James L. Holly, M.D.

Glutathione and Oxidative Stress - Part I By: James L. Holly, MD

Oxidative Stress refers to effects from endogenous (produced in the body) toxins (free radicals) produced in the body by normal metabolism and exogenous toxins from the environment. Historically, oxidative stress was not as important because our environment was not as filled with toxins as it is today. Additionally, people ate what they grew, or what they "caught," or killed. Those foods were natural and healthy. Even the meats which were eaten were healthier because they contained less fat. Actually, men and women have taken antioxidants for centuries, but didn't know it. They called them "vegetables."

Remember the "antioxidant network?" This is a term applied to five antioxidants which work together to help protect the body against the effects of free radicals and aging.

They are:

- Vitamin C
- Vitamin E
- CoQ10
- Alpha Lipoic Acid
- Glutathione

Before reading further, here is the conclusion: Because of oxidative stress placed on our bodies by normal metabolism, bad habits, bad food and bad environmental conditions, all adults should be taking supplemental dosages of these antioxidants. As will be shown, Glutathione is the most difficult because it is questionable whether supplements of glutathione effectively increase glutathione blood levels. Therefore glutathione levels should be "boosted" in the body by taking the building blocks which raise glutathione levels. Some of those "building blocks" are the essential branched amino acids found in whey, cysteine, Vitamin C and N-acetylcysteine. The recommended dosages of each of these will be given in the conclusion to our discussion of Glutathione next week. The following week, we will discuss whey, what it is and how it helps your body stay healthy.

What is Glutathione?

Glutathione is a small protein composed of three amino acids: cysteine, glutamic acid and glycine. It is involved in detoxification of the liver and the body. Glutathione to toxins, such as heavy metals, solvents, and pesticides, and transforms them into a form that can be excreted in urine or bile.

Glutathione is also an important antioxidant, counteracting the effects of free radicals produced in the body by oxidation reactions. In preliminary research, dietary glutathione intake from fruit and raw vegetables has been associated with protection against some forms of cancer. Glutathione has also inhibited cancer in test tube and animal studies. In preliminary research, higher glutathione levels have also been associated with good health in older adults.

Glutathione Supplements Absorbed by Rats but not by Man

Glutathione supplements appear to be efficiently absorbed in rats. However, the same may not be true for glutathione supplements in humans. For example, when seven healthy subjects were given a single application of up to 3,000 mg of glutathione, there was no increase in blood glutathione levels. The authors of the study concluded, "it is not feasible to increase circulating glutathione to a clinically beneficial extent by the oral administrating of a single application of 3,000 mg of glutathione." The absorption of glutathione may be better in rats because unlike the gastrointestinal tract of rats, the human gastrointestinal tract contains significant amounts of an enzyme that breaks down glutathione. Very preliminary evidence has suggested that absorption of glutathione can occur in the mouth when glutathione tablets are placed between the teeth and the inner cheek.

An unpublished preliminary study of eight colon cancer patients also found that oral glutathione appeared to have anticancer activity. Nonetheless, because questions exist about the extent to which oral glutathione can be absorbed, some doctors are concerned that oral preparations may be either less effective than other forms or not effective at all.

How to Raise Glutathione Levels

Some supplements other than oral glutathione may be more effective in raising blood levels of glutathione. For example, in one trial, blood glutathione levels rose nearly 50% in healthy people taking 500 mg of vitamin C per day for only two weeks. Vitamin C raises glutathione by helping the body manufacture it. In addition to vitamin C, other nutritional compounds that may, according to preliminary research, help increase glutathione levels include:

- alpha lipoic acid,
- glutamine,
- methionine.
- S-adenosyl methionine (SAMe), and
- whey protein.

• Vitamin B6, riboflavin and selenium are required in the manufacture of glutathione.

The extent to which any of these nutrients effectively increase glutathione levels in humans remains unclear.

Dietary Glutathione

Where is it found? Dietary glutathione is found in:

- fresh and frozen fruits and vegetables,
- fish and meat.
- Asparagus,
- avocado and
- walnuts are particularly rich dietary sources of glutathione.

Glutathione can be taken in supplement form but may not be effective. The production of glutathione by the body can be boosted by taking supplemental:

- N-acetylcysteine or
- L-cysteine plus
- L-methionine.

Studies suggest that this may be a better way or raising glutathione levels than taking glutathione itself.

Intravenous Glutathione

Studies using intravenous or intramuscular glutathione have found it to be useful for preventing or treatment of:

- blood clot formation,
- the side effects and increasing the efficacy of chemotherapy drugs;
- Parkinson's disease;
- blood pressure in people with diabetes; and
- sperm counts in men with low sperm counts
- symptoms in people with chronic rhinitis via a nasal spray.

Glutathione's Defense of the Body

Glutathione helps to defend the body against damage from:

• cigarette smoking -- see below for the dramatic and frightening result of a single puff of smoke from a cigarette

- exposure to radiation
- cancer chemotherapy
- toxins such as alcohol
- As a detoxifier of heavy metals and drugs, it aids in the treatment of blood and liver disorders
- Glutathione protects cells in several ways:
- Neutralizes oxygen molecules before they can harm cells.
- With selenium, it forms the enzyme glutathione peroxidase, which neutralizes hydrogen peroxide -- one of the most aggressive and harmful free radicals produced by the oxidation reaction in cells.
- as a component of another antioxidant enzyme, glutathione S-transferase, which is a broad-spectrum liver-detoxifying enzyme.
- Glutathione also protects individual cells and the tissues of the arteries, brain, heart, immune cells, kidneys, lenses of the eyes, liver, lungs, and skin against oxidant damage.

Glutathione also:

- Plays a role in preventing cancer, especially liver cancer.
- May have an anti-aging effect.
- Where is Glutathione Found in the Body?

Glutathione is not technically an amino acid, however, due to its close relationship is normally grouped with the amino acids. Most glutathione is found in the liver where it detoxifies many harmful compounds to be excreted thru the bile. Some glutathione is released directly by the liver into the bloodstream where it helps to maintain the strength of your red blood cells and also protecting your white blood cells.

Glutathione can also be found in the lungs and in your body's intestinal tract system. It is required for carbohydrate metabolism. Glutathione also appears to have anti-aging effects by aiding in the breakdown of oxidized fats that may contribute to atherosclerosis. As we get older glutathione levels in the body get lower and this can cause an increase in the aging process. Thus glutathione enhancement may be useful to prevent this from occurring.

Glutathione Deficiency

Glutathione deficiency may be indicated by:

- coordination problems,
- mental disorder,
- tremors,
- twitching,
- nervous system disorder, and
- difficulty in balancing.

• Glutathione depletion leads to cell death, and has been documented in many degenerative conditions. Mitochondrial glutathione depletion may be the ultimate factor determining vulnerability to oxidant attack.

Glutathione exists in two forms:

- 1. The antioxidant "reduced glutathione" tripeptide is conventionally called glutathione and abbreviated GSH.
- 2. The oxidized form is a sulfur-sulfur linked compound, known as glutathione disulfide or GSSG.

The GSSG/GSH ratio may be a sensitive indicator of oxidative stress.

Glutathione Recycles Other Antioxidants

Through its significant reducing power, GSH also makes major contributions to the recycling of other antioxidants that have become oxidized. When an antioxidant does the work of inactivating a free radical, it becomes inert. Glutathione has the capacity to "re-activate" the other antioxidants in the "network" (Vitamin C, Vitamin E, Alpha Lipoic Acid and CoQ10) extending their life and usefulness and increasing the antioxidant capacity of your foods and supplements.

Next week, we will continue our discussion of Glutathione. The good news is that now more than ever you can take positive steps to improve your health. Good health is often a choice of what you eat and what you do.

Remember, it is your life and it is your health.