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To Provoke or Not to Provoke Heavy Metals

Cases in which plaintiffs claim health problems associated with heavy metal toxicity due to products they have ingested, including dietary supplements, seem to be filed with more regularity. Mercury, lead and arsenic are targeted frequently as the alleged causes of neuropathy, "foggy headiness," heart palpitations and other health problems.¹ Some of these plaintiffs appear to rely upon faulty medical data to substantiate their claims. For example, some physicians may provoke heavy metals out of their patients' tissues and into their urine and then compare those heavy metal



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jch@dillinghammurphy.com dillinghammurphy.com levels to reference ranges for unprovoked urine tests, resulting in false positive results.

What Are Heavy Metals?

Heavy metals are defined as metals with relatively high densities, high atomic weights or high atomic numbers. Some heavy metals are essential nutrients for humans. For example, iron is required for the transport of oxygen needed for cellular respiration and zinc is needed to heal wounds.

Where Are Heavy Metals Found?

Many heavy metals are ubiquitous in that they occur naturally, so nearly everyone has some low-level exposure throughout their lifetime. They can be found in fruits and vegetables. If these plants are used to feed livestock, then the metals will leech into the livestock. Water obtained from natural springs often contains some heavy metals. The point is that we all have small amounts of heavy metals in our bodies, but our bodies generally reach a steady state in which the heavy metals are absorbed and excreted with no adverse consequences.

Heavy Metals Can Be Poisonous

There is no doubt that exposure to certain heavy metals in abnormal concentrations can cause adverse health consequences. The most common example is children ingesting lead via paint. In some situations, the health problems associated with heavy metal toxicity can be corrected by stopping further exposure followed by time to allow the body to naturally lower the level of heavy metals.

Toxicology Evaluations

A physician who suspects a patient is suffering from heavy metal toxicity will conduct a thorough medical examination, including an oral history to determine if the patient has been exposed to heavy metals. The physician also will try to correlate the patient's symptoms to one or more metals. One of the most beneficial tools for a toxicologist is an exposure assessment, which is the process of estimating or measuring the magnitude, frequency and duration of exposure to a substance. These assessments can help determine if the patient has ingested metals in a sufficient quantity to produce adverse health effects. Unfortunately, these important steps in a toxicology evaluation may not always be performed by treating physicians.

Measuring the Level of Heavy Metals

If a toxicology evaluation results in a physician suspecting heavy metal toxicity, then the physician probably will order a urine test. The patient's urine is collected and evaluated for the presence of heavy metals expressed as micrograms per grams of creatinine (ug/g). There are two types of urine tests for heavy metals: unprovoked and provoked. Unprovoked urine collection means the patient does not take an agent to entice the body to excrete metals. Provoked urine collection means the patient takes a chelating agent to encourage the body to excrete metals. Chelating agents are chemical compounds that react with metal ions to form a stable, water-soluble complex that can be excreted by the body.

Chelation therapy can be beneficial in those situations when a physician determines an exposure to heavy metals, adverse health consequences from the exposure, stopping further exposure is not sufficient to remedy the condition, and the patient needs additional help ridding the body of heavy metals.² The issue with chelating agents develops when they are used to determine if chelation therapy is necessary. A number of labs, including the Mayo Clinic, have developed reference ranges for heavy metals in unprovoked urine. A reference range is a scientific consensus for comparison, or a frame of reference, for health professionals to interpret a set of test results. However, there are no consensus guidelines for the interpretation of results of provoked urine testing. This lack of consensus for provoked references ranges is a function of variables, e.g., the variety of chelating agents, the various routes of administration of those agents (intravenous infusions, intramuscularly, orally, etc.), inconsistent doses of agents and inconsistent urine collection procedures.

Lacking reference ranges for provoked urine tests, physicians sometimes compare the provoked test results with unprovoked reference ranges. A provoked urine sample almost always looks elevated when compared to unprovoked ranges, but the results do not necessarily reflect an abnormal body burden of the presumed toxicant. This testing does little more than document a normal response to the chelator. Patients may then be mistakenly told their bodies have dangerously high levels of heavy metals and as a result, they should be "detoxified" to reduce these levels. However, experiments have established that provocation raises urine levels of heavy metals as much in people exposed to heavy metals as in unexposed control subjects and that the rise is

temporary, ought to be expected, and is not evidence of a dangerous medical condition.

Comparing Apples to Oranges

Other problems that litigators need to watch for include the length of the urine collection process and controlling for creatinine in the urine. Unprovoked reference ranges are based upon 24hour urine collections. However, it is not uncommon for physicians to prescribe provoked urine tests that require only a six-hour collection period. With provoked tests, most of the extra heavy metal excretion occurs toward the beginning of the test. This means a specimen obtained over a six-hour period and not the standard 24-hour period results in the reported heavy metal levels being higher. Also, the test results sometimes are controlled for creatinine, which falsely elevates the concentration of heavy metals reported. The end result is that even a "normal person" would tend to have a high result. An example helps drive the point home.

A person excretes 1 g of creatinine (Cr) into the urine in 24 hours and has a daily urine volume of 1 L. The same person excretes 0.4 ug/dL mercury into the urine over a day, which is 4 ug Hg/L. The urine mercury excreted over the course of one day is equal to 4 ug/g Cr. If urine is collected for six hours and controlled for creatinine, the mercury level would be expected to continue to be 4 ug/g Cr (since 250 mg Cr, 1 ug Hg, and 250 ml of urine are expected to have been collected over six hours). However, if a chelating agent were administered prior to collection of urine, the result would change. Assuming the

excretion of mercury triples in the first six hours after chelator administration and then returns to baseline, the 24-hour excretion of mercury would increase to 6 ug, while the creatinine excreted over the same 24 hours would remain stable. However, if the urine was collected only for the first six hours and then controlled for creatinine, the 3 ug of Hg collected along with 250 mg of Cr would then be converted to 12 ug Hg/g creatinine. By cutting the urine collection period to six hours and controlling for creatinine, the results reported to the patient and provider has doubled. Thus, in this example, creatinine correction would be deceptive.

Conclusion

Attorneys litigating heavy metal toxicity cases need to ask a series of questions. Has the plaintiff undergone a thorough toxicology evaluation? Has a urine test been conducted with a provoking agent? Have the results of a provoked urine test been compared to reference ranges for unprovoked urine tests? Have the urine test results been corrected for creatinine? If the answer to any one of these questions is yes, you may have a very strong defense to a claim of heavy metal toxicity.

¹ Some heavy metals are subject to California's Proposition 65, which requires that products include detailed warning labels if they contain chemicals known to the State of California to cause cancer, birth defects or other reproductive harm. Please refer to the Spring 2017 edition of *Paradigm* for the author's article discussing Proposition 65.

² The purpose of this article is not to debate the value of chelation therapy, but there is significant debate about the practice. For example, some medical practitioners claim chelation therapy can treat a variety of ailments other than heavy metal toxicity, including heart disease, cancer and autism. The American Heart Association and the American Cancer Society have stated that there is no scientific evidence to demonstrate any benefit from this form of therapy.