N-ACETYL-CYSTEINE (NAC)

(A Synthetic Derivative Of the Amino Acid Cysteine)

To appreciate the benefits --- and the damage --- from NAC supplementation you must first realize that nearly all its effects on the Stage of Life progression --- from Immuno-Neuro-Endocrine Stress --- to chronic inflammation --- to INFLAM-AGING --- come from its intracellular conversion --- or failure of its conversion --- to GLUTATHIONE.

------- In this document we will highlight the few beneficial effects of NAC supplementation that may not entirely relate directly to its endogenous incorporation into the intracellular Glutathione antioxidant system. But first, we will emphatically warn you to …

NEVER SUPPLEMENT WITH NAC
UNLESS CONCOMMITANTLY WITH GLYCINE.

After oral administration, NAC is rapidly absorbed, with peak plasma concentrations reached between 30 minutes and 1 hour. NAC is absorbed in the small intestine and undergoes first-pass liver metabolism to cysteine, which is used by the liver to synthesize Glutathione. The hepatic pool of Glutathione is replenished before Glutathione and NAC are released into the plasma.

Glutathione is "The Master Anti-oxidant" --- formed intracellularly from Glycine + NAC.

Due to its apparent antioxidant and anti-inflammatory properties, NAC has gained extraordinary popularity in Alternative Medicine, and among health food store shoppers and nutritionists. Regrettably, however, pathology models fail to justify NAC supplementation. The irony is that NAC is promoted as an anti-aging antioxidant --- yet paradoxically, NAC supplementation accelerates the aging process.

All presumptive anti-aging benefits attributed to NAC's antioxidant effects --- including benefits to atherosclerosis, arthritis, and many other inflammatory conditions --- only occur after NAC has been converted to Glutathione. But any NAC that is not combined with Glycine to produce Glutathione can wreak devastation. The truth that "nature cure" lovers refuse to face is that NAC supplementation:

- accelerates the aging process in animal studies

- suppresses anti-aging gene expression (particularly inhibiting SKN-1-mediated transcription)

- nullifies the beneficial effects of exercise

- perturbs global gene expression

- blocks essential ROS (Reactive Oxygen Species) action in their role as ubiquitous and important signaling molecules that regulate cellular homeostasis, differentiation, proliferation, repair, and aging. (Yes, it is true --- despite Alternative Medicine propaganda to the contrary, not all ROS are bad, and in fact they are essential to cellular health and longevity, and to immune system response.)

- interferes with thyroid function

- interferes with methionine metabolism

- interferes with tyrosine metabolism

- facilitates the overgrowth of yeast and fungal infections

- In a legitimate study done to test for the (wishful thinking) benefits of N-acetylcysteine on patients with idiopathic pulmonary fibrosis --- researchers had to stop the study because so many patients died.

N-acetylcysteine is also promoted by the Health Food Mythologists as a heavy metal chelator. N-acetylcysteine is not only useless as a chelator of heavy metals, but is actually dangerous. The problem is that N-acetylcysteine will bind to toxic metals and mobilize them from connective tissue (most typically bone, where heavy metals tend to be dumped so they are not too harmful), then redeposit the toxic metal in vital organs --- the brain in particular. The reason is because the kidneys have no means of eliminating the cysteine-metal compound, so it re-circulates until it is dumped randomly somewhere else in the body.

There may be clinical benefits (--- most of which derive only from conversion to Glutathione ---) in …

- inhibition of inflammatory/NF-kB signaling and expression of pro-inflammatory cytokines

- chronic obstructive pulmonary disease (COPD) (--- as a mucolytic)

- chronic bronchitis (--- as a mucolytic)

- cystic fibrosis (--- as is a mucolytic)

- breaking down bacterial biofilms (H. Pylori of the gastric mucosa, and bacterial invasion of the upper respiratory tract)

- protection against fluoridated water and toothpaste oxidative damage to the oral cavity

- (in the blood --- but more significantly in the endothelium (via Glutathione)) decreasing peroxidation of LDL cholesterol

- anti-fibrotic effects on lung fibroblasts (via Glutathione)

NAC has anti-inflammatory and anti-apoptotic properties in Insulin Resistance. These effects may be in addition to benefits from its conversion to Glutathione. Glutathione subsequently blocks some of the inflammatory effects associated with Insulin Resistance, particularly the elevated Advanced Glycation End-products (AGE). NAC modulates certain signaling pathways in both insulin target cells and pancreatic β cells.

Obesity plays a major role in Insulin Resistance progression because it causes Metabolic and Oxidative Stress, resulting in dysfunctional β cells and activation of pancreatic stellate cells, which cause fibrosis. ----- In high fat (corn oil) diet-induced obese diabetic mice, NAC supplementation maintains healthy β cells and decreases activation of stellate cells. There is significantly improved glucose tolerance and insulin sensitivity, along with decreased hyperinsulinemia.

Oxidative Stress, neuro-inflammation and neurogenesis are commonly implicated in cognitive decline. NAC is a Glutathione precursor with potent antioxidant, pro-neurogenesis, and anti-inflammatory properties. Data suggest significant cognitive improvements following NAC treatment in a variety of CNS contexts. (However, many of the studies on this topic used therapies in conjunction with NAC.)

NAC (after passing into cells to combine with Glycine to form Glutathione) has major antioxidant benefits in the brain --- and Oxidative Stress is associated with cognitive deficits. NAC also mitigates the negative effects of inflammation on cognition --- suppressing over-activation of the brain's inflammatory cells and dysregulation of the key neurotransmitter Glutamate.

NAC eliminates cognitive decline following surgery in patients older than age 60.

It is very difficult to determine which of the above conditions benefit entirely from NAC supporting endogenous Glutathione production and how many of the benefits derive from NAC acting independently.

NAC supplementation alone will produce its desired effect of intracellular Glutathione production only to the extent Glycine is available intracellularly to combine with the NAC. NAC supplementation beyond the intracellular Glycine availability for Glutathione production becomes a major source of Reductive Stress --- and actually shortens Lifespan, while exacerbating many states of pathophysiology associated with Reductive Stress --- including particularly cardiovascular disease.

While studies have shown life extension benefits from Glycine + NAC supplementation (--- in association with elevating intracellular Glutathione in defense against Endogenous Aging), no study has ever reported extension of life in animals or humans by supplementing NAC alone.

Glycine + NAC supplementation does not attempt to override or replace cellular defenses that combat Oxidative Stress and/or Reductive Stress. Instead, by providing precursors to boost Glutathione synthesis and concentration, Glycine + NAC works by supporting the ability of cells to auto-regulate their own Glutathione --- regardless of the individualized need of cells in different organs.