# Covid-19 and DHA: A Hypothesis of Immune Cell Mechanism and Response

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## Preface

Unlike antibiotics that "kill" bacteria, and terminate infections, there is no medicine that is "toxic" to viruses. Another approach against viruses is suggested here to materially reduce the effect of viruses, and in particular, the coronavirus that causes Covid-19. The hypothesis is based on boosting the immune system by supplementing with DHA in phospholipid form (PL-DHA).

Potential remedies to protect against viruses should address the functioning of the immune system. The approach suggested here is intended to be a tool to assist the body's natural immune response without adding complications.

Recent studies have documented that DHA plays a role in reducing inflammation within the human and mammalian immune responses in a number of ways.[1] This paper advances the hypothesis that PL DHA may provide an effective boost to immune cell functioning that may play a role in recovery from the coronavirus. This boost derives from the anti-inflammatory properties of PL-DHA and how they interact with the immune response.

## DHA's Remarkable Capability

The DHA molecule is located at the very tip of the Spermatozoon (Sperm cells) where it attaches to the egg cell wall. The molecule functions, in part, to punch a hole in the cell wall and thereby creates channels to transfer its DNA coding into the egg cell. Without DHA, the egg's cell membrane will not be opened to prepare the protein transfer channels for fertilization. The channels initiated by the DHA molecule work as gateway switches in many of the cell signal transduction channels within the cell membrane. [2]

The cell membranes of all living organisms, as well as viruses including coronaviruses, are made of phospholipid bilayers, PL-bilayers for short. The outer surface of these phospholipid bilayers is hydrophilic, while the inside is hydrophobic and functions to bind the two layers together. This cell membrane structure is so prevalent in nature that all cells, including cancer cells, bacteria, and coronaviruses are structured similarly.

These PL-bilayers create an envelope around the essential proteins and amino acids, the DNA and RNA elements of the organelle, as well as the intracellular water within the cells. The PL bilayers, contain channels that conduct signal transduction both intra- and inter- cellularly in the body.

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[1] "Omega-3 Fatty Acids and Inflammatory Processes" Phillip C. Calder. *Nutrients* **2010**, *2*, 355-374; doi:10.3390/nu2030355

[2] "Crystal structure and dynamics of a lipid- induced potential desensitized-state of a pentameric ligand-gated channel": Basak et al. eLife 2017;6:e23886. DOI: 10.7554/eLife.23886:

*Author's Note: In the Basak et al study, only a single DHA molecule was found around the channel structure. This may indicate that DHA may be the trigger of the channel structure self assembly process.

Viruses don't communicate. They can't even replicate by themselves until they invade living cells, and steal the amino acids and fatty acids. Alone, they are too small to have all necessary elements to replicate themselves, such as metabolism, or nutrient transport.

The human immune system has at least17 different types of cells. The way the entire system functions is not completely understood, though it is commonly accepted that some viruses are considered to be incurable, at least to some degree.

Reactive Oxidative Species

ROS (Reactive Oxidative Species) are oxygen atoms that hold unpaired free electrons (e-), comprised of a negative ion of oxygen (O-), or hydroxyl ion (OH-) in the body, that functions as a kind of disinfectant that our immune cells use to destroy foreign cells. When a macrophage, mast cell, or phagocyte (immune system cells) engulf an invading pathogen, the cell(s) employ this ROS weapon to internally destruct any pathogens present. This process is called a "respiratory burst" and serves to change the RNA folding, and thereby destroys the pathogen from within. Also used in this effort are protease which are protein hydrolyzing enzymes found inside the cells that function to break down the pathogen's protein.

While not all immune cells conduct phagocytosis, the phagocytes, and/or macrophages, that do function to destroy invading pathogens may die in the process; the incapacitated pathogens remain contained inside the body, and the entirety of the "dead cells" are excreted as "puss" and "phlegm" from the body.

It is suggested here that eosinophil cells may use the internal respiratory burst as a weapon against nearby viruses. If virus envelopes (PL-bilayers) have Phospholipid DHA (PL DHA) attached as the channel initiator, there is the potential for the virus envelopes to be easily neutralized immediately upon contact. Although a far greater understanding of this process is needed, we do know that the DHA molecule in the PL bilayer envelope acts as an electron conductor and neutralizes the pathogen.

The body's immune cells' weapon of choice is ROS, but just as you should not ingest disinfectants, ROS should not be present everywhere in the body. Uncontrolled ROS damages healthy organs, joints, and potentially every part of the body. An uncontrolled immune over-reaction will result in chronic inflammation, and as is the case with disinfectants, an ROS overdose will result in an agonizing death. In other words, ROS in the body is a double edged sword.

Danger of Oxidation to Extracted PUFA

Current manufacturing methods to produce PUFA (polyunsaturated fatty acid) supplements involve extracting the oil from the host making the extracted oil susceptible to damaging oxidation. Oxidized PUFA such as EPA, ALA, ARA, and DHA become super toxic ROS in the body once they oxidize. Each double bond (covalent bond) of carbon carries a free electron. Peroxidized double bonds cause what is known as a "peroxidation chain reaction" which further damages the PUFA. Elevated dosages of these supposed antioxidants, that should reduce inflammation, will oxidize in the body and destroy healthy and immune cells alike, and ultimately accelerate aging and encourage premature death. ONLY un-oxidized PUFA is healthy.

Any amount of peroxide inside the PUFA is an unwanted toxin. PUFA supplements, once extracted, do not have the antioxidant enzymes that normal cells possess, such as Superoxide

Dismutase (SOD) and catalase that function to clean and remove the ROS inside the cells. PUFA supplements add tocopherols (synthetic Vitamin E) as an antioxidant to protect against such damaging oxidation. However, tocopherols function as an absorbent, and once saturated with the oxidants, lose their protective nature. Delivering PUFA supplements in the form of gel capsules offer little extra protection against oxidation. Packaging that includes the use of a pump bottle to deliver each serving (the packaging common for animal Omega 3 supplements) actually "pump" additional oxygen into the bottle once opened, thereby negating the package's stated shelf life. Within a few weeks of use, peroxide builds up inside as more PUFA molecules continue to oxidize and can remain undetected even in the absence of a rancid smell. Many otherwise unexplainable illnesses can develop that can be explained by the use of an already oxidized supplement.

PL-DHA's known ability to attach to the membrane surface and then penetrate inside the PL-bilayers is due to its unique 3 dimensional structure that is not evident in other Omega 3 PUFA's such as EPA and ALA. This penetration property of DHA is the critically important feature of its functionality in our body.[3]

SARS-CoV-2

The structure of the SARS-CoV-2 virus consists of a PL-bilayer envelope surrounding the core RNA. The structure has a crown like spike protein receptor, that is probably formed from the center of the bilayer clusters attached to it. It is reported that this spike protein is oriented to attach to the human ACE2 enzyme protein, whose function is to regulate blood pressure in the body.[4]

SARS-CoV—2 viruses are about 120 nm in diameter and may be less than 1/millionth of the volume size of phagocytes or macrophages. Due to this minute size it may not be possible for immune cells to consume all the viruses by phagocytosis. However, normal cells that are infected and start transmitting the danger signal protein (which calls the first responders to react) may be contained by the phagocytes before bursting the replicated SARS-CoV-2 viruses and spreading them through the body. Viruses that are external to these infected cells need to be engulfed as well in order to be destroyed by phagocytes. One of the "weapons of choice" by the immune cells in this regard is the "respiratory burst" of the ROS that is mentioned above.

PL-DHA and SARS-CoV-2 Virus

PL DHA has the ability to attach and penetrate SARS-CoV-2 virus envelopes.[5] This penetration functions to increase the so called membrane fluidity on the envelope bilayer, to create a channel for the electron burst through the membrane to the inside of the cell. The effectiveness of the

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[3] "Eicosapentaenoic acid and docosahexaenoic acid (EPA and DHA) have distinct membrane locations and lipid interactions as determined by X-ray diffraction". Sherratt, et. al. *Chemistry and Physics of Lipids 212 (2018) 73–79.*

Author's Note: In this article, Sheratt et al describe the EPA inside the arbitrarily enlarged bilayers. There is no mechanism by which EPA can fatten the bilayers. A different explanation is that EPA did not have the ability to penetrate into the bilayers. This author believes it is the geometry of the molecules that prohibit EPA's penetration, while allowing DHA's penetration into the bilayers.

[4] https://www.wired.com/story/meet-ace2-the-enzyme-at-the-center-of-the-covid-19-mystery/.6/1/2020.

[5]"Eicosapentaenoic acid and docosahexaenoic acid (EPA and DHA) have distinct membrane locations and lipid interactions as determined by X-ray diffraction". Sherratt, et. al. *Chemistry and Physics of Lipids 212 (2018) 73–79.*

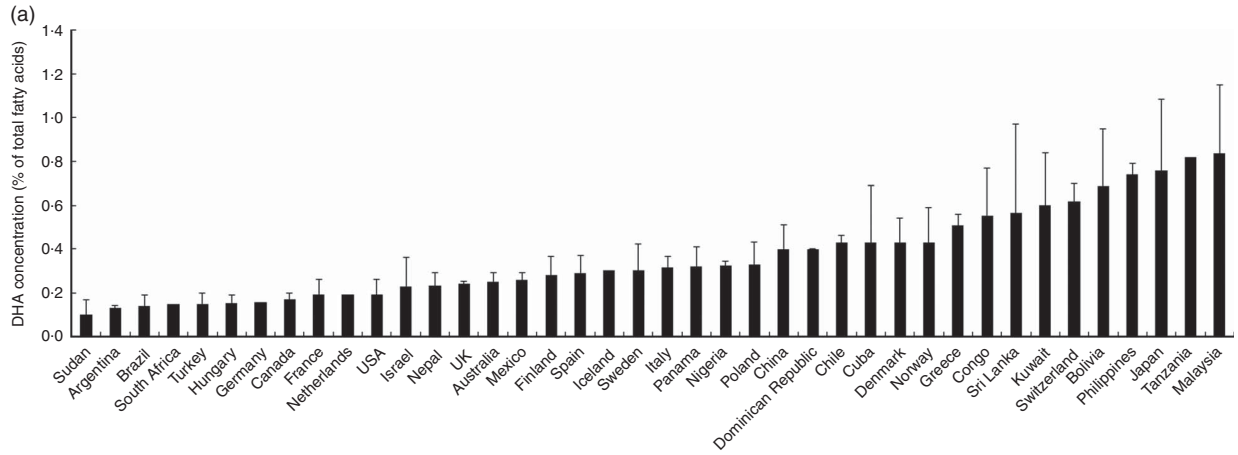
respiratory burst is enhanced if it reaches the RNA that is protected inside the PL-bilayers, to alter the replicability of the RNA,  leading to ultimate incapacitation of the virus.

The proposed immune boost created by this action is the increased supplementation level of PL-DHA in the fluid throughout the body to potentially heal the damaged cells' signaling capability. And for defense against the SARS-CoV-2 virus, PL-DHA  may amplify immune cell effectiveness.

Supporting Evidence[6]

Strong correlations exist between DHA levels in the populations of different countries and the control of Covid-19 spread. DHA levels in the world's populations are compared between DHA levels in lactating mother's breast milk compared to that from the average US lactating woman. Malaysia, Tanzania, The Philippines, and Japan contain more than five times the DHA than found in the average US lactating woman have been reported to have a remarkably lower number of per capita SARS-CoV-2 infection.

DHA Concentration by Population as Represented in Lactating Mothers' Milk




Source: Footnote 6.

Lower infection rates in Japan have largely been attributed to better tracking and societal behavior to contain the virus.[7] However, considering Japan's much closer proximity and contact with China, its very dense population centers encourage quickly accelerating community spread of disease.

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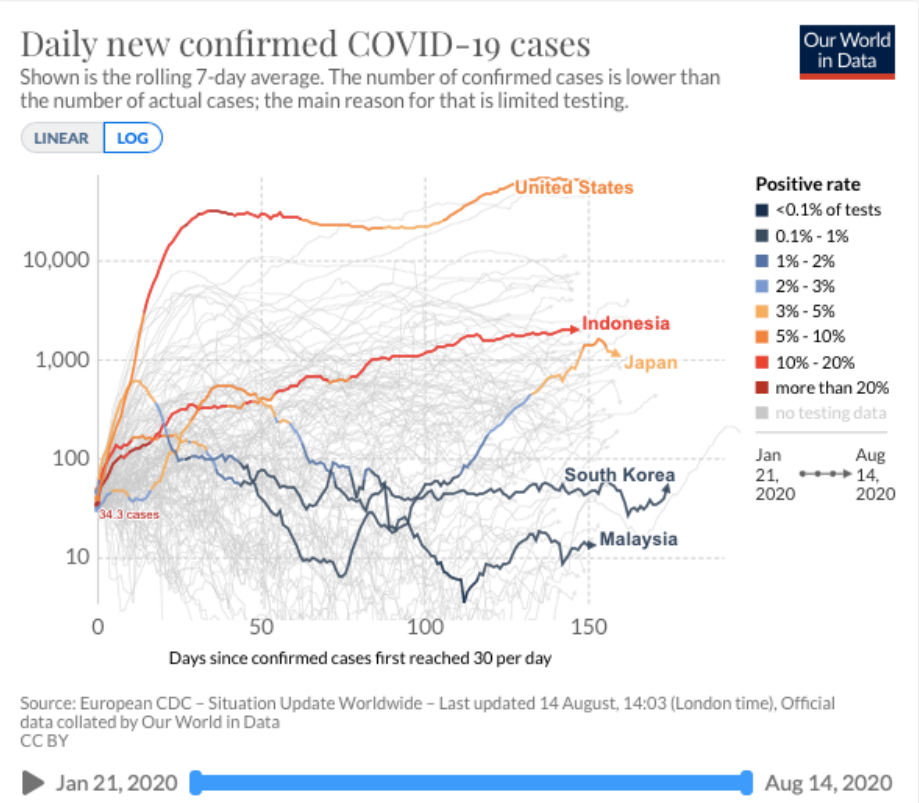
[6] "An updated review of worldwide levels of docosahexaenoic and" arachidonic acid in human breast milk by region", Fu et. al, *Public Health Nutrition: 19(15), 2675–2687*

Author's Note: Although S. Korean data is specifically missing from this report, S. Korea is reported to also experience a very low per capita covid-19 infection rate.

[7] Ibid

Unlike China, information from these countries are not withheld. Japan has 10 times the population density than that of the US, while S. Korea has about 15 times the population density of the US, while Malaysia and Tanzania are equally populous as S. Korea. The very low death rates per capita (less than 1/100 of the US infection rate) of these countries even compared to their surrounding countries cannot be explained by so called "more effective tracking"[8] nor by the "mutation theory that says the virus mutated after coming to Europe to become more contagious".[9] These anomalies are beyond coincidence. Despite these high population densities with so few cases per capita compared to countries such as the US, perhaps many more people in these four countries might have been equally infected, but not become symptomatic enough to merit testing. This may have occurred because of their high levels of internal DHA molecules that combat the early virus symptoms. [10] Neither can such low levels of infection be explained by the mutation theory that these countries experienced a less contagious strain of the virus, nor that they had much better tracking technology of infected individuals than US. Instead the explanation lies in the fact that the populations of every one of these countries consume a greater amount of fish in their diets and as a result have higher levels of DHA in their bodies to combat potential SARS-CoV-2 infection.
These countries may have had hundreds of times more cases than reported, and because their populations have more DHA in their bodies, the symptoms were not manifest enough to require testing. The correlation suggests that with increased levels of PL-DHA supplementation to boost the immune system, Covid-19 can become a more manageable health crisis.




[8]https://www.telegraph.co.uk/news/2020/07/22/infectious-covid-19-mutation-dominant-globally-fueling-faster/?yptr=yahoo

[9]Case Investigation and Contact Tracing Part of Multipronged Approach to Fight Covid-19 Pandemic. CDC 4/29/2020.

[10] https://ourworldindata.org/coronavirus./Daily New Confirmed Covid-19 Cases.8/14/2020.

The Case for PL-DHA against Covid-19

Among the Omega 3's, PL-DHA is suspected to penetrate the PL-bilayers of an organism including the SARS-CoV-2 virus. Generally, elevated amounts of currently available PUFA supplements come with elevated amounts of tocopherols. Manufacturers use tocopherol acetate as the antioxidant, to be an oxidant absorber. Tocopherol is not a water soluble antioxidant, and it does not get excreted as easily as vitamin C. Moreover, tocopherols only function to absorb the oxidant. Once saturated, tocopherols lose some of their anti-oxidation capacity. Elevated amounts of oxidized tocopherols play a negative role in the body. Excessive fluid build up in the cranial ventricle is known to be a symptom of childhood schizophrenia, and tocopherol build up is the marker for oxidative stress in the brain. In our opinion, adding tocopherols to any extracted Omega 3 product is a band-aid that tries to fix the imperfection created by the manufacturing community's extraction processes that rely on damaging heat and over concentration of the PUFA during post processing.

The source of all DHA is micro-algae. Accordingly, the most natural food source for DHA is un-extracted and unpreserved whole food explaining why oily fish or other sea food (including crustaceans) should be consumed. These creatures all acquire their DHA by feeding on the ocean algae. However, in lieu of acquiring DHA nutrition from eating lots of fresh fish, PL-DHA that is neither extracted, nor dried with damaging heat should, with proper validation, prove valuable in the fight against the SARS-CoV-2 virus when properly provided supplements are added to the diet.

Summary

We know that DHA is able to penetrate the PL-bilayers increasing membrane fluidity. The DHA molecule is responsible for cell signaling, and possibly initiates cell signal channel self assembly. By creating a space in the PL bilayer with its free electrons, DHA allows ROS to enter the bilayer.

DHA's cell signaling ability might further allow immune cells to use "respiratory burst" through the channel created by the PL-DHA to alter the RNA inside the SARS-CoV-2 virus envelope, thereby incapacitating it from further replication. It is evidenced that a variety of immune cells use respiratory burst against SARS-CoV-2 either inside the cells by phagocytosis, or on nearby cells. If sufficient DHA molecules exist in the body that can attach to SARS-CoV-2 virus surfaces, the effectiveness of the "respiratory burst" to reach into RNA will be increased and thereby reduce the impact of the virus.

There is a strong correlation between DHA levels in the populations of countries that consume more DHA, as represented by DHA levels in the breast milk of their lactating mothers', and the control of Covid-19 spread. The infection rates of the countries whose population have significantly higher average DHA levels in their bodies, have remarkably lower levels of reported covid-19 cases and mortality. Consequently this suggests the hypothesis that PL-DHA may provide an effective boost to immune cell functioning that may play a role in recovery from the coronavirus. Further investigation to prove the value of PL DHA as an effective tool against the SARS-CoV-2 virus is merited.