INFLAM-AGING CONTROL

= STRENGTHENING THE GLYCOCALYX
&
REPLENISHING INTRACELLULAR GLUTATHIONE

NUTRI-SPEC = Nutrition Specificity = Driven toward a specific target

= Driven by a specific goal.

What is your specific Target? === INFLAM-AGING Control

What is your specific Goal? === LIVE STRONGER LONGER

With Nutri-Spec, you address the two autonomous pathways of INFLAM-AGING. You recognize that Exogenous Aging begins at the moment of conception and is driven by external forces imposed by the environment. You are equally aware of Endogenous Aging that begins at age 23 and is driven by biological clocks that begin to dominate the immune system, the nervous system, and the hormonal system (= Immuno-Neuro-Endocrine Stress) at that age.

Exogenous INFLAM-AGING is …

--- Catabolic in character

--- Involves oxidative stress

Endogenous INFLAM-AGING is …

--- Anabolic in character

--- Involves reductive stress

What is the mechanism at work in each of these seemingly opposite pathways of aging?

Here is the startling reality --- a realization you can only come to appreciate within the context of your Nutri-Spec paradigm. ----- Both Exogenous INFLAM-AGING and Endogenous INFLAM-AGING are pushed into patho-physiology by exactly the same mechanism.

The damaging effects of each INFLAM-AGING pathway involve the same process === depletion of protective tissue sulfation that causes tissue structural and functional breakdown. That breakdown drives both Exogenous and Endogenous INFLAM-AGING.

Endogenous INFLAM-AGING is further compounded by depleted intracellular Glutathione. Repletion cannot be achieved in inadequately sulfated tissues.

Yes, defense against both Exogenous INFLAM-AGING that determines Health Span and Endogenous INFLAM-AGING that determines Lifespan can only be achieved by an adequate supply of Thiosulfate at the tissue level and at the cellular level.

It may be that your most powerful immune system support --- and your most powerful Live Stronger Longer support --- a supplement that also enhances cellular energetics, while also maintaining normal cellular membrane permeability --- is …

OXY TONIC - - -

because - - - Oxy Tonic (= pure, natural Thiosulfate) is by far your most powerful means to replenish tissue sulfation.

A few years ago, NUTRI-SPEC received this from a doctor in South Africa:

"Please will you pass this email and attachment on to Dr. Schenker.

"I have been associated with Heidi Du Preez over the last two years as she worked so hard to finish this work and then had to jump through so many hoops to get it published, but at last it has happened, and I can now pass this on to you, Guy. I have been itching to get it to you since reading the first draft a year ago. From your point of view, it ONCE AGAIN just proves how far ahead you have been for so many years. You already created and published the BALANCING PROCEDURE many years ago --- accolades to you!!!!"

The attachment was …

du Preez HN, et al. Pathogenesis of COVID-19 described through the lens of an under-sulfated and degraded epithelial and endothelial glycocalyx. FASEB J. 2022 Jan;36(1):e22052. https://pubmed.ncbi.nlm.nih.gov/34862979/.

This study by du Preez advances a quantum leap forward the work of Revici (1950s & 60s) --- and 30 years of NUTRI-SPEC clinical experience. Even I --- with nearly 40 years of using Thiosulfate for my patients and recommending it to you --- am astonished at how…

EVERY BODY SYSTEM AND ORGAN IS CRITICALLY UNDER THE INFLUENCE OF THIOSULFATE.

Yes, there is more power in your BALANCING PROCEDURE than in the entire pharmacopeia of "natural" medicine, or in all the countless bottles of nonsense that fill the shelves of your local health food store.

To grasp the essence of anti-INFLAM-AGING, you must understand the importance of ---

THE GLYCOCALYX = A Membrane Around Every Cell Membrane.

The Glycocalyx (Glyx) is a dense layer of protein and carbohydrate chains forming a mesh that extends into the extracellular matrix, and is involved in many critical tissue processes. The Glycocalyx is composed of tissue membrane–bound glycoproteins, proteoglycans (PGs), and highly sulfated Glycosaminoglycan (GAG) side–chains. Chondroitin Sulfate is one GAG that contributes significantly to the structure and function of the Glycocalyx.

The highly sulfated Glyx interacts with many proteins, and is involved in

- developmental processes
- regeneratory processes
- infectious processes
- inflammatory processes

The density and position of Thiosulfate groups on the Glyx structure will mainly determine these protein interactions, and therefore the biological activity of the sulfated tissue membrane.

The Glycocalyx surrounds every cell, and its complex mesh of Thiosulfate-containing proteins and carbohydrates is the key to defense against both Exogenous INFLAM-AGING and Endogenous INFLAM-AGING. Its tissue-stabilizing effects provide protection against the INFLAM-AGING stresses of ---
- metabolic imbalances and inefficiencies
- deficient autophagy
- pro-aging effects of Senescent Cells.

The Epithelial Glycocalyx is the interface between our internal cells and the external environment. If it is compromised, we are vulnerable to the onslaught of viruses, mold, bacteria, and environmental toxins or allergens.

The Glyx also lines the surface of arterial endothelial cells, in a mesh-like structure that floats into the lumen of the vascular system. This Endothelial Glycocalyx contributes to vascular permeability and vascular tone, and also plays a major role in controlling immune response, inflammatory response, and coagulation response.

The Glyx is highly negatively charged. On the cell surface that negative charge, plus the specific structures of the many Thiosulfate molecules, allows the Glyx to regulate tissue permeability. GAG chains comprising the Glyx are long, hydrophilic, negatively charged polysaccharides --- including heparin sulfate and chondroitin sulfate. Along with non-sulfated hyaluronic acid and sialic acid, the GAGs act as a receptor and a reservoir for cell adhesion proteins, growth factors, cytokines, matrix components, enzymes, enzyme inhibitors, and pathogen virulence factors --- thereby regulating tissue distribution, biological availability, and activity of these proteins.

----- Such Glyx–protein interactions, critical to metabolic function, are largely dependent on the density and position of Thiosulfate in the Glyx structure. The sulfated Glyx provides a negative charge density for both the Epithelial and Endothelial tissue surface layer --- and thus prevents the binding of negatively charged toxins and pathogens.

Maintaining both the degree of GAG sulfation and the negative charge density are critical to protection against INFLAM-AGING.

Sulfation occurs in all tissues and is defined as the transfer of a sulfate group to different substrates, such as GAGs, proteins, lipids, hormones, and drugs. The control and degree of sulfation of such a wide range of substances indicate that "this pathway is involved in many aspects of life" (= direct quote from du Preez).

Do you appreciate the magnitude of du Preez's comment on Glyx functions? ----- She is saying that Thiosulfate (Oxy Tonic) largely determines biological function of all cells!!!

Truly --- you have the capacity to reach deeply into the Immuno-Neuro-Endocrine (INE) stresses underlying inflammation --- inflammation that causes the extraordinary nutrition needs that compound over the years into INFLAM-AGING.

----- With NUTRI-SPEC, you touch your patients deeply. ----- And, what is the most effective way and the quickest way you can probe the INE stresses at the tissue level that remain a dark mystery to other doctors? How can you directly intrude upon the vicious cycles (positive feedback loops) = = = INE Stress causing increased nutrition demands, leading to Metabolic Imbalances --- then, Metabolic Imbalances creating new INE stresses ----- `round and `round in an ever-escalating whirlwind of patho-physiology --- that relentlessly causes a decline in both Health Span and Lifespan (Exogenous INFLAM-AGING & Endogenous INFLAM-AGING).

Effective & Quick? Replenish tissue membrane sulfation with Oxy Tonic (via your BALANCING PROCEDURE), and back that up with the sulfation support of the ADAPTOGENS & REJUVENINS of your Activator & Rejuvenator.

After reading some of the conclusions from du Preez's incredible work, you should be asking yourself, "Do I want to restore structure and function to tissues throughout all my patients' epithelial, endothelial and other tissue membranes with Oxy Tonic (and other NUTRI-SPEC supplements) --- or --- do I want to be an alternative healthcare provider of "remedies" based upon "research" that is a little more than propaganda?"

We have looked at the study by du Preez --- and how it builds upon the fundamentals of Revici's work from the 1940's and 50's --- showing how Thiosulfate is not only the most powerful antioxidant in the body (as part of glutathione and superoxide dismutase) --- but also is essential to both the structure and function of all epithelial membranes, as well as all endothelial membranes ---

and --- how Thiosulfate is critical for immune system function --- all the benefits that derive from feeding a strong Glyx.

TRULY --- NOTHING HAPPENS IN THE HUMAN BODY WITHOUT THE SUPPORT OF --- THIOSULFATE --- YOUR OXY TONIC.

The variable structure of ubiquitous GAG (Glycose Amino Glycan) molecules is largely dependent on the availability of Thiosulfate (Oxy Tonic). Quoting from du Preez --- "That variability explains the remarkable tissue-specific activities of thiosulfate --- influencing cell-, tissue-, and organism-level development, homeostasis, and pathogenesis".

The metabolic functions of Oxy Tonic are amazingly diverse. Adequately sulfated GAGs modulate the activity of numerous molecules --- such as …

- anticoagulant factors
- cytokines
- growth factors
- albumin
- as well as protective enzymes such as superoxide dismutase (SOD).

Oxy Tonic incorporated into GAGs of the Glyx contributes to the regulation of:

- inflammation
- vascular permeability and tone
- coagulation
- lipid metabolism
- white blood cell adhesion
- and protection against oxidative stress.

----- More from du Preez: “Therefore, any changes in GAG structure-enhanced functions are associated with a wide range of patho-physiological consequences --- such as …

○ Capillary Leak Syndrome and consequent edema formation
○ platelet aggregation
○ hyper-coagulation
○ accelerated inflammation
○ loss of vascular responsiveness.

“Most of the interactions and functions of tissue endothelial and epithelial membranes rely on the pattern and degree of sulfation --- and the resulting negative charge density. The affinity and biological activity of GAGs increase as the degree of sulfation increases. Nevertheless, the GAG-composed membrane is a delicate layer, and removing of one specific component thereof may result in the loss of function of the total. Thiosulfate not only regulates physiological processes, but is implicated in many pathologies, including cancer, infections, and vascular diseases.”

DOES THAT SOUND IMPORTANT?

--- MAYBE CRITICAL?

--- TRULY ESSENTIAL ---

to how you want to serve your patients (--- and build a thriving practice)? ----- Or, do you want to be yet another peddler of “natural remedies” --- no better than all the other “nature cure” practitioners your patients may choose --- indeed, no more advanced than your local health food store?

Immune System function? ----- How about both …

BARRIER FUNCTION

AND

PATHOGEN EVASION? -----

The GAG chains of both the epithelium and the endothelium, when heavily sulfated (Thiosulfate/Oxy Tonic), present a global negative charge that interacts

electrostatically with viruses and other pathogens. When membranes are under-sulfated, microbes and toxins exploit these weak membranes, thus more easily penetrating the cells. ----- So,

YOUR OXY TONIC LIES AT THE NEXUS BETWEEN PATHOGEN INVASION AND HOST DEFENSE.

DOES THAT SOUND IMPORTANT?

MAYBE CRITICAL?

TRULY ESSENTIAL?

Yes, for you, your family, and your patients, maximizing immune system defense absolutely requires that you maintain tissue saturation with Oxy Tonic.

In epithelial tissues, your Oxy Tonic allows the membrane to work with white blood cells to secrete many defensive compounds such as …

- antibodies
- lysozymes
- nitric oxide
- and many others.

Collectively, these defensive compounds form a physical barrier with direct anti-microbial and anti-toxin activity --- and are critical to a major function of the immune system --- to tag foreign proteins for elimination by phagocytes.

Your major takeaway is that …

THIOSULFATE SERVES AS THE PRIMARY MODULATOR AND EXPRESSER OF MEMBRANE DEFENSIVE COMPOUNDS.

Do you get it? ----- Inadequate sulfation --- which only YOU can correct in your patients with NUTRI-SPEC protocols (--- and which they will never get from any alternative healthcare provider, and certainly not from their health food store purchases) may be the most important benefit you provide your patients.

And --- what Herculean effort must you put forth to restore thorough sulfation to your patients' epithelial & endothelial membranes? How much time must you invest in achieving for your patients the critical selective permeability of tissue membranes? How many zillions of $$$s must your patients invest to maximize the immune function of organic and vascular membranes?

Wake up to the happy truth!

As du Preez has shown, the rate-limiting factor in maintaining thorough membrane structure and function through sulfation is merely the availability of Thiosulfate = (Oxy Tonic). The many GAG molecules incorporated into epithelial and endothelial membranes are easily built, even when defending against patho-physiology, when Thiosulfate is available.

Effort? Time? Expense? ---- No, no, and no.

You need nothing more than your BALANCING PROCEDURE --- to determine for each individual patient the ideal combination of Oxy Tonic, Electro Tonic, and Oxy D-Plus.

The reason we call it the "BALANCING PROCEDURE" is because the anti-anabolic (anti-Anaerobic) and anti-catabolic (anti-Dysaerobic) nutrients in those three supplements will individualize the balance between Thiosulfate, Glycerol, and Sterols to establish the ultimate in membrane function.

But please understand that your BALANCING PROCEDURE to supply all your patients with their individualized amount of Oxy Tonic needed for membrane sulfation --- is NOT a "treatment" for infections, nor for any other Immune System Stress. With Oxy Tonic you improve the healthy function of everything --- from skin function to brain function to the function of every organ in the body.

Now, here is where du Preez's study serves as a major "AH HA!" moment for NUTRI-SPEC practitioners. Consider that …

Her study (plus research by Gerontologists) also shows the role that chronic inflammation and an under-sulfated Glyx play in all the comorbid conditions (tubby tummy, high blood pressure, auto-immune diseases, diabetes, etc.) that derive from both Exogenous INFLAM-AGING and Endogenous INFLAM-AGING.

Your patients nearly all need Oxy Tonic (via The BALANCING PROCEDURE), to mitigate the extraordinary nutrition needs of tissues depleted by the leading states of dis-ease in our culture.

We have asked you countless times --- do you have patients suffering from:

--- tubby tummy?
--- high blood pressure?
--- auto-immune diseases?
--- diabetes?
--- high cholesterol and/or high triglycerides?
--- chronic pain?
--- chronic fatigue?
--- depression/anxiety?

The NUTRI-SPEC paradigm emphatically emphasizes that we do not " treat" these diseases --- but rather that these diseases cause extreme nutrition needs ---- and it is these specific nutrition requirements you can supply with NUTRI-SPEC.

Do you see that nearly every condition or symptom that brings patients into your office tells you there is a nutrition deficiency of Thiosulfate (Oxy Tonic)? ----- This is why we exclaim over and over again that your BALANCING PROCEDURE is crucial --- as a continuous Metabolic Spark --- assuring your patients they will maximize the nutrition requirements to serve …

- tissue membrane selective permeability
- tissue energetics
- tissue pH balance
- tissue oxidation/reduction balance

Thiosulfate and N-Acetylcysteine (NAC) and a few other sulfur donors contribute to the Thiosulfate pool --- the rate–limiting molecule in tissue sulfation.

NAC (--- which, with Glycine, is a major component of your Activator & Rejuvenator) is not only a precursor to Glutathione (when combined intracellularly with Glycine), but also contributes to the structure of the Glyx --- and as well to the formation of Taurine, Coenzyme A, and albumin.

Different tissues and cell types vary in Glyx structure, and the Glyx structure can vary between individuals, and within the same individual with age. Indeed, maintaining a healthy Glyx, along with maintaining intracellular Glutathione, is a major key to controlling Endogenous INFLAM-AGING.

The GAG chain length and the number and location of sulfate groups determine the binding affinity to the specific proteins, and therefore tissue function. The degree of sulfation exerts the main Glyx influence on tissue metabolic activity apart from the barrier function of the Glyx.

Any change in Glyx function is correlated with a wide range of patho-physiological consequences that accelerate INFLAM-AGING. The Thiosulfate–saturated Glyx not only regulates physiological processes, but when inadequately sulfated, is implicated in many pathologies --- including cancer, infectious and vascular diseases, and neurodegenerative disorders.

We cannot emphasize enough that loss of tissue membrane sulfation is a part of a vicious cycle --- whereby stripping of the Thiosulfate from tissues increases an individual's susceptibility to certain clinical conditions --- and those conditions of IMFLAM-AGING, in turn, further decrease the integrity of the Glyx.

Just the aging process itself --- and particularly Endogenous INFLAM-AGING associated with Glutathione depletion and development of Senescent Cells --- is associated with rising inflammatory cytokines such as TNF alpha, Interleukin-1-beta, Interleukin-6, and Interleukin-10, along with Matrix Metalloproteinases (MMPs), plus Reactive Oxygen Species and Reactive Nitrogen Species.

While elevation of these inflammatory substances accelerates the process of Endogenous Aging, the breakdown of Glyx integrity increases the production of these INFLAM-AGING agents = Vicious Cycle!

Similarly, hyperglycemia and hypertension are conditions that strip the Glyx of Thiosulfate --- yet the resulting GAG nutrition deficiency also increases the inflammation associated with those conditions = Vicious Cycle!

Let us take a little more comprehensive look at one aspect of du Preez's research --- the effects of your Oxy Tonic on …

CARDIOVASCULAR DISEASE.

The Thiosulfate (Oxy Tonic) compounds are especially pronounced on both epithelial and endothelial (arterial) membranes. Plasma proteins such as albumin, fibrinogen, and antithrombin are also bound within the endothelial tissue. Looking at the arterial intima specifically, we see how crucial is the dependence of these tissues on the presence of Thiosulfate.

When there is adequate sulfation of the arterial intima, your patients will have perfect functional interplay between the Thiosulfate of the membrane and the plasma proteins that are essential for vascular health --- as well as the interplay with fibrinogen and antithrombin that is critical to prevent what you, as a NUTRI-SPEC practitioner, know as Electrolyte Stress Imbalance.

Thiosulfate (Oxy Tonic), therefore, plays an essential role in maintaining and regulating a wide range of blood vascular functions, including …

- vascular permeability
- coagulation activity
- inflammatory responses = causing Arteriosclerosis
- protecting tissues from viral entry

The number of Thiosulfate groups in various domains of the arterial GAGs determines the binding affinity to fibrinogen and anti-thrombin --- the critical proteins involved with heart attacks and strokes.

The degree of sulfation (supplied by Oxy Tonic via The BALANCING PROCEDURE) predominantly determines the negative charge of the membranes --- which defines pathogen invasion, receptor binding sites, and the electrostatic binding of proteins --- including albumin, leukocytes, red blood cells, and platelets.

You can see a nice summary comment in this direct quote from Preez: “It is important to note that sulfation reactions in the human body affect all cells, and metabolism of many endogenous and exogenous molecules, such as hormones, drugs, and xenobiotics”.

Endothelial cell activation in inflammation is instigated by a catabolic reaction, followed by a long-term anabolic response. The anabolic response may be mediated by mTOR, the driver of Endogenous INFLAM-AGING.

Adipose tissue releases Cytokines/Chemokines, Adipokines, and toxic free fatty acids. The result is INFLAM-AGING, Coagulation, Fibrinolysis, Insulin Resistance, and Leptin Resistance. These changes are associated with the excess TNF-alpha, IL-6, and IL-1-beta caused by the inadequately sulfated Glyx.

Adiponectin deficiency (= associated with obesity, elevated Triglycerides, Type 2 Diabetes, Hypertension and Metabolic-Syndrome) is associated with Endothelial Glyx sulfation deficiency. Deficient sulfation of the Endothelial Glyx promotes excess Inducible Nitric Oxide, and thus an increase in neurovascular permeability. That results in adhesion of circulating inflammatory cells on the Endothelial wall, plus coagulation and platelet aggregation.

Leptin resistance (= associated with obesity and adipocyte-driven inflammation) is associated with poor sulfation of the Endothelial Glyx.

The maintenance of oncotic pressure is another fundamental aspect of vascular health, and of your Water/Electrolyte Imbalance Analysis. Disruption of membranes by inadequate sulfation leads to loss of barrier function with subsequent edema formation. It can also cause the loss of albumin in the urine that you pick up with your Multi Stix test strip.

Properly sulfated membranes are crucial for the maintenance of vascular barrier functions and fluid dynamics. An essential function of sulfated membranes is maintaining correct oncotic pressure in the capillary bed, in addition to facilitating the absorption and reabsorption of molecules across capillary membranes.

This concept of membrane permeability has been the very foundation of Nutri-Spec for 40 years. The balance between Oxy Tonic, Electro Tonic, and Oxy D-Plus --- MAINTAINED ON AN INDIVIDUALIZED BASIS for each of your patients --- is essential for selective membrane permeability.

Maintained on an INDIVIDUALIZED basis? ----- How? ----- With your BALANCING PROCEDURE, of course. All your patients need the benefits derived from maintaining Metabolic Balance between Oxy Tonic, Electro Tonic & Oxygenic D+. Add Activator + Immuno-Synbiotic + Rejuvenator --- and there is nothing more important you can do to assure all patients they will ---

LIVE STRONGER LONGER.

Your BALANCING PROCEDURE will …

- Individualize Metabolic Balance --- simple, inexpensive and applicable to all your patients

- Restore membrane permeability

- Break the viscous cycles between INE Stress ← → Metabolic Imbalances

- Break the viscous cycles between INE Stress ← → INFLAM-AGING

- Electrolyte Stress Imbalance? ----- Control the deadly imbalances of fibrinogen & anti-thrombin that drive the loss of cardiovascular health

- Restore capillary membrane integrity that breaks down in both Electrolyte Stress & Electrolyte Insufficiency Imbalances --- thus ensuring nutrient absorption and toxin elimination

----- Yes, your BALANCING PROCEDURE is …

THE KEYSTONE IN YOUR WALL OF INFLAM-AGING DEFENSE.

Now --- consider once again the comment --- "Thiosulfate (Oxy Tonic) shows remarkable tissue-specific activity --- influencing cell-, tissue-, and organism-level development, homeostasis, and pathogenesis prevention."

This gem of metabolic truth should cause a tingle of excitement. This statement is nearly a direct quote from the du Preez study on Thiosulfate.

Think of it …

- at the cell level of biological organization …
- at the tissue level …
- at the systemic level …

… your patients' need for Oxy Tonic is ubiquitous --- as it plays a critical role in:

- development
- homeostasis (= Metabolic Balance + Vital Reserves)
- pathogenesis prevention (= Immune Balance & Immune Strength)
- INFLAM-AGING defense

YOU CANNOT GET MORE FUNDAMENTAL --- in meeting the needs of all your patients than supplying them with Thiosulfate ----- via …

YOUR BALANCING PROCEDURE.

REPLENISHING INTRACELLULAR GLUTATHIONE

Thiosulfate --- particularly as NAC combining with Glycine, is essential to the intracellular formation of Glutathione. And, low Glutathione is a predisposing factor to tissue membranes being stripped of sulfation. Clearly, this is a vicious cycle --- with loss of tissue sulfation and low cellular Glutathione reinforcing each other.

Intracellular combination of [NAC + Glycine] to produce Glutathione is the highest priority for NAC. It is only after the need for Glutathione is satisfied that a significant amount of remaining NAC can go on to produce hydrogen sulfide, Thiosulfate, Taurine, Coenzyme A, and albumin.

Severe immune system stress will cause depletion of sulfur amino acids due to oxidative stress, reductive stress or inflammation-induced proteolysis --- so amino acid replenishment becomes critical. Both Thiosulfate and [NAC + Glycine] supplementation successfully replenish sulfur amino acids.

One study shows that after oral administration of 400 mg NAC in a single dose, the level of plasma cysteine increases --- and that is following amino acid depletion caused by strenuous exercise in sedentary men.

> Leelarungrayub D., et al. N-Acetylcysteine supplementation controls total antioxidant capacity, creatinine kinase, lactate, and TNF-alpha against oxidative stress induced by graded exercise in sedentary men. Oxidative Medicine and Cellular Longevity. 2011:2011:329643. https://pubmed.ncbi.nlm.nih.gov/21904641/.

Since [NAC + Glycine] is rate-limiting in Glutathione synthesis and in intracellular synthesis of GAGs and other Thiosulfate molecules, intracellular NAC will favor Glutathione synthesis in those suffering from Endogenous Aging. If there is an increased demand for Glutathione because of inflammatory stress --- such as during viral infection, mixed mold mycotoxicosis, endurance exercise,

over-training of any type of exercise, or chronic disease of any kind --- it will have an inhibitory effect on all organic sulfate synthesis. That is to say --- will create an extraordinary nutrition need for Thiosulfate.

This is why replenishing sulfation in those suffering a depleted Glyx is far better achieved by supplementing with Thiosulfate directly, rather than with [NAC + Glycine]. Why? Another Vicious Cycle. ----- Patients with Thiosulfate deficient Glyx + intracellular Glutathione deficiency suffer a steadily increasing burden of NF-Kappa B, TGF - Beta, and inflammatory cytokines such as TNF-alpha and IL-6. But these markers of INFLAM-AGING block the action of the enzyme that allow NAC to form Glutathione, and to convert NAC to Thiosulfate to produce GAGs needed for a strong Glyx. The resulting further Glutathione and Thiosulfate depletion causes even more inflammation, which further = = = vicious cycle.

The ideal is to supplement with both --- a balanced blend of [NAC + Glycine] along with Thiosulfate (Oxy Tonic). (Important Note: NAC must only be supplemented accompanied by Glycine. NAC supplementation in the absence of adequate Glycine is damaging, and accelerates INFLAM-AGING.)

Many studies show that endogenous Glutathione, along with endogenous production of heparin sulfate, Chondroitin Sulfate, and Taurine --- and, with all the other sulfur compounds produced from Thiosulfate to maintain the integrity of the Glyx --- decreases with physiological aging (Endogenous INFLAM-AGING). Lipoic acid is a Sulfur-containing Adaptogen that has been classified by Gerontologists as a "Rejuvenin" --- demonstrating many beneficial effects in controlling Endogenous INFLAM-AGING.

In most health conditions with a chronic inflammatory or autoimmune component, the enzyme that converts NAC to Glutathione or to GAGs is inhibited. The plasma level of Cysteine will actually be elevated, but there will be a very low plasma concentration of Thiosulfate. NAC supplementation will be of limited benefit, and a far better clinical approach is to saturate with Thiosulfate (Oxy Tonic) to bypass the enzyme deficiency. = Your BALANCING PROCEDURE is the quickest way to achieve Thiosulfate Saturation --- and do so in a way that meets the specific, individualized need of every patient.

THE BROAD ARRAY OF THIOSULFATE BENEFITS

Inflammatory Markers

Thiosulfate supplementation is not only an effective sulfur donor --- research shows it has specific tissue protection through inhibition of Nuclear Transcription Factor Kappa B (NF-kB) as well as TNF-alpha-induced production of cytokines, and also Reactive Oxygen Species --- thereby preventing up-regulation of IL-6.

It is well established in the research literature that Thiosulfate is a potent antioxidant, and anti-reductant, and anti-inflammatory agent. The down-regulation of NF-Kappa B signaling reduces many oxidative stress biomarkers, such as excess Inducible Nitric Oxide --- and decreases Prostaglandin E2 in macrophages. Many of these beneficial effects of Thiosulfate supplementation derive from the increase in intracellular inorganic sulfate, and also enhanced Glutathione production and Glyx sulfation.

NAC administration significantly reduces the inflammatory markers C-Reactive Protein (CRP) and Serum Ferritin.

Microbial Pathogens

For pathogens to gain access to epithelial and endothelial membranes, they need to first penetrate through the Glyx. Recent research studies indicate that interactions between the sulfated Glyx and viruses determine viral adherence and infectivity. The Glyx is the first point of contact for all pathogens that infect. It is found that COVID-19 has many more Thiosulfate-binding domains compared to other viruses, leading to increased infectivity.

Most viral particles have a negative charge at body fluid pH --- which is why the Epithelial Glyx so effectively repels viral particles. Under-sulfated Glyx will not only increase susceptibility to viral infection, but will also hamper the ability to control the immune and inflammatory response and coagulation.

Properly sulfated with Thiosulfate (Oxy Tonic), membranes present a global negative charge that can interact electrostatically with viruses and other pathogens. When the epithelium and endothelium are under-sulfated, viruses and toxins exploit these weak interactions to increase their concentration at the cell surface and enhance their chances of gaining cell entry.

Your Oxy Tonic is at the interface between pathogen invasion and immune defense. But more than merely a physical barrier to microbes, the properly sulfated membrane modulates the expression and release of many of the immune system's defensive compounds.

Imagine a tissue membrane --- either an epithelial membrane or an endothelial (vascular) membrane. That membrane actually serves two metabolic functions that are in a way opposite --- yet both functions depend entirely on adequate Thiosulfate from your Oxy Tonic (--- and this is why every patient can only be fully protected by going through the BALANCING PROCEDURE). The membrane you are envisioning has to both remain selectively permeable --- yet also provide a barrier against toxins and microbial pathogens.

Here is an extended quote from du Preez highlighting once again the essential metabolic functions of properly sulfated tissues --- that you can achieve with Oxy Tonic (--- and supported by your other supplements that contain negative valence sulfur --- including Activator, Rejuvenator, Taurine, Adapto-Max and Oxy-Max.

"Thiosulfate lies at the nexus between pathogen invasion and host defense.

"Adequate sulfation is responsible for the secretion of many defensive compounds into the mucosal fluid, such as mucins, antibodies, defensins, collectins, lysozyme, histamines, and nitric oxide. Collectively, these different defensive compounds form a physical barrier with direct antimicrobial activity, and the ability to opsonize pathogens to aid their clearance. When adequately sulfated (OXY TONIC!), The Glyx Modulates the Expression and Release of these Defensive Compounds.

"In various disease conditions, a decrease in sulfation shown from biopsies were associated with albumin (protein) in the urine. A broad spectrum of inflammatory diseases with different etiology contributes to membrane dysfunction by several associated pathways --- and initiate albuminuria. Intensive care unit Covid-19 patients frequently show albuminuria."

We must emphasize here again the presence of a vicious cycle. Breakdown in sulfation (=the need for Thiosulfate supplementation) contributes to the breakdown of both the permeability function and the barrier function of epithelial tissues throughout the body, as well as endothelial membranes throughout the vasculature.

The tissue degradation due to inadequate thiosulfate leads to inflammatory pathology ---

--- but then the inflammation causes further degradation of the membranes ---

--- which perpetuates and expands Immuno-Neuro-Endocrine Stress --- with more inflammation, then more tissue depletion of sulfate ---

--- and a never-ending expansion of patho-physiopathology, and ultimately, severe acute or chronic pathology.

This vicious cycle typifies both Exogenous and Endogenous INFLAM-AGING.

THE DEGREE OF THIOSULFATE ION PRESENCE AND ITS POSITION ON THE GLYX PLAYS THE BIGGEST ROLE IN DETERMINING VIRAL ATTACHMENT AND PENETRATION INTO THE CELL.

du Preez's study, largely using Covid-19 to illustrate how critical is tissue sulfation, presents evidence that an under-sulfated Glyx not only predisposes to viruses, but also results in a dysregulated Immune Response and subsequent "cytokine storm", resulting in shedding and degradation of the Glyx --- leading to adhesion of immune cells, increased vascular permeability, inflammation, oxidative stress and coagulation --- thus increasing the risk of life-threatening organ dysfunction.

DOCTOR, DO YOU GET IT?!

What du Preez is highlighting here is a fundamental theme of NUTRI-SPEC --- a feature of patho-physiology that we have emphasized again and again ---

THE VICIOUS CYCLE.

Do you see it? Deficiency of Thiosulfate not only decreases resistance to infections --- but here is the important part --- it causes a subsequent aberrant Immune Response involving the creation of a "cytokine storm" --- the excessive Immune Response (that is actually responsible for severe symptoms and death in COVID-19).

Research shows that Angiotensin–Converting Enzyme II is often elevated in those susceptible to certain viral infections. But the over-expression of ATII is a

secondary phenomenon --- since a healthy sulfated Glyx tissue is an effective barrier to ATII over-expression. ----- NAC modifies the function of the Renin/Angiotensin system, which is probably mediated via inhibition of Angiotensin II activity.

Proteases, such as thrombin, are shown to exacerbate the breakdown of the Glyx. Therapeutic use of protease inhibitors should be considered by Medical Doctors for those experiencing extreme Immuno-Neuro-Endocrine Stress. One such inhibitor that has been thoroughly tested is the antibiotic Doxycycline. Doxycycline inhibits matrix MMP activity, which is shown to significantly reduce Glyx shedding, and therefore leukocyte adhesion to the Endothelial Glyx. It is theorized that early administration of NAC or Thiosulfate with Doxycycline could play an essential role in preserving the Glyx during acute inflammatory immune response.

As part of its role as a defender against tissue damage from toxins and microbial infection, the Glyx, under the influence of NAC and Thiosulfate, also supports immune system function by binding viruses and suppressing replication, while reducing inflammation --- but also has the ability to break down biofilms created as defense by microbial invasions. ----- NAC also has clinical benefits in cough and dry eyes, and as a mucolytic.

As it increases both Glutathione and GAG formation, Thiosulfate and [NAC + Glycine] supplementation can modulate various smoking-related symptoms, including air space enlargement in heavy smokers who received 600 mg twice daily of NAC for 6 months.

MORE ON THIOSULFATE, ALBUMIN, AND ONCOTIC PRESSURE

Low Glyx sulfation results in albumin leakage, which reduces tissue turgor, along with decreasing oncotic pressure in the vascular system. Low plasma albumin and/or albumin lost in the urine is frequently found in patients with diabetes, hypertension, and chronic heart failure --- all conditions indicating an individual is deficient in Glyx sulfation.

Supplementing with Thiosulfate and [NAC + Glycine] is in no way a treatment for those pathologies --- but their existence unequivocally indicates a nutritional need for additional Thiosulfate.

---- Plasma albumin also plays a vital role in fat metabolism by binding fatty acids and maintaining them in a soluble form. Hyperlipidemia, therefore, occurs in clinical situations of low plasma albumin. Thus, elevated triglycerides and oxidized LDL are additional indicators of the need to preserve health with Thiosulfate and [NAC + Glycine] supplementation.

Whey is high in both albumin and Cysteine. Supplementation with Whey (that has not been denatured by high temperature processing) may be beneficial for those who need Thiosulfate supplementation --- particularly if they show low plasma albumin, albuminuria, or are edematous. Whey supplementation may achieve some of the benefits of human albumin supplementation, which has been shown to protect the Glyx against sulfation depletion --- and decreases adhesion of leukocytes, and reduces interstitial edema ...

> Dogne S, et al. Endothelial Glycocalyx as a shield against diabetic vascular complications. Arteriosclerosis, Thrombosis, and Vascular Biology. 2018 Jul;38(7):1427-1439. https://pubmed.ncbi.nlm.nih.gov/29880486/.
>
> Kolarova H, et al. Modulation of Endothelial Glycocalyx structure under inflammatory conditions. Mediators of Inflammation. 2014 Apr 3;2014:694312. https://pmc.ncbi.nlm.nih.gov/articles/PMC3997148/.
>
> Aldecoa C, et al. Role of Albumin in the preservation of Endothelial Glycocalyx integrity and the microcirculation. Annals of Intensive Care. 2020 Jun 22;10:85. https://pmc.ncbi.nlm.nih.gov/articles/PMC7310051/.

Additionally, largely due to its beneficial effects on the Glyx, albumin has immunomodulatory and anti-inflammatory, antioxidant, anticoagulant and antiplatelet-aggregation properties …

> Meli I. Assessing the role of albumin in the formation of Endothelial Glycocalyx layer using a Microfluidic in Vitro Model. Bern, Switzerland: Master of Science Department for Biomedical Research. Thesis submission date: 02 Feb 2019.

MICROBIOTA AND TISSUE SULFATION

Sulfate compound synthesis (such as GAGs and Glutathione) in a healthy person mostly depends on the extent of re-using sulfur from sulfate to synthesize new sulfur compounds. These conversions occur largely through intervention of microorganisms in the gut. Thus, a significant contribution to health maintenance of the Glyx through sulfation can be achieved with probiotic and prebiotic supplementation.

> Amadi B, et al. Reduced production of Sulfated GAGS occurs in Zambian in children with Kwashiorkor but not Marasmus. The American Journal of Clinical Nutrition. 2009;89 (2). https://ajcn.nutrition.org/article/S0002-9165%2823%2923984-2/fulltext?utm_source=copilot.com.

Avoid antibiotics as much as possible. (When an antibiotic must be used, Doxycycline is the ideal choice whenever applicable --- since it is a protease inhibitor that protects the Glyx from Thiosulfate depletion.) All individuals should routinely supplement with a Synbiotic combination of Probiotics and Prebiotics. That supplementation should be at least doubled when antibiotics must be taken. Gut dysbiosis is an underlying risk factor for inadequate Glyx sulfation.

SINCE THE RATE-LIMITING FACTOR TO SULFATION IS SIMPLY THE AVAILABILITY OF INORGANIC SULFATE (OXY TONIC) ---

--- it is therefore important to explore the factors contributing to, and those that deplete, Thiosulfate, and thus also affect sulfation of the Glyx.

Steroids, Acetaminophen, Aspirin, Ibuprofen, Naproxen, and other NSAIDS contribute to the depletion of inorganic sulfate. Those drugs should be avoided if at all possible. When they must be taken, then additional supplementation with Thiosulfate, [NAC + Glycine], along with Lipoic Acid and perhaps Taurine and Chondroitin Sulfate is essential.

High calcium intake, particularly high calcium intake relative to magnesium, will exacerbate inflammation associated with an inadequately sulfated Glyx. Calcium induces stress in the Endoplasmic Reticulum that deranges hydrogen sulfide metabolism, causing membrane depolarization, which in turn releases even

more calcium --- thus maintaining a vicious cycle exacerbating inflammatory stress signaling and cell death. This excess calcium can be a severe problem in enteral and parenteral feeding --- ironically given to those ill, when tissues are already stripped of Thiosulfate.

> Wilkinson L, et al. Cysteine Dioxygenase; Modulation of Expression in Human Cell Lines by Cytokines and Control of Sulfate Production. Toxicology in Vitro. 2002; 16 (4). https://www.sciencedirect.com/science/article/abs/pii/S0887233302000310?via%3Dihub.

> Entez Bahar, et al. ER Stress-Mediated Signaling: Action Potential and Calcium as Key Players. Int and Mol Sci. 2016, 17(9), 1558. https://www.mdpi.com/1422-0067/17/9/1558?utm_source=copilot.com.

High doses of Vitamin C may cause conversion of that ascorbic acid to oxalate. Both Vitamin C and oxalates require conjugation through sulfation and will contribute to both Epithelial Glyx and Endothelial Glyx dysfunction.

> Hatch M, et al. Effect of megadose of ascorbic acid on serum and urinary Oxalate, Eur Urol. 1980;6(3):166-9. https://pubmed.ncbi.nlm.nih.gov/7371664/.

> Dunne JW, et al. The effect of ascorbic acid on the sulfate conjugation of ingested noradrenaline and dopamine. Br. J Clin Pharmacol. 1984 Mar;17(3):356-60. https://pubmed.ncbi.nlm.nih.gov/6712869/.

Other factors predisposing to low tissue sulfation are low vitamin D, and increased dietary intake of fructose and polyunsaturated oils. Both high concentrations of glucose and high blood concentrated of free polyunsaturated fatty acids are associated with deficient Endothelial Glyx sulfation.

Even though [NAC + Glycine] is rate-limiting for Glutathione production --- and Thiosulfate is rate-limiting for GAG production --- pyridoxal five-phosphate (the coenzyme form of Vitamin B6) is a critical cofactor for both Glutathione and GAG production.

Molybdenum and Pyridoxal 5-Phosphate and Vitamin D are important cofactor nutrients in sulfur metabolism.

The benefits of supplementing with Quercetin and Melatonin can only be achieved when there is adequate sulfation of the Glyx --- because these nutrients require sulfation to be metabolized. Thiosulfate and/or [NAC + Glycine] should also therefore be supplemented any time Quercetin or Melatonin are used.

Since NAC and Thiosulfate have powerful anticoagulatory effects, supplementation sometimes requires that blood thinning medications need to be adjusted downward.

Brain endothelial cells are particularly vulnerable to tissue membrane sulfation inadequacy. Both low Glutathione and low Thiosulfate saturation of the Glyx cause INFLAM-AGING --- and that INFLAM-AGING, in turn, causes damage to the Endothelial Glyx --- but --- the Endothelial Glyx was already impaired by the Glutathione and GAG insufficiency. The result is vascular inflammation and a prothrombotic state, and ischemia --- which further induces INFLAM-AGING --- which further causes Endothelial Glyx Thiosulfate loss.