URINE TOXIC METALS

Meridian Valley LAB

801 S.W. 16th St., Suite 126
Renton, WA 98055

Tel: (425) 271-8689
Fax: (425) 271-8674

LAB#:
PATIENT:
ID:
SEX: Male
AGE: 53

POTENTIALLY TOXIC METALS

METALS	RESULT µg/g CREAT	REFERENCE RANGE	WITHIN REFERENCE RANGE / ELEVATED / VERY ELEVATED
Aluminum	**37**	< 25	
Antimony	**0.1**	< 0.6	
Arsenic	**33**	< 120	
Beryllium	**< dl**	< 0.5	
Bismuth	**0.4**	< 10	
Cadmium	**0.7**	< 2	
Lead	**11**	< 5	
Mercury	**3.3**	< 3	
Nickel	**12**	< 10	
Platinum	**< dl**	< 1	
Thallium	**0.06**	< 0.7	
Thorium	**< dl**	< 0.3	
Tin	**0.8**	< 9	
Tungsten	**0.04**	< 0.7	
Uranium	**0.04**	< 0.1	

CREATININE

	RESULT mg/dL	REFERENCE RANGE	2SD LOW / 1SD LOW / MEAN / 1SD HIGH / 2SD HIGH
Creatinine	**110**	45- 225	

SPECIMEN DATA

Comments: **953324**
Date Collected: **11/14/2008**
Date Received: **11/19/2008**
Date Completed: **11/20/2008**
Method: **ICP-MS**
<dl: **less than detection limit**
Provoking Agent: **DMPS EDTA**
Collection Period: **timed: 6 hours**
Volume:
Provocation: **POST PROVOCATIVE**

Toxic metals are reported as µg/g creatinine to account for urine dilution variations. **Reference ranges are representative of a healthy population under non-challenge or non-provoked conditions.** No safe reference levels for toxic metals have been established.

V10.00

URINE ESSENTIAL ELEMENTS

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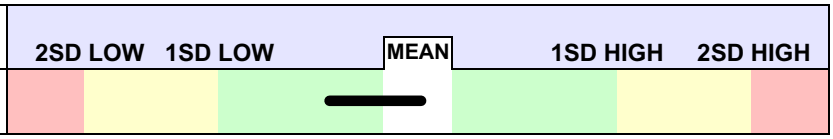
ESSENTIAL ELEMENTS

ELEMENTS	RESULT µg/mg CREAT	REFERENCE RANGE
Sodium	1600	900- 5000
Potassium	1140	750- 3000
Phosphorus	480	200- 1000
Calcium	360	45- 300
Magnesium	140	35- 230
Zinc	17	0.1- 1.5
Copper	0.25	0.007- 0.07
Sulfur	890	250- 1100
Manganese	0.039	0.0005- 0.008
Molybdenum	0.005	0.015- 0.16
Boron	1.6	0.6- 5.1
Chromium	0.046	0.008- 0.13
Lithium	0.009	0.009- 0.1
Selenium	0.11	0.04- 0.3
Strontium	0.13	0.04- 0.3
Vanadium	0.012	0.004- 0.035
Barium	0.002	< 0.013
Cobalt	0.0006	< 0.03
Iron	0.34	< 0.4
Zirconium	0.0004	< 0.003

CREATININE

	RESULT mg/dL	REFERENCE RANGE
Creatinine	110	45- 225



SPECIMEN DATA

Comments: 953324
Date Collected: 11/14/2008
Date Received: 11/19/2008
Date Completed: 11/20/2008

Method: ICP-MS
<dl: less than detection limit
Provoking Agent: DMPS EDTA

Collection Period: timed: 6 hours
Volume:
Provocation: POST PROVOCATIVE

Essential elements are reported as µg/mg creatinine to account for urine dilution variations. **Reference ranges are representative of a healthy population under non-challenge or non-provoked conditions.** Detoxification therapies can cause significant elevations of certain essential element levels (e.g. Cu, Zn). V10.00

INTRODUCTION

This analysis of urinary elements was performed by ICP-Mass Spectroscopy following acid digestion of the specimen. Urine element analysis is intended primarily for: diagnostic assessment of toxic element status, monitoring detoxification therapy, and identifying or quantifying renal wasting conditions. It is difficult and problematic to use urinary elements analysis to assess nutritional status or adequacy for essential elements. Blood, cell, and other elemental assimilation and retention parameters are better indicators of nutritional status.

1) 24 Hour Collections
"Essential and other" elements are reported as mg/24 h; mg element/urine volume (L) is equivalent to ppm. "Potentially Toxic Elements" are reported as µg/24 h; µg element/urine volume (L) is equivalent to ppb.

2) Timed Samples (< 24 hour collections)
All "Potentially Toxic Elements" are reported as µg/g creatinine; all other elements are reported as µg/mg creatinine. Normalization per creatinine reduces the potentially great margin of error which can be introduced by variation in the sample volume. It should be noted, however, that creatinine excretion can vary significantly within an individual over the course of a day.

If one intends to utilize urinary elements analysis to assess nutritional status or renal wasting of essential elements, it is recommended that unprovoked urine samples be collected for a complete 24 hour period. For provocation (challenge) tests for potentially toxic elements, shorter timed collections can be utilized, based upon the pharmacokinetics of the specific chelating agent. When using EDTA, DMPS or DMSA, urine collections up to 12 hours are sufficient to recover greater than 90% of the mobilized metals. Specifically, we recommend collection times of: 9 - 12 hours post intravenous EDTA, 6 hours post intravenous or oral DMPS and, 6 hours post oral bolus administration of DMSA. What ever collection time is selected by the physician, it is important to maintain consistency for subsequent testing for a given patient.

If an essential element is sufficiently abnormal per urine measurement, a descriptive text is included with the report. Because renal excretion is a minor route of excretion for some elements, (Cu, Fe, Mn Zn), urinary excretion may not influence or reflect body stores. Also, renal excretion for many elements reflects homeostasis and the loss of quantities that may be at higher dietary levels than is needed temporarily. For these reasons, descriptive texts are provided for specific elements when deviations are clinically significant. For potentially toxic elements, a descriptive text is provided whenever levels are measured to be higher than expected. If no descriptive texts follow this introduction, then all essential element levels are within acceptable range and all potentially toxic elements are within expected limits.

For essential elements, the mean and the reference ranges apply to human urine under non-challenge, non-provocation conditions. Detoxification therapies can cause significant deviations in essential element content of urine. For potentially toxic elements, the expected range also applies to conditions of non-challenge or non-provocation. Diagnostic or therapeutic administration of detoxifying agents frequently raise the urinary levels content of potentially

toxic elements. Descriptive texts appear in this report on the basis of measured results and correspond to non-challenge, non-provocation conditions.

CAUTION: Even the most sensitive instruments have some detection limit below which a measurement cannot be made reliably. Any value below the method detection limit is simply reported as "< dl." If an individual excretes an abnormally high volume of urine, urinary components are likely to be extremely dilute. It is possible for an individual to excrete a relatively large amount of an element per day that is so diluted by the large urine volume that the value measured is near the dl. This cannot automatically be assumed to be within the reference range.

ALUMINUM HIGH

This individual's urine aluminum is higher than expected; urine is the primary mode of excretion for absorbed aluminum.

Common sources of bioavailable aluminum include: aluminum cookware, flatware and especially coffee pots; aluminum hydroxide anti-acid formulations; some types of cosmetics, especially deodorants; some colloidal minerals and some herbs or herbal products. Aluminum cookware is particularly of concern if acid foods are cooked such as tomato paste (contains salicylates). In cosmetics and deodorants,aluminum chloride may be present as an astringent. In water purification, alum (sodium aluminum sulfate) may be used to coagulate dispersed solids and improve water clarity. Alumina or Al2O3 is very stable chemically and not bioavailable. Silica limits the solubility of aluminum and aluminum silicate is not very bioavailable. Clays, bentonite for example, contain aluminum that has poor bio-availabilty. Aluminum food containers are manufactured with polymer or plastic coatings that prevent direct food-aluminum contact provided such coatings are not damaged.

In the GI tract, phosphates react with aluminum ions forming insoluble aluminum phosphates. If this phosphate-blocking were 100% efficient, then virtually no aluminum would be absorbed. Evidently, this phosphate-forming process is incomplete because body tissue levels (such as hair) usually contain measurable amounts of aluminum. In the body aluminum follows a path of increasing phosphate concentration: plasma, cytosol, cell nucleus. Once in the nucleus, it adversely affects protein formation. Long-lived cells such as neurons are susceptible to long-term accumulation. Al is considered neurotoxic. Without intervention, aluminum accumulates continually in the body with the highest concentration occurring at old age or death.

A hair element test can be used to corroborate increased body burden of aluminum. An oral provocation with the amino acid glycine, 80 mg/Kg body weight (in divided doses) 24 hours before a diagnostic EDTA chelation with subsequent urine collection can be done to confirm aluminum excess. (Eliminate food/beverage sources of Al during this procedure.)

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LEAD HIGH

This individual's urine lead is higher than expected which means that lead intake or body burden is higher than that of the reference population.

Sources of lead include: old lead-pigment paints, batteries, industrial smelting and alloying, some types of solders, glazes on (foreign) ceramics, leaded (anti-knock compound) fuels, bullets and fishing sinkers, artist paints with lead pigments, and leaded joints in some municipal water systems. Most lead contamination occurs via oral ingestion of contaminated food or water or by children mouthing or eating lead-containing substances. The degree of absorption of oral lead depends upon stomach contents (empty stomach increases uptake) and upon the body's mineral status. Deficiency of zinc, calcium or iron may increase lead uptake. Transdermal exposure is slight. Inhalation has decreased significantly with almost universal use of non-leaded automobile fuel.

Lead accumulates in bones and inhibits formation of heme and hemoglobin in erythroid precursor cells. Before this happens, however, lower levels of lead can cause other problems. These are: impaired vitamin D metabolism, decreased nerve conduction rates, and developmental problems for children including: loss of IQ, hearing impairment, delayed growth, and behavior disorders. Transplacental transfer of lead to the fetus can occur at very low lead concentrations in the body. At relatively low levels, lead can participate in synergistic toxicity with other elements (cadmium, mercury).

Confirming tests for lead excess are: urinary lead following provocation with intravenous EDTA, or DMPS, or oral DMSA and hair element analysis. Whole blood analysis can be expected to reflect only recent exposures and does not correlate well with total body burden of lead (Carson, Ellis and McCann, Toxicology and Biological Monitoring of Metals in Humans, Lewis Publishers, p. 130, 1987). Preliminary studies performed at DDI indicate significantly increased fecal lead following I.V. vitamin C.

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MERCURY HIGH

This individual's urine mercury is higher than expected but not sufficiently high to assume pathophysiological effects. Symptomatology depends on many factors: the chemical form of absorbed Hg and its transport in body tissues, presence of other synergistic toxics (Pb, Cd have such effects),presence of disease that depletes or inactivates lymphocytes or is immunosuppressive, organ levels of xenobiotic chemicals and sulfhydryl-bearing metabolites (e.g. glutathione), and the concentration 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 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. Note that in mercury contamination of long duration, renal excretion of mercury (and normal metabolites) may become impaired, and the urine level of mercury might be only mildly elevated or not elevated at all due to renal failure.

Mercury is used in: dental amalgams (50% by weight), explosive detonators; some vaccines in pure liquid form for thermometers, barometers, and laboratory equipment; batteries and electrodes ("calomel"); and in fungicides and pesticides and in the paper industry. The fungicide/pesticide use of mercury has declined due to environmental concerns, but mercury residues persist from past use. Emissions from coalfired power plants and hospital/municipal incinerators are significant sources of mercury poollution.

Methylmercury, the common, poisonous form, occurs by methylation in aquatic biota or sediments (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 the food is contaminated with one of the previously listed forms/sources. A daily diet of fish can cause 1 to 10 micrograms of mercury/day to be ingested; the majority of which is organic, methylmercury.

Depending upon body burden and upon type, duration and dosage of detoxifying agents, elevated urine mercury may occur after administration of: DMPS, DMSA, or D-penicillamine. Mercury accumulation can also be assessed by comparing pre- and post-I.V. vitamin C fecal mercury levels (DDI observations). Blood and especially blood cell analyses are only useful for diagnosing very recent or ongoing organic (methyl) mercury exposure.

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2. World Health Organization: "Methylmercury" Environ. Health Criteria 101 (1990); "Inorganic Mercury" Environ. Health Criteria 118 (1991) WHO, Geneva, Switzerland.
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NICKEL HIGH

This individual's urine nickel is elevated which may or may not be of significance. Urinary excretion of nickel bound to cysteinyl or thiol compounds (such as glutathione) or to amino acids (histidine, aspartic acid, arginine) is the predominant mode of excretion. With the exception of specific occupational exposures, most absorbed nickel comes from food or drink, and intakes can vary by factors exceeding 100 depending upon geographical location, food type, and water supply. Depending upon chemical form and physiological factors, from 1 to 10% of dietary nickel may be absorbed from the gastrointestinal tract into the blood. Urine reflects recent exposure to nickel and may vary widely in nickel content from day to day due to the above factors.

Sources of nickel are numerous and include the following.

. Cigarettes (2 to 6 mcg Ni per average cigarette)
. Diesel exhaust (particulates may contain up to 10 mg/gram)
. Foods, especially: cocoa, chocolate, soya products, nuts, and hydrogenated oils
. Nickel-cadmium batteries
. Nonprecious, semiprecious dental materials
. Nickel-containing prostheses
. Electroplating, plated objects, costume jewelry
. Pigments (usually for ceramics or glass)
. Catalyst materials (for hydrogenation processes in the food, petroleum and petrochemical industries)
. Arc welding
. Nickel refining and metallurgical processes

Most clinically observed nickel contaminations are manifested as dermatoses - contact dermatitis and atopic dermatitis. However, Ni hypersensitizes the immune system causing hyperallergenic responses to many different substances. Because nickel can displace zinc from binding sites on enzymes, it can have inhibiting or activating effects on such enzymes. Nickel sensitivity is observed to be three to five times more frequent in women than in men.

Other laboratory tests or clinical findings that would be indicative of nickel excess are; hair element analysis, presentation of multiple allergic sensitivities, dermatitis, positive patch test for "Ni allergy", proteinuria, hyperaminoaciduria (by 24-hour urine amino acid analysis). Detoxification treatments with administration of EDTA or sulfhydryl agents (DMPS, DMSA, D-penicillamine) may increase urine nickel levels depending upon: body burden and mobility in tissues, duration of treatment, dosage and other factors.

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5. Ambient Water Quality Criteria for Nickel, US EPA NTIS, Springfield, VA. Publ No. PB81-117715,1980.

CALCIUM HIGH

Urine analysis is not a preferred way to assess body calcium stores. Nutritional sufficiency of calcium should be assessed through dietary analysis. Whole blood calcium level, serum calcium ion level, parathyroid hormone determinations, and bone density measurement are tests that are more indicative of calcium status.

High urinary calcium may be an artifact of diet, or of nutritional supplementation of calcium, or of excessive use of vitamin D or of vitamin A. Very high protein diets may cause increased uptake and excretion of dietary calcium. Cessation of these dietary inputs typically normalizes the urinary calcium level within several days.

High urinary calcium is associated with detoxification therapies in which EDTA is administered. High urine calcium also can be a consequence of immobilization or extended bed rest. Steroid therapy and glucocorticoid excess can raise urinary calcium levels.

Pathological conditions that may feature elevated urinary calcium include: renal acidosis, hyperparathyroidism, hyperthyroidism, diabetes mellitus, ulcerative colitis and some cases of Crohn's disease, sarcoidosis, acromegaly, myeloma, carcinoma of the thyroid or metastatic to bone, and Paget's disease.

Osteoporosis is NOT reliably indicated by urine calcium measurement only because the calcium loss is typically too slow and insidious to significantly raise urinary calcium.

BIBLIOGRAPHY FOR CALCIUM

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ZINC HIGH

High urinary zinc may or may not correspond to global zinc excess or to zinc loss from body tissues, because the major route for zinc excretion is via the bile, intestinal transport and feces. Typically, from two to ten percent of total zinc excretion occurs via urine; a similar amount occurs in sweat; the remainder (about 80 to 95%) occurs via biliary secretion to the intestine and is

excreted in feces. Urine levels may fluctuate without reflecting or influencing body stores.

Very high urinary zinc levels are expected to result from EDTA detoxification therapy; 3 to 20 mg/L is commonly measured in the 12 hours following intravenous administration of EDTA. Lesser elevations of urine zinc also are expected to result from sulfhydryl agent detoxification therapy (DMPS, DMSA, D-penicillamine). One to five mg/L is commonly found in the 24 hours following administration of these agents. Zinc repletion may be beneficial or required during such therapies.

Breakdown of tissue releases zinc into extracellular fluids and increases urinary zinc levels. This may be observed following or in conjunction with: accidental injury, surgery, catabolism of diseased/disordered tissue, starvation (ketosis) and diabetes. Zinc wasting may occur in alcoholic cirrhosis.

Zinc overload or toxicity can occur from ingestion of zinc contaminated food or drink; galvanized pipes or pails can be sources. Occupational or environmental exposure to zinc fumes may produce an acute contamination or poisoning. Elevated urinary zinc beyond two standard deviations high (without provocation) warrants investigation of possible sources of zinc excess, or of tissue catabolism or injury.

Excessive amounts of zinc in body tissues may displace copper and/or iron from tissue binding sites and may provoke anemia. Symptoms consistent with chronic zinc toxicity include: lethargy, difficulty writing and with fine motor skills, light-headedness, and renal failure. Immediate symptoms (within 12 hours) of acute zinc excess via ingestion include: nausea, vomiting, diarrhea, exhaustion, headache, dizziness, and myalgia. Other laboratory findings consistent with zinc toxicity would be: elevated leukocyte count, elevated serum amylase and lipase, elevated whole blood zinc concentration, elevated hair zinc level (if the zinc excess is chronic).

BIBLIOGRAPHY FOR ZINC

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COPPER HIGH

Significantly elevated copper in urine can be secondary to provocative challenge with sulfhydryl (-SH) bearing agents such as D-penicillamine (”Cuprimine”), DMSA, or DMPS. Large, multi-gram doses of vitamin C (ascorbic acid), administered orally or intravenously, may slightly or moderately increase excretion of copper.

Increased urinary copper can be an artifact of nutritional supplementation with copper or come from drinking water that is high in copper content. Acidic water carried in copper pipes can dissolve some copper which increases the copper intake if used for drinking or cooking. Molybdenum supplementation at high levels or if inappropriate may cause increased copper excretion; molybdenum and copper are mutually antagonistic in terms of body retention.

Bacterial or other infections may cause hypercupremia with attendant or delayed hypercuprinuria. This is transient and follows the inflammatory stage of the disease. Published studies such as Vivoli, Sci Total Environ, 66 p. 55-64, 1987 have correlated increased urinary copper with increased blood pressures in hypertensives. Biliary obstruction or insufficiency can decrease normal excretion of copper via the bile while increasing blood and urinary levels. Proteinuria also may feature increased copper levels.

Hyperaminoacidurias that include histidinuria can result in urinary copper wasting because histidine is a powerful chelator of copper. Hyperaminoacidurias that include histidine can be of many origins including:genetic factors, chemical or elemental toxicities, infectious agents, hyperthyroidism, sugar intolerances,nephrotic syndromes, etc.

In Wilson's disease, urinary copper is generally increased (above 100 micrograms/24 hours) without provocation or chelation. Use of D-penicillamine or DMPS as a provocative diagnostic procedure can yield a 5 - 10X increase in urinary copper levels in normal individuals. In contrast, Wilson's disease patients may then excrete 50-100 times the normal levels or 1000 to 2000 mcg/24 hr. (Walshe, J. Rheumatology (supp/7) 8 p.3-8, 1981).

Urine analysis (unprovoked) is not an adequate procedure to assess copper stores or copper metabolism. Blood levels, erythrocyte copper content, erythrocyte superoxide dismutase activity, and serum ceruloplasmin are other more indicative measurements for copper status.

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MANGANESE HIGH

High urinary manganese may or may not correspond to global manganese excess or manganese loss from body tissues because the major route for manganese uptake, reuptake, and excretion is via the bile, intestinal transport and feces. Typically, less than onehalf of one percent of total manganese excretion occurs via urine, 3-5% occurs in sweat; the remainder (approx. 95%) occurs via intestinal transport (bile) and feces. Hence urinary manganese may be increased in patients with biliary obstruction or cirrhosis. Urinary manganese levels may

fluctuate without reflecting or influencing body stores.

Elevated urinary manganese can occur following intravenous administration of EDTA; levels up to 50 micrograms per 24 hours are commonly seen without evidence of manganese overload (DDI experience). Elevated urinary manganese also occurs following oral administration of D-penicillamine with levels up to 25 micrograms per 24 hours commonly seen. DMSA and DMPS treatments also may result in similar increases in urinary manganese levels.

Manganese excesses in urine (without provocative challenge) are featured in renal wasting syndromes, nephritis, biliary insufficiency or obstruction, and dietary overload or inappropriate or excessive supplementation. Some hormones and drugs inhibit biliary excretion of manganese resulting in increased urinary excretion. Dopamine, glucagon and cyclic AMP are reported to do this. Environmental or industrial sources of manganese include: mining, metals or ores refining and processing, metal alloying, welding, some types of batteries, glazes and pigments, catalysts (petrochemical, plastics and synthetic rubber industries), and the gasoline additive, ”MMT”. Ground water used as drinking water may contain manganese, and a 1975 USEPA survey of city drinking waters showed variability from < 5 to 350 mcg/L (”Drinking Water and Health”, U.S. Printing & Publishing Office, Nat. Acad. of Sci., Washington DC, 1977). Some herbs and teas may contain high concentrations of manganese.

Relative to other essential trace elements, excessive manganese retention can be quite neurotoxic. Inhalation, as a result of occupational exposure, is the route of assimilation that is most harmful. Some symptoms and manifestations of manganese excess or poisoning are: psychiatric disturbances (hyperirritability, hallucinations, violence), tremor, Parkinson’s-like symptoms, anorexia, sexual impotence, and speech disturbance.

Because urine is not a reliable indicator of manganese status, other laboratory tests are advised if manganese excess is suspected. These are: whole blood manganese analysis, blood cell elements, and hair elemental analysis.

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MOLYBDENUM LOW

This individual’s molybdenum level is lower than one standard deviation below the mean of the reference population which means that this individual’s urine molybdenum level corresponds to the lowest 17% (approximately) of that population.

Molybdenum is an essential activator of some important enzymes in the body: sulfite oxidase (catalyzes formation of sulfate from sulfite), xanthine oxidase (formation of uric acid and

superoxide ion from xanthine), and aldehyde oxidase (processes aldehydes). Over 50% of absorbed Mo is normally excreted in urine; the remainder is excreted via bile to the feces or is excreted in sweat.

The level of molybdenum in urine may be a transient finding and may not reflect body tissue or liver levels. In copper deficiency, retention of molybdenum is increased (tissue levels could be normal or high), while urine levels might be subnormal. In renal insufficiency, molybdenum (and other elements) can be low in urine. Creatinine clearance and blood metabolite levels should be measured if a renal transport disorder is suspected.

Individuals receiving prolonged total parenteral nutrition (”TPN”) may have low body tissue and urine levels of molybdenum because it is occasionally omitted from TPN formulations.

Molybdenum in foods is mostly in soluble complexes, and only a small amount is required daily (100 to 200 micrograms, adults). Therefore, frank molybdenum deficiency is uncommon. However, GI dysfunctions, poor-quality diet, and stressors can combine to produce inadequate molybdenum. Tungsten is a powerful antagonist of molybdenum retention, copper less so. Episodic exposures to high levels of either may result in periods of low Mo excretion that follow prior periods of high Mo excretion. Sulfites, aldehydes and high amounts of purines in the diet may increase need for and retention of molybdenum. Prolonged use of dithiol chelators (DMPS, DMSA) or MSM can result in poor molybdenum status as indicated by low levels in red blood cells (DDI observations).

A multielement hair analysis plus analyses for serum and urine uric acid can be used to confirm or rule out molybdenum insufficiency.

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