Oxidative Stress Analysis 2.0

Profile Components

RESERVE
Glutathione (GSH)
Total Antioxidant Capacity (TAC)
Cysteine (Cys-SH)
Cystine (Cys-S-S-Cys)
Cysteine/Cystine Ratio
Sulphate
Cysteine/Sulphate Ratio
PROTECTIVE ENZYMES
Superoxide Dismutase (SOD)
Glutathione Peroxidase (GPx)
DAMAGE
Lipid Peroxides

What is Oxidative Stress?

Oxidative Stress occurs when the production of reactive oxygen species (ROS) outweighs the body's ability to remove them, thus shifting this equilibrium in the direction of oxidation (e.g. rusting). The instability of free radicals and other ROS causes them to extract electrons from neighboring molecules in a chain reaction, causing cellular damage in the process. Reducing agents, including dietary antioxidants, nutritional supplements, and antioxidant enzymes provide protection against free radical damage.

Oxidative stress has an integral relationship with the inflammatory cascade, which produces ROS, and is considered a driving force in the aging process. Oxidative stress has been implicated in a growing list of disorders, including cancer, atherosclerosis, arthritis, diabetes, macular degeneration, chronic fatigue syndrome, fibromyalgia, and neurodegenerative diseases.

Antioxidant needs vary significantly between individuals. Therefore, evaluating one's reduction/oxidation ("redox") balance can help pinpoint imbalances that are exacerbating or setting the stage for chronic illness, thus serving as a springboard for customized intervention. In this process we evaluate the individuals' unique biochemistry, including the availability of anti-oxidant RESERVES, the functionality of protective ENZYMES, and the presence (of absence) of tissue DAMAGE. Any imbalances are then treated specifically.

Overview of Pattern Interpretation:

Oxidative stress results from an imbalance between ROS production and antioxidant protection. Because Cystine is the oxidized form of Cysteine, a low Cysteine/Cystine Ratio can indicate a redox imbalance in the body, i.e., oxidative stress.

When prolonged or severe, oxidative stress eventually results in tissue damage and increased risk of disease, as indicated by an elevated Lipid Peroxides (reflecting oxidative damage to lipids in the body). The optional marker, 8-OHdG, can also shed light on oxidative damage to proteins.

The body's most important endogenous antioxidants include glutathione (GSH) and the enzymes, superoxide dismutase (SOD), glutathione peroxidase (GPx) and catalase. In the face of oxidative stress, the body generally compensates by increasing the synthesis of glutathione from component amino acids, and increasing the activity of antioxidant enzymes. Therefore, higher levels of GSH, SOD, or GPx suggests oxidative stress but also a healthy response to it. Normal Lipid Peroxides would suggest that despite the oxidative stress, oxidative damage has not yet occurred. However, it is still helpful to identify sources of oxidative stress and nutritionally protect these reserves.

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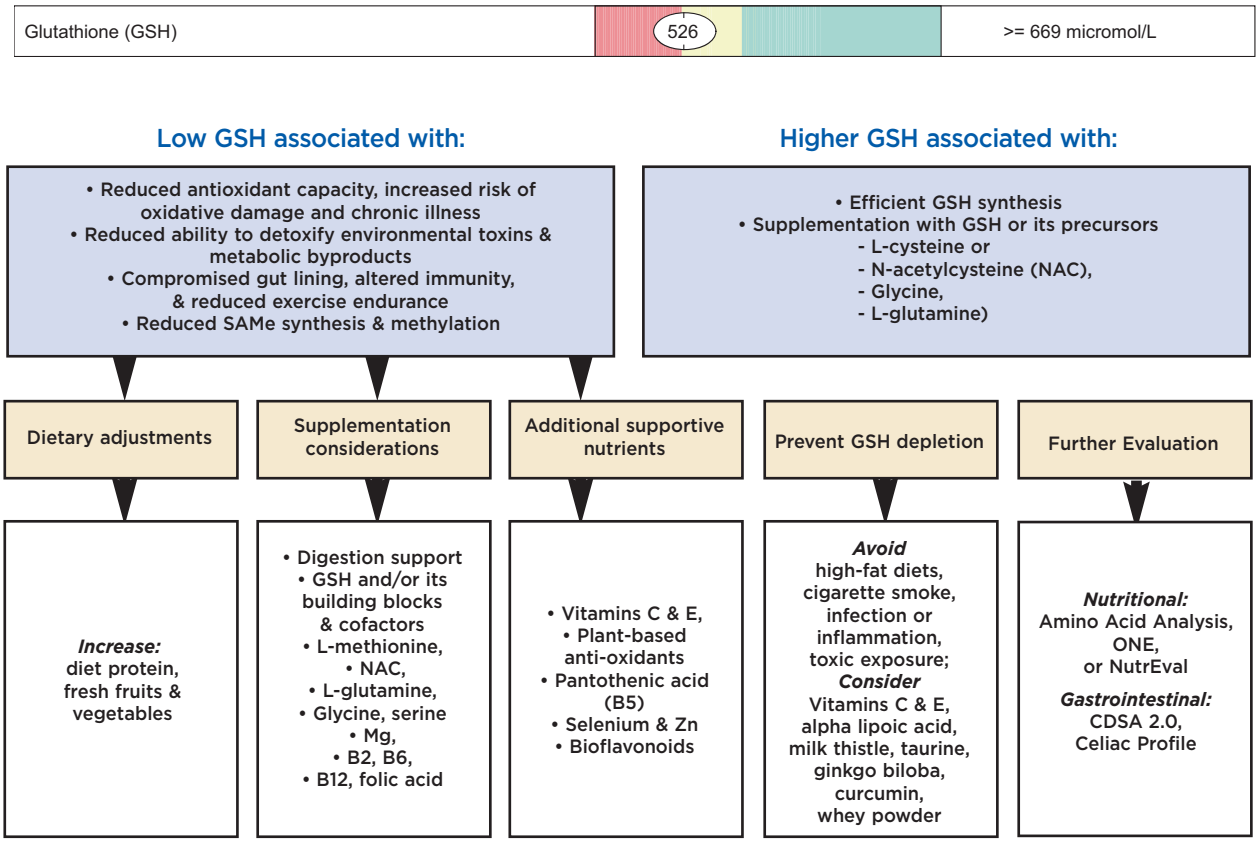
Reserves—
Glutathione (GSH)

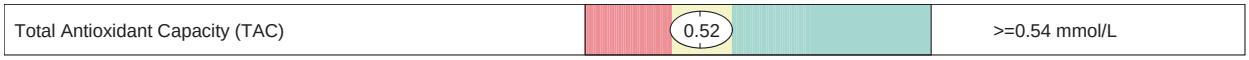
Glutathione (GSH) is a tripeptide made up of Glutamine, Glycine, and Cysteine and is the body's most potent endogenous anti-oxidant. GSH plays a central role in resistance to oxidative stress, functioning as an intracellular antioxidant, as well as a detoxifying agent for many xenobiotics. Low GSH contributes to oxidative stress and is thus a risk factor for many chronic diseases.



Reserves—

Total Antioxidant Capacity (TAC)

Antioxidants work synergistically, and wide individual variations exist regarding anti-oxidative capacity and needs. As a result, measuring total antioxidant response provides a more reliable indicator of antioxidant capacity than measuring single antioxidants. **Total Antioxidant Capacity (TAC)** reflects the collective power of reducing agents to neutralize free radicals for each individual.



Low TAC is associated with:

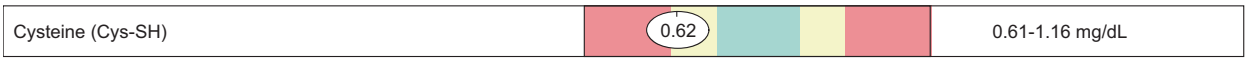
Oxidative stress and a need for greater antioxidant protection

Treatment Options to increase TAC

Identify sources of oxidative stress	Dietary adjustments	Antioxidant support	Further Evaluation
Infection, inflammation, Xenobiotic exposure, Toxic metals exposure, Etc.	***Increase:*** fresh fruits & vegetables ***Eliminate:*** trans fats	Mixture of water- and fat-soluble antioxidants: • Vitamins C & E, • GSH + precursors & co-factors *(see GSH, previous page)* • β-carotene, • α-lipoic acid • CoQ10 • Resveratrol • EGCG (green tea extract)	***Nutritional:*** Amino Acid Analysis, ONE, or NutrEval ***Gastrointestinal:*** CDSA 2.0, Celiac Profile ***Environmental:*** Elemental Analysis (urine, RBCs)

Cysteine

Cysteine is the rate-limiting amino acid for GSH, but also functions as an extracellular antioxidant and is a precursor for taurine, inorganic sulfate, acetyl-Coenzyme A, and protein synthesis.



Low Cysteine associated with:

• Reduced antioxidant capacity and ability to form GSH; increased risk of oxidative damage and chronic disease
• Possible low methionine (cysteine's precursor) or SAMe (can be depleted during GSH upregulation)
• Possible high homocysteine (Hcy) and/or low B6 (converts Hcy to cysteine)
• Repeated DMSA administration (cysteine excretion)
Possible cystinuria (inborn wasting of cysteine)

Higher Cysteine associated with:

• Supplementation with L-cysteine, N-acetylcysteine (NAC), L-methionine, or glutathione
• Possible blocks in cysteine metabolism (also see Cysteine/Sulfate Ratio, below)
• Possible cytotoxicity

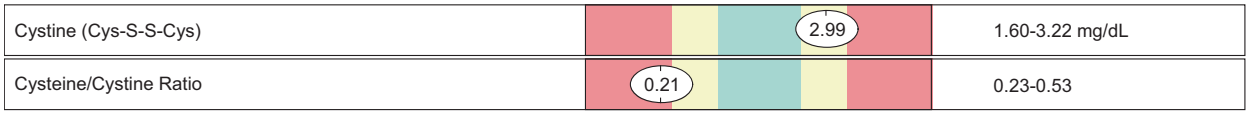
Treatment Options to increase GSH

Dietary adjustments	Supplementation considerations	Further Evaluation	Support cysteine's metabolism	Further Evaluation
Increase: dietary protein; vegetarian sources of methionine include corn, soy, sunflower seeds, oats, chocolate, cashews, walnuts, almonds, sesame seeds	N-acetylcysteine (NAC is more stable than L-cysteine), L-methionine, or GSH ***(Note: Reduce Hg toxicity prior to using high doses of NAC, as NAC may redistribute Hg in the body)***	***Nutritional:*** Amino Acid Analysis (24 hrs, to rule out cystinuria), ONE, or NutrEval ***Gastrointestinal:*** CDSA 2.0, Celiac Profile	**Mg** (cysteine to Mg), **B6 as p5p** (cysteine to taurine), **molybdenum** (cysteine to sulfate; see Cysteine/Sulfate Ratio); Additional supportive nutrients include B2, B12, folate, C, E, Zn	Rule out high homocysteine (can increase production of cysteine)

Reserves—

Cystine and 'Cysteine/Cystine Ratio'

Cystine is the oxidized disulfide form of cysteine (Cys) and is the predominant form of cysteine in the blood due to its greater relative stability. High cystine compared to cysteine, however, suggests a shifted redox balance and oxidative stress. The **Cys/CySS Ratio** is a reliable indicator of extracellular redox potential in the body. Low ratios have been noted in many chronic diseases.



Low Cysteine/Cystine Ratio associated with:

- Shifted reduction/oxidation (redox) balance in the direction of oxidative stress
- Aging, smoking, increased risk of disorders such as type 2 diabetes, atherosclerosis, cancer

Higher Cysteine/Cystine Ratio associated with:

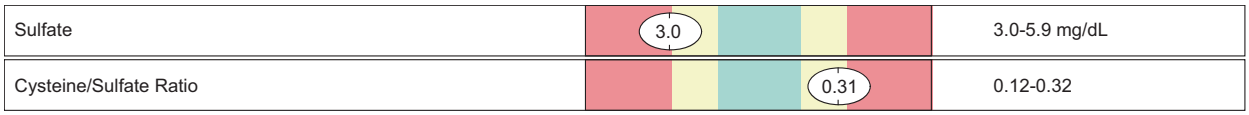
- Favorable 'redox' balance and antioxidant protection (see section for high Cysteine, if relevant)

Treatment Options to reduce Cystine and/or increase Cys/CySS Ratio

Dietary adjustments	Supplementation considerations
Increase: diet protein, fresh fruits & vegetables	• Broad-spectrum antioxidants; • GSH precursors and cofactors (see GSH above); • Other supportive nutrients include Vitamins C, E, Mg, Zn, quercetin, methylcobalamin

Sulfate and 'Cysteine/Sulfate Ratio'

Sulfate is produced from cysteine via sulfoxidation. Inorganic sulfate is a critical factor as part of Phase II detoxification reactions. Sulfate is also essential for mucin formation in the GI tract, and glycosaminoglycans in joint cartilage. Sulfoxidation defects result in low sulfate and increased risk of illness. The **Cysteine/Sulfate Ratio** reflects the efficiency of this 2-step conversion.



High Cysteine/Sulfate Ratio and/or low Sulfate is associated with:

- Leaky gut, environmental illness, food sensitivities, rheumatoid arthritis
- Alzheimer's, Parkinson's disease, motor neuron disease
- Sulfoxidation impairment (imbalance in enzymes, cysteine dioxygenase or sulfite oxidase)
- Low GSH (cysteine is used preferentially for GSH before being used for sulfate production)
- Sulfite excess (can lower TAC and increase lipid peroxides)
- Excessive exercise (can deplete GSH and sulfate)
- Sulfate depletion from chronic arthritis or IBD
- Oxidative stress and a need for greater antioxidant protection

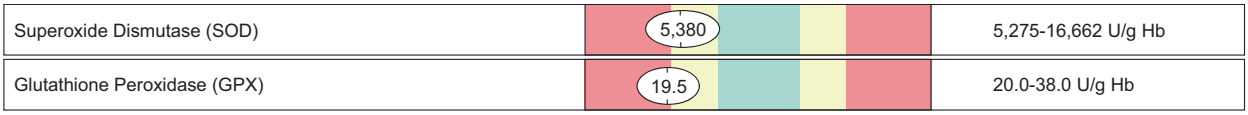
Treatment Options to increase TAC

Dietary adjustments	Supplementation considerations	Additional supportive nutrients	Identify causes of sulfate depletion
Increase: dietary protein	**Molybdenum** (Mo) (sulfite oxidase co-factor) [NB: low uric acid or sulfite/aldehyde intolerance hint at **Mo** deficiency] Rule out excess copper or tungsten (which can induce **Mo** deficiency)	• B2, B5, Mg • MSM (takes burden off cysteine) • Sulfate salts (e.g., Epsom salts) • Glucosamin sulfate • Chondroitan sulfate • Na/K-sulfate	Rule out chronic use of drugs metabolized via Phase II Sulfation (e.g., acetaminophen, prednisone

Protective Enzymes—

Superoxide Dismutase & Glutathione Peroxidase

Superoxide Dismutase (SOD) and **Glutathione Peroxidase (GPx)** are endogenous antioxidant enzymes that protect against oxidative stress. SOD converts superoxide anion to hydrogen peroxide (H2O2), which is then inactivated by glutathione peroxidase (GPx) or catalase. SOD constitutes a critical step. However, if SOD is not balanced by GPx, H2O2 may still promote oxidative damage.



Low SOD and Low GPx suggests:

- Deficient antioxidant support, increased risk of oxidative damage; normal Lipid Peroxides would suggest no cellular damage at this point
- Possible heavy metal toxicity
- Possible depletion of reserves due to chronic oxidative stress
- Nutrient deficits, esp. zinc, copper, selenium, and vitamin B6

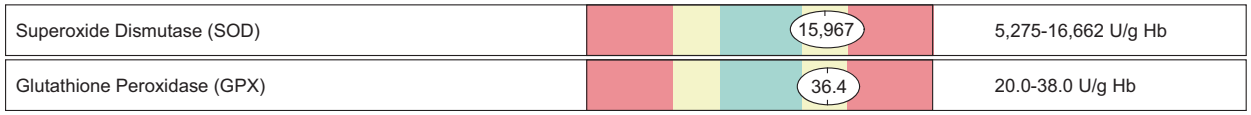
Treatment Options

Identify sources of oxidative stress

Inflammation or infection,
Environmental toxicity,
Impaired glucose tolerance,
Alcoholism,
Homocysteinemia

Supportive nutrients considerations

- Zinc & copper (cytosolic SOD cofactors)
- Mn (mitochondrial SOD cofactor)
- Selenium (GPx cofactor)
- Vitamins B6, B12, folate
- Vitamins C & E, β-carotene, bioflavonoids
- Mg, Taurine, resveratrol, green tea catechins
- Melatonin



High SOD with high GPx suggests:

- Upregulation of both enzymes due to oxidative stress;
- Normal *Lipid Peroxides* would suggest no cellular damage at this point (yet)

Treatment Options

Identify sources of oxidative stress

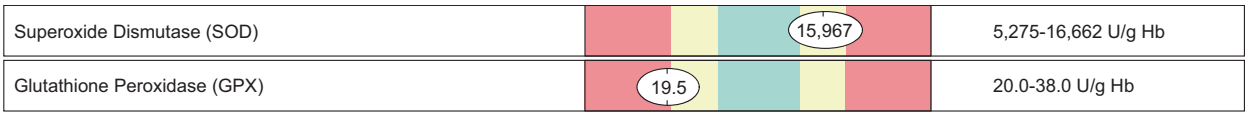
Inflammation or infection,
Environmental toxicity,
Impaired glucose tolerance,
Alcoholism,
Homocysteinemia

Supportive nutrients considerations

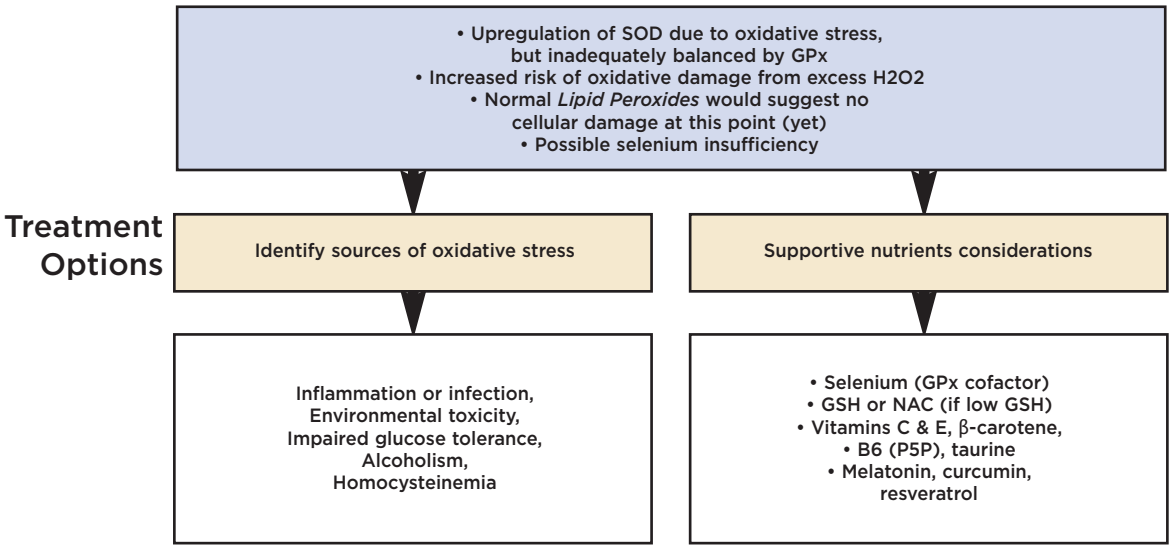
Ensure availability of enzyme cofactors:
- Zinc, copper, selenium

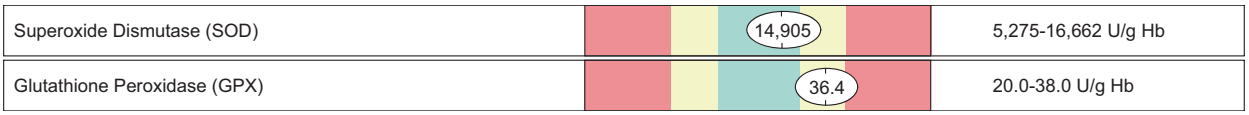
Other supportive agents include:
- Vitamins C and E,
- Propolis, curcumin

Protective Enzymes—
Superoxide Dismutase & Glutathione Peroxidase (continued)

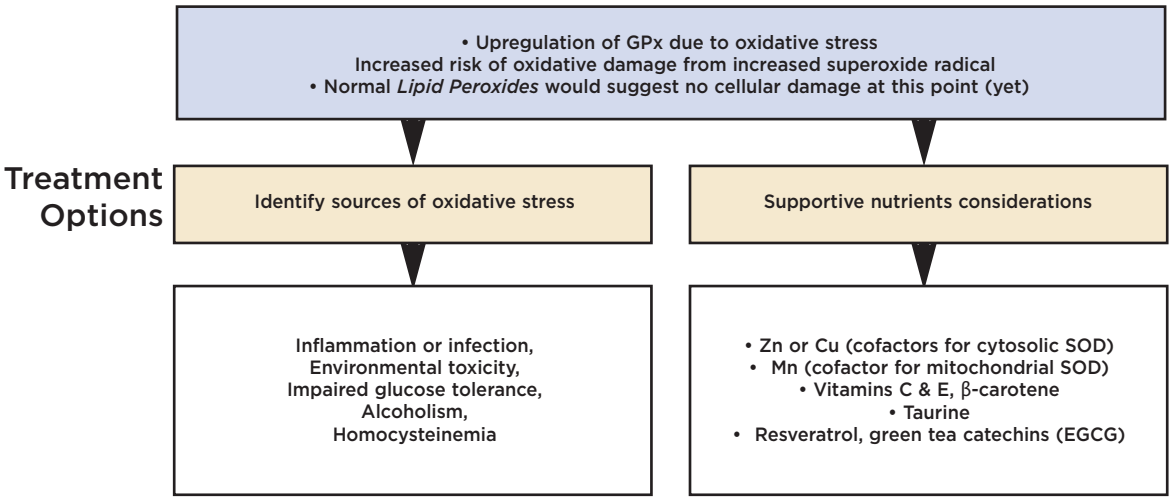


High SOD with normal or low GPx suggests:





High GPx with low/ normal SOD suggests:



Damage—
Lipid Peroxides

Lipid Peroxides are a direct indicator of oxidative damage to polyunsaturated fatty acids (PUFAs), suggesting that production of ROS has been inadequately balanced by antioxidants, esp. fat-soluble. Lipid peroxidation in cell membranes results in cellular dysfunction and is increased in many disease states. Lipid Peroxides are also increased in tissues that are poisoned by toxins.

High Lipid Peroxides are associated with:

- Oxidative damage to lipids in the body due to excessive ROS production
- Oxidative damage to lipids in the body due to deficient antioxidant protection
- High-fat diet, excess Fe or Cu, smoking, obesity with insulin resistance, heavy metal toxicity, excessive exercise, protein energy malnutrition, periodontitis, chronic disease
- Essential Fat (EMFA) deficiencies from ROS attack), GSH, B6 (deficiency promotes mitochondrial decay), Mg (required for GSH synthesis), B2 (required for GSH reduction), Zn

Treatment Options to increase TAC

Dietary adjustments	Supplementation considerations	Additional supportive nutrients	Further Evaluation
Increase: fresh fruits & vegetables ***Eliminate:*** trans fats	**Antioxidants, esp. at-soluble:** • Vitamins A & E • CoQ10 • Carotenoids **Herbal antioxidants:** • garlic • green tea • curcumi, • propolis • grapeseed	• GSH, including precursors and cofactors (see Glutathione) esp. if GSH is low • Fish oils • Other PUFAs	***Environmental:*** Elemental Analysis (urine, RBCs) ***Nutritional:*** Amino Acid Analysis, Organic Acids, EMFA, ONE, or NutrEval; **Eliminate** excess Iron or Cu (promotes hydroxyl radical production)

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