Dr. Chestnut's Research Review

 SPECIAL FREE VERSION

A Comprehensive Research Summary of the Importance of Omega-3 Fatty Acids and Vitamins A+D for Baseline Immune Function, Inflammation Regulation, and Baseline Health/Comorbidity Status AND An Evidence-Based Approach to Maximizing Immune Function and Significantly Reducing Risk from COVID-19, Influenza, and other Respiratory Viruses

As the fall "cold, flu, and COVID" season is approaching it is imperative to ensure that you and your staff have knowledge and certainty regarding the most evidence-based, most effective approaches to improving baseline immune function, resolving chronic inflammation, and improving baseline health – for yourselves and your patients.

The data is unequivocal, the most significant variables determining infection, serious outcomes from infection, hospitalization, ICU admission, and death, whether talking about COVID-19 or Influenza, are baseline immune function and baseline health. Nobody can scientifically, logically, or ethically argue against the fact that comorbidities such as obesity, diabetes, heart disease, lung disease, and chronic inflammation are far more important determinants of morbidity and mortality than any other variables, including age and infection with SARS-Co-V-2 or Influenza virus.

Hundreds of millions, if not billions of people, of all ages, got infected with the EXACT SAME COVID-19 virus variants, just as they do with influenza virus in any given year, yet only a tiny percentage had serious outcomes or died (not everyone got infected with the same variant, but hundreds of millions got infected with each variant). Thus, without any debate, the variables determining morbidity and mortality from infection ARE NOT THE VIRUS or INFECTION STATUS, or AGE, because morbidity and mortality status vary significantly from person to person within similar age groups – in individuals infected with the same virus/variant.

The most significant variables determining whether you, your staff, your patients, or your loved ones get infected, have a serious outcome, or die from COVID-19 or influenza, or any respiratory illness, are baseline immune status, baseline inflammatory status, and baseline health/comorbidity status. This is true FOR ALL AGES!

Remember, only a tiny percentage of even those over 80 yrs of age die from COVID or die from Influenza. "It's NOT the seed, it's the soil" as the expression goes. This universal truth, though so obvious but so ignored during every flu season, has never been so undeniable as during the past few years of the COVID-19 pandemic.

A full 1/3 of care home residents die every year – and this was true long before COVID-19. The average lifespan after admission to a care home is about 2.5 years. These are frail, vulnerable, elderly with a very short life expectancy. They deserve protection, but that protection could NEVER come from locking down healthy people, vaccinating healthy people with a vaccine that does not prevent infection or transmission, wearing masks that cannot filter out an aerosol virus, or social distancing when the aerosolized virus can easily survive for ours as it circulates through entire rooms. We failed the elderly frail because we failed to follow the real science.

Worse, we blamed the unvaccinated and the unmasked for their deaths when in fact it was the infected who were the threat to the elderly and neither the vaccine nor the masks prevented infection, or prevented the infected from infecting these most vulnerable of our citizens. Rather than admit the truth, that the fully vaccinated elderly in care homes continued to die, even when staff were also fully vaccinated and masked, public health authorities instead chose to blame their failure to protect these vulnerable elderly on the unvaccinated. REPUGNANT beyond comprehension.

The COVID-19 illness pandemic was not a pandemic of SARS-CoV-2 infection, it was a syndemic of comorbidities which made people susceptible to serious COVID-19 illness outcomes from SARS-CoV-2 infection. The COVID-19 illness pandemic was a syndemic of chronic lifestyle illness (comorbidities) and the novel SARS-CoV-2 respiratory virus (likely bioengineered).

It was absurd to try to control a rapidly mutating virus with vaccines that targeted only a small portion of that virus (spike protein and not the nucleocapsid etc) that could rapidly mutate and thus could never provide sterilizing immunity, individual immunity, herd immunity, or prevent infection or transmission. It was diabolical to lie about the effectiveness of these vaccines and to mandate them and, worse, to punish with loss of employment, public humiliation, and bullying, those who chose not to take them. What an incredible lack of medical ethics, integrity, and decency.

The scientific, evidence-based, logical, and ethical solution was to target the soil, to target the baseline immune status, inflammatory status, and baseline health/comorbidity status of the population.

And, for those who wanted to take an experimental vaccine/gene therapy, to make that available with informed consent regarding individual risk from COVID-19 and potential benefit/harm from the gene therapy/vaccine. The data is irrefutable that risk from COVID-19, and thus potential benefit from the vaccine, varied widely based on identifiable risk factors/comorbidities. Further, since the vaccine does not prevent infection or transmission, no valid scientific or ethical argument could be made to recommend vaccination to "protect others" - this was simply fraudulent propaganda.

There is simply no data to support even offering, let alone recommending, these vaccines for healthy children or young adults and refusing a child or young adult access to education based on vaccination status was not only unethical it was criminal.

There also should have been informed consent that was honest about the fact that there was insufficient data to claim the vaccines were safe or that they could prevent infection or transmission. All that was required, as always, was honesty and ethics. Sadly, we got neither.

The same is true for social distancing, lockdowns, and masks. As it turns out there was no valid evidence to support any of these public health measures to be mandated rather than personal choice. What a complete failure this has been! The only thing that should have been mandated was to stay home if you felt sick or had a fever!

This is what I argued from the onset of this pandemic based on the first published data which showed that serious morbidity and mortality was determined not by the virus or even by age, but by comorbidity status.

For varying but equally unjustifiable reasons these irrefutable facts got rejected by public health authorities and governments and labelled as misinformation – even when they were put forward by tens of thousands of world-renowned, highly credentialed, highly published medical experts like those who created or signed onto the Great Barrington Declaration.

The shocking, sad, inexcusable truth is that the vast majority of misinformation came from public health authorities, governments, and complacent media, educators, and healthcare practitioners.

What resulted was the greatest, most damaging, most divisive, most ineffective public health blunder in history. These truths are slowly coming to light, but most are still censored or cancelled or dishonestly labelled as misinformation.

David L. Katz MD, MPH May 6, 2022 The Better Pandemic That Might Have Been. https://www.linkedin.com/pulse/better-pandemic-might-have-been-david-l-katz-md-mph/

"The underlying cause of the toll of COVID in the U.S. and many other nations was the prior, neglected pandemic of cardiometabolic disease. The cause of all that cardiometabolic mayhem is, in turn, diet and lifestyle at odds with the requirements of human health. A culture designed to feed corporate profits at the expense of public health underlies all of that."

"The pandemic of lifestyle-related chronic disease was, if not altogether fixable during the compressed timeline of the COVID pandemic, at a minimum, addressable to very good effect."

"We need not, for example, have waited to weigh the human costs of a diabetes/COVID feedback loop. Tallying years of living lost to a pernicious interaction known from the earliest days of this pandemic is not just senseless- it is scandalous, and tragic."

"We might, rather, have rapidly expanded access to lifestyle medicine, diabetes prevention and management programming, and for that matter- free fruits and vegetables, nuts and beans, recipes and vouchers, sports and exercise equipment."

"Instead, "follow the science" devolved to dogma limited to masks and vaccines, while ignoring the causes of causes, constraining vision to its traditionally myopic span, and seemingly disavowing sense."

"The COVID disease; the heavy-handed, one-size-fits all COVID "cures"; competing ideologies where epidemiology ought to have prevailed; and the systematic neglect of the underlying causes of the causes of our woes contributed, all, to a massive toll of preventable harm. There is a far better pandemic that might have been. If we learn the lessons of this one, maybe next time it will be."

Lobestein et al . (2021) COVID-19 and Obesity: The 2021 Atlas: The Cost of not addressing the global obesity crisis. World Obesity Federation www.worldobesity.org

"As we show in this report, increased bodyweight is the second greatest predictor of hospitalisation and a high risk of death for people suffering from COVID-19. Only old age rates as a higher risk factor."

**It is extremely important to understand that age itself was not a causal risk factor, well over 95% of the elderly who got COVID-19 survived. Age is a correlative risk factor because the elderly are much more likely to have Vit D deficiency, to have chronic inflammation, to exercise less, to have poor nutrition, and, of course, to have comorbidities.*

A full 1/3 of care home residents die every year – and this was true long before COVID-19. The average lifespan after admission to a care home is about 2.5 years. These are frail, vulnerable, elderly with a very short life expectancy. They deserve protection, but that protection could NEVER come from locking down healthy people, vaccinating healthy people with a vaccine that does not prevent infection or transmission, wearing masks that cannot filter out an aerosol virus, or social distancing when the aerosolized virus can easily survive for ours as it circulates through entire rooms. We failed the elderly frail because we failed to follow the real science.

Worse, we blamed the unvaccinated and the unmasked for their deaths when in fact it was the infected who were the threat to the elderly and neither the vaccine nor the masks prevented the infected from infecting these most vulnerable of our citizens. Rather than admit the truth, that the fully vaccinated elderly in care homes continued to die, even when staff were also fully vaccinated and masked, public health authorities instead chose to blame their inability to protect these vulnerable elderly on the unvaccinated. REPUGNANT beyond comprehension.

"The unprecedented economic costs of COVID-19 are largely due to the measures taken to avoid the excess hospitalisation and need for treatment of the disease. Reducing one major risk factor, overweight, would have resulted in far less stress on health services and reduced the need to protect those services from being overwhelmed."

"We show that in those countries where overweight affects only a minority of the adult population, the rates of death from COVID-19 are typically less than one tenth the levels found in countries where overweight affects the majority of adults."

"We also show that the drivers of overweight – especially high levels of consumption of processed foods – are associated with mortality from COVID-19."

"Lastly, we show that COVID-19 is not a special case: a number of other respiratory viruses lead to more severe consequences in people living with excess bodyweight, giving good reasons to expect the next pandemic to have similar effects."

Steenkamp, L. et al. (2021) Small steps, strong shield: directly measured, moderate physical activity in 65,361 adults is associated with significant protective effects from COVID-19 outcomes. Br. J Sports Med.

"Adults with high and moderate physical activity levels had significantly better outcomes than those with low activity when contracting COVID-19. The apparent protective effects of regular physical activity extended to those with concomitant chronic medical conditions."

"The largely immunoprotective effect of aerobic activity is multifaceted. It involves reductions in inflammation, the mobilisation of lymphocytes, alterations in cytokine profiles, enhanced immunosurveillance and the amelioration of psychological stress."

"Before the emergence of COVID-19, epidemiological data suggested that physically active people are less likely to report symptoms of upper respiratory illness and that regular physical activity can protect the host from many types of viral infections including influenza, rhinovirus and the reactivation of latent herpes viruses."

Merino et al. (2021) Diet quality and risk and severity of COVID-19: a prospective cohort study. GUT (BMJ)

"Compared with individuals in the lowest quartile of the diet score, high diet quality was associated with lower risk of COVID-19 and severe COVID-19."

"Our study suggests that efforts to address disparities in COVID-19 risk and severity should consider specific attention to improve nutrition as a social determinants of health."

It was NOT THE UN-vaccinated that drove the pandemic, or overburdened the system, it was, as always, the UN-heathy, the UN-FIT, and the OVER-weight, caused by choosing to live an UN-healthy lifestyle!! This was/is true prior to, during, and after COVID.

Thus, the question that needed answering, and the question that needs answering going forward, is what are most evidence-based, clinically effective ways to improve baseline immune function status, baseline inflammatory status, and baseline health/comorbidity status?

The answer, of course, is to encourage people to Eat Well – Move Well – Think Well®. In other words, utilizing Evidence-Based Lifestyle Solutions (see my public website at www.eatwellmovewellthinkwell.com) or my practitioner website at (www.innatechoice.com or www.thewellnesspractice.com) for more FREE information and resources.

The evidence is overwhelmingly clear that the above clinical approach is the most evidence-based available in terms of improving/restoring immune function, improving/restoring the ability to control and regulate inflammation, and improving baseline health and preventing/improving/resolving comorbidities such as obesity, diabetes, and heart disease.

The fact that unhealthy lifestyle is the leading cause of low baseline immune function, chronic inflammation, low baseline health status, and comorbidities such as obesity, diabetes, and heart disease is irrefutable and the evidence is unequivocal. As is the fact that a healthy lifestyle is the only proven way to restore baseline immune function, prevent and/or resolve chronic inflammation, restore baseline health, and prevent/improve/resolve comorbidities. I have written a 500-page book on this topic, 'Live Right for Your Species Type' which irrefutably proves this with hundreds and hundreds of citations from peer-reviewed articles. For those interested in further reading or those who might doubt the veracity of the above statements I highly recommend you visit one of my websites and get a copy.

Having said all of the above, in this Research Review I am going to provide a summary of the research proving that the Evidence-Based COVID-19 and Flu Prevention and Risk Reduction Protocol I have been advocating since long before the COVID-19 pandemic, that I advocated during the COVID-19 pandemic, and that I will continue to advocate long after the COVID-19 pandemic, represents the most evidence-based, most clinically effective clinical protocol for COVID-19, flu, and other respiratory illness prevention and risk reduction.

Why is this irrefutably and provably true? Because the Innate Choice® Evidence-Based COVID-19 and Flu Prevention and Risk Reduction Protocol represents an evidence-based, proven clinically effective protocol for improving/restoring immune function, improving/restoring the ability to control and regulate inflammation, and improving baseline health and preventing/improving/resolving comorbidities such as obesity, diabetes, and heart disease (and cancer, and virtually all other chronic health and quality of life issues).

What is important to know is that omega-3 fatty acids and Vitamins A and D play vital, significant, and synergistic roles in every aspect of viral immune defense, regulation and resolution of inflammation, the epigenetic expression of healthy structure and function and thus baseline health, and the prevention/improvement/resolution of chronic illnesses/comorbidities.

These essential nutrients play a significant causal role in the variables determining risk of infection and risk of serious morbidity and mortality from COVID-19 or influenza, or any respiratory illness. These variables, which are HIGHLY INFLUENCED by these essential nutrients, are, as previously mentioned, and as will be constantly repeated for emphasis, are: baseline immune status, baseline inflammatory/inflammation regulatory status, and baseline health/comorbidity status.

The Significant Role of Omega-3 and Vitamins A+D in Baseline Immune Function

Rastogi, A. et al. (2020) Short term, high-dose vitamin D supplementation for COVID-19 disease: a randomized, placebo-controlled, study (SHADE study). Postgrad Med J doi:10.1136/ postgradmedj-2020-139065

"Vitamin D influences the expression of various genes involved in the immune system (innate immunity, adaptive immunity) and the downstream inflammatory cascade, thus affecting the susceptibility to and severity of bacterial and viral infections."

"Vitamin D can induce anti-microbial peptide cathelicidin in neutrophils, NK cells and monocytes."

"In a recent meta-analysis of intervention trials, vitamin D supplementation was observed to reduce the incidence of acute respiratory tract infections. Similarly in SARS-CoV-2 infection vitamin D deficiency may lead to a proinflammatory cytokine milieu, thus augmenting the disease severity."

"It has been observed that vitamin D-deficient individuals have increased COVID-19 risk and mortality."

Annweiler, G. et al. (Nov 2020) Vitamin D supplementation associated to better survival in hospitalized frail elderly COVID-19 patients: The GERIA-COVID Quasi-Experimental Study. Nutrients 12, 3377

"Importantly, a recent unbiased genomics-guided tracing of the SARS-CoV-2 targets in human cells identified vitamin D among the three top-scoring molecules manifesting potential infection mitigation patterns through their effects on gene expression."

"In particular, by activating or repressing several genes in the promoter region of which it binds to the vitamin D response element, vitamin D may theoretically prevent or improve COVID-19 adverse outcomes by regulating i)

the renin–angiotensin system (RAS), ii) the innate and adaptive cellular immunity, iii) the physical barriers, and iv) the host frailty and comorbidities."

Gutierrez, S. et al. (2019) Effects of Omega-3 Fatty Acids on Immune Cells. Int. J. Mol. Sci. 20, 5028; doi:10.3390/ijms20205028.

"Alterations on the immune system caused by omega-3 fatty acids have been described for 30 years. This family of polyunsaturated fatty acids exerts major alterations on the activation of cells from both the innate and the adaptive immune system, although the mechanisms for such regulation are diverse."

"Although the specific mechanisms of action of omega-3 fatty acid regulation of immune cells function present several cell type-specific features, it is worth mentioning that omega-3 fatty acids, via in vitro stimulation or via dietary supplementation, effectively incorporate into the cellular membrane of all the immune cells investigated to date."

"Macrophages have a fundamental role as part of the innate immune system. They patrol multiple organs in a constant search for invading pathogens. They are able to recognize specific pathogen-associated molecular patterns (PAMPs) thanks to the toll-like receptors (TLRs) present on their surface. After pathogen recognition, they initiate the elimination process of the pathogen by engulfing it (phagocytosis) and secreting anti-microbial molecules such as reactive oxygen species (ROS). Simultaneously, they produce and secrete a large variety of cytokines and chemokines in order to recruit and activate other immune cells from both the innate and the adaptive immune system to mount an efficient immune response to completely eliminate the threat."

"The impact of omega-3 fatty acids on macrophage function has extensively been investigated since the 1980s. Since then, there are three main properties of macrophage biology that have been identified to be altered by omega-3 fatty acids: the production and secretion of cytokines and chemokines, the capacity of phagocytosis, and the polarization into classically activated or alternatively activated macrophages."

"Neutrophils are the first cells to be recruited to the site of inflammation and have an important role in the clearance of pathogens. However, neutrophils can also interact with the adaptive immune system by promoting naïve T cells to transition into T helper1 cells and can present antigens to B-cells in the spleen."

"Omega-3 fatty acids have been shown to improve the phagocytic capacity in neutrophils in mice. In vitro, adding DHA to extracted peritoneal neutrophils leads to a 35% increase in phagocytic capacity as well as a two-fold increase in fungicidal capacity."

"This effect has partly been confirmed in humans too. Ten volunteers were given fish oil supplementation containing 26% EPA and 54% DHA daily for two months. Thereafter, the phagocytic capacity of the neutrophils in the blood was increased by 62%." "In humans, supplementation with 54% DHA and 26% EPA for two months increased ROS (Reactive Oxygen Species) production in phorbol-myristate-acetate stimulated neutrophils."

"Generally, ALA, DHA, and EPA exert an inhibitory effect on the activation of immune cells from both the innate and the adaptive branch. Interestingly, some specific immune functions are promoted by dietary omega-3 fatty acids in specific immune cell types, i.e., phagocytosis by macrophages and neutrophils or Treg differentiation, suggesting that omega-3 fatty acids do not act as unspecific immune-repressors."

What this all means, is that the immune system cannot function properly, be up-regulated properly, or be down-regulated properly, without sufficient intake of omega-3 fatty acids. It would be biologically erroneous to think of omega-3 fatty acids as either anti-inflammatory, immune system up-regulating, or immune system down-regulating. It is much more accurate to view omega-3 fatty acids as essential nutrients which are required for the proper overall function and regulation of immune responses.

When appropriate, omega-3 fatty acids are important to prevent chronic inflammation and hyper-immune responses. At other times, when appropriate, omega-3 fatty acids are important to allow up-regulation of immune function such as when a virus is detected and up-regulation of macrophages and neutrophils is required. Inflammation is a stage of healing and is required for healing and for immune response. It is hyper-inflammatory responses and/or chronic inflammation which is harmful.

Omega-3 fatty acids are not what controls or determines the immune response, omega-3 fatty acids are essential nutrients that are required ingredients or tools of the immune response. Deficiency of omega-3 fatty acids causes immune dysfunction, sometimes in the form of pro-inflammation or hyper-activity, and sometimes, as in the case of viral infection, in the form of downregulated innate immune response via macrophages and neutrophils which, in turn, causes a decreased T-Cell response to viruses because macrophages and neutrophils signal the T-Cell response.

Borsche et al. (2021) COVID-19 Mortality Risk Correlates Inversely with Vitamin D3 Status, and a Mortality Rate Close to Zero Could Theoretically Be Achieved at 50ng/ml 25(OH)D3: Results of a Systematic Review and Meta-Analysis. Nutrients 13, 3596

“One strong pillar in the protection against any type of virus infection is the strength of our immune system.”

“Today, a compelling body of experimental evidence indicates that activated vitamin D3 plays a fundamental role in regulating both innate and adaptive immune systems. Intracellular vitamin D3 receptors (VDRs) are present in nearly all cell types involved in the human immune response, such as monocytes/macrophages, T cells, B cells, natural killer (NK) cells, and dendritic cells (DCs).

“As a consequence of this knowledge, the scientific community now agrees that calcitrol is much more than a vitamin but rather a highly effective hormone with the same level of importance to human metabolism as other steroid hormones.”

“In this publication, we will demonstrate that vitamin D3 deficiency, which is a well-documented worldwide problem, is one of the main reasons for severe courses of SARS-CoV-2 infections. The fatality rates correlate well with the findings that elderly people, black people, and people with comorbidities show very low vitamin D3 levels.”

“The blood level ensuring the reliable effectiveness of vitamin D3 with respect to all its important functions came under discussion again, and it turned out that 40–60 ng/mL [100-150 nmol/L] is preferable, which is considerably above the level required to prevent rickets [the level the RDA is based upon and, sadly, the level still advocated by most healthcare practitioners].”

**The problem is that many studies of vitamin D either only include very small, deficient doses or, as invalidly, include single very high injected bolus doses – both of which have been proven to be ineffective. Then, when systematic reviews are written, these studies with invalid dosing, which often get poor results, which vastly outnumber the number of studies with proper dosing, make it appear that the evidence for vitamin D is far less robust than it is. When only studies using valid dosing of vitamin D are pooled and analyzed the benefits of vitamin D become indisputable. Further, it is clear that there is a demonstrable bias against natural, unpatentable natural supplements that do not require a visit to a medical doctor, or a written prescription. See my Jan 2021 Research Review, of the Benskin review of the vitamin D literature for further evidence.*

"Long before the SARS-CoV-2 pandemic, an increasing number of scientific publications showed the effectiveness of a sufficient vitamin D3 blood level in curing many of the human diseases caused by a weak or unregulated immune system. This includes all types of virus infections, with a main emphasis on lung infections that cause ARDS [acute respiratory distress syndrome], as well as autoimmune diseases."

"However, routine vitamin D3 testing and supplementation are still not established today. Unfortunately, it seems that the new findings about vitamin D3 have not been well accepted in the medical community. Many official recommendations to define vitamin D3 deficiency still stick to the 20 ng/mL established 100 years ago to cure rickets."

"Additionally, many recommendations for vitamin D3 supplementation are in the range of 5 to 20 µg per day (200 to 800 international units), which is much too low to guarantee the optimal blood level of 40–60 ng/mL [100-150 nmol/L]"

Prietl, B. et al. (2013) Vitamin D and Immune Function. Nutrients, 5, 2502-2521; doi: 10.3390/nu5072502

"Early evidence that vitamin D acts as important stimulant for innate immunity came from reports about tuberculosis treatment with cod liver oil. More current studies specify how calcitriol enhances the antimicrobial effects of macrophages and monocytes, which are important effector cells, fighting against pathogens."

"Human cathelicidin which causes destabilization of microbial membranes, is up-regulated in response to infections in humans and acts against bacteria, viruses and fungi."

"Besides enhancing chemotaxis and phagocytic capabilities of innate immune cells, the complex of calcitriol, VDR, and retinoid X receptor directly activates the transcription of antimicrobial peptides such as defensin β2 (DEFB) and cathelicidin antimicrobial peptide (hCAP18)."

**You will see more about the importance of Vitamin D and Vitamin A working synergistically later. The VDR is the Vit D receptor, the retinoid X receptor is the Vit A receptor.*

"This finding supports the theory that the vitamin D status regulates antimicrobial protein levels and may be crucial in infection control."

Defensin and cathelicidin are anti-microbial proteins (AMPs) which are used by the cells of the innate immune system to kill invading viruses. This is a DIRECT effect of Vitamin D on the functional status and potency of the innate immune defense against viruses.

Huang, Z. et al. (2018) Role of Vitamin A in the Immune System. J. Clin. Med. 7, 258; doi:10.3390/jcm7090258

"Vitamin A (VitA) is involved in the development of the immune system and plays regulatory roles in cellular immune response and humoral immune processes. VitA has demonstrated a therapeutic effect in the treatment of various infectious diseases."

"With deficient VitA intake, the resistance of keratinized epithelial tissues to foreign pathogens decreases, and it is no longer able to exert its mechanical barrier function, thus reducing innate immune function and promoting respiratory tract infections, diarrhea, and other diseases in children."

"Research has shown that crucial immune organs need constant dietary intake to maintain VitA concentrations, and RA (retinoic acid) was previously shown both to promote the proliferation and to regulate the apoptosis of thymocytes."

"In mice, VitAD (Vit A deficiency) leads to a defect in both T cell-mediated and antibody-dependent immune responses."

"Retinoid acid plays crucial roles in the regulation of the differentiation, maturation, and function of cells of the innate immune system. Innate immune cells are comprised of macrophages and neutrophils, which initiate immediate responses to pathogen invasion through phagocytosis and activation of natural killer T cells which perform immunoregulatory functions through cytotoxic activity."

"Regulatory T cells (Treg) are a subpopulation of T cells that maintain immune tolerance and regulate the autoimmune response."

"Local injection of Tregs failed to prevent development in a collagen-induced arthritis model, whereas the injection of ATRA-pretreated Tregs successfully inhibited the development of arthritis."

WOW! Read that again. Without sufficient Vitamin A, the Treg cells (regulatory T-cells) which serve to regulate the immune and inflammatory responses to prevent hyper-inflammation and autoimmune responses, failed to prevent the development of collagen-induced arthritis – scar tissue induced arthritis. BUT, when the Treg cells were exposed to sufficient Vitamin A, they did successfully inhibit the development of arthritis!!!

You will see in later citations that omega-3 fatty acids, Vitamin D, and Vitamin A are all required for the proper expression of and function of Treg cells and thus the proper function of the immune system.

"ATRA (Retinoic Acid Receptor Ligand) also enhanced the stability and functionality of human natural Treg cells under the inflammatory conditions. ATRA prevented the transformation of Tregs to Th17 cells and other inflammatory cells by inhibiting the expression of IL-6R on the cell surface of peripherally induced Tregs. Therefore, ATRA enhanced IL-2 function, an important immunomodulator, and promoted naïve T cell transformation into natural Tregs while inhibiting the IL-6-induced transformation of naïve T cells into Th17 cells. Additionally, ATRA also has the ability to induce and promote the development and function of human-induced Treg cells."

"VitA has both promoting and regulatory roles in both the innate immune system and adaptive immunity; therefore, it can enhance the organism's immune function and provide an enhanced defense against multiple infectious diseases."

Ikeda, U et al. 1,25 dihydroxyvitamin D3 and all-trans retinoic acid synergistically inhibit the differentiation and expansion of Th17 cells. Immunology Letters 2010. 134(1):7-16.

"The active form of vitamin D3 is an immunoregulatory hormone with beneficial effects on Th1 cell-mediated inflammatory diseases."

"Thus, we initially reveal that Vit D and Vit A have synergistic effects on the generation of Th17 cells, suggesting that the combination would provide a promising novel therapy for Th17 cell-related immune diseases including skin inflammation."

Bettoun Burris, et al. Retinoid X Receptor Is a Nonsilent Major Contributor to Vitamin D Receptor-Mediated Transcriptional Activation. Molecular Endocrinology 17: 2320–2328, 2003

"In summary, we describe a unique and unexpected facet of intermolecular cross-talk between VDR and RXR and demonstrate that RXR actively participates in RXR-VDR-mediated gene transcription by directly recruiting coactivators in response to 1,25-(OH)2D3."

In layperson terms vitamin A (retinoid) is required to activate the expression of vitamin D controlled genes and vice-versa. In other words, without sufficient amounts of vitamin A, the actions of vitamin D can be impaired or even blocked. Vitamin A and Vitamin D work synergistically.

Mawson, A. (2013) Role of Fat-Soluble Vitamins A and D in Pathogenesis of Influenza: A New Perspective. Infectious Diseases http://dx.doi.org/10.5402/2013/246737.

"This paper presents a new model of the etiopathogenesis of influenza, suggesting that host resistance and susceptibility depend importantly on the ratio of vitamin D to vitamin A activity. Retinoid concentrations within normal physiological limits appear to inhibit influenza pathogenesis whereas higher background concentrations (i.e., very low vitamin D : A ratios) increase the risk of severe complications of the disease."

Levine, SA. The importance of a balanced approach to vitamin D supplementation. Journal of Orthomolecular Medicine. 2011;26(1):15-20.

"Vitamin A and vitamin D balance, enhance, and contain each other through the retinoid X receptor (RXR)."

"Because they share a receptor, if we supplement either vitamin D or vitamin A in an unbalanced fashion, we create a functional deficiency of the one not supplemented."

This is EXACTLY why I created OmegA+D Sufficiency which contains half omega-3 fish oil and half cod liver oil which contains naturally occurring, fully formed Vitamin A and D. I also add extra Vitamin D to ensure sufficient daily intake of the 3 MOST IMPORTANT essential nutrients for immune system defense against viruses such as influenza, coronavirus, and rhinovirus – Omega-3, Vit A, and Vit D. There simply is not a more evidence-based, more important, more effective, more beneficial, or more valuable supplement in the world.

The Significant Role of Omega-3 and Vitamins A+D in Regulating and Resolving Inflammation

Borsche et al. (2021) COVID-19 Mortality Risk Correlates Inversely with Vitamin D3 Status, and a Mortality Rate Close to Zero Could Theoretically Be Achieved at 50ng/ml 25(OH)D3: Results of a Systematic Review and Meta-Analysis. Nutrients 13, 3596

"The most life-threatening events in the course of a SARS-CoV-2 infection are ARDS and cytokine release syndrome (CRS). It is well established that vitamin D3 is able to inhibit the underlying metabolic pathways because a very specific interaction exists between the mechanism of SARS-CoV-2 infection and vitamin D3."

"Angiotensin-converting enzyme 2 (ACE2), a part of the renin-angiotensin system (RAS), serves as the major entry point for SARS-CoV-2 into cells. When SARS-CoV-2 is attached to ACE2 its expression is reduced, thus causing lung injury and pneumonia. Vitamin D3 is a negative RAS modulator by inhibition of renin expression and stimulation of ACE2 expression. It therefore has a protective role against ARDS caused by SARS-CoV-2. Sufficient vitamin D3 levels prevent the development of ARDS [acute respiratory distress syndrome] by reducing the levels of angiotensin II and increasing the level of angiotensin I."

"There are several additional important functions of vitamin D3 supporting immune defense:

1. Vitamin D decreases the production of Th1 cells. Thus, it can suppress the progression of inflammation by reducing the generation of inflammatory cytokines.
2. Vitamin D3 reduces the severity of cytokine release syndrome (CRS). This "cytokine storm" causes multiple organ damage and is therefore the main cause of death in the late stage of SARS-CoV-2 infection. The systemic inflammatory response due to viral infection is attenuated by promoting the differentiation of regulatory T cells [Tregs].
3. Vitamin D3 induces the production of the endogenous antimicrobial peptide cathelicidin (LL-37) in macrophages and lung epithelial cells, which acts against invading respiratory viruses by disrupting viral envelopes and altering the viability of host target cells.
4. Experimental studies have shown that vitamin D and its metabolites modulate endothelial function and vascular permeability via multiple genomic and extragenomic pathways.
5. Vitamin D reduces coagulation abnormalities in critically ill COVID-19 patients."

Laird, E. et al. (May 2020) Vitamin D and Inflammation: Potential Implications for Severity of Covid-19. Irish Medical Journal; Vol 113; No. 5.

"Recent research has highlighted a crucial supportive role for vitamin D in immune cell function, particularly in modulating the inflammatory response to viral infection."

"At a cellular level, vitamin D modulates both the adaptive and innate immune system through cytokines and regulation of cell signaling pathways. Vitamin D receptor (VDR) is present on both T and B immune cells; Vitamin D modulates the proliferation, inhibition and differentiation of these cells."

**Remember, sufficient and proper synergistic amounts of Vit A are required to upregulate the VDR receptors on immune cells! A proper ratio of Vit D:Vit A is required.*

"In experimental models of lipopolysaccharide-induced inflammation, vitamin D is associated with lower concentrations of the pro-inflammatory cytokine Interleukin- 6 (IL-6), which plays a significant role in Covid-19 induced acute respiratory distress syndrome (ARDS)."

"Vitamin D also reduces lipolysaccharide-induced lung injury in mice by blocking effects on the Ang-2-Tie-2 and renin-angiotensin pathways that are highly relevant to Severe Acute Respiratory Syndrome Coronavirus2 (SARS-CoV-2) pathogenicity."

"A 'sufficient' vitamin D serum level is linked to a switch from a pro- to anti-inflammatory profiles in older adults."

This is also why Vit D is so important for chiropractic patients. Vit D induces "a switch from a pro- to anti-inflammatory profiles" and inflammation is at the root of spinal pain and degeneration. Inflammation is also at the root of heart disease, cancer, diabetes, obesity, and virtually every other chronic illness. This is why sufficient intake of Vit D has been clinically shown to prevent, reduce the severity of, and/or reduce virtually every chronic illness. Add sufficient intake of omega-3 fatty acids, which have also been proven to induce "a switch from a pro- to anti-inflammatory profiles" and you can begin to understand the ENORMOUS CLINICAL BENEFIT of OmegA+D Sufficiency™!!

Panigraphy et al. (2020) Inflammation Resolution: a dual prolonged approach to averting cytokine storms in COVID-19? Cancer and Metastasis Reviews 39: 337-340.

"Severe coronavirus disease (COVID-19) is characterized by pulmonary hyper-inflammation and potentially life-threatening "cytokine storms". Controlling the local and systemic inflammatory response in COVID-19 may be as important as anti-viral therapies."

"Endogenous lipid autacoid mediators, referred to as eicosanoids, play a critical role in the induction of inflammation and pro-inflammatory cytokine production."

Omega-3 fatty acids (eicosanoids), are essential for the production of lipid mediators called resolvins that play a significant role in what is known as the resolving phase of inflammation – hence the term resolvins.

"A paradigm shift is emerging in our understanding of the resolution of inflammation as an active biochemical process with the discovery of novel endogenous specialized pro-resolving lipid autacoid mediators (SPMs), such as resolvins." [And Treg Cells!]

"Resolvins and other SPMs stimulate macrophage mediated clearance of debris and counter pro-inflammatory cytokine production, a process called inflammation resolution."

"In contrast to classic anti-inflammatory agents, endogenous pro-resolution lipids [omega-3 fatty acids] can terminate the inflammatory response by promoting the clearance of cellular debris."

"Specialized proresolving mediators (SPMs), including resolvins, lipoxins, and protectins, are bioactive lipid autacoids that mediate endogenous resolution by stimulating macrophage phagocytosis of cellular debris and countering the release of proinflammatory cytokines/chemokines."

"Importantly, loss of inflammation resolution mechanisms plays a role in sustaining pathologic inflammation."

"Endogenous resolution processes have been identified in the termination of infectious diseases, including influenza, and could thus be harnessed for averting dysregulated inflammation and associated mortality in COVID-19."

"SPMs (specialized pro-resolving mediators) [from **omega-3 fatty acids**"]:

1. stimulate macrophage phagocytosis and efferocytosis
2. decrease pro-inflammatory cytokine production
3. inhibit leukocytosis and thereby decrease the inflammatory infiltrate, and
4. may stimulate the adaptive immune response and the production of anti-SARS-CoV-2 antibodies."

"Targeting individual pro-inflammatory cytokines may not be sufficient to prevent COVID-19 progression."

"Importantly, SPMs [specialized pro-resolving mediators from Omega-3 fatty acids] terminate self-sustaining inflammatory processes, such as those induced by COVID-19, by broadly inhibiting proinflammatory cytokine production and promoting a return to tissue homeostasis."

"Moreover, conventional anti-inflammatory agents such as NSAIDs and COX-2 inhibitors, while limiting the eicosanoid storm, may be "resolution toxic" as they indiscriminately inhibit eicosanoid pathways that produce resolution mediators and thereby prevent active resolution."

This is why NSAIDS don't work for chronic back pain or other chronic pain and why they only work for acute pain for a VERY SHORT period of time. NSAIDS "indiscriminately inhibit eicosanoid pathways that produce resolution mediators and thereby prevent active resolution". NSAIDS inhibit the body's innate ability to resolve inflammation – chronic use is inflammation resolution-toxic!

Szabo, Z et al. (2020) The Potential Beneficial Effect of EPA and DHA Supplementation Managing Cytokine Storm in Coronavirus Disease. Frontiers in Physiology 11: Article 752

"In the recent COVID-19 (caused by SARS-Cov-2 virus) pandemic a subgroup of patient death is attributed to the so-called "cytokine storm" phenomenon (also called cytokine release syndrome or macrophage overactivation syndrome)."

"LC-PUFAs (long chain polyunsaturated fatty acids) such as EPA (eicosapentaenoic acid) and DHA (docosahexaenoic acid) are noteworthy because of their direct influence in the immunological response to viral infections."

"Evidence suggests that n-3 LC-PUFAs can modulate the immune response and function in many ways. Among these complex immunomodulatory effects, interleukin-6 (IL-6) and interleukin-1ß (IL-1b) - because of the suspected central regulatory role in the "cytokine storm" - should be highlighted. These cytokines can be affected by dietary EPA and DHA intake."

"Summary: Based on the available data, the supplementation of EPA and DHA in COVID-19 patients appears to have potential beneficial effect in managing the "cytokine storm.""

"Therefore, the use of EPA and DHA supplementation should be considered as both a supportive therapy and a prevention strategy in SARS-Cov-2 infection."

Grant et al. (April 2020) Evidence that Vitamin D Supplementation Could Reduce Risk of Influenza and COVID-19 Infections and Deaths Nutrients 12, 988; doi:10.3390/nu12040988

"Through several mechanisms, vitamin D can reduce risk of infections. Those mechanisms include inducing cathelicidins and defensins [anti-microbial proteins or AMPs] that can lower viral replication rates and reducing concentrations of pro-inflammatory cytokines that produce the inflammation [cytokine storm] that injures the lining of the lungs [Acute Respiratory Distress Syndrome or ARDS], leading to pneumonia, as well as increasing concentrations of anti-inflammatory cytokines."

As I described in my March and April 2020 Research Reviews, vitamin D is required by the phagocytes (macrophages and neutrophils) of the innate immune system in order for these cells to be able to synthesize and release sufficient amounts of anti-microbial proteins which these cells use to kill viruses.

Vitamin D (and omega-3 and Vit A) is also required for the proper function of T-regulatory (Treg) cells of the adaptive immune system. Treg cells are essential for controlling and regulating the inflammatory response. When Treg cells are deficient in Vit D [or omega-3 or Vit A] they cannot properly control inflammation and this can lead to what is known as the cytokine storm (inflammatory storm) which is the underlying cause of Acute Respiratory Distress Syndrome – which is what kills people with COVID-19 and pneumonia secondary to flu.

Prietl, B. et al. (2013) Vitamin D and Immune Function. Nutrients, 5, 2502-2521; doi: 10.3390/nu5072502

"In principle, vitamin D exposure leads to a shift from a proinflammatory to a more tolerogenic immune status, including very diverse effects on T cell subtypes: Calcitriol suppresses T helper (Th) cell proliferation, differentiation and modulates their cytokine production. In particular, treatment of T cells with calcitriol or analogs inhibits the secretion of proinflammatory Th1 (IL2, interferon-γ, tumor necrosis factor α), Th9 (IL9) and Th22 (IL22) cytokines but promotes the production of more anti-inflammatory Th2 cytokines."

"Tregs act to suppress proinflammatory responses by other immune cells and aim to prevent exaggerated or autoimmune responses. They are potently induced by different forms of vitamin D."

Gutierrez, S. et al. (2019) Effects of Omega-3 Fatty Acids on Immune Cells. Int. J. Mol. Sci. 20, 5028; doi:10.3390/ijms20205028.

"In recent years, however, a new role for omega-3 fatty acids and their derivatives as signaling molecules has emerged."

"Both omega-3 and omega-6-derived metabolites have important immune-regulatory functions. These metabolites are generally known as specialized pro-resolving mediators (SPMs) and can be classified in different families—prostaglandins, leukotrienes, thromboxanes, maresins, protectins, and resolvins."

"Probably the most renowned property of omega-3 fatty acids is their ability to reduce inflammation and their beneficial effect on inflammation-related disorders. For some of these diseases, it has been suggested that the cell type responsible for the inflammatory modulation by omega-3 fatty acids is macrophages."

"Omega-3 fatty acids have been shown to be incorporated into phospholipids in the cell membrane of neutrophils at the expense of the omega-6 fatty acids linoleic and arachidonic acid. Once the omega-3 fatty acids have been incorporated into the phospholipids, they can be metabolized by neutrophils into prostaglandins, leukotrienes, thromboxanes, maresins, protectins, and resolvins. Omega-3 fatty acids, and their metabolites, modulate neutrophil function in several ways, including neutrophil migration, phagocytic capacity, as well as the production of reactive oxygen species and cytokines."

"Interestingly, some specific immune functions are promoted by dietary omega-3 fatty acids in specific immune cell types, i.e., phagocytosis by macrophages and neutrophils or Treg differentiation, suggesting that omega-3 fatty acids do not act as unspecific immune-repressors."

Treg or T-regulatory cells are massively important in preventing a hyper-inflammatory response and/or autoimmune response. Hyper-inflammation (ARDS) is one of the main causal factors in severe outcomes from COVID-19 and influenza. Omega-3 fatty acids and vitamins D and A are required to activate Treg cells and without sufficient amounts of these essential nutrients proper activation of the immune response, and proper control and regulation of the inflammatory response, are impossible.

Significant Role of Omega-3 and Vitamins A+D in Baseline Health/Prevention of Illness/Comorbidity

Borsche et al. (2021) COVID-19 Mortality Risk Correlates Inversely with Vitamin D3 Status, and a Mortality Rate Close to Zero Could Theoretically Be Achieved at 50ng/ml 25(OH)D3: Results of a Systematic Review and Meta-Analysis. Nutrients 13, 3596

"Over the last decades, knowledge regarding the mechanisms through which vitamin D affects human health has improved dramatically. Vitamin D turned out to be a powerful epigenetic regulator, influencing more than 2500 genes and impacting dozens of our most serious health challenges, including cancer, diabetes mellitus, acute respiratory tract infections, chronic inflammatory diseases, and autoimmune diseases such as multiple sclerosis."

Prietl, B. et al. (2013) Vitamin D and Immune Function. Nutrients, 5, 2502-2521; doi: 10.3390/nu5072502

"Vitamin D deficiency is also associated with the development of cardiovascular diseases, various types of cancer and autoimmune disorders, such as type 1 diabetes mellitus (T1D), multiple sclerosis (MS) and inflammatory bowel disease."

Bronas, U. & Dengel, D. Influence of vascular oxidative stress and inflammation on the development and progression of atherosclerosis. Am J Lifestyle Med. 4 (6) 521-34

Due to the overwhelming evidence of benefit, the American Heart Association now recommends the use of omega-3 fatty acid supplements for the primary and secondary prevention of coronary heart disease.

Larsson, SC, et.al. Dietary long-chain n-3 fatty acids for the prevention of cancer: a review of potential mechanisms. Am J Clin Nutr 2004;79:935-45.

"Omega-3 fatty acids lower the risk of cancer through their suppressing effect on the biosynthesis of eicosanoids [molecules from omega-6 fatty acids that promote inflammation, suppress the immune cells that eliminate cancer cells, and stimulate cancer cell growth]."

Jemal A, et al. Cancer statistics, 2007. CA Cancer J Clin. 2007 Jan-Feb;57(1):43-66.

"Vitamin D-sensitive cancers are responsible for 257,000 deaths (46% of all cancer deaths in U.S. in 2007)."

Lappe, JM et al. Vitamin D and calcium supplementation reduces cancer risk: results of a randomized trial. Am J of Clin Nutr 2007;85:1586-1591.

Four-year study on vitamin D supplementation showed a 77% reduction in all invasive breast cancers in women who received vitamin D supplementation versus those who did not supplement.

Mohr SB et al. Meta-analysis of Vitamin D sufficiency for improving survival of patients with breast cancer. Anticancer Research. 2014;34:1163-1166.

"High serum vitamin D was associated with lower mortality from breast cancer."

"Patients with the highest concentration of Vitamin D had approximately half the fatality rate compared to those with the lowest concentration."

Mozaffarian et al. Plasma phospholipid long chain n-3 fatty acids and total and cause-specific mortality in older adults. Ann Intern Med. 2013;158:515-525

"After adjustment for demographic, cardiovascular, lifestyle, and dietary factors both individual and combined levels of EPA, DPA, and DHA were associated with lower total mortality."

"Across quintiles, individuals with higher EPA, DPA, and DHA levels had 17%, 23%, and 20% lower risk, respectively, and those with higher total 3-PUFA levels had 27% lower risk."

**Note the increased combined effect of EPA, DPA, and DHA (OmegA+D contains all 3!!)*

Li & Huang. Anti-obesity effects of conjugated linoleic acid, docosahexaenoic acid, and eicosapentaenoic acid. Mol Nutr Food Res. 2008 52: 631-45

"Omega-3 fatty acids promote weight loss and fat loss by inhibiting fat synthesis, enhancing fat break-down and thermogenesis [fat burning], and preventing fat storage."

Evidence of Clinical Effectiveness of Omega-3 Fatty Acids and Vitamins A+D for prevention and risk of serious outcome from COVID-19 and Flu

D'Ecclesiis et al. (2022) Vitamin D and SARS-CoV2 infection, severity and mortality: A systematic review and meta-analysis. PLoS ONE 17(7): e0268396.

"All the studies showed an increased risk of Covid- 19 positive test in subjects with lower 25(OH)D levels (Fig 1), and the SRR [summary relative risk] indicated a significant double increased risk of infection for subjects with low serum VD levels compared to the highest level: SRR = 2.18."

**More than double the risk of infection with COVID-19 in those with low Vit D levels!!*

"Sixteen studies investigated the association between VD levels and severity of Covid-19 in terms of patient need for ICU admission or ventilation requirement or intubation" "The SRR indicated a significant double increased risk of severity [of COVID illness] for subjects with low serum 25(OH)D levels (SRR = 2.38)."

**More than double the risk of ICU admission or being put on ventilation for those with low Vit D levels!*

"Nineteen studies investigated the association between baseline VD levels and mortality of Covid-19 patients. The SRR for these studies suggested a significantly double increased risk of death for subjects with low level of 25(OH)D (SRR = 2.35)."

**More than double the risk of death for those with low Vit D levels!*

Borsche et al. (2021) COVID-19 Mortality Risk Correlates Inversely with Vitamin D3 Status, and a Mortality Rate Close to Zero Could Theoretically Be Achieved at 50ng/ml 25(OH)D3: Results of a Systematic Review and Meta-Analysis. Nutrients 13, 3596

"**Conclusions**: The datasets provide strong evidence that low D3 is a predictor rather than just a side effect of the [COVID-19] infection. Despite ongoing vaccinations, we recommend raising serum 25(OH)D levels to above 50 ng/mL to prevent or mitigate new outbreaks due to escape mutations or decreasing antibody activity.

**This level of serum vit D requires exponentially greater daily intake than the current RDA, which is based on the amount required to prevent rickets not the amount required to reach the human genetic requirements for sufficiency. I have outlined the required amounts, based on body weight, in my Innate Choice® 'Evidence-Based COVID-19 and Flu Prevention and Risk Reduction Supplementation Protocol' which I have included at the end of this review.*

"Thus, similar to other virus infections such as influenza, we have to expect that the effectiveness of vaccination is limited in time, especially with the current vaccines designed to trigger an immunological response against a single viral protein. We have already learned that even fully vaccinated people can be infected."

"However, these infections are the basis for the ongoing dissemination of the virus in a situation where worldwide herd immunity against SARSCoV- 2 is rather unlikely. Instead, humanity could be trapped in an insuperable race between new mutations and new vaccines, with an increasing risk of newly arising mutations becoming resistant to the current vaccines."

"A rapidly increasing number of publications are investigating the vitamin D3 status of SARS-CoV-2 patients and have confirmed both low vitamin D levels in cases of severe courses of infection and positive results of vitamin D3 treatments."

"Therefore, many scientists recommend vitamin D3 as an indispensable part of a medical treatment plan to avoid severe courses of SARS-CoV-2 infection, which has additionally resulted in proposals for the consequent supplementation of the whole population. A comprehensive overview and discussion of the current literature is given in a review by Linda Benskin [138].

**I reviewed the excellent paper by Linda Benskin in my Jan 2021 Research Review, 'Evidence-Based COVID-19 Prevention and Risk Reduction: A Literature Summary and Clinical Recommendations'. I highly recommend you read or reread that Research Review and/or get a copy of the Benskin paper (Benskin, L. (2020) A Basic Review of Preliminary Evidence That COVID-19 Risk and Severity Is Increased in Vitamin D Deficiency. Frontiers in Public Health. Vol 8, Article 513).*

"This study illustrates that, at a time when vaccination was not yet available, patients with sufficiently high D3 serum levels preceding the infection were highly unlikely to suffer a fatal outcome. The partial risk at this D3 level seems to vanish under the normal statistical mortality risk for a given age and in light of given comorbidities. This correlation should have been good news when vaccination was not available but instead was widely ignored."

"Nonetheless, this result may offer hope for combating future variants of the rapidly changing virus as well as the dreaded [and extremely common] breakthrough infections."

"This result strengthens the hypothesis that a fatal outcome from COVID-19 infection, apart from other risk factors, is strongly dependent on the vitamin D status of the patient. The mathematical regressions suggested that the lower threshold for healthy vitamin D levels should lie at approximately 125 nmol/L or 50 ng/mL 25(OH)D3, which would save most lives, reducing the impact even for patients with various comorbidities."

Imagine how much suffering and death could have been prevented with universal vitamin D supplementation!

"This is—to our knowledge – the first study that aimed to determine an optimum D3 level to minimize COVID-19 mortality, as other studies typically limit themselves to identifying odds ratios for 2–3 patient cohorts split at 30 ng/mL or lower. Another study confirmed that the number of infections clearly correlated with the respective D3 levels, with a cohort size close to 200,000. A minimum number of infections was observed at 55 ng/mL [150 nmol/L]."

"This result was also confirmed in a 2012 study, which showed that one of the fatal and most feared symptoms of COVID-19, the out-of-control inflammation leading to respiratory failure, is directly correlated with vitamin D levels. Cells incubated in 30 ng/mL vitamin D and above displayed a significantly reduced response to lipopolysaccharides (LPS), with the highest inflammatory inhibition observed at 50 ng/mL."

"This result matches scientific data on the natural vitamin D3 levels seen among traditional hunter/gatherer lifestyles in a highly infectious environment, which were 110–125 nmol/L (45–50 ng/mL) [174]. There is a major

discrepancy with the 30 ng/mL D3 value considered by the WHO as the threshold for sufficiency and the 20 ng/mL limit assumed by D-A-CH countries."

"Three directors of Iranian Hospital Dubai also state from their practical experience that among 21 COVID-19 patients with D3 levels above 40 ng/mL (supplemented with D3 for up to nine years for ophthalmologic reasons), none remained hospitalized for over 4 days, with no cytokine storm, hypercoagulation, or complement deregulation occurring."

"Thus, we hypothesize that long-standing supplementation with D3 preceding acute infection will reduce the risk of a fatal outcome to practically nil and generally mitigate the course of the disease."

EXACTLY what my Evidence-Based Chiropractic and Lifestyle Protocols, my books, and my lectures have been advocating for decades!

"Based on these circumstances, the SARS-CoV-2 pandemic is becoming the second breakthrough in the history of vitamin D3 association with disease (after rickets), and we have to ensure that full advantage is being taken of its medical properties to keep people healthy."

Benskin, L. (2020) A Basic Review of Preliminary Evidence That COVID-19 Risk and Severity Is Increased in Vitamin D Deficiency. Frontiers in Public Health. Vol 8, Article 513

"Early researchers reported three striking patterns. Firstly, the innate immune system is impaired by vitamin D deficiency, which would predispose sufferers to viral infections such as COVID-19. Vitamin D deficiency also increases the activity of the X-chromosome-linked "Renin-Angiotensin" System, making vitamin D deficient individuals (especially men) more susceptible to COVID-19's deadly "cytokine storm" (dramatic immune system overreaction)."

"Secondly, the groups who are at highest risk for severe COVID-19 match those who are at highest risk for severe vitamin D deficiency. This includes the elderly, men, ethnic groups whose skin is naturally rich in melanin (if living outside the tropics), those who avoid sun exposure for cultural and health reasons, those who live in institutions, the obese, and/or those who suffer with hypertension, cardiovascular disease, or diabetes."

"And thirdly, the pattern of geographical spread of COVID-19 reflects higher population vitamin D deficiency. Both within the USA and throughout the world, COVID-19 fatality rates parallel vitamin D deficiency rates."

"Among the 47 original research studies summarized here, chart reviews found that serum vitamin D levels predicted COVID-19 mortality rates (16 studies) and linearly predicted COVID-19 illness severity (8 studies). Two causal modeling studies and several analyses of variance strongly supported the hypothesis that vitamin D deficiency is a causal, rather than a bystander, factor in COVID-19 outcomes."

"Unlike influenza, children under age 10 are almost completely spared in COVID-19. This unusual risk factor pattern presented a mystery that spawned studies showing that COVID-19 fatalities are especially high in areas with lower levels of sunshine due to latitude or air pollution, except when population vitamin D intake is high. In fact, the risk groups for severe COVID- 19 match the risk groups for vitamin D deficiency exactly, and there is biological plausibility: vitamin D is known to modulate the immune system, helping prevent both under-reaction

that allows upper respiratory infections to be contracted, and the over-reaction referred to in COVID-19 as the "cytokine storm".

"The 141 articles presenting primarily biological plausibility evidence overwhelmingly support the assertions that vitamin D sufficiency increases resistance to viral infections and helps prevent every symptom of severe COVID-19 that results in fatalities. They show that vitamin D deficiency can also explain every major risk factor, including the mystery of why children seem relatively protected and why males, the elderly, and people with naturally melanin-rich skin are especially vulnerable."

"The 47 studies summarized here demonstrate that vitamin D deficiency explains the geographical differences in COVID-19 case and fatality rates. They provide overwhelming correlational evidence for the hypothesis, and causal evidence as well. COVID-19 mortality was predicted by vitamin D in 16 studies and vitamin D levels or sunlight predicted contracting COVID-19 in 17. Both causal modeling studies and eight chart reviews demonstrated that lower 25(OH)D was linearly associated with more severe COVID-19 outcomes."

"The evidence strongly suggests that vitamin D deficiency is an easily modifiable risk factor and correcting it is potentially life-saving. Suppressing this evidence out of fear that the public might believe supplements will make them "immune" to COVID-19 is not only elitist, but it is inconsistent with existing public policy approaches. Many mitigation strategies are publicized. None are seen as conferring immunity."

"This succinct but comprehensive review of the evidence found that despite almost complete absence of official government guidelines favoring vitamin D supplements to potentially decrease COVID-19 risk and severity, support among clinicians and other researchers for correcting and preventing vitamin D deficiency with modest daily vitamin D supplementation during the COVID-19 pandemic is very strong, worldwide."

Rastogi, A. et al. (2020) Short term, high-dose vitamin D supplementation for COVID-19 disease: a randomized, placebo-controlled, study (SHADE study). Postgrad Med J doi:10.1136/ postgradmedj-2020-139065

"It is noticed that those receiving vitamin D supplementation have fewer respiratory tract infections."

"However, the immune-modulatory effect of vitamin D is likely to be observed at 25(OH)D levels, which are considered higher than that required for its skeletal effects."

"The 25(OH)D levels at day-14 were 51.7 ng/ml and ng/ml, $p<0.001$ with a median increase of 42.4 ng/ml and 5.1 ng/ml ($p<0.01$) in the intervention and control group, respectively."

"10 out of 16 (62.5%) participants in the intervention group achieved SARS-CoV-2 negativity compared to 5 out of 24 (20.8%) participants in the control arm."

"In conclusion, a high dose, oral vitamin D supplementation to augment 25(OH)D >50 ng/ml helped to achieve SARS-CoV-2 RNA negativity in greater proportion of asymptomatic vitamin D-deficient individuals with SARS-CoV-2 infection along with a significant decrease in inflammatory marker. SARS-CoV-2 RNA negativity by cholecalciferol supplementation may help in reducing transmission rates of the highly contagious SARS-CoV-2 infection."

Yilmaz, K. & Sen, V. (2020) Is vitamin D deficiency a risk factor for COVID-19 in children? Pediatric Pulmonology 55:3595-3601.

"**Conclusion**: This is the first to evaluate vitamin D levels and its relationship with clinical findings in pediatric patients with COVID-19. Our results suggest that vitamin D values may be associated with the occurrence and management of the COVID-19 disease by modulating the immunological mechanism to the virus in the pediatric population."

Kaufman, H.W. et al. (Sept 2020) SARS-COV-2 positivity rates associated with circulating 25-hydroxyvitamin D levels. PLoS ONE 15(9): e0239252.

"SARS-CoV-2 positivity is strongly and inversely associated with circulating 25(OH)D levels, a relationship that persists across latitudes, races/ethnicities, both sexes, and age ranges."

"A previous study found that each 4 ng/mL increase in circulating 25 (OH)D levels was associated with a 7% decreased risk of seasonal infection, a decrement of approximately 1.75% per ng/mL."

"This is remarkably similar to the 1.6% lower risk of SARS-CoV-2 positivity per ng/mL found in our adjusted multivariable model."

"For the entire population those who had a circulating level of 25(OH) D <20 ng/mL had a 54% higher positivity rate compared to those who had a blood level of 30– 34 ng/mL."

"The risk of SARS-CoV-2 positivity continued to decline until the serum levels reached 55 ng/mL. This finding is not surprising, given the established inverse relationship between risk of respiratory viral pathogens, including influenza, and 25(OH)D levels."

Castillo, M.E. et al. (Sept 2020) Effect of calcifediol treatment and best available therapy versus best available therapy on intensive care unit admission and mortality among patients hospitalized for COVID-19: Journal of Steroid Biochemistry and Molecular Biology 203 105751

"Results: Of 50 patients treated with calcifediol, one (2%) required admission to the ICU, none died, and all were discharged without complications."

"Of the 26 patients not treated with calcifediol, 13 (50 %) required admission to the ICU and two died."

"Our pilot study demonstrated that administration of a high dose of Calcifediol or 25-hydroxyvitamin D, a main metabolite of vitamin D endocrine system, significantly reduced the need for ICU treatment [and death] of patients requiring hospitalization due to proven COVID-19."

Laird, E. et al. (May 2020) Vitamin D and Inflammation: Potential Implications for Severity of Covid-19. Irish Medical Journal; Vol 113; No. 5.

"This impact on the regulation of inflammation is of particular importance in older adults, the obese, and those with chronic conditions, as they may already be pre-set for a higher inflammatory response if exposed to Covid-19. A heightened inflammatory response in people who are vitamin D deficient may therefore increase the potential for 'cytokine storm' and consequent ARDS."

“In this short report we observed that low 25(OH)D concentrations appear to be associated with increased mortality from Covid-19.”

“Countries with a formal vitamin D fortification policy appear to have the lowest rates of infection whilst countries with no policy and highest deficiency rates appear to be more adversely affected.”

McCartney, D.M. and Byrne, D.G. (April 2020) Optimisation of Vitamin D Status for Enhanced Immuno-protection Against Covid-19 . Irish Medical Journal; Vol 113; No. 4.

“Vitamin D supplementation has also been shown to reduce the risk of respiratory infection.”

“Recent studies have shown an inverse relationship between serum vitamin D levels and risk of acute respiratory tract infection.”

“Notably, a September 2019 meta-analysis by Zhou and colleagues incorporating data from 21,000 subjects across eight observational studies showed that those with a serum vitamin D level <20ng/ml (i.e. <50nmol/l) had a 64% increased risk of community-acquired pneumonia.”

“Vitamin D deficiency is common and may contribute to increased risk of respiratory infection including Covid-19.”

“We recommend that all older adults, hospital inpatients, nursing home residents and other vulnerable groups (e.g. those with diabetes mellitus or compromised immune function, those with darker skin, vegetarians and vegans, those who are overweight or obese, smokers and healthcare workers) be urgently supplemented with vitamin D to enhance their resistance to Covid-19, and that this advice be quickly extended to the general adult population.”

I make the same recommendation - and was doing so LONG BEFORE COVID!!

Trinity College Dublin. "Vitamin D determines severity in COVID-19 so government advice needs to change, experts urge: Researchers point to changes in government advice in Wales, England and Scotland." ScienceDaily, 12 May 2020. www.sciencedaily.com/releases/2020/05/200512134426

“The authors propose that, whereas optimising vitamin D levels will certainly benefit bone and muscle health, the data suggests that it is also likely to reduce serious COVID-19 complications.”

“This may be because vitamin D is important in regulation and suppression of the inflammatory cytokine response, which causes the severe consequences of COVID-19 and 'acute respiratory distress syndrome' associated with ventilation and death.”

"Here we see observational evidence of a link of vitamin D with mortality. Optimising vitamin D intake to public health guidelines will certainly have benefits for overall health and support immune function.”

“But vitamin D can also support the immune system through a number of immune pathways involved in fighting SARS-CoV-2. Many recent studies confirm the pivotal role of vitamin D in viral infections.”

Carpagnano et al. (June 2020) Vitamin D deficiency as a predictor of poor prognosis in patients with acute respiratory failure due to COVID 19 Journal of Endocrinological Investigation https://doi.org/10.1007/s40618-020-01370.

"Hypovitaminosis D is a highly spread [prevalent] condition correlated with increased risk of respiratory tract infections. The world is in the grip of the Coronavirus disease 19 (COVID 19) pandemic. In these patients, cytokine storm is associated with disease severity."

"Conclusions: High prevalence of hypovitaminosis D was found in COVID-19 patients with acute respiratory failure, treated in a RICU [intensive care units]. Patients with severe vitamin D deficiency had a significantly higher mortality risk."

Merzon, E. et al. (July 2020) Low plasma 25(OH) vitamin D level is associated with increased risk of COVID-19 infection: an Israeli population-based study doi: 10.1111/FEBS.15495

"Conclusion: Low plasma 25(OH)D level appears to be an independent risk factor for COVID-19 infection and hospitalization."

Panagiotou & Gabriella. (July 2020) Low Serum 25-hydroxyvitamin D (25[OH]D) levels in patients hospitalised with COVID-19 are associated with greater disease severity. Clinical Endocrinology doi:10.111/CEN.14276

"Conclusions: Higher prevalence of VDD [Vitamin D deficiency] was observed in patients requiring ITU admission compared to patients managed on medical wards."

Martineau et al. Vitamin D supplementation to prevent acute respiratory tract infections: systematic review and meta-analysis of individual patient data. BMJ 2017;356: i6583

"Vitamin D supplementation reduced the risk of acute respiratory tract infection among all participants."

"In subgroup analysis, protective effects were seen in those receiving daily or weekly vitamin D without additional bolus doses but not in those receiving one or more bolus doses."

**This is important – bolus doses (large doses – usually injected) are NOT effective – yet, many cite studies with bolus doses as evidence that Vit D supplementation is ineffective!! The ignorance level regarding Vitamin D supplementation is staggering.*

Conclusions: "Vitamin D supplementation was safe and it protected against acute respiratory tract infection overall. Patients who were very vitamin D deficient and those not receiving bolus doses experienced the most benefit."

Prietl, B. et al. (2013) Vitamin D and Immune Function. Nutrients, 5, 2502-2521; doi: 10.3390/nu5072502

"Low serum 25(OH)D levels have been associated with upper respiratory tract infections (URTI), including influenza, chronic obstructive pulmonary disease and allergic asthma".

"In a Swedish RCT in 140 immunodeficient patients, daily intake of 4000 IU cholecalciferol over one year significantly reduced infectious symptoms, the total number of specific pathogens in the nasal fluid and the use of antibiotics in the vitamin D compared to the placebo group."

Aloia, J et al. Epidemic Influenza and Vitamin D. Epidemiology and Infection 2007, Vol 135 (7) pp. 1095-1098

In a 3 year trial taking 800 IU/day of Vitamin D reduced the incidence of colds and flu by **70%.**

After two years they increased the Vit D to 2000 IU/day and the incidence of colds and flu was reduced by almost 100% (only 1 of 104 subjects developed cold or flu in the final year).

Camargo, C.A.; Ganmaa, D.; Frazier, A.L.; Kirchberg, F.F.; Stuart, J.J.; Kleinman, K.; Sumberzul, N.; Rich-Edwards, J.W. Randomized trial of vitamin D supplementation and risk of acute respiratory infection in Mongolia. Pediatrics 2012, 130, e561–e567.

"In a randomized controlled trial of 247 Mongolian children with vitamin D deficiency in winter, with double-blinding and 99% follow-up, vitamin D supplementation significantly halved the risk of acute respiratory infections."

Dr. Chestnut's Research Review
SPECIAL FREE VERSION

Innate Choice® COVID-19/Influenza Prevention and Risk Reduction Supplementation Protocol

GEL CAPS:

First month:
1 caps of OmegA+D Sufficiency™ **per 40lbs/18kg body weight** [i.e. **4 caps/day** for 160 lb person]
3 drops of Vitamin D Sufficiency™ **per 40lbs/18kg body weight** [i.e. **12 drops/day** for 160lb person]
*This provides 10,000 IU/day of Vit D and sufficient and synergistic amounts of Omega-3 and Vit A.

Ongoing:
1 caps of OmegA+D Sufficiency™ **per 40lbs/18kg body weight** [i.e. **4 caps/day** for 160 lb person]
1/2 drop of Vitamin D Sufficiency™ **per 40lbs/18kg body weight** [i.e. **2 drops/day** for 160lb person]
*This provides 5,000 IU/day of Vit D and sufficient and synergistic amounts of Omega-3 and Vit A.

LIQUID:

First month:
1 TSPS of OmegA+D Sufficiency™ **per 80lbs/18kg body weight** [i.e. **2 tsps/day** for 160 lb person]
3 drops of Vitamin D Sufficiency™ **per 40lbs/18kg body weight** [i.e. **12 drops/day** for 160lb person]
This provides 10,000 IU/day of Vit D and sufficient and synergistic amounts of Omega-3 and Vit A.

Ongoing:
1 TSPS of OmegA+D Sufficiency™ **per 80lbs/18kg body weight** [i.e. **2 tsps/day** for 160 lb person]
1/2 drop of Vitamin D Sufficiency™ **per 40lbs/18kg body weight** [i.e. **2 drops/day** for 160lb person]
*This provides 5,000 IU/day of Vit D and sufficient and synergistic amounts of Omega-3 and Vit A.

*To order please go to www.innatechoice.com (the new combined website for Innate Choice® and The Wellness Practice®.

Read and practice well my esteemed, evidence-based, ethical, learned, expert chiropractic colleagues.

With appreciation for all you do for your patients and communities,

Dr. C