

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

Part X

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HEALTH & WELLNESS

PERSONAL JOURNAL.

Hey, Friend, Take a Hike
Socializing While Exercising WHAT'S YOUR WORKOUT? D2

A Long Weekend
For Quarterbacks
SPORTS D6

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Is This the End of Popping Vitamins?

By SHIRLEY S. WANG

The case for dietary supplements is collapsing.

A succession of large-scale human studies, including two published earlier this month in leading medical journals, suggests that multivitamins and many other dietary supplements often don't have health benefits—and in some cases may even cause harm.

The data have prompted some nutrition researchers to say taking vitamins is a waste of money for those without a specific nutrient deficiency or chronic illness. Such findings have also fueled a debate about whether the field should continue conducting expensive human trials to figure out whether particular supplements affect health.

"The better the quality of the research, the less benefit (supplements) showed," says Marion Nestle, professor of nutrition, food studies, and public health at New York University. "It's fair to say from the research that supplements don't make healthy people healthier."

For instance, vitamins E and B-12 are often touted as being good for the heart, but several studies have failed to find that they lower risk of cardiovascular disease, according to the Office of Dietary Supplements, part of the National Institutes of Health. Vitamin C hasn't been shown in many studies to lower a person's risk of getting a cold. Calcium, while important to bone health, doesn't lower risk of heart disease or cancer and may increase risk of kidney stones.

"We have an enormous body of data telling us that plant-rich diets are very healthy," says Josephine Briggs, head of the National Center for Complementary and Alternative Medicine, another NIH center. "As soon as we take these various antioxidants (and other nutrients) out and put them in a pill, we're not consistently getting a benefit."

Researchers and nutritionists are still recommending dietary supplements for the malnourished or people with certain nutrient deficiencies or medical conditions. For instance, folic acid—the supplement form of folate—reduces the likelihood of a common birth defect if taken by pregnant women.

Studying the effects of vitamins and supplements in the real world is difficult, since people eat foods with multiple nutrients that can interact with supplements and skew results. And observational trials can only

\$28 billion
Total sales of dietary supplements in the U.S. last year, up 4.4% from 2009

Please turn to page D4

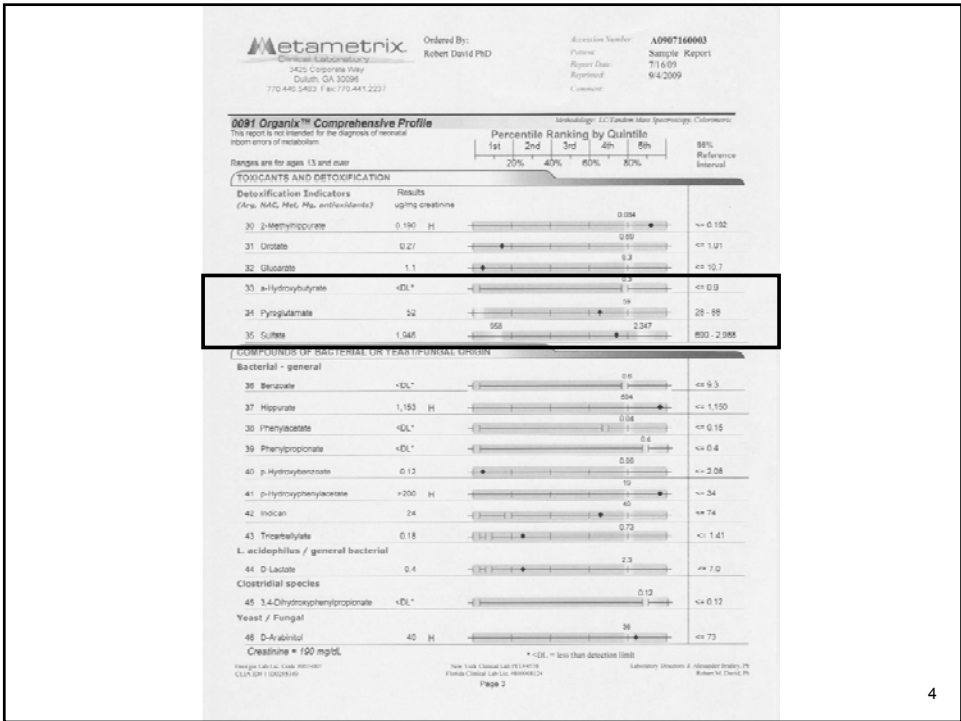
A balanced diet is the best way to get needed vitamins, researchers say.

Scary Movies and Real-Life Risks

Thrill-seekers handle People with

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Organic Acids – Part 10

Dr. Jeff Moss

Summer of Work Exposes Medical Students to System's Ills • NYTimes.com Page 1 of 3

The New York Times

September 9, 2009

Summer of Work Exposes Medical Students to System's Ills

By Jacob R. Gersberg

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 less transparent.

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 become specialists in seeing Medicaid patients, to watch patients with prescriptions on Wal-Mart's \$4 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&sh=4&sm=4&st=4 9/9/2009

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**Nutrition and
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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."

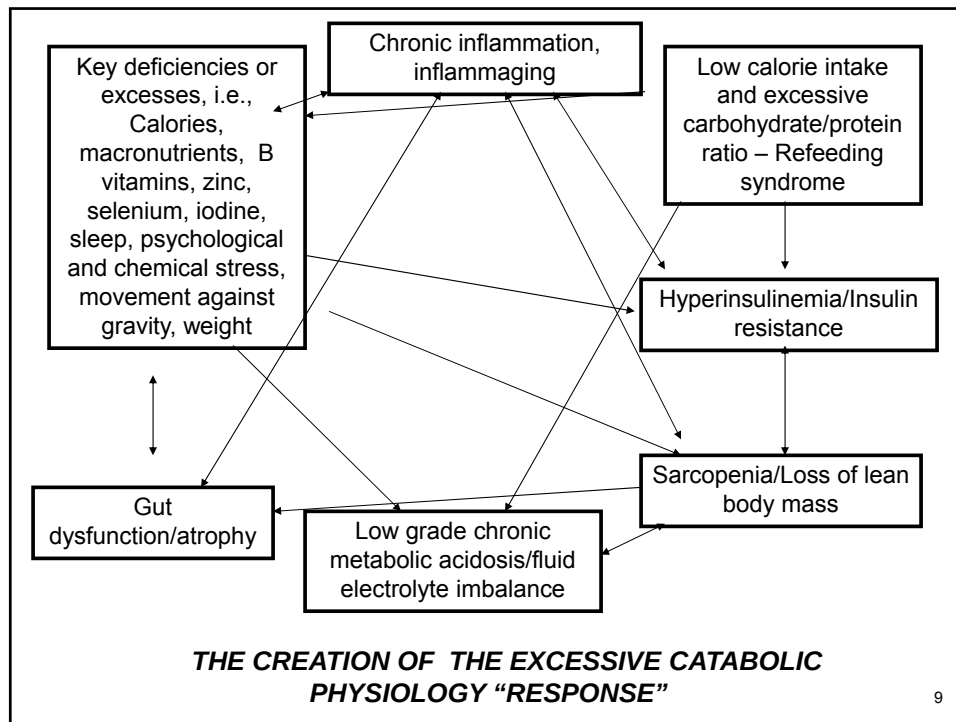
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Invited Review

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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, noradrenaline 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].

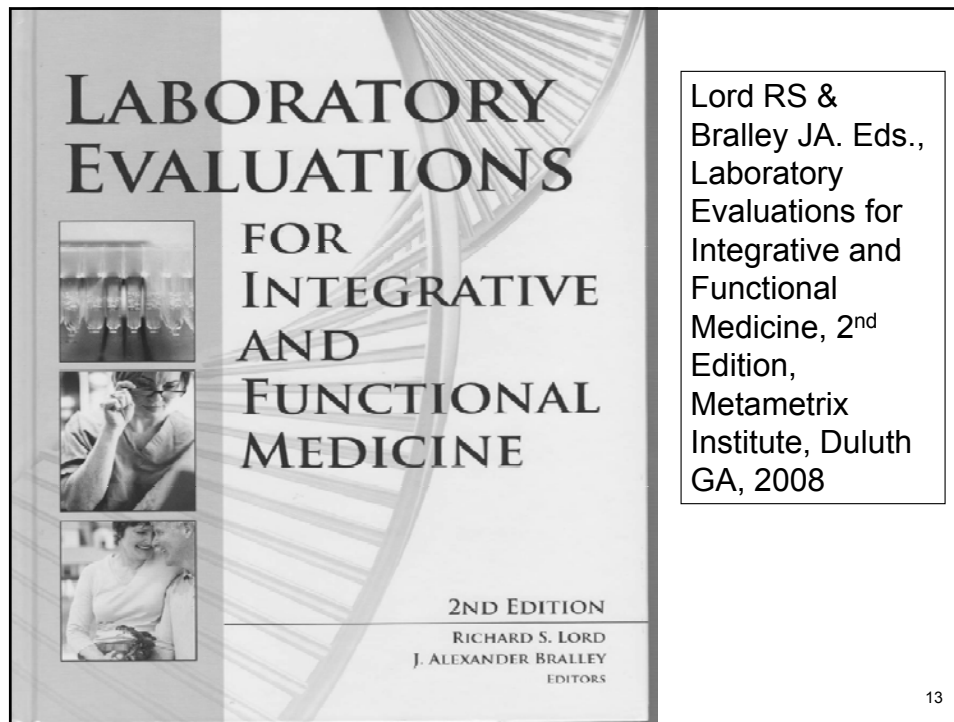
¹ Nausea, vomiting, bowel problems.

² Result from depressed inpatient population.

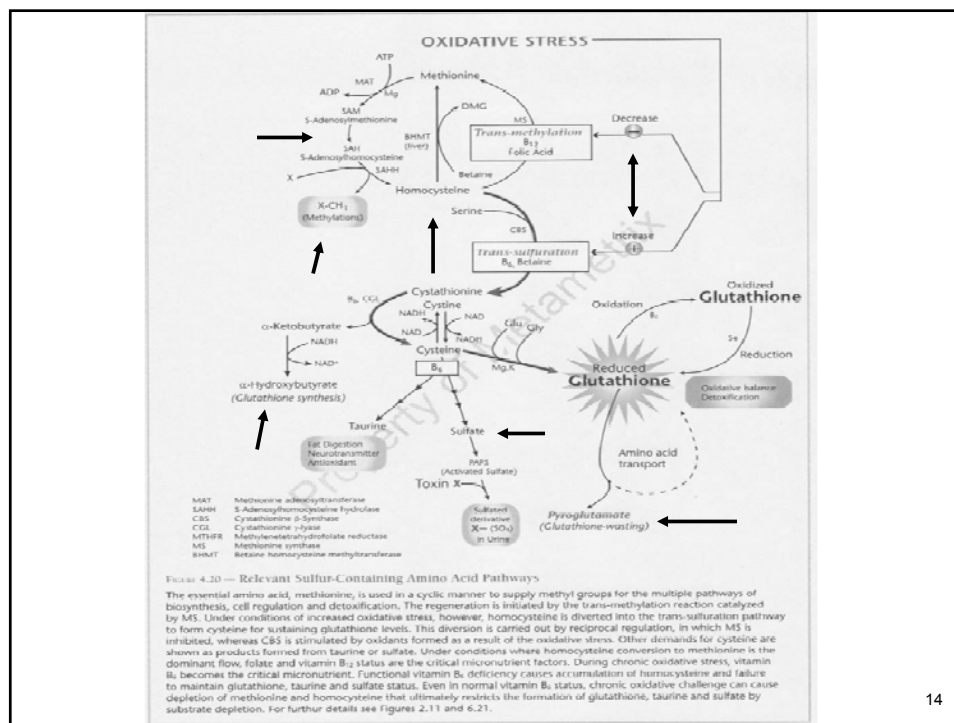
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Sulfur metabolism: The metabolic “big picture”

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Rate of 'preventive' mastectomy rising

Health spotlight



Follow coverage at breastcancer.usatoday.com.

Some doctors call trend alarming

By Liz Szabo
USA TODAY

Lisa Bonchek Adams was only 37, with a new baby and two older children, when her doctor noticed something during a routine breast exam. Her doctor didn't feel a lump, but one breast felt "different" from the other.

A few weeks later, Adams learned that she needed a mastectomy. Follow-up tests indicated there were cancer cells throughout Adams' left breast, dispersed too widely to be removed with a lumpectomy.

That's when Adams made a surprising decision. She asked her surgeon to remove both of her breasts, not just the one with cancer.

A small but growing number of young women are choosing this kind of aggressive surgery, called contralateral prophylactic mastectomy. Women such as Adams say the surgery allows them to take control of a frightening disease.

Some doctors say such surgeries are unlikely to help the average woman or improve her survival.

"I think women feel like, 'I'm going to go through this once, and I don't want to go through this worry again,'" says Adams, 42, of Darien, Conn. "I wanted to do everything I could to have as much time with my children."

Across the country, the number of

COVER STORY

Please see COVER STORY next page ►

USA Today, October 16, 2011

WELL | Tara Parker-Pope

Mammogram's Role as Savior Is Tested

Has the power of the mammogram been oversold?

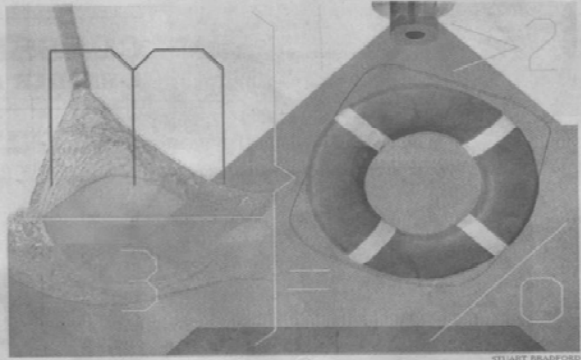
At a time when medical experts are rethinking screening guidelines for prostate and cervical cancer, many doctors say it's also time to set the record straight about mammography screening for breast cancer. While most agree that mammograms have a place in women's health care, many doctors say

The number of women helped by screening is lower than many think.

widespread "Pink Ribbon" campaigns and patient testimonials have imbued the mammogram with a kind of magic it doesn't have. Some patients are so committed to annual screenings they even begin to believe that regular mammograms actually prevent breast cancer, said Dr. Susan Love, a prominent women's health advocate. And women who skip a mammogram often beat themselves up for it.

"You can't expect from mammography what it cannot do," said Dr. Laurence Esserman, director of the breast cancer center at the University of California, San Francisco. "Screening is not prevention. We're not going to screen our way to a cure."

A new analysis published Monday in Archives of Internal Medicine offers a



stark reality check about the value of mammography screening. Despite numerous testimonials from women who believe "a mammogram saved my life,"

than most people think. The Dartmouth researchers conducted a series of calculations estimating a woman's 10-year risk of developing breast cancer and her

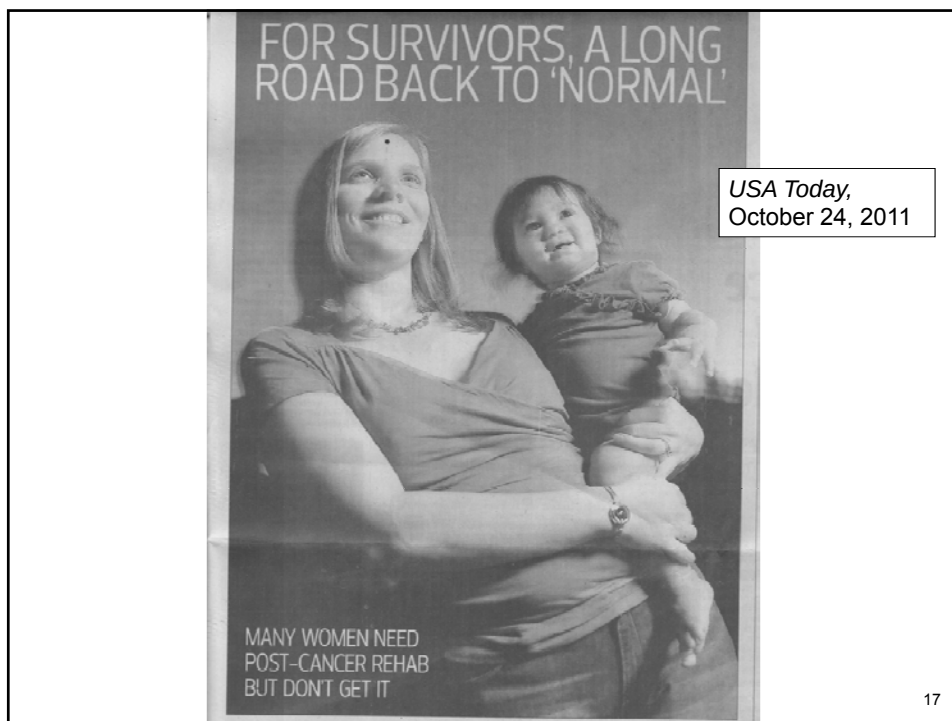
by the test, conclude two Dartmouth researchers, Dr. H. Gilbert Welch and Brittney A. Frankel.

Dr. Welch notes that clearly some women are helped by mammography screening, but the numbers are lower

screening trials as well as the benefits of improvements in treatment. Among the 60 percent of women with breast cancer who detected the disease by screening, only about 3 percent to 13

Continued on Page 6

The New York Times, October 25, 2011



Antidepressant use skyrockets 400% in two decades

Most who take the medications are not in therapy, report says

By Janice Lloyd
USA TODAY

Use of antidepressant drugs has soared nearly 400% since 1988, making the medication the most frequently used by people ages 18-44, a report from the Centers for Disease Control and Prevention shows.

Eleven percent of Americans ages 12 years and older took antidepressants during the 2005-08 study period, the authors write. They add that though the majority of antidepressants were taken to treat depression, the drugs also can be used for anxiety disorders and other conditions.

The data are from the National Health and Nutrition Examination Surveys, which included information from 12,637 participants about pre-

scription-drug use, antidepressant use, length of use, severity of depressive symptoms and contact with a health professional.

Mental-health professionals not associated with the survey cited several reasons as possible explanations for the spike:

- The struggling economy and the record number of layoffs and home foreclosures. "These
- Ad campaigns waged by pharmaceutical companies citing benefits of the drugs.
- Families who might be reimbursed by health insurance companies for a prescription but may delay getting therapy from a mental-health professional because of the cost of treatment.

In fact, less than one-third of Americans taking one antidepressant and less than one-half of those taking multiple antidepressants have seen a mental-health professional in the past year, the report shows.

"Unfortunately, some families are looking for a quick fix, but a pill is never going to get to the root of the problem," says David Palmiter, a psychologist and author of *Working Parents, Thriving Families That Make a Difference*.

Ducharme agrees. "That is the thing that bothers me the most," she says. "These drugs can be dangerous, and there needs to be follow-up care."

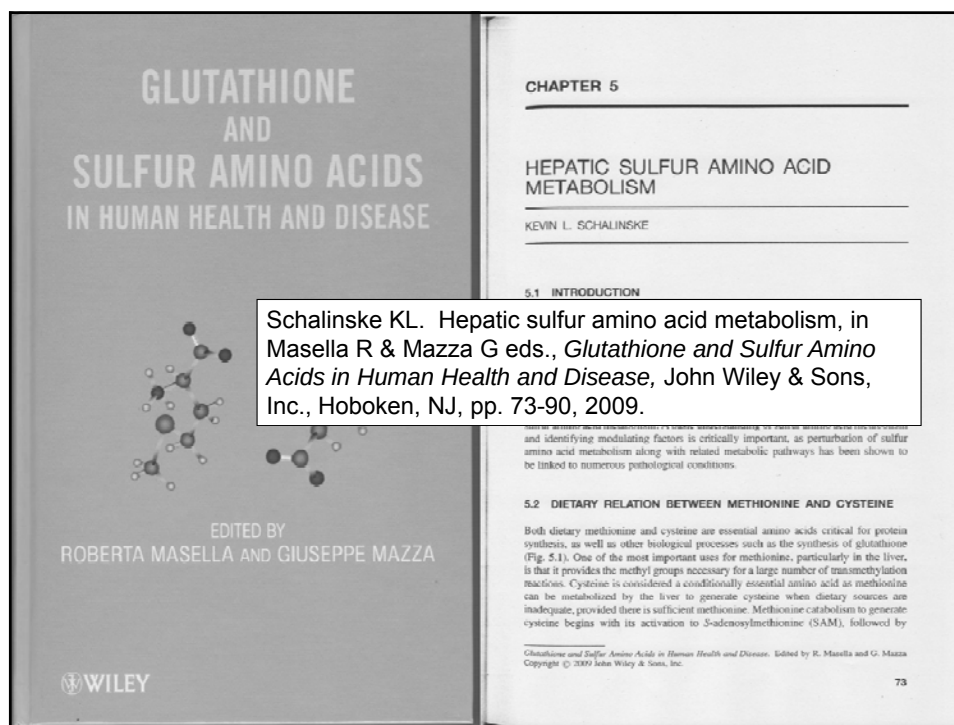
The survey also found that nearly one in four women ages 40 to 59 are taking antidepressants. Women are more likely to take antidepressants; however, among those taking antidepressants, men were more likely than women to have seen a mental-health professional in the past year.

The survey found that about one in 25 teens take the medication.

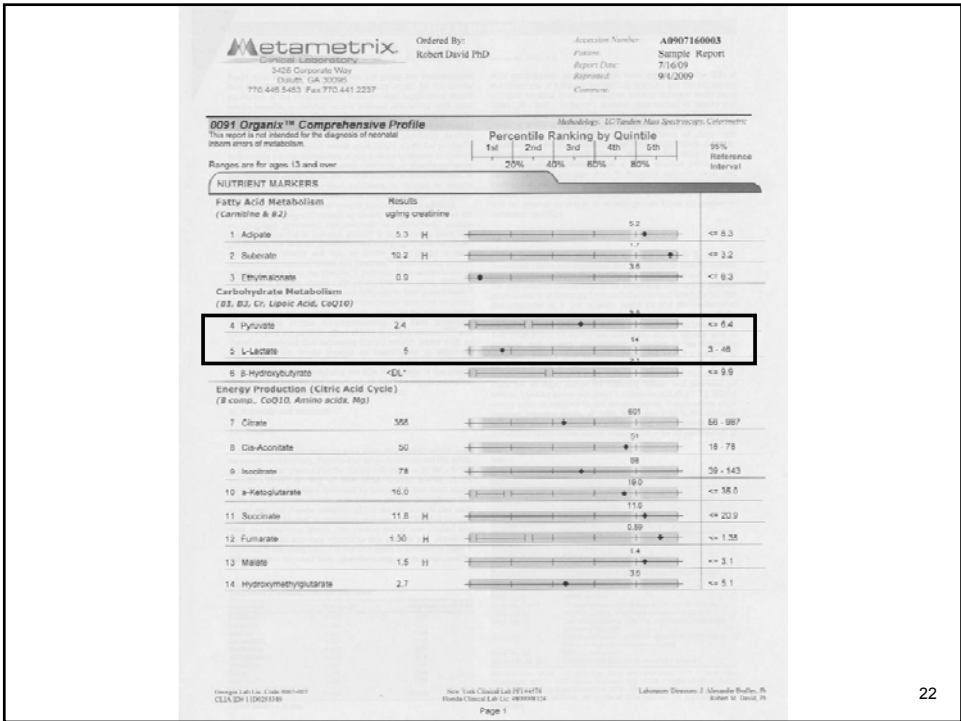
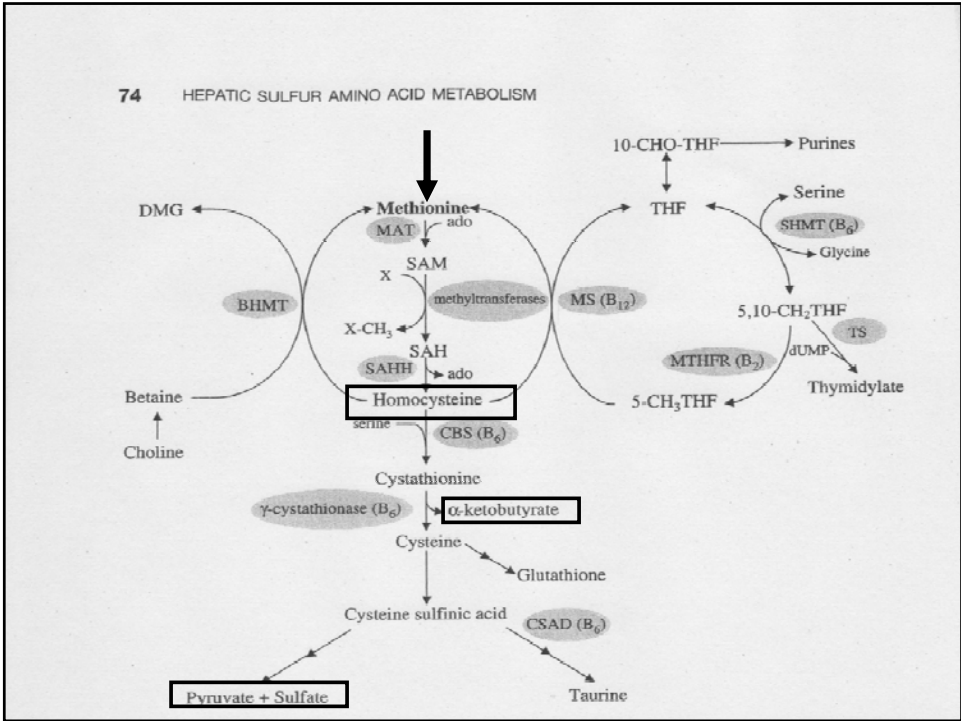
USA Today, October 20, 2011

Sulfur metabolism: Basic biochemistry and physiology

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Organic Acids – Part 10
Dr. Jeff Moss



- “Homocysteine exists at a metabolic branch point in that it can be remethylated back to methionine, or can be irreversibly catabolized via the transsulfuration pathway to generate cystathionine and subsequently cysteine.”
- “Mudd and Poole demonstrated that approximately half of the homocysteine is metabolized by transsulfuration to cystathionine and the other half is remethylated back to methionine.”

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- “Methionine is the primary donor of methyl groups, in the form of S-adenosylmethionine (SAM), for biological methylation reactions.”
- “Following all SAM-dependent transmethylation reactions, S-adenosylhomocysteine (SAH) is generated, which is a potent inhibitor of most methyltransferases.”
- “Because SAM is a positive modulator of methyltransferase activity, the intracellular ratio of SAM to SAH is considered an index of transmethylation potential.”

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“...cysteine can be converted to pyruvate and inorganic sulfate as a means to meet energy needs by gluconeogenesis and remove sulfur from the body via the urine, respectively.”

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Information on SAM

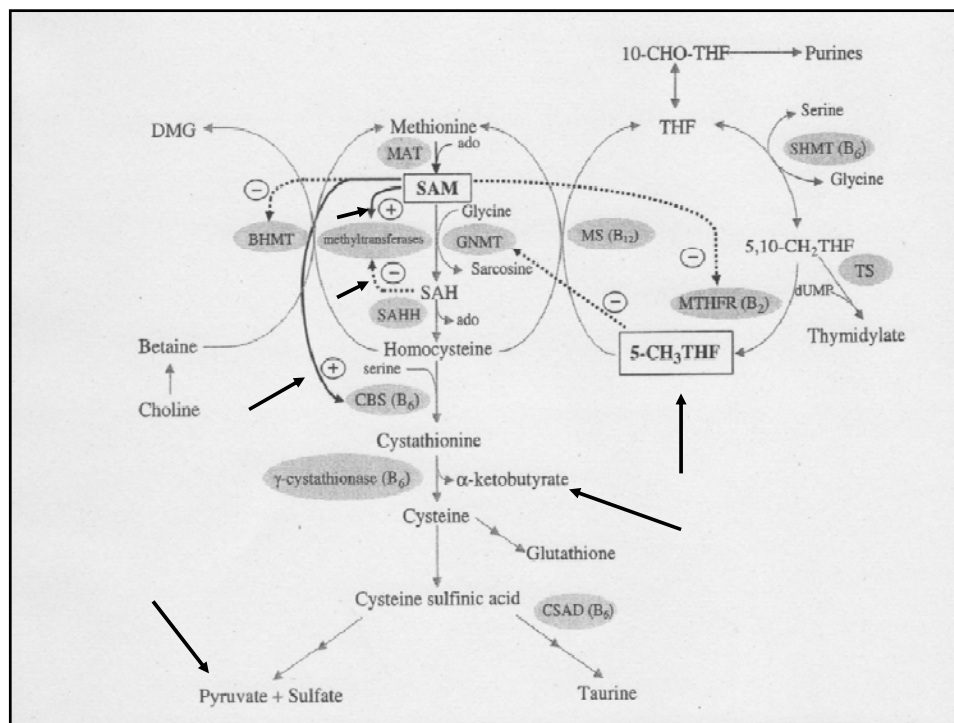
- “SAM inhibits the activity of methyltetrahydrofolate reductase (MTHFR) allosterically, thereby reducing 5-CH₃THF production...”
- “SAM-dependent methyltransferase reactions include the synthesis of carnitine from lysine, the activation and inactivation of neurotransmitters, and the methylation of DNA for epigenetic control of gene expression.”

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Impact of high protein diet

- “In brief, the excess methionine is activated to SAM, which exerts its allosteric control on methyltransferases, MTHFR, and cystathionine beta-synthase (CBS).”
- “Collectively, this results in the increased catabolism of methionine through the transmethylation and transsulfuration pathway, diminishes methionine generation by homocysteine remethylation, and disposes of excess methyl groups.”

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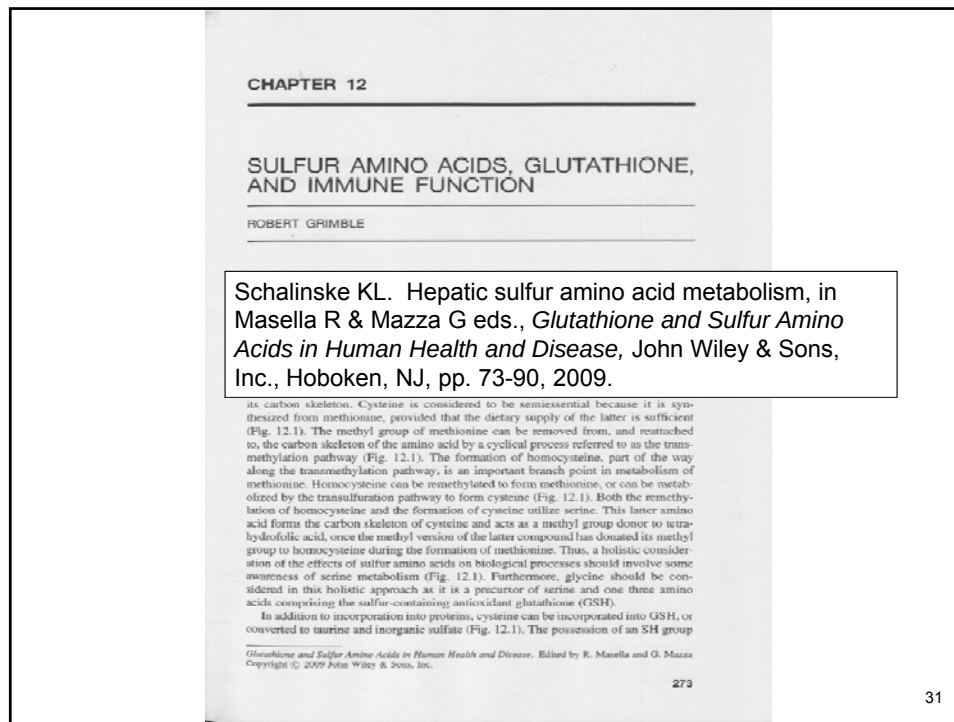


“Thyroid status, both hyper- and hypothyroidism, has been shown to perturb both the hepatic folate-dependent one-carbon pool and regulatory proteins involved with sulfur amino acid metabolism...”

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**Sulfur metabolism:
The impact of chronic
inflammation**

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- “...when the diet is low in sulfur amino acids cellular methionine is highly conserved.”
- “Flux down the transsulfuration pathway, which ultimately leads to methionine catabolism, increases only as dietary methionine intake increases.”

How does the body respond to environmental stressors?

- “The immune system has great capacity for immobilizing invading microbes, creating a hostile environment for them and bringing about their destruction.”
- “It can also become activated, in a similar way to the response to microbial invasion, by a wide range of stimuli and conditions.”

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- “These include burns, penetrating and blunt injury, the presence of tumor cells, environmental pollutants, radiation, exposure to allergens, and the presence of chronic inflammatory diseases.”
- “The strength of the response to this disparate range of stimuli will vary, but it will contain many of the hallmarks of the response to invading pathogens.”
- ***“The immune response has a high metabolic cost, and inappropriate prolongation of the response will exert a deleterious effect on the nutritional status of the host.”***

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What happens to sulfur with chronic illness?

- “Infection with human immunodeficiency virus (HIV)...has been shown to cause substantial excretion of sulfate in the urine during the asymptomatic phase of the disease.”
- “The losses reported were equivalent to 10 g of cysteine per day, in contrast to losses of approximately 3 g/d for healthy individuals on a ‘Westernized diet.’”

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- “Large decreases in plasma glycine, serine, and taurine concentrations occur following infection and injury.”
- “These changes may be due to enhanced utilization of a closely related group of amino acids, namely glycine, serine, methionine, and cysteine.”

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- “Many substances produced in enhanced amounts in response to pro-inflammatory cytokines are particularly rich in these amino acids.”
- “These substances include GSH (comprised of glycine, glutamic acid, and cysteine), metallothionein (the major zinc transport protein), in which glycine, serine, cysteine, and methionine make up 56% of the total amino acids, and a range of acute phase proteins which contain up to 25% of these amino acids in their structure.”

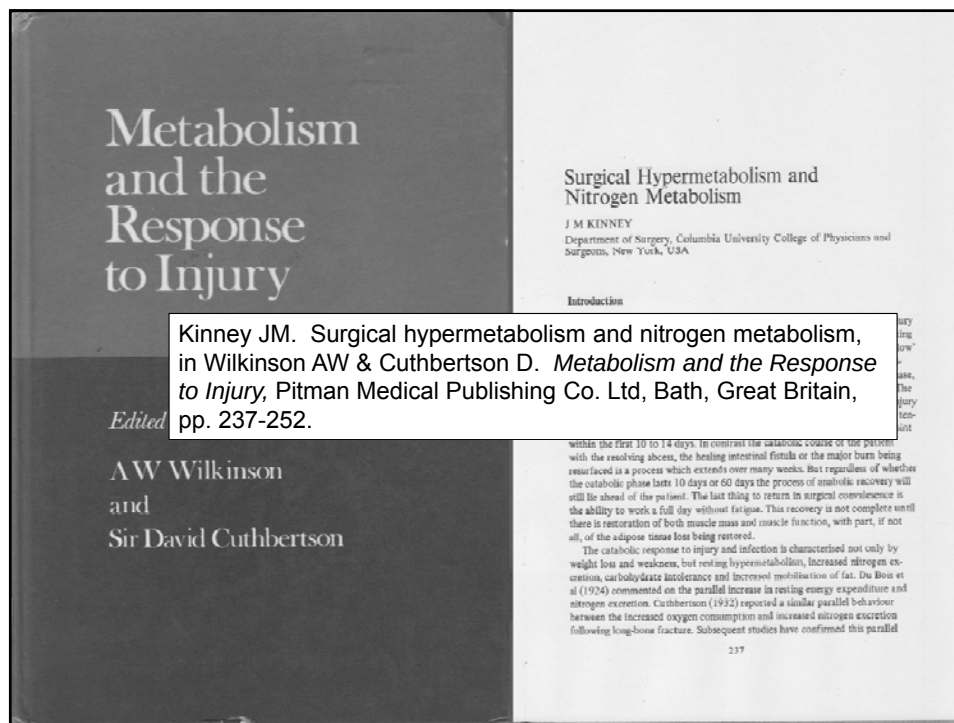
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“If an increased demand for sulfur and related amino acids is created by the inflammatory response then provision of additional supplies of these amino acids may assist the response.”

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Sir David Cuthbertson: The father of research on the impact of illness on nutritional status

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Ebb and flow

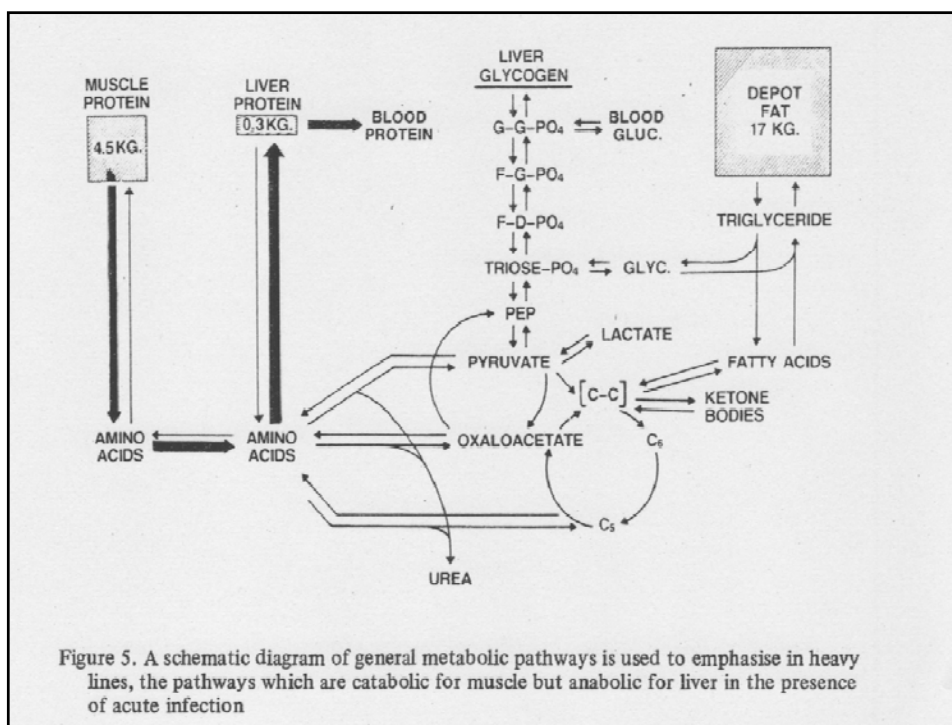
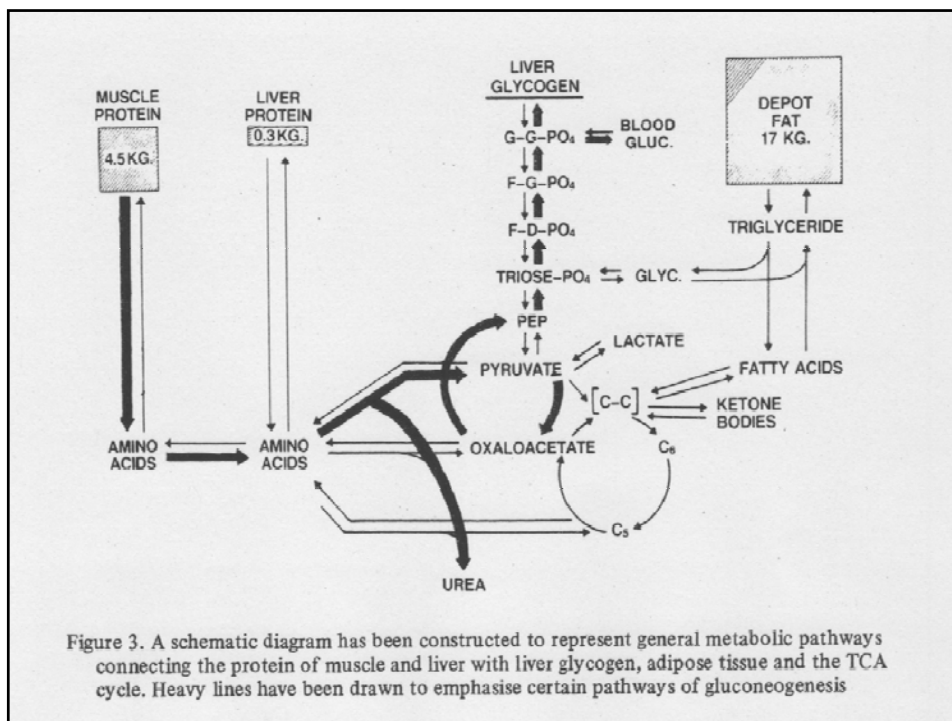
- “Cuthbertson followed his initial observations on the metabolic response to injury by dividing the response into the early or ‘ebb’ phase of depressed vitality lasting for a day or so, and followed by resurgence of vitality which he termed the ‘flow’ phase and which seemed to bear a certain resemblance to inflammation.”

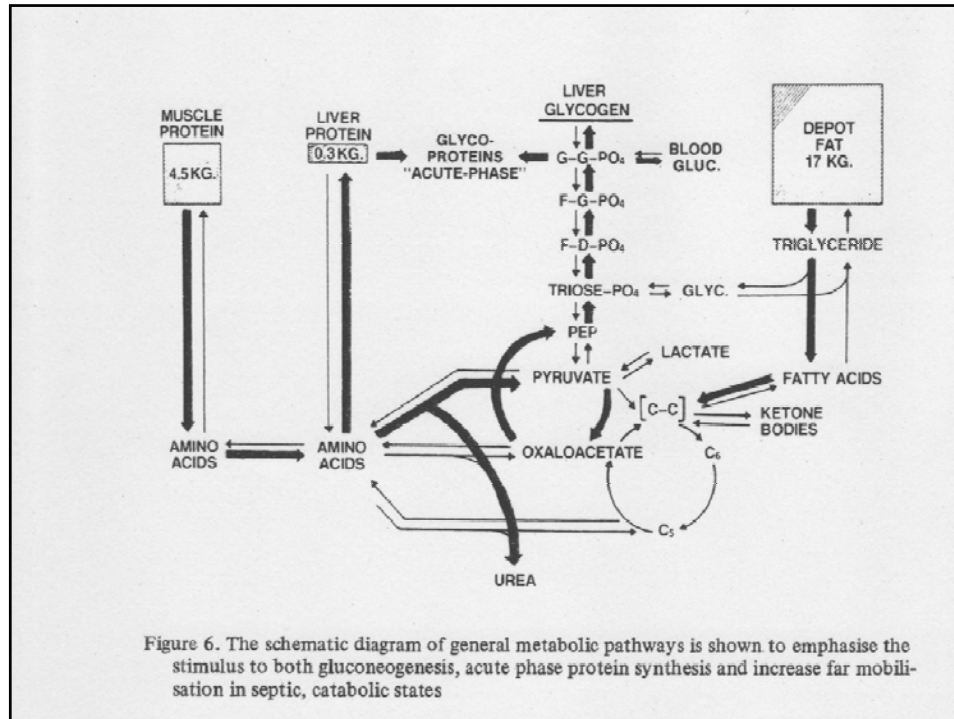
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Ebb and flow

- “The flow phase can be divided into a catabolic phase, lasting days to weeks, and the later anabolic phase, lasting weeks to months.”
- “The catabolic response to injury and infection is characterized not only by weight loss and weakness, but resting hypermetabolism, increased nitrogen excretion, carbohydrate intolerance and increased mobilization of fat.”

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XXX. THE DISTRIBUTION OF NITROGEN AND SULPHUR IN THE URINE DURING CONDITIONS OF INCREASED CATABOLISM.

By DAVID PATON CUTHBERTSON.
From the Biochemical Laboratory of the Royal Infirmary and Pathology Department, Glasgow University.
(Received January 1st, 1931.)

As the result of a series of analyses of the urine of normal subjects on standard diet...

Cuthbertson DP. The distribution of nitrogen and sulphur in the urine during conditions of increased catabolism, *Biochem J*, Vol. 25, No. 1, pp. 236-44, 1931.

Whilst Folin's general hypothesis has been accepted, doubts have been expressed as to whether these various excretory products can be exactly divided into two such groups.

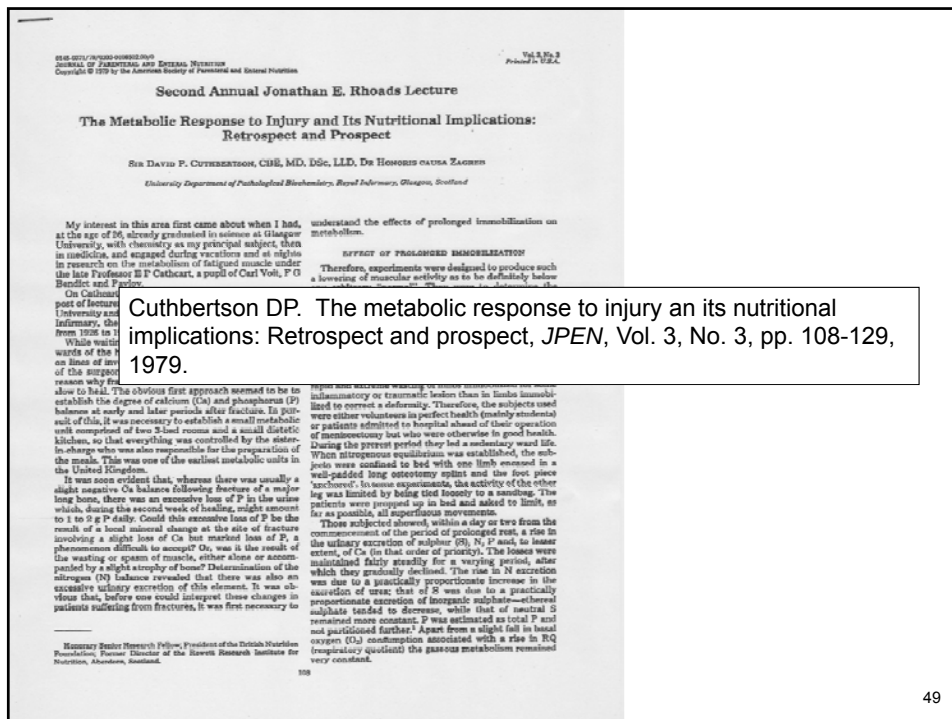
More recent work has demonstrated the difficulty of correlating the creatinine output with the total tissue or endogenous metabolism. Shaffer (1907; 1908, 21), Spriggs (1907, 1, 2), Paton (1910) and Denon and Osterberg (1922) conclude that creatinine is an index of only one phase of this tissue metabolism—that which is peculiarly related to muscle. Spriggs also concluded from his observations that the bulk of the endogenous creatinine output is "a product of the internal structural metabolism of muscle and not of its contraction." Some 30 years ago Sivic (1901) and Burian and Scher (1901) showed severally that uric acid is to a large extent independent of the total amount of nitrogen eliminated. Folin states that while uric acid does not exhibit the quantitative constancy that is found in the case of creatinine at least a certain part of it represents the breaking down of living protoplasm which must be supposed to be essential to the continuation of life. The reduction in the uric acid output when the total metabolism of protein is reduced is irregular and different for different individuals. Folin (1917) has more recently suggested that uric acid might be included as a principal endogenous catabolite.

- “More recently the present author has investigated, in part, the effect of tissue injury on metabolism.”
- “It was found that the urinary excretion of sulphur, nitrogen and phosphorus rose rapidly to a maximum generally within 3 to 6 days from the time of injury.”
- “The S:N ratio suggested that some sulphur-rich tissue, such as muscle, might be the main source of the material catabolised.”

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- “It is obvious in the first place that the source of these nitrogen and sulphur losses cannot be food intake. They must come from the increased catabolic changes in the tissue cells and body fluids.”
- “Urea and inorganic sulphate are the chief products of increased endogenous catabolism.”

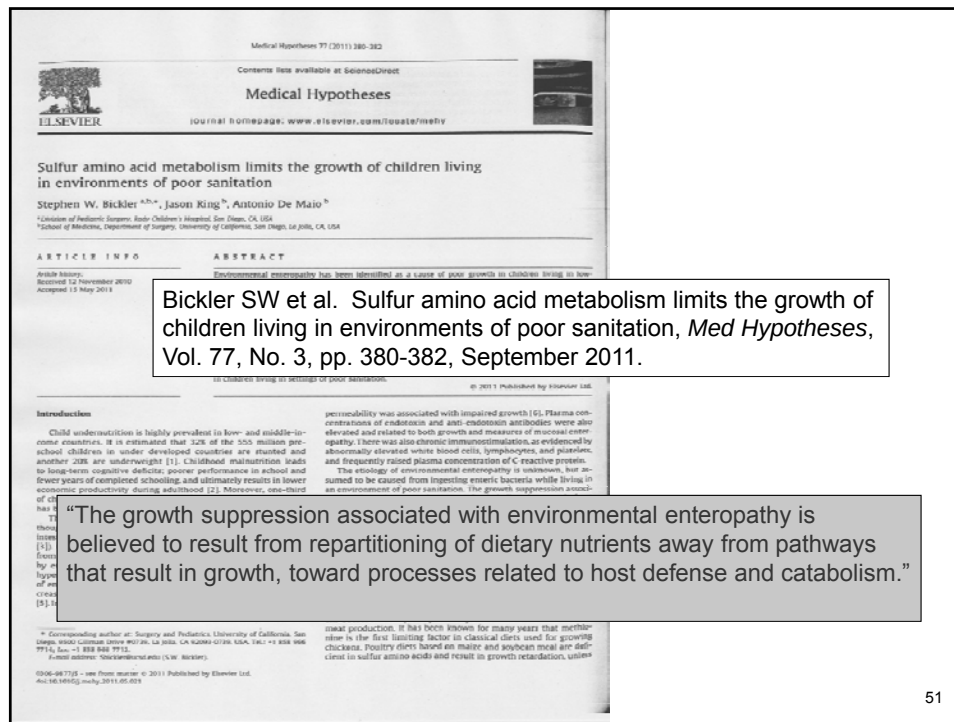
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Cuthbertson DP. The metabolic response to injury an its nutritional implications: Retrospect and prospect, *JPEN*, Vol. 3, No. 3, pp. 108-129, 1979.

The impact of prolonged immobilization

- “Those subjected showed, within a day or two from the commencement period of prolonged rest, a rise in urinary excretion of sulfur (S), N, P and, to a lesser extent, of Ca (in order of priority).”
- “The rise in N excretion was due to a practically proportionate increase in the excretion of urea; that of S was due to a practically proportionate excretion of inorganic sulphate...”



- “In environments of poor sanitation, where chronic and recurrent infections are common, we propose that increased oxidative stress drives methionine influx toward cystathionine production.”
- “This ‘cystathionine siphon’ limits remethylation of homocysteine, a process that intersects with a cellular proliferation pathway.”

- “The principle of a ‘cystathionine siphon’ is illustrated by experimental data in humans demonstrating that even a mild inflammatory challenge such as immunization can drive methionine flux towards cystathionine.”
- “...Mercer et al. showed an increased ratio of transulfuration to transmethylation and decreased ratio of remethylation 2 days following vaccination.”

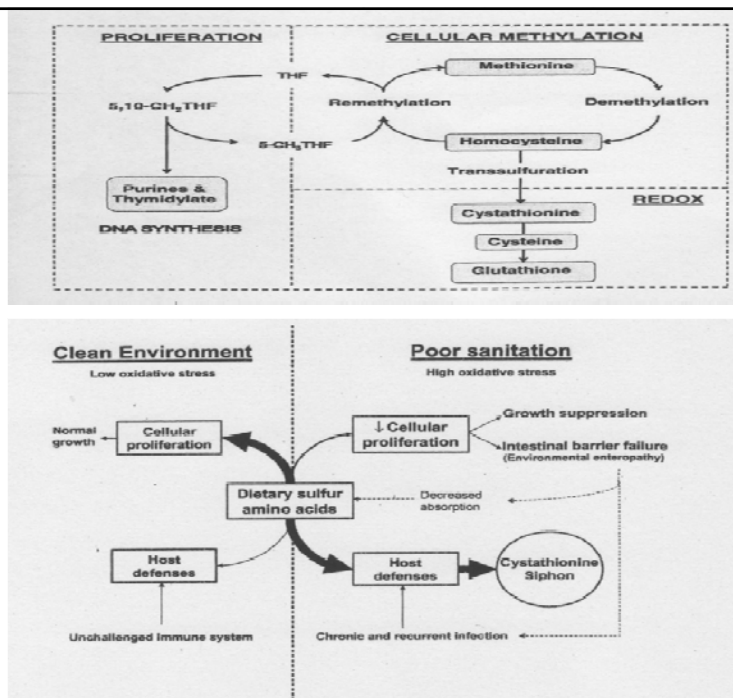
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- “Increased cystathionine β -synthase (CBS) activity could be one mechanism for our proposed ‘cystathionine siphon.’”
- “Both lipopolysaccharide and $\text{TNF}\alpha$ are known to increase CBS activity in vivo.”
- “Enterocytes have a rapid turnover. Therefore, a decrease in protein synthesis is likely to negatively impact cell proliferation and function, and could lead to failure of the intestinal barrier.”

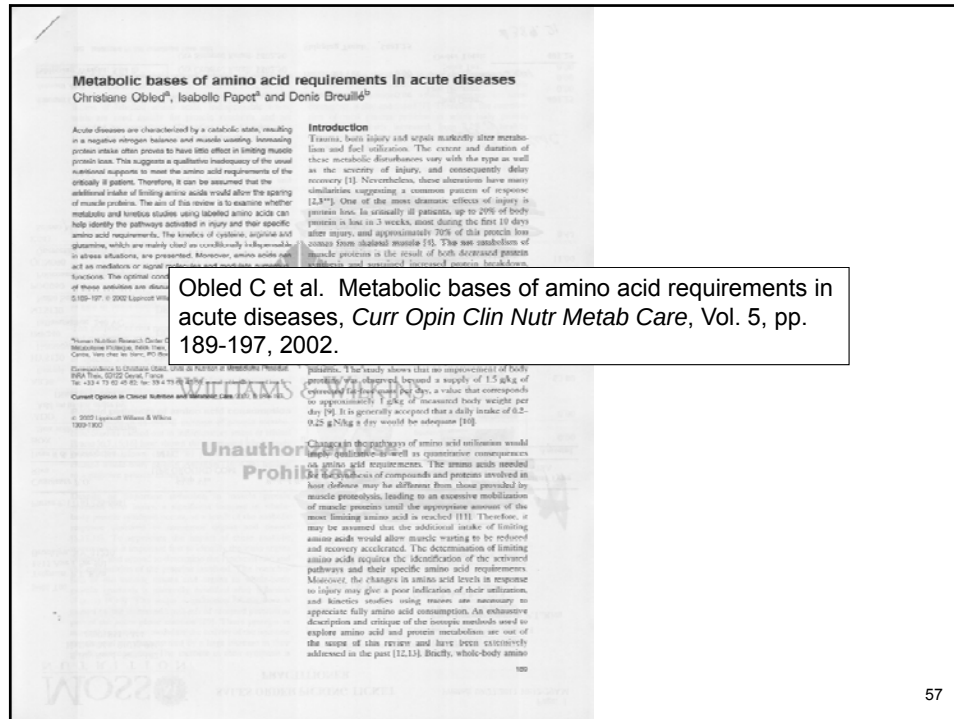
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“Further, limiting dietary sulfur amino acids preferentially affects the jejunal mucosa.”

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- “The amino acids needed for the synthesis of compounds and proteins involved in host defence may be different from those provided by muscle proteolysis, leading to an excessive mobilization of muscle proteins until the appropriate amount of the most limiting amino acid is reached.”
- ***“Preston et al estimated that the synthesis of 1 g fibrinogen would require the degradation of 2.6 g muscle protein.”***

- “The synthesis of cysteine from methionine has been found to increase 2.7 fold 2 days after infection in rats.”
- “Taken together, these results indicate an increased cysteine requirement in diseases.”
- “...catabolic states and chronic diseases are generally associated with the depletion of glutathione pools...”

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Methionine kinetics are altered in the elderly both in the basal state and after vaccination¹⁻³

Sabine Mercier, Denis Breuille, Caroline Buffiere, Jean Glanville, Isabelle Papet, Philippe Ponsard, Mirand, and Christine Dillard

ABSTRACT
Background: Inflammation is known to affect amino acid metabolism. Aging is associated with an increased prevalence of inflammatory conditions but the metabolism of methionine has been poorly explored in the elderly.
Objectives: The aim of this study was to compare methionine kinetics between elderly and young subjects and to explore the effect of aging on the response to a meal by a vaccination.

Design: Seven elderly volunteers (aged 72-85 years) were studied. Methionine, leucine, and methionine kinetics were measured by methyl-¹⁴C-methionine in the post-vaccination state.
Results: Before vaccination, the rate of methionine metabolism was similar in elderly and young subjects. After vaccination, the rate of methionine metabolism was significantly increased in elderly subjects compared to young subjects.

Conclusions: The post-vaccination increase in methionine metabolism observed in elderly subjects is similar to that observed in young subjects. This finding suggests an increased demand for methionine during aging. *Am J Clin Nutr* 2006;83:291-8.

KEY WORDS: Methionine kinetics, vaccination, elderly.
INTRODUCTION
Aging is associated with increased concentrations of inflammatory components in the blood, including acute phase proteins and cytokines. Indeed, marked changes in acute phase proteins occur even among apparently healthy elderly individuals. Concentrations of C-reactive protein, serum glycoprotein, or fibrinogen have been found to be slightly but significantly elevated in elderly subjects (1-3). Moreover, concentrations of the negative acute phase protein albumin are low (2-4). Such changes are representative of subclinical inflammation. Indeed, a deregulation of the immune system occurs in the elderly (5). Elevated circulating concentrations of interleukin 6 and an imbalance between proinflammatory and antiinflammatory cytokines have been reported during aging (6, 7). However, the metabolic and nutritional implications of this low-grade inflammatory state are unclear.

The low-grade inflammation present in the elderly could affect the immune response to additional injury or diseases. An increased risk of death in developing diseases has been reported in elderly persons with elevated concentrations of cytokines or markers of inflammation (8, 9). Indeed, cytokines are involved in the regulation of methionine metabolism, which is a precursor of cysteine and glutathione, which are important compounds for host defense against oxidative stress (10).

In humans, methionine kinetics have been widely studied in healthy young subjects in relation to the markers of methionine metabolism, such as homocysteine (11-13). By contrast, to our knowledge, only one study has been devoted to methionine metabolism in the elderly (24), and the influence of inflammation on methionine metabolism has not been explored.

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Mercier S et al. Methionine kinetics are altered in the elderly both in the basal state and after vaccination, *Am J Clin Nutr*, Vol. 83, pp. 291-8, 2006.

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- “It is well established that the acute phase response leads to important metabolic changes in general and in protein and amino acid metabolism in particular, ie, the metabolism of individual amino acids, especially methionine and cysteine.”
- “In injury, the contribution of the transsulfuration pathway to methionine flux increases, which suggests an increased cysteine requirement in diseases.”

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- “The preferential methionine metabolism toward cysteine synthesis observed after vaccination suggests an increased requirement of sulfur amino acids even in mild inflammatory situations.”
- “The main finding of this study is a higher proportion of methionine entering the transsulfuration pathway in elderly subjects before vaccination.”

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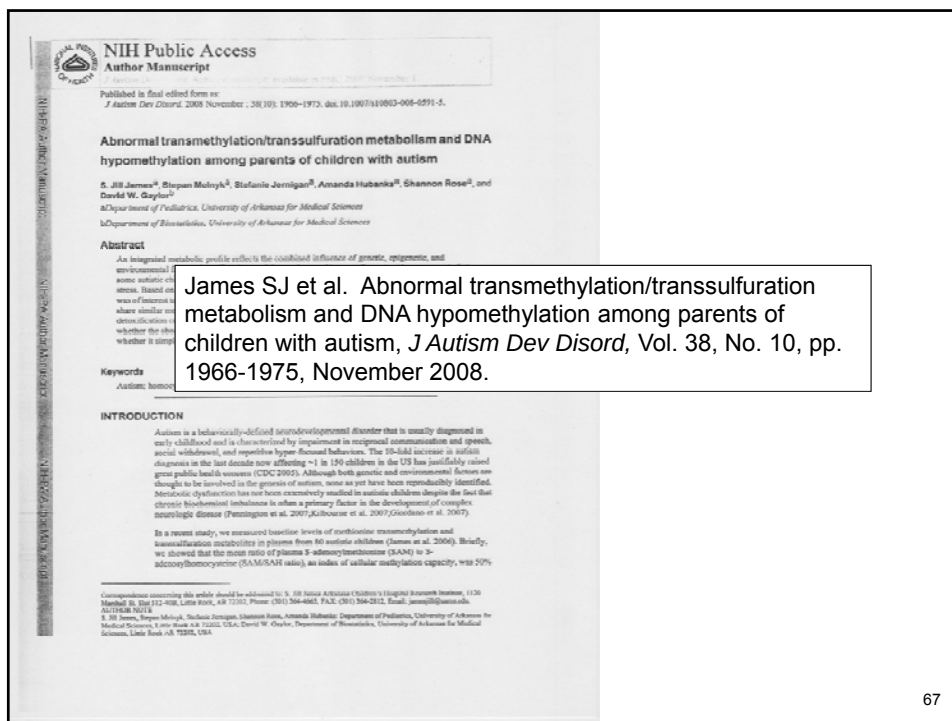


- “The metabolic results indicated that plasma methionine and the ratio of S-adenosylmethionine (SAM) to S-adenosylhomocysteine (SAH), an indicator of methylation capacity, were significantly decreased in the autistic children relative to age-matched controls.”
- “In addition, plasma levels of cysteine, glutathione, and the ratio of reduced to oxidized glutathione, an indication of antioxidant capacity and redox status, were significantly decreased.”

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- “Differences in allele frequency and/or significant gene-gene interactions were found for relevant genes encoding the reduced folate carrier (RFC 80G>A), transcobalamin II (TCN2 776G>C), catechol-O-methyltransferase (COMT 472G>A), methylenetetrahydrofolate reductase (MTHFR 677C>T and 1298 A>C), and GSTM1).”

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- “The results of this study demonstrate for the first time that some parents of children with autism exhibit significant metabolic deficits in methylation capacity (↓SAM/SAH) and in glutathione-mediated antioxidant and detoxification capacity (↓GSH/GSSG).”
- “In summary, we have discovered a significant metabolic imbalance in transmethylation and transsulfuration pathways in many parents that is similar to the imbalance previously observed in many autistic children.”

- “A decrease in the GSH/GSSG redox ratio has been associated with several genetic polymorphisms, chronic dietary deficiencies, and pro-oxidant environmental exposures.”
- “Glutathione can also be decreased by chronic psychological stress and severe anxiety.”
- “The two pathways of transmethylation and transsulfuration are metabolically interdependent such that chronic deficit in glutathione will feed back to inhibit SAM synthesis and create a chronic self-perpetuating cycle that progressively decreases GSH levels.”

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“The fact that both pathways were adversely affected in many parents suggests that the initiating factors were chronic in nature.”

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Organic Acids – Part 10

Dr. Jeff Moss

Metabolic biomarkers of increased oxidative stress and impaired methylation capacity in children with autism^{1,2}

S. Jill James, Paul Carter, Supun Mellek, Stefanie Jernigan, Laurence Joud, David W Geyko, and James A Neuhouser

ABSTRACT
Background: Autism is a complex neurodevelopmental disorder that usually presents in early childhood and that is thought to be influenced by genetic and environmental factors. Although abnormal metabolism of methionine and homocysteine has been associated with other neurologic disorders, these pathways have not been evaluated in persons with autism.
Objective: The purpose of this study was to evaluate concentrations of metabolites in the methionine cycle and the transsulfuration pathway in children with autism.
Design: Plasma concentrations of SAM, SAH, 5-methyltetrahydrofolate, homocysteine, cystathionine, cysteine, and total glutathione were measured in 20 children with autism and 20 children with normal mental and physical development.
Results: Relative to the control children, the children with autism had significantly lower baseline plasma concentrations of methionine, SAM, homocysteine, cystathionine, cysteine, and total glutathione and significantly higher concentrations of SAH, homocysteine, and oxidized glutathione. This metabolic profile is consistent with impaired capacity for methylation and/or a faulty transfer of SAM to SAH.
Conclusion: The metabolic profile of children with autism is consistent with impaired capacity for methylation and/or a faulty transfer of SAM to SAH.
KEY WORDS: Autism, disorder, biomarkers, oxidative stress, methylation, folinic acid, betaine, injectable methylcobalamin.

James SJ et al. Metabolic biomarkers of increased oxidative stress and impaired methylation capacity in children with autism, *Am J Clin Nutr*, Vol. 80, pp. 1611-7, 2004

"The intervention trial was effective in normalizing the metabolic imbalance in the autistic children."

Folinic acid, Betaine, Injectable methylcobalamin

INTRODUCTION
 Autism is a neurodevelopmental disability that is usually diagnosed before age 3 and is characterized by deficits in social interaction and communication skills.
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"Although clinical improvements in speech and cognition were noted by the attending physician, they were not measured in a quantifiable manner and are therefore not reported here."

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Thank you!!

OR CRUMB

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