Cancer and Oral Care of the Patient

Cancer is a condition that is characterized by uncontrolled growth of aberrant neoplastic cells. Cancerous cells kill by destructive invasion of tissues, that is, by direct extension and spread to distant sites by metastasis through blood, lymph, or serosal surfaces. Malignant cells arise from genetic and acquired mutations, chromosomal translocations, and overexpression or underexpression of factors (oncogenes, growth factor receptors, signal transducers, transcription factors) that cause cells to lose their ability to regulate deoxyribonucleic acid (DNA) synthesis and the cell cycle. Cellular abnormalities of malignancy result in three common features: uncontrolled proliferation, ability to recruit blood vessels (i.e., neovascularization), and ability to spread. Cancer is a major public health problem in the United States and in other developed countries. Currently, one in four deaths in the United States is due to cancer

Epidemiology: Incidence and Prevalence

Each year, about 1.2 million new cases of cancer are diagnosed in the United States, and about 560,000 persons die of the disease. In 1998, for the fi rst time, the total number of new cancer cases and cancer death rates in the United States declined. However, when deaths are aggregated by age, cancer has surpassed heart disease as the leading cause of death for those younger than age 85.. Among men, cancers of the prostate, lung and bronchus, and colon and rectum account for more than 56% of all newly diagnosed cancers. Prostate cancer alone accounts for about 33% (234,460) of cases in men. On the basis of cases diagnosed between 1995 and 2001, an estimated 91% of new cases of prostate cancer are expected to be diagnosed at local or regional stages, for which 5-year relative survival approaches 100%.

Estimated new cases*

Males			Females		
Prostate	234,460	33%	Breast	212,920	31%
Lung and bronchus	92,700	13%	Lung and bronchus	81,770	12%
Colon and rectum	72,800	10%	Colon and rectum	75,810	11%
Urinary bladder	44,690	6%	Uterine corpus	41,200	6%
Melanoma of the skin	34,260	5%	Non-Hodgkin lymphoma	28,190	4%
Non-Hodgkin lymphoma	30,680	4%	Melanoma of the skin	27,930	4%
Kidney and renal pelvis	24,650	3%	Thyroid	22,590	3%
Oral cavity and pharynx	20,180	3%	Ovary	20,180	3%
Leukemia	20,000	3%	Urinary bladder	16,730	2%
Pancreas	17,150	2%	Pancreas	16,580	2%
All sites	**720,280**	**100%**	**All sites**	**629,510**	**100%**

Estimated deaths

Males			Females		
Lung and bronchus	90,330	31%	Lung and bronchus	72,130	26%
Colon and rectum	27,870	10%	Breast	40,970	15%
Prostate	27,350	9%	Colon and rectum	27,300	10%
Pancreas	16,090	6%	Pancreas	16,210	6%
Leukemia	12,470	4%	Ovary	15,310	6%
Liver and intrahepatic bile duct	10,840	4%	Leukemia	9,810	4%
Esophagus	10,730	4%	Non-Hodgkin lymphoma	8,840	3%
Non-Hodgkin lymphoma	10,000	3%	Uterine corpus	7,350	3%
Urinary bladder	8,990	3%	Multiple myeloma	5,630	2%
Kidney and renal pelvis	8,130	3%	Brain and other nervous system	5,560	2%
All sites	**291,270**	**100%**	**All sites**	**273,560**	**100%**

Figure 26-1. Ten leading cancer types of estimated new cancer cases and deaths, by gender, United States, 2006. This indicates the most common cancers that were expected to occur in men and women in 2006. Among men, cancers of the prostate, lung and bronchus, and colon and rectum account for more than 56% of all newly diagnosed cancers. Prostate cancer alone accounts for about 33% (234,460) of incident cases in men. On the basis of cases diagnosed between 1995 and 2001, an estimated 91% of new cases of prostate cancer were expected to be diagnosed at local or regional stages, for which relative 5-year survival approaches 100%. (From Jamal A, Siegel R, Ward E, et al. Cancer statistics, 2006. CA Cancer J Clin 2006;56:106-130. © 2006 The American Cancer Society.)

CLINICAL PRESENTATION

Signs and Symptoms

Cancer often presents as a palpable mass that increases in size over time. Preceding development of the tumor, subtle changes occur that are dependent on the anatomic site involved and the cell type of origin. Initial features may include a change in surface color, a lump, enlarged lymph nodes, or altered organ function. Symptoms include pain and paresthesia.

Tumors permitted to increase in size often result in a reddened epithelial surface (caused by increased blood vessels) that ulcerates.

Staging

Most cancers are assigned a stage (I, II, III, or IV) by the medical team on the basis of the size of the tumor and how far it has spread. Generically speaking, Stage I is localized and is confi ned to the organ of origin. Stage II is regional in nearby structures. Stage III is extensive beyond the regional site, crossing several tissue planes, and Stage IV is widely disseminated. This system often is supplemented by detailed and specifi c staging systems developed for particular cancers and generally does not apply to leukemia because leukemia is a disease of the blood cells that does not usually form a solid mass or tumor. The TNM system is frequently employed, whereby *T* stands for tumor size, *N* represents nodal involvement, and *M* indicates metastases. The prognosis of patients depends in large part on the stage of disease at the time of diagnosis.

Laboratory Findings

The diagnosis of cancer is based on microscopic examination of an adequate sample of tissue taken from the lesion. Tissue can be obtained by cytologic may be subjected to flow cytometry, chromosomal analyses, in situ hybridization, or other molecular procedures for identifi cation of specifi c cancer markers, ploidy, and DNA analysis. Serum tumor markers such as carcinoembryonic antigen (CEA) for colorectal carcinoma (CA 15-3 or CEA in breast cancer and CA 125 for ovarian cancer) have low sensitivity for the detection of earlystage cancers but are useful in monitoring disease progression and response to therapy smear, needle biopsy, or incisional or excisional biopsy. Cells

.MEDICAL MANAGEMENT

Treatment strategies for patients with cancer are based on elimination of fast multiplying cancer cells without killing of the host. Therapeutic modalities include surgery; radiation (external beam or implants); cytotoxic, chemotherapeutic, and endocrine drugs; and possibly, stem cell or bone marrow transplantation

.

TABLE 26-2
Chemotherapy Drugs of Choice for Common Cancers

Cancer	Drugs of Choice
Breast	*Risk reduction:* Tamoxifen
	Adjuvant: Doxorubicin + cyclophosphamide ± fluorouracil followed by paclitaxel; cyclophosphamide + methotrexate + fluorouracil; tamoxifen for receptor positive and hormone responsive
	Metastatic: Doxorubicin + cyclophosphamide ± fluorouracil; cyclophosphamide + methotrexate + fluorouracil
	Tamoxifen or toremifene for receptor positive and/or hormone responsive
	Paclitaxel + trastuzumab for tumors that overexpress HER2 protein
Cervix	*Locally advanced:* Cisplatin ± fluorouracil
	Metastatic: Cisplatin; ifosfamide with mesna; bleomycin + ifosfamide with mesna + cisplatin
Colorectal	*Adjuvant:* Fluorouracil + leucovorin
	Metastatic: Fluorouracil + leucovorin + irinotecan
Head and neck	Cisplatin + fluorouracil or paclitaxel
Kaposi's sarcoma	Liposomal doxorubicin or daunorubicin; doxorubicin + bleomycin + vincristine
Leukemia and lymphoma	See Table 24-2
Liver	Hepatic intra-arterial floxuridine, cisplatin, doxorubicin or mitomycin
Lung	
Non–small cell Small cell	Paclitaxel + cisplatin or carboplatin; cisplatin + vinorelbine; gemcitabine + cisplatin; cisplatin or carboplatin + etoposide (PE)
Melanoma	*Adjuvant:* Interferon alfa
	Metastatic: Dacarbazine
Multiple myeloma	Melphalan or cyclophosphamide + prednisone; vincristine + doxorubicin + dexamethasone (VAD)
Prostate	Gonadotropin-releasing hormone (GnRH) agonists (leuprolide or goserelin) ± antiandrogen (flutamide, bicalutamide, or nilutamide)
Renal	Interleukin-2

Modified from Drugs for Cancer. Med Lett Drugs Ther 2000;42:83-92.

Treatment Planning Modifications

Pretreatment Evaluation and Considerations. The dentist should be aware of the type of treatment selected for the patient and whether the cancer stands a good chance of being controlled. A patient who is to receive palliative therapy may not want replacement of missing teeth; however, this patient must be free of active dental disease that could worsen during cancer therapy. By contrast, a patient who has cancer in Stage I or II and no evidence of regional spread can be managed for future dental care as a normal patient, except that the dentist should consider recalling this patient for more frequent examinations for evidence of metastases, recurrence of the lesion, or presence of a new cancer. This is particularly important for

patients with oral cancer who are at increased risk for a second primary cancer in the respiratory system, upper digestive tract, or oral cavity. The risk for a second oral cancer in smokers whose habits remain unchanged is about 30%, as compared with 13% for those who quit. A pretreatment oral evaluation is recommended for all patients with cancer before cancer therapy is initiated to attain the following:

• Rule out oral disease that may worsen during cancer therapy.

• Provide a baseline for comparison and monitoring of sequelae of radiation and chemotherapy damage.

• Detect metastatic lesions.

• Minimize oral discomfort during cancer therapy.

This evaluation should include a thorough clinical and radiographic examination and review of blood laboratory findings. Edentulous regions should be surveyed so that impacted teeth, retained root tips, and latent osseous disease that may worsen during immunosuppressive cancer therapy can be ruled out. A panoramic fi lm is acceptable; however, supplemental bitewing and Periapical fi lms may be required for adequate visualization of dental and osseous structures. Pretreatment care should include oral hygiene instructions, encouragement of a noncariogenic diet, calculus removal, prophylaxis and fl uoride treatment, and elimination of all sources of irritation and infection. In children undergoing chemotherapy, mobile primary teeth and those expected to be lost during chemotherapy should be extracted, and gingival opercula should be evaluated for surgical removal to prevent entrapment of food debris. Orthodontic bands should be removed before chemotherapy is begun. If head and neck radiation and immunosuppressive chemotherapy are scheduled, the following recommendations should be considered:

• Reduction in radiation exposure to noncancerous tissues (salivary glands) with lead-lined stents, beamsparing procedures, or the use of anticholinergic (biperiden) or parasympathomimetic (pilocarpine HCl [Salagen]) drugs during and after radiotherapy should be discussed with the radiation oncologist and the patient.

• Nonrestorable teeth with poor or hopeless prognosis, acute infection, or severe periodontal disease that may predispose the patient to complications (e.g., sepsis, osteoradionecrosis) should be extracted; sharp, bony edges

trimmed and smoothed; and primary closure obtained. Chronic infl amatory lesions in the jaws and potential sources of infection should be examined and treated or eradicated before radiation or chemotherapy. Adequate time for wound healing should be provided for extractions and surgical procedures before radiation therapy or myelosuppressive chemotherapy is induced

Symptomatic nonvital teeth should be endodontically treated at least 1 week before initiation of head and neck radiation or chemotherapy. However, dental treatment of asymptomatic teeth even with periapical involvement may be delayed. One should prioritize treatment of infections and extractions, periodontal care, and treatment of irritations before providing treatment of carious teeth, root canal therapy, and replacement of faulty restorations. Temporary restorations may be placed and some types of treatment (e.g., cosmetic, prosthodontic, endodontic) can be delayed when time is limited. To optimize oral health and reduce the risk of oral complications such as mucositis and infection, tooth scaling and prophylaxis should be provided before cancer therapy is initiated. Removable prosthodontic appliances should be removed during therapy. Patients who will be retaining their teeth and undergoing head and neck radiation therapy must be informed about problems associated with decreased salivary function, which include xerostomia, the increased risk of oral infection, including radiation caries, and the risk for osteoradionecrosis.

Dental preparation of the patient with cancer who is about to undergo surgical treatment is not as critical as for the patient about to undergo head and neck radiation and chemotherapy. However, active oral infection should be treated, teeth that are broken down should be removed, and teeth that may be used for retention of a prosthetic appliance can be restored as needed. The better the dental health of the patient, the lower is the risk that dental infection may complicate the healing process. For the patient with oral cancer, the dentist should consider consultation with the maxillofacial prosthodontist, so that proper coordination of the patient's dental and tooth replacement needs can be ensured during the presurgical and postsurgical phases of treatment.

Oral Care During Cancer Therapy. The oral health of the patient with cancer must be maintained during cancer therapy because oral complications

develop in a significant number of patients (more than 400,000) who receive cancer radiation and chemotherapy. Oral infections and potential problems should be eliminated before cancer therapy is provided to patients who are undergoing head and neck radiation and inpatient chemotherapy; routine dental care should be delayed until after cancer therapy has been completed. Patients given outpatient chemotherapy require provision of dental treatment at appropriate times between cycles. This section discusses oral complications that occur during and after chemotherapy and irradiation of head and neck structures that may require modifications in oral health care management.

Management of Complications of Radiation and Chemotherapy. General management considerations for radiation and chemotherapy include Acute toxicity reactions are seen during and immediately after radiation and chemotherapy. Acute toxicities are directly proportionate to the amount of radiation or cytotoxic drug to which tissues are exposed and are more evident in rapidly dividing cells. Delayed toxicities may occur several months to years after radiation therapy is provided. Radiation therapy induces cell necrosis, microvascular damage, and parenchymal and stromal damage. Production of oxygen-free radicals from ionizing radiation is one of the leading causes of cell damage. Cells that have rapid turnover are more susceptible to damage. For this reason, hypoxic cells and slowly replicative cells are more resistant to radiation than are those that are well oxygenated and mitotically active.

Most chemotherapeutic agents cause alopecia, breakdown of the mucous membranes (mucositis), depression of the bone marrow (infection, bleeding, anemia), gastrointestinal changes (diarrhea, malabsorption), and altered nutritional status; they may also induce cardiac and pulmonary dysfunction. Bone marrow suppression and mucositis associated with chemotherapy are predictable, dose dependent, and usually manageable. Patients receiving chemotherapy may manifest erythema and ulceration of the oral mucosa, infection of the surrounding tissues, excessive bleeding with minor trauma, xerostomia, anemia, and neurotoxicity

Mucositis. Mucositis, infl ammation of the oral mucosa, results from the direct cytotoxic effects of radiation or antineoplastic agents on rapidly

dividing oral epithelium and the upregulation of proinflammatory cytokine expression (see Appendix C). Mucositis occurs in up to 40% of patients who are undergoing chemotherapy and is often a dose-limiting factor for chemotherapy and a cause of dose interruption in radiation therapy. It develops more often in nonkeratinized mucosa (buccal and labial mucosa, ventral tongue) and adjacent to metallic restorations by the end of the second week of radiation therapy (if the dose is 200 cGy per week). Mucositis develops most often between the seventh and fourteenth days after chemotherapy is provided (especially VP16, epotoside, methotrexate) when effects of the drugs produce an extremely low WBC count (nadir). It generally subsides 1 to 2 weeks after completion of treatment. Young patients with cancer who have higher division rates have a greater prevalence of chemotherapy-induced mucositis than do older patients with cancer. Mucositis produces red, raw, and tender oral mucosa with epithelial sloughing similar to that seen in a severe oral burn. Oral ulcerations may result from breakdown of the epithelial barrier and from infection by viral, bacterial or fungal organisms. Patients typically report ulceration, pain, dysphagia, loss of taste, and difficulty in eating, which increases the risks for oral and systemic infection. If the major salivary glands have been irradiated, xerostomia. may occur after the onset of mucositis. Complications of mucositis and xerostomia make the patient extremely uncomfortable and increase the diffi culty associated with maintaining proper nutritional intake.. During this acute phase, the goals are to maintain mucosal integrity and to promote oral hygiene. Patients are generally treated in the following ways: • A bland mouth rinse (salt and soda water) to keep ulcerated areas as clean as possible

• Topical anesthetics (viscous lidocaine 0.5%) and/or an antihistamine solution (benzydamine HCl [Tantum rinse], diphenhydramine [Benadryl], promethazine [Phenergan]) that can provide pain control or that may be combined with milk of magnesia (Maalox), Kaopectate, or sucralfate to serve as a coating agent (for protection of ulcerated areas)

• Antimicrobial rinses such as chlorhexidine • Anti-infl ammatory agents (kamillosan liquidim or topical steroids [dexamethasone])

• Adequate hydration

• A diet consisting of soft foods, protein, and vitamin supplementation at therapeutic levels
• Oral lubricants and lip balms containing a water base, a beeswax base, or a vegetable oil base (e.g., Surgi-Lube)
• Humidifi ed air (humidifi ers or vaporizers)
• Avoidance of alcohol, tobacco, and irritating foods (e.g., citrus fruits and juices, hot, spicy dishes. Dentures should not be worn until the acute phase of mucositis has resolved. Dentures should be cleaned and soaked with an antimicrobial solution daily for the prevention of infection.. Secondary infections. During radiation and chemotherapy, patients are prone to secondary infection. Because of the quantitative decrease that occurs in actual salivary fl ow, and because of compositional alterations in saliva, several organisms (bacterial, fungal, and viral) may opportunistically infect the oral cavity. Moreover, if the patient is immunosuppressed as the result of chemotherapy, and if the WBC count falls to below 2000 cells/mm3, the immune system is less able to manage these infections. Opportunistic infections are also common in patients who receive chemotherapy and broad-spectrum antibiotics. The organism that most frequently opportunistically infects the oral cavity in individuals undergoing cancer therapy (who have hyposalivation and immunosuppression) is *Candida albicans.* Cytologic study, potassium hydroxide (KOH) staining, microscopic examination, and *Candida*-specifi c cultures are often performed to establish a defi nitive diagnosis. Candidal infections may produce pain, burning, taste alterations, and intolerance to certain foods, especially acidic citrus fruits or spicy foods. They present clinically in four different forms, ranging from denuded epithelium to hyperplastic lesions. During cancer therapy, the most common type is pseudomembranous candidiasis, which produces white plaques that are easily scraped off, leaving behind tiny petechial hemorrhages. Slightly less prevalent is the erythematous, atrophic form, which manifests as a red patch accompanied by a burning sensation . Other forms of candidiasis (i.e., angular cheilosis and the less common hypertrophic form, which presents as a thick, white plaque that cannot be scraped off) are more commonly detected in patients with chronic hyposalivation. Candidiasis is best managed with the use of topical oral antifungal agents. These include nystatin (oral suspension

100,000 international units [IU]/mL 4 to 5 times daily), clotrimazole (Mycelex lozenges 10 mg 5 times day), and other preparations (e.g., vaginal topical antifungal agents). Prophylactic use of antifungal agents may be required in patients undergoing chemotherapy who have frequent recurrent infections. Ketoconazole (Nizoral), fl uconazole (Difl ucan), or itraconazole (Sporanox) may be used if systemic therapy is warranted, or if patients develop unusual oral fungal infections (Torulopsis, aspergillosis, mucormycosis) or fungal septicemia (possibly from the oral cavity). Alternatively, the physician may place the patient on granulocyte (monocyte) colony-stimulating factor (G[M]-CSF) that elevates the neutrophil count to normal levels and can contribute to resolution of the lesions. Bacteria or viruses may be the cause of other secondary infections. Oral bacterial infections may appear with typical signs of swelling, erythema, and fever. Alternatively, these features may be masked in patients with lowWBC counts due to chemotherapy. In immunosuppressed patients, a shift occurs in the oral fl ora to Gram-negative organisms that normally inhabit the gastrointestinal or respiratory tract, such as *Pseudomonas, Klebsiella, Proteus, Escherichia coli,* or *Enterobacter.* The most common presentation is an oral ulceration. Thus, dentists should culture all nonhealing oral ulcerations in such patients, and these specimens should be sent for diagnosis and antibiotic sensitivity testing. If a bacterial infection is suspected, appropriate antibacterial therapy should be initiated. Antimicrobial sensitivity data are important for the selection of an effective antibiotic when the clinical course shows little or no improvement over several days. Recurrent herpes simplex virus (HSV) eruptions occur often during chemotherapy if antiviral agents are not prophylactically prescribed. They are infrequent during radiation therapy. Herpes recurrences in patients with cancer who are undergoing chemotherapy tend to be larger and to take longer to heal than herpetic lesions found in nonimmunocompromised patients . Antiviral agents (e.g., acyclovir, famciclovir, valacyclovir) are recommended prophylactically for HSV antibody–positive patients who are undergoing chemotherapy, to prevent recurrence. A daily dose of at least 1 g acyclovir/equivalent is needed to suppress HSV recurrences. Because these ulcers mimic the appearance of aphthous and may occur on nonkeratinized mucosa in immunocompromised patients with cancer, culture or use of an

enzyme-linked immunoassay is important for accurate diagnosis. Laboratory tests also help to distinguish the infection from other oral herpes virus infections such as varicella zoster and cytomegalovirus that can occur in these patients. Antiviral sensitivity testing should be considered for patients with unresolving or extensive infection and for those in poor general health. Bleeding. Patients with cancer who undergo total body irradiation or high-dose chemotherapy, or who have bone marrow involvement due to disease, are also susceptible to thrombocytopenia. Gingival bleeding and submucosal hemorrhage as a result of minor trauma (e.g., tongue biting, toothbrushing) can occur when the platelet count drops to below 50,000 cells/mm3. Palatal petechiae, purpura on the lateral margin of the tongue, and gingival bleeding/oozing are common features. Gingival hemorrhage is aggravated by poor oral hygiene. When gingival tissues bleed easily and the platelet count is severely reduced, the patient should avoid vigorous brushing of the teeth and should begin using softer devices such as toothettes or gauze wrapped around a finger and dampened in warm water or an antimicrobial solution (chlorhexidine in water, prepared by the pharmacist). During this stage, patients should be instructed not to use toothpicks, water-irrigating appliances, or dental fl oss. To control gingival bleeding, local measures, such as pressure applied with a gelatin sponge along with thrombin or microfi brillar collagen placed over the area or an oral antifi brinolytic rinse (aminocaproic acid [Amicar] syrup, 250 mg/mL) placed in a soft vinyl mouthguard, can be used to control bleeding. If local measures fail, medical help should be obtained and platelet transfusion considered. Neural and chemosensory changes. Many patients who are receiving radiation therapy experience a diminished sense of taste, probably as a result of damage to the microvilli of the taste cells. Patients who are given chemotherapeutic agents complain of bitter tastes, unpleasant odors, and conditioned aversions to foods. To minimize sensory stimulation, the dentist should avoid wearing cologne or perfume when in contact with patients who are undergoing radiation/chemotherapy. In most patients, the ability to taste is restored within 3 to 4 months after completion of radiotherapy. In cases of chronic loss of taste, zinc supplementation has been reported to improve taste perception. Silverman29 recommends 220 mg of zinc 2 times per day for patients with severe chronic loss of taste. However, currently, no effective

treatment is available that completely restores damaged taste. Neurotoxicity is an adverse effect of chemotherapeutic agents, particularly vincristine and vinblastine. Although this complication commonly arises in the peripheral nerves, patients may experience odontogenic pain that mimics irreversible pulpitis caused by these agents. Pain is more common in the molar region and can be bilateral. Proper diagnosis requires the clinician to be familiar with the chemotherapeutic drug regimen and is aided by the absence of clinical or radiographic abnormalities.

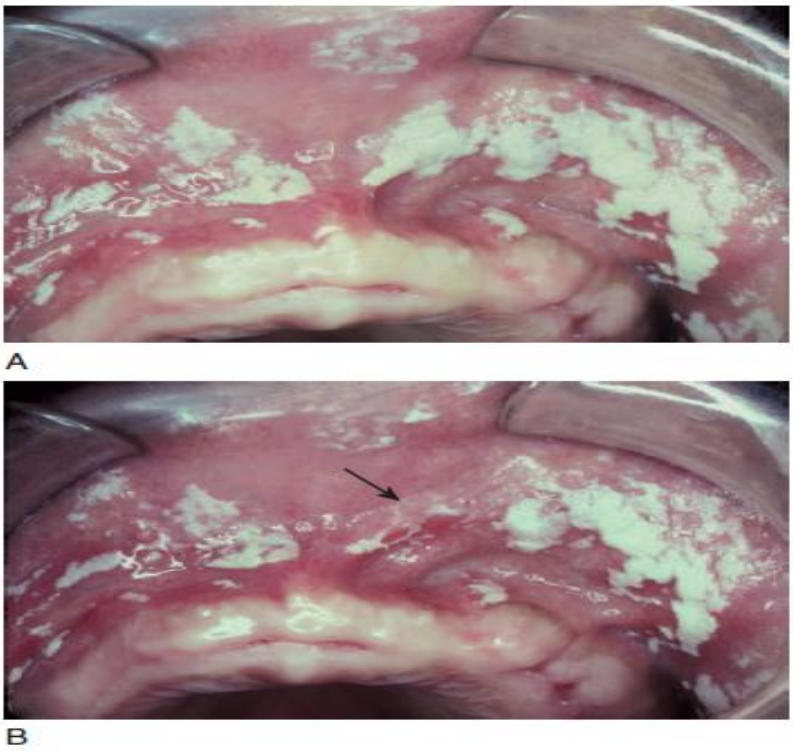
Post–Cancer Treatment Management

After cancer therapy has been provided, consultation with the physician is recommended to determine whether the patient is cured, in remission, or completing palliative care. If cancer therapy has been completed and remission or cure is the outcome, the patient with cancer should be placed on an oral recall program. Usually, the patient is seen once every 1 to 3 months during the fi rst 2 years and at least every 3 to 6 months thereafter. After 5 years, the patient should be examined at least once per year.

This recall program is important for the following reasons:

• A patient with cancer tends to develop additional lesions
• Latent metastases may occur
• Initial lesions may recur
• Complications related to therapy can be detected and managed

The usual long-term complications associated with cancer and its therapy include chronic xerostomia, loss of taste, altered bone, and related problems. Recall appointments are also important to ensure that the dentate patient continues to maintain good oral hygiene (including daily brushing, flossing, and continued use of daily fluoride gel applications); detection of oral soft tissue and hard tissue disease can occur early, before inflammation and infection involve the underlying bone, leading to necrosis. Patients who have completed palliative care should be afforded preventive oral care and dental procedures that they desire and can withstand.



A

B

Figure 26-17. Pseudomembranous candidiasis. **A,** Classic "curdled milk" appearance of the oral lesions of pseudomembranous candidiasis. This patient had no apparent risk factors for candidiasis development. **B,** Removal of one of the pseudomembranous plaques *(arrow)* reveals a mildly erythematous mucosal surface. (From Allen CM, Blozis GG: Oral mucosal lesions. In Cummings CW, Fredrickson JM, Harker LA, et al (eds): Otolaryngology: head and neck surgery, ed 3, St. Louis, 1998, Mosby.)

BOX 26-12

Recommendations for Invasive Oral Procedures in the Cancer Patient Undergoing Chemotherapy in an Outpatient Setting

Provide routine care when
- The patient feels best—generally, 17 to 20 days after chemotherapy
- Granulocyte count* >2000 cells/mm^3
- Platelet count*† >50,000 cells/mm^3

*Consultation with a physician is recommended when values are lower than indicated here, and there is a need for antibiotic prophylaxis.
†Platelet values lower than 50,000 may cause significant bleeding.

Hyposalivation and Its Sequelae. Salivary gland tissue is moderately sensitive to radiation damage. Because of this, acinar tissue that is within the fi eld of radiation can be permanently damaged during head and neck radiation therapy, resulting in hyposalivation. The degree of hyposalivation that occurs is directly related to the radiation fi eld and dose (i.e., the dose delivered to the major salivary glands) and to baseline salivary function. Dosages in excess of 3000 cGy are the most damaging, especially if shielding or medication is not provided to the patient during radiation. Irradiated salivary glands become dysfunctional owing to acinar atrophy, vascular alterations, chronic infl ammation, and loss of salivary parenchymal tissue. Usually, a 50% to 60% reduction in salivary fl ow occurs during the fi rst week after irradiation therapy is provided. After radiation therapy has been given, saliva is reduced in volume and altered in consistency, pH, and immunoglobulin concentration. It becomes mucinous, thick, sticky, and ropy because serous acini are more sensitive than mucous acini to radiation. Unfortunately, pathologic changes often progress several months after radiotherapy has ceased, and radiationinduced salivary gland damage and dysfunction are permanent. In most cases, no salivary gland function is recovered.

The direct effects of hyposalivation include extreme dryness of the oral mucosa. Of major signifi cance are the discomfort, inconvenience, and substantial diminution of quality of life that accompany oral dryness.

Clearly, saliva is an important host defense mechanism against oral disease, and it serves a variety of important functions in the oral cavity. In a healthy mouth, copious saliva containing essential electrolytes, glycoproteins, immunoglobulins, hydrolytic enzymes (amylase), antimicrobial enzymes, and a number of other important factors continually lubricates and protects the oral mucosa. Saliva in normal quantities and composition serves to cleanse the mouth, clear potentially toxic substances, regulate acidity, buffer decalcifying acids, neutralize bacterial toxins and enzymes, destroy microorganisms, and remineralize enamel with inorganic elements (e.g., calcium, phosphorus), thus maintaining the integrity of the teeth and soft tissues. When the normal environment of the oral cavity is altered because of a decrease in or total absence of salivary fl ow or because of alterations in salivary composition, a healthy mouth becomes susceptible to painful deterioration and decay. Dry, atrophic, and fi ssured oral mucosa and soft tissues usually result from the hyposalivary condition, along with accompanying ulcers and desquamation,opportunistic bacterial and fungal infections, infl amed and edematous tongue, caries, and periodontal disease. Extreme diffi culty in lubricating and masticating food (sticking to the tongue or hard palate) and in swallowing food (dysphagia) is common; this is among the most devastating and potentially most systemically damaging manifestations of hyposalivation in these individuals. Additionally, lack of or altered taste perception (i.e., hypogeusia or dysgeusia) and tolerance for certain acidic foods (e.g., citrus fruits, acetic acid, vinegar) are substantially altered in these individuals. As a result, nutritional intake may be impaired. Manifestations of salivary hypofunction in patients who have undergone irradiation therapy for head and neck cancer include severe xerostomia (less than 0.2 mL/ min unstimulated salivary fl ow), mucositis, cheilitis, glossitis, fi ssured tongue, glossodynia, dysgeusia, dysphagia, and a severe form of caries called *radiation caries*. Radiation caries is estimated to occur 100 times more often in patients who have received head and neck radiation than in normal individuals. It can progress within months, advancing toward pulpal tissue and resulting in periapical infection that extends to surrounding irradiated bone. Extensive infection and necrosis may tive. A gel form of artifi cial saliva that provides longlasting relief, especially at night, is Oral Balance. This contains two antimicrobial enzymes (lactoperoxidase and

glucose oxidase) that normally are found in saliva. Patients should be encouraged to drink plenty of water and other fl uids, with the exception of diuretics such as coffee or tea. Ethanol and tobacco should be avoided or minimized because these dry the oral mucosa. Also, post– radiation treatment patients who sip drinks constantly to keep the oral mucosa moist should avoid sipping drinks that contain a fermentable carbohydrate or carbonic acid because exposed cementum and dentin break down rapidly (in less than 6 months), resulting in radiation caries. Sugarless mints, candies, and chewing gum are benefi cial in producing some additional moisture. Considerable research has been performed on various sialogogue drugs such as pilocarpine HCl (Salagen), anethole trithione (Sialor), and, recently, cevimeline (Evoxac). Pilocarpine is the prototype parasympathomimetic drug that has been derived from the pilocarpus plant. It is an alkaloid, muscarinic/cholinergic agonist that is known to stimulate smooth muscle and exocrine secretions. Pilocarpine has been extensively tested in safety and effi cacy trials, and it appears to be very promising as a sialogogue. Parasympathomimetic drugs appear to be effective for stimulating salivary fl ow in most patients who have some residual salivary acinar function. However, certain adverse effects occur, and patients have to be carefully screened (i.e., for cardiovascular disease, diabetes, concomitant medications) before being placed on these drugs. Of particular note is that approximately 50% of patients who use pilocarpine and experience increased salivary fl ow notice symptomatic improvement in their dry mouth. Although the drug promotes salivary fl ow and provides endogenous benefi cial constituents to the oral cavity, patients may need adjunctive artifi cial salivas to feel more comfortable/

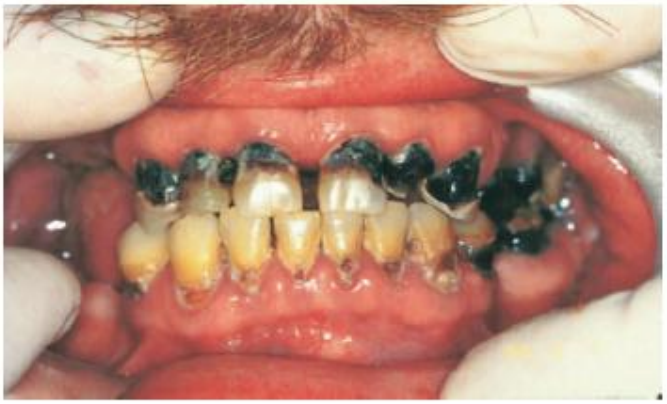


Figure 26-19. Note the extensive cervical caries in a patient who received radiotherapy. (Courtesy R. Gorlin, Minneapolis, Minn.)

Fungal Infection. Opportunistic infection with *C albicans* is prevalent in postirradiation patients, with more than 80% of these individuals exhibiting infection with the fungus if proper diagnostic testing is used (see Secondary Infections, earlier).

Tooth Sensitivity. During and after radiotherapy, the teeth may become hypersensitive; this event may be related to decreased secretion of saliva and the lowered pH of secreted saliva. Topical application of a fl uoride gel should be of benefi t in reducing these symptoms.

Muscle Trismus. Radiation therapy of the head and neck can cause damage to the vasculature of muscles (obliterative endoarteritis) and thus trismus of the masticatory muscles and joint capsule. To minimize the effects of radiation on muscles around the face and muscles of mastication, a mouth block should be placed when the patient is receiving external beam irradiation. The patient also should perform daily stretching exercises to improve trismus and should apply warm, moist heat. One exercise requires the patient to place a given number of tongue blades inside the mouth at least 3 times a day for 10- minute intervals. With a slow increase in the number of tongue blades, muscle stretching occurs and improved function ensues.

Prosthodontics. Patients should avoid wearing their dentures during the fi rst 6 months after completion of radiotherapy because mild trauma to the

altered mucosa can result in ulceration and possible necrosis of underlying bone (see Osteoradionecrosis, later). Once patients start to wear their dentures, they must be told to come to the dentist if any sore spots develop, so dentures can be adjusted. Ill-fi tting dentures should be replaced by new ones. In severe cases of chronic xerostomia, a small amount of petrolatum can be applied to the mucosal surface of the denture to enhance adhesion. Implants may be placed 12 to 18 months after radiation therapy has been provided, but clinician knowledge of tissue irradiation fi elds, degree of healing, and vascularity of the region is required because, for example, implants placed in the maxilla and the anterior mandible present less of a risk for osteoradionecrosis than those placed in the posterior mandible.

Osteoradionecrosis. Osteoradionecrosis (ORN) is a condition that is characterized by exposed bone that fails to heal (present for 6 months) after high-dose radiation to the jaws. ORN results from radiation-induced changes (hypocellularity, hypovascularity, and ischemia) in the jaws. Most cases result from damage to tissues overlying the bone rather than from direct damage to the bone. Accordingly, soft tissue necrosis usually precedes ORN and is variably present at the time of diagnosis. Risk is greatest in posterior mandibular sites for patients whose jaws have been treated with in excess of 6500 cGy, who continue to smoke, and who have undergone a traumatic (e.g., extraction) procedure. Risk is greater for dentate patients than for edentulous patients, and periodontal disease enhances risk. Nonsurgical procedures that are traumatic (e.g., curettage) or that cause a reduction in blood supply to the region (e.g., use of vasoconstrictors) can result in ORN. Spontaneous ORN also occurs. This risk continues throughout a patient's lifetime.If the dentist is unsure of the amount of radiation that was received and if invasive procedures are planned, the radiation oncologist should be contacted to determine the total dose given to the head and neck region before care is initiated. Clinicians should be aware that risk of ORN increases with increasing dose to the jaws (e.g., 7500 cGy presents a greater risk than 6500 cGy). Patients determined to be at risk should be provided appropriate preventive measures. Protocols to reduce the risk of ORN include selection of endodontic therapy over extraction, use of nonlidocaine local anesthetics that contain no or low concentrations of epinephrine, atraumatic surgical procedures (if surgery is necessary), prophylactic

antibiotics plus antibiotics during the week of healing (penicillin VK for 7 days), and hyperbaric oxygen administered before invasive procedures are performed. Hyperbaric oxygen involves sequential daily dives under 2 atmospheres of oxygen pressure in a chamber. The use of prophylactic antibiotics to prevent infection after surgical procedures in post–radiation treatment patients minimizes bacterial invasion of the surgical site. However, the effectiveness of such coverage may be greatly reduced by altered blood fl ow to the affected bone. The dentist should be aware that reduction in blood fl ow after radiotherapy is much greater in the mandible than in the maxilla because of the limited source Figure 26-20. Osteoradionecrosis. Exposed necrotic bone in the posterior mandible edentulous ridge of a patient who previously received radiation therapy to the head and neck region. and lack of collateral circulation; this accounts for the greater frequency and severity of ORN in the mandible. The use of hyperbaric oxygen treatment at the time of extraction is gaining support but is costly and cannot be repeated later with the same effect. Once necrosis occurs, conservative management usually is indicated. Exposed bone should be irrigated with a saline or antibiotic solution, and the patient should be directed to use oral irrigating devices to clean the involved area. However, extreme pressures should be avoided when these devices are prescribed. Bony sequestra should be removed to allow for epithelialization. If swelling and suppuration are present, broadspectrum antibiotics are used. Severe cases benefi t from hyperbaric oxygen treatment (60- to 90-minute dives 5 days per week, for a total of 20 to 30 dives). Cases that do not respond to conservative measures may require surgical resection of involved bone.

Bisphosphonate-Associated Osteonecrosis. As was mentioned previously, bisphosphonate-associated osteonecrosis (BON) is potentially a very serious oral complication of cancer therapy. In patients who develop BON spontaneously, the most common initial complaints are the sudden presence of intraoral discomfort and the presence of roughness that may progress to traumatization of oral soft tissues surrounding the area of necrotic bone. Therefore, the diagnosis of BON is based on the medical and dental history of each patient, as well as on the observation of clinical signs and symptoms of this pathologic process.

Treatment strategies that would yield consistent resolution and healing of BON have not yet been developed. In fact, many cases have had poor outcomes in spite of therapy and have progressed to extensive dehiscence and exposure of bone. Treatment strategies have included local surgical debridement, bone curettage, local irrigation with antibiotics, and hyperbaric oxygen therapy. However, none of these therapeutic modalities has proved successful. Therefore, the inability to manage lesions of BON compromises the oncologic, nutritional, and oral management of affected patients. Prevention of this condition is of paramount importance for these patients, so that they can receive the anticancer therapies so necessary for the best possible outcome of their neoplastic disease.

Carotid Atheroma. Patients who have received neck irradiation (more than or equivalent to 45 Gy) are more likely to develop carotid artery atheroma (calcifi ed atherosclerotic plaque) after treatment than are risk-matched control patients who have not been irradiated. These lesions may be detected by panoramic radiography and represent a risk factor for stroke that warrants referral of the patient to a physician for evaluation.

Recommendations for Preventing Osteoradionecrosis in the Head and Neck–Irradiated Patient

1. Extract teeth with questionable and hopeless prognosis at least 2 weeks before radiotherapy.
2. Avoid extractions during radiotherapy.
   - The mandible is at greater risk than the maxilla.
   - Posterior sites are at greater risk than anterior sites.
3. Minimize infection.
   - Use prophylactic antibiotics.
   - Give 2 g penicillin VK orally 1 hour before the surgical procedure.
   - After surgery, continue with penicillin VK 500 mg 4 times daily for 1 week.
4. Minimize hypovascularity after radiotherapy.
   - Use nonlidocaine local anesthetic (e.g., Prilocaine plain or forte) for dental procedures.
   - Minimize or avoid vasoconstrictor use; if necessary, consider low-concentration epinephrine (1:200,000 or less).
   - Consider hyperbaric oxygen.*
5. Minimize trauma.
   - Endodontic therapy is preferred over extraction (assuming the tooth is restorable).
   - Follow atraumatic surgical technique.
   - Avoid periosteal elevations.
   - Limit extractions to two teeth per quadrant per appointment.
   - Irrigate with saline, obtain primary closure, and eliminate bony edges or spicules.
6. Maintain good oral hygiene.
   - Use oral irrigators.
   - Use antimicrobial rinses (chlorhexidine).
   - Use daily fluoride gels.
   - Eliminate smoking.
   - Attend frequent postoperative recall appointments.

Suggestive Reading

James W Little, Craig S Miller, Nelson L Rhodus. Dental management of medically compromised patient, 9th edition, Elsevier, 2018