



مسئولیت متن و شکل بدوش نویسنده مضمون میباشد، عقیده نویسنده لزوماً نظر افغان جرمن آن لائن نمی باشد



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ترجمه: رحمت آریا

## جنگ های بی پایان راه حلی برای طولانی ترین جنگ امریکا میکانیزم جدید برای صلح دوامدار جهانی نقش کرونا - ۱۹ قسمت بیست و ششم و آخری

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### فصل سیزدهم

فرضیه اسکوربیک اسید به عنوان یک شیوه برای آزمایشات کلینیکی وقایوی و درمانی:

اسکوربیک اسید (AA) ، ویتامین C در سال ۱۹۱۲م کشف شد ، در سال ۱۹۲۸م به عنوان یک ویتامین ضروری بصورت خالص در آورده شد و در سال ۱۹۳۳م برای استفاده تجارتي بصورت مرکب تهیه شد.

در سال ۱۹۳۷م البرت سنت جیورجی و والتر نورمن بخاطر بخشی از کشف ویتامین C، جایزه نوبل دریافت کردند. سازمان صحت جهانی ویتامین C را در میان ادویه جات ضروری، و مطمئن ترین و موثرترین نوع ادویه جات مورد نیاز در یک سیستم صحتی فهرست کرده است. هرچند بقرط با آن آشنا بود ، اما در سال ۱۷۴۷م توسط جیم لیند جراح نیرو های سلطنتی به عنوان میوه جات سیتروس مورد استفاده قرار گرفت و از سال ۱۷۹۶م به بعد به همه کارگران نیروی بحری سلطنتی به عنوان آب لیمو داده شد.

متن مکمل مقاله طبی به انگلیسی

### WHAT MORE CAN BE DONE TO STOP COVID-19 CRISIS?

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### Summary

This is a brief review of corona viruses and our experiences with critically-ill ICU patients. It is connected with our investigation of Albert Szent Gyorgyi- Linus Pauling, and their supporters' use of vitamin C as therapeutics. The main thrust of the article is for justification of double blinded controlled randomized large group studies to investigate the statistical validity of reduction of cases, case severity and CFR(Case

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یادونه: دلینکي د لیکنيزي بني پاروالي د لیکوال په غاړه ده ، هیله من یو خپله لیکنه له رالیرولو مخکي په خیر و لولی

Fatality Rate) of COVID-19 with high-dose vitamin C administration as prophylaxis and therapy. Our hypothesis is for vitamin C's possible mechanism of action based on the equation of chemicaloxidative replication vs reductive anti-oxidation forces.

## Introduction

Coronavirus COVID-19 cases and mortality, case fatality rates are rising in the United States and around the world. A number of early research successes in vaccines have created optimism that we all have been seeking. It must be noted that our past experiences with SARS-viruses for which we still do not have either effective prophylaxis or therapeutics, still leaves us quite vulnerable. The seasonal influenza (Coronavirus) vaccines have shown reduction of cases, shortening the course and severity of the influenza illness. This is quite acceptable, but for facing a highly virulent COVID-19, we must be prepared epidemiologically, prophylactically and therapeutically to reduce its further spread and CFR, and also be prepared for resurgence of future deadlier phenotypes. This is becoming exceedingly challenging with increasing urbanization and globalization. Another venue would be to keep searching for low cost, low toxicity, less labor-intensive, easily acceptable means with achievable world-wide distribution. Meanwhile, there is little reason for panic, since humanity has faced worse onslaughts like influenza of 1918 which had a >10% mortality compared to the present COVID-19 with < 3 %. However, in the twenty-first century, America cannot accept the loss of even the minimal estimates of deaths in excess of 250,000 by the end this year. [1], [2], [3], [4]

## A Brief Medical Literature Review and Our Personal Experiences

Since 1933, coronaviruses have been known to be the cause of common cold (Coryza). However, coronaviruses' mutation and transmission through increasing numbers of animal vectors, has become more threatening globally in the past two centuries. We neither know how SARS, HIV, and Ebola-like viruses acquired their destructive capacity, nor do we understand the mechanism by which they destroy human organs. Furthermore, it has been suggested that with the expansion of cities, towns and villages into wilderness around the globe, people become in closer contact with wild life animals. Unfortunately, some seeking rare animals for culinary or medicinal effects, hunt them and deliver them to wet markets - which act as large-scale incubators for myriads of microbes known and unknown.

As history remains the acid test of validity of all sciences, physicians and scientists should remember that every bit of scientific discovery has been built on the efforts of previous generations. In 1937, Albert Szent-Györgyi received the Nobel Prize in Physiology/Medicine "for his discoveries in connection with the *biological combustion process with special reference to vitamin C and the catalysis of fumaric acid*". Interestingly, he gave all of his Nobel prize money to Finland in 1940 for its war against Soviet occupation. His *basic scientific investigation was focused on the chemistry of cellular respiration, identifying fumaric acid and other steps, which later became known as the Krebs Cycle for the generation of ATP/ADP as the source of energy for all life forms*. He had said that "a discovery must be, by definition, at variance with existing knowledge", and divided scientists into two categories: the Apollonian and the Dionysian. He called scientific dissenters, who explored "*the fringes of knowledge, Dionysian*." saying, "*In science the Apollonian tends to develop established lines to perfection, while the Dionysian rather relies on intuition and is more likely to open new,*

*unexpected alleys for research...*" Ralph Moss, one of his protégés, in his long career performing cancer research, wrote a biography entitled: "Free Radical: Albert Szent-Györgyi and the Battle over Vitamin C". [5]

Access to the well-preserved permafrost specimens of 1918 Flu from Alaska in 1997, yielded the genome sequence of 1918 virus, classifying it as SARS-CoV-1 and the present COVID-19 as SARS-CoV-2 revealing their many similarities. [6]

### A Brief Review of Clinical Course of SARS-CoV-2

An early study was published in the NEJM in April, 2020. *These were the data among 393 patients admitted to two New York hospitals which had similar general presentations as found in all larger group studies from China.*

The 393 COVID-19 patients in New York had the following: *Clinical Presentation* - Median age 62 years; 61% male. *Symptoms and signs*: Cough in 79%; fever 77%; dyspnea 56%; muscle pain 24%; diarrhea 24%; vomiting 19%. *Lab Results*: Lymphopenia in 90% (loss of lymphocytes), thrombocytopenia 27% (loss of platelets). *Elevated Inflammatory Markers*; ferritin, D-dimer, C-reactive protein (CRP) and Procalcitonin. *Therapies*: Invasive mechanical ventilation in 33%; of which 33% extubated; 10% died; 66% discharged from hospital, and 24% with no outcome data. [7]

The Table below is from the author's lecture at Haikou, China on November 5, 2013 during the 2012-13 SARS epidemic showing mortalities of avian flu coronaviruses similarities and place of occurrence.

<u>Virus Type</u>	<u>Year</u>	<u>Numbers</u>	<u>Mortality</u>	<u>Vector</u>	<u>Location</u>	<u>Other Data</u>	<u>&amp;</u>	<u>Findings</u>
H5N1	1997	?	2		Far-east	Autopsy		Very high cytokine levels, IFN, TNF
SARS-CoV	2003	774/8,098	10%	Avian	Far-east	No		None
H5N1	2003	4/4	100%	"	Vietnam	"		"
H5N1	2004	32/46	70%	"	Thailand, Vietnam	"		"
H5N1	2005	43/98	44%	"	Vietnam, Cambodia, China	"		"
H5N1	2006	79/115	69%	"	Indonesia, China, Iraq, Egypt	"		"
H5N1	2007	59/88	67%	"	Cambodia, PR China, Indonesia	"		"
H5N1	2008	34/44	75%	"	Cambodia, China, Egypt, Indonesia	"		"
H5N1	2009	32/73	44%	"	Indonesia, Cambodia, China, Egypt	"		"
H5N1	2010	24/48	50%	"	Indonesia, China, Djibouti, Egypt	"		"
H5N1	2011	34/62	55%	"	Cambodia, China, Indonesia, Bangladesh	"		"
H5N1	2012	20/32	63%	"	Vietnam, Cambodia, China, Egypt	"		"
H7N9	2013	45/135	33%	"	PR China	"		"
SARS-CoV-1	1918-19	1/3 world popl.	>2.5 - 10%		Global			
SARS-CoV-2	2019-	25 million	>0.7 - 3.5%		Global			

WHO Report 2003-2013 Overall Mortality of H5N1 60%

Figure 1  
(New data of SARS-CoV-1 and SARS-CoV-2 are added to the above figure)

While SARS-CoV-2 and SARS-CoV-1's clinical symptoms and signs and their genomic structures are quite similar, SARS-CoV-2's economic devastation, with social, psychological impact and rapid spread, are astoundingly different from the flu of 1918. However, back then we did not have WHO, CDC, UN, UNESCO, etc., etc. Presently, we

certainly stand in a better situation with much greater assets, such as antibiotics and many other advances in science and technology to get this pandemic under control with a unified worldwide cooperative approach.

## **A Glance at Pathophysiology of SARS-CoV-2**

Coronaviruses transmitted by animals have been the cause of diseases such as severe acute respiratory syndrome SARS, with the most likely vector being birds, Ebola virus disease EVD (CoV-2005-2020 in Congo, Africa), zoonotic vector unknown; middle east respiratory syndrome MERS (CoV-2012 in Arabia), camels as the vector, and coronavirus COVID-2019 (classified as SARS-CoV-2 Wuhan, China), bats are as the most likely vector. Dormant viruses in animals such as bats mutate and when transmitted to humans demonstrate greatly enhanced virulence. We do not know the nature of this destructive mechanism and its utilization! [8], [9], [10], [11]

On February 11, 2020, the new severe acute respiratory syndrome (SARS) related to coronavirus was named by the WHO as Corona Virus Infection Disease-2019 (COVID-19). An uncontrolled immune-response to COVID-19 infection was observed to appear as a *systemic hyperinflammatory response syndrome (SIRS)*, which earlier had been called as "*cytokine storm*" or *cytokine release syndrome (CRS)*.

### **Cytokine Release Syndrome (CRS)**

The mechanism of action of SARS virus starts first with: a) attachment, b) penetration, c) replication, d) death of host-cell, and the spread of the myriads of virus from intracellular into extracellular fluid spaces, where the immunologic defense system of the host turns awry as numerous pro-inflammatory and anti-inflammatory agents as cytokines and chemokines collide. At this point of CRS, the host's homeostasis (biological equilibrium) breaks down making the host very sick requiring hospitalization and possibly ICU care. [12]

The term 'Cytokine Storm' first appeared in an article published in 1993 as the conflict between graft-vs-host disease. [13] This phenomenon has been observed in infections with cytomegalovirus [14], Epstein-Bar virus hemophagocytic lympho-histiocytosis [15], group A streptococcus infection [16], in severe acute respiratory syndrome with coronavirus (SARS-COV) [17], and H5N1 avian flu infection in 2005. [18]. It must be emphasized that it also appears in non-infectious conditions such as polytrauma, major burns, in severe pancreatitis, and in multiple organ failures seen ICUs from other causes. [19]

Cytokines are low molecular-weight protein molecules involved in intercellular signaling and communication, such as interferons (IFNs type I, II, and Type III). [20] Another important family of cytokines are *Interleukins(IL)*, which are mostly involved as *immune system regulators and in immune cells differentiation and activation*. [21] In cytokine dynamics, for instance, TNF (tumor necrosis factor) promotes generation of IL-1, which produces changes in endothelial physiology within its local microenvironment. [22]

At this point, we leave the complex regulation of pro- and anti-inflammatory cytokines, host susceptibility to cytokine storm, and the genomics of cytokine storm to the experts. [23], [24], [25], [26]

## Increased Capillary Permeability Syndrome

In our laboratory and others, the destructiveness of cytokines have been shown to be commensurate to the degree of capillary leak and capillary damage. Consequences of cytokine storm are often anasarca (generalized leaky capillaries with generalized edema), expansion of extracellular and intracellular fluid compartments creating a physiologic “dead space”, forecasting sequential organ failure. Professor Thomas Randall as an expert in fluid-electrolyte balance called this fluid dynamics as “third spacing” in 1952. [27], [28]

The reduction of such an excessive inflammatory immune-response may be considered as a potential therapeutic target for control of severe COVID-19 infection, other infections, and non-infectious causes. [29], [30], [31], [32], [33], [34], [35], [36]

## The Imperatives for COVID-19 Crisis

To mitigate COVID-19's profound devastations while waiting for effective vaccines, the demonstration of other possible medically safe preventive and therapeutic venues may be a reasonable approach. Our review of the medical literature and many years of experience in our laboratory as clinician-scientists have brought us to the following conclusions:

- 1) *People should realize the magnitude and seriousness of the COVID-19 assault, and must enable themselves to deal with it psychologically as well as epidemiologically and must adjust their behavior accordingly for now and for near future.*
- 2) The governments of 193 nation-states in the United Nations, the great philanthropists, NGOs, all world-peace organizations, giant multinational corporations, and news media should lead a multiprong effort to persuade peoples around the World to abide by a “United Nations International COVID-19 Agenda” developed by an “International COVID-19 Conference or Committee”.
- 3) Science based public health and epidemiologic measures should be carried out with greater intensity internationally.

Before delving deeper into SARS viruses and stimulating more research in this field, we must study the past attempts for their cure, as drugs and other means, which have been tried without success, so we don't lose precious time! [37]

Most of the data for large group studies enumerated below, came from China - where they had their first encounters with COVID-19 in early December of 2019 and SARS H5N1 as early as 1997 with research experience ever since 2003. In late March, early April 2020 papers, the following cytokines and chemokines were found with high blood concentrations: IL1- $\beta$ , IL1RA, IL7, IL8, IL9, IL10, basic FGF2, GCSF, GMCSF, IFN $\gamma$ , IP10, MCP1, MIP1 $\alpha$ , MIP1 $\beta$ , PDGFB, TNF $\alpha$ , and VEGFA. Some of the severe cases admitted to ICU showed high elevations of pro-inflammatory (self-destructive) cytokines (IL2, IL7, IL10, GCSF, IP10, MCP1, MIP1 $\alpha$ , and TNF $\alpha$ ). [38], [39], [40], [41]

In a number of medical articles the occurrence of a cytokine storm in COVID-19 cases have been confirmed clinically, and in laboratory. In such patient reactions, autopsies showed more tissue death called ‘Apoptosis’ compared to normal death ‘Necrosis’ of cells. [42], [43] In early 1990s *apoptosis* was found as a genetically programmed



autonomous cellular dismantling which *does not elicit normal inflammatory response*. [44], [45]

## **Hypothesis for Ascorbic Acid as a Venue for Clinical Trials of Prophylaxis and Therapy**

Ascorbic Acid (AA), vitamin C was discovered in 1912, isolated as an essential vitamin in 1928 and was synthesized for commercial use by 1933.

Partly for Vitamin C discovery, Albert Szent-Györgyi and Walter Norman Haworth were awarded the Nobel Prize in 1937. [46], [47] *The World Health Organization listed Vitamin C among essential medicines, and the safest and most effective medicines needed in a health system.* [48] Although it was known to Hippocrates, it was used as citrus fruits by Royal Navy Surgeon James Lind in 1747 and given as lemon juice to all Royal Navy crewmen ever since 1796. [49], [50]

One of a handful two-time Nobel Laureates, Linus Pauling for chemistry and Peace Prize (1954, 1965) respectively, advocated mega-dose oral use of vitamin C for common cold and influenza in his 1970 book. He pioneered the Orthomolecular Medicine of modern era of preventive and nature-based therapeutics. [51] Vitamin C has been shown as a powerful anti-oxidant boosting immune system of lymphocytes, the natural killer cells. [52], [53], [54], [55], [56]

Aside from patients with genetic conditions of glucose-6-phosphate dehydrogenase (G6PD) deficiency developing hemolytic anemia, patients with underlying renal disease developing hyperoxaluric or uric acid stone, and liver-hemosiderosis patients, no other side-effects of high-dose vitamin C have been reported. [57], [58] [59], [58], [59], [60], [61]

It is known that Vitamin C plays an important role in metabolic functions, i.e., activation of vitamin B, folic acid, converting cholesterol to bile acids, and amino acid tryptophan to serotonin. As a scavenger vitamin C is a powerful antioxidant that protects humans from damage of free radicals. [62], [63]

## **Data from Columbia University Intravital Microscopy Laboratory Studies (College of Physicians & Surgeons)**

1. Intravital microscopic studies have shown us that we can look upon extensive capillary vascular system in human body, as a major human organ, which by surface area exceeds the skin covering us; *BSA (Body Surface Area) = 1.7 square meters vs Capillary System = 500-700 sq. meters, more than 200 folds (500/1.7 = 294).*
2. Our intravital microscopy video, photographic, and quantitative dye studies have shown *histamine* to be a *powerful agent in destruction of capillary's delicate endothelial cell-lining and its basement membrane made of collagen.*
3. Coronaviruses attack mucus membranes of upper respiratory tract (nose, throat, larynx) and after replication (incubation period) destroy those cells creating a 'cytokine storm', which overwhelms the tracheobronchial tree down to the alveolae.
4. The tracheobronchial tract lined with columnar epithelium, and the *goblet* cells which produce the protective *mucus* of approx. 50-75 ml per day, is carried by ciliary motion to the upper trachea and coughed out or swallowed. SARS viruses' cytokine storm

destroys the delicate cilia and the alveolar membrane, eliminating the surfactant (dipalmitoyl-phosphatidylcholine). The leaking serum from capillaries flood the collapsed alveolae, and with accumulated mucus interfere with the oxygen transport-system resulting in severe acute respiratory syndrome (SARS). [64], [65], [66], [67], [68], [69], [70], [71], [72], [73], [74], [75], [76], [77], [78], [79], [80], [81], [82], [83], [84], [85], [86], [87], [88], [89], [90], [91]

Linus Pauling and Albert Szent-Gyorgyi's works with vitamin C have undergone extensive biochemical, physiological and pharmacologic studies lacking only, the investigation of vitamin C's effect on capillary bed, the largest vital organ of our body. [92]

While most animals can manufacture their own Vitamin C, humans, primates, most species of bats, teleost fish, and guinea pigs cannot. This may well be the basis of its large-dose requirements for optimal homeostasis, for its human tolerance, and non-toxicity in case of very high serum levels with adequate hydration for long periods. [93]

### **A Possible Prophylaxis for COVID-19**

Pauling's book "Vitamin C and Common Cold" of 1970 [94], created an unresolved controversy to this day, between medical establishment of clinician MDs and scientist PhDs. After more than a decade, following his death in 1994, when he still possessed a sharp mind at age 93, many physicians and PhD scientists began to recognize his great contributions. For prophylaxis of cold and influenza he suggested the intake of > 4 g Vitamin C several times per day. The mega-doses of ascorbic acid (Vitamin C), because of its acidity, and, may be other unknown factors, cause diarrhea, mild headaches and other mild side-effects. For prophylaxis our recommendation during the COVID-19 pandemic is to take orally one gram capsule of Ester C (calcium-ascorbate) or other acid-neutralized AA, two of 1000 mg caps every eight to six hours, a total of 6-8 grams per day as a supplementary. For those unable to tolerate big capsules or tablets; the caps can be opened or tablets turned into powder, vitamin C being water soluble may be mixed with any preferred fruit juice as a drink. With mega-dose ascorbic acid of > 4000 mg per day, one should take 1000-1500 ml of water or non-alcoholic drinks.

With beginning of an infection and or a positive test for COVID-19, an ancillary treatment may be started with the intake of vitamin C, 3-4 g per 4 hrs., to obtain steady blood-levels, 2 g every 2 hrs. for a 7-14 day-period may suffice with antacids (TUMS), as needed. It should be tapered down to prophylactic levels of 6-8 grams or 4 grams per day. *There have been no documented severe side-effects and fatality for vitamin C overdose since its commercialization in 1930s.*[95], [96], [97], [98]

### **COMMENTS AND SUGGESTIONS**

Linus Pauling and others have studied the effects of vitamin C (Ascorbic Acid) in influenza, heart disease and cancer in collaboration with several physician-scientists and clinicians. One of his books states, "*Vitamin C has value in preventing and treating not only the common cold and influenza but also other viral diseases and various bacterial infections. It's main mechanism of action is through strengthening the immune system.*" In another section of his book, "*The amount of protection increases with increase in the amount of ingested vitamin C and becomes nearly complete (optimal) with 10 g to 40 g per day at the immediate onset of influenza.*" Professor Pauling reminded us that *vitamin*

*C in medical literature is described as “virtually non-toxic”, and adds that there has been no reported case of death from Vitamin C overdose. [99], [100], [101], [102]*

It must be mentioned that following survey of medical literature, several dozens of patients treated with mega-doses of Vitamin C were found with various positive results. [101], [102], [103]

Many detractors of Professor Linus Pauling have always called for prospective, randomized, double blinded controlled large clinical cohort studies. Although, as a physician/scientists, we cannot enumerate any such perfect studies from the medical literature, however, there are a few - less than perfect ones in following references. [104], [105], [106], [107], [108], [109], [110]

For many years we have wondered why high doses of vitamin C is required for overcoming certain severe inflammatory and infectious diseases. Below are some theories or hypotheses that may explain the basis on which we make the above suggestions for the use of optimal doses of vitamin C for strengthening of the immune system in COVID-19 victims and neutralizing free radicals, in conjunction with other traditional therapies while waiting for effective vaccines and drugs for now and SARS-CoV-n of the future. [111]

## THE

### THEORY OF MECHANISM OF ACTION OF COVID-19

There is an accepted concept as to how the virulent influenza viruses make people sick. The virus being 100-200 times smaller than the host cell, as one of my mentors Professor André Cournand (Nobel Laureate 1956/Columbia University), believed that the smaller the foreign molecules introduced into blood stream, the less likely that human immune system would recognize them. As SARS-CoV virus attaches itself with its spike-proteins to the host cell, using the host-cell wall's ACE2 to weaken it, forms a pinched-off vesicle around itself enabling it to enter the host-cell cytoplasm. With the host-cell wall membrane covering it, it stealthily attacks and takes-over the mitochondria of host-cell where Krebs Cycle's stream of ATP & ADP provide *energy* for its life and rapid replication needs. SARS-CoV-2 has a 10-20 fold greater affinity for host ACE2 compared to SARS-CoV-1, and is believed to be one of the causes for its faster transmissibility. [112] Viruses vary in their speed of multiplication but it is recognized that being 10-20 times smaller than bacteria (Flu virus 0.12  $\mu\text{m}$ , E.coli 2  $\mu\text{m}$ ), they multiply many times faster than bacteria. Viruses multiply more like spores, unlike bacteria. A bacteria involved in certain gangrenes, like E. coli is known to divide once every 20 minutes, whereas in the case of coronaviruses it's not known but suspected that their rate of replication is much faster, likely in terms of seconds. Some virologists refer to virus multiplication as budding or 'sporing'. This phenomenon becomes numerically uncountable and therefore should be measured experimentally in terms of 'virus mass' ( $V_{\text{mp}}$ ). The epidemiological phenomenon of microbial spread among persons, is expressed by  $R_0$  or  $R$  naught, which is an exponential multiplication starting with 1, 2, 4, 16 ... or 3, 9, 81...) depending on  $R_0$  number. For example, the number of laboratory-confirmed COVID-19 cases worldwide has been ten times greater than the total SARS-CoV-1 1918-flu cases. Many assume  $R_0$  number to be similar to viral replication, which more likely is not, but could be a parallel phenomenon. This may account for the fact why medical literature does not reveal the speed of SARS's multiplication per minute or by second, except that they do increase their mass exponentially. So we may represent the viral replication as SARS-CoV- $R_0$  in mathematical terms as:



## Multiplication Rates

$$\text{SARS-CoV-1} = (3)^2 \times T \text{ min}$$

$$\text{SARS-CoV-2} = (6.5)^2 \times T \text{ seconds}$$

## CHARACTERISTIC ACTIONS OF VITAMIN C

Albert Szent-Györgyi, the great scientist and a humanist had said, "To express the marvels of nature in the language of science is one of man's noblest endeavors."

### Characteristic Actions of Vitamin C (Ascorbic Acid, AA)

- Vitamin C protects capillary endothelial cells, decreasing capillary leak.
- Vitamin C is a powerful anti-oxidants (Electron Donor).
- Vitamin C strengthens human immune defense system.
- Vitamin C neutralizes histamine at one-to-one-molecular ratio.
- Vitamin C is required for collagen production and healing.
- Vitamin C may reduce coronavirus multiplication?
- Vitamin C may reduce the magnitude of 'Cytokine Storm'?

Figure 1

Vitamin C is a donor and gives its two-electron arm to a demander. Anti-oxidants are electron donors but none is as powerful as the expensive human serum albumin (HAS 66-69kD with 200 +/- charges with a net -18) and equally the recombinant rHSA. [73/115]

## Theory of Energy Demand of SARS-CoV-n at Sub-molecular Level

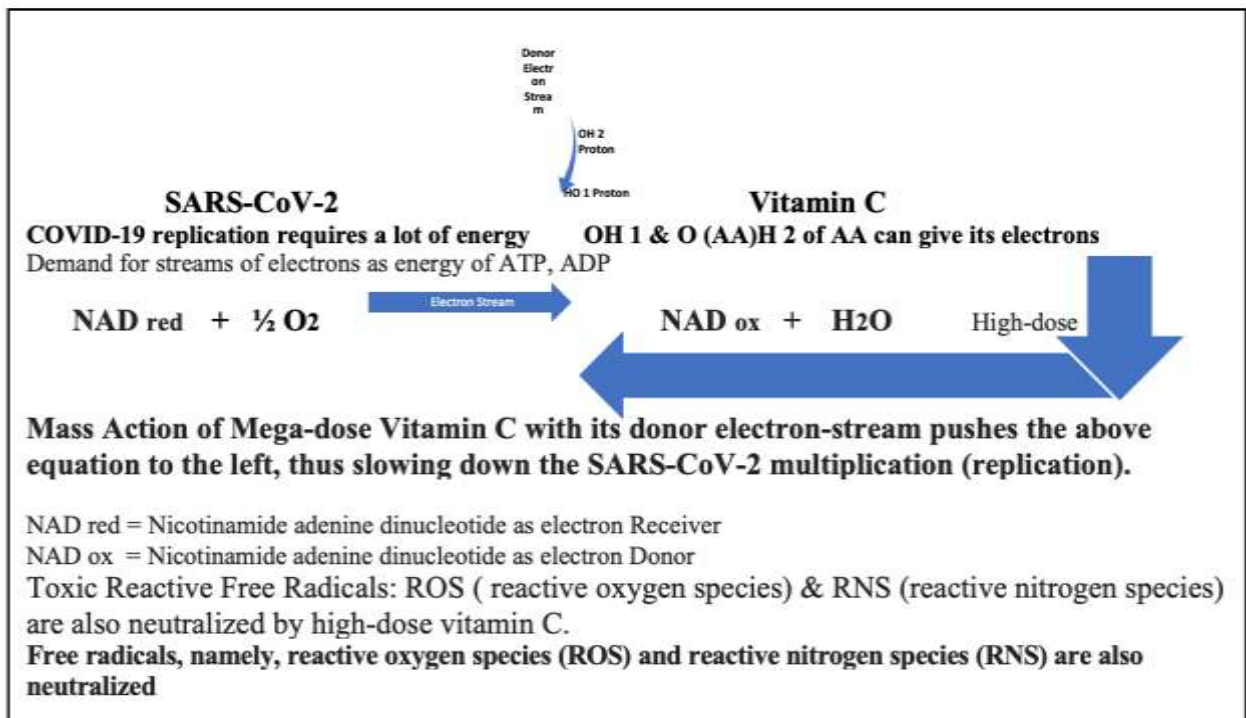


Figure 2

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For life and multiplication (replication) SARS-CoV-2 requires a lot of energy; through oxidation losing its electrons by consuming high energy sources of ATP & ADP becomes an Electron Receiver (electron acceptor). Vitamin C having 1-2 available electrons, gives them from its OHs because of its intrinsic chemical structure as an Electron Donor. Professor Lehninger says “Each electron donor has a characteristic *electron pressure* and each electron acceptor has a characteristic *electron affinity*. ... Electron donors may be arranged in a thermodynamic series of decreasing electron pressures, just as phosphate compounds can be arranged in a series of decreasing phosphate transfer potentials. In such a series it will be the thermodynamic tendency for electrons to flow from the most negative compound, (i.e. anti-oxidant Ascorbic Acid, author’s) that having the highest electron pressure, to compounds lower in the scale.” Albert L. Lehninger, a brilliant biochemist scientist of Johns Hopkins School of Medicine, put bioenergetics in these terms, “*The bioenergetics is the term used to denote the study of energy transformations in living organisms, which is intrinsically connected to Life with Multiplication and Regeneration.*” Since the cell is the basic unit of structure and function in living organisms, biological energy transformations are considered most basic at the cellular level. [113]

One of the well-known clinicians, Robert F. Cathcart III, MD, treated >11,000 patients with doses of 4 to 40 g per day for common cold, viral pneumonia, bacterial infections, arthritis, neuralgias, hay fever/asthma, candidiasis, etc. During his long career he treated a number of advanced cancer patients with Vitamin C - in excess of 100 g per day. Cathcart observed some improvement of his patients without any identifiable toxicity, but he also observed the reduction of chemotherapy side-effects. Cathcart said, “What makes ascorbate truly unique is that very large amounts can act as a non-rate-limited antioxidant free radical scavenger.” After more than seventy years of lacking scientific methodological studies for treatment of a number of diseases with mega-doses of Ascorbic Acid, there is a great need for double-blinded controlled prospective and randomized large patient-group studies, which may be readily conducted under present circumstances surrounding COVID-19. [114], [115], [116]

## Disclosures

None of the authors is involved in a conflict of interest. Co-authors had worked in my Intravital Microscopy Lab at Columbia Medical School (Black Building)

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