

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

## Part VI

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1

The New York Times

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September 9, 2009

## Summer of Work Exposes Medical Students to System's Ills

BY KEVIN BACH

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 idealism tempered.

Jacob R.  
more the  
eschemed  
Olsgaard  
treatment

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 match patients with prescriptions on Wal-Mart's \$4 list. And they saw firsthand what Mr. Olsgaard 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. Ohgaard said.

Not sur  
devalue

"You had  
reimburs  
expenses

For its part, 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 216.

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 givers.

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 little to fix.

[http://www.nytimes.com/2009/09/09/health/policy/09medschool.html?\\_r=1&th=&mc=th&...](http://www.nytimes.com/2009/09/09/health/policy/09medschool.html?_r=1&th=&mc=th&...) 9/9/2009

2

## Using the Organic Acids Test – Part 6

Dr. Jeff Moss



**Nestlé Nutrition Workshop Series  
Clinical & Performance Program, Vol. 8**

### **Nutrition and Critical Care**

**Luc Cynober  
Frederick A. Moore**



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.”

3

Clinical Nutrition (2004) 23, 1256-1266



REVIEW

### **Acute and “chronic” phase reaction—a mother of disease**

**Stig Bengmark**

Department of Surgery and Liver Institute, UCL, London, UK

Received 23 July 2004

**KEYWORDS**  
Acute phase response;  
Chronic phase response;  
Metabolic syndrome;  
Cellular membranes;  
Endothelial cells;  
Abdominal obesity;  
Insulin resistance;  
Growth hormones;  
Free fatty acids;  
Alzheimer disease;  
Parkinson disease;  
Neurodegenerative disease;  
Atherosclerosis;  
Coronary-vascular disease;  
Cancer;  
Breast cancer;  
Colorectal cancer;  
Prostatic cancer;  
Diabetes;  
Crimson;  
Fatty liver;  
Gallbladder disease;  
Chronic renal disease;

**Summary** The world is in diseases. Almost half of the mortality is due to these chronic diseases. And they are these diseases are associated consumption of calorie and also under-consumption of a function of the innate immune changes induced in response the subsequent development chronic diseases. The end of importance, and the function of the underlying cells; their ability to obtain nutrients and antioxidants and to eliminate waste products. The abdominal adipocytes seem to play a key role, as they have the ability to in stressful situations release much of proinflammatory cytokines, PPAR- $\alpha$  and free fatty acids compared to elsewhere in the body. The load on the liver of these various substances in often of greater magnitude than the liver can handle. Some of the most common chronic diseases and their potential association with acute and “chronic” phase responses and metabolic syndrome are discussed separately. The need for studies with lifestyle modifications is especially emphasized.  
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**Bengmark S. Acute and “chronic” phase reaction – a mother of disease, *Clin Nutr*, Vol. 23, pp. 1256-66, 2004**

4

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Invited Review

Neurosignals 2009;17:144-152  
DOI: 10.1159/000188102

Received: April 26, 2008  
Accepted after revision: June 1, 2008  
Published online: February 4, 2009

**NeuroSignals**

Neuroscience  
Neurobiology  
Neuroendocrinology  
Neuroimmunology  
Neuropsychiatry  
Neuropsychology  
Neurotoxicology

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

Kuan-Pin Su

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Key Words

Major depressive disorder • Depression • Docosahexaenoic acid • Arachidonic acid • Prostaglandins • Thromboxanes • Lipoxygenase • Cyclo-oxygenase

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 aetiology 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 behaviour. Based on recent evidence, omega-3 polyunsaturated fatty acids (n-3 PUFAs, or ω-3 fatty acids) are enlightening a promising path to discover the unsolved of depression, sickness behaviour 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 PUFAs, 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 dysfunction of neuronal membrane stability and transmission

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 40 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

prostaglandin  $E_2$  synthesis, which might be linked to the somatic manifestations and physical comorbidity in depression. The role of n-3 PUFAs in immunity and mood function 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 PUFAs in depression and its common comorbid physical conditions and to propose mechanisms by which they may modulate molecular and cellular functions.

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6

# Using the Organic Acids Test – Part 6

## Dr. Jeff Moss

**Table 1.** Overlapping of symptoms of acute sickness behaviour associated with IFN- $\alpha$  therapy and the somatic symptoms in MDD

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

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

<sup>1</sup> Nausea, vomiting, bowel problems.<sup>2</sup> Result from depressed inpatient population.

7

Free Radical Biology & Medicine 50 (2011) 1215–1221

Contents lists available at ScienceDirect

Free Radical Biology & Medicine

journal homepage: www.elsevier.com/locate/freeadbiomed

Original Contribution

**Mitochondrial complex I impairment in leukocytes from type 2 diabetic patients**

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**ARTICLE INFO**

Article history:  
Received 19 August 2010  
Received in revised form 11 January 2011  
Accepted 13 January 2011  
Available online 22 January 2011

**Keywords:**  
Antioxidant  
Complex I  
Diabetes  
Mitochondria  
Oxidative stress  
Reactive oxygen species  
Free radicals

**Abstract**  
Mitochondrial function in diabetic patients, evidenced by a decrease in mitochondrial O<sub>2</sub> consumption, an increase in ROS production, decreased GSH/GSSG ratio, a drop in CBI levels, and an undermining of the mitochondrial membrane potential. Furthermore, an impairment of mitochondrial complex I was detected. This study supports the hypothesis of an association of type 2 diabetes and the rate of impaired mitochondrial function. We also propose that one of the targets of oxidative stress responsible for diabetes is mitochondrial complex I.

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**“The study population consisted of 182 diabetic patients and 50 body composition- and age-matched controls. We assessed anthropometric and metabolic parameters and mitochondrial function by evaluating mitochondrial oxygen (O<sub>2</sub>) consumption, reactive oxygen species (ROS) production, glutathione (GSH) levels, GSH/GSSG ratio, mitochondrial membrane potential, and mitochondrial complex I activity in polymorphonuclear cells from diabetes type 2 patients.”**

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These authors contributed equally to this work.

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doi:10.1016/j.freeradbiomed.2011.01.019

- “The pathogenesis of mitochondrial dysfunction in obesity or diabetes-related disease is multifactorial and includes mitochondrial uncoupling and oxidative damage.”
- “There is considerable evidence that a chronic, low-grade inflammatory response is ongoing in and actually precedes type 2 diabetes and related syndromes, and this inflammation may be due, in part, to the effects of hyperglycemia or other metabolic abnormalities on white blood cells.”

9

- “The results of this study demonstrate, as expected, an increase in waist circumference and fasting levels of triglycerides, IL-6, TNF- $\alpha$ , homocysteine, US-CRP, HbA1C, glucose, [and] insulin...in type 2 diabetic patients.”
- “Furthermore, we have demonstrated that grade of mitochondrial function impairment in PMNs that takes place during type 2 diabetes.”
- “This effect was evident in the decrease in mitochondrial O<sub>2</sub> consumption, the increase in ROS production, the enhanced TNF- $\alpha$  levels and the decrease in GSH/GSSG ratio related to oxidative stress, the drop in GSH levels, and the diminished mitochondrial membrane potential that we observed in these patients.”

10

- “Recently, it has been reported that insulin signaling per se also regulates mitochondrial O<sub>2</sub> consumption and ATP synthesis rates.”
- “...our study also supports previous observations of mitochondrial dysfunction as a complication of hyperglycemia- and hyperlipidemia-induced ROS production in skeletal muscle from mice.”

11

- “...the increase in the production of ROS, decrease in GSH levels and GSH/GSSG ratio, and reduction in the mitochondrial membrane potential-all characteristics of diabetes-point toward a dysfunction within the respiratory chain that compromises the functioning of the mitochondrion as a source of energy.”

12

- “ROS are highly toxic to various sites of the mitochondrial respiratory chain, and inhibition of complex I would seem to be the most likely consequence of the toxicity.”
- “Furthermore, a reduction of complex enzyme activity leads to an accumulation of electrons in the initial part of the transport chain (complex I and coenzyme Q), which facilitates the direct transfer of electrons to molecular O<sub>2</sub>. This ultimately results in the generation of ROS.”

13

***“These data support the hypothesis that mitochondrial activity, and concretely mitochondrial complex I, may represent an important new pharmacological target for the prevention and treatment of type 2 diabetes.”***

14

# Organic Acids

## Neurotransmitter Metabolism Markers

15

### Considerations for the Catabolic Patient

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

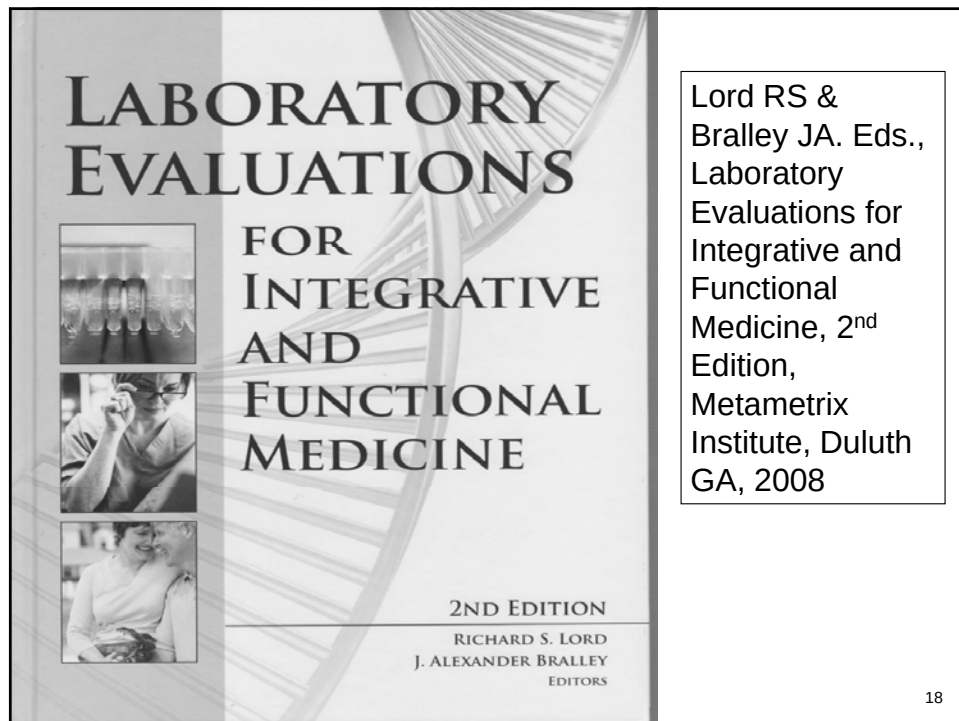
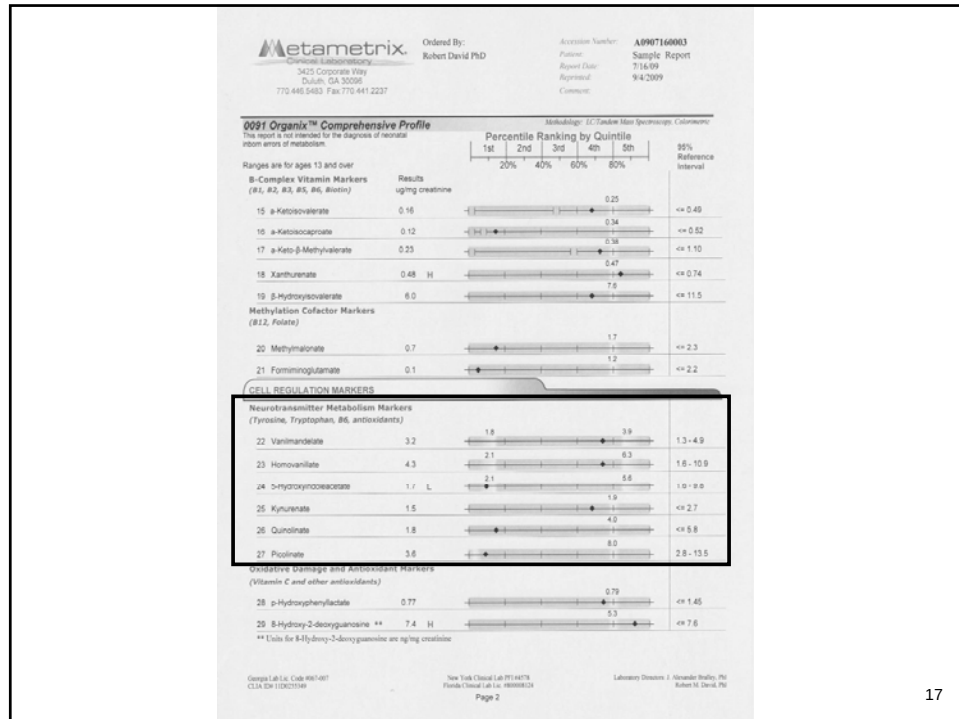
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## Using the Organic Acids Test – Part 6

### Dr. Jeff Moss



**Controversy:**

**Urinary neurotransmitters  
vs.  
urinary neurotransmitter  
metabolites**

19

- “Accurately determining the central nervous system (CNS) level of neurotransmitters has proven difficult.”
- “This may be in part because neurotransmitters are rapidly formed and degraded in nervous tissue, leaving neurotransmitter concentrations in other tissues largely unrelated to CNS levels.”
- “An exception is the reflection of CNS levels of serotonin by platelet or platelet-rich plasma serotonin concentrations and corresponding associations with serotonin-related pathologies.”

20

- ***“Even when 24-hour collection specimens are used, urinary serotonin is found to vary widely among healthy males under clinically controlled conditions.”***

21

- “Regarding dopamine, even in the extreme chronic elevation conditions of neuroblastoma, direct urinary dopamine to creatinine ratios were far less revealing than the dopamine catabolite vanilmandelic acid.”
- “In a retrospective study of 5,933 adults and 467 children conducted over a 57-month period, high 24-hour urinary dopamine levels were found in less than 3% of adults, and those instances were associated with overcollection, drug effects, and neural crest tumors.”

22

- ***“...studies specifically seeking evidence of dysregulation of dopaminergic activity in the brain have failed to find any relationship with urinary dopamine levels.”***
- “Therefore, whatever clinical utility may be claimed for measurement of urinary neurotransmitter concentrations should not be associated with any effects related to actual levels in brain or spinal cord neurons.”

23

Catecholamines:

Vanilmandelate (VMA)

Homovanillate (HVA)

24

- “Vanilmandelate, also known as vanilmandelic or vanillyl-mandelic acid (VMA), is the main urinary metabolite of the catecholamines, epinephrine, and norepinephrine.”
- “Homovanillate (HVA) is the main metabolite of dopamine that appears in urine.”
- “In controlled laboratory animal experiments, low urinary levels of VMA and HVA have been associated with low CNS levels of these neurotransmitters.”

25

- “Low levels of these neurotransmitters are associated with symptoms that include depression, sleep disturbances, anxiety and fatigue.”
- “Because these neurotransmitters are products of the amino acid tyrosine, treatments aimed at improving protein digestion and supplementation with tyrosine may normalize CNS levels.”

26

- “Elevated levels of VMA and HVA signal an increased rate of synthesis and degradation in normal tissue or abnormal production by tumor tissue.”
- “In absence of such disease processes, increased catecholamine synthesis results from the synergism of pituitary adrenocorticotrophic hormone (ACTH) and adrenal cortisol.”

27

## The Stress Response: An Expanded Definition

“The stress response is characterized by a stimulation of the sympathetic nervous system and increased secretion of both epinephrine from the adrenal medulla and glucocorticoids from the adrenal cortex. All these stimuli can be expected to reduce insulin sensitivity.”

Seematter G et al, Relationship between stress, inflammation and metabolism, Curr Opin Clin Nutr Metab Care, Vol. 7, pp. 169-173, 2004

28

## The Stress Response: An Expanded Definition

“Mental stress significantly enhances plasma catecholamines and cortisol concentrations, but does not acutely impair insulin sensitivity. It can, however, be postulated that repeated mental stress may lead to chronic alterations in cortisol and catecholamine concentrations, and to insulin resistance.”

Seematter G et al, Relationship between stress, inflammation and metabolism, Curr Opin Clin Nutr Metab Care, Vol. 7, pp. 169-173, 2004

29

## The Stress Response: An Expanded Definition

“For several decades, on the basis of experiments performed on rats, it had been thought that circulating epinephrine acted directly on the pituitary to control the release of ACTH. In this formulation the first step in the adrenal ‘stress response’ was thought to be the liberation of epinephrine; this in turn released ACTH, leading to hypersecretion by the adrenal cortex.”

Wurtman RJ. Stress and the adrenocortical control of epinephrine synthesis, Metabolism, Vol. 51, No. 6, Suppl 1, pp. 11-14, 2002.

30

## The Stress Response: An Expanded Definition

“However, subsequent experiments on humans failed to demonstrate any consistent effect of circulating epinephrine on ACTH secretion. Hence, it is no longer believed that epinephrine controls glucocorticoid secretion. Rather, the converse is true; glucocorticoids control epinephrine synthesis, and thereby affect its secretion.”

Wurtman RJ. Stress and the adrenocortical control of epinephrine synthesis, *Metabolism*, Vol. 51, No. 6, Suppl 1, pp. 11-14, 2002.

31

## The Stress Response: An Expanded Definition

“A common mechanism links the secretion of these hormones, even though the adrenal medulla and cortex have different embryologic origins and biochemical properties and very different mechanisms controlling their activities...”

Wurtman RJ. Stress and the adrenocortical control of epinephrine synthesis, *Metabolism*, Vol. 51, No. 6, Suppl 1, pp. 11-14, 2002.

32

## The Stress Response: An Expanded Definition

“This mechanism is made possible by an intra-adrenal portal vascular system, which provides the medulla with uniquely high concentrations of glucocorticoids. These high concentrations are needed to induce the medullary enzyme, phenylethanolamine-N-methyltransferase (PNMT), which controls the synthesis of epinephrine from norepinephrine.”

Wurtman RJ. Stress and the adrenocortical control of epinephrine synthesis, *Metabolism*, Vol. 51, No. 6, Suppl 1, pp. 11-14, 2002.

33

## The Stress Response: An Expanded Definition

“...prolonged chronic stress can enhance epinephrine synthesis and secretion within the adrenal, the brain, and both organs.”

Wurtman RJ. Stress and the adrenocortical control of epinephrine synthesis, *Metabolism*, Vol. 51, No. 6, Suppl 1, pp. 11-14, 2002.

34

## The Stress Response: An Expanded Definition

“Our hypothesis suggests that high levels of glucocorticoids should, if anything, reverse the actions of catecholamines.”

Munck A et al, Physiological functions of glucocorticoids in stress and their relation to pharmacological actions, Endocr Rev, Vol. 5, No. 1, pp. 25-44, 1984.

35

## Sympathetic Compensation

“When stress is prolonged the repeated cortisol peaks during occasions of stress cause elevated cortisol secretion, which eventually is followed by a decreased ‘winding down’ of the stress-induced cortisol peaks, followed by a decreased, rigid cortisol secretion, a ‘burn-out,’ where low morning cortisols are a hallmark.”

Bjorntorp P & Rosmond R. The metabolic syndrome - a neuroendocrine disorder? Br J Nutr, Vol. 83, Suppl 1, pp. S49-57, March 2000.

36

## Sympathetic Compensation

“At this stage sympathetic nervous system activity is increasing, which might be considered as a compensatory phenomenon to maintain homeostasis or allostasis in various somatic systems.”

Bjorntorp P & Rosmond R. The metabolic syndrome - a neuroendocrine disorder? Br J Nutr, Vol. 83, Suppl 1, pp. S49-57, March 2000.

37

## Sympathetic Compensation

“Patients with posttraumatic stress disorder (PTSD) have decreased cortisol and increased catecholamine secretion.”

Baker DG et al, Plasma and cerebrospinal fluid interleukin-6 concentrations in posttraumatic stress disorder (Abstract), Neuroimmunomodulation, Vol. 9, No. 4, pp. 209-17, 2001.

38

## Sympathetic Compensation

“Exaggerated norepinephrine responses and heart rate increases, as well as delayed ACTH release, were observed among female fibromyalgia patients compared with age-matched female controls. Delayed ACTH release after IL-6 administration in fibromyalgia is consistent with a defect in hypothalamic CRH neuronal function.”

Torpy DJ et al, Responses of the sympathetic nervous system and the hypothalamic-pituitary-adrenal axis to interleukin-6: a pilot study in fibromyalgia (Abstract), Arthritis Rheum, Vol. 43, No. 4, pp. 872-80, April 2000.

39

## The Damaging Power of “Uncontrollable” Stress

CHROUSOS AND GOLD

1843

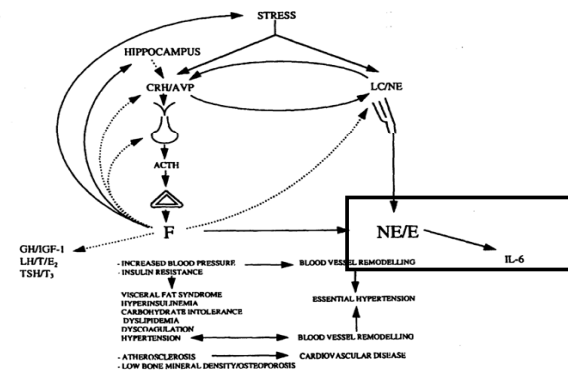
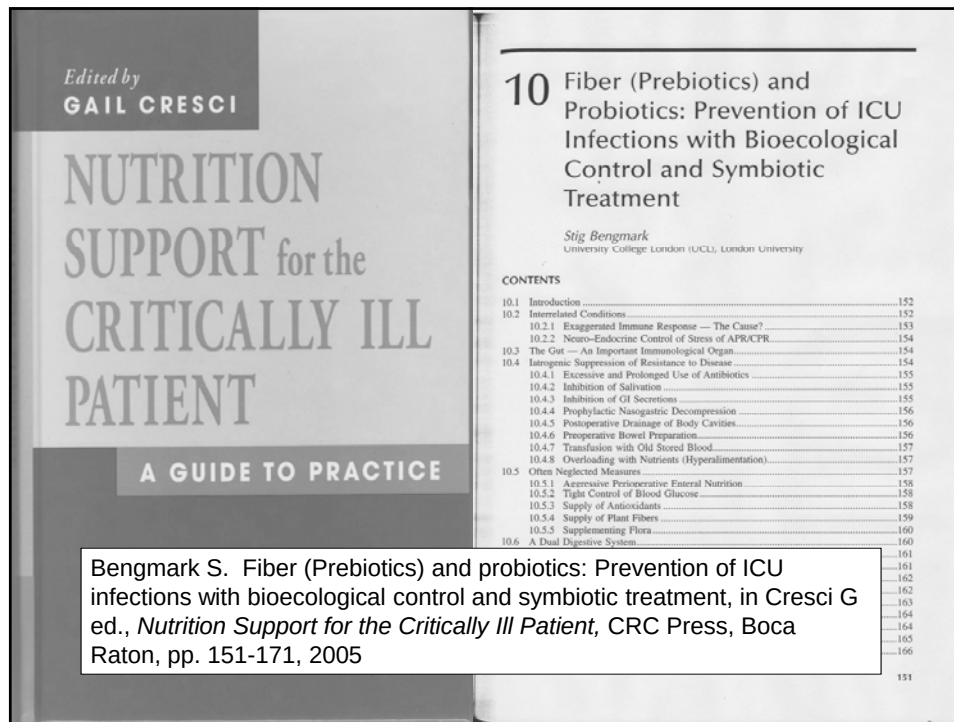


FIG. 1. A schematic representation of the stress system. The CRH/AVP neurons are reciprocally connected with the noradrenergic neurons of the LC/NE system in a positive reverberatory circuit. The HPA axis is controlled by several negative feedback loops, which tend to normalize the time-integrated secretion of cortisol, yet glucocorticoids stimulate the amygdala and, hence, the fear center. Activation of the HPA axis leads to suppression of the GH/IGF-1, LH/testosterone/estradiol, and TSH/T<sub>3</sub> axes; activation of the sympathetic system increases IL-6 secretion. Chronic increases in cortisol, catecholamines, and IL-6 and chronic suppression of the GH/IGF-1, LH/TE and TSH/T<sub>3</sub> axes lead to visceral obesity, hypertension, atherosclerosis, osteoporosis, and immune dysfunction and their sequelae resulting in increased morbidity and mortality. Symbols: Solid lines indicate stimulation; interrupted lines indicate inhibition. Abbreviations: HPA, hypothalamic-pituitary-adrenal; CRH, corticotropin-releasing hormone; AVP, arginine-vasopressin; LC/NE, locus coeruleus/norepinephrine system; GH, growth hormone; IGF-1, insulin-like growth factor-1; LH, luteinizing hormone; T, testosterone; TSH, thyrotropin; T<sub>3</sub>, triiodothyronine; F, cortisol; NE, norepinephrine; E, epinephrine; IL-6, interleukin-6.

Chrousos GP & Gold PW, Editorial: A healthy body in a healthy mind--and Vice Versa--The damaging power of “Uncontrollable” Stress, J Clin Endocrinol Metab, Vol. 83, No. 8, pp. 1842-1845, 1998.

40

Using the Organic Acids Test – Part 6  
Dr. Jeff Moss



|                                                                                                                                                                                                       |     |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----|
| Fiber (Prebiotics) and Probiotics: Prevention of ICU Infections                                                                                                                                       | 153 |
| <b>TABLE 10.1</b><br><b>Conditions of Acute and Chronic Phase Response</b>                                                                                                                            |     |
| APR and CPR                                                                                                                                                                                           |     |
| General hypermetabolism with higher resting energy expenditure                                                                                                                                        |     |
| Increased hepatic gluconeogenesis                                                                                                                                                                     |     |
| Increased glucose turnover and decreased muscle glucose uptake                                                                                                                                        |     |
| Hyperlipidemia                                                                                                                                                                                        |     |
| Adipose tissue lipolysis                                                                                                                                                                              |     |
| Increased production of nonesterified fatty acids                                                                                                                                                     |     |
| Increased whole-body protein turnover                                                                                                                                                                 |     |
| Increased hepatic protein synthesis                                                                                                                                                                   |     |
| Decreased muscle amino-acid uptake                                                                                                                                                                    |     |
| Insulin resistance                                                                                                                                                                                    |     |
| Increased production of cytokines                                                                                                                                                                     |     |
| Increased endotoxin in blood                                                                                                                                                                          |     |
| Elevated levels of catecholamines, cortisol, and glucagon ←                                                                                                                                           |     |
| <i>Sources:</i> From Simons, J.P., Schools A.M., Buurman, W.A., Wouters, E.F., <i>Clin. Sci.</i> 97, 215, 1999; and Preston, T., Slater, C., McMillan, D.C., et al., <i>J. Nutr.</i> 128, 1355, 1998. |     |

## Some final points on HVA and VMA

43

- “Dietary copper deficiency results in higher dopamine and lower norepinephrine levels in rats due to lower activity of dopamine- $\beta$ -monooxygenase, even though copper deficiency leads to greater production of the enzyme as well as tyrosine monooxygenase.”
- “Interpretation of urinary HVA must take into account dietary influences. A large fraction of ingested quercetin is metabolized by intestinal bacteria to homovanillic acid.”

44

- “...urinary HVA levels can also be raised by ingestion of bananas, which have concentrations of dopamine relative to other foods.”
- “Both urine VMA and HVA levels were higher in the workers exposed to aluminum, although serum aluminum was not significantly different.”
- “Compared with controls, the exposed workers in this study had significant differences in neurobehavioral tests.”

45



***Thank you!!***

46