

Using organic acids to
resolve chief complaints
and improve quality of life in
chronically ill patients

Part IX

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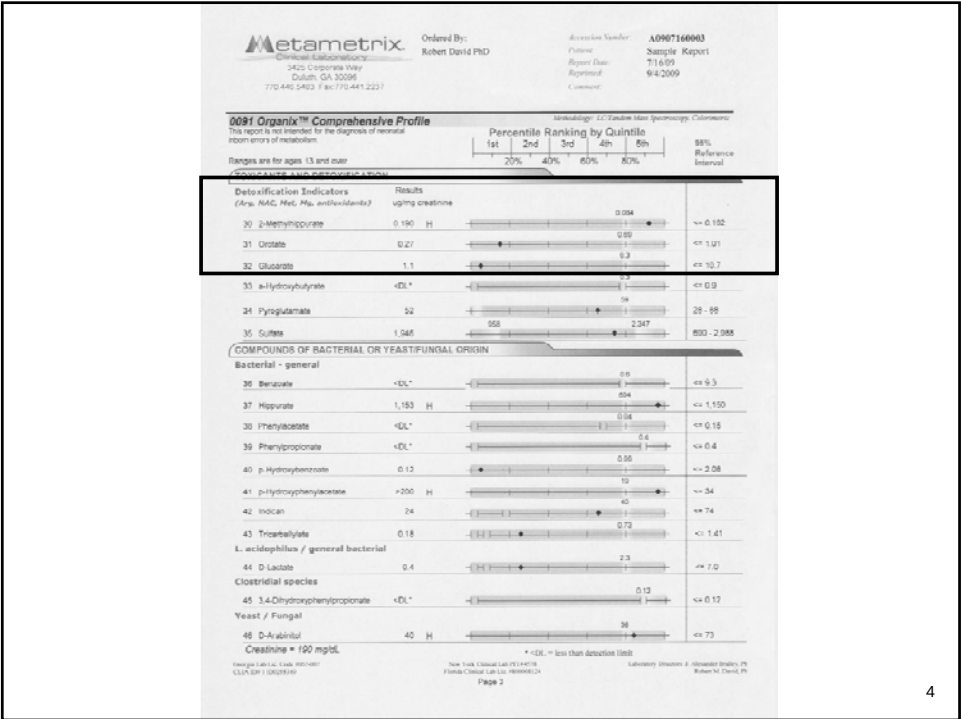
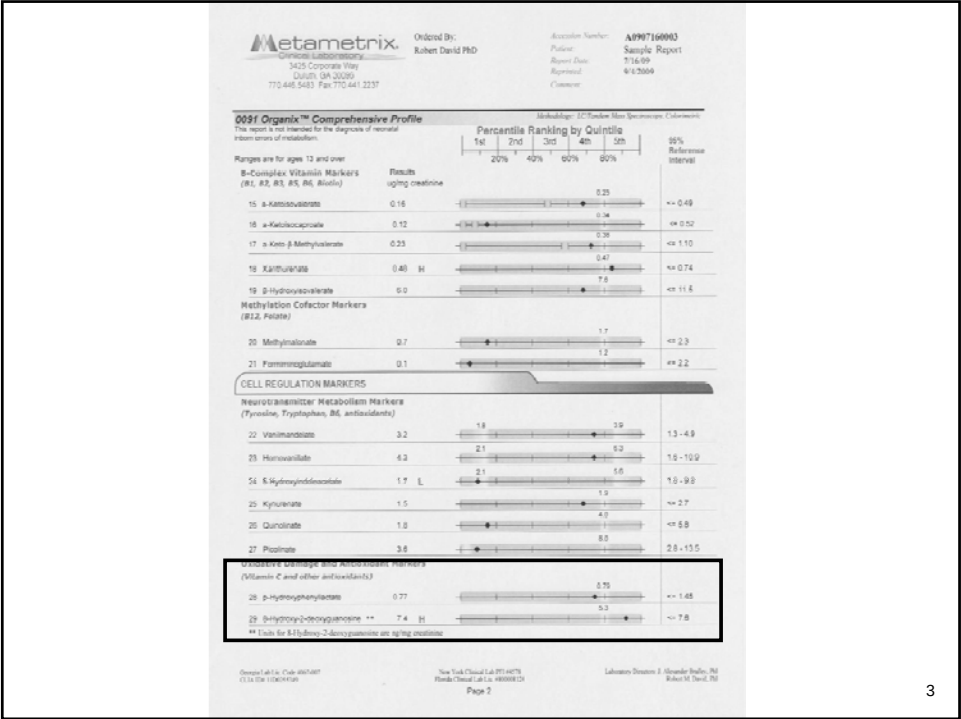
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Oxidative damage and
antioxidant markers

Detoxification markers

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Organic Acids – Part 9
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Organic Acids – Part 9

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Summer of Work Exposes Medical Students to System's Ills • NYTimes.com
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September 9, 2009
Summer of Work Exposes Medical Students to System's Ills
BY STEVEN LEON

SEATTLE — This summer, medical students from the University of Washington took a long look under the hood of the health care system they are about to inherit, and many returned to campus last week with their eyes wide open and their skulls tingling.

Summer of work exposes medical students to system's ills, *The New York Times*, September 9, 2009

The students learned not only to deliver babies and suture wounds, but also to order unnecessary tests as protection against lawsuits, to hector specialists into seeing Medicaid patients, to march patients with prescriptions on Wal-Mart's 3¢ list. And they saw firsthand what Mr. Olguard called "a tidal wave of chronic disease" — diabetes, hypertension, obesity, depression — that left many questioning how much any one physician could really accomplish.

"I often wondered what we were actually doing to help people," Mr. Olguard said.

"...a tidal wave of chronic illness..."

For 21 years, the University of Washington School of Medicine has dispatched its rising second-year students across the Northwest to provide primary care in rural or underserved areas. The monthlong program is elective, but a record number of students took part this year — 117 from a class of 248.

The school has a cooperative agreement to train medical students from Alaska, Idaho, Montana and Wyoming, none of which has a medical college of its own. The summer program is one of several vehicles, along with loan forgiveness enticements, designed to lure students back to their home states to practice in areas with a shortage of primary care doctors.

This year, the students set out as negotiations were intensifying in Washington over wholesale changes to the health care system they will soon be joining. Whether there will be improvements to the system remains to be seen, but few students returned thinking there was time to lose.

http://www.nytimes.com/2009/09/09/health/policy/09medschool.html?_r=1&ft=health&ft=... 9/9/2009

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Baracos VE. Overview on metabolic adaptation to stress, pp. 1-13.

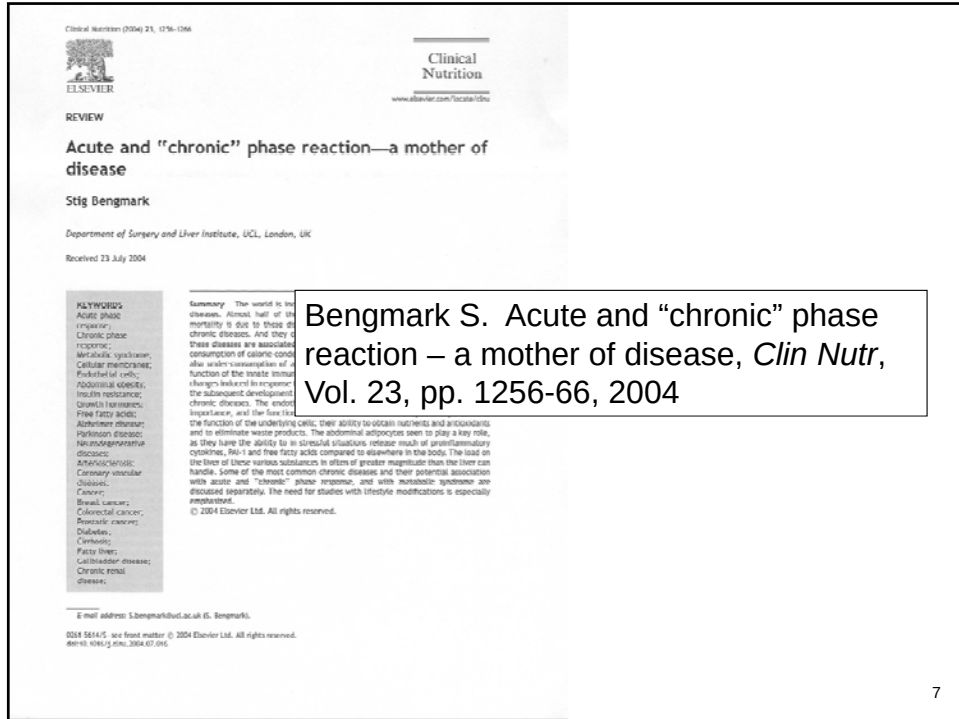
"An understanding of the nature of stress is fundamental to the rational design of nutrient mixtures to feed patients whose homeostasis has been altered by one or more stressors."

"All stresses may be presumed to be associated with characteristic modifications in the metabolism of lipids, carbohydrates, amino acids, and micronutrients."


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Considerations for the Catabolic Patient

Signs & Symptoms	Consider	Treatment Plan	Monitor	Supplementation
Signs & Symptoms: - Feeling "lousy" - Fatigue - Cravings - Depression/anxiety - Poor quality sleep - Poor digestion/absorption/leaky gut - Chronic pain/infection	Optimize pH	Optimize fluid and electrolyte balance	Morning urinary pH -pH paper	Potassium bicarbonate -K Alkaline (Moss) Magnesium -Magnesium Glycinate (Vital Nutrients)
Clinical Findings: - High % body fat - Low bone density - High fasting insulin - Heavy metal burden - Calcium to phosphorus ratio 3:1 - High normal globulin - Cholesterol (220-280) - High LDL, low HDL - High triglycerides - Low normal serum potassium, high normal serum sodium - High normal BUN with normal creatinine - Low urinary sulfate - Genomic variations	Optimize muscle mass (reduce sarcopenia) and amino acid levels	Pay special attention to protein and amino acids	Body composition -Bioelectric impedance scale Grip strength: -dynamometer	Amino acids -Cusano Amino Base (Metabolic Maint.) Protein powders/bars -UltraLam products (Biogenesis) -Paleo products (DFH)
	Reducing inflammation	Reduce inflammation Address food allergies	Inflammatory biomarkers: -ILS-CRP -Fibrinogen levels -WBC -Differential	Anti-inflammatory agents -Inflammix (Olympia) -E3a Line (Protocol) -Pain Guard (Perque) Fish Oils -Ultra Pure Fish oil (Vital Nutrients) Food allergy blends -AllerGymes (DFH)
	Improving insulin sensitivity	Watch carbohydrate/protein ratio	Fasting glucose Fasting insulin Cravings	Metabolic Synergy (DFH)
	Optimize dietary carbohydrate/protein ratios	Replete protein deficiencies and reduce carbohydrate intake along with improvements in dietary quality	Diet diary Optimal protein intake -1.0 -1.2 g/kg body weight	Protein powders/bars -Paleo products (DFH) -UltraLam (Biogenesis)
	Optimize GI function	Dietary changes, supplementation of digestive aids	Patient signs and symptoms	Betaine HCl (Vital Nutrients) DigestCymex (DFH) Intestinal Repair Complex (Biogenesis)
Optimize micronutrient deficiencies/imbalances	Supplementation of multis Possible emphasis on vitamin D, iodine, and zinc	Serum 25 OH vitamin D Fatigue/serum thyroid indicators Zinc taste test	Multi-Nutrients (Vital Nutr) Vitamin D (Vital Nutr) Isole (Moss) Zinc Supreme (DFH)	

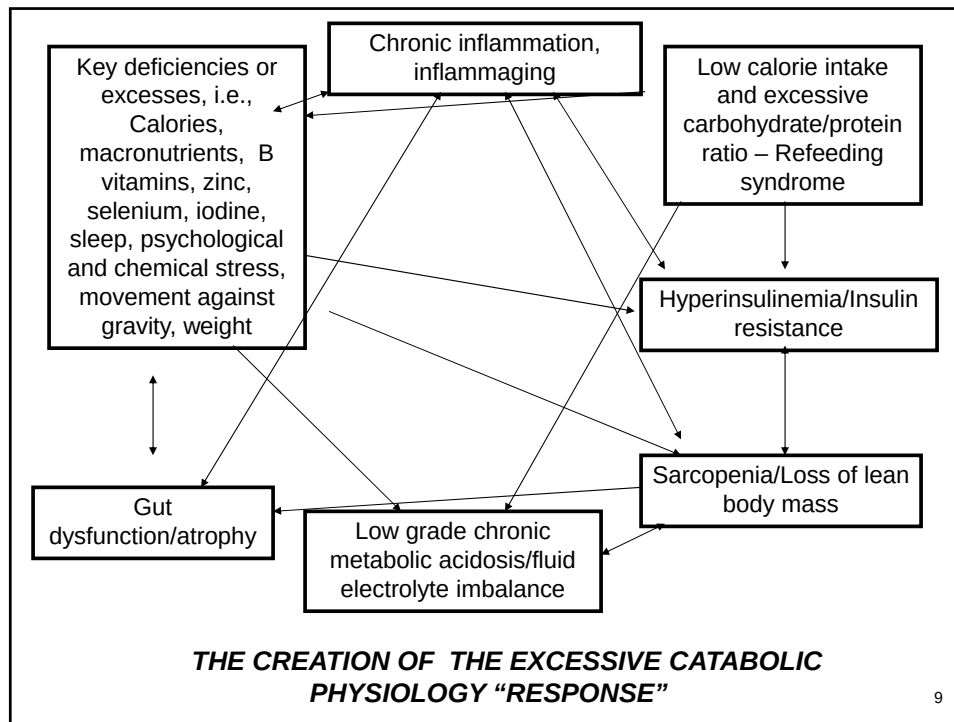
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Organic Acids – Part 9

Dr. Jeff Moss



Invited Review

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Biological Mechanism of Antidepressant Effect of Omega-3 Fatty Acids: How Does Fish Oil Act as a ‘Mind-Body Interface’?

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Key Words:
Major depressive disorder · Docosahexaenoic acid · Arachidonic acid · Prostaglandins · Inflammation · Lipid · Phospholipase A2 · Cytocytogenesis

Abstract
The unsatisfactory results of monoamine-based antidepressant therapy and the high occurrence of somatic symptoms and physical illness in patients with depression imply that the serotonin hypothesis is insufficient to approach the etiology of depression. Depressive disorders with somatic presentation are the most common form of depression. Somatization, the bodily symptoms without organic explanation, is similar to cytokine-induced sickness behavior. Based on recent evidence, omega-3 polyunsaturated fatty acids (n-3 PUFA), or n-3 fatty acids are enlightening a promising path to discover the unshared of depression, sickness behavior and to link the connection of mind and body. The PUFAs are classified into n-3 (or omega-3) and n-6 (or omega-6) groups. Eicosapentaenoic acid and docosahexaenoic acid, the major bioactive components of n-3 PUFA, are not efficiently synthesized in humans and should therefore be obtained directly from the diet, particularly by consuming fish. Docosahexaenoic acid deficiency is associated with dysfunctions of neuronal membrane stability and transmission, prostaglandin E₂ synthesis, which might be linked to the somatic manifestations and physical comorbidity in depression. The role of n-3 PUFA in immunity and mood regulation supports the promising hypothesis of psychoneuroimmunology of depression and provides an excellent interface between ‘mind’ and ‘body’. This review is to provide an overview of the evidence about the role of n-3 PUFA in depression and its common comorbid physical conditions and to propose mechanisms by which they may modulate molecular and cellular functions.

Introduction
Major depressive disorder (MDD) is a serious psychiatric illness with a high lifetime prevalence rate [1]. However, the current treatment for this high burden disease is not satisfactory. Less than 50% of patients achieve full remission with optimized medication treatment [2] despite that more than 10 antidepressants with mechanisms related to serotonin, norepinephrine and/or dopamine

Su KP. Biological mechanism of antidepressant effect of omega-3 fatty acids: How does fish oil act as a ‘mind-body interface’? *Neurosignals*, Vol. 17, pp. 144-152, 2009

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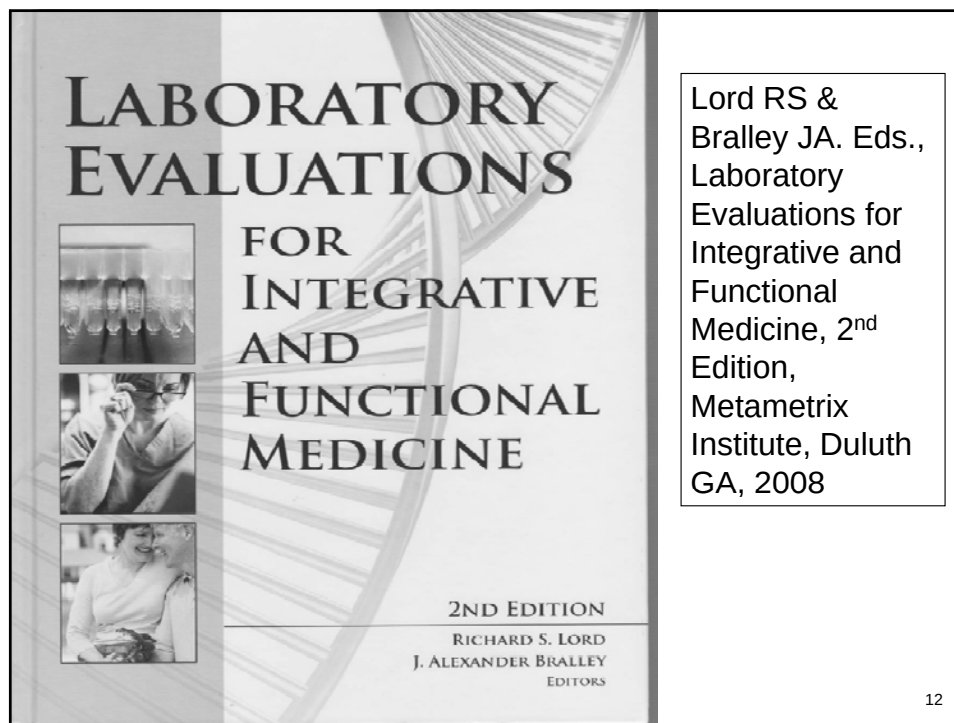
Table 1. Overlapping of symptoms of acute sickness behaviour associated with IFN- α therapy and the somatic symptoms in MDD

Symptoms	Prevalence in IFN- α therapy ^a , %	Prevalence in MDD ^b , %
Fatigue/asthenia	39-90	73
Headache	27-67	33 ^e
Gastrointestinal symptoms	50 ^c , 1	34-47 ^f
Psychomotor slowing	40 ^c	59-65 ^f
Insomnia	20-39 ^d	63
Irritability	35 ^d	50
Arthralgia	9-36	31 ^e
Musculoskeletal pain	26-32	62-80 ^g , 2
Abdominal pain	15-20	21 ^c
Anorexia	13-19	40
Anxiety	13-18 ^d	57
Poor concentration	14 ^d	51

^a [46], unless otherwise specified; ^b [99], unless otherwise specified; ^c [100]; ^d [101]; ^e [102]; ^f [103]; ^g [104].

¹ Nausea, vomiting, bowel problems.² Result from depressed inpatient population.

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Oxidative damage and antioxidant markers

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p-Hydroxyphenyllactate

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“Individuals with elevated p-hydroxyphenyllactic acid, a carcinogenic tyrosine metabolite, tend to have decreased ascorbic acid (vitamin C) in liver, adrenal glands and blood.”

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- “The methyl ester methyl-p-hydroxyphenyllactate (MeHPLA) is an important cell growth-inhibiting agent.”
- “Tumor cells contain esterase activities that hydrolyze the compound to the free acid HPLA.”
- “Thus, the effects of elevated HPLA may be due to depletion of MeHPLA.”

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- “...HPLA is an important regulator of normal and malignant cell growth, and it may mediate the cancer-promoting effects of estrogen.”
- “MeHPLA is deficient in a variety of rat and mouse mammary tumors and human breast cancer preparations, and this deficiency correlates with the loss of regulatory control.”

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- “Elevated levels of HPLA result in a dramatic decrease in ascorbic acid concentration in the liver, adrenal glands, and blood.”
- “High doses of ascorbic acid (100 mg/kg body weight daily) were shown to arrest or significantly inhibit the excretion of HPLA in patients with hemoblastoses and nephroblastoma.”

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***“Tissue saturating levels of vitamin C
should be considered in patients
with elevated HPLA.”***

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Consider the vitamin C flush

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8-Hydroxy-2-deoxyguanosine (8-OHdG)

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- “When inflammatory markers like quinolinate or metabolic enhancers like p-hydroxyphenyllactate are elevated, there is a need to know the overall impact of increased production of reactive oxygen species (ROS).”
- ***“8-Hydroxy-2'-deoxyguanosine (8-OHdG) is a product of oxidative damage to DNA.”***

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- “8-OHdG is formed in a pro-mutagenic DNA lesion due to reaction of oxygen radicals with guanosine groups in DNA.”
- “It is recognized as a useful marker in estimating DNA damage induced by oxidative stress.”
- “In studies published in 2006, human conditions where oxygen radical damage has been assessed by measuring urinary 8-OHdG include ultraviolet protection of skin, bladder cancers, hemodialysis, cardiomyopathy, insomnia, environmental toxin exposures, diabetes, effects of cigarette smoke, arsenic poisoning, and depression.”

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- “Formation of 8-OHdG is sufficiently sensitive to reveal even mild chronic effects of ROS.”
- “8-OHdG levels rise with age in adults with mild hypercholesterolemia and/or mild hypertension.”
- “Lower levels of antioxidants may predispose to oxidative stress, which is manifested by higher levels of 8-OHdG.”
- “Levels of 8-OHdG were significantly higher in atherosclerotic patients, and vitamin C levels were significantly lower.”

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- “Moderate alcohol consumption seems to have the overall effect of reducing DNA damage in some individuals as shown by the decrease in 8-OHdG levels.”
- “Diabetics tend to have higher urinary 8-OHdG excretion than healthy controls...”

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Review Article

Urinary 8-oxo-7,8-dihydro-2'-deoxyguanosine as a biomarker in type 2 diabetes

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Abstract
Lifestyle development in type 2 diabetes patients is discussed, followed by an evaluation of the potential of urinary 8-oxodG as a clinical biomarker in type 2 diabetes.

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1. Introduction

“The available evidence indicates that compared with healthy subjects, type 2 diabetes patients have increased urinary 8-oxodG excretion, and type 2 diabetes patients with complications have increased 8-oxodG excretion compared with those without complications.”

2. Urinary 8-oxodG excretion seems to be closely associated with glycemic control in patients, and various kinds of intervention that improve outcome in patients also reduce 8-oxodG excretion.”

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Detoxification markers

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2-Methylhipurate

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- “2-Methylhippurate is a by-product of the detoxification of the common solvent xylene, which is oxidized via hepatic P450 oxidase enzymes to 2-methylbenzoate.”
- “This organic acid is then conjugated with glycine to form the peptide product, 2-methylhippurate.”

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- “Xylene is a very common solvent found in paint thinners and building products, fuel and exhaust fumes, and industrial degreasers and solvents.”
- “Spray-painting workers show elevated methylhippurate, indicating recent exposure to xylene.”
- “Both spot urine specimens collected at the end of the work day and 24-hour urine specimens showed high correlation with time-averaged paint-worker exposures.”

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Orotate

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- “When there is insufficient capacity for detoxifying ammonia via the urea cycle, carbamoyl phosphate leaves mitochondria and stimulates the synthesis of orotic acid (orotate).”
- “Increased orotate production is a sensitive indicator of arginine deficiency.”

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- “In addition, orotate requires magnesium for its metabolism.”
- “Although a normal level in a urinary organic acid panel may not necessarily indicate magnesium sufficiency, high levels should alert one to a significant possibility of intracellular magnesium insufficiency, especially patients with kidney failure.”

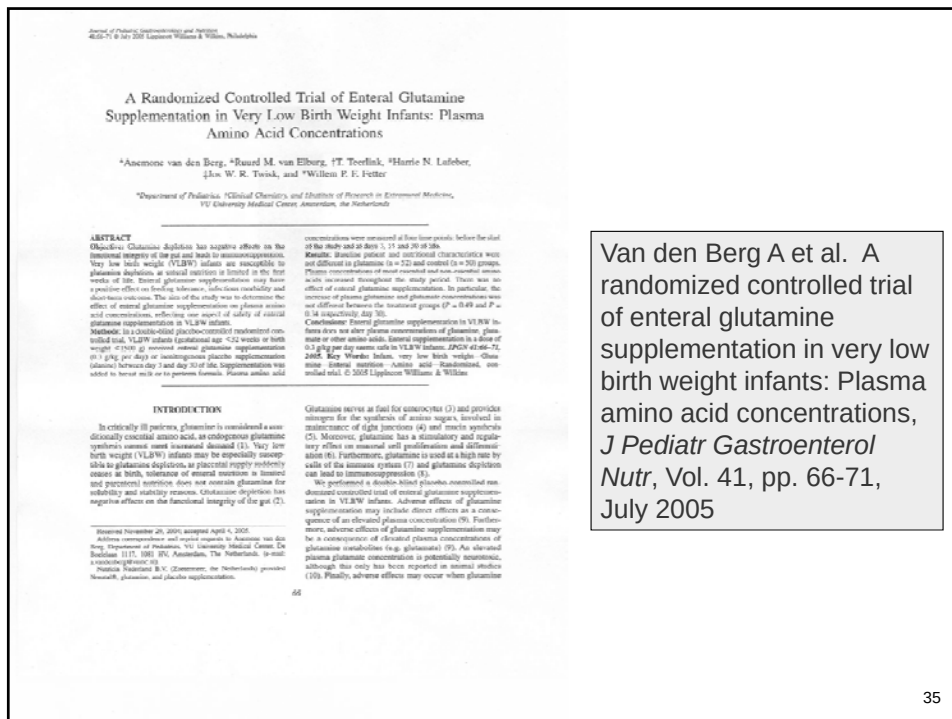
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- “Oral glutamine supplementation at levels about 10g/d in adults can result in elevation of urinary orotate due to increased ammonia generated from hepatic oxidative deamination reactions.”

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- **“Enteral glutamine supplementation in VLBW infants does not alter plasma concentrations of glutamine, glutamate or other amino acids. Enteral supplementation in a dose of 0.3 g/kg per day seems safe in VLBW infants.”**

- “In the studies on enteral glutamine supplementation, including our study, plasma glutamine concentrations did not change, whereas in three of four studies on parenteral supplementation, plasma glutamine concentrations were increased in the glutamine-supplemented group.”
- “The difference can be attributed to the fact that enterally administered glutamine is almost entirely metabolized by the gut and does not reach the systemic circulation.”

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- “We found that enteral glutamine supplementation did not alter plasma concentrations of glutamate, a glutamine metabolite that is potentially neurotoxic.”
- “This is in line with previous studies on enteral and parenteral glutamine supplementation in VLBW infants. As a consequence, neurotoxicity caused by an elevated plasma glutamate concentration in VLBW infants receiving glutamine supplementation seems unlikely.”

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Glucarate

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- “Glucaric acid (glucarate) is a by-product of the predominant liver hepatic phase I detoxification reactions involving cytochrome P450 oxidation of glucose to glucuronic acid, the substrate for phase II conjugation reactions.”
- “Measurement of glucarate in urine serves as a specific biomarker for glucuronidation.”
- “Elevations in urinary glucarate specifically suggest exposure to pesticides, herbicides, fungicides, petrochemicals, alcohol, and drugs.”

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***“...glucarate excretion is an indicator
of overall hepatic detoxification
demand.”***

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TABLE 6.10— CLASSES OF COMPOUNDS CLEARED BY GLUCURONIDATION⁴⁰¹

Class	Examples
Polycyclic aromatic hydrocarbons	Benzo(a)pyrene, benzantracene, naphthalene
Various nitrosamines	Cured meats, tobacco products, rubber products, pesticides
Fungal toxins	Aflatoxin
Steroid hormones	Estrogen, testosterone
Heterocyclic amines	Well-done, fried, or barbequed meats
Pharmaceutical drugs	Aspirin, lorazepam, digoxin, morphine
Vitamins	Vitamins A, D, E and K

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- “Urinary glucarate is influenced by oral glucarate supplementation (usually as calcium-D-glucarate), because most absorbed glucarate is cleared in the urine.”

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Thank you!!

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