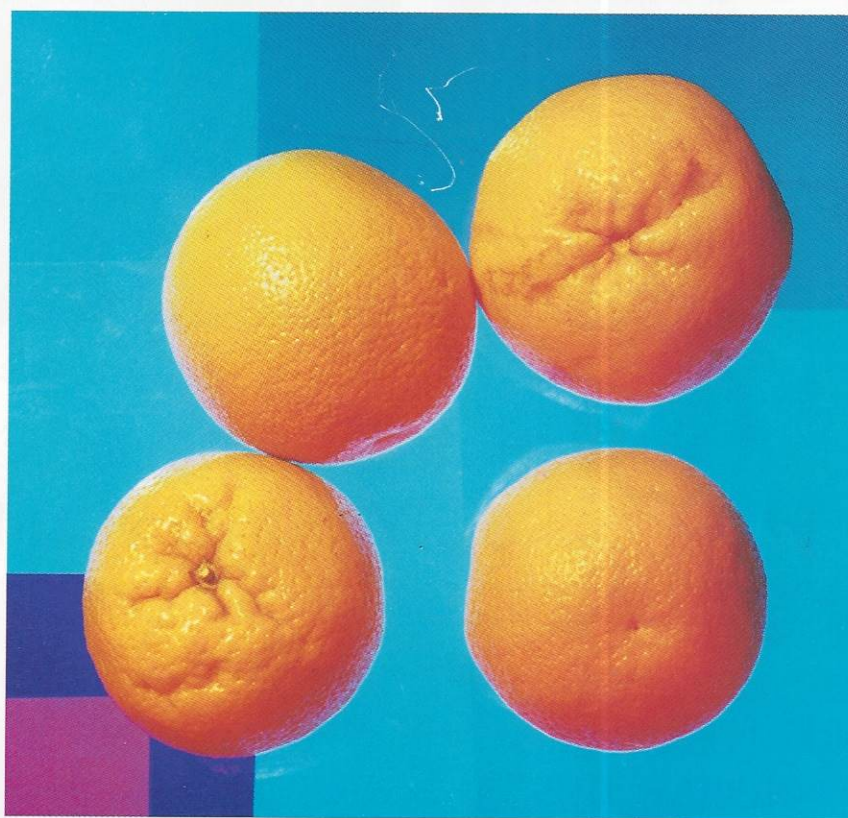


# GENERAL DENTISTRY

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Testing and placebo effect - Page 523



# Vitamin C and dental healing: Testing and placebo effect

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Vitamin C, or ascorbic acid ( $C_6H_8O_6$ ), has been administered for many years as a healing medication. As early as 1939, it was reported that vitamin C supplements enhanced the rapid recovery of surgical patients.<sup>1</sup> In pioneering experimental research, Bourne demonstrated that increased vitamin C intake correlated with infection reduction in hospital patients.<sup>2</sup> Since then, it has been prescribed for treatment of a broad spectrum of biomedical disorders, including the common cold, cancer, cataracts, burns, wounds, and other physical injuries.<sup>3-14</sup>

Use of ascorbic acid remains controversial, possibly because the optimal daily requirement of the vitamin is not well established.<sup>15,16</sup>

A recent review of publications discloses that recommended daily allowances (RDAs) range from 30 to 10,000 mg.<sup>17</sup> Sauberlich estimates that the average adult normally maintains about 1,500 mg of ascorbic acid in the body and that scurvy occurs when the body pool falls below 300 mg.<sup>18</sup> The body pool of vitamin C is esti-

mated as 20 mg/kg, which is maintainable with an intake of 100 to 140 mg/day.

The role of vitamin C supplementation in dental healing is not well defined, despite longstanding recognition of periodontal disease, gingivitis, and other forms of dental inflammation as possible symptoms of vitamin C deficiency.<sup>20-22</sup> One of the reasons for such uncertainty is the lack of standardization and controls in experimental trials of ascorbic acid in dental health research.<sup>23</sup>

As a follow-up to an initial investigation that indicated that vitamin C was effective in promoting rapid recovery and reduced complications from minor oral surgery, the present study was conducted to retest the hypothesis by use of a double-blind vitamin C/placebo experimental design.<sup>24</sup>

## Materials and methods

In an earlier study, vitamin C was administered after surgery to 277 tooth extraction patients, who were compared with 175 control patients who received no vitamin C following the procedure.<sup>24</sup> In this follow-up study, a new sample of 161 consecutive extraction patients who attended the same dental/oral

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## Self-instruction article for Exercise No. 16

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surgery clinic was analyzed to test for a placebo effect.

Before extractions were performed, each subject completed a questionnaire to give details about age, gender, occupation, residence, marital status, medical history, prescription medications, allergies, and smoking habits. Data were compiled for statistical purposes according to two criteria, the Statistical Package of the Social Sciences<sup>25</sup> and the Biomedical Computer program.<sup>26</sup>

The senior author performed all extractions with elevation techniques described by Howe,<sup>27</sup> Killey and Kay,<sup>28</sup> and McGowan.<sup>29</sup> To ensure standardization, the same types of instruments, local anesthetics, sutures, postoperative pain medications, etc., that were used in the previous phase of the research were used in this follow-up study.<sup>24</sup>

Each patient received a printed list of standardized instructions for postsurgical dental care and dietary modification, as is given rou-



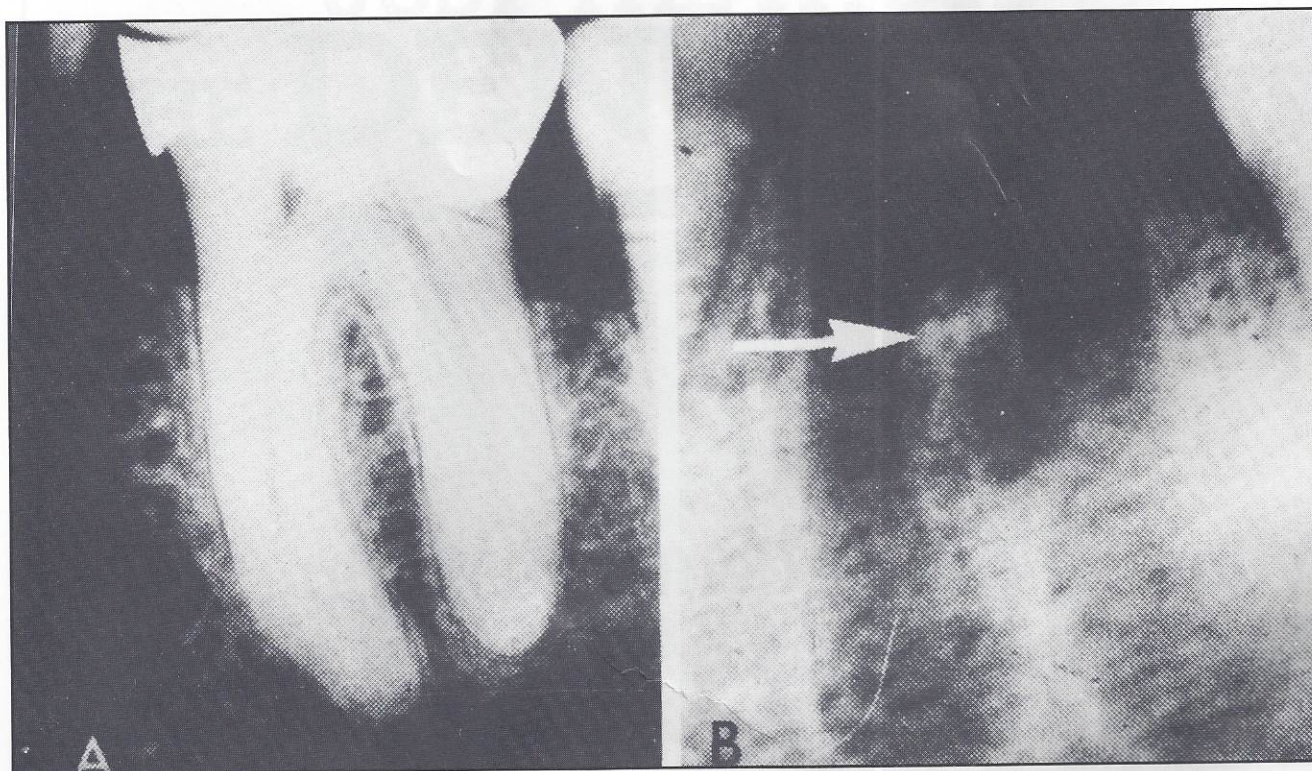


Fig. A case of alveolgia (dry socket). Radiograph of a molar before extraction (A); its socket 1 week postoperatively (B) exhibits ghost imaging and bony osteitis (arrow).

tinely to all clinic extraction patients. A form also was provided for patients to list all food and drink intake during the recovery period.

A 3-week supply of a 1,500 mg/day dose of vitamin C (Mobil Corp., Fairfax, VA), (500 mg t.i.d. with meals) was provided to alternate patients (N = 81) before they left the clinic. The remainder of the sample (N = 80) was given the same number and dose of identically appearing placebos (Schering-Plough Co., Madison, NJ) in a double-blind experimental trial, i.e., neither the patients nor the investigator knew which tablets contained vitamin C. All subjects were telephoned, and tablet counts were recorded during the week following surgery to maximize compliance with the regimens.

All patients returned for suture removal and follow-up evaluation exactly one week after their extraction procedures. Each individual was re-interviewed regarding pain, medication side effects, diet, and other postsurgical as-

pects. The Melzack scale was used to measure the degree of expressed pain.<sup>30</sup>

Healing rates were monitored and scored. Two categories of dental healing were defined, based on criteria suggested by Dubois et al.:<sup>31</sup>

*Type 1: Slow healing*—Expression of pain and request for additional analgesic; edema and purulent material; weak to moderate granulation-bed formation; administration of antibiotic prophylactic (erythromycin or penicillin, or both).

*Type 2: Rapid healing*—No expression of pain, or expression of mild pain with no need for additional analgesic; no edema or other swelling; no clinically evident infection (i.e., no purulent material); complete granulation bed formation; no need for antibiotics or other medications.

The incidence of alveolgia (dry socket), an extremely painful form of faulty postextraction healing, was recorded as an objective measure of recovery complication with use of the same double-blind approach (Fig.).<sup>32</sup>

## Results

The age-gender composition of the present sample (N = 161) is presented in Table 1. The 79 men and 82 women ranged from 10 to 88 years of age; 54 percent were young adults (20 to 39 years old). The following occupations were reported: Salaried labor (office, factory, etc.) 38 percent; professional or self-employed, 20 percent; student, 19 percent; supervisory or managerial, 7 percent; and unemployed (including retirees and housewives), 16 percent. Among respondents, 23 percent had been under the extended care of a physician; 13 percent indicated having allergies to various foods and drugs. About 90 percent of the extracted teeth were molars; of these, the majority were third molars.

Healing progress in relation to vitamin C or placebo administration is shown in Table 2. As in the previous investigation, subjects who used vitamin C healed more rapidly than placebo patients; differences were statistically signifi-



cant at the 0.01 level according to  $\chi^2$  and matched (paired)  $t$ -test values. Four types of  $\chi^2$  (Pearson, continuity correction, likelihood ratio, and Mantel-Haenszel) indicate that the sampling error ( $p = .0002$  to  $.0009$ ) does not cause statistical differences between users of vitamin C and placebos.

Incidence of alveolalgia among users of vitamin C or placebos also is outlined in Table 2. Only 1 (1.2 percent) of the 81 users of vitamin C was found to have dry socket. On the other hand, dry socket was diagnosed among 10 percent of the placebo users.

Variations in healing rate according to gender ( $p = .85$ ), age ( $p = .75$ ), occupation, and marital status are not statistically significant. Table 3 reflects the lack of association between gender and healing progress among subjects. Allergies, prescription medications, and previous medical history also were not correlated with healing progress.

The present data also suggest a lack of association between expression of postoperative pain and use of vitamin C or placebos. Table 4 shows the number of patients who reported mild or severe pain at the follow-up interview one week postoperatively.

Patients' nutrient intake following extractions was analyzed extensively. Ingestion of protein, calories, vitamins (A, B<sub>6</sub>, B<sub>12</sub>, and C), and minerals (magnesium, calcium, iron, zinc, copper, and manganese) was determined and quantified from patient diaries. Three of these dietary components correlated statistically with healing-progress categories: vitamins A, and C, and calcium. Subjects with higher intake values in all components generally healed more rapidly.<sup>33</sup>

Only 17 individuals (10.6 percent) of the total sample indicated that they smoked cigarettes. Statistical analyses of this subgroup, compared to the entire sample, revealed no significant differences in healing. As in the previous investigation, no patients reported the most common side effects

**Table 1. Age-gender composition of the sample**

Age group (years)	Men	Women	Total
10-19	10	8	18
20-29	30	31	61
30-39	13	13	26
40-59	18	20	38
60-89	8	10	18
Total	79	82	161

**Table 2. Healing progress and incidence of alveolalgia (dry socket) among vitamin C and placebo users**

Postoperative medication	% who healed slowly	% who healed rapidly	Incidence of dry socket %
Vitamin C (N = 81)	12.3	87.7	1.2
Placebo (N = 80)	37.5	62.5	10.0
Total (N = 161)	24.8	75.2	5.6

**Table 3. Effect of gender on healing**

	Slow healing	Rapid healing
Men (N = 79)	19 (24%)	60 (76%)
Women (N = 82)	21 (25.5%)	61 (74.5%)

**Table 4. Pain reported**

	% reporting mild pain	% reporting severe pain	% reporting no pain
Vitamin C users (N = 81)	24.7	22.2	53.1
Placebo users (N = 80)	23.7	22.5	53.8

of vitamin C overdose, such as diarrhea and other gastrointestinal disturbances.<sup>34</sup>

## Discussion

The present results, obtained with a double-blind experimental design, correlate with the earlier finding that vitamin C supplementation is potentially effective in promoting rapid recovery and fewer complications following tooth extraction. This finding is especially significant in view of the fact that patients' demographic and clinical characteristics (age, gender, occu-

pation, marital status, health history, etc.) were negligible influencing factors in healing progress in both studies. An important outcome of vitamin C administration is the reduced incidence of alveolalgia, a painful extraction complication caused by improper formation of the granulation bed and subsequent inflammation and possible infection of the open tooth socket.

The lack of statistically significant differences between reports of postoperative pain among vitamin C and placebo users does not



support published evidence that ascorbic acid may act as an analgesic in various parts of the body.<sup>35</sup> On the other hand, placebos have been found to have a curative/therapeutic effect on pain, hypertension, seasickness, migraine, anxiety, depression, dermatitis, and asthma.<sup>36,37</sup>

Recent research suggests that ascorbic acid may enhance dental healing through a combination of different biochemical and physiological mechanisms. A number of investigations, for example, have demonstrated that vitamin C promotes wound repair through construction of scar (connective) tissue.<sup>38,39</sup> Ascorbic acid is a catalyst in the body's synthesis of collagen, a nondietary protein that is the principle constituent of connective tissue.<sup>19,40-42</sup> The role of vitamin C in collagen production and subsequent wound healing is summarized by Rubin: "The major vitamin necessary for wound healing is vitamin C. Collagen synthesis, which closes the wound, cannot take place without this vitamin. Deficiencies in ascorbic acid lead to wounds that fail to heal, fractures that do not repair, and capillaries that become fragile. Collagen not only closes the wound, but also provides tensile strength to the tissue."<sup>38</sup>

Ascorbic acid has a role in the metabolic conversion (hydroxylation) of the amino acids proline and lysine to form hydroxyproline and hydroxylysine. These modified amino acids represent the key structural components of collagen, and account for more than one-third of its composition.<sup>17,39,43</sup> Recent experimental research points to two vitamin C-related mechanisms in this metabolic process: ascorbic acid heightens the activity of hydroxylase, an essential enzyme in collagen biosynthesis, and also causes a two- to threefold increase in collagen-specific RNA levels in human skin cells.<sup>41,44</sup> Once manufacture of collagen molecules and construction of scar tissue begin, additional vitamin C apparently triggers further growth and proliferation of connective

tissue cells (up to four times the normal rate) as well as an increase in extracellular matrix density.<sup>39,45,46</sup>

Another potential advantage is that ancillary vitamin C stimulates the immune system by accelerating formation and increasing antimicrobial activity of antibodies.<sup>7,10,47</sup> Vitamin C supplementation has been credited with elevating white blood cell production and activity, including the antibacterial leukocyte enzymes hexose monophosphate and interferon.<sup>11,13</sup> Ascorbic acid also assists in metabolic conversion of oxygen to superoxide, a substance that impairs bacterial development.<sup>6</sup> According to a recent study, the lymphatic system and lymphocyte functions also are stimulated by extradietary intake of vitamin C.<sup>48</sup>

A number of other biochemical effects of ascorbic acid in the body also might help to improve wound management and recovery. Such effects include increased iron absorption from food, strengthening of blood clots, increased white blood cell diapedesis, and reduced red blood cell hemolysis.<sup>40,47,49</sup> In addition to rapid wound closure, some investigators have proposed a number of other positive results from dental applications of ascorbic acid, including reduced post-operative gingival inflammation and bleeding, antihistamine and detoxification activity, and reduced swelling and edema.<sup>35,50,51</sup> Negative findings also have been reported.<sup>52</sup>

### Summary

The present study augments a growing body of evidence that indicates supplemental vitamin C may be beneficial in speeding healing following tooth extraction and in reducing the likelihood of alveolgia and other complications. No adverse side effects were encountered from administration of vitamin C in our studies or in a recent investigation involving intake of 10 g/day; thus, carefully tested higher dosages ("megadose therapy") might be applied successfully to patients with alveolgia or orthognathic conditions.<sup>8</sup>

Hanck comments on the relative

safety of ascorbic acid in medicine: "The few literature references suggesting adverse effects of ascorbic acid are outnumbered by a large number of clinical studies in which no adverse effects have been observed. Up to 5 g of ascorbic acid daily may be administered safely even over a long term."<sup>53</sup>

Further research is recommended to determine whether vitamin C is of similar value in hastening proper recovery from other oral surgical procedures. Vitamin C is a relatively safe, inexpensive, over-the-counter product that may be more effective in dental healing than previously known.

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