not be used to treat oral leukoplakia in cigarette smokers or heavy alcohol users, and its risk-benefit ratio for patients who do not smoke or drink alcohol remains uncertain. If beta-carotene is used to treat oral leukoplakia, patients should be monitored for progression to malignancy.

Conclusion

The available evidence suggests that vitamin A, lycopene, vitamin E, and selenium can each induce remission in some patients with oral leukoplakia. Using these nutrients in combination might be more effective than using any single nutrient by itself. Although beta-carotene also appears to be effective for some patients, the risks of beta-carotene may outweigh the benefits, particularly in smokers and alcohol drinkers. Preliminary results with black tea are promising, and tea could be included as part of an overall treatment program.

Nutritional therapy is an attractive option for oral leukoplakia, because of its relative lack of adverse effects. However, nutritional therapy appears to be less effective than conventional treatments, and nutritional therapy by itself might be less effective than conventional therapy for preventing progression to oral cancer. In contrast, the combination of nutritional and conventional therapy might produce better results than conventional therapy by itself. It is not clear whether it is safe to administer vitamin A supplements to patients who are receiving vitamin A analogues such as isotretinoin, although there is evidence that treatment with isotretinoin could promote the development of vitamin A deficiency or lead to impaired vitamin A metabolism.[22] Regardless of what treatments patients with oral leukoplakia receive, they should be monitored closely for progression of the lesions.

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261 *Periodontal disease and gingivitis*

Periodontal disease is a chronic bacterial infection that affects the gums (gingivae) and other tissues that support the teeth. If only the gums are involved, it is called gingivitis. The most common type of gingivitis is caused by the accumulation of bacterial plaque, which leads to a chronic inflammatory process. Manifestations of gingivitis may include red, swollen, tender, and bleeding gums; receding gums; pockets separating the gums from the teeth; and bad breath. If gingivitis is not adequately treated, the inflammatory process may spread to the periodontal ligaments and alveolar bone, eventually destroying these structures and causing teeth to loosen and fall out.

Risk factors for periodontal disease include cigarette smoking and poor oral hygiene. Conventional therapy consists primarily of oral hygiene measures (regular tooth brushing, flossing, and dental check-ups). These local measures are frequently, though not universally, successful. In advanced cases, antimicrobial agents, flap surgery to remove plaque below the gum line, or bone and tissue grafts may be recommended.

Dietary factors

The importance of nutrition. Nutritional factors play a role in immune function and tissue integrity, both of which could influence a person's resistance against the microorganisms that cause periodontal disease. The relationship between nutrition and periodontal disease is illustrated by observations regarding "trench mouth" (acute necrotizing ulcerative gingivitis), a common and severe affliction among World War I soldiers that was caused by spirochetes and other microorganisms. This condition was found to be associated almost invariably with signs of pellagra or pre-pellagra (vitamin B_3 deficiency),[1] and improved rapidly after treatment with 250–600 mg/day of niacin.[2] Similarly, monkeys fed a diet marginally deficient in vitamin C developed more severe gingivitis from experimentally induced dental plaque than did animals fed a normal diet.[3]

The decrease in micronutrient intake that results from consumption of refined, processed foods might increase a person's susceptibility to periodontal disease. In addition, localized deficiencies of certain nutrients may develop in periodontal tissues as a result of chronic infection and inflammation, leading to a vicious cycle of worsening disease and more severe deficiencies. Various dietary modifications and nutritional supplements may therefore be useful for preventing and treating periodontal disease.

Refined sugar. Periodontal disease developed in hamsters fed a diet containing 56% sucrose.[4] In a cross-sectional study of 2,437 young adults, high intake of added sugars was associated with an increased prevalence of periodontal disease.[5] In a study of healthy dental students with minimal gingivitis, those assigned to consume large amounts of sucrose (100 or 225 g/day) had a significant worsening of gingivitis after as little as 4 days. In contrast, students assigned to eliminate refined carbohydrates from their diet had a significant improvement in gingivitis.[6] These findings suggest that sucrose consumption contributes to the development of periodontal disease.

Allergy. Since periodontal disease is an inflammatory condition, and since allergic reactions cause inflammation, allergies to foods or other substances might exacerbate periodontal disease in some patients.

In a case report, a 32-year-old man with chronic periodontal disease that had failed to respond to conventional therapy reported that every time he drank milk there was a bad aftertaste and odor. Three weeks after discontinuing milk, the foul taste and odor were gone and gingival bleeding had ceased.[7] While the aftertaste and odor may have been due to lactose intolerance, it is likely that the gingival bleeding was caused by allergic inflammation.

An analysis of 48 toothpastes sold in Finland revealed that nearly half contained one or more compounds widely recognized as allergens. A total of 27 different allergens were identified in these products. Contact with allergens present in toothpaste has been observed to cause gingivitis in some cases.[8]

The frequency with which allergy triggers or exacerbates periodontal disease is not known. However, allergy should be considered as a possible contributing factor to periodontal disease in patients whose clinical history suggests the presence of allergies (chapter 7).

Nutritional supplements

Folic acid. Gingivitis developed in baboons fed a folic acid-deficient diet.[9] In an observational study, the prevalence of gingivitis was increased in women taking oral contraceptives,[10] which are known to promote folate deficiency.

It has been suggested that localized folate deficiency may exist in inflamed gingival tissue despite normal plasma levels, and that this localized deficiency may reduce the resistance of gingival tissue to irritants. Folic acid has also been found to bind to plaque-derived endotoxin, thereby potentially reducing the level of antigenic stimulation and inflammation caused by plaque.[11] In several clinical trials, folic acid supplementation reduced the severity of gingivitis. Folic acid administered as a mouth rinse tended to be more effective than folic acid in tablets. The greater efficacy of the mouth rinse may be due to direct absorption of topically applied folic acid into gingival tissue, as demonstrated by a 6-fold increase in the gingival tissue folate concentration after a single dose (5 ml of a 0.1% solution, swished for 5 minutes).[12]

Thirty dental students and auxiliary personnel (aged 21–32 years) were randomly assigned to receive, in double-blind fashion, 0.1% folic acid mouth rinse or placebo mouth rinse for 60 days. The subjects used 5 ml of the solution twice a day, rinsing for 5 minutes before expectorating. Gingival inflammation, as assessed by the gingival index and bleeding index, was significantly less in the group receiving folic acid than in the placebo group ($p < 0.05$).[13]

Sixty patients with gingivitis were randomly assigned to receive, in double-blind fashion, 0.1% folic acid mouth rinse or placebo mouth rinse for 4 weeks. The patients used 5 ml of the solution twice a day, rinsing for 1 minute before expectorating. Compared with placebo, folic acid resulted in significant improvements in parameters of gingival health (i.e., reductions in the mean number of color change sites and bleeding sites; $p < 0.001$).[11]

Thirty healthy volunteers were randomly assigned to receive, in double-blind fashion, 4 mg/day of folic acid orally or placebo for 30 days. Gingival inflammation decreased significantly in the folic acid group ($p < 0.05$) and worsened slightly in the placebo group.[14]

Thirty women in their eighth month of pregnancy were randomly assigned to receive, in double-blind fashion, placebo mouth rinse and placebo tablets, placebo mouth rinse and folic acid tablets (5 mg/day), or 0.1% folic acid mouth rinse and placebo tablets for 4 weeks. The women used 5 ml of the mouth rinse twice a day, rinsing for 1 minute before expectorating. Compared with placebo, folic acid mouth rinse significantly reduced the severity of gingivitis ($p < 0.001$). Oral folic acid was also more effective than placebo, but the difference was not statistically significant ($p < 0.1$).[15] Similar results were seen in another study in which the respective treatments were administered for 14 days during months 4 and 8 of pregnancy.[16]

Coenzyme Q_{10}. Biochemical evidence of localized coenzyme Q_{10} (CoQ_{10}) deficiency (demonstrated by an enzyme stimulation assay) was found in diseased gingival tissue of patients with periodontal disease, when compared with healthy gingival tissue from the same patients and with gingival tissue from healthy controls.[17–20] While it is not clear whether localized CoQ_{10} deficiency is a cause or a consequence of periodontal disease, such a deficiency could lead to impaired immune function and reduced healing capacity. Oral CoQ_{10} supplementation has been shown to increase CoQ_{10} levels in gingival tissue of patients with periodontal disease.[21] Several clinical trials have shown that CoQ_{10} is an effective treatment for periodontal disease.[21–25]

Seven patients with advanced periodontitis requiring surgical intervention received 50 mg/day of CoQ_{10} for 3 weeks. Disease severity, as measured by the periodontal score, improved significantly. Pocket depth also decreased significantly; such an improvement is said to be uncommon in patients with advanced disease.[21]

Eighteen patients with periodontal disease were randomly assigned to receive, in double-blind fashion, 50 mg/day of CoQ_{10} or placebo for 3 weeks. Outcome measures included pocket depth, purulent exudate, tooth mobility, gingival swelling, bleeding, redness, pain, and itching. Improvement was seen in all 8 patients receiving CoQ_{10} and in 3 of 10 patients receiving placebo ($p < 0.01$).[22]

In a study of 10 men with periodontitis, 30 periodontal pocket sites were randomly assigned (blinding not clear) to topical application of CoQ_{10} (85 mg/ml dispersed in soybean oil) or placebo (soybean oil alone). The solutions were applied with a small syringe once a week for 6 weeks. During the last 3 weeks, root planing and subgingival scaling were performed at all sites. During the first 3 weeks, significant reductions in gingival crevicular fluid flow, probing depth, and attachment loss were found only at sites treated with CoQ_{10}. After mechanical treatment was performed during the second 3 weeks, significant improvements were seen at all sites, regardless of whether CoQ_{10} was administered. However, only CoQ_{10}-treated sites showed significant improvements in the modified gingival index and in bleeding.[23] Thus, topical application of CoQ_{10} improved periodontitis, when administered as sole treatment or in combination with conventional periodontal therapy.

Vitamin C and flavonoids. Vitamin C and flavonoids each contribute to gingival health by promoting tissue integrity and exerting anti-inflammatory effects. Studies have shown that vitamin C deficiency can promote or exacerbate gingivitis. In monkeys and guinea pigs, feeding a diet containing suboptimal amounts of vitamin C increased the severity of experimentally induced gingivitis.[26,27] In healthy male volunteers, restriction of vitamin C intake to 5 mg/day for 4 weeks resulted in a significant increase in gingival inflammation and bleeding. These changes were reversed by vitamin C supplementation.[28]

In an observational study, a significant inverse correlation was found between dietary vitamin C intake and the extent of periodontal disease. Periodontal health appeared to improve with increasing vitamin C intakes up to 126 mg/day, beyond which no further improvement was seen.[29] Plasma vitamin C levels were significantly lower in 20 patients with periodontal disease than in healthy individuals. In patients with periodontal disease associated with low vitamin C levels, gingival inflammation could not be eliminated by local treatment unless vitamin C supplements were also given.[30] In several clinical trials, vitamin C supplementation (alone or in combination with flavonoids) decreased the severity of gingivitis.[31–35]

One hundred two healthy volunteers with varying degrees of gingivitis were randomly assigned to receive, in double-blind fashion, placebo or 300 mg/day of vitamin C, with or without 300 mg/day of citrus flavonoids, for 3 weeks. Half of the subjects also received local therapy (scaling of one-half of the mouth). Mean improvement in gingivitis was significantly greater in people receiving vitamin C than in those receiving placebo, both on the scaled and unscaled sides. The combination of vitamin C and flavonoids was significantly more effective than vitamin C alone. The beneficial effect of vitamin C plus flavonoids alone (i.e., without local therapy) was at least as great as that of local therapy alone.[34]

Fifty-eight patients (mean age, 45 years) with chronic periodontitis were assigned (apparently without randomization) to consume 2 grapefruits per day for 2 weeks or to serve as a control group. Grapefruit is a good dietary source of vitamin C and flavonoids. Prior to treatment, the mean plasma vitamin C concentration was significantly lower in the patients than in healthy controls. Gingival bleeding improved significantly ($p < 0.001$) in the group consuming grapefruit, but did not change in the control group.[35]

In other studies, supplementation with 100–500 mg/day of vitamin C, with or without flavonoids, for 3–6 weeks had no beneficial effect on gingivitis.[36–38] While there is no clear explanation for these conflicting results, they might be explainable in part by differences in baseline nutritional status, gingivitis severity, and oral hygiene.

Vitamin C and flavonoids are safe and inexpensive, and they have multiple health benefits. Therefore, despite the conflicting results of research, patients with gingivitis should be advised to consume adequate amounts of these nutrients, either through dietary modification or supplementation. It is not known whether supplementation with vitamin C and flavonoids in doses higher than those used in the studies would provide additional benefit. Administration of such doses might increase the concentration of these nutrients in periodontal tissues, potentially resulting in a greater therapeutic effect. That possibility is supported by anecdotal evidence that topically applied vitamin C (which presumably penetrates directly into gingival tissues and produces high tissue

vitamin C concentrations) is highly beneficial for patients with gingivitis (see below).

Topical vitamin C. According to anecdotal reports, some dentists have obtained "uniformly excellent" results using topical sodium ascorbate (buffered vitamin C) for prophylaxis and treatment of gum disease. After the teeth are brushed and the mouth is rinsed, 1–2 g of sodium ascorbate is placed in the dry palm of the hand, picked up on the wet toothbrush, and massaged gently into all areas of the teeth and gums. The mouth is not rinsed; rather, the sodium ascorbate is left in contact with the mouth tissues. If it causes excessive salivation, it may be swallowed. This treatment is said to soothe damaged gum tissue and to increase the healing rate.[39] Ascorbic acid should not be used topically, as its acidity can erode dental enamel.

Vitamin E. Thirty-eight patients with chronic periodontitis received scaling and root planing and were randomly assigned to receive or not to receive 300 IU of vitamin E every other day for 3 months. Compared with no vitamin E, vitamin E supplementation significantly improved median scores for plaque index, gingival index, bleeding on probing, and clinical attachment level.[40]

Calcium and vitamin D. Dogs fed a low-calcium (0.12% by weight), high-phosphorus (1.2% by weight) diet developed periodontal disease, characterized by progressive loss of alveolar bone.[41] It has been suggested that calcium deficiency or a low calcium-to-phosphorus ratio in the diet might contribute to the development of periodontal disease in humans.

Observational data suggest that suboptimal vitamin D status is a risk factor for periodontal disease. In cross-sectional studies of participants in the Third National Health and Nutrition Examination Survey, inverse associations were found between serum concentrations of 25-hydroxyvitamin D and the prevalence of both gingivitis and periodontal disease.[42,43] In some studies, supplementation with calcium, alone or in combination with vitamin D and other nutrients, resulted in an improvement in periodontal disease, although no benefit was seen in other studies.

In an uncontrolled trial, administration of 1 g/day of calcium for 6 months to 10 patients with periodontal disease resulted in the disappearance of, or marked improvement in, bleeding; a reduction in tooth mobility and pocket depth; and improvement in, or disappearance of, gingivitis. The osseous structures of the alveolar region showed radiographic improvement in 7 of 10 cases.[44]

Thirty-three patients with generalized periodontal disease were randomly assigned to receive, in double-blind fashion, placebo or a daily supplement providing 750 mg of calcium, 375 IU of vitamin D, and trace amounts of iron, copper, magnesium, silica, manganese, and zinc for 1 year. Sixty percent of the patients in the active-treatment group improved, as compared with 16.7% of those in placebo group ($p < 0.01$).[45]

Tooth loss was assessed in 145 healthy subjects (mean age, 71.5 years) who completed a randomized placebo-controlled trial that examined the effect of calcium (500 mg/day) and vitamin D (700 IU/day) supplementation on bone loss from the hip. After 18 months of supplementation, the proportion of subjects who had lost one or more teeth was 52% lower in the active-treatment group than in the placebo group (13% vs. 27%; $p < 0.05$).[46] Whether or not the tooth-preserving effect of calcium and vitamin D was due to an improvement in periodontal disease was not addressed in this study.

In another double-blind study, supplementation with 1 g/day of calcium for 6 months resulted in a slight improvement in plaque index, gingival index, and probing depth, but these improvements were not greater than those seen in the placebo group.[47]

Assuring adequate calcium and vitamin D intake carries little risk and has the potential to improve periodontal health and prevent tooth loss. Supplementation with calcium and vitamin D, when indicated, should therefore be a component of the overall management of periodontal disease. Administration other nutrients that promote bone health (chapter 166) would also be a reasonable approach for preventing and treating the alveolar bone loss that occurs in periodontal disease.

Fatty acids. In a small double-blind trial, supplementation with 3 g/day of borage seed oil (BSO) for 12 weeks resulted in clinical improvement in patients with periodontitis. BSO appeared to be more effective than 3 g/day of fish oil or the combination of 1.5 g/day of BSO and 1.5 g/day of fish oil.

Twenty-four patients (mean age, 41 years) with periodontitis were randomly assigned to receive, in double-blind fashion, 3 g/day of BSO, 3 g/day of fish oil, 1.5 g/day each of BSO and fish oil, or placebo for 12 weeks. The modified gingival index (a measure of gingival inflammation) and probing depth improved more in the BSO group than in the placebo group ($p < 0.02$ and $p < 0.05$, respectively), whereas neither of the other treatments was significantly more effective than placebo. Combination treatment was less effective than BSO alone.[48]

In another double-blind trial, supplementation with the fatty acids present in fish oil was beneficial.

Sixty patients (mean age, 45 years) in India with chronic periodontitis were randomly assigned to receive daily, in double-blind fashion, 180 mg of eicosapentaenoic acid and 120 mg of docosahexaenoic acid or placebo for 12 weeks. All patients received scaling and root planing. Compared with placebo, significant improvements were seen in the active-treatment group in gingival index, sulcus bleeding index, pocket depth, and clinical attachment level ($p < 0.05$ for each).[49]

Zinc and copper. Zinc and copper have anti-inflammatory activity and also play a role in immune function and bone health. These nutrients might therefore be useful for preventing and treating periodontal disease. In a study of 51 healthy subjects, a significant inverse correlation was found between serum zinc levels and the degree of alveolar bone loss.[50] Low serum zinc does not necessarily indicate zinc deficiency, because serum zinc levels fall in response to inflammation (which is a manifestation of gingivitis). However, observations in cattle suggest that deficiencies of zinc, copper, and other trace minerals can promote the development of periodontal disease.[51]

Multivitamin-multimineral. In short-term double-blind studies, supplementation with a multivitamin or a multivitamin-multimineral preparation improved measures of periodontal health in both children and adults. The multivitamin appeared to be somewhat more effective than vitamin B complex or vitamin C alone.

Two hundred sixty-seven healthy children (mean age, 11 years) were randomly assigned to receive, in double-blind fashion, one of the following treatments daily for 4 weeks: placebo, vitamin C (75 mg), vitamin B complex (1.2 mg of thiamine, 1.5 mg of riboflavin, 15 mg of niacinamide, 1.2 mg of pyridoxine, 5 mg of calcium pantothenate, 3 µg of cyanocobalamin, and 40 µg of biotin), or a multivitamin containing vitamin C and B vitamins as above plus 4,000 IU of vitamin A and 400 IU of vitamin D. Compared with placebo, there was a nonsignificant improvement in the periodontal index (a measure of periodontal health) in the groups receiving vitamin C alone and vitamin B complex alone, and a significant improvement in the group receiving the multivitamin.[52]

Thirty-three male volunteers (aged 19–71 years) were randomly assigned to receive, in double-blind fashion, a multivitamin-multimineral supplement or placebo daily for 21 days. The supplement contained vitamin A (12,500 IU), vitamin D (50 IU), vitamin E (50 IU), thiamine (10 mg), riboflavin (5 mg), pyridoxine (2 mg), niacinamide (25 mg), calcium pantothenate (10 mg), vitamin C (150 mg), magnesium sulfate (80 mg), zinc sulfate (80 mg), and manganese chloride (4 mg). After 7 days, the mean gingival index had improved by 22% in the active-treatment group and was significantly lower (indicating better gingival health) than in the placebo group ($p = 0.004$).[53]

B vitamins after flap surgery. In a double-blind trial, supplementation with a B-complex vitamin enhanced healing after flap surgery for periodontitis.

Thirty patients undergoing flap surgery for periodontitis were randomly assigned to receive, in double-blind fashion, a B-vitamin supplement or placebo for 30 days following surgery. The supplement provided daily 50 mg each of thiamine, riboflavin, niacinamide, calcium pantothenate, and pyridoxine; 50 µg each of biotin and cyanocobalamin; and 400 µg of folic acid. Compared with placebo, active treatment resulted in significantly better wound healing, as demonstrated by better clinical attachment levels ($p < 0.03$) at 6 months after surgery.[54]

Probiotics. In several double-blind trials, administration of lozenges containing *Lactobacillus reuteri* DSM 17938 and *L. reuteri* ATCC PTA 5289 was beneficial[55–58] or possibly beneficial[59] for patients with chronic periodontitis. In a study that included long-term follow-up, the improvements persisted for at least 49 weeks after the treatment was discontinued. The same probiotic preparation administered as a chewable tablet was ineffective in another study,[60] possibly because the shorter contact time with the oral cavity (compared with lozenges) decreased the likelihood of colonization. This patented probiotic combination is known as Prodentis. The lozenges are available in Europe and elsewhere, but at the time of this writing are not available in the United States.

Thirty patients with chronic periodontitis were treated with scaling and root planing and were randomly assigned to receive, in double-blind fashion, probiotic lozenges twice a day (morning and evening after tooth brushing) or placebo lozenges for 3 weeks. The probiotic lozenges (Prodentis; BioGaia, Lund, Sweden) contained at least 10^8 colony-forming units each of *Lactobacillus reuteri* strains DSM 17938 and ATCC PTA 5289. Evaluations were performed at baseline and on days 21, 90, 180, and 360. Compared with placebo, the probiotic significantly improved plaque index, gingival index, bleeding on probing, probing depth, and attachment gain at every time point.[56]

Case report. I saw a 49-year-old woman with moderately severe periodontal disease who had been told by her periodontist that she needed extensive surgery. She was advised to take 60 mg/day of CoQ_{10}, to use 5 ml of 0.1% folic acid mouth rinse twice a day, and to brush buffered vitamin C (calcium ascorbate) powder gently into the gums once a day. After 1 month of treatment, the periodontist remarked with surprise that her condition had improved substantially and that she no longer needed surgery.

Conclusion

In my experience, nutritional interventions are frequently beneficial for patients with periodontal disease and gingivitis. Dietary modifications that may be worthwhile include avoidance of refined carbohydrates and, when appropriate, identification and avoidance of allergens. Nutritional supplements that may be useful include folic acid mouth rinse, CoQ_{10}, vitamin C and flavonoids, buffered vitamin C topically, calcium and vitamin D, borage seed oil, and a multivitamin-multimineral preparation that contains zinc and copper. A specific probiotic preparation also appears to be of value. As is frequently the case with nutritional therapy, a combination of treatments may be more effective than any one treatment by itself.

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262 Xerostomia

Xerostomia is dryness of the mouth resulting from insufficient saliva production. Consequences of xerostomia may include halitosis, impaired speech and taste sensation, altered dietary habits, and an increased incidence of dental caries (saliva contains factors that prevent caries).

More than 400 medications can cause xerostomia, and medication use is the most common cause of this disorder. Other causes include Sjogren's syndrome and certain other autoimmune diseases, diabetes, mouth-breathing, excessive alcohol intake, nutritional deficiencies, and radiation therapy. The prevention of radiation therapy-induced xerostomia is discussed in chapter 337.

Conventional treatment focuses in large part on measures to prevent dental caries. In particular, regular use of xylitol chewing gum may be worthwhile, because it stimulates saliva flow and reduces the growth of cariogenic bacteria (i.e., *Streptococcus mutans*). Chewing of hard cheese at the end of meals also stimulates saliva flow and appears to promote re-mineralization of enamel.[1] These interventions are discussed in chapter 258. Commercially available artificial saliva preparations are also used.

Dietary factors. Because patients with xerostomia may have altered dietary habits, a diet history should be obtained, and appropriate dietary modifications and nutritional supplements should be recommended.

Patients with food allergy may have a tendency to mouth-breathe, which can result in dry mouth. Therefore, food allergy should be considered as a potential exacerbating factor in selected patients. The evaluation and management of food allergy is discussed in chapter 7.

Green tea catechins (lozenges). In a double-blind trial, use of lozenges containing green tea catechins increased saliva output in patients with xerostomia.

Sixty patients with xerostomia were randomly assigned to receive, in double-blind fashion, lozenges containing a proprietary preparation of green tea catechins (MighTeaFlow; Nomax, Inc., St. Louis, MO) every 4 hours (maximum, 6 per day) or placebo for 8 weeks. All lozenges contained 500 mg of xylitol; the amount of green tea catechins was not stated. In the active-treatment group, compared with baseline, there was a significant 3.9-fold increase in unstimulated saliva output and a significant 2.1-fold increase in stimulated saliva output (stimulated by chewing neutral wax). Saliva output did not change significantly in the placebo group.[2] Subgroup analysis of the 10 patients in this study who had Sjogren's syndrome is presented in chapter 158.

Zinc. In rats, dietary zinc deficiency resulted in an impairment of salivary secretion.[3] Some practitioners have observed that, in patients who have a combination of xerostomia and disorders of taste sensation, both of these abnormalities often improve following zinc supplementation.[3,4] In an uncontrolled trial, zinc supplementation improved xerostomia in elderly patients with low serum zinc levels.

Serum zinc levels were measured in 93 patients (mean age, 64 years) with xerostomia, hypogeusia (decreased taste sensation), or both of these disorders. Thirty-eight of the 63 patients with xerostomia had a low serum zinc concentration and were prescribed zinc. The dosage of zinc was not specified, but in a case report presented in the article, the dose was 68 mg/day (as zinc sulfate). After zinc supplementation, subjective symptoms of xerostomia resolved in 7.9% of the patients and improved in an additional 50% (total resolved or improved, 57.9%). Hypogeusia resolved or improved in 73% of the patients in whom xerostomia resolved or improved.[4] Further information about the treatment of hypogeusia is presented in chapter 271.

Vitamin C. Vitamin C is present in relatively high concentrations in salivary acinar cells and may therefore play an important role in saliva production.[5] Human volunteers fed a vitamin C-deficient diet for 3 months developed several of the manifestations of Sjogren's syndrome, including xerostomia and keratoconjunctivitis sicca, in addition to the usual signs of scurvy.[6] While frank scurvy is rare in Western societies, vitamin C deficiency or marginal vitamin C status should be considered as a potential exacerbating factor in certain patients with xerostomia, such as those with cancer, diabetes, or advanced age.

Probiotics. Overgrowth of yeast in the oral cavity is common among elderly people, and may be a contributing factor to xerostomia in some cases. In a double-blind trial, administration of a combination of probiotic strains resulted in a modest improvement in xerostomia in elderly people. It is not known whether other probiotic strains would have a similar effect.

Two hundred seventy-six elderly people (mean age, 79 years) were randomly assigned to consume, in double-blind fashion, 50 g/day of cheese that did or did not contain probiotic bacteria for 16 weeks. The probiotic cheese contained *Lactococcus lactis* and *Lactobacillus helveticus*, and 10^7 colony-forming units (cfu)/g of each of 3 probiotic strains (*L. rhamnosus* GG, *L. rhamnosus* LC705, and *Propionibacterium freudenreichii* ssp *shermanii* JS) was added to the cheese. The control cheese used only *L. lactis* as a starter culture. Salivary secretion rates (unstimulated, and stimulated by chewing paraffin wax) were measured at weeks 0 and 16. Hyposalivation was defined as an unstimulated salivary flow rate < 0.1 ml/minute and a stimulated flow rate < 0.8 ml/minute. The prevalence of a high salivary yeast count ($\geq 10^4$ cfu/ml) decreased in the probiotic group from 30% to 21% and increased in the control group from 28% to 34% ($p = 0.004$ for the difference in the change between groups). The prevalence of hyposalivation decreased in the probiotic group from 23.6% at baseline to 18% after 16 weeks, and increased in the control group from 19.4% at baseline to 26.9% after 16 weeks ($p = 0.05$ for the difference in the change between groups).[7]

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263 Other oral diseases

Geographic tongue

Geographic tongue (benign migratory glossitis) is an inflammatory condition of the tongue characterized by areas of red, slightly depressed, smooth patches on the tongue surrounded by a distinct white border. The lesions are usually asymptomatic, although they may cause burning, discomfort, or mild soreness aggravated by hot and spicy foods or citrus fruits. The cause of geographic tongue is not well understood. The lesions often resolve spontaneously and then reappear on other areas of the tongue.

Food allergy. Geographic tongue is frequently observed in people with allergic conditions. In one study, 48% of 126 patients with asthma and/or rhinitis had geographic tongue, compared with 19% of healthy controls ($p < 0.01$).[1] In my experience, geographic tongue resolves in some patients after they identify and avoid allergenic foods, and recurs if the offending foods are eaten.

Zinc. Of 25 patients with symptomatic geographic tongue, 21 (84%) had marginally low serum zinc concentrations. Of 12 patients with low serum zinc who took 45 mg of zinc (as zinc sulfate) 3 times per day, 10 (83%) became asymptomatic, with complete resolution of the geographic tongue occurring in 4 cases.[2] Long-term zinc supplementation should be accompanied by a copper supplement (1–4 mg/day, depending on the zinc dose), in order to prevent zinc-induced copper deficiency (chapter 31).

Vitamin B_6. One practitioner reported that pyridoxine (50 mg 3 or 4 times per day) is effective in the treatment of geographic tongue that is aggravated by constipation, neuroleptics, and antispasmodics.[3]

Gingival hyperplasia

Gingival hyperplasia is an overgrowth of gingival tissue that occurs as a side effect of certain medications, such as phenytoin, cyclosporine, and some calcium-channel blockers (especially nifedipine). Complications of gingival hyperplasia may include bleeding, pain, displacement of teeth, and periodontal disease. Risk factors for gingival hyperplasia include gingivitis and the presence of dental plaque. Conventional treatment includes proper oral hygiene and discontinuation or reduction of the dose of the implicated medication. Surgery (gingivectomy) is recommended in severe, refractory cases.

Folic acid. Treatment with phenytoin frequently causes a decrease in serum folate levels. In a study in cats, supplementation with folic acid prevented phenytoin-induced gingival hyperplasia.[4] In a double-blind trial, supplementation with 0.5 mg/day of folic acid for 6 months significantly decreased the incidence of gingival hyperplasia, compared with placebo (21% vs. 88%; $p < 0.001$), in children (aged 6–15 years) who had begun taking phenytoin within the previous month.[5] In addition, oral administration of folic acid improved phenytoin-induced gingival hyperplasia in patients who had laboratory evidence of folate deficiency, but was ineffective in those with normal folate status. The dosages used in these studies were 3 mg/day, 5 mg/day, and 5 mg/week, respectively, and treatment was given for periods of 16 weeks to 1 year.[4,6,7]

In one study, folic acid administered as a mouth rinse significantly improved phenytoin-induced gingival hyperplasia in patients who had initially normal serum folate levels. Folic acid mouth rinse was more effective than both oral folic acid and placebo.

Fifteen patients with phenytoin-induced gingival hyperplasia and normal serum folate concentrations were randomly assigned to receive, in double-blind fashion, placebo mouth rinse and placebo tablets, placebo mouth rinse and folic acid tablets (4 mg/day), or 0.1% folic acid mouth rinse and placebo tablets for 6 months. The patients used 5 ml of mouth rinse twice a day, rinsing 2 minutes before expectorating. Compared with baseline, folic acid mouth rinse significantly reduced the severity of gingival hyperplasia ($p < 0.05$). In contrast, there was a nonsignificant improvement in the group receiving oral folic acid and a nonsignificant worsening of gingival hyperplasia in the placebo group.[8]

The apparently greater efficacy of folic acid mouth rinse, as compared with folic acid tablets, may be due to the fact that topically applied folic acid is directly absorbed into gingival tissue.[9] One might speculate that phenytoin treatment causes localized folate deficiency in gingival tissue, without necessarily causing folate deficiency elsewhere in the body. That could explain why topically administered folic acid is beneficial in patients who do not have laboratory evidence of folate deficiency.

It should be noted that administration of large doses of folic acid (such as 15 mg/day) may decrease serum concentrations of phenytoin and other anticonvulsants, potentially interfering with seizure control (chapter 131). Such interactions are presumably less likely to occur with folic acid mouth rinse than with folic acid tablets, as long as most of the mouth rinse is expectorated after use. In the study described above,[8] the mean serum folate concentration increased less in patients receiving folic acid mouth rinse than in those receiving folic acid tablets.

There is no evidence that treatment with cyclosporine or calcium-channel blockers causes folate deficiency or abnormalities of folate metabolism, and folic acid has not been studied as a treatment for gingival hyperplasia induced by these drugs.

Glossitis

Glossitis is an inflammation of the tongue that may result in swelling, redness, soreness or tenderness, and loss of papillae. Causes include infection, irritation, allergic reactions, and nutritional deficiencies.

Food and contact allergies. In a case report, a 7-year-old male had periodically painful lesions on the tongue, which was diagnosed as transient lingual papillitis (an inflammatory disease of the tongue). The condition was found to be due to fish allergy and resolved when fish was removed from the diet.[10] Glossitis due to contact sensitivity to cinnamonaldehyde, a component of some toothpastes, has been observed in some patients.[11] Other allergens present in toothpaste might also trigger glossitis in susceptible individuals. An evaluation of 48 brands of toothpaste sold in Finland revealed that almost 50% contained one or more compounds widely recognized as allergens.[12]

Allergy to foods, food additives, or components of toothpaste should therefore be considered as potential etiologic factors in patients with glossitis.

B vitamins. Glossitis is common in patients who are deficient in vitamin B_{12}[13–15] or folic acid,[16,17] and correction of these deficiencies results in improvement or resolution of glossitis. Glossitis has also been reported to improve in some patients after supplementation with riboflavin,[18,19] niacinamide,[17] or pyridoxine.[20] In one study, 6 patients with glossitis that had failed to respond to other B vitamins had a resolution or marked improvement of the condition after treatment with pantothenic acid.[21]

It is common for people who are deficient in one B vitamin to be deficient in others as well. Therefore, individuals who have glossitis that is suspected to be due to B-vitamin deficiency should, in most cases, be treated with the entire vitamin B complex.

Iron. In a study of 378 adults with iron deficiency, 11% experienced soreness of the tongue, 11% had absent filiform papillae, and an additional 38% had a lesser degree of papillary atrophy.[22] Symptoms of glossitis can occur with relatively modest degrees of iron deficiency. For example, some patients experience soreness of the tongue before their hemoglobin level falls.[23] In patients with glossitis due to iron deficiency, the abnormalities of the tongue can be reversed with iron supplementation.

Hydrochloric acid. According to a review article published in 1933, glossitis can be a manifestation of hypochlorhydria. In some hypochlorhydric patients, treatment with hydrochloric acid resolved the glossitis, but the condition usually recurred when hydrochloric acid was discontinued.[24] It is not clear whether acid-replacement therapy resolved glossitis by improving the absorption of B vitamins or iron, or by some other mechanism. The diagnosis and treatment of hypochlorhydria is discussed in chapter 112.

Halitosis (bad breath)

Common causes of halitosis include periodontal disease, sinusitis, respiratory-tract infection, poor dental hygiene, dry mouth, esophageal reflux, certain systemic illnesses (e.g., diabetes, liver disease, and renal failure), and use of tobacco.

In my experience and that of other practitioners, unexplained halitosis is related in some cases to food allergy[25] or hypochlorhydria.[26] Some patients have found that halitosis resolves after identification and avoidance of allergenic foods. In patients with hypochlorhydria, administration of hydrochloric acid with meals (chapter 112) often eliminates halitosis. Halitosis has also been observed as a side effect of a low-carbohydrate (Atkins) diet.[27] One double-blind trial found that the use of a probiotic-containing chewing gum resulted in a modest improvement in halitosis,[28] but in another double-blind trial, probiotic tablets dissolved in the mouth were ineffective.[29]

In patients with Sjogren's syndrome (a condition associated with dry mouth), supplementation with N-acetylcysteine (200 mg 3 times per day) improved halitosis, apparently by increasing the flow of saliva.[30]

Orthodontics

Orthodontics involves the use of braces or other appliances to correct a malocclusion (an improper bite resulting from misalignment of the teeth or jaw).

Does breastfeeding prevent malocclusion? Bottle feeding causes babies to develop a habit of forward thrusting of the tongue and also leads to weak development of the some of the facial muscles. This combination of changes in pressures and balance is thought to affect oral-facial development. It has been hypothesized that breastfeeding leads to increased development of the orbicularis oris, masseter, and buccinator muscles, thereby favorably influencing the growth of the mandible.

In a cross-sectional study of 9,698 children living in the United States, the incidence of malocclusion declined with increasing duration of breastfeeding (p for trend < 0.001). Children who were breastfed more than 6 months had levels of malocclusion considerably lower than those of bottle-fed children. The authors of this study calculated that approximately 44% of all cases of malocclusion are due to inadequate duration of breastfeeding (i.e., less than 12 months).[31]

Nutritional influences in orthodontic treatment. In people receiving orthodontic treatment, remodeling of the bone and connective tissue structures surrounding the teeth occurs at a more rapid rate than normal. This rapid remodeling presumably increases the requirement of these tissues for a wide range of nutrients. For example, in guinea pigs fed a vitamin C-deficient diet, abnormalities in the periodontal ligament and surrounding bone were accentuated by application of light force from an orthodontic appliance.[32] Achieving optimal results from orthodontic treatment presumably depends on obtaining an adequate supply of all nutrients that play a role in building bone and connective tissue. These include protein, calcium, magnesium, vitamin C, B vitamins, trace minerals, and vitamin K (chapter 166).

Tooth pain (chronic)

One practitioner reported that chronic dental pain resulting from exposed roots or temporomandibular joint dysfunction can be ameliorated in some patients by avoidance of specific foods or by supplementation with large doses of vitamin C (sodium ascorbate). To determine whether either of these treatments would be effective, patients restricted their diet to a single food for 4 days or supplemented with "bowel tolerance" doses of vitamin C (described in chapter 22) for 4 days. Of 21 patients with sensitive roots, 10 experienced complete elimination of pain after supplementing with sodium ascorbate for 4 days. No further details were provided regarding the dietary intervention or long-term use of vitamin C.[33]

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