LAB #: Sample Report
PATIENT: Sample Patient
ID:
SEX: Male
DOB: 01/01/1975 AGE: 43

CLIENT #: 12345
DOCTOR: Sample Doctor
Doctor's Data, Inc.
3755 Illinois Ave.
St. Charles, IL 60174 U.S.A.

Toxic & Essential Elements; Packed Red Blood Cells

ESSENTIAL AND OTHER ELEMENTS				
		RESULT / UNIT	REFERENCE INTERVAL	PERCENTILE 2.5th 16th 50th 84th 97.5th
Calcium	(Ca)	**9** µg/g	8-25	
Magnesium	(Mg)	**61** µg/g	39-59	
Potassium	(K)	**87** mEq/L	78-97	
Phosphorus	(P)	**592** µg/g	520-670	
Copper	(Cu)	**0.676** µg/g	0.52-0.8	
Zinc	(Zn)	**15.4** µg/g	8-14	
Iron	(Fe)	**996** µg/g	810-1020	
Manganese	(Mn)	**0.027** µg/g	0.008-0.029	
Selenium	(Se)	**0.295** µg/g	0.16-0.49	
Boron	(B)	**0.017** µg/g	0.01-0.11	
Molybdenum	(Mo)	**0.0001** µg/g	0.0002-0.001	

TOXIC METALS				
		RESULT / UNIT	REFERENCE INTERVAL	PERCENTILE 95th 99th
Arsenic	(As)	**0.0092** µg/g	< 0.008	
Cadmium	(Cd)	**< 0.0005** µg/g	< 0.002	
Cesium	(Cs)	**0.0057** µg/g	< 0.015	
Chromium	(Cr)	**0.0002** µg/g	< 0.0005	
Lead	(Pb)	**0.007** µg/g	< 0.06	
Mercury	(Hg)	**0.0278** µg/g	< 0.01	
Thallium	(Tl)	**< 0.00004** µg/g	< 0.00005	

SPECIMEN DATA

Comments:

Date Collected: **02/21/2019**
Date Received: **02/23/2019**
Date Reported: **02/26/2019**

Methodology: **ICP-MS**

PACKED BLOOD CELL ELEMENTS REPORT

INTRODUCTION

This analysis of elements in packed blood cells was performed by ICP-Mass Spectroscopy following acid digestion of the specimen in a closed microwave system. For a given element, these procedures measure the sum of the amounts of surface-adhering and intracellular content, regardless of chemical form. For units of measurement, mg/l is approximately equivalent to ppm, and mcg/l is approximately equivalent to ppb.

The packed cells are not washed, and therefore, a very small amount of residual plasma remains as part of the specimen. Washing would eliminate some important plasma membranebound elements. Because the cells are not washed, the DDI reference range may vary from published ranges for intracellular content of washed erythrocytes. Blood cell specimens that are not adequately centrifuged, per the kit instructions, may yield distorted or invalid results because of excess plasma content.

Packed blood cell analysis is intended to be a diagnostic method of assessing insufficiency or excess of elements that have important functions inside blood cells or on blood cell membranes. Additional testing of whole blood or serum/plasma or other body tissues may be necessary for differential diagnosis of imbalances. Additional testing also may be necessary to assess specific dysfunctions of assimilation, transport, retention, or excretion of elements. Packed blood cell element analysis is additionally intended to determine elevated or excessive levels of five potentially toxic elements that can accumulate in erythrocytes: thallium, arsenic, cadmium, lead, and mercury.

If an element is sufficiently abnormal per the blood cell measurement, a descriptive text is included with the report. For elements with essential or beneficial functions, a text will print if the measured result is below -1.5 standard deviations from the mean of the reference population, or if the result is above +1.5 standard deviations from the mean of the reference population. For potentially toxic elements, a text prints whenever the measured result exceeds the expected range. If no descriptive element texts follow this introductory discussion, then all essential cell elements were measured to be within +1.5 SD, and all measured potentially toxic elements were within expected ranges.

Doctor’s Data states the reference range as +1 SD from the mean of the reference population. This is considered to be the nutritionally and physiologically optimal range for elements with essential or beneficial functions. Physiological imbalance corresponds to levels beyond +1 SD but pathological consequences are not expected until the blood level is beyond +2 SD. Element levels beyond +2 SD may only be temporary nutritional problems or they may reflect a failure of homeostasis to control blood quantities. Pathological consequences depend upon cell and tissue functions which are disrupted by such levels.

MAGNESIUM HIGH

Magnesium is an electrolyte mineral, an enzyme activator, and a constituent of skeletal tissue. In blood, the concentration of cellular Mg is about twice that of serum Mg. For the whole body: 65% of Mg resides in skeletal tissue, 34% exists in intracellular space, and only 1% is in extracellular fluids. Hence, the intra-cellular content and function predominates in terms of magnesium’s biological activity. Functionally, Mg is required as an activator of many enzymatic steps in carbohydrate, amino acid and fatty acid metabolisms. Phosphorylation processes, ATP formation and utilization, and metabolisms of thiamin, riboflavin and pyridoxine are magnesium dependent.

Intracellular Mg is the important fraction for enzymatic activities. RBC Mg content is deemed the most diagnostic in terms of assessing Mg status; serum Mg levels may or may not correlate with cellular levels and function (Harper et al Review of Physiological Chemistry, 17th ed, Lange Med. Pub., 1979, p 579).

Expected symptoms of hypermagnesemia include: peripheral vasodilation, hypotension, skin warmth, nausea, vomiting, ataxia, and loss of voluntary muscle control, CNS depression and a sleeplike state similar to anesthesia. Clinical conditions or causative factors for hypermagnesemia are: renal insufficiency (the most common cause), overuse of magnesium salts as a cathartic, inappropriate nutritional supplementation, parenteral overdose, excessive MgSO4 therapy, and Addison's disease. Also, there are literature reports of hypertension with elevated erythrocyte Mg (Kjeldsen, S.E. et al, "Increased Erythrocyte Magnesium in Never Treated Essential Hypertension" Am. J. Hypertension 3(7), 1990 pp 573-75; also Kjeldsen et al, Scand. J. Clin. Lab. Invest. 50, 1990 pp 395-400).

Other diagnostic tests for assessing Mg status are: serum or whole blood magnesium measurement, urine element analysis to assess renal excretion level, and renal (creatinine) clearance determination.

BIBLIOGRAPHY FOR BLOOD CELL MAGNESIUM, HIGH

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2. Jacobs D.S. et al Laboratory Test Handbook, Williams & Wilkins, Baltimore MD, 1990, pp 259-60.

3. Levine B.S. and J.W. Coburn "Magnesium, the Mimic/Antagonist of Calcium" N.E.J. Med. 10 no.9, May 1984, pp 1253-54.

4. Braunwald E. et al. Harrison's Principles of Internal Medicine,11th ed, McGraw-Hill, New York, NY, 1987, p 846.

ZINC HIGH

Zinc (Zn) is an activator or cofactor for many enzymatic steps in human metabolism. Digestive enzymes (carboxypeptidase and aminopeptidase) contain Zn; an important enzyme controlling chemical energy conversion (lactate dehydrogenase) requires Zn, as do alcohol dehydrogenase and carbonic anhydrase. A form of the oxidantresponse mediating enzyme, superoxide dismutase ("SOD"), is activated by zinc and copper. Absorption of Zn occurs mainly in the small intestine, and Zn uptake can be competitive with that of iron. Zinc is distributed throughout body tissue; about one-fifth of total body stores of Zn are in skin. Plasma or serum Zn concentration normally varies from about 0.6 to 1.3 mg/dl; RBC Zn normally varies from 0.9 to 1.6 mg/dl.

Zinc inside erythrocytes is bound to Cu,Zn-SOD, carbonic anhydrase, and other proteins.

Erythrocytes can absorb ”excess” zinc at metalloenzyme binding sites and by binding to intracellular phosphates and thiols. Very excessive zinc (due to oral supplementation of 150 mg/d) is documented to induce hypochromia in individuals with sickle cell anemia (Prasad, et al, JAMA, 240, 1978 pp 2166-68). Sideroblastic anemia also is attributed to zinc overload (Forman, et al, West. J. Med. 152, 1990 pp 190-92).

Causal conditions related to elevated Zn levels include: inappropriate or over-supplementation of zinc salts, parenteral overdose, inhalation of Zn dust or fumes, iron deficiency, copper deficiency, constant diet of unusually high-Zn foods (mussels, oysters, mushrooms and yeast), and ingestion of zinc-contaminated food or drink (possible if galvanized metal containers are used).

Symptoms consistent with chronic Zn excess include: fatigue and lethargy, difficulty writing and with fine motor skills, lightheadedness, and renal failure. Immediate symptoms (within 12 hours) of acute Zn toxicity via ingestion include: nausea, vomiting, diarrhea, exhaustion, headache, dizziness, and myalgia. Other laboratory findings consistent with Zn excess would be: elevated leukocyte count, elevated serum amylase and lipase, elevated serum Zn levels, and elevated hair Zn level if the Zn excess is chronic.

BIBLIOGRAPHY FOR BLOOD CELL ZINC, HIGH

1. Falchuk K.H., Chapt 28 in Harrison’s Principles of Internal Medicine, 13th ed, McGraw-Hill, New York, NY, 1994 pp 481-82.

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4. Forman W.B. et al, ”Zinc Abuse - An Unsuspected Cause of Sideroblastic Anemia”, Western J. Med. 150 (2), Feb. 1990 pp 190-92.

5. Lantzsch H-J and H. Schenkel, ”Effects of Specific Nutrient Toxicities in Animals and Man: Zinc” in CRC Handbook Series in Nutrition and Food, Sect. E, vol. I, CRC Press, West Palm Beach, FL1978 pp 291-307.

MANGANESE HIGH

Manganese (Mn) is required as an activator for several enzymes in humans including some that control entry of carbohydrate and protein metabolites into the tricarboxylic acid cycle so that oxidative phosphorylation can occur. Pyruvate decarboxylase is such an enzyme. Isocitrate dehydrogenase (in the tricarboxylic acid cycle) and arginase (in the urea cycle) are also activated by manganese. The mitochondrial matrix form of the superoxide dismutase (SOD) enzyme requires Mn. Manganese is concentrated in mitochondria-rich tissue such as liver, kidney, pancreas and brain.

Erythrocyte Mn concentration normally is 10x to 20x that of serum. In erythrocytes, Mn+2 binds strongly to porphyrin (not a functional use of Mn). In other cells, Mn is active in the mitochondria, cell nucleus, and endoplasmic reticulum. The formation of Mn porphyrin in RBCs reflects accumulation of Mn in the body but does not necessarily indicate detrimental or toxic effects.

Non-municipal drinking water, especially water from private wells, can be a source of manganese that can moderately increase blood levels. Individuals on an extended course of therapeutic medication may present whole blood Mn up to 2x the upper limit of the expected range (DDI observation based on communications from attending physicians). In liver diseases, mitochondrial Mn (as in Mn-SOD) can be released into the blood stream. Elevated blood cell Mn may or may not result. Other clinical conditions associated with elevated blood cell Mn include biliary insufficiency, gallbladder diseases or biliary obstruction. Calcium deficiency is reported to enhance uptake and retention of Mn.

Documented symptoms and effects of elevated Mn include: fatigue, headache, low systolic blood pressure, drowsiness followed by insomnia, and sexual impotence. Deterioration of memory, asthenia, and tremor, clinical features similar to Parkinson's disease, may occur. Acute contamination or Mn poisoning may result in euphoria, hallucinations and inappropriate laughter ("manganese madness"). Mn is considered neurotoxic partly due to its interference with adrenal catecholamine metabolism; tetrahydrobiopterin levels are reduced causing reduced dopamine formation from tyrosine (Daniels and Abarca, Neurotoxicology and Teratology 13,1991,pp485-87).

Confirmatory tests for excessive manganese are (1) hair mineral analysis with hair Mn concentration exceeding about 2 ppm; (2) urine analysis featuring significantly elevated urine levels following oral challenge of D-penicillamine.

BIBLIOGRAPHY FOR BLOOD CELL MANGANESE, HIGH

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3. Donaldson J. and A. Barbeau, "Manganese Neurotoxicity: Possible Clues to the Etiology of Human Brain Disorders", Metal Ions in Neurology and Psychiatry, Alan Liss Inc., New York, NY 1985 pp 259-85.

4. Kondakis X.G., et al, "Possible Health Effects of High Manganese Concentration in Drinking Water" Arch. Environ. Health 44 no.3,1989 pp 175-78.

5. Parenti M. et al, "Role of Dopamine in Manganese Neurotoxicity", Brain Research 473, 1988 pp 236-40.

6. Calne D.B. et al, "Manganese and Idiopathic Parkinsonism: Similarities and Differences" Neurology 44 no.9, 1994 pp 1583-86.

7. Chin-Chang H. et al "Chronic Manganese Intoxication", Arch of Neurology 46, 1989 pp 1104-06.

MOLYBDENUM LOW

Molybdenum (Mo) is an essential nutrient that functions as an obligatory cofactor for the iron- and flavin-containing enzymes aldehyde oxidase, xanthine oxidase, and sulfite oxidase. Aldehyde oxidase oxidizes and detoxifies the pyrimadines, purines, and pteridines. Xanthine oxidase/ dehydrogenase catalyzes the formation of uric acid from hypoxanthine and sulfite oxidase catalyzes the transformation of sulfite to sulfate. Insufficient sulfite oxidase activity can result in deranged cystiene metabolism.

Mo is readily absorbed (40 - 80%) and transported as a complex with protein in blood. Blood levels of Mo are regulated primarily by urinary excretion. Recent surveys indicate that many diets do not provide the recommended safe and adequate intake of 50 - 350 mcg Mo/day. (1) Good sources of Mo include milk products, whole grains, dried legumes, and organ meats.

Symptoms of overt Mo deficiency have only been described for a patient on long-term total parenteral nutrition. However, prolonged exposure to tungsten (T.I.G. welding) or dietary sulfates, aldehydes, and large amounts of purines diet might possibly result in an acquired Mo deficiency. A possible link between Mo deficiency and increased risk for esophageal cancer has been reported. (2)

Mo deficiency would be expected to be associated with abnormally low levels of uric acid in blood and sulfate in urine.

(1) Nielsen, F.H. Ultratrace Minerals, chapter 15 in Modern Nutrition in Health and Disease, 8th ed., vol. 1, Lea & Febiger, 1994.
(2) Falchuk, K.H. Disturbances in Trace Elements, in Fauci, A.S. et. al., eds, Harrison's Principles of Internal medicine, 14th edition, Mc Graw Hill, 1998.

ARSENIC HIGH

Blood cell arsenic (As) exceeds the expected level for this individual. Usually, arsenic clears the blood rapidly after a point-in-time exposure. The finding of elevated blood cell As suggests: (1) recent exposure, (2) chronic or on-going exposure, (3) decreased metabolic capacity to clear As. Arsenic has two oxidation states or valences, As+3 and As+5. As+3 is more reactive and toxic. Both forms of As accumulate primarily in skin and skeletal tissue; also in liver, kidney and spleen. Over one-half of ingested or absorbed As is normally excreted via urine and feces in 2 to 8 days.

In blood cells, As binds primarily to globulin, but generally As seeks out thiols and sulfhydryl binding sites. The vitamin cofactor, lipoic acid, is particularly affected, and this may be the reason for inhibition of alpha-ketoacid oxidation. Much of the enzymatic inhibition caused by As occurs in cells with mitochondrial structures (not erythrocytes). Arsine gas, AsH3, does react rapidly with erythrocytes, combining with hemoglobin and causing hemolysis, hemoglobinuria and hematuria.

An important detoxication pathway for As involves methylation with methyl groups donated by S-adenosylmethionine; methylated arsenic can produce a garlic-like breath odor.

Early symptoms of arsenic excess include: fatigue, malaise, eczema or allergic-like dermatitis,

and increased salivation. Increased body burden of arsenic can lead to further manifestations: skin hypopigmentation, white striae on fingernails, hair loss, stomatitis, peripheral neuropathy, myocardial damage, hemolysis, and anemia (aplastic with leukopenia).

Sources of arsenic include: contaminated foods (especially seafood), water or medications. Industrial sources are: ore smelting/refining/processing plants, galvanizing, etching and plating processes. Tailing from or river bottoms near gold mining areas (past or present) may contain arsenic. Insecticides, rodenticides and fungicides (Na-,K-arsenites, arsenates, also oxides are commercially available). Commercial arsenic products include: sodium arsenite, calcium arsenate, lead arsenate and ”Paris green” which is cupric acetoarsenite, a wood preservative. Elevated blood As of undetermined source is reported in hemodialysis patients.

Hair element analysis can be done for corroborative evidence of arsenic excess. Blood arsenic levels are not dose-related and may not accurately reflect As body burden. Urine analysis following provocation with D-penicillamine or DMSA can corroborate excess, but sequestered As may not show in early trials.

BIBLIOGRAPHY FOR BLOOD CELL ARSENIC

1. Carson B.L. et al. Toxicology and Biological Monitoring of Metals in Humans, Lewis Publishers, Chelsea, MI, 1987 pp 24-33.

2. Tsalev D.L. and Z.K. Zaprianov Atomic Absorption Spectrometry in Occupational and Environmental Health Practice, vol 1, CRC Press, Boca Raton, FL, 1983 pp 87-93.

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5. Heyman A. et al. ”Peripheral Neuropathy Caused by Arsenical Intoxication” New Eng. J. Med., 254, no. 9, 1956 pp 401-9.

6. DeKimpe J. et al, ”More Than Tenfold Increase of Arsenic in Serum and Packed Cells of Chronic Hemodialysis Patients” Am. J. Nephrology 13, 1993 pp 429-34.

MERCURY HIGH

Packed cell mercury (Hg) is measured to exceed the expected range. In whole blood, mercury eventually partitions between plasma and cells in various proportions depending upon its chemical form. For inorganic Hg (salts), the RBC/plasma ratio is about 1.0 or less which means that inorganic Hg is equally distributed, or there is somewhat more inorganic Hg in the plasma. For elemental Hg the RBC/plasma ratio is about 2. For organic mercury, the RBC/plasma ratio exceeds 10, which means that at least 90% of organic mercury, such as methylmercury, accumulates in the erythrocytes. However, blood cells may not be indicative of past exposures if the Hg has cleared the blood and deposited in other tissues. This can take up to 2 months after a point-in-time exposure to organic mercury.

The symptomatology of Hg excess can depend on many factors: the chemical form of absorbed Hg and its transport in body tissues, presence of other synergistic toxics (Pb, Cd, organic xenobiotics), presence of disease and status of immune function, and the availability of protective nutrients, (e.g. zinc, selenium, vitamin E). Early signs of mercury contamination include: decreased senses of touch, hearing, vision and taste, metallic taste in the mouth, fatigue or lack of physical endurance, and increased salivation. Symptoms may progress with moderate or chronic exposure to include: anorexia, numbness and paresthesias, headaches, hypertension, irritability and excitability, and immune suppression, possibly immune dysregulation. Advanced disease processes from mercury toxicity include: tremors and incoordination, anemia, psychoses, manic behaviors, possibly autoimmune disorders, renal dysfunction or failure.

Mercury is commonly used in: dental amalgams, explosive detonators, in elemental or liquid form for thermometers, barometers, and laboratory equipment; batteries and electrodes (”calomel”); and in fungicides and pesticides. The fungicide and pesticide use of mercury (including that in paints) has declined due to environmental concerns, but mercury residues persist from past use. Methylmercury occurs in aquatic biota in both freshwater and ocean sediments. Methylmercury accumulates in aquatic animals and fish and is concentrated up the food chain reaching high concentrations in large fish and predatory birds. Except for fish, the human intake of dietary mercury is negligible unless food is contaminated with one of the previously listed forms/sources.

Corroborating diagnostic tests for assessment of mercury burden are hair element analysis (for past or chronic exposures),and urine analysis following administration of sulfhydryl agents(DMPS, DMSA, D-penicillamine).

BIBLIOGRAPHY FOR BLOOD CELL MERCURY

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