

# **Functional Medicine University's Functional Diagnostic Medicine Training Program**

## **INSIDER'S GUIDE RBC MINERALS/TOXIC METALS INTERPRETATION AND TREATMENT**

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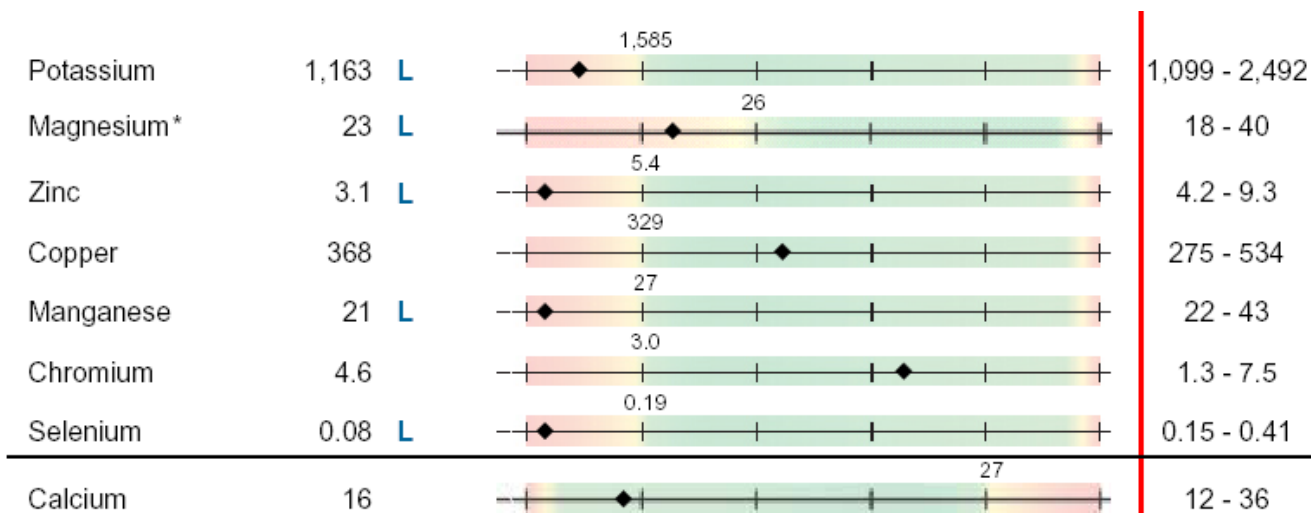
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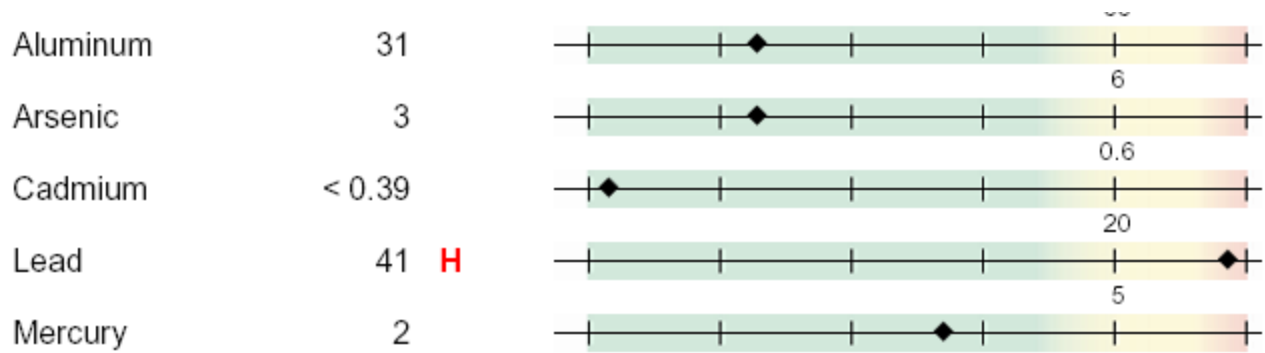
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## RBC minerals/Toxic Metals

### Interpretation and treatment





#	Name		Metabolic Association	Potential Intervention
<b>Nutrient Elements</b>				
1	Calcium	Ca	Myriad cell regulatory effects	See Calcium section
2	Chromium	Cr	Insulin target cell binding	200 - 400 µg/d
3	Copper	Cu	Detox pathways	3 - 4 mg/d
4	Magnesium	Mg	ATP energy transfer	200 - 400 mg/d
5	Manganese	Mn	Biosynthetic pathways	5 - 15 mg/d
6	Potassium	K	Neuromuscular function	Fresh fruits & vegetables
7	Selenium	Se	Antioxidant protection	200 - 1000 µg/d
8	Vanadium	V	Cholesterol, triglycerides	200 - 1000 µg/d
9	Zinc	Zn	Cofactor for numerous enzymes	15 - 60 mg/d
<b>Toxic Elements</b>				
			<b>Accumulation Site</b>	
11	Aluminum	Al	Lung	Avoidance
12	Arsenic	As	Skin, Bladder, Lung	
13	Cadmium	Cd	Kidney	Zinc
14	Lead	Pb	Bone	Calcium
15	Mercury	Hg	CNS/Brain	Selenium

Red blood cell (RBC) analysis is an invaluable diagnostic method for measuring concentrations of elements in erythrocytes providing a look at how well cellular levels are maintained because erythrocyte mineral levels reflect mineral status over a period of 4 months (the life cycle of an erythrocyte).

Other specimens, like urine or plasma, are affected by daily dietary fluctuations. In the process of their formation in bone marrow, erythrocytes acquire nutrient elements like zinc according to the availability of each element. The same may be said for the toxic elements, which means that high levels of these raise suspicion of chronic tissue penetration due to toxic exposure and inadequate detoxification mechanisms. All of the essential trace elements are dependent on stomach acid production for intestinal absorption.

## Key Clinical Points on Erythrocyte Nutrients

### **Calcium (Ca)**

Erythrocyte calcium levels are indicators of **ionic calcium** and are not related to dietary calcium.

There are approximately 179 biological functions of calcium. Every cell is dependent on the presence of ionic calcium. It is used in teeth and bones and the movement of muscles. It is required for the rhythmic action of the heart and the intestines. It is essential for the clotting of blood. It plays a role in infections, pregnancy, and in the maintenance of the acid-alkaline balance.

### **Ionic Calcium is the only physiologically active form of Calcium.**

Because ionic calcium is the only physiologically usable form of calcium, calcium from all sources, whether from diet or from bones, organs, and tissues, must first be broken down into ionic form before it can be utilized by the body for any of the 179 plus biological functions.

Erythrocyte calcium is associated with the etiology of heart disease and stroke playing a vital role in the induction of blood pressure elevation. Total erythrocyte calcium is elevated in hypertension and in postnatal hypoxic ischemic encephalopathy.

### **Chromium (Cr)**

Chromium accumulates primarily in spleen and heart tissue. Numerous clinical studies have proven that chromium impacts sugar metabolism through its role in uptake of insulin, and losses of chromium in urine are related to increased mobilization in response to the stimulus of frequent blood sugar peaks. Chromium also aids in lowering LDL cholesterol and raising HDL cholesterol. The best dietary sources include **liver, brewer's yeast, nuts, and whole grains.**

### **Copper (Cu)**

Copper is a co-factor in lipid metabolism, liver detoxification and neurological control. This may be a giant statement but sometimes the cause and cure of high cholesterol can be as simple as correcting a copper deficiency by its involvement in lipid metabolism.

Most copper is concentrated in liver, brain, and hair but is present in all other tissue. Best dietary sources are **whole grains, nuts, seeds, beans, liver, and shellfish.**

Most of the copper present in erythrocytes is bound to the enzyme **superoxide dismutase (SOD)**, which protects the cells from oxidative damage.

Dietary deficiency of copper is seen as low levels of erythrocyte copper and SOD, even in early stages of copper depletion.

Impairment of function due to copper deficiency may result from reduced activities of the enzymes, ceruloplasmin, monoamine oxidase, lysyl oxidase in connective tissue, and SOD.

Loss of these biochemical functions can lead to anemia, neural degeneration, lung and bone problems, CVD, and accelerated aging.

About 80% of erythrocyte copper is associated with SOD, while most plasma copper is bound to ceruloplasmin. Patients with Wilson's disease, an inherited copper accumulating disease, show elevated erythrocyte copper resistant to copper-lowering treatments. In these cases,

copper accumulates in liver and brain where it causes tissue degeneration, apparently due to the stimulation of protein and oxidative DNA damage.

## ***Magnesium (Mg)***

Magnesium is a critically important nutrient for many bodily functions which serves as a cofactor in approximately three hundred enzyme systems.

The magnesium content of red blood cells is a good marker of short-term magnesium status and low levels indicate nutritional deficiency.

Deficiencies of magnesium can cause a wide variety of problems including hypertension, diabetes, and the pre-menstrual syndrome.

Magnesium has also been found to be useful in the treatment of congestive heart failure, tachycardia, and other arrhythmias.

Symptoms frequently associated with magnesium deficiencies are **neuromuscular tremors, fasciculations, and gross muscle spasms**. Due to the relationship of magnesium to nervous tissue the earliest signs of deficiency is commonly the appearance of dullness and listlessness, nausea and loss of appetite, alopecia (rapid hair loss), tremors, and convulsions.

Magnesium also plays a vital role in normal cardiac function, and insufficiency has been increasingly associated with cardiovascular disease.

The major dietary sources of magnesium are **nuts, beans, and dark green vegetables**.

## ***Manganese (Mn)***

Like magnesium and zinc, manganese is involved with a significant number of **enzymes** involved with metabolism, especially those involved in **connective tissue maintenance, fatty acid synthesis, and Krebs cycle pathways**. In addition, manganese deficiency contributes to **glucose intolerance**. Manganese absorption is impaired by calcium, phosphate, and iron. Manganese also aids in production of estrogen and progesterone. The best source of manganese is found in **fruits, whole grains, and leafy green vegetables, pecans, peanuts, pineapples, hazelnuts, avocado and seaweed**

## ***Potassium (K)***

The **best single measure of body potassium status is erythrocyte potassium**.

Nervous and muscle tissues have strong requirements for potassium to maintain excitability. Depletion of body potassium can lead to a wide range of effects, including **hypertension, heart arrhythmias, and muscle weakness**.

The use of **vegetable juices, citrus juices, bananas, melons, and other fruits and vegetables** will increase potassium levels.

## **Selenium (Se)**

A primary role of selenium in erythrocytes appears to be the **activation of the enzyme glutathione peroxidase**, whereby glutathione reacts with oxygen radicals. Protein-containing foods in which the selenium is bound to amino acids, such as meats, grains, brazil nuts and seafood, are good sources of selenium.

Selenium functions primarily as an **activator of enzymes necessary for cellular protection from oxidative damage and maintenance of normal redox potentials**.

## **Vanadium (V)**

It is retained by liver and bone and transported on the blood protein transferrin. Vanadium lowers **cholesterol synthesis and may lower plasma triglycerides** in humans. It promotes mineralization of bones and teeth and may protect against cavities. It also has an apparent role insulin release.

Parsley, black pepper, dill, mushrooms and shellfish are good sources of vanadium.

## **Zinc (Zn)**

Growth and repair of any tissue is dependent on zinc as an activating cofactor for **DNA/ RNA polymerase**. For this reason, zinc is vital to the normal healing of wounds and skin disorders.

Zinc is required for normal immune function. In fact, there are many similarities between the immunologic affects of zinc deficiency and those of AIDS. Low zinc is associated with **low T-helper lymphocytes**. If intake of calcium, copper, or iron is excessive, tissue zinc may become depleted. If zinc is elevated, problems that might occur include iron nonresponsive anemia due to related copper deficiency and increased vascular disease risk from lowered HDL cholesterol. Sources of zinc in the diet include whole grains, nuts, seeds, and seafoods, especially shellfish. Low alkaline phosphatase may be a warning of zinc insufficiency.

## **Toxic Metals**

Toxic metals may exchange between blood plasma and erythrocytes after a person is exposed. The concentration of these metals in erythrocytes also is determined by the content of the tissue where erythrocytes originate: **the bone marrow**.

The marrow exchanges the metals with the mineral matrix of bone. Thus, elevated erythrocyte levels of a toxic metal may reflect a deep tissue accumulation of the element. The distribution of elements between bone and various soft tissues varies with each element.

The question of why a patient has developed a high toxic metal load is frequently difficult to answer. Obvious sources of high exposure from industrial occupations where heavy metals are used are easily identified, but chronic low-level exposures can escape notice.

## **Aluminum (Al)**

The best-known toxic effects of aluminum are dialysis encephalopathy and dementia in uremic patients. These cases have provided valuable insight about other toxic effects of aluminum, including **impaired memory, dementia, aphasia, ataxia, convulsions, and characteristic EEG changes**. Urine is the major elimination route of aluminum, so once a chelating agent has mobilized and bound the element, it is relatively easily eliminated. Potential sources include **antiperspirants, soda cans, baking soda, and toothpaste**.

## **Arsenic (As)**

Evidence links arsenic exposure and risk to vascular disease related to atherosclerosis. Long-term arsenic exposure in drinking water shows a relationship to **carotid atherosclerosis**.

Ingested arsenic has also been linked to cancers of the **skin, bladder, and lung**.

Sources of arsenic include: contaminated water supplies, paint pigments, smelting industry, microelectronics industry, wood preservatives (outdoor decks, playground equipment), pesticides, herbicides and fungicides.

Unidentified causes of **peripheral neuropathy** may be reason to rule out arsenic toxicity.

## **Cadmium (Cd)**

Cadmium competes with zinc at all cellular binding sites resulting in loss of enzyme activity.

The fact that cadmium is bound by the abundant zinc sequestering protein, metallothionein, and that this protein occurs in high concentration in kidney makes cadmium one of the most easily removed toxic elements.

During chronic exposure, the **kidney contains a major part of the body burden of cadmium** leading to potential damage to proximal tubules. Any intervention that increases the passage of metal chelating agents through the kidney will lower total body burden of cadmium.

Common related symptoms include: hypertension, femoral pain, osteopenia, vascular disease and emphysema.

Potential sources include **drinking water, processed foods, engine exhaust emissions, soft drinks from galvanized pipes, canned evaporated milk, cigarette smoke, paint pigments, and silver polish**.

**Treatment to consider is** EDTA suppository. Reduce toxin absorption via bentonite, dietary fiber (beans, cooked vegetables, oatmeal).

Adding competing nutrient such as zinc is helpful.

## **Lead (Pb)**

Lead toxicity causes paralysis and pain in the **extremities due to effects on demyelination, axonal degeneration, and presynaptic block**. **Normocytic, sideroblastic anemia** is the

consequence of lead's inhibiting effects on enzymes in the heme biosynthesis pathway. Other clinical signs associated with lead toxicity are **kidney damage, epigastric pain and nausea, and male and female reproductive failure.**

Lead toxicity commonly affects sensory, visual, auditory, and cerebellar (coordination) functions, reflecting the nervous system impact of this element. Patients may have paraesthesia in the region around the mouth and in the hands immediately after exposure.

Various intravenous chelation agents, including penicillamine and EDTA, have been shown to be effective in reducing lead body burden. Increased dietary calcium helps lower the intestinal absorption of lead. Potential sources of lead include:

- leaded house paint
- drinking water from lead plumbing
- pesticides
- newsprint.
- leaded or soldered joints in water systems
- contaminated herbal preparations
- teas
- chips of old lead-containing paint
- art supplies
- colored glass kits
- bullets,
- fishing sinkers,
- balance weights
- radiation shields
- lead-acid batteries
- bearing alloys
- babbitt metal
- certain ceramic glazes or pigments
- sewage sludge
- soils
- vegetation along highways

Calcium, zinc and/or iron deficiency conditions enhance uptake of ingested lead. In the body, absorbed lead soon leaves blood plasma and accumulates in erythrocytes where it binds to hemoglobin and thiols and also to the cell membrane.

Eventually, lead leaves the blood and deposits primarily in bone tissue and also in the aorta, kidneys, and other organs. This element can bind to enzymes, proteins and membranes that present **sulfhydryl, phosphate, amino and hydroxyl groups**. Lead interferes with enzymes that form heme, shortens erythrocyte life span, disrupts iron transport in erythropoietic cells, affects renal transport of uric acid, reduces cytochrome P-450 activity in children, and is synergistically toxic with cadmium and mercury.

In children, manifestations of lead excess may include encephalopathy with loss of IQ, and behavioral disorders. Adults and children may present with anorexia, metallic taste, insomnia, headaches, fatigue, anemia, reticulocytosis, and uricemia. Erythropoietic porphyria or porphyrinuria may occur.



## **Mercury (Hg)**

Conditions ranging from childhood autism to adult neurological dysfunction and dementia can result from the toxic effects of mercury. Mercury tends to form very stable bonds with various amino acid side chains of proteins, making it difficult to remove quickly. The major part of mercury in blood is bound to hemoglobin in red cells.

Sulfur-containing agents, such as **dimercaptosuccinic acid (DMSA)**, are the more effective agents for removing mercury from tissues. The **most important protective agent is dietary selenium**, which helps reduce the toxic effects of mercury.

Potential sources include **dental amalgams, broken thermometers, cosmetics, and predator or fresh water fish**, contaminated shellfish or seafood, contaminated water supplies, dental amalgams and/or recent dental work, laboratory equipment, barometers, thermometers, certain specially-formulated fungicides, old paint containing Hg fungicide and mining and smelting operations.

Signs and symptoms consistent with Hg contamination are variable and may include: metallic taste, increased salivation, paresthesias with decreased senses of hearing touch and vision, hypertension, headaches, fatigue, insomnia, and fine muscle tremor possibly displayed as poor handwriting.

A hallmark symptom is **emotional disturbance**, sometimes a bipolar depression but often a form of excitability and lack of ability for mental concentration.

## **Tin**

Tin is a potentially toxic element and is primarily in the erythrocytes but leaves blood and cells rapidly and is distributed to liver, bone, and kidney tissues.

Various organic tins affect various enzymes involved in **sugar metabolism, oxidative phosphorylation, and T-lymphocyte function**. Organic tin is mainly excreted via urine.

Effects of organic tin overload include: **ataxia, headaches, blurred vision, vertigo, hyperglycemia, and glucosuria**. Dystrophic changes to hepatocytes and bile ducts may occur, causing liver pain. Nephrosis, leukopenia, lymphopenia and reduced immune response are attributed to triphenyl tin.

Possible sources of tin include: tin-plated cans with damaged polymer coatings, toothpaste and perfumed soaps, metal alloys (including brass, bronze, pewter, babbitt, printers' alloy), soldered joints in cans and water systems, polyvinylchloride ("PVC") plastic manufacture (Sn is a heat stabilizer), dyes and pigments.

**Credit is contributed to the following lab for their advancement in the field of functional medicine:**

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