DOCTOR'S DATA INC

LAB #: U000000-0000-0
PATIENT: Sample Patient
ID: PATIENT-S-00001
SEX: Female
AGE: 61

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

Toxic Metals; Urine

TOXIC METALS		RESULT µg/g creat	REFERENCE INTERVAL	WITHIN REFERENCE / OUTSIDE REFERENCE
Aluminum	(Al)	**210**	< 35	
Antimony	(Sb)	**0.5**	< 0.4	
Arsenic	(As)	**40**	< 117	
Barium	(Ba)	**11**	< 7	
Beryllium	(Be)	**< dl**	< 1	
Bismuth	(Bi)	**0.2**	< 15	
Cadmium	(Cd)	**2.2**	< 1	
Cesium	(Cs)	**8.9**	< 10	
Gadolinium	(Gd)	**0.4**	< 0.4	
Lead	(Pb)	**31**	< 2	
Mercury	(Hg)	**15**	< 4	
Nickel	(Ni)	**22**	< 12	
Palladium	(Pd)	**< dl**	< 0.3	
Platinum	(Pt)	**< dl**	< 1	
Tellurium	(Te)	**< dl**	< 0.8	
Thallium	(Tl)	**0.4**	< 0.5	
Thorium	(Th)	**< dl**	< 0.03	
Tin	(Sn)	**1.9**	< 10	
Tungsten	(W)	**1.2**	< 0.4	
Uranium	(U)	**0.2**	< 0.04	

URINE CREATININE	RESULT mg/dL	REFERENCE INTERVAL	-2SD -1SD MEAN +1SD +2SD
Creatinine	**26.7**	35 - 225	

SPECIMEN DATA

Comments:

Date Collected: 5/16/2014
Date Received: 5/17/2014
Date Completed: 5/19/2014
Method: ICP-MS

pH upon receipt: Acceptable
<dl: less than detection limit
Provoking Agent: DMPS CAEDTA
Creatinine by Jaffe Method

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

Results are creatinine corrected to account for urine dilution variations. **Reference intervals and corresponding graphs are representative of a healthy population under non-provoked conditions.** Chelation (provocation) agents can increase urinary excretion of metals/elements.

V13

LAB #: U000000-0000-0
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SEX: Female
AGE: 61

CLIENT #: 12345
DOCTOR:
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3755 Illinois Ave.
St. Charles, IL 60174

Essential Elements; Urine

ESSENTIAL AND OTHER ELEMENTS		RESULT/UNIT per creatinine		REFERENCE INTERVAL	PERCENTILE 2.5th 16th 50th 84th 97.5th
Sodium	(Na)	**330**	mEq/g	43.5- 226	
Potassium	(K)	**79**	mEq/g	22- 82	
Phosphorus	(P)	**530**	µg/mg	250- 1300	
Calcium	(Ca)	**1040**	µg/mg	35- 350	
Magnesium	(Mg)	**480**	µg/mg	25- 230	
Zinc	(Zn)	**34**	µg/mg	0.1- 2	
Copper	(Cu)	**0.6**	µg/mg	0.01- 0.09	
Sulfur	(S)	**1490**	µg/mg	308- 1650	
Manganese	(Mn)	**0.099**	µg/mg	0.0005- 0.01	
Molybdenum	(Mo)	**0.12**	µg/mg	0.016- 0.18	
Boron	(B)	**1.3**	µg/mg	0.8- 6.8	
Chromium	(Cr)	**0.003**	µg/mg	0.0005- 0.01	
Lithium	(Li)	**0.023**	µg/mg	0.01- 0.2	
Selenium	(Se)	**0.18**	µg/mg	0.034- 0.28	
Strontium	(Sr)	**0.41**	µg/mg	0.06- 0.54	
Vanadium	(V)	**0.002**	µg/mg	0.0002- 0.004	
					68th 95th
Cobalt	(Co)	**1.9**	µg/mg	< 0.008	
Iron	(Fe)	**3**	µg/mg	< 2	

URINE CREATININE	RESULT mg/dL	REFERENCE INTERVAL	-2SD -1SD MEAN +1SD +2SD
Creatinine	**26.7**	35- 225	

SPECIMEN DATA

Comments:

Date Collected: 5/16/2014
Date Received: 5/17/2014
Date Completed: 5/19/2014
pH Upon Receipt: Acceptable
<dl: less than detection limit
Provoking Agent: DMPS CAEDTA
Collection Period: timed: 6 hours
Volume:
Provocation: POST PROVOCATIVE
Method: ISE;Na, K Spectrophotometry; P ICP-MS; B, Ca, Cr, Co, Cu, Fe, Mg, Mn, Mo, Se, Sr, S, V, Zn Creatinine by Jaffe method

Results are creatinine corrected to account for urine dilution variations. **Reference intervals and corresponding graphs are representative of a healthy population under non-provoked conditions.** Chelation (provocation) agents can increase urinary excretion of metals/elements.

V13

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.

Reference intervals and corresponding graphs shown in this report are representative of a healthy population under non-provoked conditions. Descriptive texts appear in this report on the basis of measured results and correspond to non-challenge, non-provoked conditions.

Chelation (provocation) agents can increase urinary excretion of metals/elements. Provoked

reference intervals have not been established therefore non-provoked reference intervals shown are not recommended for comparison purposes with provoked test results. Provoked results can be compared with non-provoked results (not reference intervals) to assess body burden of metals and to distinguish between transient exposure and net retention of metals. Provoked results can also be compared to previous provoked results to monitor therapies implemented by the treating physician. Additionally, Ca-EDTA provoked results can be used to calculate the EDTA/Lead Excretion Ratio (LER) in patients with elevated blood levels.

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 (Al) markedly exceeds the expected level. Urine is the primary mode of excretion for absorbed Al, and this high level indicates ingestion or absorption of relatively high amounts of Al.

Common sources of bioavailable Al include: aluminum cookware, flatware and especially coffee pots; aluminum hydroxide anti-acid formulations; some types of cosmetics, especially deodorants; 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 Al so Al silicate is not very bioavailable orally. Clays, bentonite for example, contain Al that has poor bio-availability. Aluminum food containers are manufactured with polymer or plastic coatings that prevent direct food-aluminum contact provided such coatings are not damaged.

In the gastrointestinal tract, phosphates react with Al ions forming insoluble Al phosphates. If this phosphate-blocking were 100% efficient, then virtually no Al would be absorbed. Evidently, this phosphate-forming process is incomplete because body tissue levels (such as hair) usually contain measurable amounts of Al. In the body Al follows a path of increasing phosphate concentration: plasma, cytosol, cell nucleus. Once in the nucleus, it may adversely affects protein formation. Long-lived cells such as neurons are susceptible to long-term accumulation. Al may be neurotoxic and is implicated as a stabilizing agent (via Al phosphate bonds) in neurofibrillary tangles in Alzheimer's disease (Science, 267, pp 793-4, 1995). In cells, Al inhibits the citric acid cycle enzyme isocitrate dehydrogenase which catalyzes formation of alpha-ketoglutaric acid. An effect of this inhibition could be hyperammonemia. Al also inhibits hexokinase, a magnesium dependent phosphorylating enzyme. Al accumulates continually in the body with the highest concentrations occurring at late in life.

Fatigue, hypophosphatemia, increased prothrombin time, and porphyria are consistent with Al excess. A hair element test may be used to further evaluate recent Al exposure. Comparison of urine Al levels before and after intravenous administration of EDTA provides an estimate of net retention of Al over time. It should be

noted that EDTA-induced increases in Al do not directly reflect Al levels that may have accumulated in the central nervious system.

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ANTIMONY HIGH

This individual’s urine antimony (Sb) is higher than expected, but potential associated symptoms and toxic effects may not be present. This is because antimony has two valences: Sb+3 and Sb+5. Sb+3 is inherently the more toxic but is mostly excreted in feces. Sb+5, less toxic, binds less well to body tissues and is excreted mostly in urine. The current analysis does not differentiate the two forms of Sb.

Antimony can be assimilated by inhalation of Sb salt or oxide dust, ingested with (contaminated) foods or fluids, or absorbed transdermally. Inhalation may occur in industrial areas that involve smelting or alloying is done (usually with copper, silver, lead, tin). Sb is present in tobacco at about 0.01% by weight; about 20% of this is typically inhaled by cigarette smoking (Carson et al., Toxicology and Biological Monitoring of Metals in Humans, Lewis Pub. p. 21, 1987). Antimony compounds are used for fireproofing textiles and plastics, and this element may be found in battery electrodes, ceramics and pigments. Antimony can be absorbed with the handling of gun powder or the frequent use of firearms. Recent studies indicate high levels of antimony in sheepskin bedding produced in New Zealand. Antimony contamination of soft plastic-bottled water is time and temperature dependent.

Symptoms of mild Sb exposure/retention may be insidious and multiple including: fatigue, muscle weakness, myopathy, and metallic taste. Chlorides and oxides of both valences of Sb can be mutagenic and may affect leukocyte function. Sb can bond to sulfhydryl (-SH) sites on enzymes and may interfere with cellular metabolism. Acute symptoms that may be associated with excessive Sb exposure/retention include: respiratory tissue irritation and pneumoconiosis with (chronic) inhalation of Sb dusts, RBC hemolysis with inhalation of stibine (SbH_3) vapor, and gastrointestinal distress if orally ingested. Skin exposure can produce ”antimony spots” or rashes which resemble chicken pox. Certain molds can produce the highlyneurotoxic stibine gas from Sb; stibine inhibits acetylcholinestelase activity.

A hair element analysis may be used to further assess Sb exposure. Antimony may be elevated in urine following administration of DMPS or DMSA if exposures to Sb have resulted in net retention; such levels may or may not be associated with overt adverse

health effects.

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Barium High

Barium (Ba) has not been established to be an essential element. Elevated levels of Ba often are observed after exposure to Ba (a contrast agent) during diagnostic medical tests (e.g. ”barium swallow”, ”upper GI series”, ”barium enema”, etc.). Elevated levels of Ba may interfere with calcium metabolism and potassium retention. Acutely high intake of soluble Ba-salts (nitrates, sulfides, chlorides) can be toxic. Chronic exposure to Ba may be manifested by muscular and myocardial stimulation, tingling in the extremities, and loss of tendon reflexes. Due to its high density, Ba is utilized to absorb radiation and is utilized in concrete shields around nuclear reactors and in plaster used to line x-ray rooms. Peanuts/peanut butter are very high in Ba so urine Ba may be elevated shortly after consumption of these foods; toxic effects would not be anticipated under such conditions.

The main use of Ba in medicine is as a contrast medium. Long-term retention of Ba can occur - granuloma of the traverse colon has been reported after diagnostic use of Ba-sulfate. Crystalline Ba-titanate is a ceramic compound which is used in capacitors and transducers. Ba is also used to produce pigments in paints and decorative glass. Soluble Ba compounds are highly toxic and may be used as insecticides. Ba-aluminates are utilized for water purification, acceleration of concrete solidification, production of synthetic zeolites, and in the paper and enamel industries.

Although Ba is poorly absorbed orally (<5%) it can be very high in peanuts and peanut butter (about 3,000 nanograms/gram), frozen and fast foods such as burgers, fries, and hot dogs (400-500 nanograms/gram). It is noteworthy that Ba intake is much higher in children than adults (Health Canada 2005, www.atsdr.cdc.gov/toxprofiles/tp24-c6.pdf).

Ba levels (and the levels of 16 other elements) in water can be assessed with water testing as provided by DDI. A possible confirmatory test for excessive Ba retention ismeasurement of blood electrolytes as hypokalemia may be associated with excessive Ba in the body. Hair

CADMIUM HIGH

This individual’s urine cadmium (Cd) level equals or exceeds twice the maximum expected level. This element is insidiously toxic with chronic accumulations affecting renal function, pulmonary and cardiovascular tissues,

bone, and the peripheral nervous system. Without intervention, the biological half-life of Cd in humans exceeds 20 years (Harrison's Principles of Internal Medicine, 13th ed, pp 2463-64).

Chronic manifestations associated with this degree of Cd excess include: hypertension, weight loss, microcytic-hypochromic anemia, lymphocytosis, proteinuria with wasting of beta2 microglobulin, emphysema and pulmonary fibrosis (if inhalation was a route of contamination), atherosclerosis, steomalacia and lumbar pain, and peripheral neuropathy. Acute inhalation of Cd dusts, fumes or soluble salts may produce cough, pneumonitis and fatigue. Manifestations of Cd toxicity may be lessened or delayed by an individual's protective and detoxication capacities. Zinc and vitamin E are protective; metallothionein and glutathione bind Cd and help detoxify itinitially.

Smoking can be a source for as much as 0.1 mcg Cd per cigarette (HEW Pub. No. NIOSH 76-192, US Govt. Printing Ofc., 1976). Some medical authorities consider Cd to be a carcinogen for lung cancer (Harrison's Principles, 13th ed, op. cit. pp 2463). Other occupational or environmental sources include: mining and smelting activities, pigments and paints, electroplating, electroplated parts (e.g., nuts and bolts), batteries (Ni-Cd), plastics and synthetic rubber, photographic and engraving processes, old drums from some copy machines, photoconductors and photovoltaic cells, and some alloys used in soldering and brazing. "Cadmium Red" as used in dental acrylics (dentures) could be a significant source of exposure for those making dentures or dentists/dental techs making fine- tune adjustments (grinding) to dentures chair side. Cadmium-free acrylic dentures are now available.

Depending upon the extent of net retention of Cd elevated urine Cd may occur after administration of EDTA, and to a much lesser extent DMPS, DMSA, or D-penicillamine.Blood Cd measurement may not be indicative (Harrison's Principles of Internal Medicine, 13th ed., pp 2463).

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NHANES II Survey" Environ. Health Persp. 91, pp 133-40, 1991.

LEAD HIGH

This individual's urine lead exceeds three times the upper expected limit per the reference population. Because a percentage of absorbed or assimilated lead is excreted in urine, the urine lead level reflects recent or ongoing exposure to lead and the degree of excretion or detoxification.

Sources of lead include: old lead-pigment paints, batteries, industrial smelting and alloying, some types of solders, ayruvedic herbs, some toys and products from China, glazes on (foreign) ceramics, leaded (antiknock 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 extensively in bone and inhibits formation of heme and hemoglobin in erythroid precursor cells. Bone lead is released to soft tissues with bone remodeling that can be accelerated with growth, menopausal hormonal changes and osteoporosis. Lead has physiological and pathological effects on body tissues that may be manifested from relatively low lead levels up to acutely toxic levels. In children, developmental disorders and behavior problems may occur at relatively low levels: loss of IQ, hearing loss, poor growth. In order of occurrence with increasing lead concentration, the following can occur: impaired vitamin D metabolism, initial effects on erythrocyte and erythroid precursor cell enzymology, increased erythrocyte protoporphyrin, headache, decreased nerve conduction velocity, metallic taste, loss of appetite, constipation, poor hemoglobin synthesis, colic, frank anemia, tremors, nephrotoxic effects with impaired renal excretion of uric acid, neuropathy and encephalopathy. At relatively low levels, lead can participate in synergistic toxicity with other toxic elements (e.g. cadmium, mercury).

Excessive retention of lead can be assessed by urinalysis after provocation with Ca-EDTA (iv) or oral DMSA. Whole blood analysis can be expected to reflect onlyrecent exposures and does not correlate well with total body burden of lead.

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MERCURY HIGH

This individual's urine mercury (Hg) far exceeds the expected level for the general population under non-provoked conditiitons. Presentation of symptoms associated with excessive Hg exposure can depend on many factors: the chemical form of Hg its accumulation in specific tissues, presence of other toxicants, presence of disease that depletes glutathione or inactivates lymphocytes or is immunosuppressive, and the concentration of protective nutrients, (e.g. zinc, selenium).

Early signs of excessive Hg exposure 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/dysregulation. Advanced disease processes from excessive Hg assimilaion include: tremors and incoordination, anemia, psychoses, manic behaviors, possibly autoimmune disorders and renal dysfunction or failure.

Mercury is commonly used in: dental amalgams (50% by weight), explosive detonators; in pure liquid form for thermometers, barometers, and laboratoryequipment; batteries and electrodes, some medicaitons and ayruvedic herbs, and Hg in fungicides and pesticides. The use of Hg in fungicides/pesticides has declined due to environmental concerns, but mercury residues persist from past use.

Methylmercury, the most common, organic form, occurs by methylation of inorganic 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. Daily ingestion of fish can result in the assimialtion 1 to 10 micrograms of mercury/day.

Depending upon the extend of cumulative Hg exposure, elevated urine mercury may occur after administration of DMPS, DMSA, or D-penicillamine. Blood and especially red blood cell elemental analyses are only useful for diagnosing very recent or ongoing organic (methyl) mercury exposure.

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NICKEL HIGH

This individual’s urine nickel (Ni) is elevated which may or may not be of significance. Urinary excretion of nickel bound to cysteine or other 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 Ni comes from food or drink, and intakes can vary by factors exceeding 100 depending upon geographical location, diet, and water supply. Depending upon chemical form and physiological factors, from 1 to 10% of dietary Ni may be absorbed from the gastrointestinal tract. Urine Ni only reflects recent exposure to Ni and may vary widely from day to day.

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, hydrogenated oils, and coffee
- Nickel-cadmium batteries (Ni-Cd)
- Nonprecious, semiprecious dental materials
- Nickel-containing prostheses
- Electroplating, metal 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 relavant Ni exposures are manifested as dermatoses - contact dermatitis and atopic dermatitis. However, Ni hypersensitizes the immune system and may cause hyperallergenic responses to many different substances. Because Ni can displace zinc from binding sites on enzymes it can affect abnormal enzymatic activity. Nickel sensitivity is observed to be three to five times more prevelant in females than in males.

Other laboratory tests or possible clinical findings that may be associated with Ni exposure are; hair elements analysis, presentation of multiple allergic sensitivities, dermatitis, positive patch test for ”Ni allergy”, proteinuria, hyperaminoaciduria (by 24-hour urine amino acid analysis). Administration of EDTA or sulfhydryl agents (DMPS, DMSA, D-penicillamine) may increase urine Ni levels; such chelator-induced elevations may or may not be associated with adverse health effects.

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TUNGSTEN HIGH

The level of tungsten (W) in this urine sample is higher than expected. After exposure and absorption via inhalation, ingestion or injection, most W is rapidly eliminated via urine and feces. W has no known biological role. Long-term chronic exposures have been associated with lung disease (pneumoconiosis or ”hard metal lung disease”) and lung cancer. Skin contact with W may produce contact eczema, pruritis, folliculitis, and neurodermatitis. Tungsten has an antagonistic relationship with molybdenum (Mo) decreasing hepatic Mo concentration and reducing the effectiveness of sulfite and xanthine oxidases.

Tungsten is a silvery-white lustrous element usually obtained as a grey powder and is mainly utilized as tungsten carbide in metal-working, mining and petroleum industries. Calcium and magnesium tungstates are widely used in filaments for electric lamps, electron tubes and television tubes. Since W has the highest melting point of all metals it is used for high-speed and hot-worked steels. Other sources of W include catalysts and reagents in biological analysis, fire and waterproofing materials, and industrial lubricants.

For people exposed to hard-metal dust, W levles can reach .014 µg/g in urine. Intestinal absorption of tungsten is rapid and seemingly significant. W is rapidly transported to the blood and then to the kidneys for filtration and eventual excretion from the body. In a rat study, elimination of W via feces was slower than that of urine but reached 52% after three days. Pulmonary absorption of W-tungstic oxide has been studied in dogs. 60% of W is rapidly deposited in the respiratory tract and 33% of that fraction reaches systemic circulation. Tungsten is also easily transferred from mother to fetus usually later in gestation.

Urinary W levels may be elevated after administration of DMPS or DMSA; comparison of urine W before and after provocation provides and estimate of net retention of W over time.

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URANIUM HIGH

This individual's urine uranium (U) is markedly higher than that of the general population. Renal excretion is the primary route of U excretion. This finding is consistent with an excessive exposure to uranium or to an unusually high body burden of this element.

Uranium is a radioactive element having 10 isotopes with half lives that exceed one hour. U238 constitutes about 99% of the naturally-occurring uranium and this is the isotope measured at DDI and reported for this individual. U238 has a half life of 4.5 X 10 to the ninth years. It decays by alpha emission to produce thorium, Th234, the initial step in a decay chain that eventually leads to lead. Alpha, beta and gamma emissions occur during this decay process. Because of the very long half life, the radioactivity danger is only slight. However, exposure to enriched or nuclear fuel grade U (high in U235) does pose a health hazard. The measured result (U238) does not reflect or imply exposure to enriched U235.

The major concern for (natural) uranium excess is toxochemical rather than radiochemical. Uranium is a chemically-reactive element, has four valences (3,4,5 or 6), and may combine with: carbonate, phosphate, citrate, pyruvate, malate, lactate, etc. in body tissues. When not excreted in urine, it may accumulate in the kidneys, spleen, liver, and in bone (substituting for calcium in hydroxyapatite). Uranium is nephrotoxic, causing damage to the glomeruli and proximal tubules. An early sign of U excess is general fatigue. Renal damage is reflected by proteinuria, hyper-aminoaciduria and glucosuria. Albuminuria and urinary catalase are findings consistent with U excess. Elevated hair U may provide further information regarding U exposure. Whole blood analysis may corroborate very recent or ongoing exposure. There are no currently available metal binding/chelating agents to assess the net retention of U that may have occured over time.

Uranium is more common than mercury, silver or cadmium in the earth's rock strata, and may be present, at low levels, in ground (drinking) water. Most commercial use of U is for nuclear fuel, but it may be present in ceramics or colored glass, especially ancient or antique, yellow-colored glass.

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Urine Sodium High

The concentration of sodium in this urine sample is higher than expected and is more than two standard deviations above the mean. A high urine sodium concentration can indicate that the kidney's capacity to reabsorb sodium might be impaired and/or that some stimulus to excrete sodium is present. Urine sodium can vary from day to day depending on the degree of water reabsorption. To get an accurate assessment of renal clearance of sodium, both urine and serum sodium can be compared - this can be done with the fractional excretion of sodium (FENa) calculation (1).

Most of the sodium in the human body can be found either in blood or lymphatic fluid. Sodium levels are regulated by aldosterone (from the adrenal cortex) which acts on the proximal tubules of the nephron to increase reabsorption of sodium and water and to increase the excretion of potassium. Urine sodium testing has a role in the assessment of sodium concentration in the extracellular fluid (ECF) - urine sodium test results should be correlated clinically with sodium and water intake, observation for clinical signs of ECF volume contraction or expansion, serum sodium levels, estimation of renal function and GFR as well as with urine osmolality.

In a normal individual, urine sodium excretion generally reflects dietary intake - the more one ingests (e.g. added dietary salt, drinking and cooking with softened water, salt poisoning, etc.) the more one excretes. High urine sodium may be associated, for example, with diuretic use or conditions such as Addison's disease (primary adrenal insufficiency).

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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.

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MAGNESIUM HIGH

This individual's magnesium level exceeds one standard deviation above the mean of the reference population which means that this individual's urine magnesium level corresponds to the highest 17% (approximately) of that population.

Elevated urine magnesium is an expected finding after administration of EDTA, with levels of 150 to 300 mg/24 hr commonly seen (adults). Elevated urine magnesium is not expected with administration of sulfhydryl agents (DMPS, DMSA, D-penicillamine).

Homeostatic regulation of blood magnesium levels is normally maintained within close limits, and homeostasis closely controls intestinal uptake and renal conservation. There are, however, many possible metabolic, hormonal, drug and (toxic) chemical influences which can increase renal excretion of magnesium, perhaps causing "magnesium wasting". These are listed below.

. Hypermagnesemia, excessive infusion of magnesium
. Hypercalcinuria/hypercalcinemia, excessive supplementation or infusion of calcium
. Hyperphosphaturia/hypophosphatemia
. Hypokalemia with urinary potassium wasting
. Hyperaldosteronism
. Hyperparathyroidism
. Alcoholism
. Hypertaurinuria/hypotaurinemia
. Diuresis: diabetes, use of thiazides, other diuretics
. Acidosis: fasting, diabetic ketoacidosis
. Renal tubular dysfunction/damage, postrenal obstruction, nephritis, Bartter's syndrome
. Nephrotoxic drugs/chemicals: amphotericin, cisplatin, aminoglycides, cyclosporin, theophylline, pentamidine.

Many pesticides, herbicides and fungicides are nephrotoxic, and may cause renal wasting; others may cause renal insufficiency, depending upon dose and time elapsed after exposure (Kuloyanova and El Batawi, Human Toxicology of Pesticides, CRC Press 1991; Sittig, Pesticide Manufacturing and Toxic Materials Control Encyclopedia, Noyes Data Corp., 1980).

Magnesium status can be difficult to assess; whole blood and blood cell levels are more indicative than serum/plasma levels. The magnesium challenge method may be most indicative: baseline 24-hour urine Mg measurement, followed by 0.2 mEq/Kg of intravenous Mg, followed by 24-hour Mg measurement. A deficiency is judged to be present if less than 80% of the Mg challenge is excreted. Ref. Jones, et al. ”Magnesium Requirements in Adults”, Med Journal Clin Nutr, 20 (1967) p.632-35.

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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).

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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

This individuals urine manganese (Mn) is higher than expected. High urinary MN may or may not correspond to global Mn excess or Mn loss from body tissues because the normal route for Mn excretion is via the bile (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 Mn may be increased in patients with biliary obstruction or cirrhosis. Urinary Mn levels may fluctuate without reflecting or influencing body stores.

Elevated urinary Mn in increased following intravenous administration of EDTA; levels increase as much as 15-X compared to pre-EDTA levels in healthy adults without evidence of manganese overload (unpublished observations, DDI). D-penicillamine. DMSA and DMPS administration also may result in increases in urinary Mn 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.

Environmental or industrial sources of Mn include: mining, refining and processing metals or ores, 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 Mn, 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 containhigh concentrations of Mn.

Relative to other essential trace elements, excessive Mn retention can be neurotoxic. Inhalation, as a result of occupational exposure, is the route of assimilation that is most harmful. Some symptoms and manifestations of excess Mn exposue include: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 Mn excess is suspected. These are: whole blood elemental analysis, red blood cell elements analysis, and possibly hair elemental analysis.

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IRON HIGH

High urinary iron may or may not correspond to global iron overload or iron loss from body tissues because the major route for iron uptake, reuptake, and excretion is via the bile, intestinal transport and feces. Urinary iron levels may fluctuate without reflecting or influencing body stores.

Very high urinary iron levels are expected to result from administration of deferoxamine (desferrioxamine, desferal) or of EDTA. For adults, urinary iron normally may vary from about 0.5 to about 2 mg per 24 hours after IM administration of deferoxamine. In cases of iron overload, this level is increased: 2-5 mg/24 hour for early or asymptomatic hemochromatosis; 9-23 mg/24 hr for symptomatic hemochromatosis (Powell and Isselbacher, Chapter 345 in Harrison's Principles of Internal Medicine, 13th Ed., 1994).

Hematuria (isolated), proteinuria with hematuria, and glomerulonephritis feature urinary loss of iron. These conditions may have infections, toxic insults, malignancies, or physical injury as possible origins. Urinary iron may be elevated by contamination with blood if the urine was collected during menstruation.

Biliary obstruction or insufficiency can decrease normal excretion of iron via the bile while increasing urinary levels. Porphyria with urinary loss of porphyrins (before heme can be formed) can feature increased urinary iron. Beta-thalassemia and alcoholic liver are also iron-wasting conditions. Excessive supplementation of iron may also cause iron overload and increased urinary iron.

Iron status is best assessed by measurement of: plasma/serum iron, total iron binding

capacity, percent of transferrin that is saturated with iron, serum ferritin level, and a CBC with hemoglobin and cell parameter analysis. The above referenced text by Powell and Isselbacher is an authoritative reference on differential diagnosis of iron overload.

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