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Vitamin C, Scurvy in Oral Medicine: A Review of Biochemistry Clinical insights, Case Reports and Advisories

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Abstract

Vitamin C as a water-soluble Vitamin, is an essential dietary requirement for human health, Avitaminosis-C results in scurvy which causes capillary fragility manifesting clinically as bruising, joint, musculoskeletal pain, oro-dental breakdown and compromised immunity.

Aim: Presented here is an overview of Vit-C physiology, listing clinical symptoms, and indicates sources of Vit-C in a North American Diet. Directions for successful dosages of Vit-C to optimize therapeutic benefit are discussed. A sound rationale with relevant clinical safe use of Vit-C is provided.

Conclusion: Vit-C stores in human physiology can be depleted and scurvy results. Fruits and vegetables are the main source of Vit-C and should be consumed regularly to avoid scurvy.

Keywords

Acid; Capillary-fragility; Collagen; Cancer; Gingivitis; Immunity; Scurvy; Vit-C

Abbreviations

Vit-C = Vitamin-C; DHCW =Dental Health Care Workers; FF&V = Fresh Fruit and Vegetables; MHCW =Medical Health Care Workers; RDA = Recommended Daily Allowances; GIT = Gastro Intestinal Tract

Introduction

Vitamin C was known as an anti-scurvy factor for centuries. Sailors who were at sea for months were notorious for developing scurvy, and scurvy prevention was procured by eating citrus. Vitamin-C was first chemically produced in 1933. Vitamin-C as a water-soluble vitamin, is known as ascorbic acid and ascorbate, and is active as L-ascorbate. Most animals, like dogs, are capable of synthesizing their own Vit-C. Anthropoid apes, including humans, some rodents, most fish and fruit-eating bats, all must obtain Vit-C from exogenous dietary sources as the gene(s) for its' enzyme is lacking in these organisms. Clinical presentations of Scurvy in the 20th Century had become rare, but is again manifesting in select communities due to ignorance, socio-economic factors and changes driven by industrialization to consumption of traditional foods. This includes The United States of America, as well as regions in Canada [1,2,3]. Although the chemistry of Vit-C is well known, as are the symptoms of scurvy and its cure, appraisals with readily available information for Medical Health Care Workers (MHCW), specifically Dental Health care Workers (DCHW), are rare and clinically targeted articles on this topic in the current 21st century are scant.

Aim: Presented here is an overview of Vit-C biochemistry, physiology, and metabolism, with emphasis listing clinical signs and symptoms with examples of Scurvy, as well a therapeutic dosing, while indicating reliable sources of Vit-C in a health-promoting diet. Recommended Daily Allowances (RDA) and directions for successful prescription dosages of Vit-C to optimize treatment and prophylaxis are discussed. A sound rationale with relevant clinically safe use of Vit-C is indicated.

Vit-C Biochemistry, Physiology and Metabolism

The biochemistry of Vit-C in plants

The biochemistry of Vit-C in plants

Vit-C Biochemistry, Physiology and Metabolism/ The biochemistry of Vit-C in plants Biochemistry of sugars, like glucose, transforms with enzymes to Vit-C, as ascorbic acid. Mankind, apes and some animals, do not have the genes and consequent enzymes, to synthesize Vit-C [4,5,6].

Physiology and Metabolism

Vit-C is an essential metabolic requirement for the growth and repair of tissues; it is a prime component in forming collagen, and the enzymatic synthesis of neurotransmission catecholamines and tyrosine to DOPA. Consequently, every tissue and organ that has a cytostructural reliant of a collagen matrix can be affected by inadequate Vit-C. All blood vessels, especially capillaries sustain their integrity with replenishment of collagen and reticulin fibers. Micro-trauma to bulging areas of limbs or organs will allow easy rupture of the capillaries with hematoma formation. Figures 1-A, 1-B. Deficient formation of collagen

induces weakening with a physical malfunction, and a combination of these properties facilitates periodontal breakdown with consequent loosening and loss of teeth. Humans do store small amounts of Vit-C in the adrenal glands, which store can be depleted without regular replacement. Vit-C is involved in the formation of steroids (Glucocorticoids, Mineralocorticoids and Sex Hormones) and Vit-C is intrinsic to the functioning of enzymes for the immune system to function. Vit-C functions as an antioxidant and consequently is important in all leucocyte enzymatic activity. Vit-C facilitates the growth of intercellular substances, changes Proline to Hydroxy-proline, Lysine to Hydroxy-lysine (in muscle), Folic acid to active folic acid, and is intrinsic to most microsomal metabolism of many drugs. Vit-C is important in sustaining immunity for optimal function and this has been claimed to be an optimizing factor in therapy for cancer [7].

Aetiology of Scurvy

Scurvy develops in individuals who are deprived of Vit-C intake. Adult scurvy takes a month or two for symptoms to manifest as reserves of Vit-C become depleted. Scurvy develops more rapidly in infants who are fed Vit-C deficient milk or formulae. Childhood Scurvy is labeled Barlow or Cheadle disease for non-breast-fed babies. Cow's milk is notorious for its' high protein, low glucose and absent Vit-C content. Human breast-milk is best, with over 200 defined factors needed for babies to thrive. Accordingly, when children have to be fed cow's milk, the cows-milk should be diluted by half, have about one teaspoonful of glucose per pint of milk (or sugar as second choice if necessary), and extra Vit-C supplement added. The addition of Vit-C is vital. This is not ideal but often resorted to when mothers don't produce lactation, or if proper infant-formula is not available, and starvation is to be eschewed. Poor diets relying on cheap processed foods often contribute to avitaminosis-C and scurvy may be part of general malnutrition. Alcohol consumption, smoking tobacco or marijuana makes extra demands on Vit-C usage and often contributes to scurvy developing. The cost, access to, and/or availability of foods with Vit-C are all confounding factors contributing to the prevalence of scurvy developing in 21st century living. Vit-C sources, minimum requirements and RDA's and doses needed are enumerated below [6,7,1,20].

Clinical Manifestations of Scurvy

Babies show cachexia, pallor, have fetid breath, bacterially coated tongue, swollen gums, peri-labial bleeding, sub-periosteal haemorrhages, defective collagen formation, capillary fragility, sub-ungual hematomata, skin bruises, and infections. Of major importance to DMHCW's is Adult Scurvy, because it affects the gums and threatens survival of the whole dentition. There is some confusion between infective periodontal disease and scurvy. Both are associated with gingival bleeding but are different conditions and demand different therapy and management [8-10]. Also, a whole group of conditions known as Haemorrhagic Diatheses should be born in mind when encountering spontaneous bleeding in the mouth [12]. Hereditary bleeding disorders occur due to the absence or deficiency of specific clotting proteins. The commonest three inherited bleeding diatheses are: von Willebrand disease, hemophilia from factor VIII deficiency, hemophilia from factor IX deficiency. Differential diagnosis may include other haemorrhagic diatheses [12]. An accurate diagnosis is essential to ensure successful therapy. Scurvy will allow for rapid progressive destruction of the periodontally affected teeth, often resulting in bleeding with eventual tooth loss. But periodontal disease developing after a Herpes infection, is not the result of

avitaminosis Vit-C, but rather to Immunosuppression combined with stagnant invasive oral biofilm ecosystems.⁸⁻¹⁰ In Scurvy oral manifestations derives from capillary fragility that allows spontaneous gingival bleeding and swelling with scurvy, and presents with oral malodor, marked lymphadenopathy, and other signs of hematmata on the body (Figures 1-A, 1-B).



Figure 1-A:

Figure 1-B:

Figure 1-A: Oral Presentation of Scurvy in a 30-year-old male, who was a cadet in training, and for months traded his daily fresh fruit portion, for tradable cigarettes; this shows his teeth and gums. There is spontaneous bleeding, swollen gums and fetid oral malodor. Figure 1-B The same case as in Figure 1-A, after one week, treated with one gram a day of Vit-C. The bleeding has stopped.

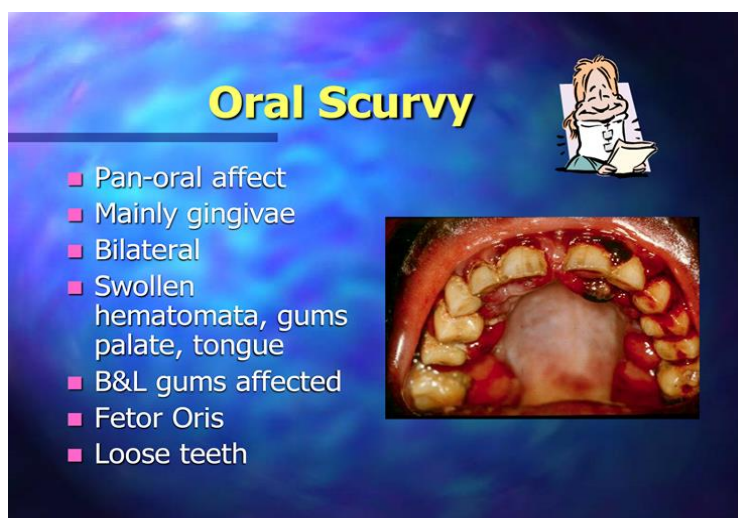


Figure 2: Oral Scurvy: Vitamin-C deficiency cannot logically be deemed the same as chronic periodontitis.

Vitamin-C is an integral part of Blood vessel walls.

Histology of Scorbutic gingiva, shows very thin vascular lining epithelium with reduced media and connective tissue. Minor trauma allows the sub-epithelial extravasation of red blood cells into adjacent connective tissues (Figures 3-A, 3-B).

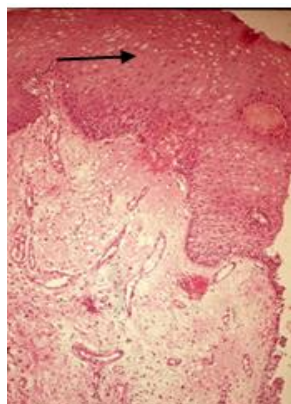


Figure 3A

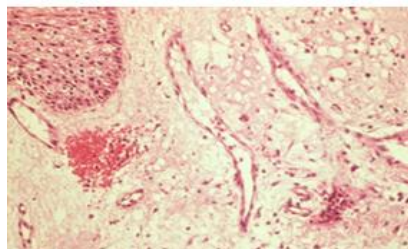


Figure 3B

Figure 3-A: Histology of Scorbutic gingiva, showing the epithelium and connective tissue. The epithelium is at the top (arrow) with the underlying connective tissue below. H & E X 20

Figure 3-B: Note the sub-epithelial extravasation of red blood cells going into the basal layer of the epithelium. This shows delicate, thin vascular capillaries and escaped red blood cells into the Connective tissue. H&E X 40

When a scorbutic patient presents, there is general malaise and lack of energy. Because scurvy was prevalent among sailors of yore, it became known as Sea Scurvy or Sailors Scurvy [12]. Patients present with bruising and different stages of skin pigmentation derived from breakdown of blood cells. There may be hemarthrosis with concomitant joint pains, and edema collects independent parts. Should scurvy be suspected, a clinical test for capillary fragility can be done. Figure 4. Blood tests should confirm the diagnosis.

Skin pigment discoloration in a scorbutic person of color, from breakdown of blood in hematomas. Lower leg and ankle oedema from liquid retention in a scorbutic person. Although very rare, Scurvy may be combined with Vit-B deficiency; it is called Alpine scurvy or Pellagra and presents with oedema and skin lesions. Scurvy and Vit-B deficiency results in Pellagra. Skin lesions, oedema, and is often part of general malnutrition.

Capillary Fragility Test

for VitC Deficiency: Hensyl W.R., Oldham J.O. 1983

- Circle 2.5 cm; upperRef: edge 4cm below crease of elbow
- Drawn on inner aspect of fore-arm
- Pressure midway between systolic & diastolic BP is applied above elbow for 15 mins[~100mb/Hg]
- Count of petechiae within circle made

- 10 → normal
- 10-20 → marginal
- >20 abnormal


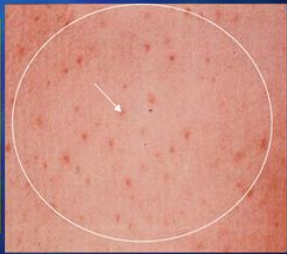



Figure 4: A clinical Capillary Fragility Test. A 2.5mm circle is marked 4cm below the elbow crease.

A blood pressure cuff is inflated midway between systolic (120mb/Hg) and diastolic (80mb/Hg) for 15 minutes. Count the number of petechiae that manifest.

Therapeutic use of Vit-C

Vitamin-C may be administered orally, or by intramuscular, subcutaneous or intravenous injection. The administration of Vit -C by eating natural Vit-C containing foods or by consuming synthetic Vit-C, is the correct and best therapy to cure and prevent Scurvy. By taking Vit-C various health claims are made for risk reduction of viral diseases like the common cold or Covid [11,12,14,]. This may be of some effect with preventing Covid with healthy people. For scurvy 1Gram a day for two weeks will cure the disease, after which a daily intake of 100mg/day should suffice [16,17,18].

Taking large doses (over 1Gram per day) is not considered beneficial and remains controversial. Excess absorbed Vit-C in the blood will be excreted by renal filtration in the urine, but may also undergo oxidative degradation metabolic changes with crystal precipitation. This habit with large doses of Vit-C can form urinary lithiasis of oxalic acid, as well as gastrointestinal discomfort, headaches, insomnia, and blushing of the skin. Consequently, it is not recommended to take large amounts of Vit-C [1].

Vit-C at 100mg./day sustains blood levels at 1.5mg/dl. Excess intake of Vit-C may precipitate renal oxalic acid lithiasis.

RDA and Natural and Dietary Sources of Vit-C

Natural sources of Vit-C in Foods have been listed and are globally well known.¹⁸ These are listed below in (Figure 5) [19,28].

There is a wide range for Recommended Daily Allowances (RDA) between 75mg and 120mg: mean 80mgm/day; The RDA for Vit-C is listed below (Table 2).

The recommended dietary allowance (RDA) for vitamin C is indicated below.

- **Men:** 90 milligrams (mg) per day for men aged 19 and older
- **Women:** 75 mg per day for women aged 19 and older
- **Pregnant women:** 85 mg per day
- **Breastfeeding women:** 120 mg per day
- **Smokers:** Men who smoke need an additional 35 mg per day

Table 2: RDA for Vitamin-C. There is a wide range for Recommended Daily Allowances (RDA) between 75mg and 120mg: mean 80mgm/day.



Figure 5: Fresh Fruit and Vegetables (FF&G) are Common sources of Vit-C [18].

Vit-C is generally available in fresh fruits and Vegetables. Broccoli and Parsley have high concentrations of Vit-C [18]. Rosehips were used during World-War II (1939-1945) in the United Kingdom of Great Britain as a local source for Vit-C.



Figure 6: Canadian sources of Vitamin-C.

In the northern Hemisphere, particularly in North America, huge amounts of fish and meat are consumed. Ptarmigan is a wild fowl, similar to-, but different from-, a chicken. [Vitamin-C Content of Native Foods and Nutrition by Health and Welfare Canada. (1985)]

In the northern Hemisphere, particularly in North America large quantities of fish and meat are consumed. Some of these flesh sources contribute to and are part of a traditional diet that contains some Vit-C, but not nearly as much as found in fresh fruit and vegetables. Cooking may reduce or destroy Vit-C content [26,27]. Other foods, many manufactured for mass consumption and are cheap, are also consumed in large quantities but do not contain Vit-C. Many consumed foods and drink contain no Vit-C. Beer, wine, and alcoholic spirits (Brandy, Vodka, Whisky, Gin, etc) do not contain Vit-C. Wheat, barley, rice semolina and tapioca and derived products do not contain Vit-C [19].

In lower socio-economic communities, fructose and sugar sweetened pop-colas, manufactured snacks and french-fries, are the cheapest, and often the most easily accessed foods for calories. Although pop-colas and chips are an easy source of calories and satisfy immediate hunger, unfortunately, a 'Cola-and-Chips' diet is not a good diet or sources of Vit-C.

Problem with Grapefruit

The name *antiscorbutic* factor was common in the eighteenth and nineteenth centuries for foods that prevent scurvy. These foods included sauerkraut, cabbage, and Citrus fruits. But grapefruit contains furanocoumarins which gives grapefruit it's unique bitter flavor, and furanocoumarin affects GIT absorption. Grapefruit interferes with CYP3A4 enzyme that detoxifies substance and inhibits protein GIT Function. Consequently there is ainterference with the absorption process with drugs resulting in no or markedly reduced effect. To compensate people may increase doses and this may lead to increased

absorption and overdose [17].

Grape-fruit interferes with drug absorption from GIT. Beta Blockers (like Atenelol, Celiprolol, Talinolol), Antibiotics (Ciprofloxacin, Levofloxacin, Itraconazole), anti-neoplastic (Etoposide), Antihistamines (like Fenoxidene) and Cyclosporine; GIT absorption are all attenuated by ingestion of grapefruit [18].

Fresh Fruit Juices as a source of Vit-C

Consumers when purchasing fresh fruits and vegetables (FF&V) demand pristine products. Consequently, these excellent sources of Vit-C have become expensive, and created a challenge for producers as what to do with undersized, bruised, excess or late harvested fruits. These FF&V products are used in other products like jams, cakes, tarts, dried-fruits, dehydrated edibles, and confections, and a huge portion of the FF&V crops are made into juices. Most FF&V contain ascorbic acid as Vit-C, (naturally sourced), but FF&V also contain many other acids. The commonest fruit carboxylic-acids prevalent are Malic (high in apples), Citric (high in Citrus), Tartaric (high in grapes). These acids, with Vit-C contribute to a high acidity and dental erosive effect from manufactured juices. The manufactured Fruit Juices with Vit -C, (natural or added), have a long shelf-life and can easily be transported in bulk. The manufactured acidic drinks also contain fermentable carbohydrates (including glucose, fructose and sucrose) and combined with the stated acidity have been strongly implicated in causing dental abfractions as erosion, abrasion, attrition and decay. Drinking these juices can be reliable a source of Vitamin-C but the frequency, mode of drinking, amount, timing, type and habits of juice consumption can impact dental a health[19-20].

Discussion

Mankind and Anthropoid apes, baboons, and monkeys, and guinea-pigs cannot naturally synthesize Vit-C, but rats, mice and dogs can, and that is why the latter animals are used for biomedical research with Vit-C. Many manufactured foods lose the Vit-C contents through their production process. Yet there are manufactured foods that add Vit-C is added to some manufactured fruit products (like Mott's Fruitsensations) which has a long shelf life (6 months). Vit-C concentrations will decrease in time proportional to the processing and storage temperature. Heat reduces Vit-C content of vegetables 60% by accelerated enzymatic destruction. Prolonged cooking aggravates this effect. Also , because Vit-C is water soluble, the vitamin leaches out into the heated-cooking water, which is filtered off and discarded [24,25]. Industrial farming methods have vastly increased the availability of fresh produce around the world. Yet challenges arising from weather and distances has impacted on times of delivery and added transport costs. In Canada availability of fresh fruits and vegetables as Kg/ per person was significantly reduced from 2013 to 2023, and has been a major influencing factor in allowing scurvy to develop in northern regions of Canada. (79.4 Kg annually per person in 2013 to 71.5 in 2023: source table 32-10-0054-01 Canada Health Statistics Canada) [27,-31].

The Recommended Daily Allowances (RDA) for Vit-C listed above indicates pregnant and breast-feeding women need more Vit-C. Alcoholics, smokers and women taking the contraceptive pill, also have higher requirements of Vit-C than the RDA [27,-31].

Using Vit-C to cure Periodontitis does not work. Periodontitis is now regarded as a chronic disease caused

by an invasive climax oral biofilm, derived from stagnant microbial ecosystems, invading the gingiva and destroying the periodontal ligaments and supporting alveolar bone, in individuals who become predisposed to this infection, (Periodontitis in its chronic or aggressive forms) by weakening their immunity from a Herpes Viral infection [8,9]. Periodontitis demands specialist management-treatment involving strident oral hygiene, sanative root plaining, possible muco-gingival surgery and concomitant chemotherapy with anti-virals, antibiotics, antiseptic mouthwashes, and biofilm moderation with antiseptic mouthwashes.

“Vit-C as a prophylaxis: Prophylaxis may be justified in those exposed to severe physical exercise or cold stress or both. So far, therapeutic supplementation has not been shown to be beneficial” Vit-C as a prophylaxis” [8]. For people predisposed to infections, like diabetics, or those metabolically stressed individuals (malnourished or scorbutic) supplementary Vit-C will improve healing.

Conclusion

Although Scurvy is rare, Oral Health Care Workers should retain a high level of suspicion for scurvy in cases with spontaneous gingival -bleeding.

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