

Organic Acids – Part 11  
Dr. Jeff Moss

Using organic acids to  
resolve chief complaints  
and improve quality of life in  
chronically ill patients  
Part XI  
Jeffrey Moss, DDS, CNS, DACBN  
[jeffmoss@mossnutrition.com](mailto:jeffmoss@mossnutrition.com)  
413-530-0858 (cell)

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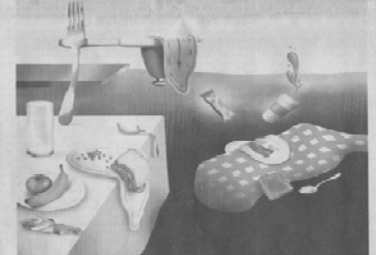
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COVER STORY USA Today, November 22, 2011

**Three squares a  
day is so yesterday**  
24/7 snacking becomes new normal



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SPORTS SCORES INSIDE THE NATION'S NEWSPAPER \$1.00

**College football**  
**SEC West takes 1, 2, 3**  
High-ranked teams upset over weekend, leaving USA Alabama and Arkansas at top 5, 4, 11

**USA TODAY**  
A GANNETT COMPANY

**Scorsese in 3-D**  
Huge in his own skin, Scorsese's film and career are the perfect blend

**Newsline**  
MONDAY, NOVEMBER 21, 2011

**USA TODAY INTERVIEW | Newt Gingrich**

**Doctors urged to limit practices**  
"The goal: to wean doctors off procedures that don't necessarily benefit patients."  
Treatment choices could be curtailed

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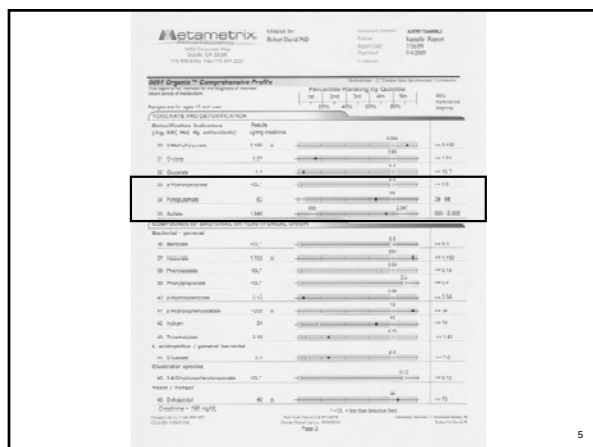
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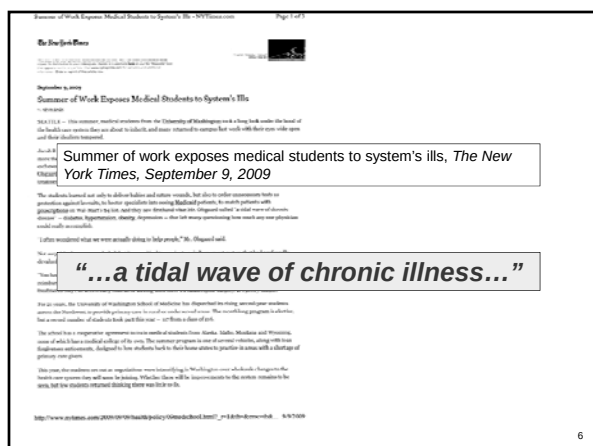
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## Sulfur metabolism – Part II: Diagnostic modalities and metabolic correction

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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."

KARGER

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ELSEVIER

REVIEW

### Acute and "chronic" phase reaction—a mother of disease

Sig Bengmark

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

Received 11 July 2004

**KEYWORDS:** Acute phase reaction; Chronic phase reaction; Inflammation; Nutrition; Stress; Sepsis; Trauma; Wound healing.

**ABSTRACT:** The acute phase reaction is a well-known phenomenon, but its role in the development of disease is still controversial. It is now clear that the acute phase reaction is a key component of the inflammatory response, and that it plays a central role in the development of disease. The chronic phase reaction is a less well-understood phenomenon, but it is now clear that it plays a central role in the development of disease. The chronic phase reaction is a key component of the inflammatory response, and that it plays a central role in the development of disease.

Bengmark S. Acute and "chronic" phase reaction – a mother of disease, *Clin Nutr*, Vol. 23, pp. 1256-66, 2004

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### Considerations for the Catabolic Patient

| Signs & Symptoms                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Consider                                              | Treatment Plan                                                                                     | Monitor                                                                  | Supplementation                                                                                                                                                  |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Feeding "fussy"</b> <ul style="list-style-type: none"><li>• Fatigue</li><li>• Cravings</li><li>• Depressive/irritable</li><li>• Poor quality sleep</li><li>• Poor digestion/absorption/energy gut</li><li>• Chronic protein/calorie deficit</li></ul>                                                                                                                                                                                                                                                                         | <b>Optimize pH</b>                                    | Optimize fluid and electrolyte balance                                                             | Monitor urinary pH<br>pH paper                                           | Proton pump inhibitors (PPIs)<br>Magnesium<br>Magnesium Citrate<br>(Vital Nutrients)                                                                             |
| <b>Optimizes muscle mass (protein synthesis) and amino acid levels</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                       | Pay special attention to protein and amino acids                                                   | Body composition:<br>muscle mass<br>muscle mass<br>lean mass<br>fat mass | Acute phase<br>Chronic phase<br>Protein synthesis<br>Amino acid products<br>(Vital Nutrients)                                                                    |
| <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 phosphate ratio 1:1</li><li>• High internal pH/blood</li><li>• Cholesterol (220-280)</li><li>• High LDL, low HDL</li><li>• High triglycerides</li><li>• Low normal serum protein, high normal serum albumin</li><li>• High normal BUN with normal creatinine</li><li>• Low urinary sulfate</li><li>• Excessive uric acid</li></ul> | <b>Reducing inflammation</b>                          | Reduce inflammation<br>Address food allergy                                                        | Inflammatory Biomarkers:<br>CRP<br>IL-6<br>TNF-α<br>IL-1β                | Anti-inflammatory agents<br>Selenium (Vital Nutrients)<br>Vitamin E (Vital Nutrients)<br>Fish oils<br>Vitamin D (Vital Nutrients)<br>Vitamin K (Vital Nutrients) |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | <b>Improving insulin sensitivity</b>                  | Watch carbohydrate/protein ratio                                                                   | Fasting glucose<br>Fasting insulin<br>Fasting triglycerides              | Metabolic Syndrome (Vital Nutrients)                                                                                                                             |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | <b>Optimize dietary carbohydrate/protein ratios</b>   | Reduce protein deficiency and reduce carbohydrate intake along with improvement in dietary quality | Urea nitrogen<br>Optimal protein intake<br>~1.0-1.2 g/kg body weight     | Protein synthesis<br>Amino acid products<br>(Vital Nutrients)                                                                                                    |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | <b>Optimize GI function</b>                           | Dietary changes, supplementation of digestive aids                                                 | Patient signs and symptoms                                               | Enzyme PKC (Vital Nutrients)<br>Digestive (Vital Nutrients)<br>Intestinal Repair Complex (Vital Nutrients)                                                       |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | <b>Optimize micronutrient deficiencies/imbalances</b> | Supplementation of malabsorption symptoms, as well as vitamins D, iodine, and zinc                 | Screen 25 OH Vitamin D<br>Fasting creatinine, thyroid, and other         | Multi-Nutrient (Vital Nutrients)<br>Vitamin D3/K2 (Vital Nutrients)<br>Iodine (Vital Nutrients)<br>Zinc (Vital Nutrients)                                        |

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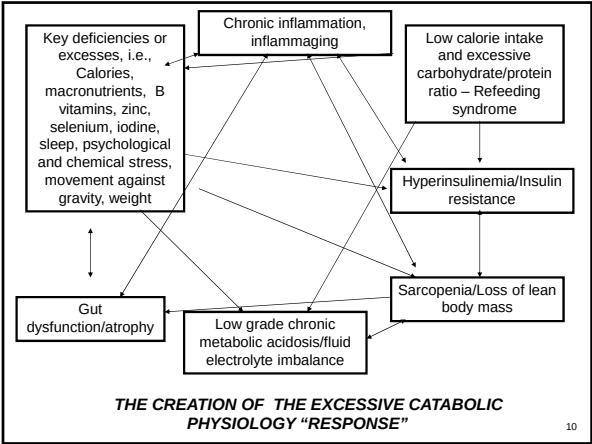
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**Biological Mechanism of Antidepressant Effect of Omega-3 Fatty Acids: How Does Fish Oil Act as a 'Mind-Body Interface'?**

**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

**Abstract:** The antidepressant effect of omega-3 fatty acids is well established, but the underlying mechanism remains unclear. This review discusses the potential role of omega-3 fatty acids in the brain, focusing on their effects on cell membrane fluidity, neurotransmitter release, and gene expression. It also explores the role of omega-3 fatty acids in the gut, where they may influence the gut-brain axis and contribute to the antidepressant effect. The review concludes that omega-3 fatty acids may act as a 'mind-body interface' by influencing both the brain and the gut, and that further research is needed to fully understand the underlying mechanism.

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

| Symptoms                  | Prevalence in IFN- $\alpha$ therapy <sup>a</sup> , % | Prevalence in MDD <sup>b</sup> , % |
|---------------------------|------------------------------------------------------|------------------------------------|
| Fatigue/asthenia          | 39–90                                                | 73                                 |
| Headache                  | 27–67                                                | 33 <sup>c</sup>                    |
| Gastrointestinal symptoms | 50 <sup>d</sup> –1                                   | 34–47 <sup>f</sup>                 |
| Psychomotor slowing       | 40 <sup>e</sup>                                      | 59–65 <sup>f</sup>                 |
| Insomnia                  | 20–39 <sup>d</sup>                                   | 63                                 |
| Irritability              | 35 <sup>d</sup>                                      | 50                                 |
| Arthralgia                | 9–36                                                 | 31 <sup>g</sup>                    |
| Musculoskeletal pain      | 26–32                                                | 62–80 <sup>h,i</sup>               |
| Abdominal pain            | 15–20                                                | 21 <sup>g</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> [39], unless otherwise specified; <sup>c</sup> [100]; <sup>d</sup> [101]; <sup>e</sup> [102]; <sup>f</sup> [103]; <sup>g</sup> [104].  
<sup>h</sup> Nausea, vomiting, bowel problems.  
<sup>i</sup> Result from depressed inpatient population.

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Sulfur metabolism:  
The metabolic “big picture”

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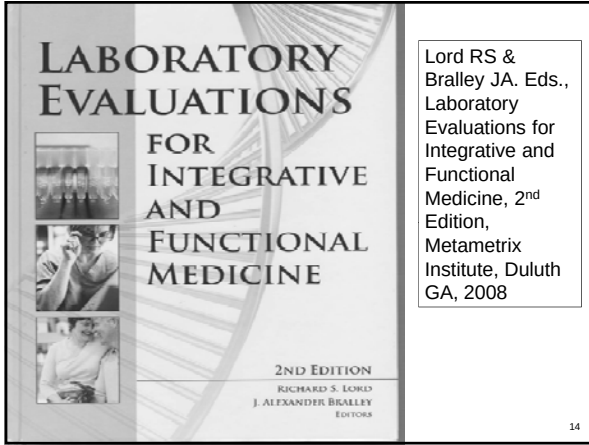
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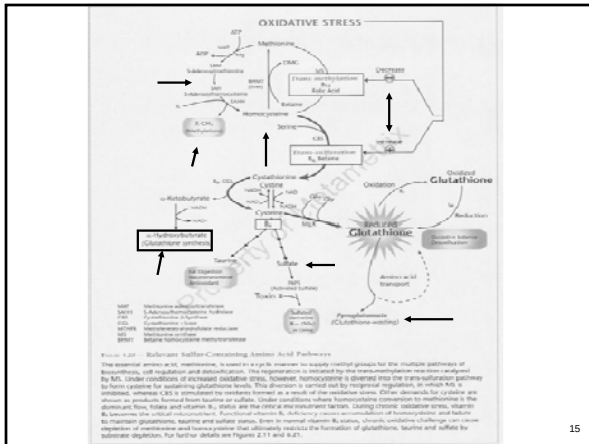
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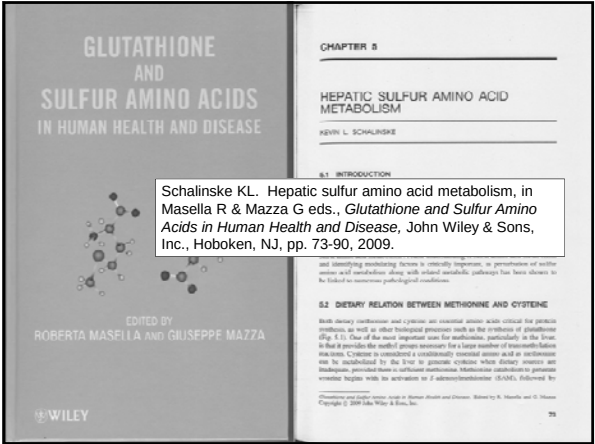
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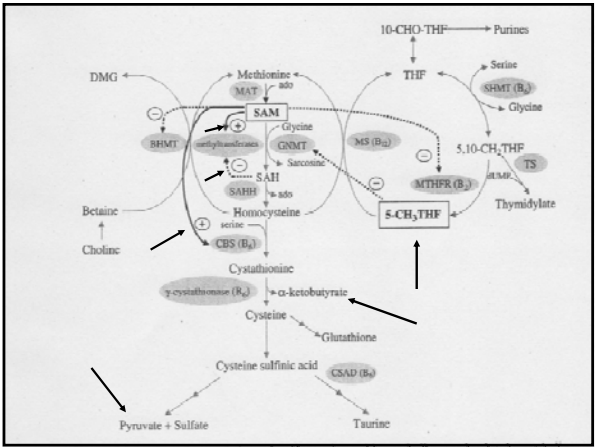
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Diagnosis of glutathione status:  
α-Hydroxybutyrate

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- “Although there is little direct evidence to date, the dominant source of urinary  $\alpha$ -hydroxybutyrate (AHB) seems to be the conversion of cystathionine to cysteine.”
- “The activity of this pathway is highly variable, changing in response to demands for protection against oxidative stress.”
- “As oxidative stress increases, the flow of homocysteine shifts away from transmethylation to methionine toward transsulfuration to cystathionine in order to increase the flux of cysteine into glutathione synthesis.”

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***“Thus, AHB production can be directly related to the rate of hepatic glutathione synthesis.”***

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### Clinical conditions associated with elevated urinary AHB

- Smoking
- Poor diet
- Lack of exercise
- Infectious diseases such as measles
- Birth asphyxia

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***“All of the conditions that have been associated with increased AHB excretion may be related to increased rates of hepatic glutathione synthesis from methionine.”***

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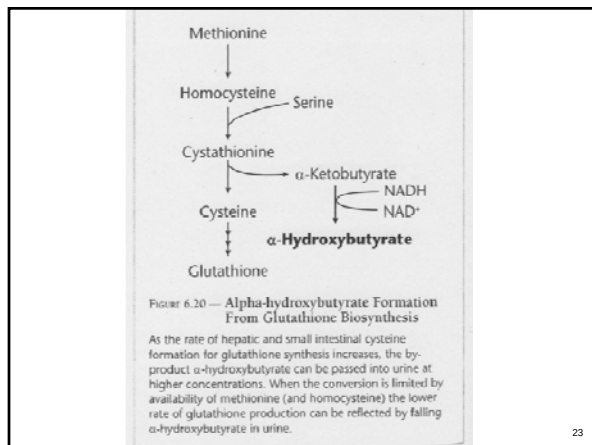
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***“When the conversion is limited by availability of methionine (and homocysteine) the lower rate of glutathione production can be reflected by falling AHB in urine.”***

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- “Elevated AHB, thus, shows increased flow through the transsulfuration pathway as required during times of increased demand for glutathione for meeting oxidative stress or for detoxification functions.”
- “Other signs, such as urinary pyroglutamate and sulfate...must be assessed to determine a patient’s ability to sustain this flow.”

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- “It is also possible to find some patients in late stages of chronic glutathione and methionine depletion who have such a low capacity to generate the transsulfuration flow that their AHB is normal.”
- “These patients generally show low plasma methionine and taurine.”

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Diagnosis of glutathione  
status:  
Pyroglutamate

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- “Pyroglutamate is created in the  $\gamma$ -glutamyl cycle (GGC), a pathway that is highly active in renal tubules and anywhere there is a high demand for glutathione.”
- “In healthy individuals, a very modest amount of pyroglutamate is spilled in the urine because the rate of pyroglutamate conversion to glutamate for glutathione reformation keeps pace with the rate of  $\gamma$ -glutamyl amino acid formation.”

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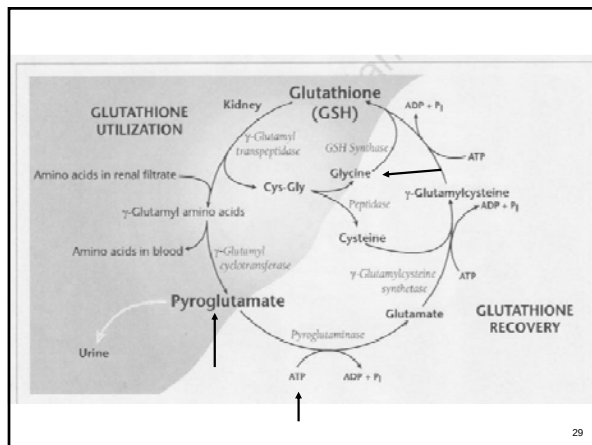
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- “As glutathione fails to be recovered in the  $\gamma$ -glutamyl pathway, a concurrent reduction in total body sulfate may be found.”
- “Studies showing an age-related decline in expression of glutathione synthesis in rat liver suggests that this problem may be more prevalent in older patients.”
- “If any compromise in energy production occurs, an increase in pyroglutamate could theoretically be noted.”

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- “Alternatively, drugs that require glutathione conjugation can cause failure to sustain glutathione adequacy. This effect has been reported with acetaminophen toxicity.”
- “Burn patients excrete higher than normal amounts of pyroglutamate, whereas their blood levels of glutathione are lowered and their rate of glycine synthesis is decreased.”

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- “Urinary pyroglutamic aciduria has been reported as a marker for glycine deficiency.”
- “If glycine conjugation demand concurrently is increased in healthy human subjects by methionine loading, then pyroglutamate excretion increases because of lowered availability of glycine.”
- “Under these conditions urinary pyroglutamate is positively related to urinary sulfate in a linear manner over the entire sulfate concentration range.”

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- “Small amounts of pyroglutamate are always present in overnight urine because it is produced as an intermediate in a cycle used in the active transport of amino acids in renal tubules.”
- “Since the appearance of a micromole of pyroglutamate in urine is accompanied by the recovery of a micromole of amino acids into the renal blood supply, we might think of the situation as one where glutathione is wasted in order to prevent massive essential amino acid loss.”

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***“Up to one-third of the glutathione circulating in blood may be used in this amino acid recovery process.”***

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- “Since pyroglutamate may be formed by heating of foods that contain high amounts of glutamic acid, urinary pyroglutamate may have dietary origins.”
- “Foods high in glutamic acid include artificial diets where glutamate is used as a flavor enhancer and high-protein foods, such as meats eggs and dairy products.”

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**Diagnosis of glutathione  
status:  
Sulfate**

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- “Sulfate is the ionic form of an inorganic rather than organic acid.”
- “It may be included on panels of urinary organic acids because of the important information it provides about sulfur metabolism.”
- “For example, the protein synthesis disruption of zinc deficiency causes decreased incorporation of cystine into proteins with concurrent large increases in urinary sulfate and taurine from cysteine degradation.”

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***“The rise in sulfate parallels the depth of zinc deficiency, indicating that, if other sulfate sources are normalized, urinary sulfate can be a metabolic marker of the severity of zinc deficiency.”***

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- “Severe depletion of organic sulfur sources will cause simultaneous high pyroglutamate and low sulfate excretion.”
- “High pyroglutamate with normal sulfate indicates inadequate organic sulfur sources for production of cysteine required for glutathione synthesis.”
- “Only organic sulfur in the form of compounds such as N-acetylcysteine or methionine along with adequate glycine will restore normal glutathione levels.”

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- “Normal urinary pyroglutamate with low sulfate levels can occur in individuals with impaired sulfate activation.”
- “In these cases, rapid replenishment of hepatic sulfate may be accomplished with either sulfur donors like N-acetylcysteine or inorganic sulfate such as sodium sulfate.”
- “On the other hand, a well nourished patient under temporary metabolic stress of detoxification from, for example, use of acetaminophen, may have elevated  $\alpha$ -hydroxybutyrate, signaling the increased rate of hepatic glutathione synthesis, but have no need for amino acid or glutathione therapy due to normal sulfate level.”

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- “An individual with limited ability to produce glutathione may show the glycine depletion sign of high pyroglutamate and low sulfate.”
- “This patient is a candidate for glutathione administration along with glycine and N-acetylcysteine or methionine, and their taurine status should be monitored, since depletion of other sulfur-containing compounds is likely.
- “Urinary sulfate has also been shown to reflect intake of sulfiting agents widely used as food additives.”

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**Treatment options  
for optimizing glutathione  
status**

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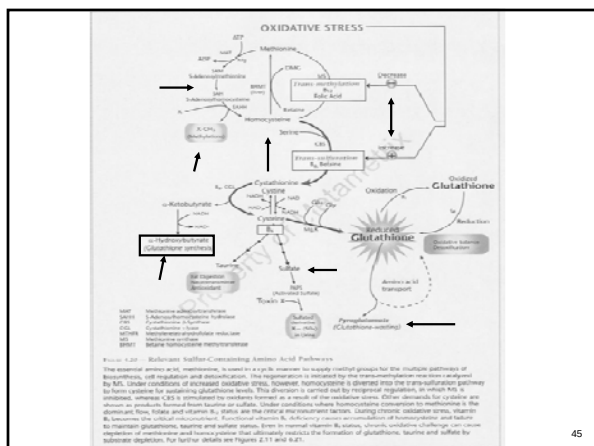
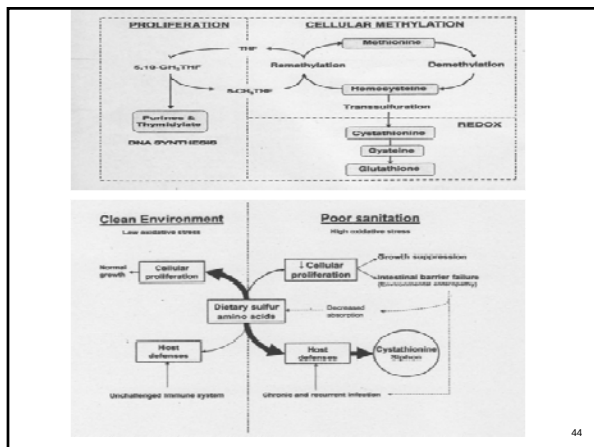
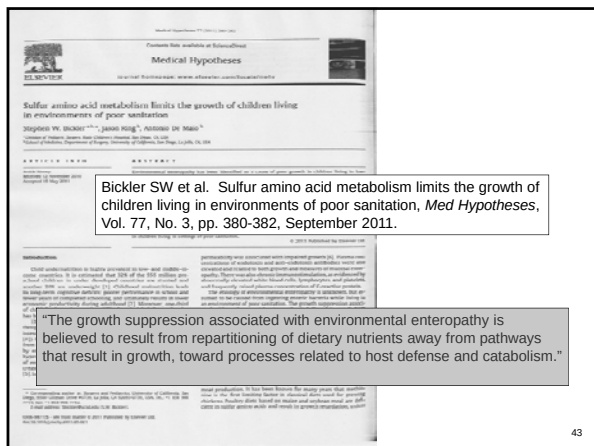
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Optimize anabolic/catabolic balance via Entry Level Clinical Nutrition

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| Considerations for the Catabolic Patient                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                       |                                                                                                         |                                                                                             |                                                                                                                                                                                                   |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Signs & Symptoms                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Consider                                                              | Treatment Plan                                                                                          | Monitor                                                                                     | Supplementation                                                                                                                                                                                   |
| <b>Signs &amp; Symptoms:</b> <ul style="list-style-type: none"><li>Fatigue, "burns"</li><li>Fatigue</li><li>Cravings</li><li>Depression/Anxiety</li><li>Poor quality sleep</li><li>Poor digestion</li><li>Atrophic body, 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 1:1</li><li>High normal globulin</li><li>Cholesterol (250-300)</li><li>High LDL, low HDL</li><li>High triglycerides</li><li>Low normal serum testosterone, high normal serum estradiol</li><li>High normal or high normal creatinine</li><li>Low urinary sulfate</li><li>Chronic infections</li></ul> | <b>Optimize pH</b>                                                    | Optimize fluid and electrolyte balance                                                                  | Monitor urinary pH of urine                                                                 | Protonix (AcidRed)<br>Alkaline (Shore)<br>Magnesium<br>Sodium Bicarbonate<br>(Vital Nutrition)                                                                                                    |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | <b>Optimize muscle mass (reduce sarcopenia) and amino acid levels</b> | Pay special attention to protein and amino acids                                                        | Body composition: Bioelectrical Impedance scale<br>Grip strength<br>Abdominal circumference | Amino acids<br>Creatine (Shore)<br>Ornithine (Shore)<br>Protein products<br>Amino acid products (Shore)<br>Fatty Acids (Shore)                                                                    |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | <b>Reducing inflammation</b>                                          | Reduce inflammation<br>Address food allergies                                                           | Inflammatory Biomarkers: CRP, ESR, RF, Rheumatoid factor, ANCA, ANF, ANCA, ANCA, ANCA       | Anti-inflammatory agents<br>Inflammation (Shore)<br>Anti-TNF (Shore)<br>Pain Guard (Shore)<br>Fish Oil<br>Alpha Pure Fish Oil<br>(Vital Nutrition)<br>Food allergy: Biotin<br>Cholesterol (Shore) |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | <b>Improving insulin sensitivity</b>                                  | Watch carbohydrate/protein ratio                                                                        | Fasting glucose<br>Fasting insulin<br>Cravings                                              | Metabolic Synergy (Shore)                                                                                                                                                                         |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | <b>Optimize dietary carbohydrate/protein ratio</b>                    | Regulate protein deficiencies and reduce carbohydrate intake along with improvements in dietary quality | Urea index<br>Optimal protein intake: 1.0 - 1.2 g/kg body weight                            | Protein products<br>Protein products (Shore)<br>Amino acid products (Shore)                                                                                                                       |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | <b>Optimize GI function</b>                                           | Dietary changes, supplementation of digestive aids                                                      | Patient signs and symptoms                                                                  | Rescue (Vital Nutrition)<br>Digestion (Shore)<br>Medical Support (Shore)<br>Digestion (Shore)                                                                                                     |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | <b>Optimize micronutrient deficiencies/imbalance</b>                  | Supplementation of nutrients<br>Provide emphasis on vitamins B, sulfur, and zinc                        | Screen 25 OH vitamin D<br>Fasting serum thyroid<br>Fasting serum<br>Zinc, body test         | Vitamin D (Vital Nutrition)<br>Vitamin D (Vital Nutrition)<br>Zinc (Shore)<br>Zinc (Shore)                                                                                                        |

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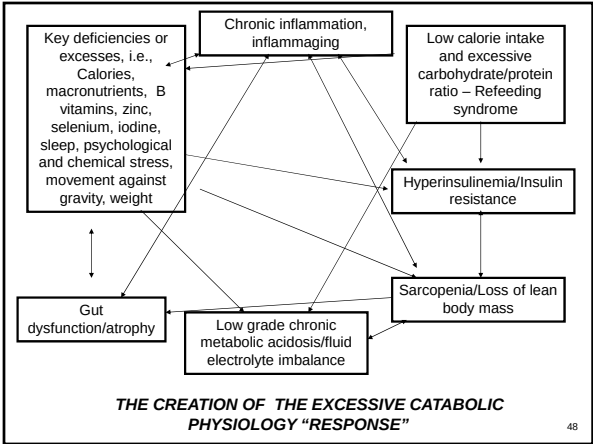
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Supplementation

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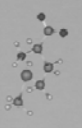
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GLUTATHIONE  
AND  
SULFUR AMINO ACIDS  
IN HUMAN HEALTH AND DISEASE



Schalinske KL. Hepatic sulfur amino acid metabolism, in Masella R & Mazza G eds., *Glutathione and Sulfur Amino Acids in Human Health and Disease*, John Wiley & Sons, Inc., Hoboken, NJ, pp. 73-90, 2009.

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ROBERTA MASELLA AND GIUSEPPE MAZZA

WILEY

CHAPTER 5

HEPATIC SULFUR AMINO ACID  
METABOLISM

KEVIN L. SCHALINSKE

5.1 INTRODUCTION

and identifying metabolic defects is critically important, as perturbations of sulfur  
amino acid metabolism along with related metabolic pathways have been shown to  
be linked to numerous pathological conditions.

5.2 DIETARY RELATION BETWEEN METHIONINE AND CYSTEINE

Methionine, homocysteine and cysteine are essential amino acids critical for protein  
synthesis, as well as other biological processes such as the synthesis of glutathione  
(Fig. 5.1). One of the most important uses for methionine, particularly in the liver,  
is that it provides the methyl groups necessary for a large number of transmethylation  
reactions. Cysteine is considered a conditionally essential amino acid as methionine  
can be converted by the liver to produce cysteine when dietary sources are  
inadequate, providing them to sulfur-rich methionine. Methionine contributes to protein  
synthesis, helps with its activation to S-adenosylmethionine (SAM), followed by  
transmethylation and S-adenosylhomocysteine (SAH) formation.

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- “A number of strategies have evolved to raise levels of glutathione in depleted individuals.”
- “There are at least three potential ways of enhancing cellular GSH content: administration of the three amino acids (cysteine, glutamic acid, and glycine) which comprise the tripeptide, either singly or in various combinations; administration of cofactors for the metabolic pathways leading to GSH production, that is, vitamin B6, riboflavin, and folic acid; and administration of synthetic compounds which become converted to precursors of GSH.”

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## Organic Acids – Part 11

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- “In HIV positive patients a whey protein formulation was clearly demonstrated to increase plasma GSH concentrations.”
- “N-acetyl cysteine (NAC) rapidly enters the cell and is speedily deacylated to yield L-cysteine.”
- “...randomized studies on asymptomatic HIV positive patients in the presence and absence of antiretroviral therapy (ART) have shown that NAC can raise blood GSH, increase natural killer cell activity, and enhance stimulation indices of T cells incubated with mitogen or tetanus toxin.”

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- “Interestingly the rise in T cell function was accompanied by a fall in plasma IL-6 in subjects receiving ART as well as the drug.”
- “Furthermore studies have shown that survival time was improved in HIV+ patients who maintained high concentrations of GSH in CD4+ T lymphocytes.”
- “It could therefore be surmised that improved T cell function and reduced inflammation are modulated by improvement in antioxidant status in these patients.”

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- “Alpha-lipoic acid provides a further means of enhancing tissue GSH content.”
- “The compound is reduced to dihydrolipoic acid, which converts cystine to cysteine.”
- “Cysteine, on gaining entry to the immune cells, is rapidly converted to GSH.”
- “Flow cytometric analysis of freshly prepared human peripheral blood lymphocytes shows that lipoic acid is able to normalize a subpopulation of cells with severely compromised thiol status rather than increasing the level in all cells above normal values.”

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## Organic Acids – Part 11

Dr. Jeff Moss

### Dosing recommendations

- N-acetylcysteine – 1500 mg/day with meals
- Lipoic acid – 300 mg/day with meals
- R-lipoic acid – 150 mg/day with meals
- Taurine – 1-2 g per day with meals

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*Thank you!!*

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