Smart Life Forum

Tim Guilford, MD

Glutathione in Health and Disease

Cubberly Community Center
4000 Middlefield Road, Room H1, Palo Alto, California

December 15, 2005 at 7:00 PM

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Future Speakers:

- January 19, David Brownstein, MD, **Iodine: Why You Need it, Why You Can't Live Without It**
- February 16, John McDougall, MD, **Why a Vegetarian Diet Works**

Mini-Presentation by Ron Snyder, President of Breakthrough, Inc. (breakthrough-inc.com)

He will present a summary of Strategic Planning Results from our October 1 SLF Board meeting. A brief outline by Phil Jacklin appears at the end of the October newsletter.

Meet Dr. Tim Guilford

He has been using a combination of “mainstream” and “alternative” therapies since the mid-1980's . The techniques include homeopathy, nutritional support and heavy metal detoxification strategies. While the approaches may differ from those currently considered “mainstream”, they are well founded in medical tradition and, where possible, documented in biochemistry. It is easiest to describe the combination he uses as “complementary” allowing a variety of approaches to many problems.

After graduating from the University of Texas Medical Branch Medical School, Dr. Guilford completed a two-year surgery internship and residency at Johns Hopkins Hospital . After that he completed a four-year residency in Otolaryngology (Ear, Nose, Throat Surgery) at the University of Michigan , and was Board certified in Otolaryngology in 1978. In the early 1980's he became interested in allergy. The need for a therapeutic approach to treat children with allergies sparked his initial interest in homeopathic medicine. Since then he has been using low-dose natural combinations to treat allergies in both children and adults. An interest in chronic diseases led to the further study of homeopathy, and to document knowledge in this area, he became licensed in the state of Nevada as a Homeopathic Medical Doctor in 1986. Continued research of the causes of chronic disease led to the exploration of the role of excess toxic metal burden. For 5 years Dr. Guilford conducted clinical research, through a licensed Investigational Review Board, on the effects of toxic metals such as mercury, on chronic disease. Toxic metal excess is being increasingly associated with many illnesses including vascular disease and neurobehavioral problems.

Main Presentation

Glutathione deficiency has been associated with an increasing array of diseases. These include

- Cancer
- Chronic illnesses
- Neurodegenerative diseases
- Cystic fibrosis (CF)
- HIV, and other viral infections
- Autism
- Aging

Reference: Biomed Pharmacother. 2003 May-Jun;57(3-4):145-55
PMID: 12818476

Glutathione is an integral part of the function of every cell in the body. The body produces as much glutathione as glucose. Okay one may say, “If Glutathione is so important, why haven't we heard of it?”

It is hard to imagine that an antioxidant material that has been called the most important antioxidant of eukaryotic cells would be so little known. How else can you describe the situation when there are almost 70,000 Medline articles describing glutathione's role in the basic science of cells, and yet there are barely a dozen clinical medical articles on the use of glutathione. To confirm this, type the single word glutathione into the Medline search engine at http://www.ncbi.nlm.nih.gov/ . Dr. Guilford says if glutathione were hiring a spokesperson, he would have to nominate the late Rodney Dangerfield. Remember, he's the comedian that came up with the line “I can't get no respect”.

What has delayed the understanding of glutathione in the clinical world? It is probably the lack of an easy way to get glutathione into the human system. There have been clinical articles showing that it is useful in the management of Parkinson's disease and even small vessel vascular disease. In both of these articles the glutathione was delivered by the use of intravenous infusion directly into the body. Glutathione in a powdered encapsulation has been available in health food stores for decades. So, why is it that glutathione has not been discovered?

The answer lies in the fact that in humans, glutathione is absorbed poorly from the gastrointestinal tract and shows up minimally in terms of systemic effect after oral ingestion. Some conjecture to explain this by claiming glutathione may be absorbed and utilized in gastrointestinal cells rather than being distributed systemically. The fate of direct oral ingestion of glutathione has been demonstrated in a clinical study showing that

3 grams of glutathione delivered by oral ingestion does not elevate plasma glutathione levels (Witschi, 1992).

The recent development of a liposome encapsulation of glutathione to create a stable, absorbable form of glutathione may be the beginning of our understanding of the clinical benefit of glutathione. ReadiSorb™ Glutathione uses a liposome that is stable in an oral preparation and is readily absorbed into the system. The combination of the active form of glutathione in a liposome may be an ideal tool to explore the role of glutathione in health maintenance. To understand the potential of this tool, let's take a look at how glutathione functions in the body and how it ameliorates the deteriorating effects of oxidation.

The tripeptide L-glutathione (GSH) (gamma-glutamyl-cysteinyl-glycine) is well known in biological and medical studies to serve several essential functions in the cells of higher organisms such as mammals. It is functional when it appears in the biochemical form known as the reduced state, GSH. When oxidized, it forms into an inactive compound, GSSG. Glutathione is not considered an essential nutrient, which means that it is normally formed in adequate amounts in the body from the combination of its amino acid components, glycine, glutamine and cysteine. The biosynthesis of reduced glutathione (GSH) depends on the enzyme gamma-glutamylcysteine synthetase to combine cysteine and glutamine and GSH synthetase to add the glycine to the first two amino acids. The availability of cysteine has been shown to be the component that limits the production of glutathione. There are certain conditions that prevent the formation of glutathione and in this state an outside supply of glutathione becomes essential. The conditional status of the supply of glutathione is apparently at play in children with autism (James).

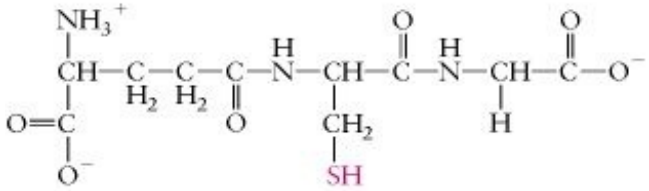
Glutathione in the reduced state (GSH) functions as an antioxidant, protecting cells against free-radical mediated damage, a detoxifying agent by transporting toxins out of cells and out of the liver, and as a cell signal by controlling the oxidative state, particularly in the immune system.

Respiration in an oxygen environment results in the formation of oxygen radicals and oxidation of lipid and proteins in cells. Oxygen metabolism in the mitochondria of the cell results in the movement of electrons derived from food after they have moved through cycles like the Krebs cycle. The energy derived from the electron is transferred to the phosphorous of ADP (adenosine di-phophate) to create ATP (adenosine tri-phophate). At the end of the sequence of transfers the depleted electron is transferred to an oxygen molecule (O) and combined with hydrogens (H) to create H 2 O, water. While this is

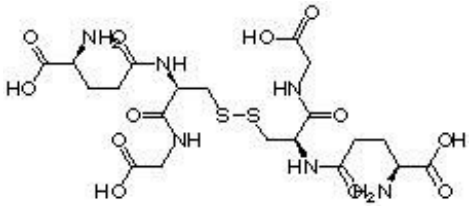
normally a fairly efficient mechanism, oxidative phosphorylation results in the production of free radicals of oxygen at least one to five percent of the time. Without antioxidant protection, the production of free radicals results in destruction of both mitochondria and normal cell structures. Mitochondria as the site of oxygen utilization in our cells are dependent on the production of glutathione from the host cell to maintain their function.

Antioxidant function depends on the ability of a material to remain in the biochemically reduced state. In this state an antioxidant is capable of quenching an oxidation reaction. In the outside world we view oxidation as rust. Inside the body the same reactions related to oxygen are occurring, but the damage shows up initially as damage to fatty membranes and proteins and eventually dysfunction in cells. Cell materials that are oxidized are not functional and generally can not be restored to a functionally state. Antioxidants maintain cell materials in the reduced or functional state. A characteristic of antioxidants such as vitamin C and glutathione is that after donating an electron to stabilized free radicals and thus becoming oxidized, antioxidants can be restored to a functional for reduced state bay another antioxidant.

The restorative relationship between antioxidants is illustrated by the continuing interaction of reduced vitamin C, vitamin E and glutathione keeping each other functional. Glutathione in the reduced state, abbreviated GSH -



The oxidation of glutathione creates two combined molecules of glutathione called GSSG.
The sulfur, which is the active site, is now combined with itself in a double bond, leaving the molecule inactive.



glutathione

The interaction of glutathione with another antioxidant of reducing agent will break the double bond and restore GSSG to the active or biochemically “reduced” state.

Tim Guilford's personal interest in glutathione developed from studies of the toxicity of mercury. As a toxin, mercury will cause the displacement of normal minerals, the interruption of enzymes systems and will deplete glutathione. The first measurable sign of mercury toxicity is depletion of glutathione in lab animals given non-lethal doses of mercury. Glutathione is a major component of the detoxification pathway known as the phase II component of detoxification. This is the main method of the removal of mercury, with a molecule of glutathione attaching to mercury to facilitate its removal. It requires at least two and in some situations three molecules of glutathione to remove a single molecule of mercury. This is because mercury must first be reduced from the +3 oxidized state to the +2 state, then to the +1 state to be combined with glutathione and removed from the lipid soluble state by glutathione. In situations where glutathione is being used up rapidly to remove toxins, the ability to form new glutathione becomes critical. It is just this type of situation in which the production of glutathione is needed, yet cannot be formed, that has been found to be present in autism. The observation of deficient glutathione as a biomarker of disease was published about a year ago by Jill James, PhD. See report by James SJ, Cutler P, Melnyk S, Jernigan S, Janak L, Gaylor D, and Neubrander J; entitled: “Metabolic biomarkers of increased oxidative stress and impaired methylation capacity in children with autism Amercan Journal of Clinical Nutrition 2004;80:1611–7. PMID: 15585776”.

A liposome is a microscopic fluid-filled pouch whose walls are made of one or more layers of phospholipid materials identical to the phospholipid that makes up cell membranes. Liposomes could be referred to as nanoscopic, i.e. on the order of one-billionth of a meter in size. The liposomes used in the present invention are between 100 and 500 nanometer in size. That small size enables liposomes to pass through many cell walls and chemical pores (like a chemical hole), which penetration of a cell could not occur if the substance was not contained in a liposome. In addition, liposomes are known to fuse with cells and

to deliver their contents into the cell. Lipids can be used to deliver materials such as drugs to the body because of the enhanced absorption of the liposome. The outer wall of the liposome is fat soluble, while the inside is water-soluble. This combination allows the liposome to become an excellent method for delivery of water-soluble materials that would otherwise not be absorbed into the body. Common materials used in the formation of liposomes are the constituents derived from constituents of the food lecithin.

ReadiSorb™ Glutathione, a liposomal encapsulation of reduced glutathione, may provide a clinical tool for the observation of the clinical effects of the oral ingestion of glutathione to maintain glutathione levels. At this time there are no clinical studies from which claims may be made. There are, however, sufficient clinical anecdotes to warrant further study. More information is available at www.readisorb.com .