

COMMENTS

Ascorbic Acid Role in Containment of the World Avian Flu Pandemic

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In this Comment, the ultimate intent is to increase survival of the anticipated global flu pandemic. The apparent failure of “medicine” to provide a completely understood and logically based biochemical prevention and treatment for all influenzas (and many other viral diseases) may be an unavoidable result of the evolving complexity of the H5N1 virus. However, clinical experience cited in all accounts, including the 2003 to 2006 period, suggest that: (i) ascorbic acid is not being administered to humans infected or at risk for influenza, and (ii) ascorbic acid is (mistakenly) believed to be a vitamin (“vitamin C”). Proper use of ascorbic acid as described here could provide effective containment for the flu pandemic. *Exp Biol Med* 232:847–851, 2007

Key words: ascorbic acid; avian flu; immunity; hyperglycemia; refined diet

Preface

In addition to the main theme of this Comment on the health improvements attainable by ascorbic acid (AA), editorial staff for *Experimental Biology and Medicine* has suggested that the author provide information on health improvements achievable by conventional methods. To accomplish this without excessive increase in length, Linus Pauling’s excellent “Regimen for Better Health” on pages

8–9 of his book (1) is suggested. Pauling’s book (1) includes a bibliography of over 400 references documenting the importance of the essential nutrients to general health; study of the book should emphasize chapter 2.

Irwin Stone’s 1972 book (2), which features forewords by two Nobel Laureates, is a unique source of references on AA (“vitamin C”) against disease. Its bibliography runs from pages 200 to 253 and contains important references cited from the medical literature of the 40 years from the discovery of AA (by Nobel Laureate Szent-Gyorgyi) through its use in clinical practice by Jungeblut, McCormick, and Klenner.

Introduction

In several publicized locations, including Vietnam, many (~50%) of the humans infected with avian flu did not die (3). As explained in this paper, these surviving patients and the medical personnel dedicated to pandemic prevention appear unaware of the need for AA or the fact that all humans can obtain it in food. Clearly, if their absorption from food is high (possibly approximately 300 mg/day; Table 1), their white cells may protect them against some level of flu virus; in addition, an oral dose of AA can increase the level of virus resisted. A theory is outlined that strengthens the prediction that a starting AA dose can be chosen that may greatly increase the number of survivors in a given population. Pauling states on page 165 of his book (1) that large-scale future survival of those infected in an avian flu pandemic should be enhanced by an AA dose given daily at 1 g/hr (and a higher dose in the people who are more ill). A high-sugar diet is undesirable for anyone, because it greatly impairs the utilization of AA and totally prevents resistance to flu.

Double-blind clinical trials of AA have been performed against the common cold and flu (1, 4). Pauling concluded that the measures to be taken for prevention and treatment of influenza through use of AA are essentially the same as for the common cold (1). He stated, at great length and on page

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Table 1. Ascorbic Acid Content of Common Foods

Food	Ascorbic acid (mg/100 g food)
Black currant	200
Red capsicum	140
Broccoli	90
Kiwifruit	90
Brussels sprouts	80
Orange	70
Green capsicum	70
Persimmon	60
Silver beet greens	50
Orange juice	40
Cauliflower	40
Spinach	30
Tomato	25
Cabbage	20

165, that AA, used properly, should be effective in preventing an influenza pandemic (1). I clarify problems caused by: (i) elevated blood sugars typical of affluent populations consuming the refined diet and (ii) the MISTAKEN belief that AA (commonly called vitamin C) is a vitamin. Although it was not initially understood, it has long been observed that hyperglycemia induces dysfunction in various processes, such as reproduction and immunity (5–10). Ely had proposed a theory that explained anomalous dysfunctions induced in hyperglycemia; he called this effect the “glucose ascorbate antagonism” (GAA; Refs. 8–10).

AA Is Not a Vitamin

AA should be regarded as one of the most important molecules. The length of human life is more dependent upon its continuous adequate supply than on most other molecules. Ascorbic acid has many thousands of functions in body processes and is needed daily in gram quantities (1). The references cited here show clearly that the popular view “ascorbic acid is a vitamin” is mistaken. This mistake is a major cause of massive tragic unnecessary morbidity and mortality, rapid aging, and shortened life spans.

A vitamin is an essential constituent of the diet required in only minute amounts for optimum health and longevity. Pauling and others have reported that several grams (more than 10 in many people) a day of AA are absolutely necessary for numerous aspects of optimum health in humans (1). The confusion over AA’s nonvitamin nature has been prolonged by continued use of the misnomer “vitamin C” for communication convenience by those who know better (even Pauling).

In early mammalian evolution, synthesis of AA evolved to provide this versatile endogenous molecule to control, organize, drive, and take part in many vital processes (11). Some mammalian species in the tropics obtained enough AA in their food to survive the low-stress environment and, as a result, lost the synthetic ability. Freedom from the need

to synthesize AA gave a genetic advantage to these animals (including prehumans) until they left the tropics.

There are about 4000 species of “normal” mammals that synthesize AA, on average approximately 50 mg/kg body wt daily or about 5 g/day (normalized to 70 kg for a human). This amount has been found to be essential for optimum health (1, 11–13), slowing aging, and resisting many human diseases, especially influenza and other maladies (1, 14–16). When in stress (e.g., pain, fear, disease), the needs and syntheses are far higher (~100-fold!), as Lewin states on page 109 of his work (15). Such synthesizing mammals, often called “normal,” were here on earth long before humans. It is important to note that in the wild state, the normal mammals do not get scurvy and do not consume a refined diet (i.e., their free sugar intake is very low). They developed and used AA as an important endogenous molecule that is necessary in large quantities for essentially all systems and functions. AA enables all normal mammals to resist most diseases, intoxications, and other disorders of humans, including tuberculosis and polio, among others. In the human body, there are thought to be about 50,000 different kinds of enzymes, a large number of which are influenced by AA (1). As AA levels fall, many enzyme systems fail, disorganizing numerous physiologic functions (17). Although humans are not synthesizers of AA, their need is the same as that of the normal mammals. When this need is met (by diet and/or supplements) and their blood sugar is maintained at a low level as described later, most humans also are protected.

The normal mammals meet the fluctuations in AA needs automatically over a wide range of conditions, due to the adaptability and efficiency of a global endocrine synchrony. Unfortunately, the human, as a nonsynthesizing mammal, does not have this synchrony but is burdened with the same daily AA requirements. Thus, humans have the life-long need (*not* an option!) to supplement inefficiently an amount that is unavoidably greater than the basic normal mammalian need. Simply providing humans the ~50 mg/kg body wt of AA as one or a small number of doses (oral or other) on a fixed schedule will not replicate the sufficiency seen in normal mammals.

We cite many reports (from a much larger number) demonstrating that high AA intake is required for optimum or “full health.” This has been defined (on page xi) to be “the greatest resistance to disease” by Albert Szent-Gyorgyi, the Nobel Prize winner who first isolated AA (2). He and Linus Pauling, the only holder of two unshared Nobel Prizes, agreed that AA is not a vitamin (1). Pauling also estimated (on page x) that most people get only 2% of the AA necessary for full health (2).

In essence, the benefits of high AA production in the synthesizing mammals are so great *and* the countless costs of inadequate AA (due to the “vitamin view”) in humans are so tragic that neither could be an accident. To *think* of AA as a vitamin is a lethal error. It dooms the thinker to a lifestyle characterized by rapid aging, much illness with related

suffering, medical costs, and early death. When AA first became available in the 1930s, its impressive effects in infectious as well as degenerative and other diseases stimulated extensive worldwide research and clinical activity, resulting in publication of more than 10,000 papers by 1975. Hundreds of these were carefully reviewed in the book by Irwin Stone (2), the biochemist who introduced Pauling to AA. However, successes of AA in clinical trials against colds and cancer in the 1960s and 1970s were compromised by the high blood glucose levels accepted as normal in developed nations (8–10, 18–20). Until the 1900s, the *low-sugar*, whole-grain, unrefined diet had produced 2-hr postprandial blood glucose values of 50–90 mg/dl. These are still seen where the primitive diet prevails (21), and they are approximately one half the glycemic levels typical of affluent populations today (20). Hyperglycemia opposes AA because glucose competitively inhibits the insulin-mediated active transport of AA against the high gradient (AA in cells is ~50 times the plasma level in health; Ref. 15, page 78). Thus, in hyperglycemia, the inability to raise intracellular AA to optimum levels compromises all biochemical processes.

Note that by 1975 the convenience of numerous antibiotics and vaccines had captured the attention of mainstream medicine, and no one felt compelled to read the old literature or practice its methods as listed below. AA was soon rejected as unpatentable and was forgotten by mainstream medicine. Nevertheless, in the last 50 years many reports have been published by research-oriented physicians (22–28). These were of viral and bacterial diseases, intoxications, etc., that were successfully (safely and economically in most patients) treated by massive doses of ascorbate (from 10 to more than 200 g/day (26).

In the 1930s, the remarkable Claus W. Jungeblut, M.D., worked in the College of Physicians and Surgeons of Columbia University. He first reported that AA in concentrations attainable in humans by a high intake could inactivate and/or protect against numerous viral and bacterial pathogens and their toxins (1, 16, 29, 30). These include the polio, hepatitis, and herpes viruses, among others. Many other researchers have published *in vitro*, *in vivo*, animal, and human evidence of AA's almost universal ability (bacteriostatic, bactericidal, virucidal, etc.) to prevent and cure infections. One of the earliest research findings was AA's ability to neutralize and render harmless many bacterial toxins (e.g., tetanus, diphtheria, and staph toxins; Refs. 2, 29, 30). It has been clearly demonstrated that oral AA 2 g/day protects against posttransfusion hepatitis (1). The high safety, efficacy, and economy of AA have been proven, but inadequate AA greatly predisposes to infectious diseases (16, 22, 29, 30). Other long-known medical benefits of AA are those for surgery and wound healing (31, 32). AA facilitates wound strength, healing rapidity, and freedom from infection. Recently, a large-scale ongoing clinical study of critically ill surgical patients has shown many benefits in those given multigram AA and vitamin E (33).

In recent decades, a number of different methods have

been developed for improving immunity against many diseases. These include: (i) the "killed-virus" polio vaccine developed by Salk that was put into use in 1955 and gave long-lasting protection without adjunctive dietary concern; (ii) gamma globulin injections, which are usually given to temporarily boost a patient's immunity against disease and also are free of dietary change (injections are most commonly used on patients who have been exposed to hepatitis A or measles); (iii) the finding that sufficient daily intake of AA is needed for immune function (AA protects against almost all infections, particularly viral); and (iv) the fact that the ultimate medical scientist, Fred R. Klenner, M.D. (from Duke Medical School, 1936), was originally a chemist and a Ph.D. student in physiology. He was inspired by Jungeblut's findings and the fact that AA is an essential nutrient, *not* a vitamin. As a result, Klenner perfected high-dose AA therapy and used it for many infectious diseases and other disorders. He reported that dosing with amounts that elevate white blood cell AA sufficiently (50–100 g/day by iv and/or oral)¹ produces prompt (~7-day) cures of polio infection, viral encephalitis, acute hepatitis (all types), adenovirus, chicken pox, measles, etc.

No valid argument or experimental evidence supports the concept that "AA is a vitamin." The fact that AA is *not* a vitamin has been proven countless times. In this era, this concept is as absurd as laughing at the germ theory to cite a recommended dietary allowance (such as ~60 mg/day) for AA. Possibly, as stated above, the most lethal misconception of our time is the notion that AA is a vitamin. This vitamin notion is a major factor in the vast morbidity and mortality cited by World Health Organization's June 2000 World Health Report (34).

Ascorbic Acid and Human Survival of Infections, Including All Influenzas

Ascorbic acid markedly enhances immune functions. Leukocytes require high AA levels to drive the metabolic pathway called the *hexose monophosphate shunt* (HMS) to supply adequate hydrogen peroxide and ribose for effective phagocytosis and mitosis. In 1971, the finding at the Bowman-Gray School of Medicine (35) that the HMS rate is *proportional to intracellular AA* should have changed all fields of medicine. Intracellular AA, as measured by buffy coat (white blood cells) AA: (i) gives a *prompt indication* of immune status and (ii) is a *universal limiting factor* that determines the rate and intensity of cell-mediated immunity. In humans and in AA-synthesizing mammals, lymphocytes multiply more rapidly and phagocytes ingest and kill more effectively *when their intracellular AA* is high. Buffy coat is the fraction of a centrifuged blood sample that contains most of the white blood cells. After centrifugation, one can distinguish a layer of clear fluid (i.e., plasma), a layer of red fluid containing most of the red blood cells, and a thin layer

¹In iv dosing, AA is always sodium ascorbate.

in between, the buffy coat (thus called because it is usually buff in hue), with most of the white blood cells and platelets.

Vitamins and other essential nutrients of a sound diet can increase immunity but not nearly as strongly as AA. Most of the poorly nourished can survive if enough AA is obtained. In a flu pandemic, those with insufficient AA will not survive, even if they are well nourished in all other ways.

Glucose Ascorbate Antagonism (GAA)

Three decades ago, after reading the Bowman-Gray 1971 report, I deduced and related to Linus Pauling a theoretical reason for the failure of clinical trials of AA against colds and cancer: It is the high blood glucose levels in developed nations (36, 40). We call this theory the GAA (8–10, 13, 38, 39). The GAA is important in the normal (low-dose) range of ~10 g/day or less of AA. The theory states that the intracellular AA levels in certain cell types, such as leukocytes and fetal cells, are “pumped up” by insulin-mediated active transport to the measured concentrations, which are ~50 times higher than in the surrounding plasma (15). This increase of intracellular AA occurs effectively if blood glucose is in the “low” (normal) range (i.e., 50–90 mg/dl). This blood sugar level was considered normal until the 1900s, but it is approximately one half the glycemic levels produced today by the typical Western diet. In even “modest” blood glucose elevations (more than ~130 mg/dl, common following most Western meals), blood glucose molecules so outnumber AAs that they competitively inhibit insulin-mediated active transport of AA into cells. Such inhibition results in low intracellular AA levels, low HMS, and cell dysfunction (namely, leukocytes do not attack tumors or pathogens, fetal cells divide too slowly, and so on); this phenomenon is the glucose “antagonism” of AA. A diet that is low in sugar or refined carbohydrates (such as white flour and white rice) is desirable for everyone, because it lowers average blood sugar and greatly enhances the utilization of AA.

The Model Dynamics of Systemic Defense Against Flu When AA Is Obtained Only in Food

The human immune system must have AA to prevent and/or cure influenza, a common viral disease. Influenza has been treated and cured medically with AA by Klenner (23–25). The size of the dose and the number of injections required were in direct proportion to the fever curve and duration of the illness.

However, it is reported that about half of the humans who contract avian influenza in Vietnam do not die. Yet, these patients may never even have heard of AA. We suggest that their survival may have occurred because the particular viral load constituting their moderate infection may have been small enough that the AA they accidentally acquired from their diets was adequate to defend them. AA is used by the immune system to increase the buffy coat AA content, enhancing defense against viruses and other pathogens.

An average young adult in marginal AA status might use one thirtieth of a gram of AA per day, or about 1 g in a whole month. Then, if he happens to have a total of only 1 g in his body, when he becomes cut off from his external supply source he would use up his entire supply in 1 month (in this simplified approximation). He could die on or about the last day of that month because there are so many (more than 10,000) functions for AA in the body, and none can be satisfied. Now, we consider a person who is malnourished but not in extremely poor health, although his resistance to many diseases is rather marginal. Such a person can still survive a mild infection of flu if the amount of flu virus is not exceeding his ability to: (i) provide sufficient white blood cells for defense; and (ii) stimulate interferon production to go into adjacent cells, preventing the virus from reproducing in them (1).

Thus, it is vital that everyone adopt a method that will provide the most reliable daily AA source. AA can normally be obtained in tablet form. However, in an avian flu pandemic or other emergency, the usual sources for this supplement (i.e., health food stores, pharmacies, etc.) would be completely exhausted and unable to meet the demands of anyone, let alone the entire population. Although inadequate, acquiring AA from food will likely be the only reliable method. Table 1 provides the AA content of common foods that can be used as sources. Five servings should average to at least 200 mg daily, especially if the higher AA-content foods are emphasized. To check other foods to eat often for their AA content, search the U.S. Department of Agriculture food composition database (41). This weak protection will require everyone to maximize AA intake, minimize exposure, and avoid sugar.

In avian flu patients, survival is a simple matter of whether AA is sufficient such that the virus dose is depleted before the AA. Clearly, when such a patient comes into medical care, if we can raise the patient’s AA at that time, by even a large fraction of a gram, his or her recovery will likely be essentially immediate in many cases. The hospital staff must judge from the patient’s temperature and other signs and symptoms (1) how severe his or her infection may be. Their judgment will determine how much AA should be given to the patient to accelerate his or her recovery. Upon the patient’s release from hospital, the medical staff should have evaluated the likelihood of the patient’s being reinfected and admonished him on reduction of exposure and improvement of diet to enhance his AA intake. Stores of supplementary AA (tablets, etc.) need to be conserved for hospital use because of large economic losses that can be suffered by avian flu countries.

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