

24 HOUR URINE TOXIC METALS

10/00



LAB #: U000000-0000-0
PATIENT: Sample Patient
SEX: Male
AGE: 47

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

POTENTIALLY TOXIC METALS

TOXIC METALS	RESULT µg/g CREAT	REFERENCE RANGE	RESULT µg/24 HOUR	REFERENCE RANGE	WITHIN REF. RANGE	ELEVATED	VERY ELEVATED
Aluminum	17	< 35	35	< 37			
Antimony	4.2	< 5	8.9	< 7			
Arsenic	43	< 100	90	< 140			
Beryllium	< dl	< 0.5	< dl	< 0.6			
Bismuth	< dl	< 30	< dl	< 30			
Cadmium	0.5	< 2	1	< 3			
Lead	0.5	< 15	1	< 20			
Mercury	4610	< 3	9690	< 5			
Nickel	1.8	< 12	3.7	< 20			
Platinum	< dl	< 2	< dl	< 2			
Thallium	0.2	< 14	0.4	< 14			
Thorium	< dl	< 12	< dl	< 13			
Tin	1.2	< 6	2.6	< 11			
Tungsten	0.2	< 23	0.4	< 22			
Uranium	< dl	< 1	< dl	< 2			

CREATININE

	RESULT mg/24 hr	REFERENCE RANGE	2SD LOW	1SD LOW	MEAN	1SD HIGH	2SD HIGH
Creatinine	2100	1100- 2800					

SPECIMEN DATA

Comments: **mercury checked on dilution- submittal marked "pre"**

Date Collected: 8/13/2001	Method: ICP-MS	Collection Period: 24 hour
Date Received: 8/17/2001	<dl: less than detection limit	Volume: 1725 ml
Date Completed: 8/18/2001		Provocation: pre

Toxic metals are reported as µg/g creatinine and µg/24 hour 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.

24 HOUR URINE ESSENTIAL ELEMENTS

10/00



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 SEX: Male
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ESSENTIAL ELEMENTS

ELEMENTS	RESULT μg/mg CREAT	REFERENCE RANGE	RESULT mg/24 HOUR	REFERENCE RANGE	PERCENTILE				
					2.5 th	16 th	50 th	84 th	97.5 th
Sodium	3510	1610- 5020	6320	1680- 6160					
Potassium	1200	850- 2970	2170	880- 3760					
Phosphorus	690	350- 1320	1240	230- 1580					
Calcium	120	67- 290	220	56- 360					
Magnesium	110	46- 200	200	50- 230					
Zinc	0.52	0.097- 1.1	0.93	0.12- 1.3					
Copper	0.021	0.011-0.048	0.038	0.011-0.068					
Sulfur	760	370- 1050	1370	280- 1910					
Iron	0.026	0.03- 0.24	0.048	0.04- 0.3					
Manganese	0.0004	.0007-0.006	0.0008	0.001-0.006					
Molybdenum	0.055	0.024- 0.13	0.098	0.026-0.176					
Barium	0.024	0.001-0.013	0.044	0.001-0.018					
Boron	1.5	1.1- 5.1	2.7	1.1- 6.2					
Chromium	0.1	0.012- 0.25	0.18	0.02-0.114					
Cobalt	0.0003	0.001-0.055	0.0005	0.001-0.055					
Iodine	0.049	0.012-0.346	0.088	0.012-0.511					
Lithium	0.014	0.009-0.088	0.025	0.008-0.107					
Selenium	0.088	0.062- 0.28	0.16	0.054- 0.39					
Strontium	0.21	0.044- 0.29	0.38	0.035- 0.44					
Vanadium	0.028	0.003- 0.03	0.05	0.003-0.038					
Zirconium	0.0001	0.001-0.006	0.0003	0.001-0.007					

CREATININE

	RESULT mg/24 hr	REFERENCE RANGE	2SD LOW	1SD LOW	MEAN	1SD HIGH	2SD HIGH
Creatinine	1800	1100- 2800					

SPECIMEN DATA

Comments:

Date Collected: 8/13/2001 Method: ICP-MS Collection Period: 24 hour
 Date Received: 2/17/2001 <dl: less than detection limit Volume: 1725 ml
 Date Completed: 2/18/2001 Provocation: pre

Essential elements are reported as μg/mg creatinine and mg/24 hour 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).

INTRODUCTION

This analysis of urine 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 urine element 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 greater than or less than 1.0 or 1.5 standard deviations from the mean value. 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, than 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 range (plus or minus 1 SD) 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 applied to conditions of non-challenge or non-provocation. Diagnostic or therapeutic administration of detoxifying agents may

significantly raise urine 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.

ANTIMONY HIGH

This individual's urine antimony is higher than expected, but associated symptoms and toxic effects may not be presented. This is because antimony (chemical symbol Sb) has two valences: Sb+3 and Sb+5. Sb+3 is 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.

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 where 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.

Symptoms of mild Sb contamination 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 interfere with cellular metabolism. Acute symptoms of Sb contamination include: respiratory tissue irritation and pneumoconiosis with (chronic) inhalation of Sb dusts, RBC hemolysis with inhalation of stibine (SbH₃) vapor, and GI distress if orally ingested. Skin exposure can produce "antimony spots" or rashes which resemble chicken pox. Certain molds can produce the highly neurotoxic stibine gas from antimony; stibine inhibits acetylcholinesterase activity.

A hair element analysis may be used as a corroborative test for increased body burden of antimony. Fecal metal analysis can be used to confirm exposure/retention of toxic Sb+3. Antimony may be elevated in urine following administration of DMPS or DMSA.

BIBLIOGRAPHY FOR ANTIMONY

1. Carson B.L. et al. Toxicology and Biological Monitoring of Metals in Humans, Lewis Publishers, Chelsea MI, pp 21-26, 1987.
2. Tsalev D.L. and Z.K. Zaprianov. Atomic Absorption Spectrometry in Occupational and Environmental Health Practice. CRC Press, Boca Raton FL, pp 85-87, 1983.
3. Scriver C.A. et al The Metabolic Basis of Inherited Disease, 6th ed. McGraw-Hill, New York NY, pp 2349-50 on PFK deficiency. 1989.

MERCURY HIGH

This individual's urine mercury equals or exceeds twice the maximum expected level. Presentation of symptoms associated with excessive mercury can depend 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.

Mercury is commonly used in: dental amalgams, explosive detonators; in pure liquid form for thermometers, barometers, and laboratory equipment; batteries and electrodes ("calomel"); and in fungicides and pesticides. The fungicide/pesticide use of mercury has declined due to environmental concerns, but mercury residues persist from past use.

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, with about three-quarters of this (typically) as methylmercury.

Depending upon body burden and upon type, duration and dosage of detoxifying agents, elevated urine mercury may occur after administration of: DMPS, DMSA, D-penicillamine, or EDTA. Elemental analysis of hair can be a corroborating test for mercury burden. Blood and especially blood cell analyses are only useful for diagnosing very recent or ongoing organic (methyl) mercury exposure.

BIBLIOGRAPHY FOR MERCURY

1. Suzuki T. et al eds, *Advances in Mercury Toxicology*, Plenum Press, New York, 1991.
2. World Health Organization: "Methylmercury" *Environ. Health Criteria* 101 (1990); "Inorganic Mercury" *Environ. Health Criteria* 118 (1991) WHO, Geneva, Switzerland.
3. Tsalev D.L. and Z.K. Zaprianov, *Atomic Absorption Spectrometry in Occupational and Environmental Health Practice*, CRC Press, Boca Raton FL, pp 158-69, 1983.
4. Birke G. et al "Studies on Humans Exposed to Methyl Mercury Through Fish Consumption", *Arch Environ Health* 25, 1972 pp 77-91.
5. Pelletier L. "Autoreactive T Cells in Mercury-Induced Autoimmunity", *J. Immunology*, 140 no.3 (1988) pp 750-54.
6. Werbach M.R. *Nutritional Influences on Illness*, 2nd ed, Third Line Press, Tarzana CA, pp 249, 647, 679, 1993.

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, aminoglycosides, 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.

BIBLIOGRAPHY FOR MAGNESIUM

1. Knochel J.P. "Disorders of Magnesium Metabolism", Chapt 360 in Harrison's Principles of Internal Medicine, 13th ed., McGraw-Hill pp. 2187-90, 1994.
2. Shils M. "Magnesium", Chapt. 8 in Modern Nutrition in Health and Disease, 8th ed. vol.1, Lea & Febiger, Philadelphia, PA, pp.164-84, 1994.
3. Harper H.A. et al. Review of Physiological Chemistry, 17th ed., Lange Medical Publications, Los Altos, CA, pp. 578-79, 1979.
4. Jones J.E. et al. "Magnesium Requirements in Adults" Med J. Clin. Nutr. 20 pp. 632-35, 1967.
- 5(a) Halpern M.J. and J. Durlach eds., Magnesium Deficiency Karger (Basel and New York), esp. pp. 146-180, 1985.
- 5(b) See also Magnesium and Trace Elements, official journal of the Am. Soc. for Magnesium Research, B.M. Altura (Brooklyn NY), Ed. in- Chief, S. Karger A.G. Postfach CH-4009 Basel, Switzerland.
6. Galland L. "Magnesium and Inflammatory Bowel Disease" Magnesium 7 no. 2, pp. 78-83, 1988.
7. Rea W.J. "Magnesium Deficiency in Patients with Chemical Sensitivity" Clinical Ecology 4 no. 1, pp 17-20, 1986.

IRON LOW

This individual's urine iron is lower than 1.5 standard deviations below the mean of the reference population which means that this individual's urine iron corresponds to the lower 10% (approximately) of that population.

Low urine iron is NOT likely to correspond to global iron deficiency in body tissues because the major route for iron uptake, reuptake and excretion is via the bile, intestinal transport and feces. Urine levels may fluctuate without reflecting or influencing body stores.

Iron can be low (along with other elements) in urine in renal insufficiency. Creatinine clearance and blood metabolite levels should be measured if a renal transport disorder is suspected.

Urine iron levels may be low in iron deficiency, and there are multiple possible causes for iron deficiency. Various editions of Review of Physiological Chemistry, (Lange Medical Publications), Harper's Biochemistry (Appleton and Lange), and Shils, Olson and Shike, Modern Nutrition in Health and Disease (Lea & Febiger, Philadelphia) have comprehensive discussions on causes and manifestations of iron deficiency.

Early signs of iron deficiency are low MCV and low or subnormal ferritin. 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 (including MCV).

BIBLIOGRAPHY FOR IRON

1. Powell L.W. and K.J. Isselbacher, "Hemochromatosis" in Harrison's Principles of Internal

Medicine, 13th Ed., McGraw-Hill, pp. 2069-2073, 1994.

2. Fairbanks V.F. "Iron in Medicine and Nutrition" in Modern Nutrition in Health and Disease, Shils, Olson and Shike eds. Lea & Febiger, Philadelphia, 1994.

3. Martin D.W. et al., Harper's Review of Biochemistry, Lange Medical Publications, Los Altos, CA. 20th ed., pp. 655-59, 1985

4. Bernat I. "Iron Deficiency" in Iron Metabolism, Plenum Press, NY pp. 215-274, 1983.

MANGANESE LOW

This individual's urine manganese is lower than 1.5 standard deviations below the mean of the reference population which means that this individual's urine manganese corresponds to the lower 10% (approximately) of that population.

Low urine manganese is very unlikely to correspond to global manganese deficiency in body tissues because the major route for manganese excretion is via the bile. Typically less than one-half 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. Urine levels may fluctuate without reflecting or influencing body stores.

In renal insufficiency, manganese (and other elements) can be low in urine. Creatinine clearance and blood metabolite levels should be measured if a renal transport disorder is suspected. Prolonged physical activity with perspiration may result in significant loss of Mn in sweat; increased Mn retention mechanisms can then cause low urine levels.

Epidemiologically, frank manganese deficiency in groups of humans has never been confirmed/published, probably because of the abundance of Mn in natural vegetable foods and because of the low Mn requirements by human metabolism. However, subnormal manganese for an individual, coincident with low urine Mn level, may occur secondary to one or more of the following conditions.

- . Junk food diet, consumption of manganese-deficient foods combined with other conditions or stressors
- . Malabsorption syndromes
 - a. Gastric hypochlorhydria
 - b. Pancreatic dysfunction/insufficiency
 - c. Inflammatory disease, food reactivities, enteropathy
 - d. Intestinal fistula, bypass or resection surgery
- . Excessive iron, zinc or cobalt in diet (competitive binding and absorption in small intestine)
- . Excessive phosphates, phytates, fiber in diet.

Because urine is not a reliable indicator of manganese status, other laboratory tests are advised if subnormal manganese is suspected. These are: whole blood Mn analysis (or multi-element profile), blood cell Mn determination, and hair Mn analysis.

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2. Tsalev D.L. and Z.K. Zaprianov, Atomic Absorption Spectrometry in Occupational and Environmental Health Practice, vol.2, CRC Press, Boca Raton FL. pp. 153-58 1983.

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