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NARROWING THE PHARMA-NUTRITION GAP

THE ANTIOXIDANT DEBATE

Which Way Next?

• ingredients • functional foods • nutraceuticals • supplements • raw materials •

GLUTATHIONE

THE KEY TO REPAIRING DAMAGED CELLS

At any given moment, thousands of our cells are dying. In fact, the saying, "We begin to die the moment we are born" is, in a matter of speaking, true. And, as paradoxical as it may seem, the cellular death that we experience is essential to living. This seemingly contradictory process is, in actuality, a brilliantly engineered survival strategy. At the core of this strategy lies the fact that our cells can become damaged. A damaged cell must either repair itself or, if the damage is too overwhelming, must be deleted so that it will not compromise the health of the tissue of which it is a part. Apoptosis, or programmed cell death, efficiently and tidily removes these damaged cells.

Apoptosis refers to a cell-initiated process of destruction and death. It is often referred to as cellular suicide because the process starts within the damaged cell. Apoptosis is the most efficient and least inflammatory way to remove damaged cells. In response to cellular damage to critical parts of the cell's DNA or organelles, molecules released as part of the damage activate repair genes. These repair genes code for certain proteins that are used to repair damage. However, if the cell cannot be functionally repaired, suicide — or apoptotic — genes are activated. These genes initiate a cascade of events within the cell that ultimately cause the cell to involute and cease to function. It is then engulfed by roving phagocytic immune cells and completely digested.

Stimulators of Apoptosis

The main trigger for apoptosis is DNA damage. In fact, DNA damaging agents such as ionizing radiation and chemotherapy rely upon apoptosis to be effective treatments against cancer. These damaging agents cause enough DNA damage to initiate apoptosis in cancerous (and some other) cells. Other agents that, when present to a sufficient degree, cause sufficient physical damage to initiate apoptosis are heat, cold, physical trauma and oxidative damage from compounds such as alcohol, tobacco smoke, industrial pollutants, infections and UV exposure. These agents damage DNA and, if the damage is too great for repair, apoptotic proteins are released.

Antioxidants and Apoptosis

We typically think of antioxidants as agents that prevent cell damage by neutralizing oxidative or free radical compounds. This function of antioxidants is fundamentally important. Given the constant exposure to oxidants in the environment, as well as the oxidative compounds released as a part of core activities such as eating, breathing and exercising, we would quickly be overwhelmed with cellular damage without the neutralizing defence of antioxidants. There is, however, an additional protective role of antioxidants that is perhaps less widely realized. Whereas apoptosis is initiated by oxidative stress, antioxidants initiate and preserve apoptosis. Antioxidants then serve a dual role; they prevent oxidative damage and, when damage has occurred, they stimulate and chaperone the apoptotic process.

The major endogenous (within the body) antioxidants involved in neutralizing free radical damage, as well as in preserving apoptosis, are glutathione, ubiquinol, SOD and catalase. Of these, glutathione is the most ubiquitous antioxidant in the human body. Glutathione is a tripeptide composed of glutamate, cysteine and glycine. It is found throughout the body and is particularly concentrated in the liver where detoxification activities are paramount. Glutathione enables apoptosis in two key ways: it defends the DNA against free radical damage, thereby preventing damage to pro-apoptotic genes; and glutathione preserves the structure and function of key cellular proteins that signal apoptosis. Without glutathione, apoptosis would be unlikely to occur. Glutathione levels are highest for about 6 hours after each meal. Our lowest level of glutathione is in the morning before our first meal. Although healthy children and young adults tend to have sufficient glutathione, its production decreases as we age. Once we reach the age of 45, we begin to produce less glutathione. Add to this any glutathione-depleting activities, and our glutathione stores can become seriously low.

Lifestyle choices that deplete glutathione include chronic excessive alcohol consumption, dietary deficiencies and constant, excessive stress. Alcohol consumption creates oxidative damage that, in turn, leads to DNA damage, thus stimulating cell repair or apoptosis. However, chronic alcohol consumption ultimately depletes glutathione, which results in impaired apoptosis. The result of this depletion is survival of alcohol-damaged cells. The proliferation of these damaged cells ultimately manifests itself in liver disease, neurological diseases, cancer and heart disease — all health conditions of alcoholism. A glutathione deficient diet is, unfortunately, far too common. Studies have found that Americans only consume from 3–150 mg of glutathione per day. The average intake is 35 mg per day. An optimal intake of glutathione is more than 250 mg per day, so the average person's diet is deficient. Additionally, foods such as cereals, bread, tea, coffee and dairy products not only lack glutathione, they destroy it.

Chronic stress is another sure-fire way to deplete glutathione. Chronic neuroendocrine stress leads to the elevation of stress hormones and an increased metabolic rate,

which is frequently accompanied by oxidative damage and depleted antioxidants. High levels of stress hormones also promote lipid storage in organ fat rather than subcutaneous fatty tissue. Fat cells secrete several proinflammatory cytokines, which increase oxidation and deplete glutathione. The result of this process is cell injury, organ damage and disease.

Glutathione Restoration

The importance of glutathione to apoptosis and, therefore, cellular viability and tissue health requires daily replenishment. Glutathione is found in a variety of foods, particularly fruits, vegetables and meats. Foods rich in glutathione include asparagus, spinach, garlic, avocado, squash, zucchini (courgette), potatoes, melons, grapefruit, strawberries and peaches. Herbs such as turmeric, cinnamon and cardamom contain flavonoid compounds that, in turn, increase glutathione production. There are also dietary precursors of glutathione. Brazil nuts, meat and seafood contain high amounts of selenium: just one or two Brazil nuts daily supplies sufficient selenium for most people to support glutathione production. Alpha lipoic acid will increase the production of glutathione and is found in red meat, organ meats (such as liver) and yeast (particularly Brewer's yeast). Riboflavin, found in sunflower seeds, spinach and avocados, is required for glutathione production. Glutathione production is dependent upon its sulphur-containing precursor amino acid, cysteine. Eggs and garlic are good sources of sulphur-containing amino acids.

In addition to diet, certain lifestyle interventions will restore glutathione to more optimal levels. In particular, activities that reduce stress have the greatest impact. One such activity is yoga. A clinical trial was conducted on healthy male volunteers from the Indian Navy who were divided into two groups — a yoga group and a control group. The yoga group was trained in yoga for 6 months. The yoga schedule consisted of prayers, asana, pranayama and meditation. The control group practiced routine physical training exercise for 6 months. Glutathione levels increased significantly ($p<0.05$) in the yoga group compared with the control group after completing the training. In a similar study, meditation was found to increase glutathione. In this study, 42 Sudarshan Kriya meditation practitioners and 42 normal healthy controls who did not practice yoga were recruited for the study. The meditators had a better antioxidant status, better stress regulation and up-regulation of repair and antiapoptotic genes.

Another viable strategy for glutathione restoration is oral supplementation with a glutathione dietary supplement. Because glutathione is naturally low in the morning, in those with insufficient overall glutathione, the early morning represents a time of very low glutathione. This translates into a window of vulnerability to oxidative insult. Supplementing glutathione, particularly in the morning, may reduce this risk. Glutathione supplementation is typically dosed between 100–300 mg daily. Despite opinions about the poor absorption of glutathione, oral glutathione is, just like other proteins, absorbed orally. There is a significant body of data that documents the bioavailability of glutathione from oral dosing.

Until Death Do Us Part: Antioxidants

The two fundamental processes that protect us from developing chronic diseases such as cancer, heart disease and neurological diseases in the face of oxidative damage are cell repair and apoptosis. Antioxidants are required for both of these protective pathways and, thus, essential for healthy life. Glutathione is perhaps the most important antioxidant in our bodies and sufficient glutathione will usher the destruction of damaged cells and preserve the repair and survival of healthy cells, ultimately supporting long-term vitality.

Cellular Suicide

One way to think about apoptosis is with an analogy. Let's say there is a forest of hundreds of oak trees, most of which are healthy. However, in the midst of this forest, there are several diseased and sickly trees. These trees are peppered throughout the forest. One way that the forest remains healthy is because those diseased trees, unable to grow and thrive like their healthy neighbours, become shaded from the sun, cannot grow their roots as deep or wide and eventually die. An opportunistic logger might then come and fell that dead tree and haul it away. This process is analogous to apoptotic cell death. The other option for the forest is if the diseased tree remains alive and spreads its disease to its neighbouring trees. Ultimately, the forest becomes weakened from disease and prone to destruction by pests or fire. This latter process is analogous in the human body to a process called necrosis. Necrosis is a process of cellular death and tissue damage initiated typically by the molecules of inflammation. Necrosis is messy, potentiates inflammation and can ultimately lead to serious illness and death. One can begin to understand the criticality of apoptosis to health and survival. In fact, defects in apoptosis can lead to cancer, autoimmune disease, chronic viral infections, atherosclerosis and neurodegenerative disorders. All of these disorders, incidentally, are characterized by tissue necrosis.

For more information

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