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## **Observations On the Dose and Administration of Ascorbic Acid When Employed Beyond the Range of A Vitamin in Human Pathology**

**Frederick R. Klenner, M.D., F,C,C.P.**

*Editor's Note:*

*Because of the unusually high amounts of ascorbic acid used in Dr. Klenner's treatment, as reported in his paper, we asked him to verify amounts mentioned. Following is his answer:*

*"To the Editor of the ICAN Journal: This will confirm that all 'quantity' factors given in my paper are correct and can be confirmed from hospital and medical office records. The notation relative to 150 grams represents the amount used for reversing pathology in a given case and was the amount given over a period of 24 hours. (The I.V. was continuous.) This was given in three bottles of 5D water, decanting only enough from 1000 cc to be replaced by the 'C' ampules.*

*"Recently the FDA has published a 'warning' that too much soda-ascorbate might be harmful, referring to the sodium ion. In reply to this I can state that for many years I have taken 10 to 20 grams of sodium ascorbate by mouth daily, and my blood sodium remains normal. These levels are checked by an approved laboratory. 20 grams each day and my urine remains at or just above pH 6."*

*Signed:*

**FRED R. KLENNER, M.D.**

### ***Ancient History and Homespun Vitamin C Therapies***

Folklore of past civilizations report that for every disease afflicting man there is an herb or its equivalent that will effect a cure. In Puerto Rico the story has long been told "that to have the health tree Acerola in one's back yard would keep colds out of the front door."<sup>1</sup> The ascorbic acid content of this cherry-like fruit is thirty times that found in oranges. In Pennsylvania, U.S.A., it was, and for many still is, Boneset, scientifically called *Eupatorium perfoliatum*<sup>2</sup>. Although it is now rarely prescribed by physicians, Boneset was the most commonly used medicinal plant of eastern United States. Most farmsteads had a bundle of dried Boneset in the attic or woodshed from which a most bitter tea would be meted out to the unfortunate victim of a cold or fever.

Having lived in that section of the country we qualified many times for this particular drink. The Flu of 1918 stands out very forcefully in that the Klenners survived when scores about us were dying. Although bitter it was curative and most of the time the cure was overnight.

Several years ago my curiosity led me to assay this "herbal medicine" and to my surprise and delight I found that we had been taking from ten to thirty grams of natural vitamin C at one time. Even then it was given by body weight. Children one cupful; adults two to three cupfuls. Cups those days held eight ounces. Twentieth century man seemingly forgets that his ancestors made crude drugs from various plants and roots, and that these decoctions, infusions, juices, powders, pills and ointments served his purpose. Elegant pharmacy has only made the forms and shapes more acceptable.

***Early specifications, action and dosages for administrations.***

To understand the chemical behavior of ascorbic acid in human pathology, one must go beyond its present academic status either as a factor essential for life or as a substance necessary to prevent scurvy. This knowledge is elementary. Listen to what appeared in Food and Life Yearbook 1939, U.S. Department of Agriculture:<sup>3</sup> "In fact even when there is not a single outward symptom of trouble, a person may be in a state of vitamin C deficiency more dangerous than scurvy itself. When such a condition is not detected, and continues un-corrected, the teeth and bones will be damaged, and what may be even more serious, the blood stream is weakened to the point where it can no longer resist or fight infections not so easily cured as scurvy." It is true that without these infinitesimal amounts myriads of body processes would deteriorate and even come to a fatal halt.

Ascorbic acid has many important functions. It is a powerful oxidizer and when given in massive amounts; that is, 50 grams to 150 grams, intravenously, for certain pathological conditions, and "run in" as fast as 20 Gauge needle will allow, it acts as a "Flash Oxidizer,"<sup>4</sup> often correcting the pathology within minutes. Ascorbic acid is also a powerful reducing agent. Its neutralizing action on certain toxins, exotoxins, virus infections, endotoxins and histamine is in direct proportion to the amount of the lethal factor involved and the amount of ascorbic acid given. At times it is necessary to use ascorbic acid intramuscularly. It should always be used orally, when possible, along with the needle.

***Scurvy historically the target; today's goal of high blood levels to cope with self-induced abuses and physiological traumas.***

If one is to employ ascorbic acid intelligently, some index for requirements must be realized. Unfortunately there exists today a sort of "brand" called "minimum daily requirements." This illegitimate "child" has been co-fathered by the National Academy of Science and The National Research Council and represents a tragic error in judgment. There are many factors which increase the demand by the body for ascorbic acid, and unless these are appreciated, at least by physicians, there can be no real progress. It is vitally important that cognizance be taken of the demand by the body for ascorbic acid far beyond so-called scorbutic levels. Briefly these demands can be summarized: 1)

The age of the individual; 2) Habits -- such as smoking, the use of alcohol, playing habits; 3) Sleep, especially when induced artificially; 4) Trauma.-- trauma caused by a pathogen, the trauma of work, the trauma of surgery, the trauma to the body produced accidentally or intentionally; 5) Kidney threshold; 6) Environment; 7) Physiological stress; 8) Season of the year; 9) Loss in the stool; 10)

Variations in individual absorption; 11) Variations in "binders" in commercial tablets; 12) Body chemistry; 13) Drugs; 14) Pesticides; 15) Body weight; 16) Inadequate storage.

***Flexible dosage standards explained as minimal standards.***

With such knowledge it is no longer possible to accept a set numerical unit in terms of minimal daily requirements. This is true because of the simple fact that people are different and these same people experience different situations at various times. With ascorbic acid, today's adequate supply means little or nothing in terms of the needs for tomorrow. Let us start thinking in terms of maximum requirements. For too long a time we have under supplied our children and ourselves by accepting through negative ignorance and acquiescence so-called standards. Based on scant data on mammalian synthesis, available for the rat, a 70-Kg. individual would produce 1.8 grams<sup>5</sup> to 4.0 grams<sup>6</sup> of ascorbic acid per day in the unstressed condition. Under stress, up to 15.2 grams.<sup>7</sup> Compare this to the 70 mg recommended for daily requirements without stress and 200 mg for the simple stress of the obstetrical patient, and you will recognize the disparity and understand why we have been waging a one man war against the establishment in Washington for 23 years.

***Ascorbic acid not synthesized by man***

Work on mammalian biosynthesis of ascorbic acid indicates that the vitamin C story as is generally accepted represents an over simplification of available evidence.<sup>8,9,10</sup> This often leads to misinterpretations and false impressions. It has been proposed that the biochemical lesion which produces the human need for exogenous sources of ascorbic acid, is the absence of the active enzyme, L-gulonolactone oxidase from the human liver<sup>11</sup>. A defect or loss of the gene controlling the synthesis of this enzyme in man, blocks the final phase in the series for converting glucose to ascorbic acid. Virus can mutate cells, X-Rays can do it and it can occur by chance. Such a mutation could have happened, denying all progenies of this mutated animal the ability to produce ascorbic acid. Survival demanded ascorbic acid from an exogenous source. This is not remarkable. Other recognized genetic diseases in which a missing enzyme causes a pathological syndrome, in man, are phenylketonuria, galactosemia and alkaptonuria.

It is worthy to note that Sealock and Goodland have ascribed to ascorbic acid the faculty of being the necessary co-enzyme in the metabolic oxidation of tyrosine. The velocity of the oxidation in this reaction is dependent upon the concentration of vitamin C. Tyrosine is essential in breaking down protein to usable amino acid. The scorbutic guinea-pig's liver is unable to oxidize tyrosine except in the presence of ascorbic acid. This suggests a lead in the study of the metabolic abnormality-Alkaptonuria-in humans.

Ascorbic acid administration will correct the alkaptonuria of the scorbutic guinea pig. Its effect on human alkaptonuria has been inconsistent. The reason: Inadequate use of ascorbic acid.

### ***Bio-chemist Irwin Stone's concept has practical value***

The inability of man to manufacture his own ascorbic acid, due to genetic fault, has been called "hypoascorbemia" by Irwin Stone.<sup>12</sup> This is another reason for abolishing the present concept of daily minimal requirements. The physiological requirements in man are no different from other mammals capable of carrying out this synthesis.

### ***Various procedures testing for the vitamin C levels and Requirements of the body.***

Various tests have been employed to determine the degree of body saturation of vitamin C, but for the most part they have been misleading. Blood and urine samples analyzed with 2:6 dichlorophenol indophenol will give values roughly 7 percent less than when testing with dinitrophenol hydrazine. Gothlin advocates the capillary fragility test which is similar to the tourniquet test of Hess in results. Both can be used to estimate the quantity of vitamin C necessary to maintain capillary integrity. The intra-dermal test of Rotter as modified by Slobody<sup>13</sup> is again gaining new recruits. In principle it is the same as the lingual test of Ringdorf and Cheraskin<sup>14</sup> since both are based on the time required to decolorize dye. The lingual test is rapid and simple to perform but it requires a syringe with a 25 gauge needle and a stop watch. Since the dye methods depend on the reduction of the reagent by vitamin C, any substance having a reducing potential lower than the dye is a possible source of interference. Twenty years ago we elected to measure, as a therapeutic gauge, the amount of vitamin C in urine by borrowing on its ability to reduce qualitative Benedict's solution. A 2 plus Benedict's reaction in a known dextrose free urine was accepted as a standard. This test was helpful in gauging requirements for simple stress, but not accurate enough when using needle therapy. Fifteen years ago we developed the Silver Nitrate-Urine<sup>15</sup> test. This test employs 10 drops of 5 percent silver nitrate and 10 drops urine which is placed in a Wasserman tube. Read in two minutes it will give a color pattern showing white, beige, smoke gray or charcoal or various combinations of any two depending upon the degree of saturation. We have found this color index test is all one will need for establishing the correct amount of ascorbic acid to use by mouth, by muscle, by vein in the handling of all types of human pathology either as the specific drug or as an adjuvant with other antibiotics or neutralizing chemicals. In severe pathological conditions the urine sample, taken every four hours, must show a fine charcoal-like precipitation with a clear supernatant liquid if positive clinical results are to be realized. Spilling in the urine is not new. Abraham and Keefer have demonstrated that when penicillin is injected intravenously, excretions in the urine account for 60 percent of the administered dose.

### ***Role played by ascorbic acid in intercellular reactions, neutralizing, possibly controlling virus production.***

In 1935 Stanley isolated a crystalline protein possessing the properties of tobacco mosaic virus. It contained two substances, ribonucleic acid (RNA) and protein. The simple structure characteristic of tobacco mosaic virus was soon found to be a basic property of many human viruses such as coxsackie virus (which I believe to be the cause of Multiple Sclerosis), Echo and polioviruses - they all contain only ribonucleic acid and protein. There exist minor variations. Adenoviruses contain deoxyribonucleic acid (DNA) and protein. Other viruses such as that causing influenza contain added lipid and polysaccharides. Deoxyribonucleic acid is used to program the large viruses, like mumps, ribonucleic acid is used to program the small viruses, like measles.

The role of the protein coat is to protect the parasitic but unstable nucleic acid as it rides the "blood highway" or "lymphatic system" to gain specific cell entry. Pure viral nucleic acid without its protein coat can be inactivated by constituents of normal blood. There are several theories as to what happens after cell entry: 1) Once inside a given cell, the virus nucleic acid sheds its protein coat and proceeds to modify the host cell by either creating mutations or by directly substituting its own nucleic acid; 2) The infectious nucleic acid, after entering a human cell, retains its protein coat and starts to produce its own type protein coat<sup>16</sup> and viral nucleic acid, so that new units can either depart to enter other cells or by destruction of the cell, thus making the infection more severe; 3) The introduction of a foreign fragment of nucleic acid in the cell-virus interaction approach as postulated by Starr<sup>17</sup>. In the Starr theory there can exist cells with partial chromosome make-up and cells with multi-nuclei. Hiliary Kropowski holds that these partial cells are 'pseudo-virions'<sup>18</sup> and are found in some tumor-virus infections. A key factor in the Starr-Kropowski thinking is that the cell maintains its biological integrity to support virus development despite the abnormal morphology and genetic deficiency. If these invaded cells could be destroyed or the invader neutralized the illness would suddenly terminate. Ascorbic acid has the capability of entering all cells. Under normal circumstances its presence is beneficial to the cell, however, when the cell has been invaded by a foreign substance, like virus nucleic acid, enzymic action by ascorbic acid contributes to the breakdown of virus nucleic acid to adenosine deaminase which converts adenosine to inosine. The net result is to lead to purines which are extensively catabolized and not to p+urines which are utilized for further nucleic acid. Ascorbic acid also joins with the available virus protein, making a new macromolecule which acts as the repressor factor. It has been demonstrated that when combined with the repressor, the operator gene, virus nucleic acid, cannot react with any other substance and cannot induce activity in the structural gene, therefore inhibiting the multiplication of new virus bodies. The tensile strength of the cell membrane is exceeded by these macromolecules with rupture and destruction. Another hypothesis is that vitamin C acts to create new "L" viruses which are impotent. Still another, that the "binding" alone is sufficient to destroy the virus.

***Promptness of massive ascorbic acid in avoiding fatal encephalitis related to stubborn head and chest colds.***

In 1953<sup>19</sup> we presented a case history and films of a patient with virus pneumonia. This patient was unconscious, with a fever of 106.8°F (A. corrected) when admitted to the hospital. 140 grams ascorbic acid was given intravenously over a period of 72 hours at which time she was awake, sitting up in bed and taking fluids freely by mouth. The temperature was normal. Since that time we have observed a more deadly syndrome associated with a virus causing head and chest colds. This is one of the adenovirus striking in the area of the upper respiratory tract with resulting fever, sore throat and eyes, and when in children can cause fatal pneumonia. More often death is indirect by way of incipient encephalitis where the child can be dead in 30 minutes. These are the babies and children found dead in bed and attributed to suffocation. It is suffocation but by way of a syndrome we observed and reported in 1957<sup>20</sup> which is similar to that found in cephalic tetanus-toxemia culminating in diaphragmatic spasm, with dyspnea and finally asphyxia.<sup>21</sup> By 1958<sup>22</sup> we had collected sufficient information from our office and hospital patients to catalog this deadly syndrome into two important stages. A 1) There is always a history of having had the "Flu" which lasted 48 to 96 hours complicated with extreme physical or mental distress; 2) A mild cold, similar to an allergic rhinitis, which lingered on for several weeks but did not incapacitate the individual.

B This stage, which is always sudden, will present itself in at least seven forms: 1) Convulsive seizures; 2) Extreme excitability resembling delirium tremens if an adult and with dancing of the eyeballs if a child; 3) Severe chill; 4) Strangling in the course of eating or drinking (bulbar type); 5) Collapse; 6) Stupor; 7) Hemiplegic type.

### ***Second Stage Findings***

Other findings of this dramatic second stage are: 1) Rapid pulse; 2) Temperature can be normal, moderately elevated or high; 3) Respirations twice to three times normal and in some cases will be suggestive of air hunger; 4) Pupils will be moderately open and in some instances (hemiplegic) one will be markedly dilated; 5) Urine negative; 6) The white blood count running from 6,000 to 25,000 with a high poly count in the differential; 7) Young patients starting the second phase with a convulsion there has been not only a history of normal bowel movements but also an enema given at the time of first examination has produced a normal stool; 8) Bladder spincted control was abnormal in our cases who convulsed or who were in coma.

### ***Neurological Changes***

It is apparent that the second stage of this syndrome is triggered by a breakthrough at the site of the blood-brain barrier. The time required for neurological changes to become evident is roughly comparable to the time necessary for similar neuropathology to be demonstrated following a severe head injury. Cerebral edema exists in both conditions. In my practice I start massive ascorbic acid therapy immediately. I have seen children dead in from 30 minutes to 2 hours because their attending physician was not impressed with their illness upon hospital admission.

An autopsy on one of these patients showed bilateral pneumonitis - all one needs to spark a deadly encephalitis. To indicate just how common this syndrome presents itself, I relate here a newspaper account of a 15 year old girl who had a mild, lingering cold for several weeks. She attended a dance party one evening and except for a complaint of feeling extremely tired, she went to bed apparently well. She was found dead in bed the following morning. An autopsy showed bilateral pneumonia. How many times have you read such an account? This is why it is necessary for everybody to take adequate supplemental vitamin C to guard against such disasters.

### ***Literature Research***

In 1960 we decided to re-search the literature before writing our paper. "Virus Encephalities As A Sequel Of The Pneumonias."<sup>22</sup> Rosenfield in 1903 described a similar syndrome under the caption "Brain Purpura or Haemorrhagic Encephalitis." Comby, in 1907, was the first to call attention to the interesting "metastatic" sequela of the pneumonias. Baker and Noran in 1945 enumerated five groups, each showing certain definite clinical characteristics which may be of both diagnostic and prognostic significance in relation to this virus syndrome. 1) Symptoms of a nonspecific nature - headache, vomiting, irritability; 2) Delirious type; 3) Convulsive type; 4) Lethargic type; 5) Hemiplegic type. These groups plus two additional types, namely: 6) Chill - blood invasion type; 7) Collapse, were as we reported them, independently, in the Tri-State Medical Journal, October 1958.

Their results: Some recovered, some died and still others lived as "vegetation" mental cripples. All of our patients recovered. Thirteen years from the time of the Baker-Noran report to the time of our report and 13 years from the time of our report to the present time. This makes the issue urgent. Physicians must recognize the inherent danger of the lingering head or chest cold and appreciate the importance of early massive vitamin C therapy.

### ***How does the brain become involved in encephalitis?--some speculations.***

Clinical problems such as these groups present, leads one to speculate on the pathways in which the virus gains entrance into the brain. We can summarize: 1) Through the olfactory nerves; 2) Through the portals of the stomach from material swallowed, either pulmonary or upper respiratory drainage; 3) Direct extension from otitis media or from mastoid cells; 4) The blood stream. Arriving in the brain the virus goes through the blood cerebro spinal fluid barrier and/or the blood brain barrier by one of three ways: a) Electrical charge; b) Chemical lysis of tissue; c) Osmosis. Bakay<sup>24</sup> reported that the permeability of the blood-brain barrier can be changed by introducing various toxic agents into the blood circulation. Chambers and Zweifach<sup>25</sup> emphasized the importance of the intercellular cement of the capillary wall in regulating permeability of the blood vessels of the central nervous system. In this syndrome the toxic substance is an adenovirus. Ascorbic acid will repair and maintain the integrity of the capillary wall.

### ***Burns - degrees explained and some therapy rational.***

In the treatment of burns ascorbic acid, in sufficient amounts, reflects itself as a truly miracle substance. In the early forties, when I was using ascorbic acid, intramuscularly, in treating bacillary dysentery, shiga type, with excellent results, Lund, Lam and many others were using, what they called, massive doses of ascorbic acid in the treatment of burns. One or two grams each day, in fluids, was the recognized dose. Burns are at the beginning first degree and some remain as just an erythema. Many times the first degree burn progresses rapidly to the second degree stage and remains as "blisters". Still others go on to third degree which usually is more pronounced on the third plus post burn day. There is a fourth stage which results from lack of knowledge in treatment. It terminates with skin grafting and plastic surgery. We believe that ascorbic acid will eliminate the fourth stage and the third stage if used as we will later program.

### ***Burns - continued descriptive and related therapies.***

The pathologic physiology of a burn wound from the moment of the accident is in a state of dynamic change until the wound heals or the patient dies. The primary consideration is the phenomenon of blood sludging originally recognized by Knisely in 1945.<sup>26,27</sup> Initially there is intravascular agglutination of red blood cells into distinctly visible, smooth, hard, rigid, basic masses. Lofstrom in 1959 demonstrated that the oxygen uptake by the tissues is greatly reduced because of the sludging and therefore reduced rate of flow. Berkeley<sup>28</sup> in 1960 concluded that this phenomenon of sludging or agglutination results in capillary thrombosis in the area of the burn, extending proximally to involve the large arterioles and venules and thereby creating tissue destruction greater than that originally produced by the burn.

Anoxia produces added tissue destruction. Lund and Levenson<sup>28</sup> found that after severe burns there is considerable alteration in the metabolism of ascorbic acid as shown by a low concentration of ascorbic acid in the plasma either with the patient fasting or after saturation tests and also low urinary excretion of vitamin C either with the patient fasting or after the injection of test doses. The extent of the abnormality closely paralleled the severity of the burn. Bergman<sup>30</sup> reported an increase demand for ascorbic acid in burns especially when epithelization and formation of granulation tissue are taking place. Lam<sup>31</sup> also reported in 1941 a marked decrease in the plasma ascorbic acid concentration in patients with severe burns. Klasson<sup>32</sup> although limiting the amount of ascorbic acid to a dose range of 300 mg to 2000 mg daily, in divided doses, found that it hastened the healing of wounds by producing healthy granulation tissue and also that it reduced local edema. He rationalized that ascorbic acid used locally as a 2% dressing possessed astringent properties similar to hydrogen peroxide. He also reported that antibiotic therapy was rarely necessary.

### ***Severe burns and related therapy.***

Harlen Stone<sup>33</sup> suggested the use of gentamicin in major burns to lower the sepsis caused by pseudomonas. Absorption of its exotoxin from the infected burn wound inhibits the bacterial defense mechanism of the reticuloendothelial system. Death can result either from the toxemia alone or from an associated septicemia.

We have found that the secret in treating burns can be summarized in five steps: 1) The use of the "old covered wagon" type cradle when indicated, with three 25 watt bulbs. The patient controls the heat by turning on and off the first bulb as needed to keep warm. No garments or dressings are allowed; 2) The employment of a 3% ascorbic acid solution as a spray over the entire area of the burn. The spray can be applied with a Devilbis unit using an ordinary portable pressure pump. The old type "flit gun can also be used or even a 50 c.c. syringe with a 20 gauge needle. The 3% solution is used every 2 to 4 hours for a period of roughly five days; 3) The use of vitamin A and D ointment over the area of the burn and this is now alternated, q4h with the 3% ascorbic acid solution; 4) The administration of massive doses of ascorbic acid by vein and by mouth. 500 mg per Kg. body weight diluted to at least 18 c.c. per gram vitamin C using 5% dextrose in water, saline in water or Ringers solution and for the initial injection, run in as fast as a 20 gauge needle or catheter will carry the flow. Cut-downs are frequently necessary and the foot-ankle area is recommended. Vitamin C solution is repeated every 8 hours for the first several days, then at 12 hour intervals. Ascorbic acid, by mouth, is given to tolerance. Loose stools is accepted as this index. Using large doses of ascorbic acid I.V. will necessitate the administration of at least one gram calcium gluconate, daily, to replace free calcium ions removed in the breakdown chemical action as ascorbic acid goes to dehydroascorbic acid, then to ketogulonic acid and later to oxalic acid"" as the calcium salt; 5) Supportative treatment; that is, whole blood and maintaining electrolite balance. If seen early after the burn there will be no infections and no eschar formations. This eliminates fluid formation, since the eschar traps will not exist and there will be no distal edema because the venous and lymphatic systems will remain open. There will be no arterial obstruction and no nerve compression. Pseudomonas will not be a problem, since ascorbic acid destroys the exotoxin systemically and locally.



Even if the burn is seen late when pseudomonas is a major problem the gram negative bacilli will be destroyed in a few days leaving a clean healthy surface. I have seen eschars 2 inches wide and 1/2 inch thick, severely infected so that stench had to be controlled with deodorizing sprays, melt away when employing the method outlined. Ascorbic acid also eliminates pain so that opiates or their equivalent are not required. In extremely extensive burns that involve back and front of the patient, the "Hoverbed" employed by the British should be considered. It uses the same principle as the hovercraft to lift a solid object. What has been overlooked in burns is that there are many living epithelial cells in the areas that grossly look like "raw muscle." With the use of ascorbic acid these cells are kept viable, will multiply and soon meet with other proliferating units in the establishment of a new integument.

### ***Regarding personal and environmental pollution-carbon monoxide.***

We are all plagued with varying degrees of chronic carbon monoxide poisoning. This is the price we pay for putting our "railroads" on our highways, smoking and being too lazy to walk. Small amounts of carbon monoxide, if constantly maintained in the alveoli, can produce serious effects. Carbon monoxide in the inspired air leads to oxygen deficiency in the tissues causing extreme exhaustion. The affinity of carbon monoxide for hemoglobin is roughly 300 times as great as that for oxygen.

In addition to active replacement of oxy-hemoglobin the presence of some proportion of carboxy-hemoglobin decreases the dissociability of such oxy-hemoglobin as remains. Carbon monoxide can be released from hemoglobin if the patient is exposed to high pressure of oxygen, 93% along with 7% carbon dioxide. This is not always available. Ascorbic acid in the blood is constantly losing molecules of water. Perfectly dry carbon monoxide and oxygen cannot unite to form carbon dioxide, but carbon monoxide and water may give rise to carbon dioxide in the complete absence of oxygen. The reactions which take place are  $CO + H_2O = HCOOH$   $CO_2 + H_2$  (Wright). Here the oxygen of the water has been used to oxidize carbon monoxide to carbon dioxide with the liberation of hydrogen. Glutathione may facilitate this cellular oxidation by acting as a hydrogen acceptor (Hopkins). Clinical experience suggests that if sufficient ascorbic acid is suddenly placed into the blood stream - 12 grams to 50 grams - that through "Flash Oxidation" a concentration of oxygen is made high enough to pull carbon monoxide from hemoglobin to form carbon dioxide. This rapidly formed carbon dioxide acts with the high oxygen tension to serve the same purpose as when given by "mask," further enhancing the chemical action taking place. Ascorbic acid will also prevent residuals such as paralysis, blindness, interference with sensations, muscle spasms or twitchings which in some cases can be permanent.

### ***Primary and lasting benefits in pregnancy.***

Observations made on over 300 consecutive obstetrical cases using supplemental ascorbic acid, by mouth, convinced me that failure to use this agent in sufficient amounts in pregnancy borders on malpractice. The lowest amount of ascorbic acid used was 4 grams and the highest amount 15 grams each day. (Remember the rat-no stress manufactures equivalent "C" up to 4 grams and with stress up to 15.2 grams).

Requirements were roughly 4 grams first trimester, 6 grams second trimester and 10 grams third trimester. Approximately 20 percent required 15 grams, each day, during last trimester. Eighty percent of this series received a booster injection of 10 grams, intravenously, on admission to the hospital. Hemoglobin levels were much easier to maintain. Leg cramps were less than three percent and always was associated with "getting out" of Vitamin C tablets. Striae gravidarum was seldom encountered and when it was present there existed an associated problem of too much eating and too little walking. The capacity of the skin to resist the pressure of an expanding uterus will also vary in different individuals. Labor was shorter and less painful. There were no postpartum hemorrhages. The perineum was found to be remarkably elastic and episiotomy was performed electively. Healing was always by first intention and even after 15 and 20 years following the last child the firmness of the perineum is found to be similar to that of a primigravida in those who have continued their daily supplemental vitamin C. No patient required catheterization. No toxic manifestations were demonstrated in this series. There was no cardiac stress even though 22 patients of the series had rheumatic hearts. One patient in particular was carried through two pregnancies without complications. She had been warned by her previous obstetrician that a second pregnancy would terminate with a maternal death. She received no ascorbic acid with her first pregnancy. This lady has been back teaching school for the past 10 years. She still takes 10 grams of ascorbic acid daily.

Infants born under massive ascorbic acid therapy were all robust. Not a single case required resuscitation. We experienced no feeding problems. The Fultz quadruplets were in this series. They took milk nourishment on the second day. These babies were started on 50 mg ascorbic acid the first day and, of course, this was increased as time went on. Our only nursery equipment was one hospital bed, an old, used single unit hot plate and an equally old 10 quart kettle. Humidity and ascorbic acid tells this story. They are the only quadruplets that have survived in southeastern United States. Another case of which I am lustly proud is one in which we delivered 10 children to one couple. All are healthy and good looking. There were no miscarriages. All are living and well. They are frequently referred to as the vitamin C kids, in fact all of the babies from this series were called "Vitamin C Babies" by the nursing personnel--they were distinctly different.

### ***How concerned should we be about oxalic acid and kidney stones?***

#### ***A technical explanation.***

One of the "scare" weapons used by the critics on high daily doses of ascorbic acid is the oxalic acid-kidney stone hypothesis. Meakins<sup>36</sup> states that the chief factors in the formation of renal calculi are perversions of metabolic processes, infection and stasis in the urinary tract. There are two schools of thought on stone formation: 1) That there is a central nucleus of colloids on which the crystalloids are precipitated; 2) That the crystalloids are deposited from the urine in which they are present in concentrated solution, in which salt and hydrogen ion concentrations are important factors. In all cases stasis and a concentrated urine appear to be the chief physiological factors. The only way that oxalic acid can be produced from ascorbic acid is through splitting of the lactone ring.

This happens above pH5. The reaction of urine when 10 grams of vitamin C is taken daily is usually pH6. Oxalic acid precipitates out of solution only from a neutral or alkaline solution-pH7 to pH10. Kelli and Zilva<sup>37</sup> reported that "Nutrition experiments showed that dehydroascorbic acid is protected in vivo from rapid transformation to the antiscorbutically impotent diketogulonic acid from which oxalic acid is derived. Values reported in the literature for normal 24 hour urinary oxalate excretions for humans range from 14 mg to 56 mg. Lamden et al.<sup>38</sup> found in a group of volunteers that the ingestion of 9 grams ascorbic acid daily resulted in oxalate spills as high as 68 mg for 24 hours and in the controls without extra vitamin C the high was 64 mg for a 24 hour period. These critics have overlooked the individual with diabetes mellitue. The amount of oxalic acid found in the diabetic patient approximates that found in the urine of a normal person taking 10 grams vitamin C each day. With the diabetic we find a paradox. Give this individual 10 grams ascorbic acid daily, by mouth, and the urinary oxalate excretion remains relatively unchanged. Diabetics are known for their diuresis. The individual who takes 10 or more grams of vitamin C each day will find that this organic compound is an excellent diuretic. No urinary stasis; no urine concentration. The ascorbic acid kidney stone story is a myth. Methylene blue will dissolve calcium oxalate stones giving 65 mg orally 2 to 3 times a day. (Dr. M. J. Vernon Smith: Med. World News, Dec. 4, 1970)

### ***Why death from insect and snake bites?***

It is estimated that 6500 deaths occur each year in the United States from snake bite. Many more from various flying insects, spiders, certain plants and some caterpillars. These are needless deaths. Several factors are at work in these pathologies: 1) The tox-albumin of the snake bite, like the copperhead or rattler; 2) Formic acid plus a toxin with a protein cover, called proteotoxin by Arthus,<sup>39</sup> such as found in bees and wasps; 3) Neurotoxin from the Black Widow, the Fiddle Spider and snakes like the Cobra and Coral; 4) Production of histamine, especially in the more severe stings and bites. Wells<sup>40</sup> in 1925 called the poison of certain spiders and snakes zootoxins and of poisonous plants, phytotoxins. Ford<sup>41</sup> in 1911 reported three classes of toxins in plants and fungi: 1) Nerve poisons-muscarine; 2) Those causing structural changes in the viscera with resulting fatty degeneration; 3) Gastrointestinal irritants.

### ***Ascorbic acid to the rescue.***

It is a demonstrated principle that the production of histamine and other end products from deaminized cell proteins released by injury to cells are a cause of shock. The clinical value of ascorbic acid in combating shock is explained when we realize that the deaminizing enzymes from the damaged cells are inhibited by vitamin C.<sup>42</sup> It has been shown by Chambers and Pollock<sup>43</sup> that mechanical damage to a cell results in pH changes which reverse the cell enzymes from constructive to destructive activity. The pH changes spread to other cells. This destructive activity releases histamine a major shock producing substance. The presence of vitamin C inhibits this enzyme transition into+the destructive phase. Clark and Rossiter<sup>44</sup> reported that conditions of shock and stress cause depletion of the ascorbic acid content of the plasma. As with the virus bodies, ascorbic acid also joins with the protein factor of these toxins effecting quick destruction. The answer to these emergencies is simple. Large amounts of ascorbic acid 350 mg to 700 mg per Kg. body weight given intravenously.

In small patients, where veins are at a premium, ascorbic acid can easily be given intramuscularly in amounts up to two grams at one site. Several areas can be used with each dose given. Ice held to the gluteal muscles until red, almost eliminates the pain. We always reapply the ice for a few minutes after the injection. Ascorbic acid is also given, by mouth, as followup treatment. Every emergency room should be stocked with vitamin C ampoules of sufficient strength so that time will never be counted-as a factor in saving a life. The 4 gram, 20 c.c, ampoule and 10 gram 50 c.c. ampoule must be made available to the physician.

### ***A case history-success due to promptness with a twelve gram injection.***

As an example of the lethal effect of certain stings and bites, I briefly relate a case history. An adult male came to my office complaining of severe chest pain and the inability to take a deep breath. Stated that he had been "stung" or "bitten" 10 minutes earlier. Thinking that it was a Black Widow and not bothering to look for fang marks, due to the gravity of the situation, I gave one gram calcium gluconate intravenously. This gave no relief. He begged for help saying he was dying.

He was becoming cyanotic. Twelve grams of vitamin C was quickly pulled into a 50 c.c. syringe and with a 20 gauge needle was given intravenously as fast as the plunger could be pushed. Even before the injection was completed, he exclaimed, "Thank God". The poison had been neutralized that rapidly. He was sent home to locate the "culprit". He soon returned with an object that looked like a mouse. It was 1 1/2 inches long with long brown hair. There was a dark ridge down the entire back. It had seven pairs of propelling units and a tail much like a mouse. The following day I took "The Thing" to Duke University where it was identified as the Puss Caterpillar. This unusual caterpillar left 44 red raised marks on the back of its victim. Except for vitamin C this individual would have died from shock and asphyxiation.

### ***Some concern answered regarding high dosage of ascorbic acid.***

Merton Lamden, a bio-chemist, writing in the New England Journal of Medicine, Feb. 11, 1971, expresses grave doubts about the safety of large doses of ascorbic acid taken by mouth. He gives a report by Paterson<sup>45</sup> on the diabetogenic effect of dehydroascorbic acid on rats. Paterson in 1950 employed only the Ketone formula of ascorbic acid, dehydroascorbic acid, which he administered, undiluted, intravenously, in extraordinary amounts. His results were based on giving rats, weighing 100 grams to 120 grams, dehydroascorbic acid in doses from 20 to 50 mg. This transposed to a man weighing 70 kilograms would represent a dose of 3,500 grams-roughly 5,000 grams ascorbic acid. Obviously the work has no relationship with the ingestion of ascorbic acid by humans. I have taken from 10 to 20 grams of ascorbic acid daily since my last visit to this college - 18 years ago. I do not have diabete mellitus and if I might digress a moment, neither have I had a kidney stone.

### ***Diabetes mellitus response to 10 grams ascorbic acid by mouth.***

Over the past 17 years we have studied the effect of 10 grams by mouth, in patients with diabetes mellitus. We found that every diabetic not taking supplemental vitamin C could be classified as having sub-clinical scurvy.

For this reason they find it difficult to heal wounds. The diabetic patient will use the supplemental vitamin C for better utilization of his insulin. It will assist the liver in the metabolism of carbohydrates and to re-instate his body to heal wounds like normal individuals. We found that 60% of all diabetics could be controlled with diet and 10 grams ascorbic acid daily. The other 40% will need much less needle insulin and less oral medication. Contrary to what Medical News Letter, (Vol. 12 # 26, Dec. 25 1970) carried to the physicians the Tes-Tape is accurate in testing urine samples.

***Observations following post-surgery cases on blood plasma levels of ascorbic acid. Deduction is evident of the need for substantial amounts of ascorbic acid prior to surgery.***

In 1960 and again in 1966, in papers delivered before the Tri-State Medical Society, I called attention to the "scurvy" levels of ascorbic acid found in postoperative patients. Plasma levels recorded before starting anesthesia and after cessation of such inhalents and completion of surgery remained unchanged. This has lead many to believe that surgery created little or no demand for supplemental "C". We found, however, that samples of blood taken six hours after surgery showed drops of approximately 1/4 the starting amount and at 12 hours the levels were down to one-half. Samples taken 24 hours later, without added ascorbic acid to fluids, showed levels 3/4 lower than the original samples. Baylor University re-search team reported similar findings in 1965. Bartlett, Jones<sup>48</sup> and others reported that in spite of low levels of plasma ascorbic acid at time of surgery, normal wound healing may be produced by adequate vitamin C therapy during the post-operative period. Lanman and Ingalls<sup>47</sup> showed that the tensile strength of healing wounds is lowered in the presence of "scurvy plasma levels". Schumacher<sup>48</sup> reported that the pre-operative use of as little as 500 mg of vitamin C given orally "was remarkably successful in preventing shock and weakness" following dental extractions. Many other investigators have shown in both laboratory and clinical studies, that optimal primary wound healing is dependent to a large extent upon the vitamin C content of the tissues. In 1949, it was my privilege to assist at an abdominal exploratory laparotomy. A mass of small viscera was found "glued together". The area was so friable that every attempt at separation produced a torn intestine. After repairing some 20 tears the surgeon closed the cavity as a hopeless situation. Two grams ascorbic acid was given by syringe every two hours for 48 hours and then 4 times each day. In 36 hours the patient was walking the halls and in seven days was discharged with normal elimination and no pain. She has outlived her surgeon by many years. We recommend that all patients take 10 grams ascorbic acid each day. Where this is not done and the surgery is elective, then 10 grams by mouth should be given for several weeks prior to surgery. At least 30 grams should be given, daily, in solutions, post-operatively, until oral medication is allowed and tolerated.

***Mononucleosis aided by ascorbic acid.***

After studying hundreds of college students, Yale researchers have evidence that strengthens the like between mononucleosis and EB virus, a herpes-like agent also associated with Burkitt lymphoma. Large doses of intravenous "C" has a striking influence on the course of mononucleosis.

In one patient who was given the last rites of her church, the girl's mother took things into her own hands when the attending physician refused to give ascorbic acid. In each bottle of intravenous fluids she would quickly "tap in" 20 to 30 grams vitamin C. The patient made an uneventful recovery. Her mother has her B.S. in Nursing and has been a long time advocate of massive "C" therapy.

### ***Could ascorbic acid have anti-cancer features?***

Schlegel<sup>50</sup> from Tulane University has been using 1.5 grams ascorbic acid daily to prevent recurrences of cancer of the bladder. He and biochemist Pipkin have been able to demonstrate that in the presence of ascorbic acid, carcinogenic metabolites will not develop in the urine. They suggest that spontaneous tumor formation is the result of faulty tryptophane metabolism while urine is retained in the bladder. Schlegel termed ascorbic acid "An Anticancer Vitamin". Along this line Glick and Hosoda<sup>51</sup> reported on work by Von Numers and Pettersson that the depletion of mast cells from guinea pigs skin was due to ascorbic acid deficiency. The possibilities indicated are that vitamin C is necessary either directly or indirectly for formation of mast cells, or for their maintenance once formed or both. Ascorbic acid will control myelocytic leukemia provided 25 to 30 grams are taken orally each day. One can only speculate on what massive therapy would do in all forms of cancer. Many pathologic conditions are cured by giving 5 million to 100,000 million units of penicillin as an intravenous drip over a period of 4 to 6 weeks. How long must we wait for someone to start continuous ascorbic acid drip for 2 to 3 months, giving 100 to 300 grams each day, for various malignant conditions?

### ***Barbiturate patients in shock normalized with ascorbic acid.***

Clemmesen<sup>52</sup> states that the important principles in management of barbiturate poisoning are anti-shock therapy, continuous oxygen and patent airways. Hadden et al.<sup>53</sup> suggest six measures as supportive treatment. An intensive care unit would be necessary to carry out these functions. All one really need do is give adequate ascorbic acid therapy. One patient who had taken 2640 mg Lotusate (talbutal) was seen in the emergency room with a blood pressure of 60/0. Twelve grams vitamin C was given intravenously with a 50 c.c. syringe and then the needle attached to a bottle of 5D water containing 50 grams ascorbic acid. Within 10 minutes the blood pressure was 100/60 demonstrating the effect of vitamin C on shock. A second bottle of 250 c.c. 5D water containing one gram emivan was started in the other arm. The patient was awake in 3 hours, taking juice with "C" added. She received 125 grams ascorbic acid by vein in 12 hours. Ascorbic acid not only assists with hepatic metabolism but also as a major diuretic flushes these compounds out by way of the kidneys. Nasal oxygen running 6 liters per minute was also employed. Another patient who had masked 2400 mg seconal with paraldehyde was awake after 42 grams of ascorbic acid had been given by vein as fast as a 20 gauge needle could carry the flow. She received 75 grams vitamin C by vein and 30 grams by mouth in a 24 hour period.

### ***Cholesterol not a problem, when daily intake of ascorbic acid is high.***

Mention should be made of the role<sup>54</sup> played by vitamin C as a regulator of the rate at which cholesterol is formed in the body; deficiency of the vitamin speeding the formation of this substance. In experimental work, guinea pigs fed a diet free of ascorbic acid showed a 600 percent acceleration in cholesterol formation in the adrenal glands. Ten grams or more each day and then eat all the eggs you want. That is my schedule and my cholesterol remains normal, Russia has published many articles demonstrating these same benefits.

### ***Lock-law relieved.***

Ascorbic acid has no equal as an adjuvant with other drugs in many conditions. With Tolserol it is curative in the treatment of Lockjaw. Both drugs must be used in proper amounts. In our case 1000 mg Tolserol given intravenously to a boy weighing 20 Kg. was the optimal amount to use. In 48 hours he was given 90 grams ascorbic acid and 3000 mg Tolserol, all intravenously.<sup>55</sup> Jungeblut<sup>56</sup> reported that vitamin C, when added to tetanus toxin "in vitro", brings about inactivation of the toxin. Two cases of Trichinosis was treated and cured using Vitamin C: and Para-Aminobenzoic acid.<sup>57</sup> Although the temperature curve was returned to normal in 36 hours it was found that nine days of treatment was necessary for permanent cures.

### ***Infectious hepatitis relieved.***

Viral hepatitis needs brief mentioning. There are two types: 1) Infectious hepatitis; 2) Needle hepatitis. Physical activity has always been considered to increase the severity and prolong the course of the disease.<sup>58</sup> In Vietnam, Freebern and Repsher showed that pick-and-shovel details had no effects on the 199 controls as against 199 kept at bed rest.<sup>59</sup> One thing is certain. Given massive intravenous ascorbic acid therapy and patients are well and back to work in from 3 to 7 days. In these cases the vitamin is also employed by mouth as follow-up therapy. Dr. Bauer at the University Clinic, Basel, Switzerland, reported that just 10 grams daily, intravenously, proved the best treatment available.

### ***Ascorbic acid therapy applied to various maladies.***

We could continue indefinitely extolling the merits of ascorbic acid. Boyd and Campbell<sup>60</sup> reported excellent results in the healing of corneal ulcers even though their massive doses was 1.5 grams daily. In one case of a corneal burn from the phosphorus off an old time match, the pain was relieved immediately with the intravenous injection of 12 grams vitamin C with a 50 c.c syringe. One gram was prescribed each hour for 50 grams. The cornea was normal in less than 24 hours. One single injection of ascorbic acid calculated at 500 mg per Kg. body weight will reverse heat stroke and one to three injections of the vitamin in a dose range of 400 mg Kg. body weight will effect a dramatic cure in Virus Pancarditis. One gram taken every one to two hours during exposure will prevent sunburn and intravenous injections will quickly relieve the pain and erathema, even the second degree burns when precautions are not taken. One to three injections of 400 mg per Kg. given every eight hours will "dry up" chicken-pox in 24 hours. If nausea is present it will stop the nausea.

These injections are usually given with a syringe in a dilution of one gram to 5 c.c fluid. This concentration will produce immediate thirst. This is prevented by having the patient drink a glass of juice just before giving the injection. Forty grams ascorbic acid by vein and 1000 mg to 2000 mg vitamin B1 intramuscularly will neutralize the person intoxicated by alcohol and will save the life if one drinks after using Antibus. 5 per cent ointment using a water soluble base will cure acute fever blisters if applied 10 or more times a day and we have removed several small basal cell epithelionhas with a 30 percent ointment.

Dr. Virno<sup>61</sup> at the eye clinic, University of Rome, Italy, reported very promising results in glaucoma with a dose schedule of 100 mg per Kg. body weight taken after meals and bed hour. He also reported that these large doses have proved to be safe. In arthritis at least 10 grams daily and those taking 15 to 25 grams daily will experience commensurate benefit. Supportive treatment must also be given. Repair of collagenous tissue is dependent of adequate ascorbic acid. Complications of smallpox vaccination are usually handled by adequate oral ascorbic acid. Several times we found it necessary to give the "C" intravenously along with Adenosine. Twenty percent ichthammol used locally with vaccinia necrosum is good psychology. In herpes zoster two grams vitamin C intramuscularly and 50 mg Adenosine 5-Monophosphoric acid, aqueous solution, also intramuscularly every 12 hours. Compound tincture benzoin locally is helpful. In massive "shingles" ascorbic acid should also be given by vein. Always as much by mouth as can be tolerated. Heavy metal intoxication is also resolved with adequate vitamin C therapy.

***General all around benefits uia one to ten grams ascorbic acid per day.***

It has been suggested that ascorbic acid metabolism may be an index of total metabolism and thus serve as a general diagnostic guide. Adults taking at least 10 grams of ascorbic acid daily, and children under ten at least one gram for each year of life will find that the brain will be clearer, the mind more active, the body less wearied and the memory more retentive.

**SUMMARY**

The types of pathology treated with massive doses of ascorbic acid run the entire gamut of medical knowledge. Body needs are so great that so called minimal daily requirements must be ignored. A genetic error is the probable cause for our inability to manufacture ascorbic acid, thus requiring exogenous sources of vitamin C. Simple dye or chemical test are available for checking individual needs. Ascorbic acid destroys virus bodies by taking up the protein coat so that new units cannot be made, by contributing to the break-down of virus nucleic acid with the result of controlled purine metabolism. Its action in dealing with virus pneumonia and virus encephalitis has been outlined. The clinical use of vitamin C in pneumonia has a very sound foundation. In experimental tests monkeys kept on a vitamin C free diet all died of pneumonia while those with adequate diets remained healthy.<sup>62</sup> Many investigators have shown an increased need for ascorbic acid iq this condition.<sup>63,64</sup> Brody in 1953 after studying vitamin C and colds in college students advised that ascorbic acid be given early and often in sufficient amounts. Regnier<sup>65</sup> reporting in review of Allergy found that the larger the dose of ascorbic acid the better were the results. Our findings resulted in a schedule of one gram each hour for 48 hours and then 10 grams each day by mouth. Those under ten at least one gram for each year of life.



## **Virus Encephalitis.**

Virus encephalitis is a deadly syndrome and must be treated heroically with intravenous and/or intramuscular injections of ascorbic acid. We recommend a dose schedule of from 350 mg to 700 mg per Kg. body weight diluted to at least 18 c.c. of 5D water to each gram of "C". In small children, 2 and 3 grams can be given intramuscularly, every 2 hours. An ice cap to the buttock will prevent soreness and induration. Ascorbic acid in amounts under 400 mg per Kg. body weight can be administered intravenously with a syringe in dilutions of 5 c.c. to each one gram provided the ampoule is buffered with sodium bicarbonate with sodium Bisulfite added. As much as 12 grams can be given in this manner with a 50 c.c. syringe. Larger amounts must be diluted with "bottle" dextrose or "saline" solutions and run in by needle drip. This is true because amounts like 20 to 25 grams which can be given with a 100 c.c. syringe can suddenly dehydrate the cerebral cortex so as to produce convulsive movements of the legs. This represents a peculiar syndrome, symptomatic epilepsy, in which the patient is mentally clear and experiences no discomfort except that the lower extremities are in mild convulsion. This epileptiform type seizure will continue for 20 plus minutes and then abruptly stop. Mild pressure on the knees will stop the seizure so long as pressure is maintained. If still within the time limit of the seizure the spasm will re-appear by simply withdrawing the hand pressure. I have seen this in two patients receiving 26 grams intravenously with a 100 c.c. syringe on the second injection. One patient had poliomyelitis, the other malignant measles. Both were adults. I have duplicated this on myself to prove no after effects. Intramuscular injections are always 500 mg to 1 c.c. solution. With continuous intravenous injections of large amounts of ascorbic acid, at least one gram of calcium gluconate must be added to the fluids each day. This is done because we have found that massive doses of ascorbic acid pulls free calcium ions from the vicinity of the platelets or from the calcium-prothrombin complex as the lactone ring of dehydroascorbic acid is opened. The first sign of calcium ion loss is "nose bleeding". This differs from the nosebleed found, at times, in cases of chicken pox or measles. Here it represents frank scurvy from vitamin C deficiency. The pathology being "Capillary fragility".<sup>66</sup>

## **Burns.**

A new treatment for burns has been outlined, which if followed will eliminate skin grafting and plastic surgery. It is probably too simple to gain early acceptance. The literature has been suggesting the value of ascorbic acid in burns for many years. Proper local application and the amount for systemic usage has been misleading. One only need see one case properly treated with ascorbic acid to appreciate its importance. If ascorbic acid can destroy the exotoxin of tetanus, as Jungeblut demonstrated, it can also destroy the exotoxin of Pseudomonas. Ascorbic acid plays an important role in maintaining fluid balance in the body. Ruskin pointed out that the vitamin activates an enzyme arginase, which breaks down the amino acid arginine, resulting in production of urea which is one key to tissue fluid balance.

### ***Pregnancy.***

The simple stress of pregnancy demands supplemental vitamin C. This amount will vary with the individual. The silver nitrate-urine test will simplify these findings. Vitamin C seems especially concerned with mesenchymal tissue. When one considers the demands of the fetus and infant, especially premature babies, it is obvious that high vitamin C intakes are required during pregnancy because this "parasite" will drain available "C" from the mother. Greenblatt<sup>68</sup> reports excellent results following the oral administration of vitamin C in the therapy of habitual abortion. In my own practice I was able to take women who had had as many as five abortions without a successful pregnancy and carry them through two and three uneventful pregnancies with the use of supplemental vitamin C. The German literature is "stacked" with articles recommending high doses of vitamin C during gestation because they believe that this substance is of great benefit in influencing the health of the mother and in preventing infections. The vital contribution of ascorbic acid to the body tissues can be summed up in the formation and maintenance of normal intercellular material, especially in the connective tissue, bones, teeth, and blood vessels. Genetic errors might be prevented if prospective mothers were advised to take 10 or more grams of ascorbic acid daily. It is significant that we found in the simple stress of pregnancy, a normal physiological process, that equivalent requirements paralleled those found in the rat when under stress. Experiments by King et al.<sup>68</sup> have shown that the need for supplemental vitamin C begins with the embryo.

### ***Kidney Stones.***

The "scare" factor of large doses of ascorbic vs, kidney stones has been laid to rest. Since the urine is usually pH6, one can see that the opening of the lactone ring is a slow process. This reaction takes place in tissues and is probably regulated by the amount of glutathione present. The important considerations are that one must have a concentrated urine, that stasis must be a factor and that the urine must be alkaline for any appreciable amounts of the crystalloids to precipitate out. This will never occur with massive ascorbic acid therapy. Furthermore, it has been shown that the controls in a given experiment had almost as much oxalic acid spill as did those volunteers taking 9 grams of ascorbic acid daily.

### ***Insect - Snake Bites.***

The quickness of results in snake bite, spider bite, hornet stings and caterpillar reactions demonstrates the usefulness in saving lives. It is best to give the vitamin intravenously with a syringe since bottle preparations are too time consuming. One precaution must be given. There exist a 2 gram ascorbic acid ampule, and ironically it is the only one to my knowledge approved by the Food and Drug Administration, which might "kill" if used undiluted in a syringe. This lethal factor is due to the preservatives added. Each ampule contains 2 grams sodium ascorbate. Vehicle contains: Monothioglycerol 0.14%; Sodium Formaldehyde Sulfoxylate 0.05%; Methyl Paraben 0.13%; Propyl Paraben 0.015%. Neutralized to pH6 with Sodium Bicarbonate; Water for injection q.s. This ampoule can be used intravenously ONLY when diluted to at least 25 c.c. to one gram.

One sometimes will be confronted with extraordinary allergic and shock symptoms along with acute respiratory obstruction. In these situation one must employ Benadryl intravenously and/or intramuscularly and an adrenocortical hormone such as Decadron. These can be given by a nurse while the ascorbic acid is being prepared. In their absence a second "syringe" dose of ascorbic acid will suffice. Fluids by mouth should be given to prevent or correct thirst which all patients seem to experience.

### ***Diabetes***

Large doses of ascorbic acid do not cause diabetes mellitus in humans as has been suggested. On the contrary 10 grams daily, by mouth, has proved to be beneficial. The fact that 10 grams will allow them to heal wounds like normal individuals will save many legs in the future. Lamden, a bio-chemist, instigated these fears by misinterpretation of the results reported by Patterson using the Ketone formula intravenously in rats.

### ***In Surgery.***

In surgery the use of ascorbic acid resolves itself into a "must" situation. The 24 hour frank scurvy levels should be sufficient evidence to encourage all surgeons to use vitamin C freely in their fluids. Proper employment of vitamin C by the surgeons will all but eliminate the post-surgery deaths.

### ***In Malignancy.***

The part very large doses of ascorbic acid given intravenously over a prolonged period offers a medical challenge. From cabbage and tomatoes grown in the carbon-14 chambers radioactive ascorbic acid can be extracted, which can be used in tracer studies. At least one re-search team has demonstrated that in cancer all available "C" is mobilized at the site of the malignancy. Lauber and Rosenfeld reported that "C" is mobilized from the tissues of the body and selectively concentrated in traumatized areas. In one hopeless case we administered 17 grams daily for 92 consecutive days without changing the blood or urine levels from that associated with scurvy. This is the reason we believe a dose range of 100 grams to 300 grams daily by continuous intravenous drip for a period of several months might prove surprisingly profitable. Blood chemistry should be followed daily with such an investigation. Schlegel found that even a dose of 1.5 grams a day, by mouth, would prevent bladder cancer.

### ***Barbiturate Poisoning.***

Our findings in no less than 15 cases of barbiturate poisoning suggested that no death should occur from this error in judgment. We also observed the dramatic effect of 12 grams intravenously on blood pressure associated with shock. The shock seen in heat stroke had been corrected by the time the injection was completed. The dose range used was 500 mg per Kg body weight.

### ***Tetanus - Trichinosis***

The use of ascorbic acid with Tolserol in the treatment of Tetanus should be accepted as universal treatment. Here again the dose must be proper. Our case as reported will serve as a guide in making these calculations. Ascorbic acid along with Para-Aminobenzoic acid is curative in Trichinosis. Both drugs are administered by mouth. It is estimated that at least 5 million cases of chronic Trichinosis exists in the United States. Just nine days of treatment would return these individuals to normal. In our cases 10 grams ascorbic acid was given daily and Para-Aminobenzoic acid was employed in high range. Four to six grams to start then three grams every 2 hours for eight times. For the remainder of the nine day schedule it was given 3 grams every two hours during the day and every three hours during the night.

### ***Viral Hepatitis.***

Ascorbic acid is the drug of choice in viral hepatitis. The dose used ranges from 400 mg to 600 mg per Kg body weight, depending on the severity of the disease. It should be given every 8 to 12 hours. Ten grams ascorbic acid daily in divided doses is also given by mouth. Those under 10 years the usual schedule of at least one gram for each year of life.

### ***Multiple Uses.***

We have reviewed many other pathological conditions in which ascorbic acid plays an important part in recovery. To these might be added Cardiovascular Diseases, Hypermenorrhea, Peptic and Duodenal Ulcers, Post-operative and Radiation Sickness, Rheumatic Fever, Scarlet Fever, Poliomyelitis, Acute and Chronic Pancreatitis, Tularemia, Whooping Cough and Tuberculosis. In one case of scarlet fever in which Penicillin and the Sulfa drugs were showing no improvement, fifty grams ascorbic acid given intravenously resulted in a dramatic drop in the fever curve to normal. Here the action of ascorbic acid was not only direct but also as a synergist. A similar situation was observed in a case of lobar pneumonia. In another case of purperal sepsis following a criminal abortion the initial dose of ascorbic acid was 1200 mg per Kg body weight and two subsequent injections were at the 600 mg level. Along with Penicillin and Sulfadiazine an admission temperature of 105.4°F. was normal in nine hours. The patient made an uneventful recovery. In one spectacular case of Black Widow<sup>69</sup> spider bite in a 3 1/2 year old child, in coma, one gram calcium gluconate and 4 grams of ascorbic acid was administered intravenously when first seen in the office. Four grams ascorbic acid was then given every six hours using a 20 c.c. syringe. She was awake and well in 24 hours. Physical examination showed a comatosed child with a rigid abdomen. The area about the umbilicus was red and indurated, suggesting a strangulated hernia. With a 4 power lense, fang marks were in evidence. Thirty hours after starting the vitamin C therapy the child expelled a large amount of dark clotted blood. There was no other residual. A review of the literature confirmed that this individual has been the only one to survive with such findings; the others were reported at autopsy. Ten grams vitamin C and 200 mg to 400 mg vitamin B-6, by mouth, daily will "shield" one from mosquito bites. Twenty percent will also require 100 m vitamin B-6 intramuscularly each week.

### ***General Nutrition.***

Vitamin C plays a very important role in general nutrition. Deficiency of this substance in sufficient amounts can be a factor in loss of appetite, loss of weight or failure to grow, muscular weakness, anemia and various skin lesions. The relationship between vitamin C and the health of the gums and teeth has long been recognized. Laboratory studies on gum-teeth connective tissue have reaffirmed this relationship.<sup>70</sup> Our son who will be 19 in July has never developed a tooth cavity. Since age 10 he has received at least 10 grams ascorbic acid, daily, by mouth. Before age 10 the amount given was on a sliding scale.

### ***Intra-Venous Application.***

Ascorbic acid must be given by needle to bring about quick reversal of various "insults" to the human body. We have found that doses must range from 350 mg to 1200 mg per Kg body weight. Under 400 mg per Kg of body weight the injection can be made with a syringe provided the vitamin is buffered with sodium bicarbonate with Sodium Bisulfite added. Above 400 mg doses per Kg body weight, and a particular ampoule described in this summary, the vitamin must be diluted to at least 18 c.c. of 5 per cent dextrose in water, saline in water or Ringer's solution. Many times Adenosine 5-Monophosphate, 25 mg in children and 50 to 100 mg in adults, given intramuscularly, is necessary to achieve results. The aqueous solution is more effective for quick results, although Adenosine in Gel can be employed. In debilitated individuals or when the pathology is serious, Desoxycorticosterone Acetate (DCA), aqueous solution, must also be added to the schedule. Usually 2.5 mg for children and 5 mg for adults is the daily intramuscular dose required. Sudden swelling of the feet indicates abnormal sensitivity and the drug must be discontinued.

It must be remembered when using ascorbic acid that experiments on man are the only experiments which can give positive evidence of therapeutic action in man. Likewise, the use of ascorbic acid in human pathology must follow the Law of Mass Action: "In reversible reactions, the extent of chemical change is proportional to the active masses of the interacting substance."

**FRED R. KLENNER, M.D.**

Reidsville, N.C.

### **APPENDIX**

**Case History: Pesticide Poisoning** - Three boys ranging in years from age seven to age 12 were walking along a North Carolina Highway. They were caught in the "spray" of a dusting airplane. The youngest boy had been covered by the other two and so received little exposure. He was seen in the emergency room of the local hospital and sent home. The other two boys had different physicians.

One lad age 12, under our care, was given 10 grams of ascorbic acid with a 50 c.c. syringe every 8 hours. The concentration was one gram for each 5 c.c. diluent. He was returned home on the second hospital day. The third boy received supportive treatment but did not receive ascorbic acid.

His body was something to see. The spray had produced an allergic dermatitis as well as a chemical burn. He died on the 5th hospital day.

**Case History: Nasal Diphtheria**-Three children, living in the same neighborhood, developed nasal diphtheria. All three children had different physicians. A little girl under our care was given 10 grams ascorbic acid, intravenously, with a 50 c.c. syringe every 8 hours for the first 24 hours and then every 12 hours for two times. She was then put on one gram ascorbic acid every two hours by mouth. She lived and is now a graduate nurse. The other children did not receive ascorbic acid and both died. Our young patient also received 40,000 units diphtheria antitoxin which was given intraperitoneal. The other children also were administered the antitoxin.

**Case History: Poliomyelitis**-Although we were able to cure many cases of polio with massive doses of ascorbic acid, one single instance demonstrates the value of vitamin C. Two brothers were sick with poliomyelitis. These two boys were given 10 and 12 grams of ascorbic acid, according to weight, intravenously with a 50 c.c. syringe, every eight hours for 4 times and then every 12 hours for 4 times. They also were given one gram every two hours by mouth around the clock. They made complete recovery and both were athletic stars in high school and college. A third child, a neighbor, under the care of another physician received no ascorbic acid. This child also lived. The young lady is still wearing braces.

**Case History: Acute Virus Infection representing Deadly Virus Syndrome.** Cases with paralysis are extremely interesting in as much as they challenge diagnostic prowess. One of our cases, a female age 58, demonstrated three different types. She entered the hospital because of a convulsive seizure. She had had a lingering cold for ten days. She experienced three additional convulsive seizures after hospital admission. The temperature was 100.8°F. pulse 140, respirations 32. She was extremely restless. Twenty-four grams ascorbic acid in 360 c.c. 5D water was given intravenously for three times at 8 hour intervals. One gram calcium gluconate was added to the first and third bottle. Twenty four hours following admission and 72 grams ascorbic acid in the blood stream, patient was awake and rational but completely paralyzed, right arm and leg. Five grams ascorbic acid was given in fruit juice every 6 hours by mouth and 6 grams ascorbic acid along with a B complex preparation was given intravenously, daily for eight additional days. The right arm and leg returned to normal 48 hours after admission. Classical pellagra was also corrected during this hospital stay.

**Case History: Repeating virus infection**-This case proved that adequate ascorbic acid therapy must be continued long enough to destroy all virus bodies, otherwise the infection will recur. In 1960, I treated a seven year old boy, off and on, over a period of six weeks, for influenza like symptoms.

Therapy included one of the mold derived drugs, sulfadiazine and 5 to 10 grams ascorbic acid by mouth. On three different occasions this treatment schedule was dramatically effective. When the child became ill for the fourth time, the administration of the above antibiotics and oral vitamin C had no reversing effect. On the third day of this illness the child suddenly became lethargic and just as suddenly to frank stupor.

The temperature which had been running low grade was now 102.6°F. At this point all oral medication was discontinued. I immediately gave six grams of ascorbic acid intravenously with a 30 c.c. syringe. He was awake and asking, "what happened" in 5 minutes. Six grams ascorbic acid was given in 4 hours and then at 6 hour intervals for two additional doses. The recovery was complete in 24 hours and remained so. Ascorbic acid was again started by mouth giving 5 grams in juice every 8 hours. After one week, this was reduced to the usual daily "take" of seven grams. I had ample opportunity to observe this case--the child was our son.

**Case History: Snake bite**-Child of 4 years was struck on the lower leg by a large highland moccasin at 7:00 P.M., while at play in the yard of her country home. Seen in the emergency room of the local hospital at 7:30 P.M., the child was vomiting, was crying because of severe pain in her leg, which she held with both hands above the "fang marks". Fever was 99.0°F. Four grams of ascorbic acid was given intravenously at 7:35 P.M. with a 20 c.c. syringe. The following 25 minutes were taken to follow a skin test on anti-venom. At this time and before the anti-venom was administered the child had stopped vomiting, she had stopped crying and was sitting on the emergency room table, laughing and drinking a glass of orange juice. She commented: "Come on, Daddy, I'm all right now, let's go home." She was allowed to return home with the understanding that her father would give me a report, by phone, each hour during the night. This he did. His report, each time, was that the child was sleeping as usual and that except for moderate swelling to the "calf of the leg", appeared normal. Seen in the office at 10:00 A.M. the following morning she still demonstrated the small amount of swelling of her leg and had 1/2 degree fever. She was given a second dose of 4 grams of ascorbic acid intravenously. Seen at 5 P.M. she had no fever but the swelling remained constant. There was no pain. The following day, 38 hours after being bitten, she was completely normal. Since this was our first case of snake bite treated with vitamin C, we elected to give an additional 4 grams of ascorbic acid on this visit. No other antibiotics were given and none was required. Since she had had a booster injection of tetanus toxoid in recent months, none was given at this time. Comparing this to an earlier case of snake bite in a 16 year old girl, struck by a moccasin of about the same size, as gauged from the fang marks, on the hand while pulling tobacco plants, and who was hospitalized for three weeks. She was given 3 doses of anti-venom. The arm was compressed continuously with magnesium sulfate solution. Swelling was four times that of the opposite arm and striae developed over the entire surface. This patient received no vitamin C other than that found in a regular hospital diet. Morphine was required to control pain. (We no longer use anti-venom.)

**Case History: An Insidious virus**-This was a child of 18 months. She was seen in the driveway to my home at about 7:00 P.M. The history was brief. The child had strangled on food while eating supper. A cursory examination given in the front seat of an automobile revealed an extremely restless, whining child.

The temperature was 98.6°F. (axillary 10 minutes-corrected). There was no obstruction to the air-ways. We did elicit the information, that the child had had a cold for several days. We also learned that the child's mother had taken her for a long stroller ride the previous day--which in this area was damp and cold. Frankly the impulse to send the child home was great.

Remembering that I had seen children dead within 30 minutes to two hours after hospital admission without treatment, I decided to buy some time. The Uncle was asked to take the child to the emergency room of the local hospital. The nurse on duty was given an order to take a rectal temperature and then give a fleets enema. If the results proved unsatisfactory, she was to repeat the procedure in 30 minutes using a normal saline solution. Approximately 45 minutes after leaving my home, the intern on duty reported by phone, that the child was unconscious to a point where she responded only to pain stimuli. The enema had not been given. Going at once to the hospital, conditions were found as described. The little patient was lying motionless on the examining table. Using a suitable size rectal tube I gave the enema with good results. The stool was normal. Rectal temperature taken at the hospital was 98.4°F. (corrected). The pulse rate was 152 per minute and respirations were 32 per minute. It was impossible to visualize the throat because the mouth was "locked" as one finds after stimulation in lockjaw. Our impression was that the virus had now entered the brain. Thirty grams of ascorbic acid, in divided doses, was given intramuscularly over a period of 36 hours. Crystalline penicillin was started on the second day and 300,000 units were administered in divided doses over the next three days. This was added to block secondary invaders. One hour following admission we applied a 4 x 4 gauze, saturated with tap water, to the child's lips. The sucking reflex was still intact, but the child immediately strangled. Turning the child head down, the small amount of water ran from its nostrils. Now it was clear. It was this "bulbar phenomenon" that was at play when the child was eating supper. The nursing log showed the temperature to be 99.0°F. (corrected) 1 1/2 hours after admission and 1 1/2 hours later it was recorded at 100.0°F. (corrected). The nursing log at this time read: "Shows no sign of consciousness." Temperature was 101.2°F. four hours after admission and was 102.4°F. (corrected) after six hours. Now the nursing log read: "Baby swallowed water without difficulty." At this point the temperature curve started back down and by 7:00 A.M. (11 hours following admission) the child was alert and taking water freely from a spoon. Twenty eight hours after the first injection of ascorbic acid the temperature was normal. Water, milk and orange juice were now taken from a bottle. Cecon (liquid vitamin C) was given by mouth. Discharge was on the 5th hospital day. The initial low fever recording indicated that the child was dying; after ascorbic acid therapy she began to respond, thus the fever. After the virus was killed, the temperature returned to normal.

Case History: Monoxide Poisoning-State highway employee carried into my office in unconscious condition. He was a known diabetic. The breathing was not Kussmaul type and his skin was warm and dry. We elicited the information that he had been found in the cab of his truck with the windows closed and the engine running. It was a cold Winter day. Entertaining a diagnosis of Monoxide intoxication we immediately gave 12 grams ascorbic acid with a 50 c.c. syringe using a 20 gauge needle. (We employ a 20 G. needle when using a 50 c.c. syringe; 21 G needle for a 30 c.c. syringe; 22 G needle for a 20 c.c. syringe and a 23 G needle for a 10 c.c. syringe.



This assists in controlling the rate of flow which is important, especially, in young children). Within 10 minutes the patient was awake, sitting up on the edge of the examining table, rubbing his eyes and saying: "Doc, what in the world am I doing up here in your office." He returned to his place of employment within 45 minutes.

**Case History #1: Acute Virus Pancarditis**-A five year old boy was admitted to the local hospital with history of having a "re-lapse" after recovery from measles. The physical findings showed a thready and feeble pulse. A distinct rub was in evidence by auscultation. The EKG showed RS-T deviations. The temperature was 105°F. Ascorbic acid calculated at 400 mg per Kg body weight was given intravenously with a syringe. Within two hours the picture had almost reverted to normal. Injection of Vitamin C was repeated in 6 hours and again at 12 hours. A fourth injection was given after 24 hours although the patient was clinically well. The child returned home on the 4th hospital day.

**Case History #2: Acute Virus Pancarditis** following a deep cold. The findings approximated those of case #1. The parents elected to take the child to Duke Medical Center. Six grams of ascorbic acid was given by needle before starting the trip to the hospital which was 60 miles away. Upon arrival at the Medical Center the child had made such dramatic response to the single injection of ascorbic acid that the parents were tempted to return home. The receiving physician questioned the sickness of the child as being out of proportion to that relayed by me during our telephone conversation. The parents assured the physician that the child had been seriously ill, but that the change came about after receiving the ascorbic acid. Although 50 grams (25 ampoules) of ascorbic acid was sent along with the parents, none was given because the physician in charge stated that he would be afraid to give that size dose, intravenously, to a child. The fact that we had administered six grams, which represented a dose of 400 mg per Kg body weight, apparently had no influence. Laboratory findings, however, confirmed our impression and the child was hospitalized for two weeks. Two additional injections of vitamin C would have cured the child in 24 hours.

**Case History: Acute Pancreatitis**-Adult Male seen in the emergency room of local hospital complaining of severe, agonizing pain in the epigastrium which radiated to the back. Nausea and vomiting were present. Serum amylase studies showed a concentration of 345. This was the 4th such attack experienced by this patient. Sixty grams ascorbic acid in 700 c.c. Dextrose in water was given intravenously. 20 mg Pantapone was given in the emergency room. No additional opiates were required. The patient made an uneventful recovery. He was placed on 10 grams ascorbic acid by mouth and has not had a recurrence in almost 5 years. He has, however, developed mild diabetes mellitus which is now controlled with diet and vitamin C.

**END**

I am in full agreement with Lancelot Hogben who said: "A scientific idea must live dangerously or die of inanition. Science thrives on daring generalizations. There is nothing particularly scientific about excessive caution. Cautious explorers do not cross the Atlantic of truth.

**Frederick R. Klenner, M.D., F.C.C.P.**

**Reidsville, North Carolina**

*A native of Pennsylvania, Dr. Klenner attended St. Vincent and St. Francis College, where he received his B.S. and M.S. degrees in biology. He graduated magna cum lauda and was awarded a teaching fellowship there. He was also awarded the college medal for scholastic philosophy. There followed another teaching fellowship in chemistry at Catholic University, Where he pursued studies for a doctorate in physiology.*

*Dr. Klenner then 'migrated' to North Carolina and Duke University to continue his studies. He arrived in time to use his knowledge in physiology and chemistry to free the nervous system of the frog for a symposium by immersing the animal in 10% nitric acid. Taken in tow by Dr. Pearse, chairman of the department, he was finally persuaded to enter the school of medicine. He completed his studies at Duke University and received his medical degree in 1936.*

*Dr. Klenner served three years in post graduate hospital training before embarking on a private practice in medicine. Although specializing in diseases of the chest, he continued to do general practice because of the opportunities it afforded for observations in medicine. His patients were as enthusiastic as he in playing guinea pigs to study the action of ascorbic acid. The first massive doses of ascorbic acid he gave to himself. Each time something new appeared on the horizon he took the same amount of ascorbic acid to study its effects so as to come up with the answers.*

*"Dr. Klenner's list of honors and professional society affiliations is tremendous. He is listed in a flock of various "Who's Who" registers. He has published many scientific papers throughout his scientific career.*

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