LAB #: B000000-0000-0
PATIENT: Sample Patient
ID: PATIENT-S-00000
SEX: Female
DOB: AGE: 71

CLIENT #: 12345
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)	**15**	µg/g	8-26	
Magnesium	(Mg)	**37**	µg/g	39-59	
Potassium	(K)	**86**	mEq/L	78-97	
Phosphorus	(P)	**578**	µg/g	520-670	
Copper	(Cu)	**0.586**	µg/g	0.52-0.8	
Zinc	(Zn)	**8.0**	µg/g	7.8-13.8	
Iron	(Fe)	**917**	µg/g	800-1010	
Manganese	(Mn)	**0.030**	µg/g	0.009-0.033	
Selenium	(Se)	**0.170**	µg/g	0.16-0.49	
Boron	(B)	**0.101**	µg/g	0.01-0.11	
Molybdenum	(Mo)	**0.0006**	µg/g	0.0002-0.001	

TOXIC METALS					
		RESULT / UNIT		REFERENCE INTERVAL	PERCENTILE 95th 99th
Arsenic	(As)	**0.0048**	µg/g	< 0.008	
Cadmium	(Cd)	**0.0013**	µg/g	< 0.002	
Cesium	(Cs)	**0.0070**	µg/g	< 0.015	
Chromium	(Cr)	**0.0013**	µg/g	< 0.0005	
Lead	(Pb)	**0.043**	µg/g	< 0.05	
Mercury	(Hg)	**0.0097**	µg/g	< 0.01	
Thallium	(Tl)	**0.00007**	µg/g	< 0.00005	

SPECIMEN DATA

Comments:

Date Collected: **03/30/2017**
Date Received: **04/03/2017**
Date Reported: **04/06/2017**

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 membrane-bound 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: antimony, 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 LOW

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 intracellular 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.

Low Mg is not an independent CVD risk factor but Mg insufficiency is associated with hypertension, hyperglycemia and, endothelial cell dysfunction by promoting a pro-inflammatory, pro-thrombotic and pro-atherogenic environment that could play a role in the pathogenesis of cardiovascular disease. Oral Mg supplementation inhibits platelet-dependent thrombosis and improves exercise tolerance and endothelial and myocardial function in patients with CVD. Epidemiological evidence links Mg deficiency to CVD. RBC Mg levels may be checked as part of an evaluation of the severity of kidney problems and/or of uncontrolled diabetes.

Intracellular Mg is the important fraction for enzymatic activities, and intracellular Mg depletion can occur despite normal blood serum concentrations (Rude R.K. et al, Magnesium and Trace Elements, Karger, 10, 1991-92 p. 117). RBC Mg content is deemed the most diagnostic in terms of assessing Mg adequacy; 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 hypomagnesemia are: fatigue, constipation, irritability of the neuromuscular system with muscle tremor or twitching, hypertension, spasmophilia, mental depression possibly with psychoses, and convulsions. Ventricular arrhythmia may occur with low Mg, especially if potassium also is low. Conditions leading to inadequate Mg include: poor quality diet, fasting or anorexia, hyperalimentation lacking in adequate Mg, GI dysfunctions and malabsorption, alcoholism, renal wasting, dialysis without replenishment, diarrhea of several days duration, excessive calcium (or vitamin D) supplementation, hyperparathyroidism, and hyperaldosteronism. Diabetes may feature Mg insufficiency. Slightly low whole blood Mg may be due to low serum proteins (to which some serum Mg is bound) while RBC Mg remains within normal limits.

Other clinical tests for assessing Mg status are: urine amino acid analysis to rule out taurine deficiency or wasting (taurine is magnesium sparing), and urine element analysis to rule out urinary wasting of Mg. The magnesium challenge method may be most indicative: baseline 24-hour urine Mg measurement, followed by 0.2 mEq/Kg intravenous Mg, followed by 24-hour urine Mg measurement. A defi-

ciency is judged to be present if less than 80% of the Mg challenge is excreted.

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ZINC LOW

Zinc (Zn) is an activator or cofactor for many enzymatic steps in human metabolism. Many digestive peptidase enzymes contain Zn; an important enzyme controlling chemical energy conversion (lactate dehydrogenase) requires Zn, as does alcohol dehydrogenase. A form of the oxidant-response 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. Individuals who have Zn deficiency have low erythrocyte carbonic anhydrase activity (Martin D.W. et al, Harper's Review of Biochemistry, 20th ed, Lange Med. Publ.,1984 p. 659). The role of low Zn and erythrocyte SOD activity in inflammatory diseases, e.g. arthritis, has been studied with inconsistent and controversial conclusions. Hemolytic anemias, especially thalassemia, can feature deficient Zn in erythrocytes.

Conditions associated with zinc deficiency include: incomplete digestive proteolysis and malabsorption, chronic diarrhea, overuse of diuretics, alcoholism, hepatic cirrhosis, renal tubular disease and nephrotic syndrome, diabetes mellitus. Excess dietary phosphates, phytates, fiber, calcium and copper can impair uptake of Zn. Excess copper levels also can interfere with zinc retention bycompetition for albumin binding sites in blood serum. Zinc binds to cysteine and histidine. Cystinuria or histidinuria enhances urinary zinc excretion; usually lowering serum zinc. Packed cell Zn may or may not be affected. Therapeutic detoxification procedures, e.g. EDTA chelation and D-penicillamine therapy, deplete body stores of Zn.

Conditions seen in Zn deficiency are: altered taste, impaired dark adaptation by the eyes, partial (usually) alopecia, poor wound healing, sexual impotency, acral dermatitis, delayed growth in children, dwarfism, and immune dysfunction with impaired T-lymphocyte activity. Elevated lactic acid in blood (lactic acidosis) may occur in Zn deficiency.

Other laboratory tests that may be diagnostic for suspected Zn deficiency are: serum Zn measurement, periodic urine element analysis during detoxification therapy, hair element analysis (low zinc corroborates deficiency, high zinc usually indicates maldistribution and zinc dysfunction), serum lactic acid (mildly elevated in Zn deficiency), erythrocyte SOD activity determination (subnormal in either Zn or Cu deficiency), and erythrocyte carbonic anhydrase activity (subnormal in Zn deficiency).

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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.

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SELENIUM LOW

Selenium (Se) has two documented functions as an enzyme activator in humans: (1) activation of the enzyme T4 to T3 prohormone deiodinase for balance in thyroid hormone level, and (2) activation of glutathione peroxidase for reduction of peroxides by oxidation of glutathione. Erythrocytes are a tissue of choice for assessing glutathione peroxidase function and selenium status. In its antioxidant function, selenium works with vitamin E. Vitamin E functions to prevent oxidation of cell membranes and fatty acids, while glutathione, via the peroxidase enzyme, works to undo oxidation after it has happened.

Symptoms and conditions that can result from Se deficiency include: increased susceptibility to viral infections, increased inflammation during infection or following exposure to xenobiotics or oxidant chemicals, hardening or sclerosing of tissue, muscle pain and tenderness, and possibly hypothyroid function with subnormal T3.

Selenium deficiency usually is the result of a poor quality diet or one which has emphasized highly refined foods. However, there are geographical regions in the world where the soil contains little Se, and even unprocessed food grown in such soils can be deficient in Se. Selenium often is lost through urinary wasting in cystinuria; hyperaminoaciduria conditions and renal transport disorders may feature Se wasting.

Laboratory tests for further assessment of Se status are: determination of erythrocyte glutathione peroxidase functional activity, measurement of serum T3 and T4, and measurement of hair Se level (barring exogenous Se contamination primarily from shampoos). 24-hour urine amino acid analysis may be informative if Se wasting is suspected.

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BORON HIGH

Boron (B) is introduced to the body mainly through food (noncitrus fruits, leafy vegetables, nuts, legumes, wine, cider, beer) and drinking water but is also found in food preservatives (sodium borate), and insecticides (boric acid). Evidence for biological essentiality in animals (including humans) has been presented. It has been proposed that boron contributes to living systems by acting indirectly as a proton donor and that it exerts a particular influence on cell membrane and structure and function. In humans boron is responsible for the hydroxylation of various substances in the body. It may enhance the production of various hormones such as testosterone, estrogen, DHEA, and 1,25 dihydroxycholecalciferol. Boron is very readily absorbed and excreted in the urine yet its concentration remains quite low in the serum. Based on urinary recovery findings, more than 90% of ingested B is usually absorbed. Boron is distributed throughout the tissues and organs of animals and humans at concentrations mostly between 4.6 and 55.5 nmol (0.05 and 0.6 µg)/g fresh weight. Among the organs that contain the highest amounts of B are bone, spleen, and thyroid. It appears to be most concentrated in the thyroid gland.

Boron has a low order of toxicity even with intakes as high as 40mg/day in some parts of the world. However, high body burden of the element may be harmful, especially to young animals (including human neonates). Reports have shown that when doses equivalent to more than 46 mmol (0.5 g) B daily were consumed, disturbances in appetite, digestion, and health occurred. Acute toxicity signs include nausea, vomiting, diarrhea, dermatitis, and lethargy. High B ingestion also induces riboflavinuria.

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CHROMIUM HIGH

The level of chromium in this sample is higher than expected. Recent evidence indicates that red blood cell (RBC) chromium levels primarily reflect exposure to toxic hexavalent chromium (Cr VI), as opposed to the nutritional status of essential Cr III. The nutrient chromium III is almost entirely excluded from entering RBCs. The level of Cr VI in RBCs has been directly correlated with Cr VI exposures (in vitro, Devoy et al. 2016).

Chromium may be ingested, inhaled or adsorbed through the skin.

Chromium VI is a well-established carcinogen. Respiratory exposure may result in bronchial asthma, respiratory tract polyps, nasal and septal ulcerations, or naso-pharyngeal irritation and inflammation. Long-term exposure may increase lung cancer risk. Ingestion of Cr VI may result in inflammatory changes in small intestine, pancreas and liver tissues (animals), and increase the risk of gastrointestinal and lung cancers. In vitro studies indicate that supra-physiological exposure to Cr VI depleted ATP and glutathione, increased oxidative stress, and induced hemolysis of erythrocytes. Ingested Cr VI is rapidly reduced to Cr III by gastric acid and enterocytes high in the small bowel, unless that capacity is overwhelmed by excessive exposure. Ingestion of antacids or proton pump inhibitors may decrease innate gastrointestinal reduction of Cr VI. In vitro studies indicate that systemically Cr VI is rapidly reduced to chromium III by glutathione, cysteine and vitamin C in cells. The intracellularly reduced Cr III binds to hemoglobin and remains in the RBCs. The reduction of Cr VI induces oxidative stress and generates unstable tetravalent and pentavalent forms that can bind to lipids, proteins, nucleic acids or DNA with toxic effects. Poor status of antioxidants may enhance damage to DNA and cells.

Sources of exposure to Cr VI include industrial groundwater pollution, manufacture and use of ferrochromium and stainless steel, wood finishing and leather tanning industries, handling of cement, airborne cement dust, porcelain teeth, stainless steel cookware, vehicle emissions, copier inks or toners and e-cigarette juice. The Centers for Disease Control recommend a complete blood count (CBC), liver function tests (ALT, AST, SGPT, and bilirubin), blood urea nitrogen (BUN) and urinalysis be performed after detection of chromium VI exposure. Industrial exposure to Cr VI increased urinary B-2 microglobulin levels when compared to controls.

Confirmatory tests for chromium excess include:

1. Measurement of hyaluronidase activity in serum (reported to increase with Cr VI overexposure).
2. Analysis of Cr in hair which shows exposure
3. Analysis of Cr in urine which does not indicate body burden but indicates recent (acute) or ongoing exposure. (rule out supplementation with Cr III)
4. Evaluate oxidative stress (DNA Oxidative Damage, urine)
5. Evaluate glutathione status (RBC Glutathione)

Resources:

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THALLIUM HIGH

The level of thallium (Tl), one of the most toxic heavy metals, is abnormally high in this specimen. Elevated levels of Tl in blood or red blood cells is indicative of either a recent acute exposure, or ongoing exposure to the metal. Such exposure is not necessarily associated with significant net retention in the body, or toxicity.

Tl has atomic properties similar to potassium (K), and therefore follows potassium distribution pathways and alters K-dependent processes. Tl binds to sulfhydryl groups of enzymes, inhibits cellular respiration, interacts with riboflavin and riboflavin-based co-factors, and disrupts calcium homeostasis.

This test result only indicates exposure to Tl. Acute Tl poisoning is associated with severe constipation, extreme abdominal pain, neuropathic pain in the lower extremities, sleeplessness and excessive thirst. Fever, conjunctivitis and stomatitis may occur. Neurological effects of Tl poisoning appear in 3 - 20 days, and include ataxia, paresthesia, delerium, stupor and psychotic changes. Cardiovascular symptoms include tachycardia, arrhythmias and hypertension. Alopecia typically occurs after about 2 - 3 weeks, and can progress to complete loss of all body hair, including the inner third of eyebrows.

Significant retention of Tl occurs with chronic, low-level exposure; chronic toxicity can occur with prolonged or repeated exposures. Mee's lines in the finger- and toenails often occur with chronic, low-level exposure or long-term survival after acute poisoning. Long-term retention is associated with scaly dermatitis, nail dystrophy, severe cachexia and polyneuritis. It should be noted that hair loss may not occur with chronic, low-level exposure.

The most notorious cause of acute Tl poisoning is oral ingestion of Tl-based rodenticides/ insecticides. Environmental exposures to Tl are related to emissions from coal-fired power plants, metal smelters (zinc, lead), and cement plants. High levels of Tl can be found in vegetables grown in the vicinity of cement plants and in areas that have Tl-enriched runoff from copper and zinc mines. Tl is used in the manufacture of optical lenses, scintillation counters, low-temperature thermometers, switching devices, green-colored fireworks, and some imitation jewelry. It is also used as a chemical catalyst, imaging agent (Tl-stress test), and a corrosion resistant alloy.

Exposure to Tl can be confirmed by analysis of a random urine specimen since low level Tl excretion in the urine persists up to 6 months after ingestion. Long-term exposure (2 - 3 months) can be assessed by using hair elemental analysis. However, net retention of Tl can only be assessed by comparison of pre- and post levels of Tl in urine (DMSA) or feces (charcoal or Prussian Blue). Prussian Blue blocks the enterohepatic resorption of Tl, and is the most effective agent.

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