Management of the Patient Undergoing Radiotherapy or Chemotherapy

Edward Ellis III



CHAPTER

CHAPTER OUTLINE

DENTAL MANAGEMENT OF PATIENTS UNDERGOING RADIOTHERAPY TO HEAD AND NECK
Radiation Effects on Oral Mucosa Radiation
Effects on Salivary Glands
Treatment of Xerostomia Radiation
Effects on Bone Other Effects of Radiation
Evaluation of Dentition Before Radiotherapy
Condition of Residual Dentition
Patient's Dental Awareness
Immediacy of Radiotherapy
Radiation Location
Radiation Dose
Preparation of Dentition for Radiotherapy and Maintenance After Irradiation
Method of Performing Preirradiation Extractions Interval Between Preirradiation Extractions and Beginning of Radiotherapy
Impacted Third Molar Removal Before Radiotherapy
Method of Dealing with Carious Teeth After Radiotherapy
Tooth Extraction After Radiotherapy
Denture Wear in Postirradiation Edentulous Patients
Use of Dental Implants in Irradiated Patients
Management ofPatients Who Develop Osteoradionecrosis

DENTAL MANAGEMENT OF PATIENTS ON SYSTEMIC CHEMOTHERAPY FOR MALIGNANT DISEASE
Effects on Oral Mucosa
Effects on Oral Microbiology Effects on Hematopoietic System
General Dental Managment Treatment of Oral Candidosis

DENTAL MANAGEMENT OF PATIENTS UNDERGOING RADIOTHERAPY *TO* HEAD AND NECK

Radiotherapy (i.e., radiation therapy, x-ray treatment) is a common therapeutic modality for malignancies of the head and neck. Approximately 30,000 cases of head and neck cancer occur each year. Many of these are managed by therapeutic irradiation. Its use is *ideally* predicated on the ability of the radiation to destroy neoplastic cells while sparing normal cells. In practice, however, this is never actually achieved, and normal tissues experience some undesirable effect. Any neoplasm can be destroyed by radiation if the dose delivered to the neoplastic cells is sufficient. The limiting factor is the amount of radiation that the surrounding tissues can tolerate.

Radiotherapy destroys neoplastic (and normal) cells by interfering with nuclear material necessary for reproduction, cell maintenance, or both. The faster the cellular turnover, the more susceptible the tissue is to the damaging effects of radiation. Thus neoplastic cells, which are usually reproducing at higher rates than normal tissue,

are selectively destroyed (relatively). In practice, normal tissues with rapid turnover rates are also affected to some degree. Therefore hematopoietic cells, epithelial cells, and endothelial cells are affected soon after treatment when radiotherapy begins.

Early in the course of radiotherapy, the oral mucosa shows the effects of treatment. The changes in and around the oral cavity as the result of destruction of the fine vasculature are most notable to dentistry. Salivary glands and bone are relatively radioresistant, but because of the intense vascular compromise resulting from radiotherapy, these tissues bear a considerable hardship in the long run.

Radiation Effects on Oral Mucosa

The initial effect of radiotherapy on the oral mucosa, which is seen in the first 1 or 2 weeks, is an erythema that may progress to a severe mucositis with or without ulceration. Pain and dysphagia may be severe and make adequate nutritional intake difficult. These mucosal reactions begin to subside after completion of the course of radiotherapy. The taste buds, also comprised of epithelial cells, show similar reactions. Loss of taste is a prominent complaint early in treatment and gradually returns, depending on the quantity and quality of saliva that remains after treatment.

The long-term effects of radiotherapy to the oral mucosa are characterized by a predisposition to breakdown and delayed healing, even after minor insult. The epithelium is thin and less keratinized, and the submucosa is less vascular, which gives a pale appearance to the tissue. Radiotherapy induces submucosal fibrosis, which makes the mucosal lining of the oral cavity less pliable and less resilient. Minor trauma may create ulcerations that take weeks or months to heal. These ulcerations are often difficult to differentiate from recurrent malignant disease.

Radiation Effects on Salivary Glands

Salivary gland epithelium has a very slow turnover rate; therefore the salivary glands might be expected to be radioresistant. However, because of the destruction of the fine vasculature by the radiation, the salivary glands show considerable damage, with resultant atrophy, fibrosis, and degeneration. This manifests clinically as xerostomia (the decreased production of saliva) and gives the patient a "dry mouth." The severity of xerostomia depends on which salivary glands were within the field of radiation. A dry mouth may be the patient's most significant complaint.

The effects of xerostomia on the oral cavity are devastating. Because saliva is the principal protector of the oral tissues, absence results in serious complications. Rampant "radiation caries" can swiftly destroy the remaining dentition and predispose the patient to severe infections of the jaws. Teeth thus affected exhibit decay around the entire circumference of the cervical portion (Fig. 18-1). Periodontitis is also accelerated in the absence of saliva. Dysgeusia, dysphonia, and dysphagia are also caused by xerostomia.

Treatment of Xerostomia

After radiotherapy, patients often complain of chronic dry mouth. At present no general agreement exists concerning how to prevent these changes. Unfortunately, in many cases, xerostomia never improves substantially, and exogenous replacement of saliva is necessary. For the simplest form of replacement, water can be sipped throughout the day. In addition, several saliva substitutes can be obtained without a prescription at the pharmacy. These substitutes contain several of the ions in saliva and other ingredients (e.g., glycerin) to mimic the lubricating action of saliva. Unfortunately, artificial salivas on the market do not possess the protective proteins that are present in the salivary secretions. The patients are therefore still prone to the problems induced by xerostomia. For comfort, however, many patients seem to be just as satisfied with plain water as artificial salivas and keep small quantities available at all times to sip.

Efforts to stimulate the patient's residual saliva have met with some success. The Food and Drug Administration (FDA) has now approved the use of two medications to stimulate the flow of saliva: (1) pilocarpine hydrochloride and (2) cevimeline hydrochloride have been shown to relieve symptoms of xerostomia for patients with xerostomia.[1] Both are parasympathomimetic agents that function primarily as muscarinic agonists, causing stimulation of exocrine gland secretion. This can increase the production of saliva, even in patients whose salivary glands have been exposed to radiation. An oral dose of 5 mg of pilocarpine four times each day or 30 mg of cevimeline three times a day has been shown to improve many symptoms of xerostomia without significant drug-related side effects.[2] The administration of these medications may prove to be beneficial for some patients with postradiation xerostomia.

Radiation Effects on Bone

One of the most severe and complicating sequelae of radiotherapy for patients with head and neck cancer is osteoradionecrosis (Fig. 18-2). Basically, osteoradionecrosis is devitalization of the bone by cancericidal doses of radiation. The bone within the radiation beam becomes virtually nonvital from an endarteritis that results in elimination of the fine vasculature within the bone. The turnover rate of any remaining viable bone is slowed to the point of being ineffective in self-repair. The continual process of remodeling normally found in bone does not occur, and sharp areas on the alveolar ridge will not smooth themselves, even with considerable time. The bone of the mandible is denser and has a poorer blood supply than that of the maxilla. Thus the mandible is the jaw most commonly affected with nonhealing ulcerations and osteoradionecrosis.

Other Effects of Radiation

Patients undergoing radiotherapy may have an alteration in the normal oral flora, with overgrowth of anaerobic species and fungi. Most researchers feel that oral flora colonizing the mucous membranes play an important role in the severity of mucositis and subsequent healing

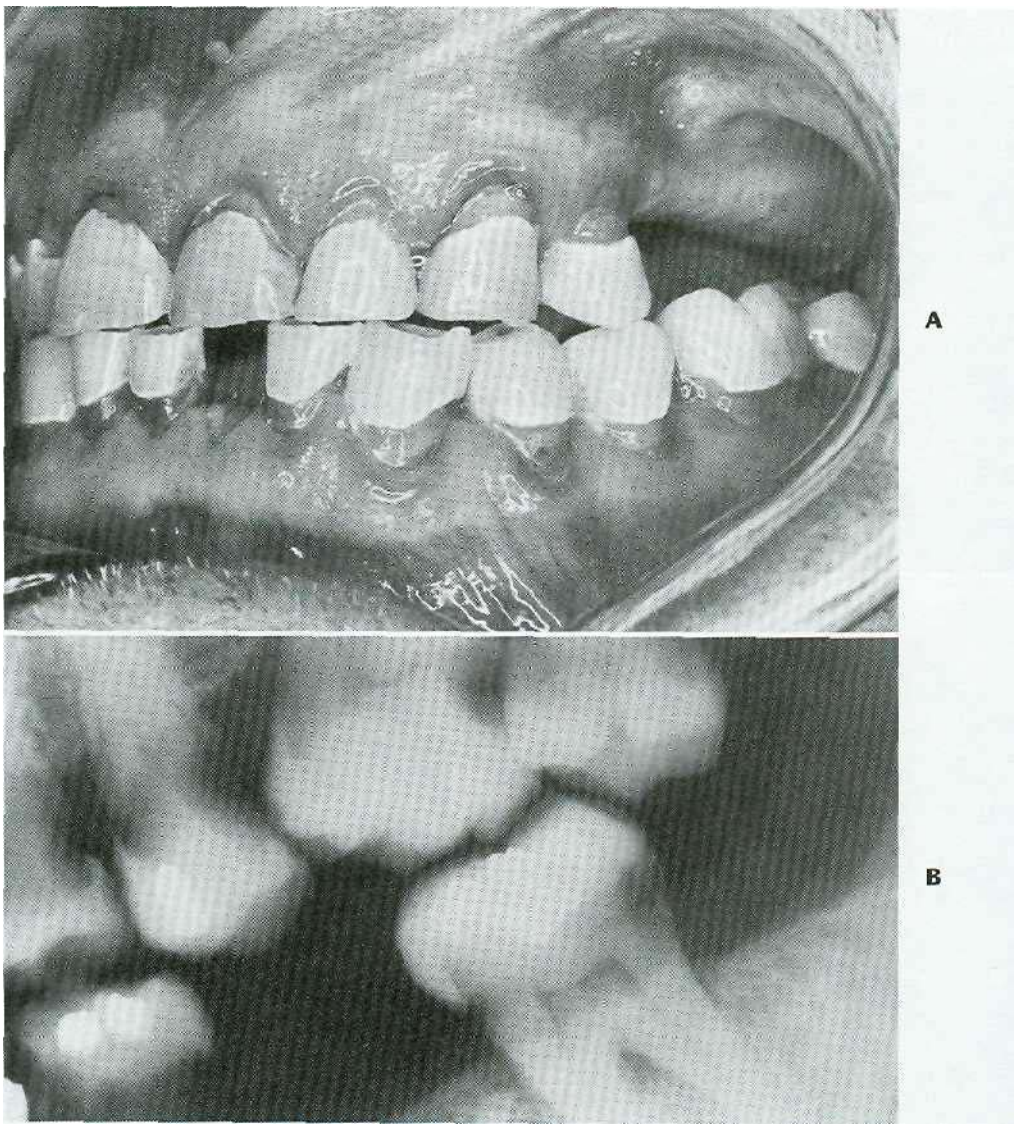


FIG.18-1 A, Typical clinical appearance of radiation caries. B, Typical radiographic appearance of radiation caries. Note the erosion around the cervical portion of the teeth.

process.[3,4] *Candida albicans* commonly thrives in the oral cavities of patients who have been irradiated. It is not known whether the alteration in the flora is caused by the radiation itself or the resultant xerostomia. Patients frequently require the application of topical antifungal agents, such as nystatin, to help control the amount of *Candida* organisms present. Another oral rinse frequently prescribed is 0.1% chlorhexidine (Peridex). This agent has been shown to have potent in vitro antibacterial and antifungal effects. When used throughout the course of radiation treatment, it has been shown in at least one study to greatly reduce the prevalence and symptoms associated with radiation-induced mucositis.[5] Its use in other studies has been equivocal.[3-6]

Evaluation of Dentition Before Radiotherapy

The most feared side effect of radiotherapy is osteoradionecrosis. Most patients who develop this complication have residual teeth throughout the course of radiotherapy. Thus the clinician may wonder what to do with the teeth before irradiation. Should teeth be extracted? This question has no categorical answer; however, several factors must be considered.[7-10]

Condition of residual dentition. All teeth with a questionable or poor prognosis should be extracted before radiotherapy. The more advanced the periodontal condition, the more likely the patient is to develop caries and continued periodontitis. Although this may not be in keeping with usual dental principles, *if in doubt, extract.* Extraction in these cases may spare the patient months or years of suffering from osteoradionecrosis.

Patient's dental awareness. The present state of the dentition and periodontium is a good clue to the past care they have received. In patients with excellent oral hygiene and oral health, the clinician should retain as many of the teeth as possible. Conversely, in patients who have neglected oral health for years, the chances are

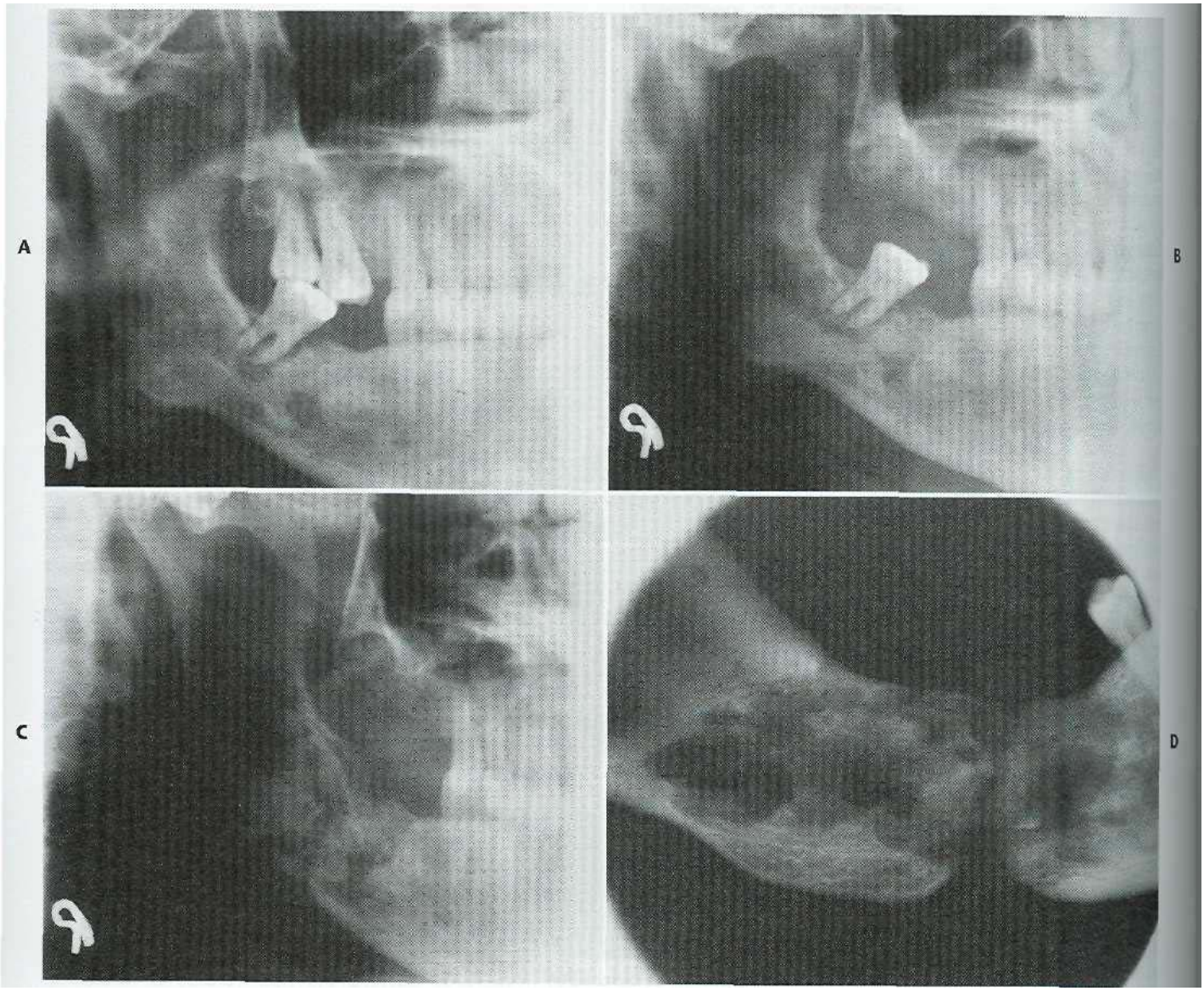


FIG. 18-2 Progressive course of osteoradionecrosis. A, Radiograph showing radiolucencies in right mandible and around apex of molar tooth. B, Six months later, during which time antibiotics and local irrigations were used, radiolucent process is spreading into ramus. Molar was removed at this time. C, Five months after tooth removal, extraction site did not heal and destructive process spread, resulting in pathologic fracture of mandible. D, Radiograph after removal of devitalized bone, showing extent of process. *(Courtesy Dr. Richard Scoot, Ann Arbor, ML)*

that they will continue to do so, especially in the face of severe xerostomia and oral pain, which will make oral hygiene even more difficult. Preradiotherapy patient preparation is similar to preorthodontic patient preparation. If an individual cannot or will not care for his or her mouth before the application of the braces, it will be impossible for him or her to do so when faced with future obstacles.

Immediacy of radiotherapy. If the radiotherapist feels that therapy must be instituted urgently, there may not be time to perform the necessary extractions and allow for initial healing of the extraction sites. In this instance the dentist may elect to maintain the dentition but must work closely with the patient throughout the course of radiotherapy and thereafter in an attempt to maintain oral health as optimally as possible.

Radiation location. The more salivary glands and bone involved in the field of radiation, the more severe will be the resultant xerostomia and vascular compromise of the jaws. Thus the dentist should discuss with the radiotherapist the locations of the radiation beams and estimate the severity of the probable xerostomia and bone changes. Xerostomia by itself may not result in severe problems if the dentition can be maintained, because the bone is still healthy. It is the combination of xerostomia and irradiated bone that usually causes the

problem. In individuals who will have radiation to the major salivary glands *and* a portion of the mandible, preirradiation extractions should be considered. Frequently the radiotherapist agrees to delay the institution of irradiation for 1 to 2 weeks if the dentist feels that time is necessary to allow the extraction sites to begin to heal.

Radiation dose. The higher the radiation dose, the more severe is normal tissue damage. The radiotherapist should discuss with the dentist the amount of radiation planned for the individual. Frequently the dose is not maximal, and tissue damage may be minimized. This tends to make the dentist more conservative in preirradiation extraction considerations.

Squamous cell carcinomas of the oral cavity make up approximately 90% of malignant tumors for which radiation therapy is used. Unfortunately, this cancer requires a very large dose of radiation (greater than 6000 rads [60 By]) to effect a result. Other malignancies, such as lymphoma, require much less radiation for a response, and the oral cavity will therefore be less affected. When the total dose falls below 5000 rads (50 Gy), long-term side effects, such as xerostomia and osteoradionecrosis, are dramatically decreased.

Preparation of Dentition for Radiotherapy and Maintenance After Irradiation

Every tooth to be maintained must be carefully inspected for pathologic conditions and restored to the best state of health obtainable. A thorough prophylaxis and topical fluoride application should be performed before radiotherapy. Oral hygiene measures and instructions should be demonstrated and reinforced. Any sharp cusps should be rounded to prevent mechanical irritation. Impressions for dental casts should be obtained for fabrication of custom fluoride trays to be used during and after treatment. Because tobacco use and alcohol consumption irritate the mucosa, the patient should be encouraged to stop these before commencement of radiation therapy.

During radiation treatment the patient should rinse the mouth at least 10 times a day with saline rinses. The patient should be placed on chlorhexidine mouth rinses twice a day to help minimize the bacterial and fungal levels within the mouth. The dentist should see the patient each week during the radiotherapy for observation and oral hygiene evaluations. If an overgrowth of *Candida albicans* occurs, nystatin or clotrimazole topical applications will bring this under control relatively rapidly. The ability of the patient to open the mouth should be carefully monitored throughout the course of radiation treatment. Radiation causes a progressive fibrosis within the muscles of mastication that makes it difficult for the patient to adequately open the mouth. Patients should be instructed in physiotherapy exercises to maintain the preradiation-treatment interincisal dimension. All patients must be weighed weekly to determine whether they are maintaining an adequate nutritional status. The combination of mucositis and xerostomia makes oral intake extremely uncomfortable. However, malnutrition causes further difficulties by delaying healing of the oral tissues and giving the patient an overall feeling of generalized illness. In severe cases it may be necessary to feed the patient via nasogastric tube to maintain a reasonable nutritional status.

After radiation treatment the dentist should see the patient every 3 to 4 months. A prophylaxis is performed during these postirradiation visits, and topical fluoride applications are made. The patient should be fitted with custom trays to deliver topical fluoride applications. The patient should be instructed in the use of the trays and in *daily* self-administration of topical fluoride applications. The use of a 1% fluoride rinse for 5 minutes each day has been found to decrease the incidence of radiation caries.[11] Over-the-counter fluoride rinses currently available can be used without a customized delivery splint with good success and seem to have better patient acceptance.

Method of Performing Preirradiation Extractions

If the decision has been made to extract some or all teeth before radiotherapy, the question becomes, "How should the teeth be extracted?" In general, the principles of atraumatic exodontia apply. However, the concepts of bone preservation are disregarded, and an attempt is made to remove a good portion of the alveolar process along with the teeth and achieve a primary soft tissue closure. With the onset of radiotherapy, the normal remodeling process is inhibited; if any sharp areas of bone exist, ulceration occurs with bone exposure. Thus the teeth are usually removed in a surgical manner, with flap reflection and generous bone removal.

Atraumatic handling of the mucoperiosteal flaps is necessary to ensure a rapid soft tissue healing. Burs or files should be used to smooth the bony edges under copious irrigation, because the remodeling capability of the tissues is greatly decreased after radiotherapy. Prophylactic antibiotics are indicated under these circumstances.

Note: The dentist is in a race against time. If the wound fails to heal, the radiotherapy will be delayed. If the radiation is delivered before the wound heals, healing will take months or even years.

Interval Between Preirradiation Extractions and Beginning of Radiotherapy

No categorical answer exists to the question of how much time should be allowed after extractions before beginning radiotherapy. Obviously, the sooner radiotherapy is begun, the more beneficial it may be. Thus when the soft tissues have healed sufficiently, radiotherapy may begin. Traditionally, 7 to 14 days between tooth extraction and radiotherapy have been suggested.[7-12,13] Most authors base their recommendations on the clinical impression that reepithelialization has occurred in this period. However, radiotherapy should be delayed for 3 weeks after extraction, if possible. This helps to ensure that sufficient soft tissue healing has occurred. The radiotherapy should be delayed further, if possible, if a local wound dehiscence has occurred. In this instance daily local wound

care with irrigations and postoperative antibiotics are mandatory until the soft tissues have healed.

Impacted Third Molar Removal Before Radiotherapy

If the patient has a partially erupted mandibular third molar, removal may be prudent to prevent peri coronal infection. In general, however, allowing a tooth that is totally impacted within the bone of the mandible to remain in place is more expeditious than removing it and waiting for it to heal.

Method of Dealing with Carious Teeth After Radiotherapy

Teeth that develop postradiotherapy caries must be immediately cared for in an attempt to prevent further spread of infection. Composites and amalgam are the materials of choice to repair the defects caused by decay. Full crowns are probably not warranted, because recurrent decay is more difficult to detect under such restorations. Oral hygiene measures, including fluoride application, must be reinforced in any patient who develops postirradiation caries.

If a tooth has necrotic pulp, endodontic intervention with systemic antibiotics can be carefully performed and the tooth ground out of occlusion and maintained. Frequently root canal treatment is difficult because of a progressive sclerosis of the pulp chamber that occurs in irradiated teeth. In such instances the tooth can simply be amputated above the gingiva and left in place.

Tooth Extraction After Radiotherapy

Can teeth be extracted after radiotherapy and, if so, how? These are probably the most difficult questions to answer. Each dentist has a view on this subject, and the literature is contradictory. Postirradiation extractions are also the most undesirable extractions the dentist will ever perform, because the outcome is always uncertain.

The answer to the question of whether extractions *can* be done after radiotherapy is certainly, yes. The more important question is, How? If the tooth is to be extracted, the dentist can either perform a simple extraction without primary soft tissue closure or a surgical extraction with alveoloplasty and primary closure. Either of these techniques yields similar results, with a certain concomitant incidence of osteoradionecrosis. The use of systemic antibiotics is recommended.

Another technique that has been shown to be effective and that is gaining in popularity is the use of hyperbaric oxygen (HBO) *before* and *after* tooth extraction. Hyperbaric oxygen therapy is the administration of oxygen under pressure to the patient. It has been shown to increase the local tissue oxygenation and vascular ingrowth into the hypoxic tissues.[14,15] The usual protocol for such treatments is to have between 20 and 30 HBO dives before extraction and 10 more dives immediately after extractions. HBO chambers are not available in all communities and, when present, are usually in select hospitals. A physician that is experienced in hyperbaric medicine manages patients referred to these facilities. The patient usually undergoes one HBO session each day. Therefore it takes 4 to 6 weeks to get the 20 to 30 treatments before surgery, and 2 weeks of treatment after surgery. In a prospective clinical trial comparing this regimen with the use of prophylactic antibiotics before dental extraction without hyperbaric oxygenation, Marx, Johnson, and Kline[16] found a significant decrease in the incidence of osteoradionecrosis (5.4% compared with 30%).

Because considerable controversy exists over how to manage an extraction surgically in a patient who has undergone irradiation, because few hyperbaric oxygenation chambers are available for use, and because the incidence of severe complications is relatively high, it is recommended that an oral and maxillofacial surgeon manage the patient who has received irradiation and requires extractions.

Denture Wear in Postirradiation Edentulous Patients

Patients who were edentulous before radiotherapy manage very nicely with well-constructed dentures. However, patients rendered edentulous just before or after radiotherapy exhibit more problems with mucosal ulcerations and subsequent osteoradionecrosis. The normal remodeling process of the alveolar bone cannot smooth even the most minor irregularities left by extraction. With denture wear, these minor irregularities cause ulceration of the mucosa.

Soft denture liners might seem an ideal solution for patients who have received irradiation. However, the silicone soft liners proved to be not particularly useful for several reasons. At present, patients are probably best served with ordinary dentures.

Denture fabrication for patients who were previously edentulous can proceed once the acute effects of irradiation have subsided. For patients who underwent extractions just before or after radiotherapy, it is prudent to see them very frequently after delivery of their dentures to make adjustments for sore spots that develop before they cause mucosal breakdown and bone exposure.

When dentures are constructed, the dentist must be certain that the denture base and occlusal table are designed so that forces are distributed evenly throughout the alveolar ridge and that lateral forces on the denture are eliminated.

Use of Dental Implants in Irradiated Patients

The dental rehabilitation of the edentulous patient who has received radiation therapy is one of the greatest challenges facing the reconstructive dentist. Many patients who have had ablative surgery for malignancy do not have the normal anatomy that makes denture wear possible. There may be no vestibules to accommodate a denture flange.

Often, portions of the tongue have been removed. There may be hard and soft tissue defects and deficits. When reconstructed, the bone may have poor form for support of a tissue-borne prosthesis. Frequently such patients have thick, nonpliable soft tissue flaps that have been grafted from distant areas and are not adherent to the underlying bone. All of these combine to make conventional denture fabrication extremely challenging. In such instances the use of implant-borne prostheses are preferred from a functional standpoint.

For years, however, a history of irradiation has been a relative contraindication to the placement of dental implants.[17] The effects of radiation on bone and soft tissue present a formidable challenge to the use of implanted metallic devices. Not surprising, success rates for implants placed into radiated tissues are reported to be lower than implants placed into nonirradiated tissues.[18,19] However, the benefits that can accrue from providing this group of patients a functional and esthetic dental reconstruction are great.

Such patients have been through a great deal of hardship. They have lost portions of their anatomy, are frequently deformed, and feel the uncomfortable effects of the radiation therapy, such as xerostomia, dysphagia, and dysgeusia. They relish the thought of being able to chew solid food with a functional dentition. Implant-borne prostheses can help achieve this goal in these difficult situations. However, the unpredictable reaction of soft and hard tissue in an irradiated patient and the surgical trauma of treatment have all combined to promote caution in such cases.

Many variables must be evaluated when considering placement of dental implants into irradiated bone, including the radiation type, dose, sites, elapsed time since the treatment, protection provided to the bone during treatment, and the patient's own physiologic responses (which themselves are affected by age, sex, genetics, smoking, and other systemic considerations). Other critical factors are whether the implants will be placed into irradiated host mandibular bone, irradiated bone grafts, or bone that has been transplanted after the radiation therapy. In the latter instance, if the mandible was reconstructed using a microvascular graft in which the blood supply to the bone is brought in from a distant source and has not been altered by the previous radiation therapy, no adverse tissue reaction should be expected after placement of dental implants.

When dental implants are to be placed into irradiated host or grafted bone, the dentist must proceed with caution. Consultation with the radiotherapist is recommended to determine the amount of radiation that has occurred to the area of the jaws where the proposed implants will be placed. It has been demonstrated that the success of implant retention is directly and positively correlated with the amount of radiation to which the bone was exposed.[19] If the amount of radiation is less than approximately 4500 rads (45 Gy), implants may be placed with care. When the amount of radiation exceeds this amount, preoperative (20 to 30) and postoperative (10) hyperbaric oxygen treatments should be considered. Hyperbaric oxygen treatments have been shown to be beneficial in such patients.[20]

The time required for osseointegration will be prolonged in irradiated patients because of the lower metabolic activity in the bone, so the implants should not be loaded for at least 6 months after placement. The dentist must pay particular attention to oral hygiene in such patients, because their tissues will not be as able to resist bacterial invasion as tissues in patients who have not been irradiated. The prosthetic design should therefore be made as cleansable as possible, with frequent use of overdentures. These patients will require more careful follow-up and hygiene measures.

In spite of the fear that implants placed into irradiated bone will lead to osteoradionecrosis, it is uncommonly reported in the literature.[21,22] However, there has been an insufficient duration of experience to predict the long-term outcome of implant prosthetics in the patient who has undergone radiation.

Management of Patients Who Develop Osteoradionecrosis

Most mucosal breakdown and subsequent osteoradionecrosis occur in the mandible. They occur most often in mandibles that have received radiation in excess of 6500 rads (65 Gy) and do not usually occur in mandibles that have received radiation doses below 4800 rads (48 Gy).[23-25] Severe pain may follow. The patient should discontinue wearing any prosthesis and try to maintain a good state of oral health. Irrigations should be instituted to remove necrotic debris (Fig. 18-3). Only occasionally are systemic antibiotics necessary, because osteoradionecrosis is not an infection of the bone but rather a nonhealing hypoxic wound.[15] Because of the decreased vascularity of the tissues, systemic antibiotics do not gain ready access to the area to perform the function for which they are intended. However, in acute secondary infections, antibiotics may be useful to help prevent spread of the infection. Any loose sequestra are removed, but no attempt is made initially to close the soft tissues over the exposed bone. Most wounds smaller than 1 cm eventually heal, although it may take weeks to months.

For nonhealing wounds or extensive areas of osteoradionecrosis, surgical intervention may be indicated. In this instance resection of the exposed bone and a margin of unexposed bone and primary soft tissue closure can be attempted (see Fig. 18-3). This is successful in many cases. Greatly improved results have recently been obtained by the use of hyperbaric oxygen therapy in conjunction with surgical intervention.[14]

Reconstructive efforts with bone grafts used for continuity defects can also be undertaken successfully in many patients who have undergone irradiation. Free microvascular grafting techniques are becoming more popular for restoring continuity defects in patients who have received radiotherapy. These bone grafts have their own blood supply from a reconnection of blood vessels and are therefore less dependent on the local tissues for incorporation and healing.

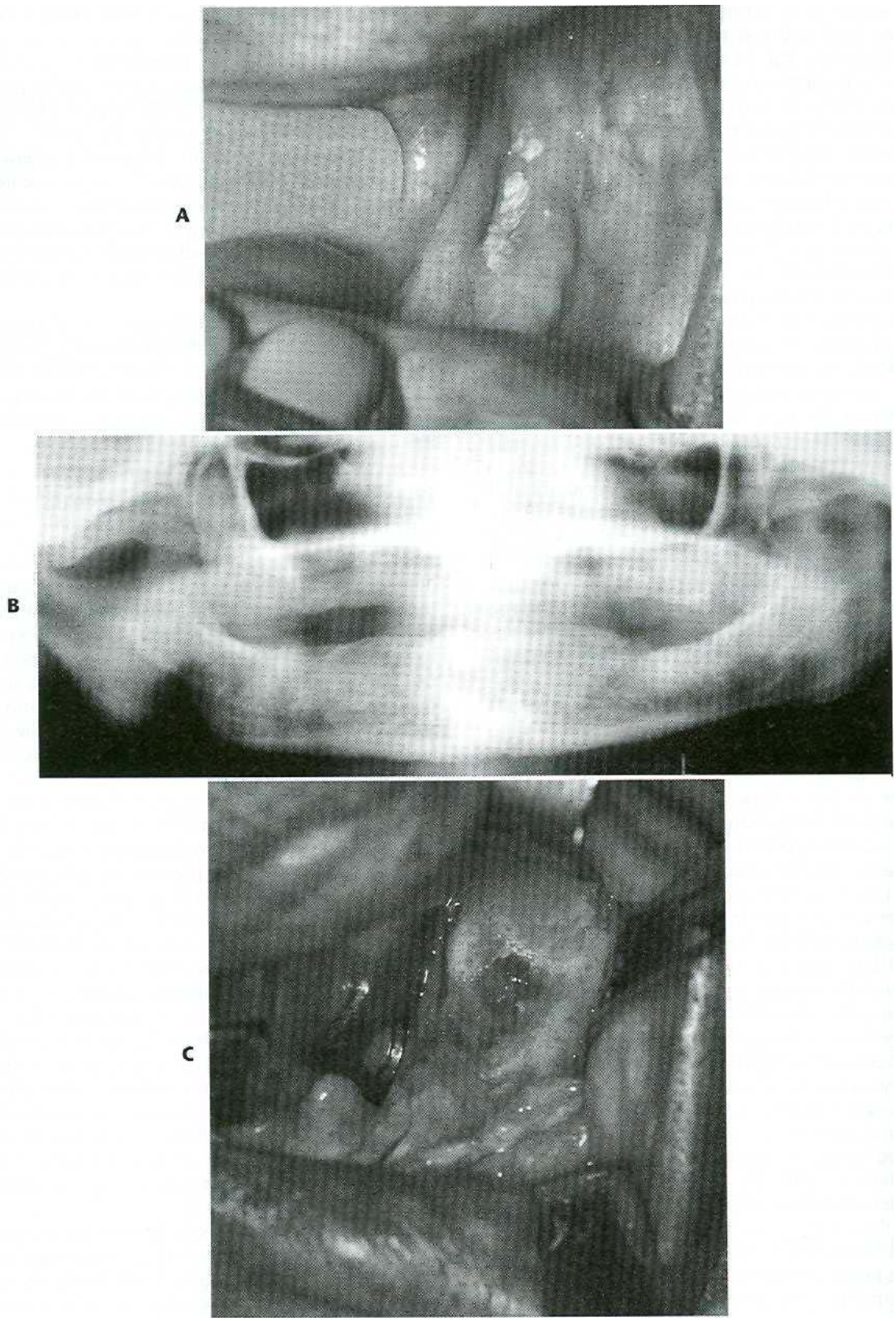


FIG. 18-3 Osteoradionecrosis of the left mandible. This patient had a full course of tumoricidal radiotherapy for squamous cell carcinoma. The dentition was removed at the time of the cancer resection. This patient was prepared for treatment of the osteoradionecrosis with pre- and postoperative hyperbaric oxygen treatments. A, Exposed devital bone along alveolar ridge of left mandible. B, Panoramic radiograph showing diffuse irregularity without good cortication of alveolar crest. C, Surgical exposure of the area shows devital bone margins and a central crater devoid of bone.

Continued

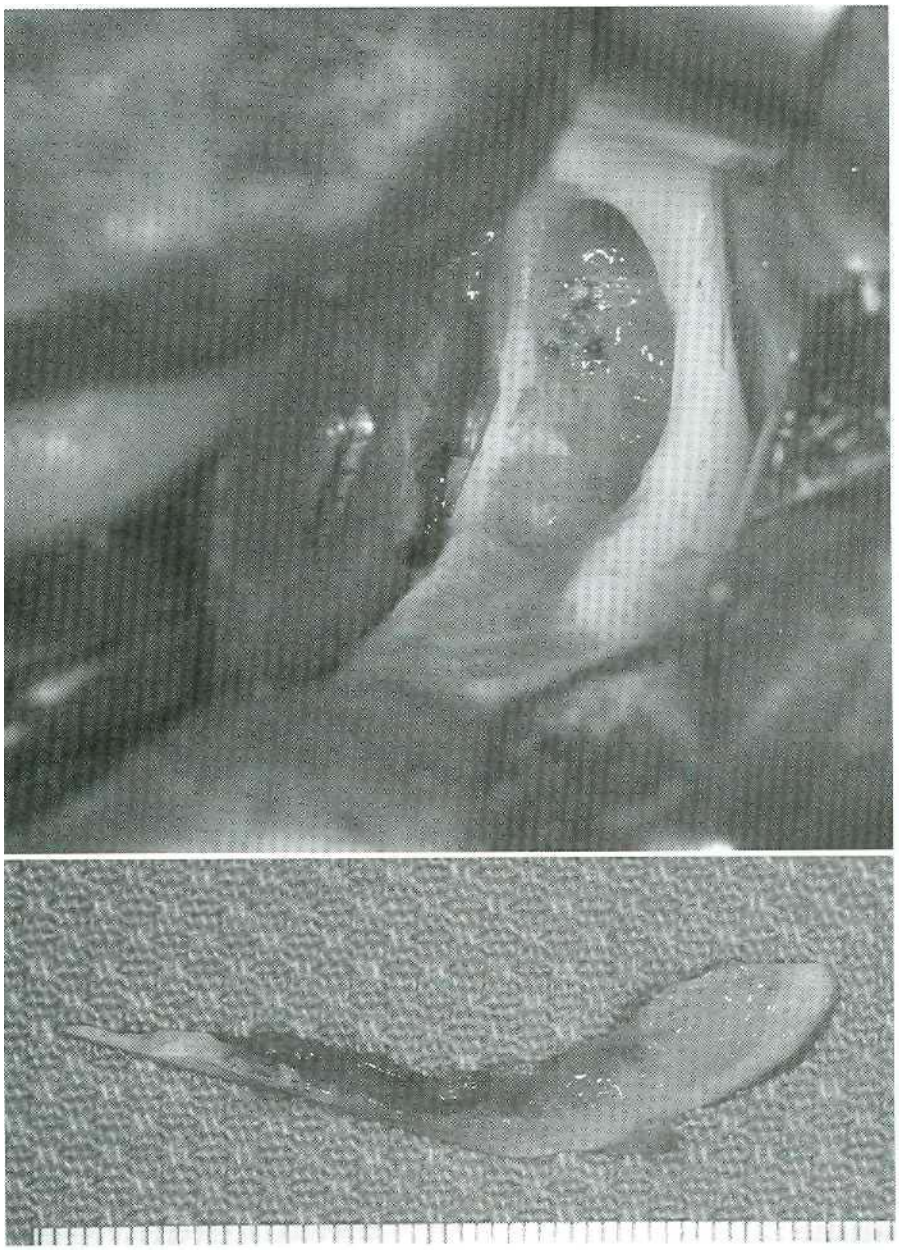


FIG. 18-3-cont'd D, The bone of the alveolar crest is removed, and the remainder smoothed with a bur until bleeding bone is encountered. The central crater is similarly burred out. E, Resected specimen of alveolar crest.

Continued

DENTAL MANAGEMENT OF PATIENTS ON SYSTEMIC CHEMOTHERAPY FOR MALIGNANT DISEASE

Destruction of malignant cells by tumoricidal chemotherapeutic drugs has proved an effective treatment for a variety of malignancies. Like radiotherapy, the antitumor effect of cancer chemotherapeutic agents is based on their ability to destroy or retard the division of rapidly proliferating cells, such as tumor cells, nonspecifically. Unfortunately, normal host cells that have a high mitotic index are also adversely affected. Normal cells most affected are the epithelium of the gastrointestinal tract (including oral cavity) and the cells of the bone marrow.

Effects on Oral Mucosa

Many chemotherapeutic agents reduce the normal turnover rate of oral epithelium, which results in atrophic thinning of the oral mucosa manifested clinically as painful, erythematous, and ulcerative mucosal surfaces in the mouth. The effects are most noted on the unattached mucosa and rarely seen on gingival surfaces. These changes are seen within 1 week of the onset of the administration of the antitumor agents. The effects are usually self-limiting, and spontaneous healing occurs in 2 to 3 weeks after cessation of the agent.

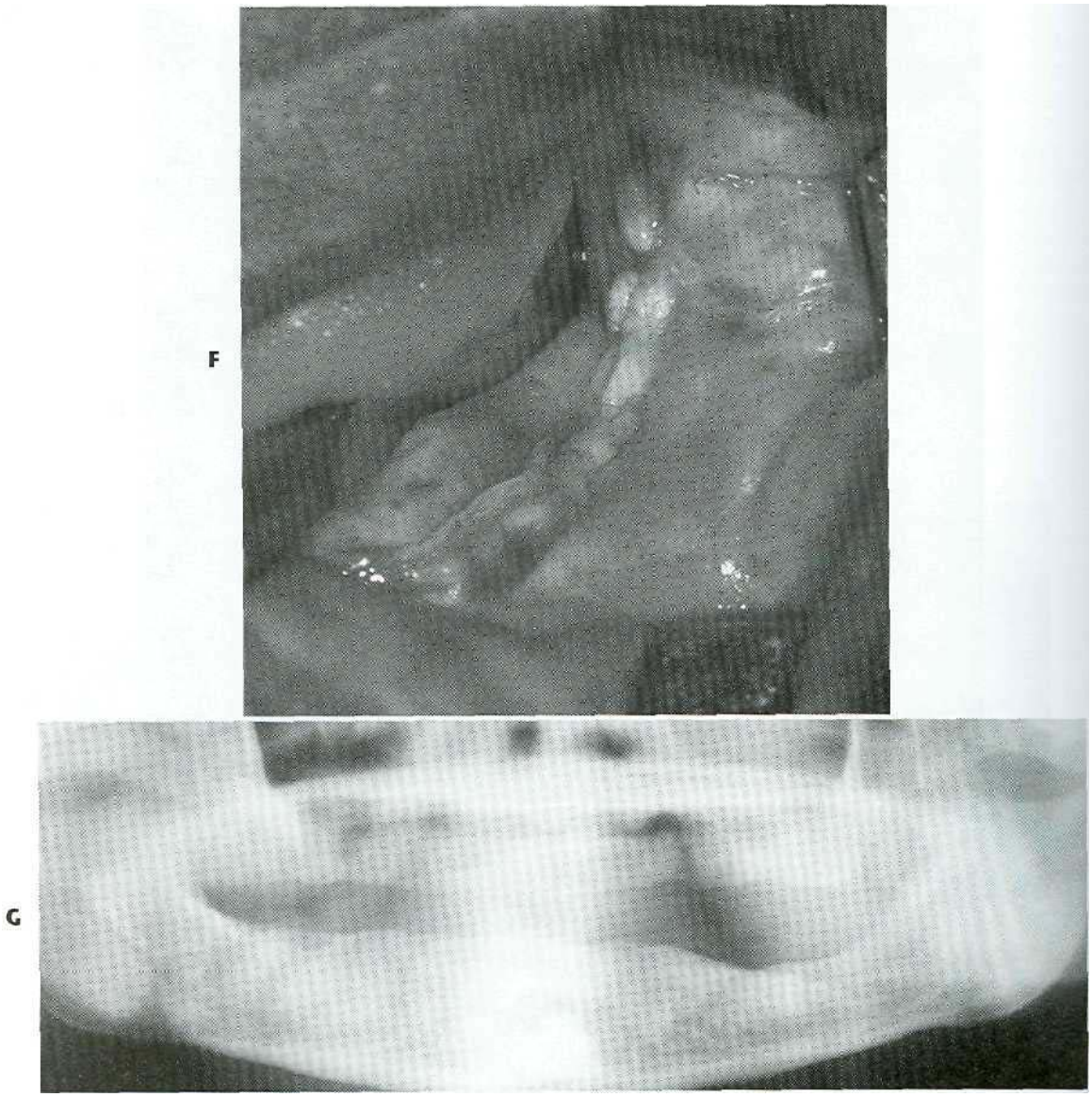


FIG. 18-3—cont'd **F,** Closure of soft tissues. G, Panoramic radiograph 8 months after surgery showing slight remodeling and healing of the bone.

Effects on Hematopoietic System

Myelosuppression, as manifested by leukopenia, neutropenia, thrombocytopenia, and anemia, is a common sequela of several forms of cancer chemotherapy. Within 2 weeks of the beginning of chemotherapy administration, the white blood cell count falls to an extremely low level. The effect of myelosuppression in the oral cavity is marginal gingivitis. Mild infections may develop, and bleeding from the gingiva is common. If the neutropenia is severe and prolonged, severe infections may develop. The microorganisms involved in these infections may be overgrowths of the usual oral flora, especially fungi; however, other microorganisms may be causative. Thrombocytopenia can be marked, and spontaneous bleeding may occur. This is especially common in the oral cavity after oral hygiene measures. Recovery from myelosuppression is usually complete 3 weeks after cessation of chemotherapy.

It is important to find out the type of neoplasm for which the patient is being treated. The type of neoplasm dictates the type of chemotherapeutic agents to be used. Many hematologic neoplasms (e.g., leukemia) are treated with chemotherapeutic agents that result in profound alterations in the function and number of bone marrow elements. Comparatively, chemotherapeutic management of some nonmarrow solid tumors may not be associated with as severe a marrow aplasia as is found in patients with hematologic neoplasms.

Effects on Oral Microbiology

Chemotherapeutic agents, because of their immunosuppressive side effect, cause profound changes in the oral flora. For example, overgrowth of indigenous microbes, super infection with gram-negative bacilli, and oppor-

tunistic infections are all common sequelae and lead, to patient discomfort and morbidity. Systemic infections are responsible for about 70% of the deaths in patients receiving myelosuppressive cancer chemotherapy.[26,27] *Oral* microorganisms have been shown to be a common source of bacteremia in these patients.[26] Thus most patients who are on chemotherapy are treated concomitantly with systemic antimicrobial agents. However, in spite of these regimens, patients frequently develop overgrowth of some organisms, most commonly the *Candida* spp.[28–30]

General Dental Management

In general, the principles of dental management for the patient who has had or will have radiotherapy apply equally well to the patient who has had or will have chemotherapy.[31,32] However, because of the intermittent nature of the chemotherapy delivered in many instances, the minimal effects on the vasculature, and the almost normal state of the individual between chemotherapeutic administrations, dental management can be much easier. The effects of the chemotherapy are almost always temporary, and, with the passage of time, systemic health improves to optimal levels, which allows almost routine dental management.

Primary concerns for the dentist should be the severity and duration of bone marrow suppression. The dentist must be aware of the dates of chemotherapy and the hematologic status of the patient before beginning dental care. If the patient is being treated for a hematologic neoplasm (e.g., leukemia), *both* the disease *and* the chemotherapy lead to decreases in the functional blood elements, Therefore these patients may be at great risk for infection and hemorrhage at any time in the course of their disease. Consultation with the patient's physician in these instances is mandatory, in most cases of nonhematopoietic neoplasm, the patient is at risk for infection and hemorrhage only during the course of the chemotherapy, after which recovery of the blood elements occurs.

The decision of when to extract teeth before treatment is based on the condition of the residual dentition, the patient's past dental hygiene practices, the immediacy of the need for chemotherapy, and the overall prognosis of the malignant disease.

Prechemotherapy dental measures that should routinely be performed are a thorough prophylaxis, fluoride treatment, and any necessary scaling. Unrestorable teeth should be removed before chemotherapy begins.

Patients who have begun chemotherapy must maintain scrupulous oral hygiene. This is difficult in the face of mucositis and ulceration, which frequently occur. No dental procedures should be performed on any patient receiving chemotherapy whose white blood cell and platelet status is unknown. In general, patients who have a white blood cell count greater than or equal to 2000 mm^3, with at least 20% potymorphonuclear leukocytes and a platelet count greater than or equal to 50,000 mm^3, can be treated in routine fashion. Prophylactic antibiotics should be administered if the patient has had chemotherapy within 3 weeks of dental treatment. If the white blood cell count and platelet levels fall below those specified, minimal oral care should be practiced, because infection, severe bleeding, or both can occur. The patient may even need to avoid flossing and to use an extremely soft toothbrush during these periods. Any removable dental appliance should be left out at these times to prevent ulceration of the fragile mucosa.

Treatment of Oral Candidosis

Initial treatment of candidosis is with topical application of an antifungal medication.[28] The advantage of using topical medication is that systemic side effects are minimized. Similarly in patients with persistent infection, advantage can be gained by continuing topical agents in addition to systemic medications. The use of this combination may allow a reduced dose and duration of systemic administration of the antifungal medication and also may reduce the potential side effects.

Topical agents are available as oral rinses, oral tablets, and creams. In general, oral rinses provide a short contact time for the drug and are therefore of less efficacy. The tablets are one of the most accepted forms of topically treating candidiasis, because they can be dissolved slowly in the mouth and provide increased exposure time of the drug with the oral flora. The cream forms of topical antifungals are helpful for *Candida* of the oral commissures or for application to the oral surfaces of prosthetic devices to prolong medication exposure.

The most commonly administered topical medication for oropharyngeal *Candida* infections is nystatin. it is available in several forms and should be applied 4 times daily.

Therapy should continue 2 weeks after cessation of clinical signs and symptoms. An alternate drug is clotrimazole. Troches of these medications are available and can be dissolved in the mouth 4 or 5 times a day. For more stubborn cases, ketoconazole or fluconazole (i.e., systemic antifungal medications) can be prescribed. However, the dentist must be careful with systemic administration of antifungal medications because of their toxic side effects. These vary widely with the type of medication and can be serious.

Another widely prescribed medication for oral candidosis is chlorhexidine mouth rinse. Chlorhexidine (Peridex) has been shown to have potent antibacterial and antifungal properties *in vitro*. Its in vivo effects are less well documented, especially for use against *Candida* spp. in immunosuppressed individuals.[3,33] However, it is used in most of such patients on the basis that it probably does no harm and may prove beneficial in many instances.

REFERENCES

1. Grisius M: Salivary gland dysfunction: a review of systemic therapies, *Oral Surg Oral Med Oral Pathol* 92:156, 2001.
2. Khan Z, Jacobsen OS: Oral pilocarpine HC1 for post-irradiation xerostomia in head and neck cancer patients. In *Proceedings of the First International Congress on Maxillofacial Prosthetics,* New York, 1995, Memorial Sloan-Kettering Cancer Center.

3. Spijkervet FK: *Irradiation mucositis,* Copenhagen, 1991, Munksgaard.
4. Spijkervet FK et al: Effect of selective elimination of the oral flora on mucositis in irradiated head and neck cancer *patients, j Surg Oncol* 46:167, 1991.
5. Matheis MJ et al: Evaluation of oral mucositis in patients receiving radiation therapy for head and neck cancer: a pilot study of 0.12% chlorhexidine gluconate oral rinse. In *Pro ceedings of the First InternationalCongress on Maxillofacial Prosthetics,* New York, 1995, Memorial Sloan-Kettering Cancer Center.
6. Ferretti GA et al: Chlorhexidine prophylaxis for chemotherapy- and radiation-induced stomatitis: a randomized double-blind trial, *Oral Surg Oral Med Oral Pathol* 70:331, 1990.
7. Beumer J, Brady F: Dental management of the irradiated patient, *Int JOral Surg* 7:208, 1978.
8. Beumer J, Curtis T, Harrison RE: Radiation therapy of the oral cavity. I. Sequelae and management, *Head Neck Surg* 1:301, 1979.
9. Beumer J, Curtis T, Harrison RE: Radiation therapy of the oral cavity. II. Sequelae and management, *Head Neck Surg* 1:392, 1979.
10. Beumer J, Curtis TA, Morrish RB: Radiation complications in edentulous patients, *JProsthetDent* 36:193, 1976.
11. Driezen S et al: Prevention of xerostomia-related dental caries in irradiated cancer patients, *J Dent Res* 56:99, 1977.
12. Bedwinek JM et al: Osteonecrosis in patients treated with definitive radiotherapy for squamous cell carcinomas of the oral cavity and naso and oropharynx, *Radiology* 119:665, 1976.
13. Starcke EN, Shannon IL: How critical is the interval between extractions and irradiation in patients with head and neck malignancy? *Oral Surg* 43:333, 1977.
14. Marx RE: A new concept in the treatment of osteoradionecrosis, / *Oral Maxillofac Surg* 41:351, 1983.
15. Marx RE: Osteoradionecrosis: a new concept in its pathophysiology, J *Oral Maxillofac Surg* 41:283, 1983.
16. Marx RE, Johnson RP, Kline SN: Prevention of osteo radionecrosis: a randomized prospective clinical trial of hyperbaric oxygen versus penicillin, *} Am DentAssoc* 111:49, 1985.
17. Hobo S, Ichida E, Garcia LT: *Osseointegration and occlusal reha bilitation,* Tokyo, 1989, Quintessence.
18. Granstrom G et al: Bone-anchored reconstruction of the irra diated head and neck cancer patient, *Otolaryngol Head Neck Surg* 108:334, 1993.
19. Visch LL, Levendag PC, Denissen HW: Five-year results of 227 HA-coated implants in irradiated tissues. In *Proceedings of the First International Congress on Maxillofacial Prosthetic?,,* New York, 1995, Memorial Sloan-Kettering Cancer Center.
20. Granstrom G, Jacobsson M, Tjellstrom A: Titanium implants in the irradiated tissue. Benefits from hyperbaric oxygen, Int *J Oral Maxillofac Implants* 7:15, 1992.
21. Albrektsson T: A multicenter report on osseointegrated oral implants, J *Prosthet Dent* 60:75, 1988.
22. Taylor TD, Worthington P: Osseointegrated implant rehabil itation of the previously irradiated mandible: results of a lim ited trial at 3 to 7 years, J *Prosthet Dent* 69:60, 1993.
23. Beumer J et al: Postradiation dental extractions: a review of the literature and a report of 72 episodes, *Head Neck Surg* 6:581, 1983.
24. Murray CG et al: Radiation necrosis of the mandible: a 10-year study. I. Factors influencing the onset of necrosis, *M J Radial Oncol Biol Phys* 6:543, 1980.
25. Murray CG et al: Radiation necrosis of the mandible: a 10-year study. II. Dental factors: onset, duration, and man agement of necrosis, *IntJ Radiat Oncol Biol Phys* 6:549, 1980.
26. Greenberg MS et al: The oral flora as a source of septicemia in patients with acute leukemia, *Oral Surg* 53:32, 1982.
27. McElroy TH: Infection in the patient receiving chemothera py: oral considerations, J *Am DentAssoc* 109:454, 1984.
28. Epstein JB: Antifungal therapy in oropharyngeal mycotic infections, *Oral Surg* 69:32, 1990.
29. Heimdahl A, Nord CE: Oral yeast infections in immuno-compromised and seriously diseased patients, *Acta Odontol Scand* 48:77, 1990.
30. Odds FC et al: Carriage of *Candida* species and *C. albicans* biotypes in patients undergoing chemotherapy or bone mar row transplantation for haematological disease, J *Clin Pathol* 42:1259, 1989.
31. DePaoIa LG et al: Dental care for patients receiving chemotherapy, *J Am Dent Assoc* 112:198, 1986.
32. Wright WE et al: An oral disease prevention program for patients receiving radiation and chemotherapy, / *Am Dent Assoc* 110:43, 1985.
33. Thurmond JM et al: Oral *Candida albicans* in bone marrow transplant patients given chlorhexidine rinses: occurrence and susceptibilities to the agent, *Oral Surg* 72:291, 1991.