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Nutritional Epigenetic Support for Fighting Viral and Toxin Exposure

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Abstract

Extrinsic epigenetic influences alter the physiological function and body habitus response to transient as well as long-term exposures and more importantly, the outcome of the response. We must prepare nutritionally and epigenetically to sustain and support optimal function which then allows the body's intrinsic mechanisms to do their job, including fighting foreign invaders (i.e. bacteria, virus, parasite, fungus) and eliminating toxins (i.e. chemicals, pollutants, xenobiotic medications and OTC drugs, heavy metals, volatile gases) each requiring bioavailable essential nutrients that power and support enzymatic reactions that are the physiological machinery behind these immune and toxic battles.

Keywords: Nutritional Epigenetics; Inflammation; Oxidative Stress; Antioxidants; Liver Detox Pathway; Toxin Burden; NFkB, Nrf2

Introduction

Fighting virus should not begin with what anti-viral to take when sick; it begins days, months, and years beforehand. In this era of pandemic COVID-19 viral infection and fear, it has been well-documented viral infection and the body's defense immune attack is associated with cytokine storm, oxidative stress, each inducing stimulation of the pro-inflammatory NFkB simultaneously alongside anti-inflammatory Nrf2 [1,2]. The intrinsic mechanism of immune cell attack to kill invading microbial species is accomplished with an oxidative respiratory burst that generates reactive oxygen species (ROS; superoxide anion, hydroxyl radicals, hydrogen peroxide) [3] as well as the pro-inflammatory cytokines especially IL-1 and IFN; many more being also generated during cytokine storms [4]. Tissue and organ damage internally as well as symptoms and illness externally present during cytokine storms and excessive oxidative stress [1,4]. The person who already existed in a chronic inflammatory state associated metabolically with excessive oxidative stress and depleted antioxidant protection has a significant predisposition to be "more ill" upon exposure to additional stressors such as virus and toxins since they too also stimulate these inflammatory and oxidative stress pathways. Co-infections [5], preexisting viral and toxin body burden, as well as bioavailable antioxidants and nutritional status are key in determining the body's response to additional threats, especially in regards to coming into contact with COV19 and these body habitus states at time of exposure directly correlate to how a person may respond [6-8].

Besides our current pandemic, we are challenged daily to microbial and toxin exposures that already strain our detox and elimination pathways alongside immune and adrenal systems. The physiological epigenetic state of the body determines the person's resilience to aforementioned stresses at the time of exposure. When we launch the attack against foreign invaders such as a virus or toxic xenobiotics our defense mechanisms generate physiological doses of potentially damaging reactive species free radicals (ROS) as part of the fight to protect the tissues and organs at the whole body molecular level [9,10]; not an isolated event during COV19 exposure. There must be a balance between free radical generation of oxidative stress and the antioxidants that ensure the oxidative stress physiologically occurring is countered and not damaging. The

physiological intrinsic mechanisms of immune support and toxic burden management are beautifully built into the genome to rapidly respond to different stimuli, threats, changes, and subsequent adaptations that need to occur to prevent symptoms, pain, disease, aging, degeneration, and disease upon exposure [1,4,6-8].

Epigenetic extrinsic influences include factors such as dietary lifestyle choices and nutritional status [11], body habitus and exercise [12], sleep [13], stress and stress management [14], relationship status, occupation [15] and prior toxic and/or viral load [1]. Extrinsic influences influence the genome through a non-mutation alteration of gene expression [16]. As a collective, each extrinsic factor cumulatively induces its epigenetic effect at the level of gene expression to support or impair optimal function through up or down regulation of the gene such influences regulate; presenting at the molecular biochemical level of optimal or aberrant function which presents to the person as outward wellness or disease. Extrinsic epigenetic influences therefore alter the physiological function and body habitus response to transient as well as long-term exposures and more importantly, the outcome of the response.

Epigenetic pro-inflammatory up-regulation of NFkB

NFkB

A body habitus of excessive cytokines epigenetically stimulates the pro-inflammatory transcription factor NFkB to activate the genes it regulates increasing the rate of synthesis of its pro-inflammatory proteins and enzymes to go to action fighting the situation at hand. This can work to the body's advantage during the short-term acute inflammatory response when we need transient high levels of protective and signaling pro-inflammatory cytokines (i.e. IL-1, IL-6, TNF, IFN) many times under the direction of the pro-inflammatory essential fatty acid omega-6 Linoleic Acid eicosanoids pathway during injuries and infections [17]. However, chronic expression of these same pro-inflammatory genes under the direction of an aberrantly up-regulated epigenetically overstimulated NFkB and persistent body habitus of excessive inflammatory cytokines can result in a negative shift towards tissue damage, destruction, degeneration, and disease expression. If the person is already preexisting in this chronic inflammatory physiologically-induced epigenetic illness state, then exposure to infection and/or additional toxic load will be exponentially detrimental as they induce their transient states of high levels of oxidative stress and inflammation [18,19].

NFkB and comorbid oxidative stress states

These types of changes occur in co-morbid metabolic disturbance disease states such as hyperglycemia-induced Diabetes Mellitus and its subsequent Metabolic Syndrome and NAFLD which are also riddled with concomitant hypertension and hyperlipidemia, and many times also with the CVD risk factor hyperhomocysteinemia. Each of the underlying pathological mechanisms of hyperglycemia, hypertension, hyperlipidemia, and hyperhomocysteine each individually induce excessive up-regulation of NFkB, as well as induce a perpetuating cycle of free radical reactive oxygen and reactive nitrogen species inducing a body habitus of oxidative stress [20] which damages and attacks the DNA backbones, tertiary protein folding structures, and fatty acids inducing lipid peroxidation [6]. Oxidative stress is one of the underlying factors in co-morbid diseases and virtually every system of pain, aging, degeneration, and disease [21].

An individual with comorbid disease and its excessive inflammation and oxidative stress has already depleted the essential nutrient bioavailability and may not have an efficient ability to launch a successful attack with minimal effects.

Epigenetic pro-inflammatory up-regulation of Nrf2

Nrf2

Oxidative stress is defined as excessive free radicals and inefficient bioavailable protective antioxidants to scavenge and quench the free radical reactive species [22]. During oxidative stress the anti-inflammatory transcription factor Nrf2 is stimulated to up-regulate the anti-inflammatory genes its responsible for thereby increasing the rate of synthesis of the antioxidant enzymes (SOD, GPx, Catalase) as well as the phase-2 liver detox conjugation enzymes required to allow for excretion of toxins, xenobiotics, and reactive intermediates passing from CYP450 phase-1 redox reactions [23].

Liver detox pathway phase-1 and phase-2

In its simplest form, the hepatic detox phase-1 and phase-2 pathways act as a first line defense against dietary and ingested toxins as they enter the body through the Hepatic Portal Vein from the intestines entering the liver. Inhaled volatile acids as well as topical toxins/chemicals also pass through the liver with access to this multi-step biochemical process that converts them to water-soluble toxic reactive species intermediates (phase-1 redox CYP450 reactions) followed by tagging them with markers of excre-

tion and elimination (phase-2 conjugation reactions). Each portal of entry route of toxin and xenobiotic exposure is dealt with by the hepatic detox pathway and relies on efficient routes of excretion of the conjugated toxin/xenobiotic including urine as filtrate, bile through feces, breathe exhaled, and sweat [9,10,24,25]. The ability to protect against hepatic damage and toxic burden overload relies on bioavailable antioxidants to quench free radicals that escaped phase-2 conjugation reactions or exceeded the bioavailable limit of the agents recruited as the conjugators. Phase-2 conjugation reactions require essential sulfur amino acids and organic sulfur agents [24]. Most people experiencing toxic overload are lacking these vital essential nutrients to properly support hepatic detox pathway and exist with a higher toxic load, many lipophilic and without excretion (marked by conjugation with these essential nutrients) become lodged in adipose [25].

An individual who bottlenecks at phase-2 conjugation from lack of bioavailable nutrient molecules is therefore more susceptible to oxidative stress from the excessive build-up of toxic intermediates that remain unconjugated from phase-1 CYP450 reactions and need an even higher amount of protective antioxidants and essential nutrients.

Antioxidants

Antioxidants present primarily in 3 mechanisms. They are solo antioxidant agents that donate a hydrogen atom in a reversible redox reaction to quench free radicals, as intrinsic antioxidant enzyme systems which convert free radical reactive species to less harmful substances which are mineral dependent reactions, and lastly by stimulating and up-regulating our anti-inflammatory Nrf2 transcription factor which increases the rate of synthesis of the latter mineral-dependent intrinsic antioxidant enzymes. The primary solo antioxidant agents include essential vitamins ascorbate and tocopherol as Vitamins C and E, the most potent intrinsic antioxidant Glutathione a tripeptide of cysteine/glycine/glutamate conditionally essential amino acids, our essential water-soluble B3 derivative NADPH, and vitally important CoQ10 known as Ubiquinol which dually sustains the generation of our energy molecule ATP at the electron transport chain, and ALA also called Alpha Lipoic Acid our disulfide antioxidant and metabolic enzyme cofactor. Though the body can synthesize CoQ10 and ALA an individual with oxidative stress, statin medication, and metabolic disorders and disease exist at a higher demand and readily deplete their bioavailability and must be supplemented for to sustain optimal function and biochemical reactions relying on them. These each rely on the other to be regenerated with the continual reversible redox reactions thereby recycling their antioxidant powers of hydrogen transfers and electron donation to free radicals. The mineral-dependent intrinsic antioxidant enzymes include Heme/Iron-dependent Catalase, Selenium-dependent Glutathione Peroxidase (GPx), and the 2 forms of Superoxide Dismutase (SOD) requiring Copper/Zinc for the cytosolic SOD and Manganese for mitochondrial SOD. These are synthesized by up-regulated Nrf2 under oxidative stress states [5,6,8,11].

Therefore, to benefit from the positive protective roles of an up-regulated oxidative stress induced Nrf2 response to support optimal liver detox pathways and antioxidant enzyme protection during infections and inflammation, each of the enzymes/pathways the Nrf2 genes support requires essential vitamins/minerals/amino acids that the body cannot synthesize… hence "Essential Nutrients".

Essential nutrients during pro-inflammatory epigenetic up-regulation

Essential nutrients (vitamins, minerals, certain amino acids and fatty acids) are essential because the body is unable to synthesize them and must rely for their bioavailability through dietary lifestyle choices followed by proper digestion and absorption. A person must eat them, digest them, and absorb them or they will not reach the organs/tissues that require them during such times of infection, injury, inflammation, and tissue regeneration. From the NFkB perspective, if there is excessive essential fatty acid of the omega-6 Linoleic Acid, as in many western diets and obesity-laden populations, there is excessive pro-inflammatory cytokines and up-regulation NFkB and heightened even more during cytokine storms, which directly induces chronic debilitating tissue damage, degeneration, and disease. An individual with deficient vitamins and minerals cannot support their antioxidant protective Nrf2 mineral-dependent enzymes demanding required Iron, Copper, Manganese, and Selenium for the antioxidant enzymes to function properly [6], rendering these individuals more susceptible to oxidative stress and inflammation. To prevent the liver detox phase-2 bottleneck all essential B-vitamins, several amino acids (especially the sulfur amino acids methionine/cysteine/NAC and taurine, conditionally essential arginine, and simplest yet universally vital glycine), sulfur itself removed by sulfur amino acid catabolism requiring iron and molybdenum as well as B2/B3 or from sulfur foods

such as onions/garlic, and brassica vegetable sulfurophane which converts hepatically to glutathione, the potent intrinsic antioxidant tripeptide of cysteine/glycine/glutamate are *ALL* required for conjugation reactions to prevent against high toxic burden [9,10]. Vitamin C and Vitamin E work closely together to protect against oxidative stress on essential fatty acids through their solo antioxidant redox reactions [26] and Vitamin C is largely required by the immune cells to launch an attack [27] and Vitamin A supports adrenal response during times of internal stress such as infection, inflammation, toxin overload [28] and immune cell activation [29]. Additionally, Vitamin D works to increase the anti-inflammatory IL-10 cytokine which prevents autoimmune switch during times of activated immune reactions [30], while it also works with Vitamin A at the epigenetic level of retinoid heterodimer VDR-RXR as transcription regulator which encodes for the IL-10 [31]. Amino acids serve as building blocks and precursors to ensure enzymes can be built and transport/ion channel proteins are bioavailable to shuttle nutrients to/from as well as in/out of cells. Protein turnover and enzyme synthesis are enhanced during times of infection and inflammation requiring even more basal levels of these precursor amino acids [32].

Conclusion

The body knows how to manage viral and toxin exposures with intrinsically orchestrated epigenetic responses…when it has the ingredients it needs to be able to launch the attack. If the body does not have bioavailable essential nutrients to launch the response there is an increased risk of becoming more ill then someone who is not deficient.

The other perspective is the current body habitus during the viral/toxin exposure. If there is a preexisting NFkB up-regulation, inflammation, oxidative stress depleted antioxidant body habitus then the viral/toxin load will be exponentially detrimental expressing as sickness and disease with a more taxing burden of recovery. The individual that presents with both nutritional deficiency plus body habitus of preexisting inflammation and oxidative stress is at an even higher risk of viral/toxin exposure of extreme symptoms and poor recovery.

Make decisions today that create the body that is prepared, ready, and able to successfully combat viral and toxin exposures. Work daily and weekly to improve nutritional intake of antioxidant, vitamin, mineral-rich produce and phytogreens, high fiber, and low carb low sugar diets, plus regular amounts meats and protein powders, healthy fats with oils and nuts/seeds, plus omega-3 fish oils and alpha linolenic acid agents such as flax and hemp.

These choices provide anti-inflammatory food sources plus all the essential nutrients while supporting optimal digestion to allow for nutrient absorption and bioavailability; these steps shift the body habitus away from overactive up-regulated NFkB [33] and will decrease the negative effects of viral or toxin induced cytokine storms during infection and exposure. While we down-regulate NFkB and provide the essential nutrients, also add-in natural agents such as Resveratrol and Curcumin which naturally stimulate Nrf2 [19] enhancing antioxidant defense and toxin removal. Furthermore, important to understand during an active infection or toxic exposure, the metabolic demand during such infection/exposure also increases the requirement of bioavailable nutrients to launch efficient responses. Providing regular daily/weekly amounts of essential vitamins/minerals, and natural antioxidants and phytogreens to support enzyme and antioxidant function will set the stage to better handle the viral/toxin exposure with less symptoms and resulting less disease expression.

Start early with support to feel and respond better if one becomes ill and exposed.

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