Management of Oral Complications from Radiation and Chemotherapy

The oral examination reveals: very dry, erythematos oral mucosal tissues with areas of erosion extending through the epithelial layers. Especially affected is the tongue, which is also fissured and atrophic with loss of papillae covered by a thin white coating. The gingivae and periodontium are quite healthy except for some erythema all around the marginal gingivae.

Nelson L. Rhodus, D.M.D., M.P.H.*
A 62-year-old male presents with the following:

Chief complaint: very sore, burning mouth which is very dry with painful sores and teeth. Patient has also lost much of his sense of taste and has difficulty eating and swallowing.

Medical history:
The patient had Stage III invasive squamous cell carcinoma of the left lateral posterior tongue, which was diagnosed two years ago. He had a surgical resection of the left tongue along with a modified neck dissection in which 31 lymph nodes were removed, two of which demonstrated malignancy. Therefore, he underwent 32 treatments of IMRT (intensity modulated radiation therapy), for a total of 6800 cGy. He has not had regular dental visits.

Patient’s dental management will include: After cancer therapy is completed and remission or a cure is the outcome, the cancer patient should be placed on an oral recall program. Usually, the patient is seen once every one to three months during the first two years and at least every three to six months thereafter. After five 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 develop, the initial lesions may recur, and complications related to therapy can be detected and managed.

The usual long-term complications associated with the cancer and its therapy include chronic xerostomia, mucosal atrophy and erosion, loss of taste, altered bone, oral infections 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 the continued use of daily fluoride gel applications). Also, early detection of oral soft tissue and hard tissue disease can be found before inflammation and infection involve the underlying bone leading to necrosis (bone death).

Salivary gland tissue is sensitive to radiation damage. Because of this, glandular tissue in the field of radiation can be permanently damaged.

*Dr. Rhodus is Professor and Director, Division of Oral Medicine, School of Dentistry, and Adjunct Professor, Department of Otolaryngology, School of Medicine at the University of Minnesota. Email is rhodu001@umn.edu.
resulting in hyposalivation. This is directly related to the radiation field and salivary gland dose and baseline salivary function.

Up to a 50% to 60% reduction of salivary flow may occur after the first week of radiation therapy. After radiation therapy, saliva is reduced in volume and pH and increased in viscosity and immunoglobulin concentration. These changes often progress several months after radiotherapy has ceased, and the radiation-induced salivary gland damage and dysfunction are permanent and irreversible. Variable degrees of a return in salivary gland function may occur, although most patients recover little to none of pretreatment levels.

The direct effects of hyposalivation include extreme dryness of the oral mucosa and associated discomfort, inconvenience, and substantial diminution of quality of life. Clearly, saliva is an important host defense mechanism against oral disease, serving a variety of important functions in the oral cavity. In a healthy mouth, saliva's essential electrolytes, glycoproteins, immunoglobulins, hydrolytic enzymes (amylase), antimicrobial enzymes, and a number of other important factors are crucial in maintaining normal oral health and function. Saliva in normal quantities and composition serves to cleanse the mouth, clear potentially toxic substances, regulate acidity, buffer decalciﬁying acids, neutralize bacterial toxins and enzymes, destroy microorganisms, and remineralize enamel with inorganic elements (e.g., calcium and phosphorus), thus maintaining the integrity of the teeth and soft tissues.

During and following radiotherapy, the teeth may become hypersensitive.

When the normal environment of the oral cavity is altered because of a decrease in or total absence of salivary flow or because of alterations in salivary composition, the mouth becomes susceptible to painful deterioration and decay. This is particularly signiﬁcant if it continues for a long time. Dry, atrophic, and ﬁssured oral mucus membranes result from dryness along with accompanying ulcers and desquamation, opportunistic bacterial and fungal infections, inﬂamed and edematous tongue, caries, and periodontal disease. Common and the most potentially devastating systemic manifestations of hyposalivation are difficulty in lubricating and chewing food (sticking to the tongue or hard palate) and difﬁculty swallowing food (dysphagia). Additionally, there is often a lack of or altered taste perception (hypogeusia or dygeusia) and tolerance for certain acidic foods and liquids. As a result, nutritional intake in these individuals may be impaired.

An additional major manifestation of salivary hypofunction in patients having undergone irradiation therapy is a severe form of caries called radiation caries. Radiation caries is estimated to occur 100 times more frequently in patients who have received head and neck radiation (>5000cGy) compared to those who have not had radiation. It can progress within months, advancing towards pulpal tissues and resulting in dental abscesses that can extend to the surrounding irradiated bone. Extensive infection and necrosis can result. An assessment of salivary flow should be made at the outset of treatment to help prevent this complication. Obviously, stimulating additional salivary flow is imperative. A prescription for concentrated ﬂuoride toothpaste (5000 ppm) should be provided to these patients for use in custom trays or for brush-on application. Fluoride varnish applied regularly is crucial to prevention of caries, especially after teeth have been restored.

Xerostomia is managed according to the three categories delineated in Table One. First is the provision of additional moisture and lubrication to the oral cavity and oropharynx by BOTH salivary substitutes and stimulation of the patient’s salivary glands. Several artificial salivas are available, some of which provide a modicum of relief. However, synthetic saliva solutions alone are not satisfactory for relief of the complaints associated with chronic, severe xerostomia. These patients will require stimulation of saliva with one of the sialogogues.

Caffeine, alcohol, and tobacco should be avoided. Also, patients should avoid sipping drinks that contain sugar, as exposed root surface may break down rapidly (in less than six months), resulting in recurrent radiation caries. Sugarless mints, candies, or chewing gum (containing xylitol) are beneﬁcial in producing some additional moisture.

Considerable research has been performed with various stimulants such as pilocarpine HCl (Salagen), anethole trithione (Sialor), and cevimeline (Evoxac). These drugs appear to be effective for stimulating salivary ﬂow in most patients who have some residual salivary function. However, certain side effects occur, and patients have to be carefully screened (i.e., cardiovascular disease, diabetes, concomitant medications) before being placed on these drugs. Of particular note is that approximately
50% of patients who use pilocarpine experience increased salivary flow and noticed symptomatic improvement in their dry mouth. Therefore, although the drug increases salivary flow and provides beneficial constituents to the oral cavity, patients may still need adjunctive artificial saliva in order to feel more comfortable.

**Tooth Sensitivity.** During and following radiotherapy, the teeth may become hypersensitive, which could be related to the decreased secretion of saliva and the lowered pH of secreted saliva. The topical application of a fluoride gel as well as fluoride varnish should help to reduce these symptoms. Specific commercially available devices are also available for this purpose.

**Muscle Trismus.** Radiation therapy of the head and neck can cause damage to the vasculature of muscles resulting in Trismus or limited oral opening. The patient should perform daily stretching exercises to improve trismus, preceded by application of warm moist heat. One exercise is for the patient to place a given number of tongue depressors in the mouth at least three times a day for ten minute intervals. By slowly increasing the number of tongue depressors, muscle stretching will occur and more normal function will ensue. Specific commercially available devices are also available for this purpose.

**Muscle Trismus.** Radiation therapy of the head and neck can cause damage to the vasculature of muscles resulting in Trismus or limited oral opening. The patient should perform daily stretching exercises to improve trismus, preceded by application of warm moist heat. One exercise is for the patient to place a given number of tongue depressors in the mouth at least three times a day for ten minute intervals. By slowly increasing the number of tongue depressors, muscle stretching will occur and more normal function will ensue. Specific commercially available devices are also available for this purpose.

**Prosthodontics.** Patients should avoid wearing their dentures during the first six months after completion of the radiotherapy because mild trauma to the altered mucosa can result in ulcerations and possible necrosis of underlying bone (see section on osteoradionecrosis). Once patients start to wear their dentures, they must be told to come to the dentist if any sore spots develop so the dentures can be adjusted. Ill-fitting 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 help with adhesion. Implants can be placed 12 to 18 months after radiation therapy, but the dentist must have knowledge of tissue irradiation fields, degree of healing, and vascularity of the region. For example, implants placed in the maxilla and the anterior mandible are less of a risk for osteoradionecrosis than those placed in the posterior mandible.

**Table One. Management of Salivary Dysfunction**

<table>
<thead>
<tr>
<th>I. Moisture/Lubrication</th>
<th>Rx Dexamethasone (Decadron Elixir) 0.5 mg/5 ml§</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Drink/sip water, liquids (that lack fermentable carbohydrate and carbonic acid).</td>
<td>± Rx Triamcinolone 0.1% (in hydrocortisone acetate) (O rabæ) (O rabæ-H CA)</td>
</tr>
<tr>
<td>B. Avoid ethanol, tobacco, caffeine, and hot, spicy, or salty foods.</td>
<td>± Rx Clotrimazole (M ycelex) 60-mg troches</td>
</tr>
<tr>
<td>C. Use xylitol candy/gum, Salix or N umoisyn lozenges.</td>
<td>± Rx Nystatin and triamcinolone ointment (M ycelex II, T ristatin II, M ytrex)</td>
</tr>
<tr>
<td>D. Artificial OTC Salivas: Oasis, Salivart, Moi-Stir, M oathkote (some patients need multiple articles). For Oral Balance, apply 1/2 tsp 5 to 6 times daily as needed, especially at night.</td>
<td><strong>III. Prevention of Caries-Periodontal Disease</strong></td>
</tr>
<tr>
<td>E. Rx Pilocarpine HCl 2% (Salagen)† 5 mg, tid or qid daily, or Rx Cevimeline (Evoxac)† 30 mg caps tid or qid daily.</td>
<td>A. Meticulous personal oral hygiene</td>
</tr>
<tr>
<td><strong>II. Soft Tissue Lesions-Soreness</strong></td>
<td>B. Avoid acidic drinks</td>
</tr>
<tr>
<td>OTC Oral Balance and Biotene mouthwash.</td>
<td>C. Toothpaste (Biotene)</td>
</tr>
<tr>
<td>Rx Diphenhydramine (Benadryl) + M aalox + nystatin elixir† (± Sacrafate) (± 0.5% viscous lidocaine)</td>
<td>D. R egular hygiene recalls and dental prophylaxis (three months)</td>
</tr>
<tr>
<td><strong>G. Fluoride varnish</strong></td>
<td>E. M echanical brushes, waterpik, N aH CO₄ rinses</td>
</tr>
<tr>
<td>+Rx Neutral N af 1.0%-trays (Prevident 5000)</td>
<td>F. X ylitol gum</td>
</tr>
<tr>
<td>+Rx Chlorhexidine gluconate (Perix, Periguard)</td>
<td><strong>III. Prevention of Caries-Periodontal Disease</strong></td>
</tr>
</tbody>
</table>

*Salivary gland dysfunction, hyposalivation, or xerostomia should be managed by the diagnosis and according to the signs, symptoms, and severity of its manifestations in the oral cavity. Decreases in the quantity, and alterations in the composition of, beneficial constituents of saliva render the patient subject to many problems. The strategies for management will vary from individual to individual as to severity and are divided into the above three major areas.

†Caution in use in patients who have chronic obstructive pulmonary disease (COPD) and patients at risk for myocardial infarction (MI).

‡Rx: Benadryl 25 mg/10 ml + nystatin 100,000 IU/ml + M aalox 4 ml; eq 15 ml.

§Rx: Decadron Elixir 0.5%/5 ml. Dispense 100 ml. Sig: 1 tsp. tid swish-swallow.
induced changes (hypocellularity, hypovascularity, and ischemia) in the jaws. Most cases result from damage to tissues overlying the bone, as opposed to 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 received in excess of 6500 cGy, who continue to smoke, and undergo a traumatic (i.e., extraction) procedure. Risk is greater for dentate patients than edentulous patients, and when periodontal disease is present. Non-surgical procedures that are traumatic (e.g., curettage) or cause a reduction of blood supply to the region (use of vasoconstrictors) can result in ORN. Spontaneous ORN also occurs. The risk remains throughout a patient’s lifetime.

If the dentist is unsure of the amount and specific location of radiation received by the patient and any invasive procedures that are planned, he or she should concur with the radiation oncologist before initiating any care. The risk of ORN increases with increasing dose to the jaws (e.g., 7500 cGy is a greater risk than 6500 cGy). Patients determined to be at risk should be provided the appropriate preventive measures.

Protocols to reduce the risk of osteoradionecrosis include selection of endodontic therapy over extraction, and the use of prophylactic antibiotics plus antibiotics during the week of healing (penicillin VK for seven days); and hyperbaric oxygen before invasive procedures.

Once necrosis occurs, conservative management usually is indicated. If swelling and suppuration (infection) are present, broad-spectrum antibiotics are used. Severe cases benefit from hyperbaric oxygen treatment 60 to 90 minute dives, five days per week (for a total of 20 to 30 dives), followed in most cases by removal of necrotic bone.

There are many severe oral complications from radiation and chemotherapy which can cause significant pain, suffering, and a diminished quality of life, not to mention substantial cost. However, many if not most of these can be prevented or reduced by early intervention and proper management by the dentist.

---

**Bibliography**