

Biomonitoring of Environmental Pollutants – Interpretation and Application of Test Results

Implications on Weight Loss, Chronic Fatigue,
Cardiovascular Disease, Diabetes as well as
General Wellness

Before we get to the lab tests....

- We need to define what a toxin is.
- We need to determine the extent of environmental toxicity.
- We need to discuss the effects of the toxins on our systems.
- Then we need to learn how to interpret the tests.

The List of Toxins

- We have the usual list of villains
 - **Heavy metals**
 - **Organochloric and organophosphic compounds**
 - **Petrochemicals**
- And the not so apparent
 - Stress
 - Infections
 - Drugs

Toxins – How Prevalent???

- According to the United States Environmental Protection Agency in 2002 through their “Toxic Release Inventory” tracking system, over 7.1 billion pounds of 650 different industrial chemicals were released in the air and water, 266 of which are linked to birth defects.
- Worldwide, the estimates approach 80 billion pounds of toxins released annually.
- Some of these toxins affect human health in microgram doses.

Toxins – How Prevalent???

- A neurotoxin known as diazinon, a commonly used insecticide, was found in nearly 1/3 of drinking water during a national water sampling program.
- 9 individuals not in the chemical industry were tested for 210 chemicals and 167 of them were found in at least one of the people with an average number of chemicals found per person was an astounding 91. Most of these chemicals did not exist 20 years ago.

Toxins - Sources

- In the August 2001 issue of **Atmospheric Environment**, researchers reported that levels of dimethyl mercury from landfills “is higher, by a factor of 30 or 40, than concentrations of total mercury in the ambient air. They also reported that the dimethyl mercury concentration was 1,000 times greater than any measurement ever!!!”

Toxins - Sources

- One of the most used cooking surfaces, Teflon, is the cornerstone of a lawsuit in the United States.
- It has been implicated as a causative factor in elevated cholesterol.
- The perfluorochemicals (PFC's) are in Stainmaster, Teflon, Scotchguard, and Gore-Tex, all from DuPont.
- The company did not reveal the known health problems caused by this chemical.
- Elevated LDL may be a marker for toxicity exposure.

Toxins - Sources

- PFC's have been found in 90% of the people tested in the United States.
- It has also been found in similar percentages of people in Korea, China, India and Japan. These were the only countries tested so far.
- 17 of 18 species of animals tested positive for PFC's!

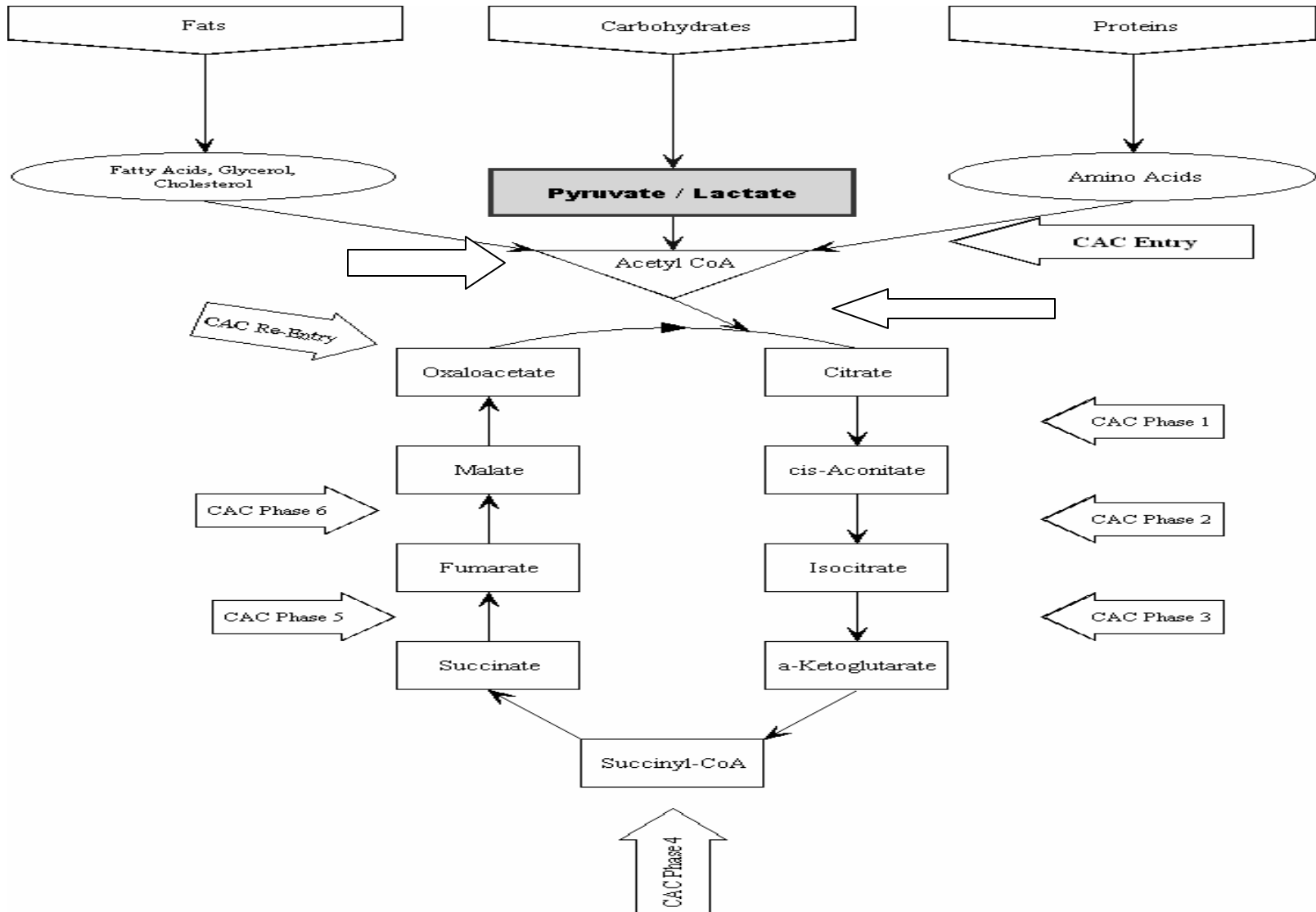
Toxins – Citric Acid Cycle Disruption

- An extreme example:
- Compound 1080 –
“The poison that keeps on killing”
- Fluoroacetate is a natural form of the slightly more toxic sodium fluoroacetate, also known as the notorious rodent poison 'Compound 1080'.
- When ingested and metabolized, fluoroacetate is transformed in cells to fluorocitrate – a strong enzyme inhibitor. Fluorocitric acid blocks the CAC Cycle completely!

Citric Acid Cycle Disruptors

- Compound 1080 is an extreme case, tartaric acid is a more common one.
- It is a common component of many foods and drinks especially wine and grapes.
- It is not a yeast by-product.
- It may interfere with the Citric Acid Cycle at the point where Malate comes in.

Citric Acid Cycle Disruptions



Basic Status Report (High/Low)

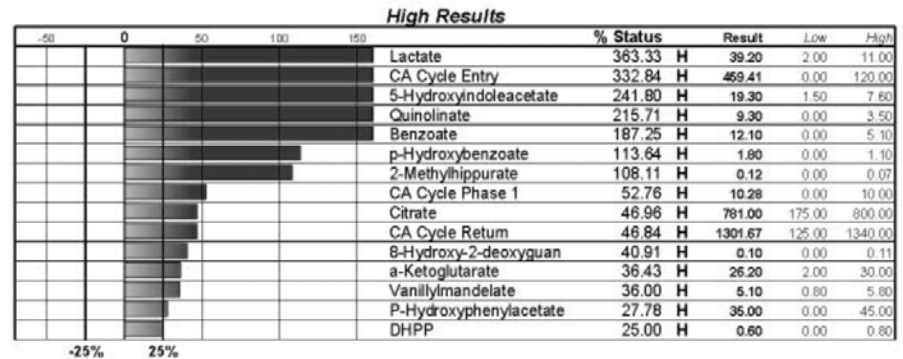
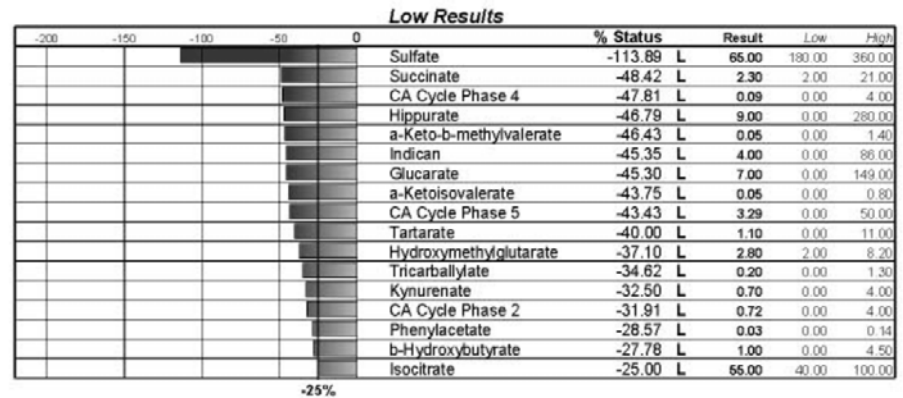
Urine Organic Acid Date: 5/22/2003

Female / Age: 34

The % Status is the weighted deviation of the laboratory result.

Sample of a patient with a citric acid cycle disruption.

The test to determine a CAC cycle problem is a urine organic acid test. Carbon Based is the first and only company to be able to pinpoint the location of the disturbance and help find the potential toxin.



Toxins effecting the Neuroendocrine System

- According to the chemical industry “The major phthalates in commerce today produced by members of the Phthalate Esters Panel do not interfere with estrogen or androgen receptors when tested in laboratory animals.”
- From the book “Our Stolen Future”
- Much of the existing literature on phthalates' toxicological properties focuses on the old approach to toxicology: high level exposure for cancer endpoints, and occupational exposure leading to adult infertility.



Note

Identification of a Toxic Mechanism of the Plasticizers, Phthalic Acid Esters, which are Putative Endocrine Disrupters: Time-dependent Increase in Quinolinic Acid and Its Metabolites in Rats Fed di(2-ethylhexyl)phthalate

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We have reported that the administration of di(2-ethylhexyl)phthalate (DEHP) increased the formations of quinolinic acid (QA) and its lower metabolites on the tryptophan-niacin pathway. To discover the mechanism involved in disruption of the tryptophan-niacin pathway by DEHP, we assessed the daily urinary excretion of QA and its lower metabolites, and enzyme activities on the tryptophan-niacin pathway. Rats were fed with a niacin-free, 20% casein diet or the same diet supplemented with 0.1% DEHP or 0.043% phthalic acid and 0.067% 2-ethylhexanol added for 21 days. Feeding of DEHP increased the urinary excretions of QA and its lower metabolites in a time-dependent manner, and the increase of these excretions reached a peak at 11 days, but feeding of phthalic acid and 2-ethylhexanol had no effect. Feeding of DEHP, however, did not affect any enzyme activity including α -amino- β -carboxymuconate- ϵ -semialdehyde decarboxylase (ACMSD), affecting the formation of QA, on the tryptophan-niacin pathway.

Key words: phthalate ester; di(2-ethylhexyl)phthalate; quinolinic acid; endocrine disrupters; tryptophan metabolism

Phthalate esters (PhE), such as di(2-ethylhexyl)phthalate (DEHP) and its monoester, mono(2-ethylhexyl)phthalate (MEHP), are low-level environment contaminants that can adversely affect rodent testis only at high doses,¹⁾ and chronic feeding of a high concentration of DEHP (1.2%) but not a low concentration (0.6%) to rodents resulted in an increased incidence of liver tumors.²⁾ DEHP has subacute-chronic toxicity mediated by peroxisome proliferator-activated receptors α (PPAR α) in liver, kidney, and testis, but DEHP can also act through PPAR α -independent pathways in mediating renal and testicu-

lar toxicity.³⁾ We have found that the growth of weaning rats fed a niacin-deficient diet was promoted by an administration of di-n-butylphthalate (DBP).⁴⁾ Furthermore, we showed that the conversion of tryptophan to niacin was significantly promoted by feeding a diet containing DBP⁵⁾ or DEHP⁶⁾ even at a low concentration (0.1%). Both plasticizers increased the formation of quinolinic acid (QA) and its lower metabolites on the tryptophan-niacin pathway, suggesting the inhibition of α -amino- β -carboxymuconate- ϵ -semialdehyde decarboxylase (ACMSD) by the PhE or their metabolites. To discover the mechanism of disruption of the tryptophan-niacin pathway by DEHP, we assessed the daily urinary excretions of QA and its lower metabolites, and enzyme activities on the tryptophan-niacin pathway.

Vitamin-free milk casein, sucrose, L-methionine, and Nam were purchased from Wako Pure Chemical Industries (Osaka, Japan). *N*¹-methyl-2-pyridone-5-carboxamide (2-Py) and *N*¹-methyl-4-pyridone-3-carboxamide (4-Py) were synthesized by the methods of Pullman and Colowick⁷⁾ and of Shibata *et al.*,⁸⁾ respectively. The mineral and vitamin mixtures were obtained from Oriental Yeast Kogyo (Tokyo, Japan), all other chemicals used being of the highest purity available from commercial sources.

The animal room was kept at a temperature of around 22°C and at about 60% humidity with a 12-hr light/12-hr dark cycle. Body weight and food intake were measured daily at around 10:00 a.m., and food and water were renewed daily. The care and treatment of the experimental animals conformed to The University of Shiga Prefecture guidelines for the ethical treatment of laboratory animals. Male rats of the Wistar strain (6 weeks old) were obtained from Clea Japan (Tokyo, Japan) and immediately placed

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Abbreviations: PhE, phthalate esters; DEHP, di(2-ethylhexyl)phthalate; MEHP, mono(2-ethylhexyl)phthalate; PPAR α , peroxisome proliferator-activated receptors α ; ACMSD, α -amino- β -carboxymuconate- ϵ -semialdehyde decarboxylase; PhA, phthalic acid; 2-EH, 2-ethylhexanol; DBP, di-n-butylphthalate; NiA, nicotinic acid; Nam, nicotinamide; MNA, *N*¹-methylnicotinamide; 2-Py, *N*¹-methyl-2-pyridone-5-carboxamide; 4-Py, *N*¹-methyl-4-pyridone-3-carboxamide; QA, quinolinic acid; AnA, anthranilic acid; KA, kynurenic acid; XA, xanthurenic acid; 3-HA, 3-hydroxyanthranilic acid; QPRT, quinolinate phosphoribosyltransferase; ACMS, α -amino- β -carboxymuconate- ϵ -semialdehyde

Phthalates increase the formation of quinolinic acid
Quinolate can induce hippocampal and neuronal damage.

Phthalates – Ubiquitous Toxin

- If you see elevated Quinolinolate, suspect phthalate exposure.
- Some time-released medications are made with plasticizers made with phthalates.
- If you see any endocrine system abnormalities, look into solvent and phthalate exposure.

Testing for Phthalates

- Until recently, phthalates could only be tested commercially using blood or fat biopsy.
- Recently, thankfully, U.S. Biotek developed the urine test for phthalates, benzene, styrene, trimethylbenzene, toluene, and xylene along with an urban pollution index.

Testing for Toxins

- As many of you know, the test is simple and requires little specimen preparation.
- The first morning urine is collected, the collection strip is saturated, allowed to air-dry, then placed into a plastic bag filled with desiccant and mailed to the lab.
- No freezing and no waiting for next day air service to pick up the sample.

Testing for Toxins

- Another very valuable calculation and result from US Biotek's lab is the Urban Pollution Index.
- The January 2005 issue of Environmental Health Perspectives and the journal Circulation (Jan 9, 2005) will publish articles on the effect of smog on being a major cause of clogged arteries and coronary heart disease.

Effects of petrochemicals

- Disruption of the Citric Acid Cycle Entry Point
 - Inability to properly utilize carbohydrates to derive energy
 - May cause weight gain or weight loss problems
 - Create a hypoglycemic condition
 - Well documented as endocrine disruptors

One effect of petrochemicals on carbohydrate metabolism

- By depleting the amino acid glycine and stressing the threonine supply in order to detoxify, you may impair the process of gluconeogenesis which in turn can lead to hypoglycemic-like symptoms and impaired insulin responses.
- Those with moderate to severe impairment in their insulin response may show abnormal weight gain due to the overproduction of fat.
- Increasing the availability of glycine is an important first step.
- This toxic response may be part of the explosion of diabetes in the developed and developing world.

Toxins – Safe at any dosage?

- According to a paper (Body Burden) by the Environmental Working Group (www.ewg.org) “A growing body of literature links low dose chemical exposures in animal studies to a broad range of health effects previously unexplored in high dose studies.”

Toxins - Dosage

- Many chemical companies and the government will cite numerous studies where they have determined the “safety” levels of many chemicals below which the effects they have observed no longer appear.
- This level is known as the LD50 – the lethal dosage for 50% of the animals tested.

Toxins - Dosage

- With some chemicals, an effect seen at a high dose is not seen at a low dose and visa versus.
- Perchlorate, a rocket fuel component, causes changes in the brain at .01 – 1 mg/kg per day but not at 30 mg/kg per day according to Argus 1998 and others.

Toxins – Biphasic Dose Response

- We see with perchlorates that an effect seen at a low dose does not appear at a higher dose.
- Research done at Carbon Based has uncovered a possibility that detoxifying too much too soon may cause a negative biphasic dose response because of too *low* of a level of toxins!

Toxins – Biphasic Dose Response

- If we detoxify too quickly we may cause the body to have an inability to deal with this biphasic dose response.
- Homeopathy may provide a way around this due to its ability to deal with such small quantities of toxins.
- We will be putting together a series of studies of in the year 2005 to see if homeopathic remedies can reduce the side effects of overly aggressive detoxification protocols.

Environmental Toxins – A Triphasic Dose Response?

- Some research has suggested that a little toxicity is good for your health.
- This has been done to justify the continued abuse of our environment and is not a valid argument.
- As mentioned previously, many of the toxins in our present day environment did not exist 30 years ago.
- Our bodies have no idea how to deal with many of them, nor do we have any idea what the health ramifications are.

Toxins - Dosage

- According to an article in the recent **Environmental Health Perspectives**, differences in temperature, humidity and atmospheric pressure affect the level at which toxic effects are seen.
- The difference can be up to 15 fold!
- Heat and humidity can greatly increase toxic effects.

Toxicity - Implications

- Laboratory animals undergoing toxicity testing showed decreased body temperatures.
- Researchers believe that the movement towards hypothermia may be a protective device used by the body to slow down the effects of the toxins.

Toxicity - Implications

- A theoretical model I have proposed over the past few years is that the greater number of people being seen today with low basal temperature is our response to an increase in toxic load.
- Lower Metabolism and low temperature = Slower Toxic Effects = More Weight Gain = Slower Weight Loss

Toxicity - Implications

- *In the July 2004 International Journal of Obesity, Dr. Angelo Tremblay of Laval University said the following:*
“Pollution seems to be a new factor affecting the control of thermogenesis in some obese individuals experiencing body-weight loss.”

So what does this have to do with Laboratory Testing?

- Because of the variability of toxicity from individual to individual, atmospheric conditions and accentuated toxicity issues we need to utilize highly sensitive laboratory interpretation methods to determine the best protocol of treatment.
- We at Carbon Based are always researching the best labs for testing.

Accentuated Toxicity

- Arsenic can disrupt the pyruvate and succinate oxidation pathways.
- This inhibition effectively blocks the Krebs cycle, which results in marked depletion of ATP stores.
- Alcohol affects the same cycle as so arsenic toxicity is accentuated by alcohol ingestion by up to 100 fold.

High-Protein Diets to the Rescue?

- Increasing protein intake is helpful in improving the detoxification capabilities of the liver and kidney.
- The protein diet opens a side door of the citric acid cycle by-passing the metabolic blockade on carbohydrate metabolism caused by environmental toxins.
- BUT!!! Long-term ketosis causes the blockade to become harder to breakdown in the long-run.

Problems with too much Protein

- Hyperammonemia is a major problem if the person has inadequate excretion capabilities, e.g. low arginine, ornithine.
- Note also that ammonia is toxic, as it will deplete alpha-ketoglutarate levels, hence depressing CAC activity, resulting in energy depletion.
- Side-effects of hyperammonemia include lethargy, brain fog, seizures, coma and death.
- Testing for ammonia levels in the blood must be done through very careful specimen preparation.
- Here is where a urine organic acid test, with its markers for ammonia build-up comes in handy.

So what to do???

- It is critical to assess the toxic load of the individual through a competent laboratory assessment.
- It is important to continue the follow-up with not only laboratory testing but clinical assessment.

Which tests to run?

- Petrochemicals
 - Urine Organic Acids
 - Environmental Pollutants
- Pesticides
 - Urine Organic Acids (for general exposure)
 - Blood Tests (only for specific exposure not for changes in treatment modalities)
- Heavy Metals
 - Hair Elements
 - RBC Mineral/Toxins
 - Urine/Fecal Metals
 - Apolipoprotein E genetic allele
- General Overview
 - SMAC 25, CBC and Differential with Thyroid Panel

Internet Based Resources

- Environmental Working Group
 - www.ewg.org
- TOXMAP
 - <http://toxmap.aquilent.com/toxmap/index.jsp>
- Environmental Health Perspectives
 - www.ehponline.org/open
- Carbon Based Corporation
 - www.carbonbased.com

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