NutriNotes

"Integrating the Nutrition-Health connection" **Vol 10, #3**

Glutathione: "Your Body's Most Powerful Protector" (GSH) Part I

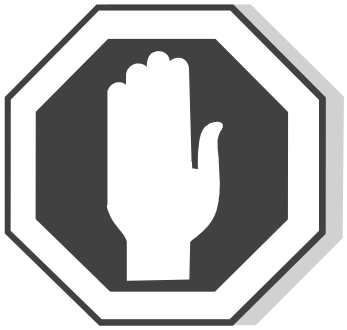
Dr. Jimmy Gutman, author of "Glutathione – your body's most powerful protector", explains why raising glutathione levels in the body can be a very good thing (Jimmy Gutman, MD, "Glutathione – your body's most powerful protector", Kudo.CA Communications, Montreal, Canada 2002). **Dr. Gutman describes glutathione (GSH)** as a cell protector, an antioxidant, a detoxifier, an immune system enhancer, an energy booster, a healing agent, an anti-aging nutrient… and a nutrient possessing many other facets. How can it be and do all these things? In this newsletter, we try to explain glutathione, how it works, why it's so important, and why it does what it does. For instance, glutathione raises ATP levels, and ATP is the currency our body needs for various biochemical reactions. Increasing ATP increases our body's ability to heal itself. Also, oxidative stress, or free radical damage, is responsible for a whole host of health complications, and glutathione can be a helpful nutrient to combat the free radicals and prevent cell injury.

Dr. Gutman describes how glutathione supplementation is used as support for stress, athletic performance, skin disorders, detoxification, pregnancy/lactation, sleep, psychoneurobiology, trauma and burns, seizures, fatigue, digestion, stomach/bowel conditions, kidney issues, arthritis, eyesight, hearing loss, sinusitis, lung problems, MS, lung disease, hepatitis, diabetes, heart disease, ear infections, stroke, cholesterol, Parkinson's and Alzheimer's (among others) and as support for general, overall health.

Glutathione is in many cells; however it is utilized mainly in the liver. It is a tripeptide, which means it's made up of three amino acids: Cysteine, glycine, and glutamate. It functions as an antioxidant, and also as the most important binder of toxins that the body possesses. When toxic substances enter Phase II of liver detoxification, they have to be "conjugated", or hooked onto something that will aid elimination. The main conjugator for these toxins is a nutrient, glutathione.

The problem with just taking glutathione as a supplement is that it is not very efficient, (it is quickly broken down in the digestive tract and eliminated), lowering the efficiency of glutathione supplementation. When taken orally, some glutathione is delivered to the liver; however, to raise glutathione levels efficiently in the body, glutathione nutrient enhancers are the most effective in accomplishing this task. Natural ingredients can serve as precursors (building blocks), or they can enhance glutathione production, by either supporting or directly raising glutathione levels. This newsletter includes descriptions of many of those nutrients that optimize glutathione levels.

Undenatured Whey Bypasses Roadblocks



Undenatured whey is an ideal way to bypass the normal roadblocks to successful cellular glutathione (GSH) production by getting glutathione precursors inside the cells. Normally, the biggest roadblock is the breakdown of glutathione in the digestive tract due to the high prevalence of an intestinal enzyme. This lowers the efficiency of glutathione supplementation. **Undenatured whey, however, is able to bypass these roadblocks, because it contains the precursor building blocks, AND the efficient delivery system** for getting the precursors **inside the cells** where they can then make glutathione.

The whey has bioactive proteins and contains cystine, which is two cysteine molecules held together by a bond that is resistant to digestion. Cysteine, being one of the three amino acids that make up glutathione, facilitates the production of glutathione inside the body's cells because it is the limiting building block. It is deficient in many diets. It does not travel to the cell well unless it is part of a larger protein, and that's where cystine comes in. Being a larger protein, the cystine in whey travels quickly to the cell and then splits into the two cysteine molecules to provide the necessary precursor for glutathione production. The whey also contains an efficient delivery system to transport the cystine to the cells. Moreover, whey contains additional building blocks for glutathione. These building blocks, and the delivery system, are heat-sensitive, but the undenatured whey eliminates this roadblock too, since it has not been exposed to heat. **Glutathione must be manufactured in the cells for efficient production.** Undenatured, unheated whey protein is considered an optimal nutritional source for glutathione production because it provides transportation of these heat-sensitive precursors (cystine and glutamyl-cystine residues) by other heat-sensitive molecules that accelerate delivery (albumin, lactoferrin and alpha lactalbumin), all contained in whey. **For individuals' sensitive to whey, they can still supplement with GSH precursors (see next page) and other nutrients that optimize GSH levels in the body.**

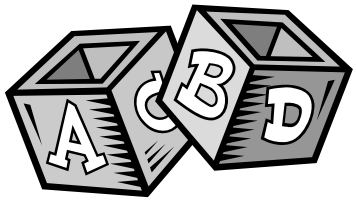
Non-whey nutrients that optimize Glutathione (GSH)

N-Acetyl-Cysteine (NAC) raises glutathione levels in the body: Cysteine facilitates the production of GSH inside the body's cells, but straight cysteine supplementation (contains two molecules of cysteine) can be irritating if taken in its direct form. Supplementing with the precursor N-acetyl cysteine resolves this problem however, and efficiently delivers cysteine to the cells for GSH.production.

Alpha Lipoic Acid enhances the function of GSH, regenerating its active form just as it does several other antioxidants. Conversely, the enzyme GSH-reductase keeps lipoic acid in its active state. It has been suggested that the protection that lipoic acid offers against radiation damage could result from improved cell viability due to increased GSH levels. Dr. Lester Packer of the U of Cal. Berkeley describes lipoic acid as providing the intact cystine, which splits into two cysteines inside the cell for GSH production.

Vitamin C, Vitamin E and Selenium are important antioxidants in a synergistic cycle of regeneration (reactivation) to keep these antioxidants (and GSH) active. Vitamin E also directly modulates GSH-related enzymes, and **selenium** is a critical component in the GSH peroxidase enzyme, the only metabolically active form of selenium in the body.

L-Glutamine provides building blocks for glutathione production. Although cysteine is usually the limiting factor in glutathione synthesis, other building blocks also help.



Milk Thistle encourages growth and regeneration of injured liver cells. **Silymarin** is the active ingredient in milk thistle. It detoxifies xenobiotics (harmful environmental toxins), and it can raise GSH levels as much as 35% in certain GSH-deficient states.

Other nutrients, such as **rosemary,** help to increase glutathione levels, whereas nutrients like **turmeric, which contains curcumin**, prevent the decrease of GSH. Some of the vitamins, such as t**hiamine (vitamin B-1) and riboflavin (vitamin B-2)** are essential components of coenzymes that maintain GSH and related enzymes in their active form. **Vitamin B-6, vitamin B-12, and folic acid** contribute to many enzyme systems, including amino acid metabolism and protein synthesis (such as the production of glutathione). **Folic acid** tends to shunt cysteine favorably in the direction of GSH. **Magnesium** and **Zinc** are necessary for many enzymatic reactions; low levels of magnesium impair an enzyme that is important in GSH synthesis, and low levels of zinc also impede glutathione synthesis, especially in red blood cells.

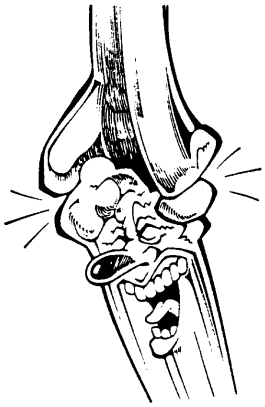
Rosemary also reduces pathogenic substances such as bacteria, raises detoxification enzymes in the liver, and decreases inflammation and liver cell injury (Ahn J. et al. 2004; Sotelo-Felix JI, et al. 2002.)

Super Oxide Dismutase and **catalase** are antioxidant enzymes that protect GSH levels. They are endogenous, or already in the body, as opposed to vitamin C or vitamin E, that we have to take up into the body. However, without proper nutrition, these antioxidant enzymes get depleted.

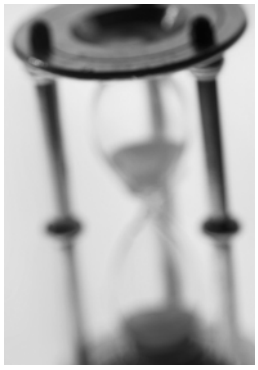
Glutathione (GSH) –
What does it support?

Actually, GSH is backed by strong research describing its dramatic health benefits. Dr. Jimmy Gutman mentions several in his book, including **health, aging, stress, athletic performance, skin disorders, detoxification, fatigue, digestion, pregnancy/lactation, sleep, psychoneurobiology, trauma and burns, seizures, stomach/bowel conditions, kidney issues, arthritis, eyesight, hearing loss, sinusitis, lung problems, MS, lung disease, hepatitis, diabetes, heart disease, ear infections, stroke, cholesterol, BPH, Parkinson's, Alzheimer's, PSA levels, balding/hair loss, infertility … and many other conditions** (Jimmy Gutman, MD, "Glutathione – your body's most powerful protector", Kudo.CA Communications, Montreal, Canada 2002). Knowing the powerful attributes of this antioxidant and toxin-binder, it stands to reason that a multitude of conditions can be supported by GSH supplementation. Let's look at just a few…

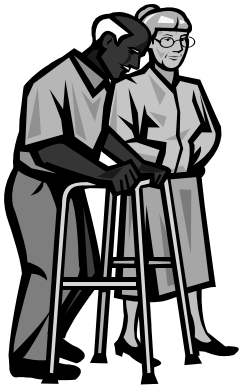
Oxidative stress, immune system function, **detoxification, rheumatoid arthritis, Parkinson's disease, hepatitis, liver cirrhosis, septic shock and diabetes:** "Thus, NAC *(which raises GSH)* offers useful adjunct therapy to **increase protection against oxidative stress, improve immune system function** and **increase detoxification of acetaminophen and other drugs**. These findings suggest that NAC therapy could be valuable in other clinical situations in which GSH deficiency or oxidative stress plays a role in disease pathology, e.g. **rheumatoid arthritis, Parkinson's disease, hepatitis, liver cirrhosis, septic shock and diabetes**" (De Rosa SC, et al. N-acetylcysteine replenishes glutathione in HIV infection. Eur J Clin Invest. 2000 Oct;30(10):915-29).



Rheumatoid arthritis is an inflammatory condition that progresses with aging. A team of rheumatologists from Leiden University Medical Center in the Nederlands diminished inflammation at a cellular level by using NAC (N-acetyl cysteine) to raise GSH in the tissues, and NAC has been known to specifically protect synovial fluid (Grootveld M, et al. The role of N-acetylcysteine in protecting synovial fluid biomolecules against radiolytically-mediated oxidative damage: a high field proton NMR study. Free Radic Res. 1999 May;30(5):351-69; Sakurada S, Induction of cytokines and ICAM-1 by proinflammatory cytokines in primary rheumatoid synovial fibroblasts and inhibition by N-acetyl-L-cysteine and aspirin. Int Immunol. 1996 Oct;8(10):1483-93).



Aging: Glutathione diffuses the free radicals that threaten tissue damage, and thus slows the approach of aging (Guttman, ibid). A plethora of evidence in the literature supports the theory that glutathione affects the aging process by its strong antioxidant, detoxification, and immune powers (Bjork K, D, Glutathione-S-transferase expression in the brain: possible role in ethanol preference and longevity.
FASEB J. 2006 Sep;20(11):1826-35; Tomas-Zapico C, Oxidative damage in the livers of senescence-accelerated mice: a gender-related response. Can J Physiol Pharmacol. 2006 Feb;84(2):213-20; Grzelak A, et al. Accumulation of oxidative damage during replicative aging of the yeast Saccharomyces cerevisiae. Exp Gerontol. 2006 Aug 4; Alvarado C, et al. Dietary supplementation with antioxidants improves functions and decreases oxidative stress of leukocytes from prematurely aging mice. Nutrition. 2006 Jul-Aug;22(7-8):767-77).



Glutathione (GSH) –
What does it support? (cont'd)

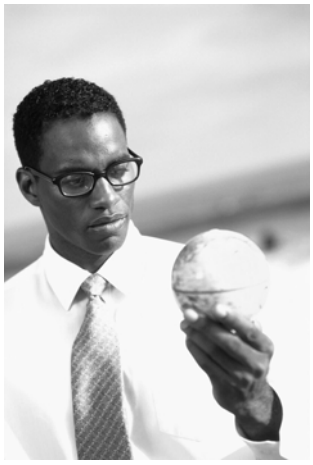
Heavy metal detox: One of the most promising aspects of glutathione research, according to the book "The Biochemical Powers of Glutathione" is the power of GSH to detoxify heavy metals (heavy metals bind to essential enzymes in the body) (Blechman, S. & Kalita, D. The Biochemical Powers of Glutathione" 1982). The National Library of Medicine is full of citations on GSH and its power to bind to metals: Swiergosz-Kowalewska R, Bednarska A, Kafel A. Glutathione levels and enzyme activity in the tissues of bank vole Clethrionomys glareolus chronically exposed to a mixture of metal contaminants. Chemosphere. 2006 May 2; Elumalai M, Antunes C, Guilhermino L. Enzymatic biomarkers in the crab Carcinus maenas from the Minho River estuary (NW Portugal) exposed to zinc and mercury. Chemosphere. 2006 Aug 31; Permina EA, Kazakov AE, Kalinina OV, Gelfand MS. Comparative genomics of regulation of heavy metal resistance in Eubacteria. BMC Microbiol. 2006 Jun 5;6:49; Mishra S, Srivastava S, Tripathi RD, Kumar R, Seth CS, Gupta DK. Lead detoxification by coontail (Ceratophyllum demersum L.) involves induction of phytochelatins and antioxidant system in response to its accumulation. Chemosphere. 2006 May 6).

Pregnancy, Lactation, Childbirth: The newborn's glutathione status will depend on the status of the mother. One of the reasons breast milk builds the immune system of the baby is because it contains glutathione precursors. It is highly important for a newborn to have antioxidant defenses against the toxic assault experienced when they enter the world. The placenta is high in GSH and filters toxins. Many of the problems of pregnancy correlate with low GSH levels; low placenta GSH is associated with harder deliveries, more difficult pregnancies, and poor post-natal health.

"There is every reason to believe that elevated glutathione levels in the mother will counteract the negative effects of many perinatal complications" (Gutman, ibid). For instance, research shows that GSH is correlated to protection against many of the problems in pregnancy, and there is "evidence to suggest that endogenous anti-oxidants (*ie GSH*) are important *(protective)* in the development of complications of pregnancy such as preeclampsia" (Perkins AV. Endogenous anti-oxidants in pregnancy and preeclampsia. Aust N Z J Obstet Gynaecol. 2006 Apr;46(2):77-83.

Sleep: The thalamus and hypothalamus are areas of the brain that are vulnerable to sleep-deprivation, and Tokyo Medical Center researchers showed that high levels of GSH not only promote sleep, but affect other hypothalamic controls as well. Glutathione may even detoxify neuronal tissues more actively during certain periods of sleep (Guttman, ibid). Several studies suggest that obstructive sleep apnea syndrome is associated with oxidative stress (Barcelo A et al. Antioxidant status in patients with sleep apnoea and impact of continuous positive airway pressure treatment. Eur Respir J. 2006 Apr;27(4):756-60). "Glutathione, a major endogenous antioxidant, is an important factor protecting against free radical-mediated neuronal degeneration. **Glutathione has also been proposed to be a sleep-promoting substance**…" (Ikeda M, et al. Brain oxidation is an initial process in sleep induction. Neuroscience. 2005;130(4):1029-40).

Glutathione (GSH) –
What does it support? (cont'd)



Benign prostatic hypertrophy (BPH): A loss of GSH enzyme activity is related to BPH and prostate cancer. Abnormal growth in the prostate often corresponds to deficiencies in GSH enzymes, such as GSH S-transferase. It is possible that a deficit in this enzyme system has a role in both prostate enlargement (BPH) and prostate cancer.

Prostate cancer: Selenium supplementation is associated with decreased occurrence of prostate cancer (selenium is an integral part of the GSH peroxidase enzyme). The function of the enzyme **glutathione S-transferase deteriorates in prostate cancer,** and inactivation of the enzyme is an early event in the malignant development.

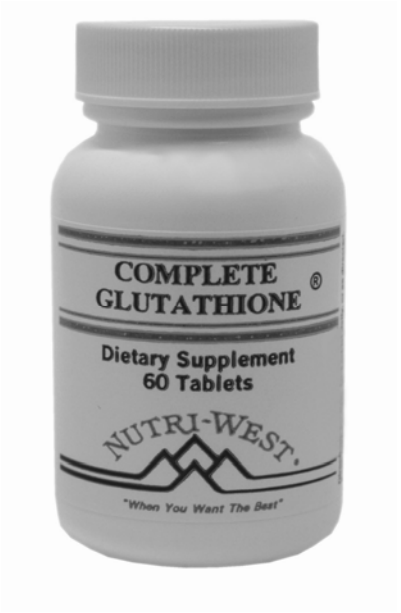
The enzyme activities of superoxide dismutase (SOD), glutathione peroxidase (GPX), catalase (CAT) and copper (Cu) and zinc (Zn) levels were estimated in the erythrocytes of 25 non-metastatic prostate cancer patients, 36 benign prostatic hyperplasia (BPH) patients and 24 age- and sex-matched healthy subjects (controls). **"We hypothesize that an altered prooxidant-antioxidant balance may lead to an increase in oxidative damage and consequently may play an important role in prostate carcinogenesis" (**Aydin A et al. Oxidative stress and antioxidant status in non-metastatic prostate cancer and benign prostatic hyperplasia. Clin Biochem. 2006 Feb;39(2):176-9).

Infertility: Male sperm disorders account for 35% of infertility cases. Oxidative stress (free radical production) is one of the main contributors to loss of sperm function. Glutathione seems to act at the epididymis during sperm formation, and improves the function of ejaculated sperm (Irvine, DS. GSH as a treatment for male infertility. Rev. Reprod. 1:6-12, 1996; Lenzi A et al. Placebo-controlled, double blind, crossover trial of glutathione therapy in male infertility. Human Reproduction 8:1657-1662, 1993).

Balding/Hair Loss. It is believed that free radicals (oxidative damage) play a role in male-pattern baldness, the most common cause of hair loss. Normal hair grows in cycles, where hair falls out in the resting, dormant cycle (telogen). Research positively correlates GSH concentration with the percentage of anagen (active growing phase) hairs, suggesting that glutathione helps maintain the hair growth cycle. Areas with hair have up to three times as much GSH. Glutathione may be influencing the hormones that target hair follicles; follicular GSH activity significantly declines as we age. Rapidly growing cells, such as hair follicles, are most susceptible to chemo toxicity, and N-acetyl cysteine, which raises glutathione levels, not only "enhances the tumor-killing effect of the drug doxorubicin on skin cancer in the lab, but also completely prevents the hair loss that normally accompanies this treatment" (D'Agostini F et al. Inhibition by oral NAC of doxorubicin-induced clastogenicity and alopecia, and prevention of primary tumors and lung metasteses in mice. International J Oncology 13:217-224, 1998; Jiminez JJ et al. Treatment with NAC protects rats from cyclophosphamide/cytarabine-induced alopecia. Cancer Investig. 10:271-276, 1992.)

Complete Glutathione

Formulated by Dr. Dan Murphy



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Synergistic Effect of Fish oil and Raised Glutathione – they work better together!!!!

Research confirms that when the glutathione antioxidant status is boosted, the anti-inflammatory effect of fish oil is INCREASED over what it is when given alone without antioxidant boosting. In a rat model of colitis, there was significant improvement of all biochemical parameters of colonic inflammation. Thus, both colonic myeloperoxidase (MPO) and alkaline phosphatase (AP) activities were significantly reduced compared with untreated colitic rats. In addition, "**a complete restoration of colonic glutathione content, which was depleted as a consequence of the colonic insult, was obtained** …; **this content was even higher than that obtained when colitic rats were treated with FO diet alone**. When compared with the control colitic group, the combined treatment was also associated with a lower colonic nitric oxide synthase and cox-2 expression as well as with a significant reduction in different colonic proinflammatory mediators assayed, i.e. leukotriene B(4), tumor necrosis factor alpha and interleukin 1beta, **showing a significantly greater inhibitory effect**" when raised glutathione was combined with fish oil "Camuesco D, et al. Intestinal anti-inflammatory activity of combined quercitrin and dietary olive oil supplemented with fish oil, rich in EPA and DHA (n-3) polyunsaturated fatty acids, in rats with DSS-induced colitis. Clin Nutr. 2006 Jun;25(3):466-76. Epub 2006 May 15".

****** Next issue will contain more health support uses for glutathione. Stay tuned for additional information!!!***