Glutathione in Health and Disease

BY PATRICIA KONGSHAVN, MSC, PHD

Glutathione (g-glutamylcysteinylglycine, GSH) is a water-soluble tripeptide composed of the amino acids glutamate, cysteine, and glycine. Present in all mammalian cells, it is widely distributed throughout the animal and plant kingdoms, underscoring its fundamental biological significance.

GSH is an endogenous antioxidant of great importance, as well as being a detoxicant of exogenous and endogenous toxic compounds. In addition, it plays a vital role in many other cell cycle-related events, including protein synthesis and gene expression. Not surprisingly, more than 25,000 medical articles on GSH have appeared over the last five years. A number of review articles have provided the basis for the material presented here.[1-7]

BENEFITS OF GSH

GSH is a key antioxidant responsible for protecting the cell from damage by reactive oxygen species (ROS) such as peroxide, superoxide anion, and the hydroxyl radical.

GSH is responsible for detoxification of xenobiotics (eg, benzene compounds, acetaminophen), as well as endogenously produced potentially toxic metabolites such as prostaglandins and leukotrienes. Much of this detoxification occurs in the liver and kidneys. These substances are converted by GSH into inactivated water-soluble conjugates that can then be easily excreted.

GSH status plays an important role in innumerable cell functions, including gene expression, DNA synthesis and repair, protein synthesis, cytokine production, enzyme activation, and signal transduction. This has a broad-reaching effect, one consequence being that GSH affects the ability of cells to proliferate in the body. It is perhaps for this reason that the immune system is particularly vulnerable to GSH deficiency since lymphocytes need to proliferate to develop an effective immune response.

GSH AND DISEASE

GSH plays crucial roles in antioxidant defense, detoxification, and the regulation of pathways essential for whole-body homeostasis. GSH deficiency contributes to oxidative stress and therefore appears to play a key role in the pathology of many diseases.

Patients with liver disease are GSH-depleted.[1,6] Altomare et al,[8] for instance, studied 35 chronic alcoholic patients and 20 nonalcoholic patients with liver disease (acute and chronic hepatitis, fatty liver, and cirrhosis) and observed decreased GSH in both groups when compared with control patients. These investigators postulated that the decreased GSH contributed to liver injury susceptibility. Thus, in patients with liver disease, GSH deficiency exists, which may predispose to further liver toxicity caused by the resultant inadequate defense mechanisms.

GSH deficiencies have been documented in a number of pulmonary diseases, including acute respiratory distress syndrome, asthma, chronic obstructive pulmonary disease, idiopathic pulmonary fibrosis (IPF), cystic fibrosis, and neonatal lung damage.[1,6] GSH concentrations in the epithelial lining fluid (ELF) are only 25% of normal values in IPF, for example.[9] The ELF normally contains 150 times more GSH than in other tissues,[6] where it serves to protect the lungs against oxidative darnage, environmental toxins, and atmospheric pollutants. Low levels of GSH lead to inflammation and oxidative stress with resultant damage to cell membranes, cellular proteins, and DNA.

The brain is highly susceptible to oxidative damage. and a depletion of antioxidants, including GSH, has been