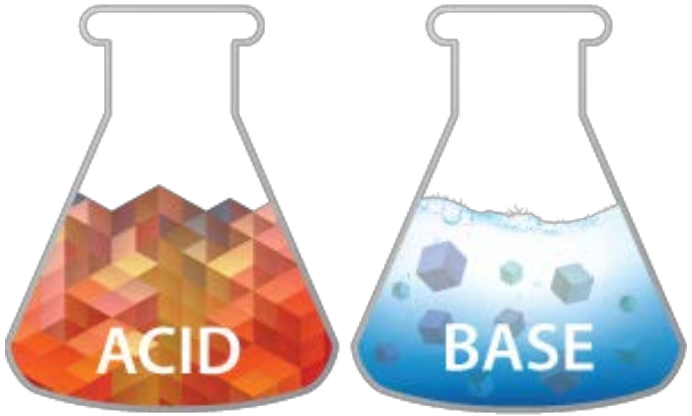

Minerals such as magnesium, calcium, and phosphate are frequently discussed in the context of the endocrine system because of the effects of vitamin D, and parathyroid hormone on the regulation of these minerals.

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

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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:

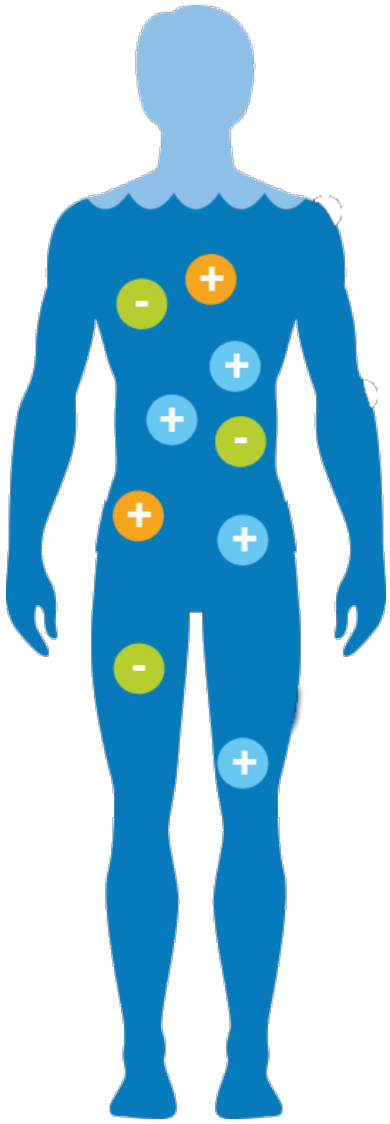
- **reduced enzyme activity**
- **mineral loss and demineralization of the bone**
- **inflammation and tissue irritability due to the corrosive nature of acids**

– all of which lead to illness.

Electrolytes and Serum Anion Gap

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

Analyte	Age	Reference Range	Optimal Range
Sodium (Na^{+})	Adult	136 – 142 mEq/L	Same
Potassium (K^{+})	Adult	3.8 – 5.0 mEq/L	4 – 4.6
Chloride (Cl^{-})	Adult	95 – 103 mEq/L	99 - 103
Carbon dioxide as bicarbonate	Adult	23 – 30 mEq/L	26 - 31
Anion Gap	Adult	10 – 20 mEq/L (K^{+} used) 8 – 16 mEq/L (K^{+} not used)	8 – 12 mmol/L (K^{+} used)



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)

Intracellular Volume (normally, more fluid is in the cells)	**24 liter (60%)**
Total Extracellular Volume	**16 liters (40%)**
Extracellular (interstitial)	11.2 liters (28%)
Extracellular (plasma)	3.2 liters (8%)
Extracellular (*transcellular)	1.6 liters (4%)

* Transcellular fluid: lumen of GI; fluids in the CNS; eye fluid; serous fluid

Electrolyte Concentrations in Extracellular and Intracellular Fluids

Analyte	Plasma (mEq/L)	Interstitial (mEq/L)	Intracellular Water (mEq/L)
Na^+	140	145.3	13
K^+	4.5	4.7	**140**
Ca^{++}	5.0	2.8	1×10^{-7}
Mg^{++}	1.7	1.0	**7.0**
Cl^-	104	114.7	3
HCO_3^- Bicarbonate	24	26.5	10
SO_4^{2-} Sulfate	1.0	1.2	----
Phosphorus	2.1	2.3	**107**
Protein	1.5	8	40
Organic anions	5	5.6	----

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.

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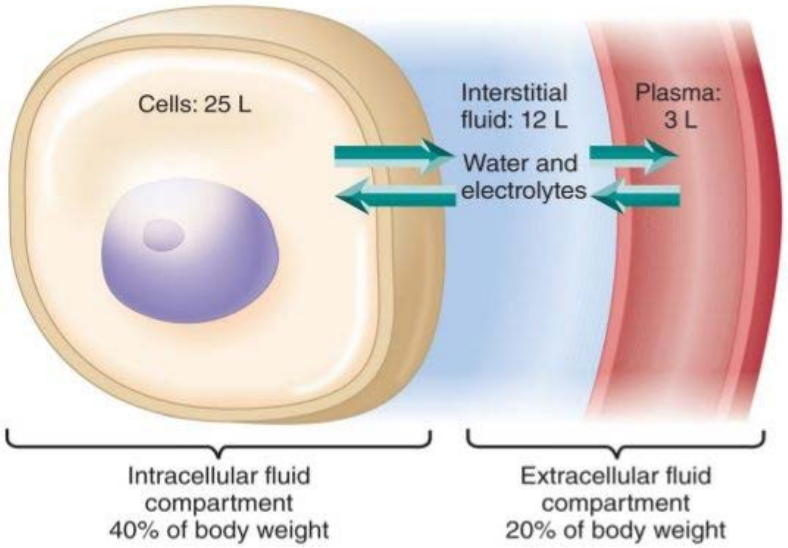
Reduced Intracellular Fluid Volume

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



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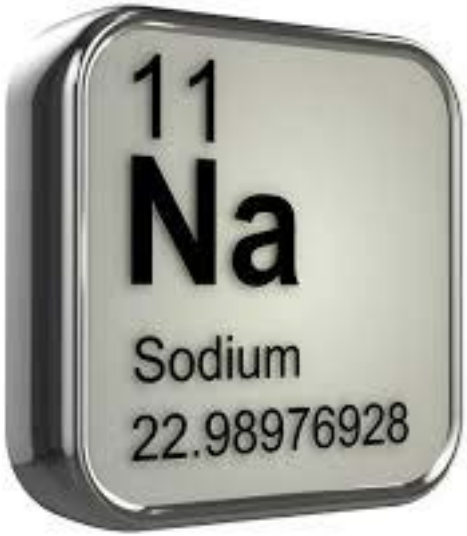
Sodium



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

Changes in serum sodium most often reflect *changes in water balance*, rather than sodium balance

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

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.

Signs and Symptoms of Abnormal Serum Potassium

Symptoms of hyperkalemia	Irritability, nausea, vomiting, intestinal colic, diarrhea
Symptoms of hypokalemia	Hypotension, weakness, cramps, loss of smooth muscle function, decreased insulin release, abnormal ECG findings (deceased T-wave amplitude, widening QRS complex, and a depressed ST segment)

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: (CO_2) in solution or bound to proteins, bicarbonate (HCO_3^-), carbonate (CO_3^{2-}), and carbonic acid (H_2CO_3).

In practice, **80 – 90% is present as bicarbonate**, and is a general guide to the body's buffering capacity. Essentially, CO_2 is primarily used as a rough guide for acid-base balance.

$$CO_2 + H_2O \longleftrightarrow H_2CO_3 \longleftrightarrow HCO_3^- + H^+$$

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

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

Increased acidosis: increase in hydrogen ion concentration and decreased HCO3 concentration

Na + unmeasured cations = Cl + HCO3 + unmeasured anions

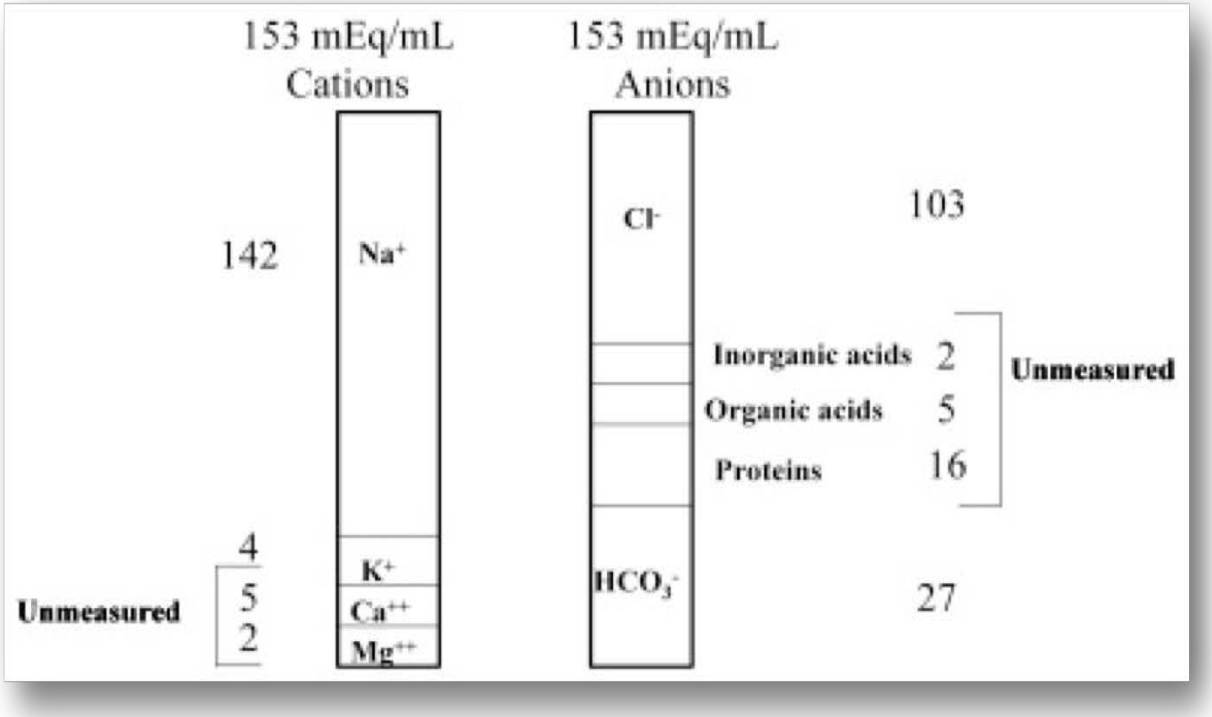
Major unmeasured cations

- Calcium
- Magnesium
- Potassium
- Gamma globulins

Major unmeasured anions

- Plasma proteins (albumin)
- Sulphate
- Phosphates
- Lactate
- Other organic anions

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.



If anion gap is increased; then there is an increase in other anions (acids) – not HCO3.

AG = Na+ - (Cl- +HCO3-) 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

Analyte	Age	Reference Range	Optimal Range
Total Calcium (bound and unbound)	Adult	9.2 – 10.5 mg/dL	9.4 – 10 mg/dL 2.35 – 2.5 mmol/L
Calcium, Ionized	Adult	4.6 – 5.3 mg/dL	
Phosphorous (P) Phosphate (PO_4)	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 1.3 – 2.1 mEq/L	.82 – 1.23 mmol/L 2.0 – 3.0 mg/dL
RBC-Mg	Adult	4.2 – 6.8 mg/dL 3.6 - 5.6 mEq/L	4.2 – 6.8 mg/dL 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 Ca = [0.8 x (normal albumin - patient's albumin)] + 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

Serum Phosphorous (Phosphate)

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

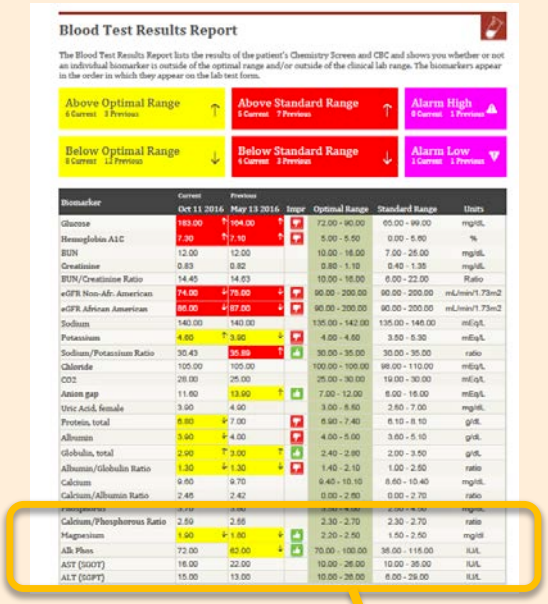
Serum Magnesium: RBC-Mg the Better Test

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,


Blood Test Results Report

The Blood Test Results Report lists the results of the patient's Chemistry Screen and CBC and shows you whether or not an individual biomarker is outside of the optimal range and/or outside of the clinical lab range. The biomarkers appear in the order in which they appear on the lab test form.

Above Optimal Range 6 Current 3 Previous

Above Standard Range 5 Current 7 Previous

Alarm High 0 Current 1 Previous

Below Optimal Range 8 Current 12 Previous

Below Standard Range 4 Current 3 Previous

Alarm Low 1 Current 1 Previous

Biomarker	Current Oct 11 2016	Previous May 13 2016	Impr	Optimal Range	Standard Range	Units
Glucose	183.00	104.00		72.00 - 90.00	65.00 - 99.00	mg/dL
Hemoglobin A1C	7.30	7.10		5.00 - 5.50	0.00 - 5.60	%
BUN	12.00	12.00		10.00 - 16.00	7.00 - 25.00	mg/dL
Creatinine	0.83	0.82		0.80 - 1.10	0.40 - 1.35	mg/dL
BUN/Creatinine Ratio	14.45	14.63		10.00 - 16.00	6.00 - 22.00	Ratio
eGFR Non-Afr. American	74.00	75.00		90.00 - 200.00	90.00 - 200.00	mL/min/1.73m2
eGFR African American	86.00	87.00		90.00 - 200.00	90.00 - 200.00	mL/min/1.73m2
Sodium	140.00	140.00		135.00 - 142.00	135.00 - 146.00	mEq/L
Potassium	4.60	3.90		4.00 - 4.60	3.50 - 5.30	mEq/L
Sodium/Potassium Ratio	30.43	35.89		30.00 - 35.00	30.00 - 35.00	ratio
Chloride	105.00	105.00		100.00 - 100.00	98.00 - 110.00	mEq/L
CO2	28.00	25.00		25.00 - 30.00	19.00 - 30.00	mEq/L
Anion gap	11.60	13.90		7.00 - 12.00	6.00 - 16.00	mEq/L
Uric Acid, female	3.90	4.90		3.00 - 5.60	2.60 - 7.00	mg/dL
Protein, total	6.80	7.00		6.90 - 7.40	6.10 - 8.10	g/dL
Albumin	3.90	4.00		4.00 - 5.00	3.60 - 5.10	g/dL
Globulin, total	2.90	3.00		2.40 - 2.90	2.00 - 3.50	g/dL
Albumin/Globulin Ratio	1.30	1.30		1.40 - 2.10	1.00 - 2.50	ratio
Calcium	9.60	9.70		9.40 - 10.10	8.60 - 10.40	mg/dL
Calcium/Albumin Ratio	2.46	2.42		0.00 - 2.60	0.00 - 2.70	ratio
Calcium/Phosphorous Ratio	2.59	2.66		2.30 - 2.70	2.30 - 2.70	ratio
Magnesium	1.90	1.80		2.20 - 2.50	1.50 - 2.50	mg/dl
Alk Phos	72.00	63.00		70.00 - 100.00	36.00 - 115.00	IU/L
AST (SGOT)	16.00	22.00		10.00 - 26.00	10.00 - 35.00	IU/L
ALT (SGPT)	15.00	13.00		10.00 - 28.00	6.00 - 29.00	IU/L

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.

Below Optimal

Magnesium ↓ 1.90 mg/dl (- 150 %)

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 dyfunction 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.

Condition	pH	Analyte	Causes
Metabolic Acidosis	↓	↓HCO_3^-	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	↑	↑HCO_3^-	Loss of HCl from stomach – vomiting Ingestion of bicarbonate Increased renal excretion of acid – diuretic therapy, potassium depletion, secondary hypoparathyroidism
Respiratory Acidosis	↓	↑CO_2	Lung disease • COPD • Advanced interstitial lung disease Thoracic deformity or airway obstruction Diseases of respiratory muscle and nerves Depression of respiratory center
Respiratory Alkalosis	↑	↓CO_2	Pneumonia Pulmonary fibrosis Pulmonary congestion CNS lesions Drugs: salicylate, progesterone

Monitoring Urinary pH

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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.**

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Next lesson: Part 5 of 8

Clinical Approach to Anemia