

[Med Hypotheses](#). 2006;67(3):578-87. Epub 2006 Apr 18.

## **A nutritional supplement formula for influenza A (H5N1) infection in humans.**

[Friel H](#), [Lederman H](#).

howardfriel@verizon.net

### **Abstract**

By early February 2006, the World Health Organization had reported 165 human cases of H5N1 influenza since December 2003, with 88 fatalities. However, the avian H5N1 influenza virus apparently is not yet efficiently transmitted between humans. Though a near-term possibility of a global H5N1 influenza pandemic remains, currently there is no vaccine or anti-viral drug that is proven to be safe and effective in preventing or treating H5N1 influenza in humans. There is thus a compelling public interest in developing alternative prophylaxis and treatment strategies for H5N1 influenza, which would need to address the complex pathogenesis of H5N1 influenza that is responsible for its apparently unusually high virulence. The authors present here a significant body of medical and scientific evidence to support the prophylactic use of a carefully designed nutritional supplement formulation that may antagonize the major pathogenic processes of H5N1 influenza in humans. Through several independently-mediated mechanisms, the formulations may: (a) degrade H5N1 virulence by directly affecting the virus itself, (b) inhibit H5N1 viral replication by maintaining cellular redox equilibrium in host cells, (c) inhibit H5N1 replication by a blockade of the nuclear-cytoplasmic translocation of the viral ribonucleoproteins and reduced expression of late viral proteins related to the inhibition of protein kinase C activity and its dependent pathways, (d) down-regulate activation and proliferation of proinflammatory cytokines in respiratory epithelial cells and macrophages that are implicated in the pathogenesis of H5N1 influenza, and (e) protect the lungs and other vital organs from virus- and cytokine-induced oxidative stress by supplying and maintaining sufficient levels of exogenous and endogenous antioxidants. Key mediators in these processes include selenium, vitamin E, NAC/glutathione, resveratrol, and quercetin. Taken prophylactically, and throughout the duration and recovery of an H5N1 infection, the nutritional supplement formula may aid humans infected with H5N1 influenza to survive with a reduced likelihood of major complications, and may provide a relatively low-cost strategy for individuals as well as government, public-health, medical, health-insurance, and corporate organizations to prepare more prudently for an H5N1 pandemic. Some evidence also indicates that the supplement formulation may be effective as an adjunctive to H5N1 vaccine and anti-viral treatments, and should be tested as such.

PMID: 16624496 [PubMed - indexed for MEDLINE]



[FASEB J.](#) 2009 Oct;23(10):3263-72. Epub 2009 Jun 19.

# Glutathione--a review on its role and significance in Parkinson's disease.

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## Abstract

Parkinson's disease (PD) is the second most common neurodegenerative disease, affecting over a million people in the United States alone, and is characterized by rigidity, bradykinesia, resting tremor, and postural instability. Its main neuropathological feature is the loss of dopaminergic neurons of the substantia nigra pars compacta. However, the pathogenesis of this loss is not understood fully. One of the earliest biochemical changes seen in PD is a reduction in the levels of total glutathione, a key cellular antioxidant. Traditionally, it has been thought that this decrease in GSH levels is the consequence of increased oxidative stress, a process heavily implicated in PD pathogenesis. However, emerging evidence suggests that GSH depletion may itself play an active role in PD pathogenesis. This review aims to explore the contribution of GSH depletion to PD pathogenesis.

PMID: 19542204 [PubMed - indexed for MEDLINE]



[Jpn Heart J.](#) 1996 Mar;37(2):177-82.

## Decreased glutathione levels in acute myocardial infarction.

[Usal A](#), [Acartürk E](#), [Yüregir GT](#), [Unlükurt I](#), [Demirci C](#), [Kurt HI](#), [Birand A](#).

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### Abstract

Although experimental studies have demonstrated that reduced glutathione (GSH) is involved in cellular protection from deleterious effects of oxygen free radicals (OFRs) in ischemia and reperfusion, there are controversial data on the correlation between the levels of erythrocyte GSH and the ischemic process. To clarify, we determined the erythrocyte GSH levels in 21 patients with acute myocardial infarction (AMI), aged 39-70, who were not given thrombolytic therapy and 21 age- and sex- matched healthy controls. Samples of blood were taken on days 1, 3, 5 and 7 from AMI patients and on the same days from the controls. The GSH levels of patients with AMI were significantly depressed by 11.5% as compared to the controls on the second day after infarction ( $7.44 \pm 1.71$  vs  $8.41 \pm 1.54$  U/gHb  $p < 0.05$ ). Although the total mean of GSH levels for all days was lower (3.8%) in patients than in the controls, this finding did not reach statistical significance ( $7.41 \pm 1.71$  vs  $7.71 \pm 1.27$  U/gHb, ns). There was no correlation between the erythrocyte GSH levels and cardiac enzyme concentrations, infarct localization, hemodynamic status according to Killip classification and the frequency of ventricular arrhythmias. This preliminary work suggests that depressed GSH levels may be associated with an enhanced protective mechanism to oxidative stress in AMI. Measurements of erythrocyte GSH can be helpful in the estimation of oxidative stress in the course of AMI. However, further research must be done to determine the primary scavenger in AMI by analyzing all the enzymes and substrates involved in the endogeneous system that controls the effects of OFRs.

PMID: 8676544 [PubMed - indexed for MEDLINE]

## Blood glutathione-peroxidase levels in skin diseases: effect of selenium and vitamin E treatment.

[Juhlin L](#), [Edqvist LE](#), [Ekman LG](#), [Ljunghall K](#), [Olsson M](#).

### Abstract

Blood glutathione-peroxidase (GSH-Px) was determined in 61 healthy subjects and 506 patients with various skin disorders. Depressed levels were observed in patients with psoriasis, eczema, atopic dermatitis, vasculitis, mycosis fungoides and dermatitis herpetiformis. Low values of GSH-Px were also found in some patients with pemphigoid, acne conglobata, polymyositis, rheumatoid arthritis, scleroderma and systemic lupus erythematoses. Vegetarian diet, malnutrition and alcohol abuse could possibly account for the low values in some patients. Fifty patients with low GSH-Px levels were treated with tablets containing 0.2 mg selenium as Na<sub>2</sub>SeO<sub>3</sub> and 10 mg tocopheryl succinate. The GSH-Px levels increased slowly within 6-8 weeks of treatment. The clinical effect was encouraging and calls for controlled studies.

PMID: 6179360 [PubMed - indexed for MEDLINE]

[Ann Clin Lab Sci.](#) 1978 Jan-Feb;8(1):23-9.

# Glutathione reductase in the red blood cells.

[Chang JC](#), [van der Hoeven LH](#), [Haddox CH](#).

## Abstract

Glutathione reductase plays an important role in protecting hemoglobin, red cell enzymes, and biological cell membranes against oxidative damage by increasing the level of reduced glutathione (GSSGR) in the process of aerobic glycolysis. The enzyme deficiency may result in mild to moderately severe hemolytic anemia upon exposure to certain drugs or chemicals. However, hereditary deficiency of the enzyme is extremely rare. Recent studies on glutathione reductase in the red cell have shown more insight in the understanding of red cell metabolism and interactions with other enzymes, especially glucose-6-phosphate dehydrogenase (G-6-PD). Glutathione reductase in serum may be a source of error in any clinical laboratory test in which an enzyme activity is determined indirectly by measuring the change in reduced nicotinamide-adenine dinucleotide (NADH) or reduced nicotinamide adenine dinucleotide phosphate (NADPH) absorbance. Glutathione reductase levels are reduced in banked blood when citrate-phosphate-dextrose (CPD) is used as a preservative. Reviewed is the role of glutathione reductase in the metabolism of the red cell and its clinical implication and usefulness.

PMID: 623427 [PubMed - indexed for MEDLINE]

[Chem Biol Interact.](#) 1991;80(1):89-97.

## Oral glutathione increases tissue glutathione in vivo.

[Aw TY](#), [Wierzbicka G](#), [Jones DP](#).

Department of Physiology, Louisiana State University Medical Center, Shreveport 71130.

### Abstract

Mice were given an oral dose of glutathione (GSH) (100 mg/kg) and concentrations of GSH were measured at 30, 45 and 60 min in blood plasma and after 1 h in liver, kidney, heart, lung, brain, small intestine and skin. In control mice, GSH concentrations in plasma increased from 30 microM to 75 microM within 30 min of oral GSH administration, consistent with a rapid flux of GSH from the intestinal lumen to plasma. Under these GSH-sufficient conditions, no increases over control values were obtained in GSH concentrations in most tissues except lung over the same time course. Mice pretreated for 5 days with the GSH synthesis inhibitor, L-buthionine-S,R-sulfoximine (BSO, 80 mumol/day) had substantially decreased tissue concentrations of GSH. Oral administration of GSH to these GSH-deficient animals gave statistically significant increases in GSH concentrations in kidney, heart, lung, brain, small intestine and skin but not in the liver. Administration of the equivalent amount of the constituent amino acids, glutamate, cysteine, and glycine, resulted in little change in GSH concentrations in all tissues in GSH-deficient animals. Thus, the results show that oral GSH can increase GSH concentrations in several tissues following GSH depletion, such as can occur in toxicological and pathological conditions in which GSH homeostasis is compromised.

PMID: 1913980 [PubMed - indexed for MEDLINE]

[Am J Physiol.](#) 1990 Oct;259(4 Pt 1):G524-9.

## Bioavailability of dietary glutathione: effect on plasma concentration.

[Hagen TM](#), [Wierzbicka GT](#), [Sillau AH](#), [Bowman BB](#), [Jones DP](#).

Department of Biochemistry, Emory University School of Medicine, Atlanta, Georgia 30322.

### Abstract

Plasma glutathione (GSH) concentration in rats increased from approximately 15 to 30 microM after administration of GSH either as a liquid bolus (30 mumol) or mixed (2.5-50 mg/g) in AIN-76 semisynthetic diet. GSH concentration was maximal at 90-120 min after GSH administration and remained high for over 3 h. Administration of the amino acid precursors of GSH had little or no effect on plasma GSH values, indicating that GSH catabolism and resynthesis do not account for the increased GSH concentration seen. Inhibition of GSH synthesis and degradation by L-buthionine-[S,R]-sulfoximine and acivicin showed that the increased plasma GSH came mostly from absorption of intact GSH instead of from its metabolism. Plasma protein-bound GSH also increased after GSH administration, with a time course similar to that observed for free plasma GSH. Thus dietary GSH can be absorbed intact and results in a substantial increase in blood plasma GSH. This indicates that oral supplementation may be useful to enhance tissue availability of GSH.

PMID: 2221062 [PubMed - indexed for MEDLINE]



[Br J Nutr.](#) 1989 Nov;62(3):683-91.

## Effect of oral glutathione on hepatic glutathione levels in rats and mice.

[Viña J](#), [Perez C](#), [Furukawa T](#), [Palacin M](#), [Viña JR](#).

Department of Physiology, University of Valencia, Spain.

### Abstract

Administration of oral glutathione (GSH) increases hepatic GSH levels in fasted rats, in mice treated with GSH depletors such as diethyl maleate and in mice treated with high doses of paracetamol. An increase in hepatic GSH levels after administration of oral GSH does not occur in animals treated with buthionine sulphoximine, an inhibitor of GSH synthesis. Administration of oral GSH leads to an increase in the concentration of L-cysteine, a precursor of GSH, in portal blood plasma. Oral administration of L-methionine produced a significant decrease of hepatic ATP in fasted rats, but not in fed rats. Administration of N-acetylcysteine or GSH did not affect the hepatic ATP levels. The results show that the oral intake of GSH is a safe and efficient form of administration of its constituent amino acids in cases when GSH synthesis is required to replete hepatic GSH levels.

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PMID: 6179360 [PubMed - indexed for MEDLINE]

[J Nutr.](#) 2004 Mar;134(3):489-92.

# Glutathione metabolism and its implications for health.

[Wu G](#), [Fang YZ](#), [Yang S](#), [Lupton JR](#), [Turner ND](#).

[Collaborators \(1\)](#)

[Lupton JR](#).

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## Abstract

Glutathione (gamma-glutamyl-cysteinyl-glycine; GSH) is the most abundant low-molecular-weight thiol, and GSH/glutathione disulfide is the major redox couple in animal cells. The synthesis of GSH from glutamate, cysteine, and glycine is catalyzed sequentially by two cytosolic enzymes, gamma-glutamylcysteine synthetase and GSH synthetase. Compelling evidence shows that GSH synthesis is regulated primarily by gamma-glutamylcysteine synthetase activity, cysteine availability, and GSH feedback inhibition. Animal and human studies demonstrate that adequate protein nutrition is crucial for the maintenance of GSH homeostasis. In addition, enteral or parenteral cystine, methionine, N-acetyl-cysteine, and L-2-oxothiazolidine-4-carboxylate are effective precursors of cysteine for tissue GSH synthesis. Glutathione plays important roles in antioxidant defense, nutrient metabolism, and regulation of cellular events (including gene expression, DNA and protein synthesis, cell proliferation and apoptosis, signal transduction, cytokine production and immune response, and protein glutathionylation). Glutathione deficiency contributes to oxidative stress, which plays a key role in aging and the pathogenesis of many diseases (including kwashiorkor, seizure, Alzheimer's disease, Parkinson's disease, liver disease, cystic fibrosis, sickle cell anemia, HIV, AIDS, cancer, heart attack, stroke, and diabetes). New knowledge of the nutritional regulation of GSH metabolism is critical for the development of effective strategies to improve health and to treat these diseases.

PMID: 14988435 [PubMed - indexed for MEDLINE]