High-Dose Vitamin C:

Increasing Vitamin C Intake to High Doses to Optimize Immune Function and Combat Illness

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**ABSTRACT**

Over the past century, a small portion of scientists have advocated for the use of high-dose vitamin C for optimization of health and immune function. However, although the scientific community agrees on the importance of vitamin C, this particular group of scientists have remained shunned within the healthcare and medical fields due to the “taboo” nature of supplements. This paper aims to explore the current RDA of vitamin C and the potential benefits of high-dose vitamin C on enhancing immunity and fighting infection. Both oral dose and intravenous vitamin C will be covered, as well as their effects on different illnesses such as pneumonia, influenza, and COVID-19. Additionally, this paper will introduce how to raise awareness on the effectiveness of high-dose vitamin C in the healthcare community so healthcare professionals can employ advocacy strategies and teach the public, specifically those in low-income areas, how to naturally increase their protection against illness.Thisreview goes beyond the simple nutritional factors of vitamin C, and delves into its pharmacological and pharmacokinetic abilities.

*Keywords:* Vitamin C, High-Dose, Immunity, Illness, Pharmacology, Pharmacokinetics

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**Introduction**

Humans have long recognized the importance of vitamin C, even before Albert Szent-Györgyi isolated the vitamin in his laboratory in 1928. Scurvy, otherwise known as prolonged vitamin C deficiency, afflicted an estimated 2 million sailors years before the cause was known. It was not until 1747, that the key correlation between scurvy and food sources of vitamin C was discovered by James Lind when he tested six different treatments on 12 sailors with scurvy. From this experiment, it was determined that out of all the proposed treatments, only citrus helped the sailors (Carpenter & Carpenter, 2012).

Through time, vitamin C was found to have more functions than preventing scurvy. It has been used in experiments as a treatment for numerous ailments, especially infectious diseases. In today’s current climate, with emerging communicable diseases such as COVID-19, it is important to further examine the role of vitamin C in illness prevention and treatment, specifically in terms of supplementing with high-dose vitamin C.

Humans in developed countries have become too acclimated to the comforts of the epidemiological transition, where focus is shifted to development of chronic disease later in life instead of emergent infectious disease. Evidently, the developed world is not safe from infectious diseases. However, research suggests that humans may be able to arm themselves against communicable diseases with high-dose vitamin C supplementation, which can naturally boost immunity and act as a treatment. Vitamin C can shorten hospital stays and decrease the severity of disease. High-dose vitamin C is a low-cost, low-risk avenue of both treatment and prevention that should be promoted and researched by hospital administrations in low-income areas to decrease duration of hospital stays and provide a way for low-income communities to reduce their high hospitalization rates (Hemila & Chalker, 2019; Cohen, 1999).

**Summary of Literature**

**What is Vitamin C?**

 Vitamin C is a water-soluble vitamin that is found in certain foods and can exist in supplement form (National Institutes of Health, 2020). Vitamin C is defined as a vitamin because it is a substance that the body needs to develop and function; humans cannot survive without it [(U.S](https://medlineplus.gov/definitions/vitaminsdefinitions.html). National Library of Medicine, 2015). Vitamin C is also called ascorbic acid. Ascorbic acid refers to the molecular compound of vitamin C (C6H8O6) (PubChem, n.d.). Amongst its main functions, Vitamin C is an antioxidant that donates electrons to unstable free radicals to prevent oxidative stress in the body and is a cofactor for 15 mammalian enzymes involved in significant bodily processes, including hormone production, gene transcription, and the biosynthesis of collagen (Padayatty & Levine, 2016). Furthermore, vitamin C acts as an antiviral through its interactions with the immune system (Carr & Maggini, 2017).

**The Discovery of Vitamin C**

 Although the existence and importance of vitamin C were acknowledged years before its official identification, it was not until 1928 when vitamin C was formally recognized by Hungarian biochemist, Albert Szent-Györgyi (Grzybowski & Pietrzak, 2013). Szent-Györgyi began medical school in 1911 and eventually obtained his medical degree in 1917, after he served as an army medic during World War I. After establishing his own medical practice, he began new research in pharmacology. While bouncing around Europe, he was able to successfully investigate electron transduction and the pH system. He later worked at the University of Groningen where he proved that oxidation and reduction are of equal importance in cellular respiration and form a cycle, which was later deemed the citric acid cycle or the Krebs cycle.

After these findings, Szent-Györgyi became interested in why leaves turn brown in the sun and the brown discoloration of human skin during Addison disease (Grzybowski & Pietrzak, 2013). With this, he discovered that there was significant involvement by a specific substance with reductive properties that also happened to be present in citrus fruit and animal adrenal glands. This substance became the new focal point of Szent-Györgyi’s work. He eventually described it as a hydrocarbon with the chemical formula C6H8O6 and published his results, calling the unknownsubstance “Ignose”, derived from the words “I don’t know” and the suffix “ose” which characterizes sugars. The name was rejected and Szent-Györgyi renamed the substance “hexuronic acid.” In 1931, Szent-Györgyi returned to Hungary and was put in charge of the Department of Medical Chemistry at the University of Szeged. It was there that he met an American physician, Joseph Svibley, who had previously researched vitamin C at the University of Pittsburg. Szent-Györgyi commissioned Svibley to explore the “anti-scurvy” properties of hexuronic acid by investigating guinea pigs with scurvy. Eventually, the two scientists confirmed that the substance was vitamin C and published their findings in April 1932. It was not until Szent-Györgyi reached out to a fellow researcher, Norman Haworth, that the term “ascorbic acid” came to light, which replaced the previous name of “hexuronic acid.”

**Vitamin C Synthesis in Humans**

 Vitamin C is essential to human development and functioning. However, humans are at a disadvantage when it comes to vitamin C because, unlike almost all animal species on earth, humans cannot synthesize their own vitamin C. Other species that cannot synthesize their own vitamin C are teleost fishes (e.g., tuna, salmon, catfish), anthropoid primates (e.g. gorillas, spider monkeys, tamarins), guinea pigs, and some bat and bird species (Basic Biology, 2015; Encyclopedia Britannica, 2020).

 Researchers have pinpointed mutations in the L-gulono-γ-lactone oxidase (GLO) gene, which codes for the enzyme responsible for catalyzing the last step of vitamin C biosynthesis, as the culprit behind human’s inability to synthesize the vitamin (Grouin et al., 2011). It is suspected that the bias for mutations in the *GLO* gene stems from the fact that losing this gene only affects vitamin C production. Further research has found that in fish, anthropoid primates, and guinea pigs, the *GLO* gene mutations are irreversible. However, *GLO* pseudogenes found in bat species and some bird species have been reactivated through evolution.

Because humans cannot store or synthesize vitamin C, it means that an adequate amount of it must be consumed through diet. Rich sources of vitamin C are citrus fruits, tomatoes and tomato juice, and potatoes. It is also found in red and green peppers, kiwi, broccoli, strawberries, Brussel sprouts, and cantaloupe (National Institutes of Health, 2020). Research suggests that there is no correlation between GLO gene losses and reactivations and diet, suggesting that not being able to synthesize vitamin C is a neutral trait. This indicates that humans did not lose the ability to synthesize vitamin C because humans consume enough of it, meaning that vitamin C intake in diet and the loss of vitamin C synthesis are unrelated (Grouin et al., 2011).

**Recommended Dietary Allowance of Vitamin C**

Recommended Dietary Allowance (RDA) is the level of dietary intake that sufficiently meets the nutrient requirement of 97-98% of healthy individuals in a specific life stage and gender group (Institute of Medicine, 2000). The current RDA of vitamin C for adults is 90 mg for men and 75 mg for women daily (National Institutes of Health, 2019). These numbers are derived from maximum neutrophil ascorbate concentrations that lead to little urinary excretion (Institute of Medicine, 2000).

However, for people with diseases that require particular nutrient requirements or those who have special health needs, the RDA only serves as a basis; the RDA can be increased or decreased based on the individual’s needs (Institute of Medicine, 2000). The fact that the RDA can be adjusted based on individual need call into question its accuracy.

**Tolerable Upper Intake Level of Vitamin C**

The Tolerable Upper Intake Level (UL) of a nutrient is the highest level of intake that will most likely not lead to adverse health effects for almost all individuals in the general population. This indicates that the body can biologically tolerate this amount. It is suggested that as intake level surpasses the UL, the risk for adverse effects goes up (Institute of Medicine, 2000).

The current UL of vitamin C for both adult women and men is 2,000 mg/day (National Institutes of Health, 2019). This number is based on intake from diet and supplements, and the adverse effect of diarrhea. The Institute of Medicine (2000) states that although most sources suggest that the general healthy population should not exceed the UL, there is support for intake above the UL in controlled clinical trials. This review will examine studies that exceed 2,000 mg per day and report no adverse effects.

**Vitamin C Deficiency**

Most Americans are not eating enough fruits and vegetables. Even though it only takes 10 mg/day to prevent vitamin C deficiency, it is the fourth leading nutrient deficiency in the United States (Carr & Maggini, 2017).

Prolonged vitamin C deficiency is called scurvy. It is characterized by the weakening of collagenous structures, which leads to poor wound healing and impaired immunity (Carr & Maggini, 2017). Scurvy occurs after a continuous period of deficiency. The early symptoms of scurvy include generally feeling unwell, fatigue, loss of appetite, nausea, diarrhea, fever, painful joints and muscles, and small bleeding around hair follicles that are visible in the skin. However, symptoms that occur in the late stages of scurvy are more extreme. These include swollen, purple gums prone to bleeding, loose teeth, bulging eyes, severe and easy bruising, dry and brownish skin, hair breakage, slow-healing wounds, reopening of scars, bleeding into joints and muscles, and premature stopping of bone growth (State of Victoria, 2012). In most extreme cases, scurvy can result in death.

Individuals afflicted with scurvy are highly susceptible to dangerous diseases. The illness most associated with scurvy is pneumonia (Carr & Maggini, 2017). If an infection occurs in someone with scurvy, vitamin C levels in the body become more depleted because of increased inflammation and metabolic requirements. Research has found that scurvy occurs after infectious disease epidemics, especially after respiratory illness outbreaks.

**Why High-Dose Vitamin C?**

In this review, high-dose vitamin C pertains to doses of vitamin C that are 200 mg and above. High-dose vitamin C can be administered in two ways: orally or intravenously (IVC). There are benefits to both. Oral supplementation of vitamin C is inexpensive and readily available, making it more accessible to the general public. Intravenous vitamin C, while less accessible since it is only administered in healthcare settings, can be more efficient than oral vitamin C because IVC bypasses the gastrointestinal tract. This means that the vitamin C skips the process of digestion, allowing the body to be able to access the vitamin C more quickly than it could with an oral dose (Padayatty & Levine, 2016).

Although there is a fundamentally established RDA for vitamin C based on the inability of humans to both synthesize and store vitamin C, there is suspicion over how much vitamin C humans are supposed to consume. One point of controversy is the current RDA. A study examining dosages of vitamin C on seven healthy volunteers for 4-6 months concluded that the current RDA is not enough (Levine et al., 1996). The determinants used to conclude this new RDA of 200 mg/day were the relationship between vitamin C dose and steady-state plasma concentration, bioavailability, urinary excretion, cell concentration, and potential adverse effects.

The volunteers in the study consumed a diet with less than 5 mg of vitamin C daily (Levine et al., 1996). The doses given to the volunteers were seven daily doses between 30 and 2,500 mg of vitamin C. The study found that neutrophils, monocytes, and lymphocytes were saturated at 100 mg daily and had vitamin C concentrations that were at least 14 times higher than plasma concentrations. Bioavailability of vitamin C was found to be complete during a single dose of 200 mg. It was also found that vitamin C was not excreted in the urine of six of the seven volunteers until the 100 mg dose. Plasma was fully saturated after a dose of 1,000 mg. Because the study found that doses of 500 mg and higher had decreased bioavailability and higher rates of excretion, the researchers suggest a new RDA of 200 mg which they suggest getting from fruits and vegetables.

However, there was no discussion in this study of what occurred during the administration of 2500 mg. Additionally, their findings state that the plateau of plasma concentrations increased from 30 mg to 1000 mg, even though graphically, it showed that saturation continued to increase until 2,500 mg. Data on doses of 1250 mg and up were also excluded from parts of the experiment.

Another area of investigation is the Tolerable Upper Intake Level of vitamin C, which is the maximum daily intake unlikely to cause harmful effects. Currently, it is set at 2,000 mg/day (Harvard T.H. Chan School of Public Health, 2020). This indicates that humans can take about five times more than the RDA. Additionally, G.H. Bourne calculated that gorillas, the closest relative to humans, consumes about 4,000 mg of vitamin C every day, causing speculation amongst the scientific community about whether 90 mg of ascorbic acid is truly enough (Milton, 2003).

Furthermore, the work of Dr. Robert Cathcart challenges the RDA and UL of orally administered vitamin C. Through his work, he found that high-dose vitamin C does not live long in the body. Blood plasma levels above 70 μM/L were found to have a half-life of about 30 minutes, meaning that doses spread out throughout the day are independent, as is their bioavailability (Hickey et al., 2005). This means that one dose of vitamin C does not carry over to the next dose of vitamin C. In terms of the RDA, one dose of 90 mg/day would stay in the body for only a short period of time before it was used up or excreted, thus suggesting that more doses are necessary to maintain adequate levels of vitamin C in the body. This idea is based on the water-solubility of vitamin C: the body quickly absorbs what it needs, then proceeds to excrete the rest. Cathcart also contests the RDA and UL by suggesting that more vitamin C is necessary when a person is ill. In fact, Cathcart found that bowel tolerance of an individual is proportional to the toxicity of a disease: the more severe the disease, the more vitamin C the body needs (Cathcart, 1992). He used bowel tolerance of ascorbic acid, the amount that a person can intake before the production of loose stool, as a marker. In his studies, Cathcart found that about 80% of his patients who could tolerate ascorbic acid, reached bowel tolerance when they took 10-15 grams of ascorbic acid dissolved in water in four to six doses over a period of 24 hours. He also found that when these same people caught a mild cold, their tolerance could increase to about 50 grams over 24 hours. In the case of a severe cold, their tolerance could raise to 100 grams; for influenza, 150 grams, and so on.

**Functions of Vitamin C**

Within its properties as a vitamin, vitamin C is the most water-soluble antioxidant in the body (WebMD, 2008a). The importance of vitamin C being water-soluble means that it is quickly absorbed and excreted; it is not stored in the body. Its antioxidant abilities help protect the body from oxidation caused by free radical damage (WebMD, 2008b). Oxidative stress occurs when there is a disturbance in the balance between the production of free radicals and antioxidant defenses (Betteridge, 2000). It is theorized that oxidative stress plays a role in cancer, cardiovascular diseases, diabetes, Alzheimer’s disease, Parkinson’s disease, and a scope of eye diseases (NCCIH, 2020). Free radicals are compounds that form when the human body converts food into energy (National Institutes of Health, 2019). These unstable molecules can then damage DNA, lipids, and proteins (National Cancer Institute, n.d.). Vitamin C donates electrons to these unstable molecules. This neutralizes them, thus inhibiting their capacity to cause damage (Lobo, Patil, Phatak, & Chandra, 2010). The human body is constantly exposed to free radicals; they are caused by elemental factors such as cigarette smoke, air pollution, and ultraviolet light [(National](https://ods.od.nih.gov/factsheets/VitaminC-Consumer/) Institutes of Health, 2019). Therefore, the intake of vitamin C is essential to protect the body from these readily available free radicals. The antioxidant functions of vitamin C are very well-known and accepted in the scientific community.

Moreover, vitamin C is a cofactor for enzymes that are involved in important biosynthetic and regulatory processes such as carnitine and collagen biosynthesis, hormone production, gene transcription, and epigenetic regulation (Bozonet & Carr, 2019). The most important of these biosynthetic processes is arguably collagen biosynthesis. Vitamin C is essential to produce healthy collagen, which is the most abundant protein found in humans. It is the main protein in connective tissue and serves as the primary structural component of the dermis, cartilage, ligaments, tendons, bones, and teeth (Lobo et al., 2010).

Additional functions of vitamin C are wound-healing, heavy metal detoxification in the body, and key player iron metabolism by promoting iron uptake (Carr & Maggini, 2017; Padayatty & Levine, 2017).

Despite the many key roles that vitamin C plays in the body, the main focus of this review is the immune-boosting properties of vitamin C. Research suggests that vitamin C is a significant player in both innate and adaptive immune responses (Carr & Maggini, 2017). Vitamin C appears to play a role in promoting differentiation and maturation of immature T-cells. It is also said to accumulate in phagocytic cells that can enhance chemotaxis, phagocytosis, and microbial killing. It promotes apoptosis and the clearance of spent neutrophils from sites of infection by macrophages, thus decreasing the risk of necrosis and potential tissue damage. Also, because of its antioxidant properties, it potentially provides protection against environmental oxidative stress of the skin by supporting the epithelial barrier function against pathogens and promoting oxidant scavenging. These functions will be further investigated regarding their effects on specific illnesses.

**Original Works of High-Dose Vitamin C**

*Dr. Linus Pauling*

 One of the founding fathers of high-dose vitamin C is Nobel laureate, Dr. Linus Pauling. Dr. Pauling received his B.S. in Chemical Engineering from Oregon State College, then received his PhD in Chemistry and minors in physics and mathematics from the California Institute of Technology. His work was mostly centered around molecular structures and theoretical work on chemical bonds (The Nobel Prize, 2020). Some of his accomplishments include the Nobel Prize in Chemistry in 1954 and the Nobel Peace Prize in 1962. The 1954 Prize was awarded to Dr. Pauling for his work on the development of quantum mechanics which greatly impacted the world of physics and chemistry by providing explanations for chemical bonding. However, it was Dr. Pauling’s advocacy against the nuclear arms race after the dropping of the atomic bombs on Hiroshima and Nagasaki that made him the recipient of the 1962 Nobel Peace Prize.

 It was not until after receiving the 1954 Prize, that Dr. Pauling began researching vitamins; he was in the midst of working with mental health patients and vitamins were proposed to be effective medications for these diseases. This launched Dr. Pauling’s controversial career on mega doses of vitamin C. His main work involved high-dose vitamin C, around 10 grams per day, and its effects on cancer (Council for the Lindau Nobel Laureate Meetings, n.d.). In his clinical cancer trial, he and another researcher gave 100 terminal cancer patients supplemental vitamin C as a part of their cancer management (Cameron & Pauling, 1976). The control group consisted of 1,000 terminal cancer patients who received the same treatment, except for the supplemental vitamin C. It was found that the average survival time of the subjects with the supplemental vitamin C lived 4.2 times longer than those without the vitamin C. Additionally, the study results yielded that 90% of the supplement patients died at a rate that was one-third that of the non-supplement patients, and that the other 10% of supplement patients had a much greater survival time.

 Dr. Pauling also expressed interest in changing the RDA for vitamin C in the 1970s. Based on cross-species comparisons, evolutionary arguments, biochemical individuality, and the amount of vitamin C in a raw plant food diet, he believed that the optimal intake of vitamin C is 2000 mg daily, with a minimum of 200 to 250 mg per day. He theorized that, “The first 250 mg leads you up to the level where the blood is saturated. You can achieve a higher volume [concentration] in the blood by a larger intake, but you get much better improvement for the first 250 mg than for additional grams” (Oregon State University, 2019). Dr. Pauling took at least 10 grams of vitamin C every day for more than 20 years. He eventually died at the age of 93 (Council for the Lindau Nobel Laureate Meetings, n.d.).

*Dr. Frederick Klenner*

Another mastermind behind high-dose vitamin C was Dr. Frederick Klenner. Dr. Klenner graduated from the Duke University School of Medicine in 1936, had three years of post-graduate hospital training, and eventually opened his own private practice (International Society for Orthomolecular Medicine, 2020a). Dr. Klenner specialized in diseases of the chest and published 28 papers. One of his main contributions to the science of vitamin C and illness his published findings on using vitamin C on patients afflicted with poliomyelitis and other viral diseases (Klenner, 1949). In 1948, he treated 60 patients with polio, distributing doses of vitamin C every two to four hours. The starting doses were between 1,000 and 2,000 mg. Once the patient’s fever dropped, the dose was then administered every six hours. As a result, all of Dr. Klenner’s patients were well within 72 hours after the treatment began.

*Dr. Robert Cathcart*

Another high-dose vitamin C researcher that made a name for himself was Dr. Robert Cathcart. He obtained his medical degree from the University of California in San Francisco in 1961, interned and completed his residency at Stanford Hospital, became the instructor for orthopedic surgery at Stanford, and created the “Cathcart Prosthesis” (International Society for Orthomolecular Medicine, 2020b). Throughout his career, Dr. Cathcart treated more than 20,000 patients with high-dose vitamin C. He also created the concept of titrating to bowel tolerance, where he treated over 9,000 patients with a variety of illnesses using high-dose vitamin C to test their tolerance of the vitamin (Cathcart, 1981). Dr. Cathcart focused much of his vitamin C work on HIV/AIDS, administering more than 10 to 20 grams intravenously to his patients (Cathcart, 1984).

**Vitamin C and Respiratory Illnesses**

*Influenza*

 Studies suggest that vitamin C has a positive impact on influenza. Influenza affects the body by creating oxidative stress which causes nonspecific damage to pulmonary tissue and can result in inflammation of the lungs. Because ascorbic acid is an antioxidant, it alleviates the infection in two ways: it neutralizes free radicals and blocks the activation of specific enzymes that enable the transfer of the influenza virus (Zarubaeva et al., 2018).

 In a prospective, controlled study consisting of students in a technical training facility, both the effectiveness of vitamin C in illness prevention and the relief of symptoms of virus-induced respiratory infections were explored (Gorton & Jarvis, 1999). The control group was made up of 463 participants, ages 18 to 32, and the experimental group had 252 students, ages 18 to 30 years. The investigators recorded the number of cold and flu symptoms of all participants for one year and compared the number of symptoms of the two groups. The control population was given pain relievers and decongestants when symptoms appeared; the experimental group was given 1,000 mg of vitamin C for the first 6 hours after symptoms appeared, and then three times daily. This study found that reported flu and cold symptoms in the experimental group decreased 85% after administration of vitamin C when compared to symptoms of the control group.

*Pneumonia*

Because of its antioxidant properties, vitamin C protects host cells against oxidative stress resulting from infections (Hemila & Louhiala, 2007). In cases of illness, phagocyte and lymphocyte concentrations of vitamin C are much higher than the plasma concentration. In experimental studies, it has been shown that vitamin C increases the function of phagocytes and the production of T-lymphocytes and interferon, and inhibits the replication of viruses. Additionally, infections such as pneumonia, result in reduced vitamin C levels in plasma, leukocytes, and urine.

 One study that illustrated the effectiveness of vitamin C on pneumonia was a randomized, double-blind place-controlled trial (Hemila & Louhiala, 2007). Its participants were hospital patients with a mean age of 81 years who were admitted with acute bronchitis or pneumonia. The patients’ mean plasma vitamin C level was 23 µmol/L. One-third of the patients had plasma vitamin C levels of just 11 µmol/L. The experimental group was given 0.2 g/day of vitamin C on top of regular treatment. The control group received treatment without vitamin C. Vitamin C was found to decrease the respiratory symptom score in the more severely ill patients; their less ill counterparts showed no effects. There were also five deaths in the control group and only one in the vitamin C group.

 Another study examining the effects of vitamin C on pneumonia patients compared a group of patients that were administered low-dose vitamin C to a group that was given high-dose vitamin C (Hemila & Louhiala, 2007). There was also a control group to which vitamin C was not administered. The lower doses ranged from 0.25 to 0.8 g/day, and the higher doses were anywhere between 0.5 and 1.6 g/day. The control group’s hospitalization duration was 23.7 days. When compared to the control group, it was found that the low-dose vitamin C group had a 19% shorter stay and the high-dose group had a 26% shorter stay. Additionally, the vitamin C groups reported more normalized chest X-rays and temperatures.

 Although these studies are not necessarily generalizable to the Western world because they were conducted in the UK and Russia, their promising results suggest that vitamin C treatment on pneumonia should be explored in westernized civilizations.

*COVID-19*

 COVID-19 is a new infectious disease plaguing the world. Because of its novelty, the disease is severely under researched. Its spread has been too quick for the world of science to keep up; there are no vaccinations at this time. However, throughout the beginning stages of the pandemic when the virus was still mostly concentrated in its country of origin, China, information regarding vitamin C as a treatment ventured to the United States. Although specific results were not released, the Second Affiliated Medical Team of Xi’an Jiaotong University made their plan of action to treat COVID-19 patients with high-dose vitamin C public. They suggested administering vitamin C in the early stages of the disease, all doses must be high doses, and has to be combined with an individualized treatment plan for the patient. This team based their plan off of their prior experience with vitamin C treatments on patients diagnosed with acute Keshan disease and severe acute respiratory syndrome (SARS) (The Second Affiliated Hospital of Xi’an Jiaotong University, 2020).

 Another advocate for vitamin C treatment for COVID-19 patients is Dr. Richard Cheng who is based out of South Carolina (Cheng, 2020). He has been promoting high-dose vitamin C in China for the past four to five years. Dr. Cheng has been stationed in Shanghai, China, since the outbreak of COVID-19. He has established two IVC clinical trials in COVID-19 patients and is currently discussing creating more IVC trials with other hospitals. He suggests IVC for more extreme cases and oral doses for less severe cases. Dr. Cheng endorses vitamin C for COVID-19 because the illness causes inflammation caused by oxidative stress which prevents the lungs from exchanging oxygen. Because vitamin C is an antioxidant, it should reduce the oxidative stress in the body.

 These vitamin C clinical trials have also made an appearance in the United States. Currently, New York State’s largest hospital system, Northwell Health, is distributing high-dose vitamin C to its COVID-19 patients. A pulmonologist and critical-care specialist, Dr. Andrew G. Weber, is giving his patients in intensive care 15,00 mg doses of IVC (Mongelli & Golding, 2020). He claims that his patients who received the vitamin C “did significantly better” than his patients that were not given vitamin C. This treatment is currently being used in numerous Northwell facilities.

**Vitamin C and ICU Duration**

 With the ability of vitamin C to fight infection, it makes sense that the longevity of ICU (Intensive Care Unit) stays would be decreased as a result of its administration. A meta-analysis was conducted on whether vitamin C had an effect on the length of stay in the ICU and the duration of mechanical ventilation (Hemila & Chalker, 2019). This meta-analysis analyzed 18 controlled trials with 2,004 patients in total. In 12 of these trials with a total of 1,766 patients, it was found that vitamin C decreased ICU stay by 7.8%. In six trials where vitamin C was administered orally in doses of one to three grams per day, the ICU stay was reduced by 8.6%. There were three trials that involved patient mechanical ventilation for more than 24 hours, and it was found that vitamin C reduced time on a mechanical ventilator by 18.2%.

**Risks of High-Dose Vitamin C**

 Although high-dose vitamin C is relatively safe, there are proposed risks.

*Kidney Stones*

 One commonly cited adverse effect of high-dose vitamin C is the formation of kidney stones. However, data regarding vitamin C and kidney stones is inconclusive. For example, numerous studies conducted on gout, abnormally high concentrations of uric acid/urate, and vitamin C have varying results [(Oregon](https://lpi.oregonstate.edu/mic/vitamins/vitamin-C) State University, 2020).

One observational study of 1,387 men showed that higher intakes of vitamin C were associated with lower serum concentrations of uric acid (Prier et al., 2018). A cross-sectional study of 4,576 African Americans demonstrates that the odds of having hyperuricemia was associated with dietary intakes that were high in fructose and low in vitamin C, or with high fructose-to-vitamin C ratios. In a prospective study that followed 46,994 men for 20 years, it was found that total daily vitamin C intake was inversely associated with incidence of gout. Higher intakes suggested a greater reduction in risk of gout. A meta-analysis performed in 2011 on 13 randomized controlled trials of healthy individuals with elevated serum uric acid levels suggested that vitamin C supplementation (a median dose of 500 mg was used daily for thirty days) reduced serum uric acid concentrations by 0.35 mg/dL. This was compared to a placebo group [(Oregon](file:///C%3A%5CUsers%5CCam%20Vazquez%5CDocuments%5C%28Oregon) State University, 2020). In a prospective case series study involving long-term IVC use in 157 adult patients, 8% of whom had a history of kidney stones, it was found that patients maintained stable renal function.

One of the largest studies regarding kidney stone risk and vitamin C are the Nurses’ Health Study (NHS) I and II, and the Health Professionals Follow-up Study (HPFS) (Ferraro et al., 2016). The NHS consisted of 156,735 women and the HPFS was comprised of 40,536 men. This study found that total vitamin C intake was not significantly associated with kidney stone risk in women, but it was for men whose intake fell between 500-999 mg/day. The same associations were found with supplemental vitamin C, although the dosage was not specified. Overall, the study found that vitamin C intake was not associated with kidney stones among men or women, who did not have dietary intakes greater than 700 mg/day.

Because the results of these studies are conflicting, those who are at risk of kidney stones should confer with a medical professional about vitamin C use.

*Hemochromatosis*

Because vitamin C has the ability to increase iron absorption, there are concerns about whether or not the vitamin will have an impact on those who have hemochromatosis, which is when the body stores too much iron. This condition is thought to affect about one million people in the U.S. (National Institutes of Health, 2019). However, there is no clear evidence that supports the claim that vitamin C endangers those who have hemochromatosis. One article states that, because the overall uptake and storage of iron in humans is controlled by a complex network of regulatory mechanisms, high-dose vitamin C will not disrupt the iron balance in healthy people and those who are heterozygous for hemochromatosis. For those who are homozygous hemochromatosis, the effects of vitamin C are understudied (Grester, 1999).

 On the other hand, for the 10 million people who are iron deficient, vitamin C can be greatly beneficial because it increases the bioavailability of iron from foods by enhancing intestinal absorption of non-heme iron (Miller, 2013; Oregon State University, 2020).

 Overall, data is inconclusive on hemochromatosis and vitamin C, but supported in terms of vitamin C and those who are iron deficient. Those diagnosed with hemochromatosis should confer with a medical professional about vitamin C use.

*Nausea, Diarrhea, and Cramps*

One of the main concerns of high-dose vitamin C is diarrhea and bloating. That is why the UL is set at 2,000 mg; this is the proposed dose before diarrhea occurs. However, the UL applies to healthy individuals. The work of Cathcart shows that when an individual is ill, the amount of vitamin C one can tolerate (bowel tolerance) increases proportionally to the severity of the illness (Cathcart, 1992). In his work, Cathcart treated over 9,000 patients with mega doses of vitamin C. From his work with these patients, he found that an individual who is healthy and well could tolerate 4 to 15 grams over the course of 24 hours. For those with a mild cold, that dose increased to 30 to 60. For his influenza patients, the dose raised to 100 to 150 grams. For pneumonia patients, the tolerated dose was between 150 and 200 grams (Cathcart, 1981).

 Not only can loose stool be avoided with high-dose vitamin C by simply monitoring one’s own body, but this tolerance will increase when an individual becomes ill, negating the idea for the UL. However, those with gastrointestinal issues should confer with a medical professional about vitamin C use.

**High-Dose Vitamin C as a Public Health Issue**

 Vitamin C is a natural, low-cost, and safe way to help people boost immunity. The literature illustrates an increasing demand for high dosages of vitamin C to optimize immune function in the body in order to protect people from serious infectious diseases. Not only is the current RDA too low, but humans need frequent doses of vitamin C throughout the day because of the body’s inability to store the vitamin (Levine et al., 1996; Hickey et al., 2005).

Additionally, vitamin C deficiency being the fourth leading vitamin deficiency in the United States indicates that American immune systems are vulnerable, especially the immune systems of those who have low socioeconomic status (SES). For instance, U.S. children from lower social classes are more absent from school because of upper respiratory infections and ear infections than their higher SES counterparts (Cohen, 1999). Furthermore, lower levels of education and higher levels of unemployment are associated with higher incidence of acute lower respiratory tract infections. Moreover, in the U.S., children up to 17-years-old from families who receive federal assistance are more likely to die of pneumonia and influenza. Hospitalizations are increased in lower income communities, specifically during flu season (Hadler et al., 2016). Using influenza hospitalization data collected in 14 Flu-Surv-NET sites covering 27 million people during the 2010-2011 and 2011-2012 flu epidemic, it was found that flu-related hospitalization incidence in higher poverty census tracts was 21.5, which was approximately twice the incidence in lower poverty census tracts.

Encouraging hospitals to administer and promote high-dose vitamin C is a symbiotic relationship: hospitals will increase efficiency and decrease costs because hospital stay durations and hospitalizations will decrease; and those in low-income areas who are more susceptible to severe illness and may not be able to afford healthcare, will be less likely to need hospital services. Therefore, action must be taken by the healthcare field to promote the use of vitamin C in hospitals in an attempt to protect the American population and hospitals themselves from the consequences of future outbreaks.

**Conceptual Framework: Social Ecological Model**

In this section, the Social Ecological Model will be used to promote high-dose vitamin C in hospitals, which, in turn, will demonstrate how promoting high-dose vitamin C in hospitals will influence the public. The Social Ecological Model describes the interaction and interdependence of the levels of society on health issues. The model includes individual factors, including knowledge, attitudes, and beliefs; interpersonal factors, such as interactions that provide social support or barriers to health behaviors; institutional and organizational factors, which are rules, policies, and informal structures that can inhibit or promote healthy behaviors; community factors, including formal and informal social norms; and public policy factors, such as laws, that regulate health actions (Rural Health Information Hub, 2020). The Social Ecological Model demonstrates the top-down effect that hospitals will have on individual health behaviors.

 At the policy level, there will be changes in regulatory practices of hospitals. All hospitals will be required to offer high-dose vitamin C as an alternate form of medicine to its patients. There must be consent forms signed by the patients in order for medical professionals to administer high-dose vitamin C. It will also be mandatory that when vitamin C is administered, research will be conducted and published, in order to help high-dose vitamin C become a more widely researched topic. All research findings must be presented at a local conference that local medical and healthcare professionals will attend. Community outreach programs based from the hospital will be required to disseminate information to the public.

 With newly established research and dissemination from hospitals about vitamin C use, the community and institutional levels will be affected. The new medical information will sway local doctors’ offices and public health departments to promoting the use of high-dose vitamin C. The new research will help establish new norms in treatments and regulations in doctors’ offices and public health departments. In order to fit these new norms, there will be restructuring of health practices in community level institutions, such as schools, due to public health efforts. Health education officials will begin to use high-dose vitamin C in its health education programs, leading to restructured health education programs in schools.

 Subsequently, policy, community, and institutional factors will influence interpersonal factors. With newly reformed education programs and health promotion efforts from both medical and public health professionals, knowledge of vitamin C and its benefits will disseminate to the public. As knowledge and familiarity of high-dose vitamin C increases, conversations will spark between people, and these people will begin to suggest this mode of viral protection and treatment to their friends and family.

 Finally, as a result of those surrounding an individual promoting the use of high-dose vitamin C, an individual will adopt the idea of high-dose vitamin C for themselves and use it as a mode of treatment and prevention.

**Recommendations for Public Health Practice**

With vitamin C being the fourth leading nutrient deficiency in the United States and the emergence of novel viral diseases, vitamin C should be promoted in the medical community through the establishment of high-dose vitamin C hospital policies (Carr & Maggini, 2017). These policies should be implemented mostly in patients with respiratory illnesses and in ICUs. These policies should especially be mandatory in low-income communities that boast higher rates of infection and hospitalizations (Cohen, 1999; Hadler et al., 2016).

 Along with these new high-dose vitamin C hospital policies, there should be increased funding for research. A lack of research is what is circulating doubt about high-dose vitamin C in the medical community. High-dose vitamin C, despite its promising effects on illnesses, is greatly under-researched. In order for the medical community to truly begin to grasp how high-dose vitamin C effects the body, there needs further exploration of the topic. Because vitamin C is low-risk and inexpensive, hospitals should be required to research the vitamin.

 Additionally, hospitals and medical centers have a responsibility to educate the public. Hospital administrations should combine their effects with local public health departments to disseminate information on high-dose vitamin C through outreach programs. With the increased susceptibility of the human body to infectious diseases, the public has a right to know how they can protect themselves. This is especially important in low income communities where people may not have the ability to eat healthy, exercise, or get vaccinations, or for those who do not believe in vaccinations. This could be a way to reach an unprotected part of the population in order to increase herd immunity. Furthermore, when new diseases emerge, health officials may not have adequate time to develop a vaccination. By promoting the use of vitamin C during these times, there may be reduced rates of illness, even without a vaccination. Overall, there should be policies in hospitals that provide patients the choice to use high-dose vitamin C as a treatment option, there needs to be increased funding of high-dose vitamin C, and there should be community outreach from hospitals and public health officials about how high-dose vitamin C can be beneficial to the public.

**Conclusion**

High-dose vitamin C is a promising avenue to disease prevention and treatment for high- risk individuals. Vitamin C is an inexpensive, readily available supplement that is easy to find in pharmacies and supermarkets, making it accessible to all populations. It is also a safe way to naturally boost immunity. By promoting the use of high-dose supplemental vitamin C, the number of vitamin C deficient Americans could decrease, and the number of Americans with optimally strong immune systems can increase. This could help protect the United States from another epidemic such as COVID-19, which has left many Americans ill, and medical professionals and hospitals overwhelmed. Additionally, implementing IVC for COVID-19 patients all across the United States could reduce the stress of hospitals by lessening hospital stays. Overall, high-dose vitamin C is low-cost, high-benefit solution to preventing and treating illnesses

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