Elemental Analysis of Hair and Urine via ICP-MS: Application to Naturopathic Medicine

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Disclaimer

- The information presented in this Webinar is the opinion of Dr. Gillson based on his research and experience.
- Dr. Gillson's opinions do not necessarily reflect the opinions of any other individual or organization.

What is Elemental Analysis?

- Measurement of the amounts of the chemical elements e.g. calcium, iron, beryllium, uranium in a sample.
- People often use the term "Mineral" analysis.
- This is a misnomer.
- Minerals are (often) complicated mixtures of various elements e.g. Samarskite: \((Y,Fe^{3+},Fe^{2+},U,\text{Th},\text{Ca})_2(Nb,Ta)_2O_8\)
- Here we are ripping the sample apart and reducing it to its component ions; we are not measuring minerals!
“Heavy” Metals

- This term is used somewhat loosely, to refer to all toxic/potentially toxic elements.
- In general, the heavy (high atomic number) toxic elements include mercury, lead, thallium and bismuth.
- There are other heavy elements that aren't especially toxic, such as uranium, thorium and tungsten.
- Elements like cadmium, antimony and silver aren't that heavy, but are also toxic.
- Beryllium, at atomic number 4, is very light, but still toxic!

Why do Elemental Analysis?

**Nutrition**
- Measure levels of elements which are normally in our body, and are known to be nutritionally relevant.
- Assess adequacy of nutrient content of diet.
- Assess ability of gut to absorb nutrients.

**Toxicity**
- Measure levels of elements which are not normally in our body, and are known or suspected to be toxic.
- Assess possibility that patient symptoms are caused by toxic elements.
- In some cases, are able to predict the extent of damage due to a toxic element e.g. cadmium in first morning urine.
Elemental Analysis of Hair and Urine

Really now, how many people are exposed to Hg and Cd?

- Particulates from the burning of coal are loaded with toxic elements.
- Coal dust burned in Asia settles on North America → water and crop contamination.
- Effluent from our own coal-burning plants isn’t helping!
- Seafood concentrates toxic elements like mercury and cadmium.
- Imported skin lightening creams may contain mercury.

Really now, how many people are exposed to Hg and Cd?

- People supplement with weird stuff like colloidal indium.
- Herbal supplements can be contaminated with toxic elements.
- Pepto Bismol contains bismuth.
- Some plants have a propensity to concentrate certain elements from soil, e.g. tobacco concentrates cadmium.
- Lead from water pipes in old houses.
Nutritionally Essential Elements

- Gastric juice is acidic for a reason.
- Digestion and assimilation worsen with age.
- Nutrient intake declines with age:
  - Psychosocial factors, poor dentition, financial considerations
- Many chronic illnesses culminate in a failure to digest and assimilate nutrients.
  - Decreased acid production
  - Decreased production of pancreatic enzymes

Conditions Associated with Essential Element Deficiency

- Eczema (Zn)
- Fatigue, poor tanning, grey hair (Cu)
- Frequent respiratory infections (Zn, Mn)
- Glucose-insulin disruption (Zn, Cr, V)
- Hormone deficiencies (Zn, B, Se)
- Thyroid problems (I, Br, Hg, Cd, Se)
- Cardiovascular disease (Cu, Mg)
- Mood disorders (Li)
- Arthritis (B, Cu)
- Poor bone health (B, Mg, Sr)
The Truth about Elemental Analysis

- Elemental analysis is often viewed suspiciously by the mainstream (especially hair analysis).
- Some hair testing labs try to sell supplements based on supposed imbalances identified by their testing.
- Over-interpretation of results can lead to overtreatment/inappropriate treatment.

The Truth about Elemental Analysis

- Elemental analysis has been around for a long time.
- There is a large mound of literature on the topic.
- Elemental analysis of hair, urine, blood cells has a valid place in medicine.
- Some of the diagnoses on the next slide should not be made unless chemical element intoxication has been ruled out.

Neurologic/Cognitive/Behavioural Problems Possibly Associated with Toxic Elements

- Tremor
- Parkinsonism
- ALS
- MS
- Peripheral neuropathy
- Dementia
- Learning disabilities?
- Autism?
Hair vs Urine

- Hair is an archaeological record.
- Length = time
- First ½” (1 cm) closest to scalp reflects previous month’s average blood level.
- Urine = security videotape of last 24 - 48 hours
- Urine = recent intake for most elements
- Urine = reflects cumulative exposure for Cd

Hair

- Hair results markedly affected by dyes, perms and bleach.
- Need undyed, unbleached, unperm fresh growth closest to scalp.
- Sample is often taken from the nape of the neck.
- Can also use pubic hair.

Hair

- Dyes, bleach, etc., may contain barium, tin, strontium, zirconium, manganese.
- The treatment may also alter the matrix of the hair such that it has a greater propensity to take up certain elements.
Hair
- Need 0.225 to 0.25 mg
- A prepaid Business Reply envelope is provided, to return the specimen to RMA.
- If you want faster turnaround, use a stamp!

External Contamination of Hair
- Sample may be contaminated with dust e.g. someone who works with drywall is exposed to aluminum and magnesium-containing dust.
  - This is avoided by incorporating a washing step at the lab, prior to digestion.
- It may be hard to distinguish elements deposited from "within" from elements adsorbed onto hair from the environment e.g. welders, swimmers.
  - Common pitfalls are noted in the interpretation.

Urine
- Can use 1st morning urine.
- 24 hour collection better than first morning if looking at nutritionally relevant elements.
- Results are reported with creatinine normalization, i.e. mass analyte/mass creatinine.
- Return shipping of specimen is via overnight FedEx.
- Most elements are stable at room temperature for one week.
Speciation

- Elements may be present in both organic and inorganic forms e.g. Arsenic
  - Arsenite (As(III))
  - Arsenate (As(V))
  - Monomethylarsonic acid (MMA(V))
  - Dimethylarsinic acid (DMA(V))
  - Monomethylarsonious acid (MMA(III))
  - Dimethylarsinous acid (DMA(III))
  - Arsenobetaine (AsB)
- Speciation is available but is only relevant in certain specialized instances.
- Complete avoidance of seafood will remove organic arsenic from the picture.

Urine Provocation Studies

- First morning urine: Baseline
- Administer oral and/or IV chelating agent: e.g. EDTA, DMSA, DMPS
- Collect urine for specified time period, 6-24 hours (usually 6 hours).
- Looking for an increase in toxic elements in 2nd sample as an indicator of body burden.

Urine Provocation Studies

- Merely looking at the Provoked numbers does not tell you what the body burden is.
- The ratio: $\frac{[X]\text{Provoked}}{[X]\text{Unprovoked}}$ is thought to better reflect body burden.
- $[X]\text{Provoked}$ is not thought to accurately reflect body burden.
- Exception: Lead
**Draft posted for public comment on the ATSDR website**: "The measurement of lead excreted in urine following an injection (intravenous or intramuscular) of the chelating agent, calcium disodium edta (CaNa2EDTA provocation) has been used to detect elevated body burden of lead in adults (2,3,4,5) and children (6,7), and is considered to be a reliable measure of the potentially toxic fraction of the lead body burden (8)."

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**Banging the Beehive**

- When you whack a beehive, bees may fly out.
- Does the number of bees flying out tell you how many were in the hive pre-whacking?
- Does the number of bees flying out tell you how many are left in the hive post-whacking?
- Provocational studies will never be the definitive way to assess body burden; there is no definitive way, short of tissue biopsy.
Urine Provocation Studies

- False Positives:
  - High level due to acute exposure (e.g. high arsenic due to fish consumption).
- False Negatives:
  - Poor absorption of chelating agent (if oral administration).
  - Glutathione deficiency (one of the cellular detox mechanisms requires glutathione).
  - Chelating agent may not have high affinity for the element of interest e.g. EDTA and Hg.

Normal Ranges Hair/Urine

- Specimens provided by NDs, MDs and other practitioners, for normal range generation.
- Normal individuals of both genders and all ages (subject to a list of exclusion criteria).
- Specimens did not come from patients!
- Provoked urine specimens are referenced to ranges established without provocation.

Determining Reference Ranges

- Specimens are analyzed.
- Results have to be fitted to a statistical model e.g. Normal Distribution.

The standard deviation is added or subtracted from the mean, to find the bounds within which a certain percentage of the population lies.

- Conventional medicine uses the wider zone (mean +/- 2 SD): "Normal" encompasses the middle 95% of the population.
- Functional medicine uses the narrower zone where "Optimal" encompasses the middle 68% of the population (mean +/- 1 SD).
Many biological variables, including hair and urine element concentrations, follow a lognormal distribution.

Skewed distribution.

The limits of the ranges aren’t symmetric about the mean.

If the quoted range is 5 – 35 the “middle” is not 20. The peak is closer to 15.

### Hair Methodology

- Wash sample with dilute detergent, rinse with pure water, dry.
- Microwave digestion with nitric acid.
- Wind up with a clear yellow liquid.
- Dilute with water and analyze.
- Run controls and certified reference materials along with samples.
- Participate in external validation programs.

Most of the results are below the mean

A “Left shift” is often seen in children and the elderly.

It is also seen with low stomach acid, and many chronic illnesses.

Treatment: digestive enzymes and other aids to digestion, improve diet.
Reasoned Approach to Interpretation of Hair Tests

- Cutler developed a set of “counting rules”
- Identified patterns for the essential elements which have < 5% probability of occurring by chance:
  - Too few green bars
  - Too many red or purple bars
  - Lopsided distribution (too few bars going left/too few going right)
- The finding of an essential element distribution which breaks one or more of these rules increases the likelihood that toxic elements are interfering with the deposition of all elements in hair (toxic and essential).
Cutler’s Approach made Simple

- RMA has coded Cutler’s logic into the Interpretation Engine.
- The Essential Element distribution is interpreted as Normal or Abnormal.
- The rest of the interpretation flows from that, exactly as Cutler outlines in his book.
What if you see something like this for the Toxic Elements?

One might conclude that the patient is carrying excessive amounts of many toxic elements.

All of Cutler's counting rules are broken here, for the essential elements.

Body seems to be "dumping" into hair and this is affecting both essential and toxic elements.

A more sensible conclusion is that one toxic element, (usually mercury or lead) is affecting the ability of hair to faithfully record what has floated by the hair follicles in the last month or so.

It is the overall pattern that makes us suspicious, rather than a line-by-line interpretation.
At face value, this person appears to have a low burden of toxic elements.

The accompanying essential element pattern also breaks Cutler's rules. Essential elements are under-represented in hair. (Too many left-going bars).

This may indicate that a toxic element is poisoning the transport of all elements into hair, even though nothing shows up in the toxic elements.

Absence of elevated toxic elements doesn't preclude possibility that a toxic element or elements is/are still a problem for this patient.
Is Cutler on the right track?

**Importers**
- There are no importers specifically designed to import toxic elements!
- Are we surprised?
- Toxic elements ride in with the non-toxic elements because they are the same size, same charge, same chemical binding tendencies.

**Sequestrators and Exporters**
- These have evolved specifically to deal with noxious things creeping into cells.
- Sequestration proteins may also have a role to play in normal physiology.
Is Cutler on the right track?

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<table>
<thead>
<tr>
<th>“Importers”</th>
<th>“Exporters”</th>
</tr>
</thead>
<tbody>
<tr>
<td>DMT-1</td>
<td>cMDAT</td>
</tr>
<tr>
<td>ZIP</td>
<td>GSX</td>
</tr>
<tr>
<td>OAT</td>
<td>ABCB6</td>
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<tr>
<td>LAT</td>
<td></td>
</tr>
<tr>
<td>CaMgATPase</td>
<td></td>
</tr>
</tbody>
</table>

“Sequestrators” metallothionein

• Symmetric distribution of essential elements
• Mostly green bars for essential elements
• Low levels of toxic elements
• Good cellular health
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**Normal balance**

- Toxic elements can induce synthesis of exporters and sequestration proteins.
- Synthesis of importers can also be upregulated, e.g. more Se is imported to offset effect of Hg.
- Capacity of sequestration proteins can be exceeded.
- Exporter and importer proteins can be inactivated by excessive amounts of toxic elements.

**Button line:**
- It is quite plausible that chaotic/statistically unlikely patterns of element deposition could arise.
- Patterns seen will depend on mix of toxic elements present, concentration of the elements in question, duration of exposure, nutritional status, genetics.
- This would be exceedingly difficult to “prove” as the system is so complex.
- Removal of toxic elements results in normalization of these patterns.

Mercury in Hair

- Hair reflects average methylmercury burden quite well, and hair methylmercury reflects brain methylmercury.
- Fish contain methylmercury, so hair reflects fish consumption, in many cases.
- Amalgam mercury also shows up in hair, but may be obscured by the “fish” signal.
- About 7% of the mercury eliminated by the body winds up in hair. (Magos-cited above.)
Effect of Hair Treatment

High As and Se is a fingerprint for use of selenium dandruff shampoo.

March 29
Hair roots Untreated

April 21
After bleaching/colouring

84 yr old male
• fatigue
• anemia

Previously very active World-class biathlete in his age group.

Was exposed to lead in his teens.

High lead

Led shift

Hair test

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Normalization of Hair Patterns with Treatment

- Cutler gives many examples in his book.
- Initial distribution pattern of essential elements is abnormal; no toxic elements show up.
- After some treatment, toxic elements begin to show up, essential element pattern remains abnormal.
- Eventually, with continued treatment, essential element pattern normalizes and toxic elements disappear again.
Elemental Analysis of Hair and Urine

Scalp

Welder

- Bipolar mood disorder
- Depression
- Anxiety
- RA

Pubic

Due to fumes adsorbing on hair?
Or…inhaled fumes putting toxic elements into blood → hair?

Before commercial detox product

After 2 months on commercial detox product

2 year old male
Language delay
Essential element distribution is normal
Dad and Grandpa are both machinists or welders. How is it getting into the house? W known to affect Mo.

**Urine Methodology**
- No digestion needed.
- Spin urine sample and decant supernatant.
- Dilute and acidify the supernatant.
- Analyze.
- Run pooled controls, commercially available controls and Certified Reference Materials.
- Participate in External Quality Assessment program.

**Cutler and Urine Elements**
- Cutler has not tried to apply his approach to urine tests.
- Unprovoked urine levels of a given element are often only a small fraction of total daily excretion of that element.
- Cannot formulate rules for what is expected when chelating agents are used: as this is not a steady-state situation.
Might take this as an indication to watch vanadium if course of chelation is undertaken.

BASELINE URINE ELEMENT TESTING

Some practitioners with long experience in this area maintain that you can draw the same conclusions from this type of unprovoked urine result as you can for hair, i.e. decreased intake of essential elements, or problems with absorption from food.

BASELINE URINE ELEMENT TESTING

What does this mean?

High Baseline Level of Hg

- 85% of mercury in blood is methylmercury.
- A high baseline level of urine Hg (> 0.9 ug/g Cr) usually indicates acute/ongoing exposure to seafood containing methylmercury.
- Exception 1: frequent inhalation of Hg vapour, e.g. continued use of a vacuum cleaner that had once been used to vacuum up liquid mercury.
- Exception 2: large amalgam surface area +/- periodontal disease +/- alot of chewing +/- alot of hot beverages/acidic beverages.
High Provoked Level of Hg

- High fish consumption.
- Large surface area of amalgam (one whopping filling is worse than 6 tiny ones).
- Ongoing exposure from some other unusual vector e.g. living on a toxic waste dump, living beside a smelter, living next to a coal-fired power plant.

Left shift
84 yr old male
- fatigue
- anemia
Previously very active World-class biathlete for his age group

Hair test
High lead
Urine "challenge" test confirms high lead seen in hair
- History of lead exposure as a teen
- Lead is stored in bone; leaches out as bone is lost with aging
- Patient needs to work with a knowledgeable practitioner to slowly clear out the lead

Post/Pre Patient “Lifts”
Documented at RMA (oral DMSA)

- Pb ≈ 20 x
- Hg ≈ 10 x
- Tl ≈ 1.8 x
- As ≈ 1.3 x
- Cd ≈ 1.2 x
- Cu ≈ 7 x
- Mn ≈ 2.5 x

If you don’t see ratios in this ballpark, you have to be concerned about:
- GSH deficiency
- Inadequate DMSA dose (30 mg/kg)
- Poor absorption

Continuous efforts at detox lead to episodic "releases" of toxic elements.
There is plenty we don’t understand about toxicity and detoxification!
Conclusion

- Elemental analysis of hair and urine has not always received the credit it deserves.
- These tests have their place in the assessment of patients, just like any other laboratory testing.
- These tests are very useful for NDs.
- Accreditation helps ensure high quality, accurate results.