

Challenge Testing for Heavy Metals

Sometimes it is difficult to show the presence of toxic metals in static samples of hair, blood and urine despite clinically significant body burdens for the metals. This is because toxic metals may accumulate in relatively non-exchangeable pools within specific tissues, e.g. brain, liver and kidneys. The result can be normal concentrations of toxic metals in blood and urine despite a significant body burden for these metals. Thus, it is reasonable for a clinician to want to corroborate a laboratory's initial "normal" or "borderline" toxic metal finding with adjunctive testing. This is justifiable if the patient's complaints and history are consistent with one or more hallmark symptoms of metal toxicity.

The best course of action for confirmation of elevated body burden is to disturb the body's stores of toxic metals so that a certain quantity will redistribute into the blood and be eliminated in the urine where it can be detected. Chelating agents are necessary for this purpose due to the fact that they have been found to specifically bind and mobilize toxic metals from tissues into circulation. Typically, a challenge consisting of an oral or IV dose of the chelating agent is administered. Urine is collected, and then analyzed for toxic metals. This result is compared with the results of pre-challenge baseline urine. A significant (>50%) increase relative to unchallenged levels or an elevation above reference levels in one or more toxic metals in the post-challenge urine indicates the presence of heavy metal body burden.

DMSA Challenge Test

DMSA (2,3 Dimercaptosuccinic acid) is an FDA-approved chelating agent which mobilizes heavy metals, such as lead and mercury, from human tissues.¹ DMSA is considered superior to EDTA for the detection of mercury or other tightly bound metals and is also considered the safest, least toxic method for detecting toxic metals.² DMSA effectively competes with the tissue binding sites to release toxic metals that are normally sequestered in bone, nerve, liver, etc.

One method used to evaluate toxic metals is to use a dose relative to body mass. Sources suggest the following: 10mg of DMSA per kg of body weight per day^{3,4} to be taken in divided doses. Each dose should be taken between meals. For a 70 kg man, this would equate to approximately 2 equal doses of 700 mg of DMSA.

Other advocates prefer to simplify dosing recommendations. They suggest a dosage for toxic metal detection in adults to be 500 mg of DMSA, as a

challenge substance, taken 4 hours apart. It is important to take each dose between meals, as the absorption of the detecting agent may otherwise be compromised. The 2x500 mg is considered a conservative, but effective dose for adults weighing between 40 and 80 kg. This protocol may be done following 1-2 days of DMSA at similar doses to allow greater time for re-equilibration of body pools.

Either a 6-8 hour (for measuring mcg/mg creatinine) or a 24 hour (for measuring mg/day) urine specimen is collected. The urine collection may begin at the time of the first 500 mg dose of DMSA. The patient voids urine for the last time at the same time of day that he/she took the first DMSA capsule on the previous day. The urine is mixed by swirling, and a portion is transferred to the plastic screw cap tube for shipping. The daily (or periodic) output of body burden of heavy metal is evaluated with elevated levels demonstrating the presence of potentially toxic body burden of heavy metal.⁵⁻⁷

EDTA Challenge Test

A review of medical literature also accounts for the use of intravenous ethylenediamine tetraacetic acid (EDTA) as a widely used therapy for detecting the presence of toxic heavy metals. EDTA is also used as a form of treatment for various age-associated diseases. The substance is used as an IV drip in the form of the disodium magnesium salt, which binds with variable avidity to all divalent metal ions. Since essential minerals are lost from the body during the therapy it is desirable to determine the extent of losses of both toxic and essential elements by performing a pre and post-chelation analysis. For this purpose, it is satisfactory to use single catches of urine and to report the data as amount of mineral per mg creatinine. Alternatively, specimens from 24-hour urine collections may be analyzed for measuring excretion in units of mg/day. Cranton has reported the changes in excretion of chemical elements with challenge by intravenous EDTA.⁸

Other Oral Challenge Compounds

In addition to DMSA and EDTA, other compounds have been reported to successfully bind heavy metals. The chelating agent d-penicillamine was one of the first agents employed for heavy metal detoxification. It effectively causes redistribution of most metals, increasing their loss in urine. Penicillamine has been used to reduce copper toxicity in Wilson's disease^{9,10} and to reduce body burden of lead in children¹¹.

More recently, DMPS (2,3-dimercapto-1-propanesulfonic acid), another sulfur-containing compound, has been

reported to be an effective agent for treatment of human acute arsenic exposure¹² and for reducing brain, kidney, and blood mercury levels in experimental animals chronically exposed to low levels of methyl mercury¹³. Challenge testing may be done using either DMPS or d-penicillamine.

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