Toxic Element Clearance Profile
in µg/g Creatinine

Genova Diagnostics®
Innovative Testing for Optimal Health

63 Zillicoa Street
Asheville, NC 28801

Patient: **SAMPLE PATIENT**
Age: 40
Sex: M
MRN:

Order Number:
Completed: September 09, 2005
Received: July 20, 2005
Collected: July 20, 2005

Toxic Elements

Results in µg/g creatinine

Element	Reference Range	TMPL	Reference Range
Lead	0.4		<= 1.4
Mercury	0.86		<= 2.19
Aluminum	1.2		<= 22.3
Antimony	0.012		<= 0.149
Arsenic	0		<= 50
Barium	0.1		<= 6.7
Bismuth	0.19		<= 0.76
Cadmium	0.05		<= 0.64
Cesium	0.0		<= 10.5
Gadolinium		0.821	<= 0.019
Gallium		0.413	<= 0.028
Nickel	0.45		<= 3.88
Niobium	0.082		<= 0.084
Platinum		0.078	<= 0.033
Rubidium	0		<= 2,263
Thallium	0.133		<= 0.298
Thorium	0.083		<= 0.124
Tin	0.78		<= 2.04
Tungsten	0.094		<= 0.211
Uranium		0.046	<= 0.026

Sulfur

Results in mg/g creatinine

Element	Reference Range	Reference Range
Sulfur*	597	367-1,328

* Elevated sulfur may indicate the presence of a chelating agent.

Creatinine Concentration

Urine Creatinine ◆ 136.00 38.00-200.00 mg/dL

Collection Information

Urine Total Volume (in milliliters): 1,200

Length of Collection: (in hours) 24.0

Provocation Comment:
Information regarding provocation was not provided.

TMPL

Tentative Maximum Permissible Limit (TMPL) - Element excretion is significantly elevated, consistent with increased body burden. Increased element concentrations can have a negative impact on overall health and well-being. These values are derived from Casaret and Doull's **Toxicology: The Basic Science of Poisons** , 5th Ed. 1996 McGraw Hill NY, NY p 997-998. Units have been standardized.

The performance characteristics of all assays have been verified by Genova Diagnostics, Inc. Unless otherwise noted with ◆ as cleared by the U.S. Food and Drug Administration, assays are For Research Use Only.

Commentary

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Commentary is provided to the practitioner for educational purposes, and should not be interpreted as diagnostic or treatment recommendations. Diagnosis and treatment decisions are the responsibility of the practitioner.

Reference Range Information:
Elemental reference ranges were developed from a healthy population under non-provoked/non-challenged conditions. Provocation with challenge substances is expected to raise the urine level of some elements to varying degrees, often into the cautionary or TMPL range. The degree of elevation is dependent upon the element level present in the individual and the binding affinities of the challeng substance.

Calcium is above the reference range. Hypercalcemia causes elevated urinary calcium except when glomerular function is impaired. Possible dietary reasons for elevated urine calcium are the use of calcium supplements or excessive use of vitamins A or D. Changes in dietary habits such as an abrupt decrease in protein intake can cause transient urinary loss of calcium and decreased calcium uptake as well. Other reasons for high urine calcium include detoxication procedures involving administration of EDTA, use of citric acid (especially if abnormal calcium distribution is present), corticosteroid use, estrogen therapy, and use of drugs or medications that mobilize calcium or reduce calcium retention.

Gallium is above the reference range. This element is chemically similar to aluminum in that absorption of gallium from the intestines is inhibited by the presence of dietary phosphate but increased by the presence of citric or malic acid (carboxylic acids). In animal studies, gallium uptake (like aluminum uptake) is increased in iron-deficiency or low plasma transferrin conditions with deposition occurring in liver, spleen, brain, renal cortex and bone. Once absorbed, humans with normal renal function excrete 4 to 55% of a total, point-in-time exposure within four days, with urine being the major route for gallium excretion.

Although chemically similar to aluminum, the scientific literature reports gallium to be somewhat less toxic. However, with chronic exposure, there can be irritation of mucosal membranes, decreased gastric function, and kidney tubular damage. Controlled acute exposures in animals produced hyperexcitability, photophobia, rapid weight loss with anorexia, and GI distress with diarrhea and bloody feces.

Gallium nitrate is a therapeutic agent used for cancer-related hypercalcemia, Hodgkin's disease and non-Hodgkin's lymphoma. Use of gallium for these purposes is expected to cause notable urinary increases. Gallium (as arsenide or phosphide) is used to manufacture semiconductor materials, light-emitting diodes ("LEDs") and microwave components. It is used instead of mercury in high-temperature thermometers and as a substitute for mercury in arc or fluorescent lamps. Dental materials including root-canal sealers may contain gallium. In scientific or laboratory equipment, it often is used for vacuum or pressure seals and may be in "vacuum grease" as well.

Lithium is above the reference range. The most frequent reason for significantly elevated urine lithium is therapeutic use of lithium carbonate for mood and bipolar disorders. Minor increases can be due to food or water content in geographic areas where soil or ground waters contain moderately elevated levels of lithium. Urine is the prominent route for excretion. Passage of this element through the blood, various tissues, and into the urine is rapid, with a biologic half-time of about 24 hours. Use of diuretics or increased intake of potassium or sodium can increase the rate

Commentary

of lithium excretion. Toxicity from excess lithium is manifested by muscle irritability and twitching, ataxia, coarse tremor, hypertonic muscles, drowsiness or sedation, and confusion. A constant polyuria, with vasopressin-resistant nephrogenic diabetes insipidus, can also occur from chronic excess.

Normal dietary lithium levels, even in high-lithium ground water locales, are orders of magnitude below those needed to evoke symptoms. Occupational or industrial exposures are common where Lithium is used in manufacture of lightweight metals, batteries, (in laptop computers and cellular phones), greases and lubricants, enamels, glazes and coatings, aluminum welding, rubber manufacture (polymerization), and organic and petrochemical syntheses.

Manganese is above the reference range. Biliary dysfunction and administration of chelating agents, especially EDTA and, to a lesser extent, D-penicillamine, can result in increased or elevated urine manganese.

At physiological levels, manganese is an essential element that functions as an activator of certain enzymes. In excess, this element can accumulate in cell mitochondria in the pancreas, liver, kidneys, and intestines, and also deposits in bone and in the brain. In the nervous system, manganese decreases dopamine and its function. Emotional instability, compulsive and aberrant behaviors are also attributed to excess manganese.

Manganese is used in the manufacture of steel and bronze alloys, batteries, electronic components, water conditioning systems (potassium permanganate for high-iron water), matches, welding rods, glazes, dyes and pigments.

Niobium is above the reference range. Once considered to be rarely encountered except in the metallurgical industry, niobium now is used in stainless steel welding, orthodontics, prostheses, magnets, and experimentally as a superconductor. The corrosion-resistant metal alloy "Inconal" contains this element.

In animal studies, niobium challenges have produced glycosuria, increased body fat and weight, myocardial insufficiency, lethargy, decreased respiration, and liver cell damage. Also in animal studies, exposure to niobium disordered other elemental distributions, causing copper and zinc to deposit in the liver and manganese to deposit in the heart.

Niobium is a common trace element in food and drink with notable levels in tea, coffee, and pepper. The element is also used to manufacture high-temperature steels and iron-aluminum alloys. A new application is niobium-titanium dental wire for orthodontics. Permanent magnets may use the element in their manufacture.

Platinum is above the reference range. Excessive platinum in food or drink is rare, and most exposures are industrial via inhalation, or as a result of the administration of "cis-platin", a chemotherapeutic agent for cancer. Elemental platinum has very low toxicity except for those who have dermal sensitivity. Most inhaled, ingested or injected platinum is excreted via urine. This excretion is biphasic with most being eliminated within several hours while the remainder may require 12 days or more for excretion. Elevated urine platinum may be observed after administration of sulfhydryl-bearing detoxification agents (DMSA or DMPS).

Platinum as a complex can upregulate heme oxygenase activity (>10x), thereby disordering heme synthesis in the liver. Platinum inhibits DNA synthesis in the same manner that it exerts its antitumor activity. Binding to and blocking

Commentary (continued)

sulfhydryl sites and inhibition of dehydrogenase enzymes are other modes of toxicity. Platinum deposits in liver and in the kidney, where chronic deposition can damage proximal tubules and cause renal insufficiency. "Platinosis", caused by chronic exposure, features rhinorrhea, coughing and sneezing, eczematous dermatitis, and a lung syndrome with dyspnea, wheezing and an asthma-like condition.

Besides cis-platin, sources of platinum include: catalytic converters on gasoline engines (cars, trucks), electroplating operations, catalyst production and catalytic equipment in the chemical process industries and petroleum refineries, precious dental materials, jewelry, smelting and refining of nickel and copper, purification of gold ores, and electronic parts such as thermocouples, resistance wires and contacts.

Thorium is above the reference range. With an exceedingly long half-life of 14 billion years (thorium-232 is measured), natural background levels are of little concern. Thorium decays (by alpha-particle emission) to radon which is much more radioactive. A recent study by the CDC found detectable amounts of thorium in urine in 39.6% of U.S. residents.

Thorium has mild biochemical toxicity. It binds to aspartic and glutamic acids in tissue pools of free-form amino acids and can be transported to some locations with these amino acids. It binds to bone glucoproteins and to chondroitin sulfate; it also inhibits digestive amylase and blood phosphatase enzymes. In addition, impaired leukocyte function may occur.

Tungsten-inert-gas("TIG") welding rods or electrodes can be a source of thorium exposure, as can mining and milling of metal ores. Some nuclear reactors use thorium in fuel-rod assemblies. Molding and casting high-temperature metal forms may involve thorium oxide, and magnesium-thorium alloys are used in the aerospace industry. Mantles for gas lanterns (used on camping trips) also contain thorium.

Uranium is above the reference range. Uranium has both radiochemical and toxicochemical hazards. By far, the most common mode of exposure to uranium that is absorbed is via drinking water that has passed through rock strata that contain this element. Inhaled uranium from rock dust, mining and excavating is a second source. Excretion is mostly by urine, but the biological residence time is long with measurable uranium in the urine for up to 18 months after an acute exposure. Urine levels of uranium can be notably elevated if the body burden is high and if uranium-mobilizing or chelating agents are used. Some of these detoxifying agents are: "Tiron" (dihydroxy-benzene disulfate), DTPA (diethylene-triamine pentaacetate), gallic acid (trihydroxybenzoic acid), and 5-amino salicylate. EDTA administration or use of citrate salts may increase urinary excretion of this element.

Fatigue, a commonly-observed symptom of chronic, low-level uranium exposure, may be due to impairment of cellular energy metabolism. The uranyl ion also bonds to phosphates, and in bone, it bonds strongly to hydroxyapatite sites, displacing calcium. Uranium bound to bicarbonate begins to produce renal damage if concentrations are high enough; hyperaminoaciduria and beta-2-microglobulinuria occur as uranium begins its attack on tubular epithelia. As renal damage becomes more severe, albuminuria, elevated blood urea nitrogen (BUN), and damage to the proximal tubules occurs, eventually leading to renal failure.

Besides the obvious potential sources of nuclear power plants and nuclear waste sites, the most likely real source is rock strata that contain uranium (igneous rocks, like granite, and phosphate strata). Dust from such strata or ground

Commentary (continued)

water that passes through can contain uranium that may be inhaled or ingested.

Zinc is below the reference range. Low urine zinc can be the result of anorexia or of a zinc-deficient diet (predominantly highly-processed foods, "junk" foods). Excessive dietary phosphates or fiber can limit the bioavailability of zinc. Gastrointestinal disorders that limit uptake of zinc include gastric hypochlorhydria, pancreatic insufficiency, celiac, sprue and inflammatory conditions affecting the upper small intestine.