

Oral Complications of Cancer Therapies

Introduction

More than 1 million Americans will develop cancer during 1989. These newly diagnosed malignancies will include 228,000 gastrointestinal cancers, 155,000 lung cancers, 143,000 invasive breast carcinomas, 40,000 lymphomas, and 27,000 cases of leukemia. Also included are the estimated 30,000 cases of oral and oropharyngeal cancer.

Management of many malignancies requires local or radical surgical excision. Other forms of cancer treatment may be employed, e.g., radiation therapy, chemotherapy, and bone marrow transplantation. Unfortunately, most cancer treatments affect normal as well as neoplastic cells and tissues. As treatments have become more intensive and therapeutically successful, the effects on normal tissues have increased. The oral cavity is a very frequent site of such side effects. As a result of treatment, as many as 400,000 patients may develop oral complications that may be acute or chronic in nature. The more powerful the treatment modalities, the greater the risk of morbidity.

At a minimum, oral complications are painful, diminish the quality of life, and may lead to significant compliance problems, often discouraging the patient from continuing treatment. Cancer treatments may produce a breach in mucosal integrity, allowing pathogenic organisms to spread systemically, further compromising the patient. At times, levels of oral morbidity may interfere with oncologic therapy, necessitating suspension of therapy until such complications resolve.

Side effects of radiation therapy to the head and neck may be noted as early as the first week. The potentially devastating occurrence of osteoradionecrosis in the irradiated patient has yet to be widely addressed in terms of multicenter, collaborative studies. The prevention and management of this and other oral complications remain as incompletely resolved clinical issues. Bone marrow transplantation (BMT) is an evolving cancer management with frequent oral complications. Although BMT was once considered desperate and reserved for treatment of end-stage leukemia, it is now used routinely as an effective tool for treatment of several other cancers. Before and after actual transplantation, the possibility of secondary dysfunctions of the oral cavity exists. The stomatotoxicity of chemotherapy and total body irradiation, the associated risk of early septicemia from oral organisms, and the possibility of acute and chronic graft-versus-host disease all may affect the ultimate treatment outcome. Literature on the subject is sparse, and there are few well-documented studies demonstrating the efficacy of treatment of oral complications of BMT.

Pretreatment therapy for oral complications can positively affect the outcomes of cancer treatment. All members of the cancer treatment

team should be fully informed of the oncologic treatment plan. Oral care should be initiated at the outset of cancer treatment with the goal of reducing morbidity and in many instances improving compliance.

This report will answer the following questions:

- Is there a role for pretherapy interventions affecting the oral cavity in reducing the incidence of oral complications in the cancer patient?
- Which pretreatment strategies are optimal to prevent or minimize oral complications?
- What are the most effective strategies for management of acute oral complications occurring during cancer therapy?
- What are the indicated strategies for management of chronic oral complications following cancer therapy?
- What are the directions for future research?

Absent from the discussion in this report are the broad and important areas of postsurgical management, including surgical reconstruction and maxillofacial prosthodontic treatment. Both the surgical and prosthodontic considerations are significant but beyond the scope of this report.

What Are the Oral Complications of Cancer Therapies?

Surgical removal of anatomical structures in the head and neck region compromises oral function to varying degrees. In chemotherapy, most complications are the result of myelosuppression, immunosuppression, and direct cytotoxic effects on oral tissues. Major clinical problems in the oral cavity that are associated with chemotherapy include mucositis, local or systemic infection, and hemorrhage. Total body irradiation and radiation for head and neck cancer have both direct and indirect effects on oral and related structures. The oral complications of radiotherapy to the salivary glands, oral mucosa, oral musculature, and/or alveolar bone include growth and developmental abnormalities, xerostomia, rampant dental caries, mucositis, taste loss, osteoradionecrosis, infection, dermatitis, and trismus. It is the recognition of the risk of these complications and their relation to outcome that prompts the discussion and necessitates agreement on the best means of management.

These complications result from the aggressive treatment of cancer; many would not occur if cancers could be detected and treated at an early phase. The emphasis in this report on the prevention and treatment of complications should not detract from the basic goal of prevention and early detection of cancer.

Is There a Role for Pretherapy Interventions Affecting the Oral Cavity in Reducing the Incidence of Oral Complications in the Cancer Patient?

Oral complications resulting from anticancer therapies can significantly affect morbidity, the patient's tolerance of treatment, and the quality of life. Death can sometimes result from severe oral complications. There is a role for pretherapy intervention in reducing the incidence and severity of oral complications. Research data demonstrate that appropriate interventions can significantly lessen morbidity and possibly decrease mortality.

There is evidence that preexisting oral disease unrelated to cancer or therapy may increase the risk of oral complications. Before the initiation of cancer therapy, a comprehensive pretreatment dental evaluation is mandated. The following objectives should be fulfilled:

- Establish baseline data with which all subsequent examinations can be compared.**
- Identify risk factors for the development of oral complications.**
- Perform necessary dental treatment to reduce the likelihood of oral complications induced by cancer treatment.**

Which Pretreatment Strategies Are Optimal To Prevent or Minimize Oral Complications?

There are many pretreatment strategies available to minimize or prevent oral complications. These afford the clinician a unique opportunity to ameliorate the side effects induced by cancer therapy. Pretreatment strategies include evaluation, treatment of preexisting dental disease, patient and family education and counseling, prevention of oral mucosal infections, interventions to modify salivary gland dysfunction, reduction of iatrogenic and disease-related neutropenia, and prevention of mucositis.

A comprehensive patient examination is paramount to identify preexisting oral problems that have the potential to affect the course of cancer therapy. To satisfy the objectives of the examination, the following data must be obtained in patients at risk for oral complications: cancer diagnosis, medical history, dental history, dental charting, periodontal charting, appropriate radiographs, and nutritional status. Some clinicians may wish to include volumetric assessment of resting and stimulated whole saliva. Additionally, study models could be obtained where deemed appropriate.

Potentially complicating oral disease should be identified and corrected as early as possible before commencement of anticancer therapy. Significant problems include poor oral hygiene, third molar pathology, periapical pathology, periodontal disease, dental caries, defective restorations, illfitting prostheses, orthodontic appliances, and any other potential sources of irritation.

Sources of infection and irritation are important targets for early intervention. At the initial dental evaluation, all cancer patients should undergo thorough oral hygiene procedures, including root planing, scaling, and curettage. These procedures are beneficial in reducing the incidence of oral complications by removing bacteria that can result in local and systemic infection. The neutrophil and platelet count must be considered before any patient undergoes an invasive procedure. This intervention should be supplemented by daily plaque removal including toothbrushing with a fluoride toothpaste and flossing, if this can be tolerated by the patient. Additionally, the use of topically applied fluorides and chlorhexidine mouth rinse has shown clinical benefit in the prevention and control of dental caries and plaque.

Dental foci may be potential sources for systemic infection and should be eliminated or ameliorated. Treatment may include dental extractions or endodontic therapy. Ideally, dental procedures, but especially dental extractions, should be completed at least 14 days before cancer therapy, if the patient's condition permits.

Most of the pretreatment as well as treatment protocols aimed at preventing or ameliorating oral complications of anticancer therapy require patient adherence to prescribed oral hygiene procedures. Patient and family education, counseling, and motivation are critical to the success of any preventive pretreatment strategy. The patient must be cognizant of the potential side effects of the anticancer regimen. The rationale for pretreatment strategies must be explained to encourage patient adherence to the therapy.

Bacterial and fungal surveillance cultures are not necessary for routine patient management. Suspicious lesions should be cultured. The use of prophylactic acyclovir should be considered in seropositive patients at high risk for reactivating herpes simplex virus infection, i.e., the bone marrow transplant patient and possibly other patients with prolonged, profound myelosuppression. The prophylactic use of acyclovir in patients who are at lower risk probably is not indicated and carries a low risk of development of acyclovir-resistant strains. Although acyclovir is a relatively safe drug, it may have side effects, including renal dysfunction and, rarely, central nervous system toxicity.

Salivary gland dysfunction is one of the most common sequelae of head and neck cancer treatment. At present, there are no agreed-upon pretreatment strategies to prevent or minimize xerostomia. However, studies are being conducted to evaluate various techniques, including

radioprotective agents and drugs such as pilocarpine that can maintain or enhance salivary gland function during radiation. The latter approach appears to be the most promising for future clinical applications.

Pretreatment strategies to reduce iatrogenic and disease-related neutropenia in cancer patients are under investigation. A pilot trial of recombinant granulocyte colony stimulating factor (rhG-CSF) administered to patients during chemotherapy resulted in restoration of the neutrophil count and function and a decrease in severity of mucositis. Mucositis is a universal and often painful consequence of chemotherapy and radiotherapy to the head and neck. At the present time, there is no other agent that is effective in preventing therapy-related mucositis. Randomized clinical trials addressing this problem are in progress.

What Are the Most Effective Strategies for Management of Acute Oral Complications Occurring During Cancer Therapy?

Acute oral complications occurring during treatment are related to the type of cancer and forms of therapy. These problems have several different clinical presentations including: mucosal inflammation and ulceration of varying etiologies, oral candidiasis, viral and bacterial infections, dental or periodontal infections, and mucosal bleeding. Treatment of oral infections is important to reduce the debilitating symptoms associated with these lesions and to minimize the risk for developing systemic bacterial or fungal infections.

Mucosal Inflammation and Ulceration

Radiation therapy for head and neck cancer causes mucositis, which can progress from erythema to ulceration. Chemotherapy given in conjunction with radiation may accelerate the onset and increase the severity of radiation mucositis. No currently available drugs can prevent mucositis. Distinguishing radiation-induced mucosal changes from other similar appearing lesions is suggested by their occurrence within the radiation fields. Appropriate cultures and smears may be necessary to diagnose fungal infection in the presence of radiation mucositis. There are several alternative drugs for antifungal therapy; however, prolonged dental contact with nystatin solution, nystatin pastilles, or clotrimazole oral troches may lead to dental caries because they contain large quantities of sugar.

Chemotherapy that does not result in profound myelosuppression can nevertheless cause mucosal ulceration by directly damaging the epithelium. The most commonly associated agents are antimetabolites such as methotrexate, 5-fluorouracil, and purine antagonists. Antitumor antibiotics, hydroxyurea, VP-16, and procarbazine can also cause nonspecific mucosal ulceration.

Oral ulceration may be associated with the underlying cancer, particularly acute leukemias, and with severe neutropenia from any cause. In these cases, the diagnosis is dependent on recognizing the association and ruling out infection. In a high percentage of patients undergoing BMT, oral mucosal lesions may occur as part of acute or chronic graft-versus-host disease. These lesions may take several forms, including erythema, lichenoid change, ulceration, or hyperkeratosis. Therapy depends on management of the underlying disease.

There are also many untested topical oral preparations that claim to reduce the symptoms of oral mucositis. The efficacy and safety of these agents have not been established. Ingredients in these combinations have included: diphenhydramine hydrochloride, kaolin and pectin, magnesium sulfate, antacids, sucralfate, corticosteroids, dyclonine, and lidocaine hydrochloride. In patients having trouble eating because of severe oral mucositis, use of local and/or systemic pain control may be necessary.

Viral Infection

Herpes simplex virus (HSV) is the most common viral pathogen associated with oral lesions in patients receiving myelosuppressive chemotherapy or BMT. A large number of patients have had prior infection with HSV as evidenced by the presence of HSV antibodies in the serum of 30 to 100 percent of adults in the general population. Under conditions of immunosuppression, the latent virus often reactivated, leading to severe oral, and occasionally, disseminated infections. Approximately 50 to 90 percent of BMT patients who are seropositive for HSV will develop HSV infections, usually within the first 5 weeks after transplantation. Similarly, a large proportion of patients with acute leukemia or others receiving intensive chemotherapy will reactivate HSV during periods of immunosuppression.

In contrast to HSV infection in immune competent individuals, HSV infections in the immunocompromised host are associated with severe ulcerations that may occur on any oral mucosal surface. In immunocompromised patients, the mucositis associated with HSV is more painful, severe, and prolonged than mucositis uncomplicated by viral infection. HSV ulcerations may be the portal of entry for bacterial and fungal pathogens. In addition, the virus may cause esophagitis and, rarely, disseminated infection.

Herpes simplex infections are often difficult to diagnose on clinical grounds alone because it may be difficult to differentiate them from mucosal lesions of other etiologies. Due to the morbidity associated with HSV infections and because of the availability of effective antiviral therapy, it is advisable to obtain viral cultures in immunosuppressed patients. Cytologic and newer diagnostic tests for the presence of viral antigens may be useful for rapid diagnosis of HSV infections. In patients

in whom the presumptive diagnosis is oral HSV infection, it is reasonable to initiate therapy with either oral or intravenous acyclovir while awaiting the results of viral diagnostic tests. The intravenous route may be preferred in severe infections and in patients unable to take oral medications.

Oral Candidiasis

Several types of oral mucosal lesions are caused by overgrowth and infection by *Candida* species, including pseudomembranous candidiasis (removable white plaques), chronic hyperplastic candidiasis (leukoplakia-like white plaques that do not rub off), chronic erythematous candidiasis (patchy or diffuse mucosal erythema), and angular cheilitis. Fungal cultures, potassium hydroxide, and gram-stained smears are helpful diagnostic tools. The white, raised, removable plaques of the pseudomembranous form of candidiasis are most obvious to the examiner. Diagnosis can be confirmed by a potassium hydroxide smear. These organisms may infect other sites in the gastrointestinal tract and cause esophagitis or diarrhea. In neutropenic patients, mucosal infection with *Candida* may lead to systemic infection.

Topical forms of therapy for oral candidiasis include nystatin and clotrimazole.

Pseudomembranous candidiasis can usually be treated with topical nystatin. Lesions of chronic oral candidiasis usually require much longer treatment, especially in patients with severe chronic xerostomia resulting from head and neck radiation therapy. In more extensive infections, such as esophagitis, oral ketoconazole may be effective. For infections not responding to the above measures, a course of low-dose intravenous amphotericin B may be indicated. Disseminated candidiasis should be managed with intravenous amphotericin B.

Bacterial Infections

Bacterial organisms in the mouth can cause localized infections, including acute sialadenitis of major salivary glands, periodontal abscess, pericoronitis, or other mucosal or dental infection. These problems usually require empirical treatment with selected antibiotics, but gingival and periodontal lesions usually require additional treatment by local debridement of bacterial plaques.

Systemic infection is a major cause of morbidity and mortality in neutropenic patients. In some cases, the oral cavity may be the portal of entry for bacterial pathogens. Whether a source of infection can be identified or not, empiric, broad-spectrum antibiotic therapy must be initiated promptly in the febrile neutropenic patient. There are several different antibiotics or antibiotic combinations that may be appropriate in this setting. Because *Pseudomonas* infections are associated with a

high mortality rate in neutropenia, the empiric regimen should include antibiotics that adequately treat this organism.

Mucosal Bleeding

Mucositis due to any cause may be accompanied by oral bleeding, especially in severe thrombocytopenia caused by leukemia, lymphoma, or myelosuppression. Disseminated intravascular coagulation is another important potential cause of thrombocytopenia or hemorrhage in immunocompromised patients. Severe thrombocytopenia may predispose patients to bleeding from routine mechanical oral hygiene procedures. In addition, these procedures may increase the risk of septicemia in patients with severe neutropenia. In these patients, dental plaque can be effectively managed by daily mouth rinsing with a chlorhexidine solution.

What Are the Indicated Strategies for Management of Chronic Oral Complications Following Cancer Therapy?

Therapeutic modalities used in the treatment of malignancy can result in changes in healthy tissues arising long after treatment has been completed. These sequelae must be addressed for the remainder of the life of the patient.

Xerostomia is an example of such a problem in patients receiving therapy for head and neck or other forms of cancer. Total body radiation, and especially local radiation to oral structures, may irreversibly affect the production of saliva by both the major and minor salivary glands. The magnitude of this problem is dependent upon the radiation dose and volume of tissue exposed. Significant xerostomia is not as frequently encountered in patients treated with chemotherapy. Concomitantly administered medications such as psychotropic and antiemetic medications should be evaluated for their xerogenic potential.

Chronic graft-versus-host disease is associated with xerostomia. Painful lichenoid lesions can also develop in these patients and thus compromise therapy unless controlled by immunosuppressive therapy. Long-term cyclosporine can lead to gingival hypertrophy.

There are no widely employed diagnostic criteria to estimate the degree or extent of xerostomia. We are still primarily dependent upon subjective impressions by both patient and clinician. A dry mouth may affect speech, taste, nutrition, and the patient's ability to tolerate dentures or other oral prostheses. Saliva also contains antimicrobial compounds and is important in the mechanical removal of pathogens from the mouth. As a consequence of decreased saliva production,

there may be an overgrowth of caries-producing organisms. This may have devastating effects on the dentition, even in individuals without prior history of dental caries. In addition, an increase in the frequency of candidiasis and in the severity of gingival/periodontal infections has been observed in some patients.

Management of chronic xerostomia involves a combination of strategies:

- **Continuous maintenance of effective oral hygiene to reduce colonization and proliferation of oral pathogens.**
- **Use of water or saliva substitutes to keep the mouth moist.**
- **Stimulation of residual salivary parenchyma to produce more saliva.**

Intensive oral hygiene methods and the use of an adequately protective topical fluoride are the most important methods of preventing the dental complications of xerostomia.

In terms of saliva substitutes, several preparations are being tested. Ideally, these should reduce patient discomfort, be long-lasting, and should substitute for salivary components that are necessary for the maintenance of mucosal and hard tissue integrity. There is a need for more effective preparations and more data on the long-term benefits of this form of therapy.

Sialogogues, such as pilocarpine and anetholetrithione, alone or in combination, are being tested to stimulate the formation of saliva. The data suggest that this approach benefits patients who have some residual functional salivary tissue, resulting in a steady increase in salivary flow and symptomatic improvement. These drugs appear to be well tolerated; side effects are minimal and readily controlled. The effectiveness of sialogogues in reducing the long-term ravages of xerostomia (e.g., radiation caries) has not been documented.

The long-term effects of radiation therapy to the head and neck region include obliterative endarteritis with resultant tissue ischemia and soft tissue fibrosis. These changes may progress with time and never resolve. Surgical wounds in the irradiated area heal poorly and chronic radiation ulcers may develop. Fibrosis of the muscles of mastication and the temporomandibular joint, while uncommon, may result in trismus. However, recurrent tumor must be ruled out.

Osteoradionecrosis (ORN), a relatively uncommon clinical event, is a consequence of hypovascularity, the cytotoxic effects of radiation on bone-forming cells and tissue, and is associated with hypoxia of the affected bone. As a consequence, when bone is injured, it is unable to heal and becomes susceptible to secondary infection.

This process can progress to pathologic fracture, infection of the surrounding soft tissues, and oral-cutaneous fistula formation. It is characterized by severe, constant pain. The risk of developing ORN is lifelong. Chemotherapy does not increase the risk of ORN.

The initiating injury resulting in ORN is frequently the extraction of a tooth from an irradiated mandible. For this reason, all teeth that might have to be removed should be extracted before starting radiation therapy. If clinical conditions permit, at least 2 weeks, and ideally 3 weeks, should be allowed for adequate healing between the extraction and the commencement of radiation therapy. Healthy teeth should be preserved. Dentures causing ulceration of the atrophic mucosa over the mandible can initiate ORN. Spontaneous ORN can also occur without any obvious injury to the irradiated mandible.

Traditional treatment of ORN with antibiotics and surgical debridement frequently fails with progressive involvement of the remaining mandible. The keystone of the treatment of ORN is the provision of adequate tissue oxygenation in the damaged bone. This is best done by using hyperbaric oxygen therapy (HBO). Multiple treatments are required. Early stages of ORN without fracture or fistulae may be cured by HBO alone. More advanced cases, in addition to HBO, require sequestrectomy or partial mandibulectomy with eventual bone grafting.

In the event that dental extraction is required following radiation, meticulous surgical technique and antibiotic prophylaxis are necessary. In those patients felt to be at particularly high risk of developing ORN, preextraction HBO should be considered. An alternative to postirradiation extraction is endodontic therapy.

Complications in the Pediatric Population

Oral complications arising from the treatment of cancer in children have characteristics in common with those observed in adults. However, because children are actively growing and developing, cancer treatment creates additional long-term problems unique to the pediatric patient. As modern therapy results in increasingly improved survival in a variety of pediatric cancers, long-term sequelae of treatment are beginning to emerge. Some reports indicate that the frequency of oral complications in pediatric patients may be higher than in adults. The nature and severity of these treatment sequelae depend on a number of factors: the type and location of the tumor, the age of the patient, the dose of radiotherapy, the aggressiveness of chemotherapy, the status of oral and dental health, and the level of dental care before, during, and after therapy.

Chronic problems involving target tissues are impaired growth and development of hard and soft tissues, which may result in orofacial asymmetry, xerostomia, dental caries, trismus, and a wide variety of dental abnormalities. The latter include delayed tooth eruption, altered

dental root development with shortening and thinning of the roots, enamel opacities, enamel grooves and pits, small teeth, small crowns, and failure of tooth development and eruption. In teeth with underdeveloped roots secondary to cancer therapy, even minimal periodontal disease will result in early loss of teeth. In general, the principles in the preventive and active treatment of xerostomia, dental caries, and trismus in adults appear to be applicable to children. However, evaluation of the efficacy and long-term consequences of these various strategies has not yet been carried out on a large scale.

These children may have lifelong dental problems requiring periodontic, orthodontic, prosthodontic, or orthognathic procedures. Supervised, consistent oral care, meticulous hygiene, and a regular dental recall schedule (to uncover problems early and determine the need for dental intervention) are key to maintenance of dental health care in children cured of their cancer.

In addition, the emotional and psychological consequences of orofacial deformities and oral dysfunction in these children deserve more attention as increasing numbers survive.

The potential for development of secondary malignancies in these survivors is a serious delayed sequela of successful cancer therapy. Although a majority of secondary malignancies reported in children consist of leukemia or lymphomas, soft tissue and bone sarcomas can occur in irradiated sites. The possibility of secondary malignancies arising in these children should heighten the clinician's awareness of this problem.

Providing education and information to the patient and family is essential for maximum treatment compliance. Direct involvement of the family is thought to result in improved adherence to treatment protocols, thereby enhancing the quality of the patient's life.

The therapeutic team should be multidisciplinary and sensitive to the patient's emotional and physical needs related to the illness. Patients traumatized by the loss of normal oral function, the presence of pain, nausea, and impairment of eating, and a life-threatening illness can become depressed. The following preventive measures should be undertaken by the therapeutic team: provide information to increase the patient's and family's understanding of the medical/oral condition, the treatment plan, and the consequences of treatment. Methods of educating the patient/family should be individualized based on the diagnosis and needs. Patience and positive reinforcement are important.

What Are the Directions for Future Research?

- Devise accurate, quantifiable, reproducible criteria for assessing and classifying oral complications of cancer therapy.

- Determine incidence and prevalence of oral complications related to different types of anticancer therapies and related risk factors.
- Study the mechanisms of cancer treatment injury to the hard and soft oral tissues at the molecular and cellular level and determine how these affect the oral environment.
- Delineate the role of latent HSV activation in the pathogenesis of mucositis due to radiation therapy and chemotherapy of solid tumors.
- Study the frequency, clinical significance, and mechanisms of development of acyclovir resistance by HSV.
- Develop radioprotective and chemoprotective agents.
- Define the role of biological response modifiers, for example, rhG-CSF, in the prevention of myelosuppression and the influence of these agents on oral tissues and oral complications.
- Define and further document through prospective studies the effectiveness of initiating current pretreatment oral care procedures on the incidence, severity, and extent of oral complications of cancer management.
- Develop more effective sialogogues and saliva substitutes and evaluate their effectiveness in preventing the complications of xerostomia.
- Determine the most effective strategies to ensure patient compliance with therapeutic regimens.
- Define the role of the family support unit in the diagnosis, prevention, and treatment of oral complications of cancer treatment.
- Conduct further studies of the role of the oral cavity as a source of systemic infection.
- Conduct controlled studies to determine and test optimal antifungal therapies.
- Define patient populations that will benefit from prophylactic antiviral therapy.
- Define the role for oral antimicrobials in the prevention of infection in neutro- penic patients.
- Devise controlled studies of chlorhexidine and other agents for the control of mucositis in specified patient populations.

- Determine whether oral markers can serve as a predictor of problems of other organs.
- Develop more precise protocols for use of hyperbaric oxygen.
- Study disorders of taste perception in patients undergoing cancer therapy.
- Determine the cost-effectiveness of preventive, diagnostic, and therapeutic management of oral complications.
- Study the effect of different topical fluoride preparations to determine the most effective forms and dosage schedules.

Many research goals can be achieved through coordination of committed members of the dental, medical, and nursing professions already actively involved in clinical investigations. Through such cooperative efforts, patients enrolled in ongoing investigations could serve to answer these important questions.

Deep concern exists that appropriate dental care may not be available due to a significant lack of appropriate levels of third-party reimbursement. This is particularly true when dental treatment necessary as part of the overall cancer management is not reimbursed.

Conclusions and Recommendations

- All cancer patients should have an oral examination before initiation of cancer therapy.
- Treatment of preexisting or concomitant oral disease is essential in minimizing oral complications in all cancer patients.
- Prophylactic acyclovir is beneficial in selected patients to prevent herpes simplex virus reactivation.
- Precise diagnosis of mucosal lesions and specific treatment of fungal, viral, and bacterial infections are essential.
- Mucosal ulcerations should alert the cancer team to the risk of systemic infection.
- Currently, the best treatments for chronic xerostomia include regular use of topical fluorides, attention to oral hygiene, and sialagogues.

- **Osteoradionecrosis can be prevented. When present, it is best managed with hyperbaric oxygen alone or with surgery.**
- **In the pediatric population, it is important to recognize the long-term consequences of radiation therapy that include the dental and developmental abnormalities and secondary malignancies.**
- **Studies of oral complications should be incorporated into ongoing and future cooperative clinical oncology group protocols.**
- **Disseminate information concerning oral complications of cancer therapies and develop strategies to assure adherence by health care providers with appropriate preventive measures.**
- **Develop and implement curricula relevant to oral complications of cancer therapy in schools of medicine, dentistry, dental hygiene, and nursing.**
- **Direct family involvement in patient care is encouraged for maximum treatment compliance.**

Panel Consultants

James J. Sciubba, D.M.D., Ph.D.
Panel and Conference Chairman
Chairman
Department of Dentistry
Long Island Jewish Medical Center
New Hyde Park, New York

Carol S. Beckert, D.D.S.
Pediatric Specialist
Troy, Michigan

Frederick A. Curro, D.M.D., Ph.D.
Director
Pain Service
St. Joseph's Hospital and Medical Center Director
Pharmacology and Clinical Sciences
Block Drug Company
Jersey City, New Jersey

Troy Daniels, D.D.S., M.S.
Panel and Conference Cochairman
Professor and Chairman
Division of Oral Pathology
University of California at San Francisco School of Dentistry
San Francisco, California

R.L. Scotte Doggett, M.D.
Medical Director
Radiation Oncology Center
Sutter Community Hospitals
Associate Clinical Professor
Department of Radiology
University of California at Davis
Sacramento, California

Erlinda Etcubanas, M.D.
Associate Director
Department of Clinical Research
Triton Biosciences, Inc.
Alameda, California

Melbahu M. Gibbs, M.S.W., L.I.C.S.W. Director
Social Work and Ambulatory Alcohol Program
Carney Hospital
Boston, Massachusetts

Keith S. Heller, M.D.
Attending-in-Charge
Head and Neck Surgery
Queen's Hospital Center Affiliate
Long Island Jewish Medical Center
New Hyde Park, New York

Ada M. Lindsey, Ph.D., R.N.
Dean and Professor
University of California at Los Angeles School of Nursing
Los Angeles, California

Gary A. Ratkin, M.D.
Past Chairman
Clinical Practice Committee
American Society of Clinical Oncology
Clinical Associate Professor
Department of Medicine
Washington University School of Medicine
St. Louis, Missouri

Carol Singer, M.D. Chief
Infectious Diseases
Long Island Jewish Medical Center
Associate Professor of Clinical Medicine
The State University of New York at Stony Brook
New Hyde Park, New York

Norton S. Taichman, D.D.S., Ph.D.
Professor and Chair of Pathology

**University of Pennsylvania School of Dental Medicine
Philadelphia, Pennsylvania**

**David Vlahov, Ph.D.
Assistant Professor
Department of Epidemiology
Johns Hopkins University School of Hygiene and Public Health
Baltimore, Maryland**

Source: National Institutes of Health

Speakers

**Linda M. Bartoshuk, Ph.D.
"Chemosensory Alterations and Cancer Therapies"
Professor of Surgery
Section of Otolaryngology
Psychology Department
Yale University School of Medicine
New Haven, Connecticut Anne R. Bavier, M.N.
"Nursing Management of Acute Oral Complications of Cancer"
Program Director
Nursing Research
National Cancer Institute
National Institutes of Health
Bethesda, Maryland Samuel Dreizen, D.D.S., M.D.
"Description and Incidence of Oral Complications of Cancer Therapy"
Professor and Chairman
Department of Oral Oncology
University of Texas Dental Branch
Houston, Texas Joel Epstein, D.M.D., M.S.D.
"Infection Prevention in Bone Marrow Transplantation/Radiation
Patients"
Medical-Dental Staff
Cancer Control Agency of British Columbia
Vancouver General Hospital
Vancouver, British Columbia
CANADA Gerald A. Ferretti, D.D.S., M.S.
"Oral Antimicrobials-Chlorhexidine"
Professor and Director
Pediatric Dental Service
University of Kentucky College of Dentistry
University of Kentucky Medical Center
Lexington, Kentucky Richard B. Friedman, D.M.D., M.P.H.
"Osteoradionecrosis: Causes and Prevention"
Associate Professor and Chairman
Division of Dental Medicine
Medical College of Virginia Hospitals
Richmond, Virginia Janice L. Gabrilove, M.D.**

"Treatment of Iatrogenic and Disease-Related Neutropenia by Recombinant Human Granulocyte Colony Stimulating Factor"

Assistant Member

Memorial Sloan-Kettering Cancer Center

New York, New York Martin S. Greenberg, D.D.S.

"The Role of the Treatment of Dental Disease in Preventing Oral Complications of Cancer Therapies"

Professor and Acting Chairman

Department of Oral Medicine

University of Pennsylvania School of Dental Medicine

Chairman

Department of Dental Medicine

Hospital of the University of Pennsylvania

Philadelphia, Pennsylvania Deborah Greenspan, B.D.S.

"Management of Salivary Dysfunctions"

Associate Clinical Professor

Department of Stomatology

University of California at San Francisco School of

Dentistry

San Francisco, California Penelope J. Leggott, D.D.S., M.S.

"Oral Complications in the Pediatric Population"

Associate Professor

Oral AIDS Center

University of California at San Francisco

University of British Columbia

Vancouver, British Columbia

CANADA Peter B. Lockhart, D.D.S.

"Oral Complications Following Induction Cancer Chemotherapy in Patients With Head and Neck Cancer"

Chairman

Department of Dentistry

Charlotte Memorial Hospital

Charlotte, North Carolina Charles L. Loprinzi, M.D.

"Studies Related to the Prevention of 5FU-Induced Mucositis"

Consultant

Mayo Clinic

Rochester, Minnesota Christine Miaskowski, Ph.D., R.N., O.C.N

"Management of Mucositis During Therapy"

Robert Wood Johnson Clinical Nurse Scholar

Department of Physiological Nursing

University of California at San Francisco

San Francisco, California Roy A.M. Myers, M.D., F.R.C.S., F.A.C.S.

"Radiation Tissue Damage"

Director

Hyperbaric Medicine

MIEMSS

University of Maryland Medical System

Baltimore, Maryland Douglas E. Peterson, D.M.D., Ph.D.

"Infection Prevention in Chemotherapy Patients"

Associate Professor of Oncology

**University of Maryland Cancer Center
Professor of Oral Diagnosis
University of Maryland Dental School
Baltimore, Maryland Spencer W. Redding, D.D.S., M.Ed.
"Role of Herpes Simplex Virus Reactivation in Chemotherapy-Induced
Oral Mucositis"
Interim Associate Dean for Advanced Education and
Hospital Affairs
University of Texas Health Science Center
San Antonio, Texas Simon W. Rosenberg, D.M.D.
"Chronic Dental Complications Following Cancer Therapy"
Assistant Attending Dentist
Department of Surgery
Memorial Sloan-Kettering Cancer Center
New York, New York Marc Rubin, M.D.
"Monotherapy for Empirical Management of Febrile Neutropenic
Patients"
Investigator
Infectious Diseases Section
Pediatric Branch
National Cancer Institute
National Institutes of Health
Bethesda, Maryland Jean E. Sanders, M.D.
"Implications of Cancer Therapy to the Head and Neck on Growth and
Development"
Associate Professor of Pediatrics
University of Washington
Associate Member
Fred Hutchinson Cancer Research Center
Seattle, Washington Rein Saral, M.D.
"Management of Acute Viral Infections"
Associate Professor of Oncology and Medicine
Johns Hopkins Hospital
Baltimore, Maryland Stephen C. Schimpff, M.D.
"Surveillance Cultures"
Executive Vice President
University of Maryland Medical System
Baltimore, Maryland Mark M. Schubert, D.D.S., M.S.D.
"Recognition, Incidence, and Management of Oral Graft-Versus-Host
Disease"
Assistant Professor
Department of Oral Medicine
University of Washington
Fred Hutchinson Cancer Research Center
Seattle, Washington Jerry L. Shenep, M.D.
"Combination Antibacterial Therapy for Febrile, Neutropenic Cancer
Patients"
Associate Member
St. Jude Children's Research Hospital
Memphis, Tennessee Sol Silverman, Jr., D.D.S., M.A.**

"Oral Defenses and Compromises as a Result of Cancer Therapy"

Professor and Chairman

Division of Oral Medicine

University of California at San Francisco School of Dentistry

San Francisco, California Stephen T. Sonis, D.M.D., D.M.Sc.

"Pretreatment Oral Assessment"

Professor of Oral Medicine

Harvard School of Dental Medicine

Chief

Dental Service

Brigham and Women's Hospital

Boston, Massachusetts Christopher A. Squier, Ph.D., D.Sc., M.A.

"Mucosal Alterations"

Professor

Department of Oral Pathology

Director

Dows Institute for Dental Research

Assistant Dean for Research

University of Iowa College of Dentistry

Iowa City, Iowa Peter Stevenson-Moore, B.D.S., C.D.S.R.C.S., M.S.D.,

M.R.C.D.(C)

"Essential Aspects of a Pretreatment Oral Examination"

Cancer Control Agency of British Columbia

Vancouver, British Columbia