Oral care for patients with cardiovascular disease and stroke

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ABSTRACT

Background. The authors describe how oral disease, particularly periodontal disease, may place certain patients at increased risk of developing cardiovascular disease and stroke.

Results. Although the precise mechanisms of interaction are not clear, two biological mechanisms that may explain the relationship are presented. In addition, the authors describe the dental management issues that need to be understood in treating patients compromised by cardiovascular disease.

Conclusions and Clinical Implications. The patient with cardiovascular disease may present a challenge to the dental health care provider, depending on the degree of hemodynamic compromise and the stability of his or her condition.

In May 2000, the U.S. surgeon general's office published its first report on oral health in America, emphasizing that oral health means much more than healthy teeth and that it is integral to general health.[1] Included in the report is an extensive review of the burden that oral health problems place on vulnerable populations. The surgeon general confirmed that many systemic diseases and conditions have oral manifestations that may be the initial signs of clinical disease. In addition, the mouth is a portal of entry as well as the site of disease for microbial infections that affect general health status. Its functions can be affected adversely by many pharmaceuticals and other therapies commonly used to treat systemic conditions.

"Oral Health in America: A Report of the Surgeon General" concluded with the recognition that "the mouth is the center of vital tissues and functions that are critical to total health and well-being across the life span." The mouth serves as "a mirror of health or disease, as a sentinel or early warning system, as an accessible model for the study of other tissues and organs, and as a potential source of pathology affecting other systems and organs."[1]

The patient with cardiovascular disease may present a challenge to the dental health care provider.

CARDIOVASCULAR DISEASE

Cardiovascular diseases make up the most prevalent category of systemic disease in the United States and in many other countries, and increase in prevalence with age.[2]

Atherosclerosis is a progressive disease process that involves the large- to medium-sized muscular and large elastic arteries. It can lead to ischemic lesions of the brain, heart or extremities, and can result in thrombosis and infarction of affected vessels, leading to death. The impact of atherosclerosis on overall health is staggering. World Health Organization statistics indicate that in 1995, cardiovascular diseases were responsible for 20 percent of deaths worldwide (14 million people). In some developing countries, cardiovascular disease accounts for about 50 percent of deaths.[3]

For years, dentists have noticed that certain characteristics are common to patients with periodontitis and patients with cardiovascular disease (Figures 1 and 2). Both cardiovascular disease and periodontal disease are more likely to occur in people who are older, in men, in people of lower educational status with fewer financial resources, in those who smoke, in people who have stress and in those who are socially isolated. The classical risk factors for cardiovascular disease—hypertension, hyper-

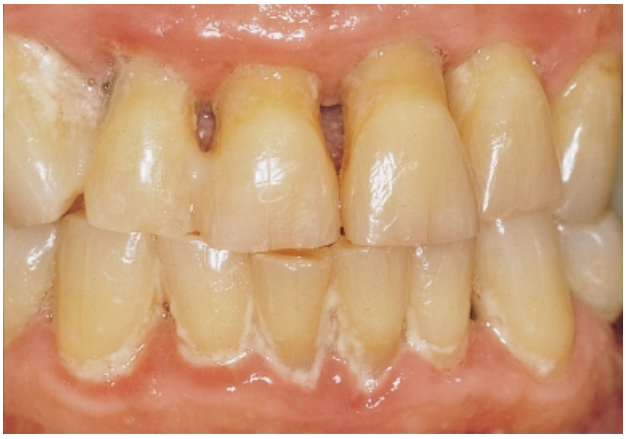

Figure 1. A 45-year-old man with coronary artery disease who smokes two packs of cigarettes per day. He has not responded well to periodontal treatment and does not practice good oral hygiene.

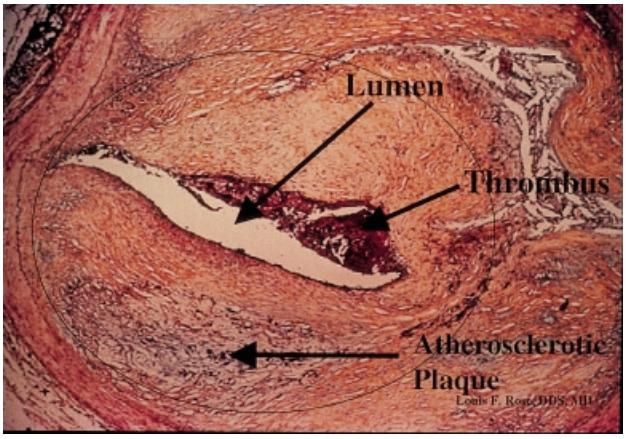

Figure 2. Histologic section of a coronary artery demonstrating atherosclerosis and thrombus formation.

cholesterolemia and cigarette smoking—account for only about one-half to two-thirds of all cases of the disease. Research has shown that atherosclerosis is more common in patients with periodontitis.[2] This suggests that periodontal disease and cardiovascular disease may have similar causative pathways.

Some scientific studies have shown a link between infections of the mouth and coronary artery disease. In one such study, Mattila and colleagues[4] compared patients who had experienced a myocardial infarction, or MI, with healthy control subjects. They found that after adjusting for age, socioeconomic status, smoking, serum lipid levels and diabetes, dental health (as measured by the Total Dental Index) was worse in subjects who had experienced an MI. In another study by Mattila and colleagues,[5] a statistically significant association was found between dental infections and atheromatosis.

In examining the effects of different oral infections on the incidence of strokes, Grau and colleagues[6] re-examined the Total Dental Index and found that only the periodontal component of the index was responsible for the association between oral infection and cerebrovascular ischemia (stroke).

Several longitudinal studies have followed a population of otherwise healthy people to determine what factors increase the risk of developing heart disease. The first National Health and Nutrition Examination Survey followed up 9,760 subjects for 14 years; DeStefano and colleagues studied these data and found that people with periodontitis at baseline had a 25 percent increased risk of having coronary artery disease.[7] After adjusting for age, sex, race, education, poverty index, marital status, systolic blood pressure, total cholesterol level, diabetes, body mass index, physical activity, alcohol consumption and cigarette smoking, the researchers found that men with periodontitis had a 1.72 relative risk compared with men without periodontitis. The authors concluded that dental disease was associated with an increased risk of cardiovascular disease, particularly in men younger than age 50 years.[7]

Potential biological mechanisms. Most of these studies[4-7] have shown that there is an association between periodontal disease and cardiovascular disease. These associations have been demonstrated across diverse populations and appear to be independent of traditional risk factors, but do not provide for a biological rationale for the association.

Two biological mechanisms that may explain the relationship between cardiovascular disease and periodontal disease are discussed in this article:

- Bacteria from periodontal disease may enter the circulation and contribute directly to the atheromatous or thrombotic processes.
- Systemic factors alter the immunoinflammatory process involved in both periodontal and cardiovascular diseases.

Role of infections in atherosclerosis. Since 1908, when Sir William Osler proposed that cardiovascular disease itself was an infection, the role of infection in cardiovascular disease has been discussed.[8] Infection is now recognized as a risk factor for atherogenesis and thromboembolic events.[5-7]

Infectious agents may cause injury directly to the epithelium and partially activate the inflammatory response seen with atherosclerosis. There is evidence that infection with certain bacteria, such as *Chlamydia pneumonae, Helicobacter pylori,* cytomegalovirus and other periodontopathic bacteria are associated with heart disease. Haraszthy and colleagues[9] studied 50 carotid atheromas via polymerase chain reaction. Seventy-two percent of the surgical specimens indicated bacterial content and 44 percent of the atheromas contained at least one of the periodontal microorganisms studied (*Porphyromonas gingivalis*, *Prevotella intermedia*, *Bacteroides forsythus* and *Actinobacillus actinomycetemcomitans*) (Figure 3[10]).

People with severe periodontitis have the strongest link to cardiovascular disease. These people also have the greatest amounts of pathogenic bacteria and systemic factors that may contribute to an altered immunoinflammatory response.

Common systemic factors involved in periodontal and cardiovascular diseases. Considerable evidence has identified atherosclerosis as an inflammatory disease. This hypothesis, which is also known as the Ross "Response-to-Injury Hypothesis,"[11,12] explains how inflammation relates to atherosclerosis. Ross' hypothesis suggests that injury to the epithelium causes the initial lesion, leading to a chronic arterial inflammatory process. During this inflammatory process, monocytes migrate through the endothelium into the underlying tissue, where there is a proliferation of smooth muscle cells.

Hydrolytic enzymes, cytokines, chemokines and growth factors are released as a result of activation of the monocytes (macrophages) into the blood vessel, resulting in further damage and focal necrosis. A major feature of this process is lipid accumulation, and the atheromatous plaque can become covered with a fibrous cap over the focal necrotic area in the later stages of this process. This fibrous cap also may erode and rupture, leading to thrombus formation, arterial occlusion and infarction.

Certain people may be genetically predisposed to experience a hyperinflammatory response when stimulated by a bacterial challenge such as periodontal disease. These people may produce higher levels of proinflammatory cytokines, particularly interleukin-1, prostaglandins (in particular, prostaglandin E_2) and tumor necrosis factor (in particular, tumor necrosis factor-α). These biological mediators can have a direct effect on the periodontal pocket, as well as on the vascular endothelium and smooth muscle. In the periodontal pocket, these mediators cause vasodilation and increased vascular permeability.

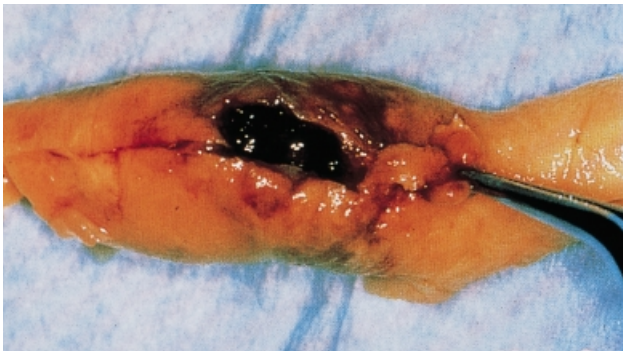

Figure 3. Carotid artery atheroma. (Reprinted with permission of the publisher from Genco and colleagues.[10])

This is followed by inflammatory cell recruitment, connective-tissue degradation and bone destruction. The result of recruitment of inflammatory cells into the major blood vessels is the proliferation of vascular smooth muscles, vascular fatty degeneration and intravascular coagulation. People who are genetically predisposed to this proinflammatory response may be at a higher risk of developing periodontal disease and cardiovascular disease.

Prospective interventional studies are needed to determine the exact link between periodontal disease and cardiovascular disease, as well as to evaluate whether periodontal treatment may reduce the risk of developing cardiovascular disease.

DENTAL MANAGEMENT OF PATIENTS WITH CARDIOVASCULAR DISEASE

The primary management goal for the patient with cardiovascular disease during dental therapy is to ensure that any hemodynamic change produced by dental treatment does not exceed the cardiovascular reserve of the patient. This is best achieved by minimizing any hemodynamic alterations during treatment (that is, by maintaining the patient's optimum blood pressure, heart rate, heart rhythm, cardiac output and myocardial oxygen demand).[13,14]

Psychological and physiological stress during periodontal treatment has the potential to significantly alter hemodynamic stability.[13,15,16] Consequently, a stress-reduction protocol is frequently

suggested for patients with significant cardiovascular compromise, which includes the following:

- shorter appointments, preferably in the morning when the patient is well-rested and has a greater physical reserve;
- use of profound local anesthesia to minimize discomfort;
- preoperative or intraoperative conscious sedation or both;
- excellent postoperative analgesia.[17,18]

We should note that almost all references suggesting a stress-reduction protocol do so on the assumption that such a protocol will minimize adverse hemodynamic alterations. There is little objective evidence, however, that such a protocol is required for the majority of patients with cardiovascular disease, or that it produces a better outcome in regard to cardiovascular complications associated with periodontal therapy.

Anesthetic agents. The use of local anesthetic agents with vasoconstrictors in patients with cardiovascular disease remains controversial. The two most commonly used vasoconstrictors are epinephrine and levonordefrin. Levonordefrin is only 20 percent as potent as epinephrine; therefore, its concentration in dental anesthetics is fivefold greater (that is, 1:20,000) than the most common concentration of epinephrine (1:100,000).

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Normal epinephrine release from the adrenal medulla can increase 20- to 40-fold during stress.[19] Such stress may be induced by pain during dental treatment. Patients receiving local anesthetic without vasoconstrictor often have significantly impaired pain control compared with those receiving local anesthetic with epinephrine.[20] For this reason, patients with cardiovascular disease may be at greater risk of experiencing massive endogenous epinephrine release secondary to poor local anesthesia than they are from the small amount of vasoconstrictor used in local anesthetics.

Most human studies examining hemodynamic variables after dental injection of 1.8 to 5.4 milliliters of 2 percent lidocaine with 1:100,000 epinephrine have found no significant changes in mean arterial pressure, blood pressure or heart rate in healthy patients or in those with mild-to-moderate cardiovascular disease.[16,19,21,22] So it is recommended that patients with mild-to-moderate cardiovascular disease receive the smallest amount of local anesthetic needed to provide profound anesthesia, with aspiration performed to prevent intravascular injection. Researchers have suggested that the use of conscious sedation to decrease stress and therefore minimize endogenous release of epinephrine may be a more important factor in ensuring hemodynamic stability in patients with cardiovascular disease than are attempts to avoid the small amount of epinephrine used in local anesthetic injections.

Although small amounts of vasoconstrictor produce little risk for the average patient with cardiovascular disease, exogenous vasoconstrictors may be contraindicated in patients with severe cardiovascular compromise, including unstable angina, recent myocardial infarction or coronary artery bypass surgery, uncontrolled dysrhythmias, severe hypertension and severe congestive heart failure.[19] Intraligamentary injection of local anesthetics with vasoconstrictor generally is contraindicated in patients with significant cardiovascular disease,[19] since the hemodynamic effects are similar to those observed after intravenous epinephrine injection.[23]

Ischemic heart disease. Ischemic heart disease, most commonly manifested as angina or myocardial infarction, is the major cause of sudden death in the United States.[16,22,24] It usually is caused by decreased coronary blood flow, increased myocardial oxygen demand or both. There are three types of angina: stable, unstable and variant (Prinzmetal's angina). It is clear from the literature that psychological or physiological stress may exacerbate ischemic symptoms. Therefore, use of a stress-reduction protocol and profound anesthesia is an integral part of periodontal therapy for these patients.[13,15,17,18]

Stable angina generally is caused by atherosclerotic narrowing of coronary vessels and presents with infrequent episodes of pain, usually precipitated by physical exertion or emotional stress. The medications most commonly used to treat patients with stable angina include nitrates such as nitroglycerin, β-andrenergic blocking agents and calcium channel blockers.[15]

Periodontal treatment planning may be altered in these patients by the need for shorter appoint-

ments, use of only small amounts of vasoconstrictor in local anesthetics and possible indications for preoperative or intraoperative conscious sedation. Supplemental oxygen delivered via a nasal canal may help prevent intraoperative anginal attacks.[17] The drugs of choice for treating an acute anginal attack are 100 percent oxygen and sublingual nitroglycerin.[15,18] The patient may be instructed to bring his or her own nitroglycerin tablets to each appointment, and the health care provider also may place nitroglycerin tablets in the emergency medical kit.

Unstable angina occurs when there is a dramatic increase in the frequency or severity of anginal attacks or when angina appears while the patient is at rest.[15,24] Patients with unstable angina generally are not candidates for elective dental therapy, and consultation with the patient's physician usually is indicated. If emergency dental care is needed, preoperative anxiolytic agents may be indicated for stress reduction and to minimize endogenous epinephrine release. The dentist should closely monitor the patient's hemodynamic status and oxygen saturation before and during treatment.

Variant angina (that is, Prinzmetal's angina) usually occurs at rest and probably is caused by coronary artery spasm.[15,25]

The other major category of ischemic heart disease frequently encountered by oral health care providers is myocardial infarction. Researchers and clinicians commonly recommend that patients not receive routine dental care for at least six months after experiencing a myocardial infarction.[18,19,24] This recommendation is based on the fact that the peak mortality rate following myocardial infarction occurs during the first year,[26] primarily resulting from the increased electrical instability of the myocardium after the infarction.[27]

During this six-month period, dental treatment generally is limited to managing acute dental needs, and consultation with the patient's physician may be needed.[28] Acute dental needs usually are addressed definitively, since continued pain may potentiate hemodynamic alterations or dangerous cardiac dysrhythmias.[17,24] A protocol similar to that described above for unstable angina may provide the best means of managing acute dental needs.[16,17] After the six-month postmyocardial infarction period, most patients may be treated with techniques similar to those used for the patient with stable angina, including relatively short appointments and a stress-reduction protocol where indicated.

Dysrhythmias. Patients with cardiac dysrhythmias may require special precautions during dental therapy. Antidysrhythmic drugs commonly are used, many of which have side effects such as gingival overgrowth or xerostomia that may impact the dentition or periodontium. The use of local anesthetics with vasoconstrictors may be contraindicated in patients with refractory dysrhythmias[19]; dental treatment may best be accomplished in a controlled medical setting with careful cardiac monitoring.[24]

Some dysrhythmias are treated with implantable pacemakers or automatic defibrillators in addition to drug therapy. Pacemakers and automatic defibrillators present a low risk of infective endocarditis and do not require prophylactic antibiotic coverage before dental therapy.[29] Older pacemaker models were unipolar and could be disrupted by equipment that generates an electromagnetic field, such as ultrasonic instruments and electrocautery units. Most pacemakers placed within the last 30 years are bipolar and generally are not affected by the small electromagnetic fields created by dental equipment.

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Automatic defibrillators often activated-without warning, which may cause sudden movement and endanger the patient in the dental setting. The dental health care provider must be aware of this potential during treatment, and may need to stabilize the operating field through use of a bite-block or other such devices.

Cerebrovascular accident. Although stroke is a cerebrovascular disorder or cerebrovascular accident, or CVA, it is discussed in the above section entitled "Cardiovascular Disease," because CVAs occur most frequently in patients with existing cardiovascular disease, especially hypertension. A stroke results from sudden interruption of blood flow to the brain, which deprives it of oxygen. The survival rate and severity of the ensuing functional deficit depend on the type of stroke and the extent of the lesion.[30] Patients with stroke frequently are treated with oral anticoagulants and may, in consultation with their physicians, need alteration of the drug regimen before

undergoing periodontal therapy.

To prevent a subsequent stroke, clinicians must treat active infections aggressively, since even minor infection may alter blood coagulation and trigger thrombus formation and ensuing cerebral infarction.[31] Dysphasia may be present in the patient with stroke and can cause changes in diet, mastication, nutrition and body weight. Inability to completely clear the mouth of food particles may result in halitosis, caries and increased risk of infection. The dental health care provider should counsel the patient about the importance of thorough oral hygiene. Weakness of the facial area or paralysis of extremities may make oral hygiene procedures extremely difficult,[30] and the dental health care provider may need to modify oral hygiene instruments for ease of use, perhaps in consultation with an occupational therapist.

The dentist may initiate a long-term regimen of chlorhexidine rinses to aid in plaque control.[30] The gag reflex may be diminished after a CVA as well, which may require particular attention during dental therapy. The patient's head position can be adjusted if needed, while thorough and constant evacuation will help prevent aspiration of foreign matter.[30]

Most cases of infective endocarditis involving oral microorganisms probably are caused by dental disease, mastication and oral hygiene procedures.

Valvular heart disease. The most important goal of dental therapy in patients with valvular heart disease is the need to prevent infective endocarditis. Dental procedures often cause a transient bacteremia that rarely lasts longer than 15 minutes,[32] but the bacteria may lodge on abnormal or damaged cardiac tissue, especially valves, which may result in endocarditis. The percentage of patients with endocarditis who have had recent dental treatment varies widely in the literature from 3 to 40 percent.[32-35]

Most cases of infective endocarditis involving oral microorganisms probably are caused not by dental treatment, but by dental disease, mastication and oral hygiene procedures.[32] Guntheroth[34] found that while dental extractions induced bacteremia in 40 percent of patients, normal mastication and tooth brushing induced bacteremias in 38 percent and 25 percent of patients, respectively.[34] He concluded that the exposure time to bacteremias during a one-month period was 1,000 times greater from routine chewing and tooth brushing than it was from a dental extraction.

Periodontal disease may predispose patients to an increased incidence of bacteremia, a fact implicit in the American Heart Association, or AHA, recommendations in regard to the prevention of bacterial endocarditis. These recommendations stress the importance of establishing and maintaining "the best possible oral health to reduce potential sources of bacterial seeding."[32] The recommendations further emphasize the role of the dentist in reducing periodontal inflammation through professional therapy and oral hygiene instruction. Because dental procedures that involve bleeding may induce a transient bacteremia, the AHA recommends antibiotic prophylaxis prior to "dental procedures known to induce gingival or mucosal bleeding, including professional cleaning."[32]

Patients at risk of developing infective endocarditis may undergo multiple courses of antibiotic therapy, increasing the risk of establishing resistant strains; alternatively, numerous procedures may be accomplished at the same appointment, if possible. It may be prudent to allow at least seven days to elapse between appointments or to select an alternate antibiotic regimen for appointments within this one-week period.[32] As a local adjunct to systemic antibiotic prophylaxis, a chlorhexidine mouthrinse has been recommended before dental procedures.

Anticoagulant therapy. Patients with prosthetic heart valves; other valvular disorders; or a history of myocardial infarction, CVA or thromboembolism frequently receive anticoagulant therapy consisting of coumadin derivatives, such as dicumarol and warfarin.[18,36]

Most patients maintain a therapeutic level of anticoagulation, resulting in a prothrombin time, or PT, of 1.5 to 2.0 times that of the laboratory control PT, although some patients may require greater levels of anticoagulation (> 2.0 times the control time).

Historically, the PT has been expressed as the ratio of the patient's actual PT (in seconds) to a control value that varies between laboratories. This PT ratio method of reporting PT is no longer used in most countries, and is being replaced in the United States by the International Normalized Ratio, or INR, method.[37] The INR, also known as the "corrected" PT ratio, is the PT value

that would have been determined had the test been done using the World Health Organization's standard thromboplastin, an international reference thromboplastin.[38] The major source of variability in reporting (due to differences in calculating) is the PT ratio to the international reference standard.

The dental health care provider may consult with the patient's physician before treatment (which can induce bleeding) to determine whether modification of anticoagulant therapy is indicated. In addition, drug interactions with warfarin and other similar agents are numerous, and these must be considered. Aspirin and other nonsteroidal anti-inflammatory drugs may dramatically increase the risk of warfarin-associated bleeding.[37,39,40] Tetracyclines may decrease vitamin K production, interfere with formation of prothrombin and increase anticoagulation.[41,42] Metronidazole may inhibit coumadin's metabolism, potentiating its anticoagulant effect, while penicillin may counteract coumadin's effect.[37]

Clinicians should alter anticoagulant therapy only in consultation with the patient's physician, since some people are more at risk of developing thrombus formation or hemorrhage than are others.[43]

Aspirin, an inhibitor of platelet aggregation, often is used to prevent thrombosis formation.[44] Because of its irreversible binding to platelets, the effect of aspirin lasts at least four to seven days. It generally is used in small doses of 325 milligrams or less and usually will not alter bleeding time significantly at this dose. However, higher doses may increase bleeding time and predispose the patient to develop postoperative bleeding. For these patients, aspirin therapy may be discontinued for several days before the dental procedure if treatment is expected to induce significant bleeding.

CONCLUSION

In May 2000, the public health community was alerted to the need to promote oral health by the first surgeon general's report on oral health. Although the precise mechanisms of interaction are not clear, sufficient evidence exists to conclude that oral lesions, especially advanced periodontic pathologies, place certain patients at increased risk of developing cardiovascular disease and stroke. These observations are leading dentists and physicians to interact more closely in caring for patients. In addition, a greater burden is being placed on the dental community to become more familiar with oral microbiology and the pharmacological approaches available to treat oral diseases that may have systemic implications.

The patient with cardiovascular disease may present a challenge to the dental health care provider, depending on the degree of hemodynamic compromise and the stability of his or her condition. Many of the dental treatment approaches used for these patients are based on consensus opinion established through years of experience and informed clinical judgment. Few of the treatment approaches are founded on controlled clinical trials that have assessed the effect of different treatment modalities on well-defined outcome criteria.

In many instances, such studies are limited by ethical or medicolegal considerations involved with placing patients at risk of developing systemic complications. Research also may be limited by the difficulty in obtaining study populations of adequate size for relatively rare disorders such as infective endocarditis. ■

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1. Oral health in America: a report of the surgeon general: executive summary. Rockville, Md.: National Institute of Dental and Craniofacial Research; 2000.
2. World Health Organization. The World Health Report 1995: bridging the gaps. Geneva: World Health Organization; 1995;16:377-85.
3. Umino M, Nagao M. Systemic diseases in elderly dental patients. Int Dent J 1993;43:213-8.
4. Mattila KJ, Nieminen MS, Valtonen VV, et al. Association between dental health and acute myocardial infarction. BMJ 1989;298:779-81.
5. Mattila KJ, Valle MS, Nieminen MS, Valtonen VV, Hietaniemi KL. Dental infections and coronary atherosclerosis. Atherosclerosis 1993;103:205-11.
6. Grau AJ, Buggle F, Ziegler C, et al. Association between acute cerebrovascular ischemia and chronic and recurrent infection. Stroke 1997;28:1724-9.
7. DeStefano F, Anda RF, Kahn HS, Williamson DF, Russell CM. Dental disease and risk of coronary heart disease and mortality. BMJ 1993;306:688-91.
8. Osler W. Diseases of the arteries. In: Osler W, ed. Modern medicine: Its practice and theory. Philadelphia: Lea & Febiger; 1908:429-47.
9. Haraszthy VI, Zambon JJ, Trevisan M, Zeid M, Genco RJ. Identifi-

cation of pathogens in atheromatous plaques. J Periodontol 2000;71:1554-60.
10. Genco, RJ, Glurich I, Haraszthy V. Overview of risk factors for periodontal disease and implications for diabetes and cardiovascular disease. Compend Contin Educ Dent 1999;19(1 supplement):40-5.
11. Ross R, Glomset J. The pathogenesis of atherosclerosis (first of two parts). N Engl J Med 1976;295:369-77.
12. Ross R, Glomset J. The pathogenesis of atherosclerosis (second of two parts). N Engl J Med 1976;295:420-5.
13. Matsuura H. The systemic management of cardiovascular risk patients in dentistry. Anesth Pain Control Dent 1993;2:49-57.
14. Council on Community Health, Hospital, Institutional, and Medical Affairs. Hypertension update: a survey of the literature of interest to dentists. 1989;118:645-6.
15. MacAfee KA 2nd, Chisdak B, Hersh EV Angina pectoris: diagnosis and treatment in the outpatient setting. Compendium 1993;14:892-900.
16. Findler M, Galili D, Meidan Z, Yakirevitch V, Garfundel AA. Dental treatment in very high risk patients with active ischemic heart disease. Oral Surg Oral Med Oral Pathol 1993;76:298-300.
17. McCarthy FM. Safe treatment of the post-heart-attack patient. Compendium 1989;10:598-604.
18. Shuman SK. A physician's guide to coordinating oral health and primary care. Geriatrics 1990;45(8):47-57.
19. Perusse R, Goulet JP, Turcotte JY. Contraindications to vasoconstrictors in dentistry, part I: cardiovascular diseases. Oral Surg Oral Med Oral Pathol 1992;74:687-91.
20. Knoll-Kohler E, Fortsch G. Pulpal anesthesia dependent on epinephrine dose in 2% lidocaine: a randomized controlled double-blind crossover study. Oral Surg Oral Med Oral Pathol 1992;73:537-40.
21. Meyer FU. Haemodynamic changes under emotional stress following a minor surgical procedure under local anesthesia. Int J Oral Maxillofac Surg 1987;16:688-94.
22. Levine E, Tzukert AA, Mosseri M, et al. Perioperative hemodynamic changes in ischemic heart disease patients undergoing dental treatment. Spec Care Dentist 1992;12(2):84-8.
23. Smith GN, Pashley DH. Periodontal ligament injection: evaluation of systemic effects. Oral Surg Oral Med Oral Pathol 1983;56:571-4.
24. Findler M, Garfunkel AA, Galili D. Review of very high-risk cardiac patients in the dental setting. Compendium 1994;15(1):58-66.
25. Farkas JA, Goebel WM. Assessing the risk of angina for dental therapy. Oral Surg Oral Med Oral Pathol 1984;58:253-6.
26. Luria MH, Debanne SM, Osman MI. Long-term follow-up after recovery from acute myocardial infarction: observations on survival, ventricular arrhythmias, and sudden death. Arch Intern Med 1985;145:1592-5.
27. Ruberman W, Weinblatt E, Frank CW, Goldberg JD, Shapiro S. Repeated 1-hour electrocardiographic monitoring of survivors of myocardial infarction at six-month intervals: arrhythmia detection and relation to prognosis. Am J Cardiol 1981;47:1197-204.
28. Cintron G, Medina R, Reyes AA, Lyman G. Cardiovascular effects and safety of dental anesthesia and dental interventions in patients with recent uncomplicated myocardial infarction. Arch Intern Med 1986;146:2203-4.
29. Gilbert GH, Minaker KL. Principles of surgical risk assessment of the elderly patient. J Oral Maxillofac Surg 1990;48:972-9.
30. Ostuni E. Stroke and the dental patient. JADA 1994;125:721-7.
31. Syrjanen J, Peltola J, Valtonen V, Iivanainen M, Kaste M, Huttunen JK. Dental infections in association with cerebral infarction in young and middle-aged men. J Intern Med 1989;225(3):179-84.
32. Dajani AS, Taubert KA, Wilson W, et al. Prevention of bacterial endocarditis: recommendations by the American Heart Association. JAMA 1997;277:1794-801.
33. Genco RJ, Grossi SG, Zambon JJ, Reynolds H, Ho A, Garrett S. Frequency of bacteremia following different modalities of periodontal treatment (abstract 842). J Dent Res 2001;80:141.
34. Guntheroth WG. How important are dental procedures as a cause of infective endocarditis? Am J Cardiol 1984;54:797-801.
35. Creighton JM. Dental care for the pediatric cardiac patient. J Can Dent Assoc 1992;58:201-7.
36. Martinowitz U, Mazar AL, Taicher S, et al. Dental extraction for patients on oral anticoagulant therapy. Oral Surg Oral Med Oral Pathol 1990;70:274-7.
37. Hirsh J, Dalen JE, Deykin D, Poller L. Oral anticoagulants: mechanism of action, clinical effectiveness, and optimal therapeutic range. Chest 1992;102:312S-26S.
38. Bussey HI. How to monitor the dosage of warfarin. Heart Dis Stroke 1993;2:388-92.
39. Wynn RL. Dental nonsteroidal anti-inflammatory drugs and prostaglandin-based drug interactions, part one. Gen Dent 1992;40(1):18-20.
40. Carr MM, Mason RB. Dental management of anticoagulated patients. J Can Dent Assoc 1992;58:838-44.
41. Fay JT, O'Neal R. Dental responsibility for the medically compromised patient. J Oral Med 1984;39:218-45.
42. Felder RS, Miller SB. Dental care of the polymedication patient. Dent Clin North Am 1994;38:525-36.
43. Scheitler LE, Hart N, Phillips G, Weinber JB. Hematologic and surgical management of the dental patient with plasminogen activator deficiency. Oral Surg Oral Med Oral Pathol 1988;66:680-2.
44. Kasco G, Terzhalmy GT. Acetylsalicylic acid and acetominophen. Dent Clin North Am 1994;38:633-44.