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Heather Majors  
410 Dirksen Senate Office Building  
Washington, D.C. 20510-6175  
[Heather\\_Majors@epw.senate.gov](mailto:Heather_Majors@epw.senate.gov)

Rebeckah F. Adcock  
Counsel, Senate committee on Environment & Public Works  
Senator James M. Inhofe (R-OK), Ranking Member  
415 Hart Senate Office Building  
Washington, D.C.  
[Rebeckah\\_adcock@epw.senate.gov](mailto:Rebeckah_adcock@epw.senate.gov)

Re. Hearing: Current Science on Public Exposures to Toxic Chemicals  
Scope: Examination of recent science analyzing public exposures to toxic chemicals

*Senate Committee: Environment and Public Works*  
*Subcommittee on Superfund, Toxics and Environmental Health*

Chairwoman Boxer, Chairman Lautenberg, Ranking Member Inhofe, esteemed Members of the Committee, and guests:

Thank you for the opportunity and honor of presenting testimony to this subcommittee on the “current science on public exposures to toxic chemicals.” I trust that this hearing on health exposures and biomonitoring will be useful, and an important component to the process of improving public health through the intended reform of the Toxic Substances Control Act of 1976 (TCSA).

Biomonitoring is a tool with clear benefits. The ability to actually measure the amount of any given chemical in the body is an important step beyond – or test of – modeling assumptions. The ability to identify lower and lower concentrations of an increasing number of substances has allowed us to recognize potential problems much earlier than in the past and has provided the impetus to act before harm occurs. The use of biomonitoring for research to investigate potential new interactions on multiple fronts is an important new area for investigation. Many of the witnesses before this committee have discussed these points in the past. I want to focus my remarks on the impact of biomonitoring on medical care and public perceptions, particularly in the area of risk communication. I leave my written comments to be read into the record, along with associated references. I am happy to respond to any questions from the committee.

### Personal Background:

I am a physician, trained and board-certified in Internal Medicine, Emergency Medicine, Medical Toxicology, with additional experience in Pathology, Occupational Health, and laboratory interpretation. I have been an attending physician in Connecticut for 22 years. I am the Medical Director of Occupational Health Services for Hartford Hospital and the Connecticut Children's Medical Center. I am the Associate Medical Director of the Connecticut Poison Control Center (CPCC), one of about 60 regional poison centers certified by the American Association of Poison Control Centers. The CPCC receives more than 30,000 calls every year from the public and medical personnel regarding possible or known toxic exposures. I am an Associate Professor at the University of Connecticut School of Medicine, and the Director of the Medical Toxicology training program at UConn, one of about 24 such programs in the country. In that role and as an educator, I am responsible for training some of the next generation of medical providers. I am a consultant to the Connecticut Department of Public Health and was a member of the Environmental Health Public Tracking Program Planning Committee. I participate in our state's biopreparedness activities. I also serve as a reviewer for 6 peer-reviewed medical journals, and am a member of the Editorial Board of the Journal of Medical Toxicology. I am a member of the Scientific Advisory Council of the Environmental Health Research Foundation, at whose invitation I agreed to testify today. I am a member of the Board of Directors of the American College of Medical Toxicology (ACMT), which is the member organization representing most of the 500 board-certified Medical Toxicologists in the country. In that capacity, I serve on the Practice Committee and am the National Director of a network between ACMT and the Agency for Toxic Substances and Disease Registry (ATSDR) of the Centers for Disease Control and Prevention (CDC). The purpose of this network is to provide the regional expertise of physician medical toxicologists to the regional ATSDR representatives and their public health partners in order to address concerns about human exposure to chemicals in the environment (either naturally-occurring or arising from human activity).

My comments are my own, and do not necessarily reflect opinions of the ACMT, its Board of Directors, or its members. I have attached for the written record an editorial published in our on-line journal (Appendix A), and a position statement of the College (Appendix B) relevant to some of the issues discussed today.

The mission of the American College of Medical Toxicology is to advance quality care of poisoned patients and public health through physicians who specialize in consultative, emergency, environmental, forensic, and occupational toxicology. Previous contracts and cooperative agreements with ATSDR have allowed ACMT to present material on chemicals as potential terrorist weapons (Toxic Industrial Chemicals and Toxic Industrial Materials) to more than 6000 public health, prehospital and medical personnel, emergency planners, and military personnel; and material on the health effects of clandestine methamphetamine laboratories to more than 1100, as well as recurring conferences at regional and national meetings.

### Potential Benefits of Biomonitoring:

Medical Toxicology is a medical subspecialty focusing on the diagnosis, management and prevention of poisoning and other adverse human health effects due to medications, occupational and environmental toxins, and biological agents.

Biomonitoring is an important tool for use in toxicology. In the current setting of unwarranted or uncertain fear about “all things chemical”, it can also be used to focus or alleviate concerns. Specifically, a robust biomonitoring program can be used to a greater or lesser extent to:

- Identify the concentration of chemicals actually taken up by the human body and the metabolic fate of those chemicals;
- Improve the accuracy or test the validity of assumptions in physiologically-based pharmacokinetic modeling or regulatory models;
- Identify susceptible populations or particular at-risk groups (e.g. genetic polymorphisms) for chemical toxicity;
- Track trends of exposure over time and in the setting of various interventions;
- Validate reference ranges for chemical exposure;
- Inform discussions regarding levels of exposure consistent with no adverse effects (thresholds);
- Provide a framework in which to evaluate individuals’ concerns about chemical exposure.

### Need for Support of Currently Existing Mechanisms to Conduct Biomonitoring:

While the viewpoints and worldview of the multiple participants in the 2006 National Research Council’s (NRC) report on “Human Biomonitoring for Environmental Chemicals” ([http://www.nap.edu/catalog.php?record\\_id=11700](http://www.nap.edu/catalog.php?record_id=11700) ) may differ, their recommendations identify not only potential benefits and research utility, but also the shortcomings and the practical difficulties of using biomonitoring to answer questions about environmental exposures and human health.

These difficulties are to be expected, given the different dosing scenarios, genetic polymorphisms, and impact of other diseases and confounders on an individual’s or population’s response to any single or mixture of substances. As reform of TSCA is considered, please bear in mind the recommendations of this group, as well as the need for funding to reach the goals espoused by this committee. The NRC’s recommendations include the need for:

- Coordinated strategy for population biomonitoring based on potential for exposure and public-health concerns;
- Development of biomonitoring-based hazard and exposure assessments and public-health; surveillance to interpret the risks posed by low-level exposure to environmental chemicals, enhancing where possible existing efforts by adding biomonitoring in order to improve interpretation;
- Focus on strategies for reporting results of biomonitoring studies;
- Review of bioethical issues inherent to biomonitoring efforts;

These are in fact the ultimate goal of such efforts as the recurring National Health and Nutrition Evaluation Survey (NHANES) and the goal of the Environmental Public Health Tracking

programs at the state and regional levels. Unfortunately, funding for state-based biomonitoring efforts, building on years of public health activities and medical concerns at the state, regional, and national levels, has been cut drastically, resulting – for example – in a 67% decrease in allocated funding this year and a reduction from a possible 33 states to only 3 states funded. The National Association of Public Health Laboratories (APHL) has issued a document identifying the priority needs of the state laboratories and emphasizing the need for coordinated funding of existing infrastructure to improve and regionalize what is now a fragmented system (<http://www.aphl.org/policy/priorities/Documents/HillDayFactSheets2009.pdf> ). Utilizing improved capabilities and capacity developed through biopreparedness efforts over the last 8 years, it is very possible to utilize the expertise and resources of state-based public health laboratories for biomonitoring projects of public health importance. I was able to attend the National Biomonitoring Planning Conference held by the APHL in Atlanta last fall (<http://www.aphl.org/aphlprograms/eh/Documents/NBMSummary2009.pdf> ). This meeting of state and federal laboratorians generated the framework for a 5 year plan to generate a data- and expertise-sharing biomonitoring program. However, this can only occur through funding and education of qualified personnel to make use of purchased equipment.

#### Limitations of Biomonitoring:

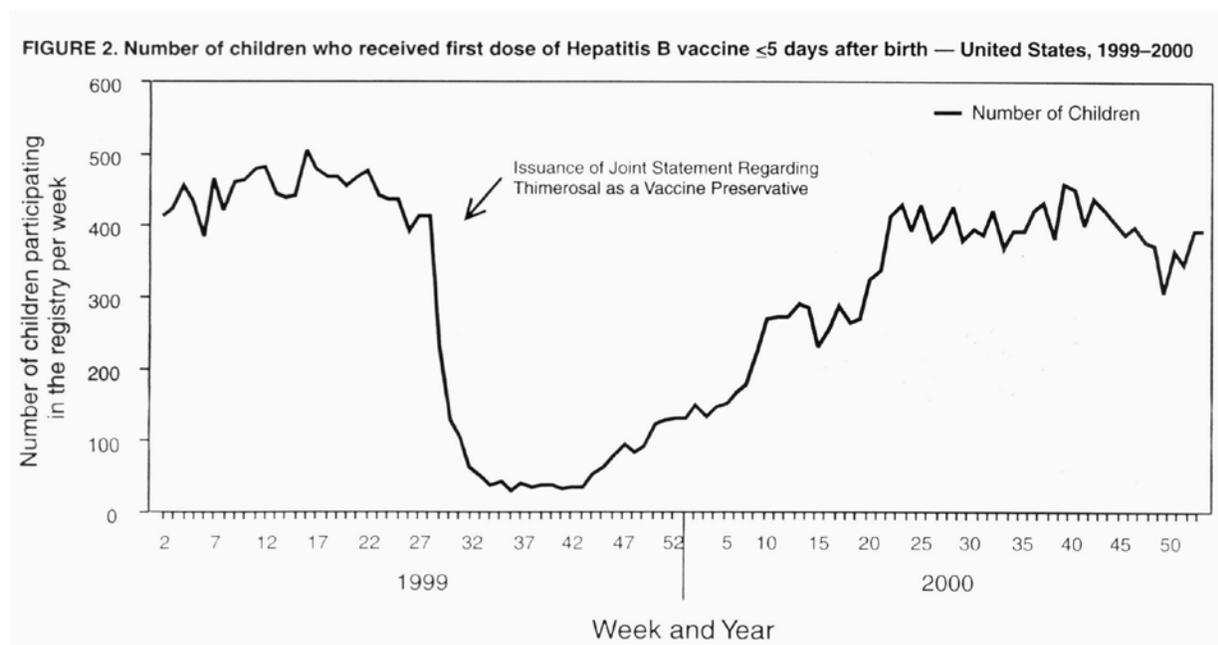
It is important to recognize the limitations of biomonitoring. Biomonitoring is a tool. It is not an answer. It does not, in and of itself, eliminate potential confounders or alternative explanations for identified associations between chemical exposure and disease. As perhaps needs reiterating, the identification of a substance confirms its presence; it does not indicate whether that substance is causing harm or benefit. Any environmental chemical will be present to some extent in those who ingest, inhale or otherwise are exposed to it. Thus, the statements that have been made in this committee and other venues that “neurotoxins”, “endocrine disruptors”, or other “harmful chemicals” are present in our (and our childrens’) bodies is meaningless, without specific relationship to dose, exposure timing, and comparison to appropriate control populations. While it is frequently stated that “scientists have developed a more refined understanding of how some chemicals can cause and contribute to serious illness”, it is also true that our ability to measure substances at very low concentrations has outstripped our ability to determine causation. In other words, scientists are able to identify spurious associations with environmental chemicals, while having difficulty accounting for confounders, thus proffering disease causations that do not, in fact, exist.

#### **The Precautionary Principle (United Nations, 1992)**

**Where there are threats of serious or irreversible environmental damage, lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent degradation.**

Unfortunately, biomonitoring can be – and has been – abused as a tool. The practical problem with overstating exposure-disease associations is seen every day by medical professionals who evaluate people who are fearful of being “poisoned” by the latest chemical touted in a study as the cause of the same disease blamed on another compound the month before. Unfortunately, there are also a number of practitioners who prey on such patients, offering therapies that are not

indicated for conditions the patient does not have. On a weekly, if not more frequent basis, I am contacted by patients or media desiring assistance in interpretation or personal application of data reported in the scientific literature or obtained from ill-considered or inappropriately-performed laboratory testing. This does not just affect the small portion of the population with fixed delusions. It potentially impacts every woman considering pregnancy, every parent wondering about their children's health, and every worker and employer. The incessant drumbeat that environmental chemicals are the source of all ills is hyperbole that should fall in the face of the evidence supported by biomonitoring.



**When the message is not communicated clearly or correctly, we end up with inappropriate response and harm, rather than the prevention of harm. This is demonstrated in the drop in vaccinations (figure above) and neonatal deaths from Hepatitis B secondary to unfounded concerns about thimerosal-preserved multi-dose vials of vaccine.**

**Similarly, increases in unvaccinated measles cases and persistently lower rates of vaccination are attributed to the unethical and dishonest study published in *The Lancet* by Wakefield et al., based on 12 patients.**

#### Practical Risk Communication Issues Concerning Exposure to Chemicals in the Environment:

How do I as a practicing toxicologist provide a scientific, understandable, and appropriate message to my patients and other concerned parties, both professionals and lay public? I have used the following criteria in my evaluation of the literature and communication with others. I would respectfully suggest that these be considered when communicating biomonitoring data to

Americans, whether at the patient-physician, scientist-peer-review literature, policy or regulatory levels.

- Identifying a substance as being of public health concern is not the same as stating it is causing individual harm. Appropriately obtained or extrapolated biomonitoring data can be used to gauge an individual's exposure compared to population norms.
- Decisions about exposure need to incorporate information about at-risk populations (and whether an individual is a member of such a group), as well as the benefits gained by use of the product or availability and potential adverse effects associated with alternatives. Biomonitoring data alone does not answer this question, but common sense should play an important role.
- Claims of association of a medical condition with historic exposures to some substance need to be evaluated in the face of current exposures. Biomonitoring data that identifies decreasing – or increasing – population exposure to chemical compounds should be incorporated into all research publications touting disease associations and should be required by editors prior to acceptance for publication.
- Using a study population to dredge for associations is reasonable for hypothesis generation. A statistical association generated post-hoc from multiple comparisons is shaky ground from which to draw conclusions, particularly when the conclusions fly in the face of existing information or known facts, or do not take into account reasonable confounders.
- It is intellectually dishonest to claim that effects of chemical exposure are so small as to be clinically unrecognizable, then attribute major clinical effects to these same exposures.



**If we consider everything a risk, then we can't avoid true dangers.**

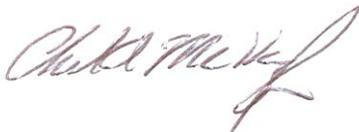
My point is that spurious associations and contradictory positions on regulation of chemicals in our environment are not going to be resolved solely by the use of biomonitoring. However, appropriate focus on those substances or exposures of most concern can be greatly influenced by the results of carefully considered, appropriately conducted and correctly interpreted biomonitoring studies.

As a practicing physician toxicologist, it is my responsibility to interpret the basic science, animal and human exposure data for people who are concerned about their risk, and to educate physicians and others who provide care for patients or information for people. Those who co-opt the biomonitoring process for their own advancement and political aims do a disservice to the entire medical and lay community with generalizations about “chemicals”, “cancer”, “neurotoxins”, “endocrine disruptors”, and other terms that are used without specific and detailed reference to dose, effect, and risk/benefit considerations, applied to both the products in use and their alternatives.

Biomonitoring is a very useful tool for documenting human exposure to environmental chemicals of concern, tracking trends in exposure, and prioritizing chemicals of most concern for possible regulation, restriction or substitution, consistent with “green chemistry” principles. Chemicals with declining prevalence or concentration in the population, as demonstrated by biomonitoring, should be treated as the historical success or cautionary stories they provide in terms of public health improvement or lack thereof. Attention and funding should be focused on those compounds that display biopersistence, bioaccumulation, biotransformation, or that generate sentinel signals from high-dose exposure (e.g. occupational) or high-risk populations (e.g. fetal/neonate); and for which concern for significant public health effects exist.

I thank the committee for this opportunity to present the views of a practicing medical toxicologist and educator on the important issues of biomonitoring, public health, and risk communication.

Sincerely,

A handwritten signature in cursive script, appearing to read "Charles McKay".

Charles McKay, MD FACMT, FACEP, ABIM  
Medical Review Officer  
Medical Director, Occupational Health Services  
Section Chief, Division of Medical Toxicology,  
Department of Traumatology and Emergency Medicine  
Hartford Hospital  
Associate Professor of Emergency Medicine  
Associate Medical Director, Connecticut Poison Control Center  
University of Connecticut School of Medicine  
Member, Scientific Advisory Counsel, Environmental Health Research Foundation Member,  
Board of Directors, American College of Medical Toxicology

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American College of Medical Toxicology Position Statement: Post-Chelator Challenge Urinary Metal Testing. [http://www.acmt.net/cgi/page.cgi?aid=2999&\\_id=52&zine=show](http://www.acmt.net/cgi/page.cgi?aid=2999&_id=52&zine=show) (last accessed 1/30/10)

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CDC EPHT: <http://www.cdc.gov/nceh/tracking/trackbiomon.htm>

CDC Funding 2009 Biomonitoring grants [http://www.cdc.gov/biomonitoring/state\\_grants.htm](http://www.cdc.gov/biomonitoring/state_grants.htm)

CDC. Fire Deaths and Injuries: Fact Sheet.

<http://www.cdc.gov/HomeandRecreationalSafety/Fire-Prevention/fires-factsheet.html>

CDC National Exposure Report: (chemicals in 4<sup>th</sup> report): [http://www.cdc.gov/exposurereport/pdf/NER\\_Chemical\\_List.pdf](http://www.cdc.gov/exposurereport/pdf/NER_Chemical_List.pdf) [212 chemicals, including 75 being checked (retrospectively – 2003-4; 1999-2000, 2001-2) for the first time]

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Oregon State's Ways and Means 2009-11 Budget Proposal:

<http://www.scribd.com/doc/15662281/Oregon-Ways-and-Means-CoChairs-Recommended-20092011-Budget>

## APPENDIX A: Internet Journal of Medical Toxicology Editorial

A Call To Arms For Medical Toxicologists: The Dose, Not The Detection, Makes The Poison  
Internet Journal of Medical Toxicology 2003; 6(1):1 (archived)  
[http://www.acmt.net/cgi/page.cgi?aid=1543&\\_id=52&zine=show](http://www.acmt.net/cgi/page.cgi?aid=1543&_id=52&zine=show)

Charles A. McKay Jr. MD FACMT, FACEP, ABIM  
Michael G. Holland, MD, FACMT, FACOEM, FACEP  
Lewis S. Nelson MD, FACMT, FACEP

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### Introduction

Over the last several decades, the analytic capability to measure very small concentrations of an increasingly vast array of chemical structures has increased dramatically. Analytic chemists can now measure certain purported toxicants at a fraction of a part per trillion.[1] To give some idea of this level of detection, the proverbial "drop in a bucket" would be measuring things at the parts per million range; parts per trillion is equivalent to a "drop in a lake"!

Unfortunately, our ability to determine what to do with this data has not progressed as fast as the analytic technology. Although a tenet of toxicology is that "the dose makes the poison", many people inappropriately fear that the very detection of a substance must equate with toxicity. As medical toxicologists, we focus on the patient's symptoms and signs and their association with exposure and delivered dose. However, many of us are faced with patients coming from other practitioners with laboratory data from a multi-element panel indicating toxicity by mercury, arsenic, or other heavy metals or excesses or deficiencies of a wide array of trace elements or hydrocarbons (so-called environmental pollutants). These laboratory tests are often presented as *de facto* evidence of toxicity or "systemic imbalance or insufficiency" without any evidence of excessive dose or exposure. Furthermore these test results are then considered the cause of a variety of poorly characterized or general symptoms. Unfortunately, "environmental ecologists" and other practitioners[2] often use these test results, which we consider clinically irrelevant, as support for a variety of scientifically unproven or clinically non-indicated treatments.

We define esoteric testing to be uncommonly performed laboratory analyses for trace elements, environmental contaminants, or endogenous enzymes obtained from samples of blood, urine, hair or other body tissue. These tests or matrices generally lack a published reporting of validated reference ranges or suffer from significant procedural difficulties. While a large number of potentially valid analytes or methods may fall into this broad definition, the widespread use of certain testing panels and laboratories by certain groups of practitioners present obvious examples of aberrant practices with which we are all familiar. (the so-called "know it when you see it" definition of quackery).

We present the following composite case and a rationale for a proposed set of criteria to assist physicians in the decision to perform esoteric testing and in the interpretation and application of results already obtained.

### Case Example

A 52 year old woman presents to the toxicology clinic complaining of generalized fatigue, difficulty with memory, and anxiety. There is a history of some weight loss over the last few months and difficulty sleeping. The patient is an ex-smoker and consumes occasional ethanol. A general physical exam is unremarkable, as is a neurological and mini-mental status exam. During

further questioning, as the toxicologist formulates a wide differential (including a number of non-toxicologic diagnoses), the patient declares, "My other doctors found I was out of balance and have too much mercury in my system. I want to know if I should have my dental fillings removed because I don't feel much better after chelation." With further discussion, it becomes clear that the patient has been to a number of practitioners, some of whom have used "alternative practices" such as kinesiology to determine she has an excess of heavy metal contamination, while others have given courses of dimercaptopropane sulphonate (DMPS) followed by urinary mercury collection and hair mercury analysis.

## **Discussion**

While poisoning by a wide variety of naturally-occurring heavy metals or industrial contaminants is well-described, the "low-level" toxicity of mercury, arsenic, and other heavy metals is more problematic. Even for elements, such as mercury, where it is generally accepted that hair analysis is a valid analytic technique[3], proper collection, analysis and interpretation is still necessary. Furthermore, the distinction between public health concerns and individual toxicity is very important. For example, it is generally accepted that mercury contamination of the environment has contributed to an increase in the mercury concentration in marine animals. All states have health advisories regarding the consumption of fresh-water fish because of concerns about mercury (and PCB) contamination. Yet these advisories are focused on the possible risk for neurotoxicity for the unborn child of a pregnant woman. While various studies have raised questions about subtle population neurodevelopmental effects from amounts of mercury 10-100 times that of the average American diet (resulting in maternal hair mercury measurements far above what is commonly reported as abnormal by hair analysis laboratories), even these authors state that none of their subjects demonstrated clinical mercury poisoning.[4] Can we reassure the vast majority of patients with vague symptoms and abnormal heavy metal screens without glossing over the patient who is truly poisoned? We believe such a balance is possible and should be one component of the medical toxicologists' practice. On an individual basis, we can educate practitioners and the general populace in our area regarding some of the cautions to take with available laboratory testing. Each of the following points deserves careful consideration:

- 1) The decision to perform laboratory testing should be based on a differential diagnosis, rather than indiscriminate testing.

It is often tempting to run a large battery of tests on patients with poorly characterized or complex presentations. Patients who carry diagnoses such as chronic fatigue syndrome, multiple chemical sensitivity, fibromyalgia are especially prone to this type of testing, since these "conditions" are essentially symptom complexes and have no known organic or toxic etiology. Also, patients with chronic, progressive or incurable disorders such as multiple sclerosis and autism may be tested for toxicants. Some physicians will order trace mineral analyses searching for a cause of these syndromes, but many unscrupulous practitioners order these tests to "prove" to patients the need for chelation or other unnecessary, and potentially dangerous, "treatments". Unfortunately, this reliance on analytic testing is often misplaced. By pure chance, the statistical likelihood of finding a test result outside a population norm will increase as the number of tests increases. In the absence of good clinical correlation, these results are usually meaningless, but can cause a good deal of confusion and concern in both patient and physician.[5] As mentioned above, the dose determines toxicity. In addition, most toxicants produce a characteristic pattern of effects; this

specificity of effect should be carefully sought in the history and physical exam, which then should guide testing patterns.

2) Critical methodological steps regarding specimen collection and laboratory analysis must be heeded.

All of these tests measure very small amounts of chemical compounds. As such, even low-level contamination of collection materials or procedures can result in false positive reports. This problem is well described with lead biomonitoring, where elevated capillary blood measurements from fingerstick testing must be confirmed with a venous sample because skin contamination with lead may result in falsely elevated blood levels. This can also occur with heavy metal testing of hair, due to external contamination by metals found in hair treatments, public water supplies or air pollution.[6] Similar problems arise with blood or urine collections.[7] In addition, dietary restrictions are necessary when analyzing body burden of heavy metals or trace elements to prevent false elevations from such agents as dietary supplements or seafood. As an example, the presence of largely non-toxic arsenobetaine and arsenocholine - "fish arsenic" - from seafood interferes with the assessment of arsenic exposure.[8] Although a further testing refinement (i.e. speciation of arsenic type) can be used for this element if there are concerns about the patient's dietary contribution, few laboratories provide this expensive service. Furthermore, this would not distinguish the contribution of arsenosugars that are present in marine algal products (often present in supplements).[9] Finally, many labs will analyze a urine specimen collected for six hours after a chelation challenge, and then compare this result with a norm based on a non-challenged collection. This result will almost always be higher than the non-challenged test but does not reflect an abnormal body burden of the presumed toxicant.[10,11,12] As an example, normal subjects may excrete several fold more mercury post-chelation than in their own pre-chelation test.[12] The results then are "flagged" as abnormal when in fact the testing has done little more than document a normal response to the chelator.

3) Laboratory tests should have well-validated reference ranges. These are lacking for many esoteric tests.

Population norms are often not standardized or are based on small numbers. In fact, some of these laboratories have developed their own reference ranges that are much lower than widely accepted ranges such as that published for hair mercury by the National Centers for Environmental Health of the CDC. This represents their belief that these toxins are more poisonous than mainstream medical science believes. The end result is many patients' results will be flagged as abnormal. In addition, accuracy is very poor for some analyses, such as hair testing by popular laboratories.[13] Many of these laboratories claim Clinical Laboratory Improvement Amendments (CLIA) certification, a federal standard for certain analytic tests, yet no such certification specifically exists for hair mineral analyses. Proficiency testing standards for hair testing do not exist, and individual labs devise their own verification methods and criteria for accuracy. Analytic laboratories should demonstrate some validity of testing, both internal (precision) and compared to standards (accuracy). Even when this is done,[14] information regarding measurements in a target population, such as those with known clinical effects from excesses or deficiencies of the given analyte, should be included.

4) Exceedance of a reference value does not necessarily imply that a patient is poisoned.

Interpretation of laboratory tests is best done in the clinical setting. Often additional clinical, epidemiological and laboratory data are necessary to establish a scientific basis for linking an elevated lab value with the presence or future risk of an adverse health outcome. In fact, for some elements and enzymes, the biologic or physiologic human health effects are not well characterized. As with the heavy metals, the effects of gross deficiencies (e.g. selenium)[15] or excesses (e.g. manganese)[16] are well described, while the effects of smaller variations from a population norm are less clear. Indeed, the experiences of certain unusual populations, such as two-three fold increases in serum manganese in patients receiving total parenteral nutrition, suggest no clinical adverse effects from these excesses.[17,18] Again, laboratories will often report determinations, usually in hair or red blood cells, compared to an unvalidated population norm, rather than as correlated with health or disease. Laboratories should provide normal ranges based on validated control populations. It is inappropriate for a laboratory to provide treatment recommendations. This is particularly true when the laboratory is associated with industries that distribute or otherwise promote treatments for the purported intoxications or deficiencies they claim to document.

### **Summary**

In general, testing for heavy metals, nutritional elements present at extremely low concentrations, or so-called environmental contaminants, should only be obtained in the following situations and with the indicated precautions:

- A properly performed clinical history and physical exam suggests the lack or excess of these chemicals or minerals/metals.
- Proper patient preparation may include dietary avoidance of food and supplements that contain the substance of interest for several days prior to the sample collection.
- The use of collections after chelation is usually unwarranted.
- If post-chelation collections are used, the range of normals must be adjusted accordingly, and the results must be interpreted with extreme caution.
- Collection should be done through a certified laboratory that is experienced in the collection and handling of these specimens to avoid contamination.
- Analysis should be at a reputable laboratory that provides data on their normative population, including the selection and number of controls, and validation of their analytic procedures.
- The laboratory should not provide treatment recommendations or sell therapy to the patient.

### **Conclusion**

There are many factors to consider before ordering a large array of esoteric laboratory tests and a number of important considerations in the interpretation of these tests. The current popularity of broad trace element or pollutant screening with subsequent "detoxification" treatment, is often inappropriate. At this time, many of these tests are best utilized as research tools, such as the current population evaluations by the National Center for Environmental Health of the Centers for Disease Control and Prevention.[19] Application of these test results to individual patients is fraught with problems. Current concerns about environmental-related illness have been misappropriated by a number of practitioners to vindicate non-indicated treatments. A large portion of our toxicology clinic population is convinced their symptoms are due to poisoning, when neither their symptom complex nor laboratory testing justify such a conclusion. It is our

contention that medical toxicologists should be at the forefront in the discussion regarding the appropriateness of toxicologic testing and its interpretation. In addition, we should be active in protecting patients from the misapplication of these tests.

### **Addendum**

The proceedings of an ATSDR panel on hair analysis have been published recently. The reference is: Harkins DK, Susten AS. Hair Analysis: Exploring the State of the Science. Environ Health Persp 2003;111:576-578.

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## **APPENDIX B: American College of Medical Toxicology Position Statement**

### **Post-Chelator Challenge Urinary Metal Testing**

*by Nathan Charlton, MD and Kevin L. Wallace, MD FACMT, posted on 10:35 AM, July 27, 2009*

[http://www.acmt.net/cgi/page.cgi?aid=2999&\\_id=52&zine=show](http://www.acmt.net/cgi/page.cgi?aid=2999&_id=52&zine=show)

Heavy metals, such as lead and mercury, are ubiquitous in the environment [1-4]. Exposure in human populations is constantly occurring, and detectable levels of lead and mercury are commonly found in blood and urine of individuals who have no clinical signs or symptoms of toxicity and may be considered background or reference values [1-5]. Although urine testing for various metals in an appropriate clinical context, using proper and validated methods, is common and accepted medical practice, the use of post-challenge (a.k.a., post-provocation) urine metal testing, wherein specimens are typically collected within 48 hours of chelation agent administration, is fraught with many misunderstandings, pitfalls and risks. The American College of Medical Toxicology issues this position statement in disapproval of the use of post-challenge urinary metal testing in clinical practice and the use of such test results as an indication for further administration of chelating agents.

In current evidence-based medical practice, urinary testing is commonly used in the biomonitoring of exposure to certain metals such as arsenic and inorganic mercury and the severity of their associated toxicity. It is accepted practice to conduct such testing, e.g., in exposed individuals with clinical evidence of peripheral neuropathy, as long as validated collection and analytical methods are employed prior to, or after, a sufficiently long time interval (e.g., 3-5 days) following administration of a chelating agent, i.e., applied to non-challenge urine specimens, and the results are compared to appropriate reference values [5, 6]. In some non-evidence-based medical practices, however, assessment of metal poisoning is frequently based on non-validated post-challenge urine metal testing, which invites inappropriate comparison to normal urine reference ranges [4-7].

Chelating agents such as dimercaptosuccinic acid (DMSA), dimercaptopropanesulfonic acid (DMPS), dimercaprol (BAL), and edetate calcium disodium (CaNa<sub>2</sub>-EDTA) bind metallic and metalloid elements and have been shown to increase their elimination from the body. Chelating agents have been found to mobilize metals in healthy individuals who have a body burden considered normal for a standard reference population, as well as in those who are determined to have a high body burden of the same metallic species [4, 8-11]. More specifically, urine specimens collected in relatively close temporal proximity to administration of chelating agents, i.e., post-challenge specimens, are expected to have increased concentrations of metallic elements. This includes elements, such as zinc, that are essential to normal physiologic functions and maintenance of good health.

Normal reference values for non-challenge urine metal test results vary among and within different populations. Ranges for these values have been established in nationally certified laboratories that meet proficiency standards for urinary metal testing [5]. However, scientifically acceptable normal reference values for post-challenge urine metal testing have not been established [10]. In addition, scientific investigation to date has failed to establish a valid correlation between prior metal exposure and post-challenge test values [10]. Despite the lack of

scientific support to do so, it is also a common practice of some laboratories and care providers to provide or apply non-challenge normal reference values as a comparative means of interpreting results of post-challenge urine metal testing [5]. Currently available scientific data do not provide adequate support for the use of post-challenge urine metal testing as an accurate or reliable means of identifying individuals who would derive therapeutic benefit from chelation.

Unfortunately, the practice of post-challenge urine metal testing and its application to assessment of metal poisoning often leads to unwarranted and prolonged oral and/or intravenous administration of chelating agents, in response to the results of serial post-challenge testing that remain elevated above non-challenge reference values. Chelation therapy based on such laboratory values, in addition to being of no benefit to patient outcome, may actually prove harmful [5, 12]; catastrophic outcomes such as acute fatal hypocalcemia have been reported following the improper use of a chelating agent, edetate disodium (Na<sub>2</sub>-EDTA) [13]. In addition, the safer formulation of this agent, CaNa<sub>2</sub>-EDTA, has been demonstrated to increase urinary excretion of essential minerals such as iron, copper and zinc [8, 14]. There is published experimental evidence that deleterious effects may occur when chelation is applied in the absence of prior lead exposure. [15] Other chelating agents such as DMSA and DMPS may also increase the elimination of certain essential elements, as well as promote target organ redistribution of metallic elements of concern such as mercury [16-18].

It is, therefore, the position of the American College of Medical Toxicology that post-challenge urinary metal testing has not been scientifically validated, has no demonstrated benefit, and may be harmful when applied in the assessment and treatment of patients in whom there is concern for metal poisoning.

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