Micro Trace Minerals Laboratory
35+ years of clinical & environmental laboratory diagnostics

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The role of Aluminum (Al) in Medicine and our Environment

In a 1998 statement the **Commission ‚Human Biomonitoring' of the German Environmental Protection Agency** points out three aspects that are important in the environmental/medical assessment of aluminum:

1. Human exposure is inevitable. Al is the third most common element on earth.
2. Al is clearly neurotoxic
3. Al has a potential role in the development and pathogenesis of Alzheimer.

The commission states that to monitor an exposure, we have three laboratory tests (blood, urine, hair) and the DFO (Deferoxamine) Test.

In this News Release we discuss the assessment of urine, before and after provocation. More under www.microtraceminerals.com

1. Aluminum Reference Range i.e. the acceptable upper range for unprovoked urine:

The German Environmental Agency is expecting to reduce urine levels to <15µg/L.
The Mayo Clinic states that a daily excretion >20 µg/L indicates exposure to aluminum.
We now use a reference range of <40µg/g creatinine, which is equal to 40 µg/L.
All of the above ranges apply to unprovoked urine i.e. urine that has not been provoked with any type of chelating agent.

Clinical Information:
Under normal physiologic conditions, the usual daily dietary intake of aluminum (5-10 mg) is completely eliminated. Excretion is accomplished by avid filtration of aluminum from the blood by the glomeruli of the kidney. Patients in renal failure (RF) lose the ability to clear aluminum and are candidates for aluminum toxicity.

A high intake of dietary aluminum results in an increase in Al-elimination. High amounts of Al can be found in tea, lemonades, colas and fruit juices packaged in aluminum cans or aluminum-lined boxes. Zeolite, algae products, food additives such as aluminum phosphate, antacids and other medications may contain aluminum, causing an increase in urine concentration.

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Urine aluminum concentrations are likely to be increased above the reference range in patients with metallic joint prosthesis. Prosthetic devices produced by Zimmer Company and Johnson and Johnson typically are made of aluminum, vanadium, and titanium. This list of products is incomplete, and these products change occasionally; see prosthesis product information for each device for composition details.

Avoiding Al seems more important than we ever expected. Research indicates that transferrin can bind aluminum, transporting it through the Blood Brain Barrier. In the brain, Al plays a role in the destruction of nerve cells. (De Sole P., et al. Possible relationship between Al/ferritin complex and Alzheimer disease. (Clin. Biochem. 2013; 46: 89-93)

The Al-concentration of unprovoked urine is a reflection of the intake and exposure that happened during the last hours prior to sampling.

In the occupationally exposed, intoxication due to inhaled aluminum is directly related to the renal Al-excretion.

The European Environmental Agencies have set a Maximum Contaminant Level (MCL) of 200µg/L for the occupationally exposed.
The US Department of Health and Human Services, Agency for Toxic Substances and Disease Registry (ATSDR) does not provide a MCL.

THE MCL ONLY APPLIES TO UNPROVOKED URINE

Diagnosis and Therapy of an acute Aluminum-Intoxication / Exposition:
Patients receiving chelation therapy with desferrioxamine (for iron- or aluminum-overload states) excrete considerably more aluminum in their urine as they would under normal conditions.

Cautions
In cases of Al-intoxication, desferrioxamine elevates serum aluminum to levels >150µg/l. However, this test is not an acceptable substitute for serum aluminum measurements and is not recommended for routine aluminum screening.

Falsely increased urine results may be obtained if the specimen is collected in nonacid-washed polypropylene collection vessels or if metal caps are used to seal the container.

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Which chelating agent is useful for the treatment of chronic or subacute aluminum intoxication?
We compared mean levels of unprovoked urine (baseline or spot urine) with mean levels of provocation urines following treatment with commonly used chelating agents.

Table 1: Comparison of mean aluminum concentration of unprovoked vs. provoked urines:

Chelating agent(s)	# of Tests (N)	Mean value µg/g crea	Max-value µg/g crea	Test value >200µg/g crea	Mean Crea value g/L
Unprovoked urine	2485	14	1256	10	1,0
DMSA oral, 500mg	249	19	262	2	0.62
DMPS, iv	2750	18	390	2	0.66
DMPS iv + ZnDTPA iv	3320	20	817	2	0.69
MgEDTA,2,5g Infusion +500mg DMSA	78	57	141	0	0.54
CaEDTA, 1,9g +500mg DMSA	95	46	200	0	0.64

DMSA: Mean values are slightly higher in the provoked urines, but the aluminum binding of DMSA and the induced renal excretion seems insignificant.

DMPS i.v.: Mean values are slightly higher for the provoked urine and about equal to DMSA values. The aluminum binding and/or renal excretion following DMPS i.v. seems insignificant.

DMPS i.v. + ZnDTPA i.v. combination therapy
Mean values for the provoked urines are slightly higher than those of the DMSA+DMPS urines. The aluminum binding of the combination treatment, including the renal excretion seem insignificant.

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CaEDTA, 1,9g i.v. plus 500mg DMSA oral, and/or NaMgEDTA, 2,5g i.v. plus DMSA oral

The mean concentration of 57µg/g crea for the urines provoked with NaMgEDTA+DMSA and the CaEDTA+DMSA provoked urines (46µg/g crea) are considerably higher than the mean values for DMSA, DMPS and the DMPS/ZnDTPA combination treatment.
The mean concentration for the CaEDTA+DMSA and the NaMgEDTA+DMSA provoked urines are above our reference range of 40µg/g crea.

Assessment:

By comparing mean concentrations of DMSA, DMPS and the combination DMPS+ZnDTPA urines, we could not determine an efficient aluminum binding and renal excretion for any of these chelating agents. These chelating agents may not be the agents of choice in the treatment of aluminum overexposure.

The mean concentration of the urines provoked with CaEDTA+DMSA i.e. MgEDTA+DMSA show an increase in Al-binding and excretion, with 57µg/g crea for MgEDTA/DMSA and 46µg/g crea for CaEDTA/DMSA. The difference may be explained by the application route. CaEDTA is often (wrongly) injected, whereas NaMgEDTA is applied as an infusion. The fluid volume may be responsible for the lower creatinine value of the urines provoked with MgEDTA +DMSA (0.54µg/g crea).

From this data, we cannot safely state that the EDTAs bind aluminum more effectively, especially in lieu of the extreme values detected in baseline urines.
Of 2485 tests, we found 10 exceeding the MCL with a mean concentration of 526µg/g crea! The maximum level was 1256µg/g crea.

We found maximum concentrations exceeding the MCL in all provocation urines, except for the MgEDTA+DMSA urines. See Table 1.

Important information:

Aluminum is widespread in our environment. This indicates that great caution has to be taken during sampling. Our urine containers are metal-free. Make sure you are not re-using sample containers.

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Protocol reminders:

- Patients must empty bladder before chelation (oral or i.v.) is started.
- To avoid contamination, we prefer that patients collect all urine in the bladder for the duration of the appropriate collection period.

Urine collection times:

- DMSA oral: 4h
- DMPS oral: 3-4h
- DMPS i.v.: 1-2h
- EDTA: Infusion time plus 45min.
- EDTA+DMSA example: If oral DMSA is provided 1h prior to the start of a 2g EDTA infusion, the collection time is 1h + infusion time + 45min = 3h45min
- ZnDTPA+DMPS: 2h

More information under http://www.microtraceminerals.com/en/chelation-newsarticles

Additional information for chronic or subacute aluminum intoxication/exposure:

Aluminum is, compared with lead or mercury, relatively nontoxic. No known physiologic need exists for aluminum.

Approximately 95% of an aluminum load becomes bound to transferrin and albumin intravascularly and is then eliminated renally. In healthy subjects, only 0.3% of orally administered aluminum is absorbed via a healthy GI. When the GI barrier is bypassed, such as with intravenous infusion or in the presence of advanced renal dysfunction aluminum has the potential to accumulate. As an example, with intravenously infused aluminum, 40% is retained in adults and up to 75% is retained in neonates. Mayor et al suggested that parathyroid hormone may increase intestinal absorption of aluminum.

Up to this time, no biological function has been attributed to this metal, and, more importantly, aluminum accumulation in tissues and organs results in their dysfunction and toxicity. Aluminum is absorbed from the GI tract in the form of oral phosphate-binding agents (aluminum hydroxide), parenterally via immunizations, via dialysate on patients on dialysis or total parenteral nutrition (TPN) contamination, via the

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urinary mucosa through bladder irrigation, and transdermally in antiperspirants. Lactate, citrate, and ascorbates facilitate GI absorption. If a significant load exceeds the body's excretory capacity, the excess is deposited in various tissues, including bone, brain, liver, heart, spleen, and muscle.

Aluminum can interfere with chromium, iron, magnesium, zinc, calcium and copper. An inadequate supply of essential elements facilitates aluminum uptake. Aluminum absorption in bone is a risk in children with an inadequate intake of dietary calcium or vitamin D. Highly stressed patients with an inadequate magnesium supply are at risk. Leaky gut syndrome or kidney problems support the aluminum uptake.

Aluminum disrupts the Vitamin B6 and Vitamin D Metabolism.

Infants should be protected from Aluminum in nanoparticle form. Vaccines are containing either the mercury-containing thiomersal or aluminum-compounds.

While aluminum cannot be avoided, we can reduce Al-uptake by optimizing the body’s nutritional balance. Providing digestive support in the form of probiotics helps.

We wish you all the best. If you find this newsletter informative, let us know.

E.Blaurock-Busch and team

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