Henry Ford Hospital Medical Journal

Volume 29 | Number 3 Article 3

9-1981

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Henry Ford Hosp Med J
Vol 29, No 3, 1981

A Role for Dentistry in Managing the Oro-Nasopharyngeal Irradiated Cancer Patient

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Radiation therapy for oral and nasopharyngeal carcinoma produces direct and indirect changes in the oral cavity. Before such therapy is begun, the cancer patient should be examined by a trained dental specialist so that associated problems such as oral mucositis, xerostomia, radiation dental caries, osteoradionecrosis, and ageusia can be addressed. During and after irradiation therapy as well, the dental specialist should be involved in the treatment program. In this way, it is possible to maintain the patient's dental system through restorative measures, mandatory use of topical fluorides, dental rinses, and preventive prophylaxis.

Radiation therapy for oral and nasopharyngeal carcinoma produces direct and indirect tissue changes in the oral cavity which cause painful, dysfunctional, esthetic, and personal problems for the irradiated oral cancer patient. With the improved prognosis with treatment in these cases, greater emphasis has shifted to rehabilitation. Such rehabilitation, both during and after radiation, can best be provided by the combined efforts of medical and dental personnel. Mucositis, xerostomia, hypogeusia or ageusia, cervical dental caries, and tissue necrosis may all occur, with varing severity, in response to radiation therapy of the head and neck. This article reviews the literature on these common oral changes and presents a dental program to treat them.

Mucositis

When irradiation is started, a characteristic reddening of the oral mucosa occurs almost immediately (1,2), and painful desquamation (1) and cervical odontogenic sensitivity (3) usually follow. During the mucositis, the incidence of infection increases (1), most commonly candidiasis (4,5). The severity of mucositis does not depend on the presence or even the successful management of the fungal organism (5) but seems to be related to the level, time, and intervals of the dosage of irradiation (6,7). Fortunately, symptoms improve progressively over two to four weeks (1,6,7).

Xerostomia

Oral irradiated patients commonly experience changes in salivary flow and consistency. Flow reduction, which begins when salivary glands receive 450R (9), is marked during the first three to seven days of therapy (8,9) (Fig. 1). At 5,000R to 6,000R, permanent salivary gland changes occur, and xerostomia becomes permanent (1,6,9-12).

Initially in all glands, histopathologic changes consist of mucous acinar damage, which results in a mucous discharge of "ropey" saliva (13). Parotid serous acini become edematous and devoid of secretory granules (12,13). Serous flow will decrease more rapidly and more completely than mucinous flow (2,12). Parenchymal degeneration (13), acinar necrosis (2,12,13), fibrosis (1,2,6,12,13), adiposis (2,12), and finally lymphocyte infiltration (12) produce permanent gland atrophy and advanced dysfunction.

Hypogeusia and Ageusia

Changes in taste acuity, as measured by the patient's ability to taste sucrose, hydrochloric acid, and quinine, begin with the first 240-400R (14). Loss of acuity then progresses until, at greater than 3,000R, 500 to 8,000 times the normal concentrations are required to elicit a normal taste response. When dosages reach 6,000R, ageusia can be permanent (1,2,6,10,11). As the patient recovers, a tenfold improvement can be expected within 20 to 60 days after

Submitted for publication: March 24, 1981
Accepted for publication: April 20, 1981

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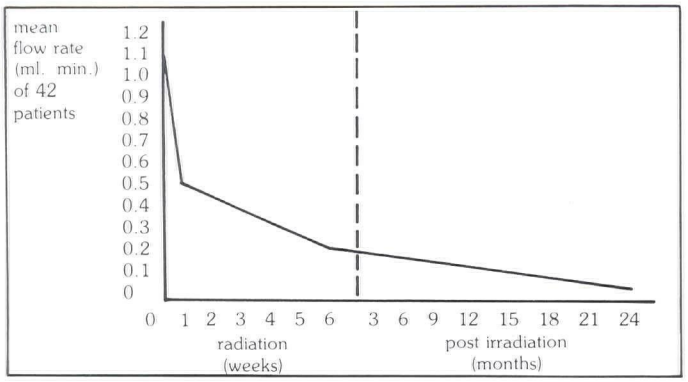

Fig. 1

Rate of salivary flow reduction. Reprinted with permission from Dreizen S, et al. Prevention of xerostomia-related dental caries in irradiated cancer patients. J Dent Res 1977;56(2):99-104. Copyright by Journal of Dental Research 1977.

irradiation (14), and full pretreatment acuity levels can be expected within two to four months (1,6,14). Hypogeusia or ageusia is probably caused by the loss of or damage to microvilli on the tongue papillae (6,11,14).

Cervical Dental Caries

A characteristic pattern of dental decay in the orofacially irradiated cancer patient (1,3,4,7,10,12,15) occurs in cervical areas and on smooth tooth surfaces not normally susceptible to decay (Fig. 2). The carious lesion tends to be large and broad, sometimes circumscribing the tooth (15) and causing carious tooth amputations (7).

In the past, it was felt that postirradiation root decay was the direct effect of ionizing beams on tooth tissue itself, but subsequent studies have shown that even teeth outside the ionizing beam become decayed (15). While in vitro studies generally show that irradiated teeth are not chemically or structurally altered (12,16,17), one in vivo study on rat teeth (18) did find some evidence of irradiation changes on tooth tissue. In contrast to the human condition, however, rodent teeth are permanently erupting to compensate for occlusal wear. The irradiation effect in this study was on developing tooth tissue, not on already formed tissue, as with human teeth.

Postirradiation decay is, therefore, felt to be due to the indirect effect of xerostomia, since a similar, if not identical, decay pattern has been reported in patients with chronically reduced salivary flow, such as narcotics addicts (19,20) and those affected with Sjogren's syndrome (21).

Microbiological effects of xerostomia

Table I illustates the important inverse relationship between Streptococcus sanguis and Streptococcus mutans in caries-free versus carious dental plaque in the general

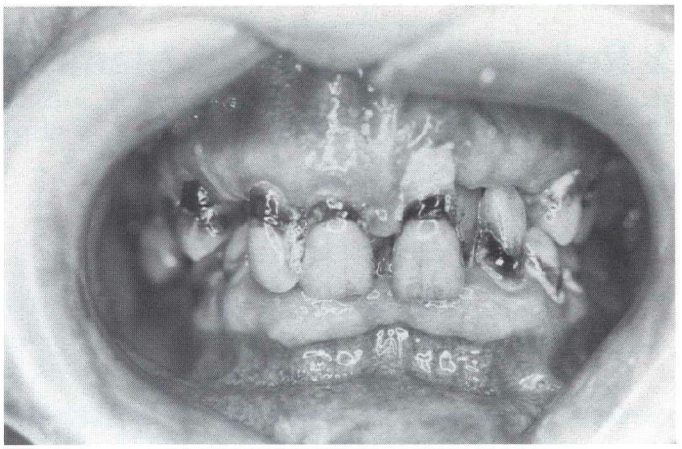

Fig. 2

Cervical dental caries in the orofacially irradiated cancer patient.

TABLE I

Bacterial Differences in Healthy and Disease (caries)-associated Plaque*

Species	% Supragingival Organisms	
	health	caries
S. sanguis	+ +	+
S. mutans	+	+ +
Lactobacilli	±	+
A. viscosus	−	+

− not detectable
± less than 1%
+ greater than 1%, less than 10%
+ + greater than 10%

* Reprinted with permission of the author from Loesche WJ. The bacteriology of dental decay and periodontal disease. In: Samuel Baron, ed. Medical microbiology. Principles and concepts. Menlo Park, Cal: Addison-Wesley, in press.

population. This relationship has been demonstrated in nonirradiated root surface decay (22,23) and in the xerostomic postirradiation oral environment (24).

S. sanguis is found in very high proportions in the normal salivary flora (27), while S. mutans and Actinomyces viscosus are found in high numbers on the teeth, unaffected by the presence of saliva (28,29). S. mutans has been found in postirradiated dental plaque in levels 25 times greater than normal when caries is active (4), while markedly reduced levels of S. sanguis have been reported in the irradiated oral cavity whether decay was active or not (4,24). In pre-irradiation oral samples, S. mutans made up 0.6% of plaque streptococci, whereas, after irradiation, it made up 44% of plaque streptococci (30).

Biochemical effects of xerostomia

The sticky, matted saliva of the irradiated patient is high in nitrogen and organic substances that provide an ideal bacterial substrate (12). Lactoperoxidase, found in saliva, inhibits the growth of S. mutans on tooth tissue (33); it prevents the organism from attaching to tooth surfaces and permits it to be swallowed (34). However, if salivary flow is reduced, this mechanism of controlling S. mutans is blunted.

Salivary pH in normal individuals is approximately 6.6 (31), but in the irradiated patient it has consistently been found to be lower (1,12). With below normal pH, the acidophilic, cariogenic plaque organisms (31) flourish; below 5.0 to 5.2, calcium and phosphate ions are labilized from the tooth surface (25). Healthy salivary flow serves to buffer the acidic pH changes and to replace leached ions because of the presence of a calcium ion concentration in normal parotid saliva of 0.75-1.5 mM and phosphate ion concentration of 4-11 mM (32). If salivary flow is reduced, both ions have lowered availability (32). The net effect of chronically lowered pH and reduced salivary buffering would be long-term labilization of calcium and phosphate from the tooth.

S. sanguis depends on salivary glycoproteins for agglutination (34,35). After agglutination, tooth colonization occurs through ionic interaction (35). The ability of S. mutans to metabolize refined carbohydrate to mucin, a sticky protein, is an important aspect of its pathogenicity and is unaffected by salivary flow. A reduction in salivary flow would then decrease the ability of S. sanguis to compete for tooth attachment and would thus favor the growth of S. mutans.

Immunological effects of xerostomia

Resistance to dental decay in normal individuals has been positively correlated with secretory IgA (S-IgA) and secretory IgM (S-IgM) levels in saliva (36,38), and with serum IgG (39). S-IgA is found in parotid and minor salivary gland fluid, predominantly in the latter (40).

The relationship between S-IgA and caries activity is also true for the irradiated patient (4). S-IgA concentration tends to increase in saliva for about two weeks after irradiation, but then it tapers off, not returning to pre-irradiation levels by three months (41). This change would correspond to the acinar degeneration previously described.

Immunological protection from decay occurs for several reasons. Because secretory immunoglobulins reduce the ability of bacteria to adhere to the tooth, the in vitro adherence of S. mutans is thus reduced (42,43), as is the epithelial lining adherence of S. mutans, S. mitis, and S. salivarius (44). Also, S-IgA inhibits the glucosyl transferase enzyme activity in S. mutans (45,46). Finally, salivary immunoglobulins can opsonize S. mutans for phagocytosis (39). The immunoglobulins of whole saliva, probably derived from serum flow (39), are associated with odontoblastic processes of pulpal origin under deep carious lesions (47), whereas secretory immunoglobulins are associated only with more shallow lesions (47), such as those seen in irradiation caries.

Single immunizations against specific cariogens do not provide immunity against decay, but rather increase decay in humans (48) and in gnotobiotic rats (49). If the rapid microbial changes that occur after irradiation for orofacial carcinoma can be equated with the effects of single immunization, it would be expected that caries would increase after irradiation.

Necrosis

Irradiating oral structures results in tissue edema, endarteritis, small vessel hyalinization, and a general reduction of effective blood flow (1,3,6). Since tissue repair and response are physiologically dependent on the amount of the blood supply and on the severity of the trauma, preventing trauma and infection is the cornerstone of an oral management program for the irradiated patient.

The most obvious traumatic episode the irradiated oral cancer patient experiences is exodontia or tooth extraction. However, prophylactic tooth extraction for patients scheduled for irradiation is markedly declining in major treatment centers (10). Rather, it is being recommended only when gross sepsis occurs and when the tooth cannot be repaired (13,50) or treated endodontically. Ideally, the extraction would take place ten days to two weeks (7,13,50) before irradiation and an alveolectomy and primary wound closure (50) would be performed at the same time.

A potential source of trauma and discomfort occurs when a prosthesis rests on the mucosa, especially on the mylohyoid ridge (7). Since this may be an obstacle in the patient's full rehabilitation, prosthetic service should be provided by a dental specialist trained in this phase of rehabilitation.

Extraction of teeth has been associated with necrosis in only 2% (13), 4% (3), and 17% (7) of reported cases. Radiation dosages were invariably greater than 6,000R (3,7) and directed primarily at the floor of the mouth (7). Postirradiation osteonecrosis occurred from three months to five years after extraction (6,7). In cases of advanced periodontitis, teeth have been safely extracted after irradiation using antibiotics and atraumatic methods (3,7). Therefore, realistic attempts can be made to save the teeth of the oropharyngeal cancer patient about to undergo irradiation.

Infection due to carious pulpal involvement or gross periodontal involvement can also cause necrosis (3,70), but these problems can easily be managed before irradiation begins in the same manner as in any nonirradiation treatment program. As the evidence grows that periodontal disease can be controlled conservatively and as stronger, more accurate, less costly, nonmetal materials are developed, realistic rehabilitation programs can be designed which are in line economically with the patient's prognosis. Fixed, permanent "temporization" that uses natural teeth and acrylic bridgework may obviate the need for mucosal-born prostheses or excessively costly fixed bridgework.

Dental Program for Problems of the Irradiated Oral Cavity

For oral and nasopharyngeal cancer patients who are to receive radiation therapy, a three-part plan is recommended that manages the patient's dental problems before, during, and after irradiation (1,3,7,13).

Before irradiation

Diagnostically clear, full mouth, intra-oral or extra-oral radiographs are mandatory for proper planning of treatment (2,3,7,10,13). By means of radiographs, intrabony pathology, partially impacted teeth, retained portions of teeth, and caries extension can all be diagnosed, at least in part. A concurrent clinical examination will reveal periodontal health, gingival recession, quality of present restorations, and potential prosthetic complications. Extraction of nontreatable teeth, prophylaxis, restoration, and oral hygiene procedures should all be accomplished at this time in the two to three weeks before the patient begins to receive irradiation.

The oral hygiene regimen should be very specific. Brushing techniques aimed at cervical and sulcular areas (Bass, Modified Scrub) with a soft, multitufted nylon bristle brush (Oral B-40, Pro Perio, Butler GUM) will effectively remove plaque. In anticipation of markedly reduced salivary flow, an oral lavage should be started. This can easily be done with a disposable Travad 1500 enema bag or the equivalent suspended over a basin and filled with one quart of warm water, in which one teaspoon of baking soda and one-half teaspoon of salt (13) have been dissolved. Artificial saliva is also commercially available for this purpose.

Finally, as an integral part of a pre-irradiation oral hygiene program, topical fluoride usage should be begun. Ideally, plastic custom trays can be made to encourage the patient to use the medication at home, since the patient's cooperation will be improved (51). A 3% NaF rinse for one minute (7), a 0.4% SnF (51), a 2% NaF gel (13), or a 1% NaF gel (8,25,27) for five minutes in custom trays (4,8) have all been used.

Topical fluoride can help to control bacteria on the tooth by reducing the surface energy of a tooth surface. It binds preferentially to charged areas and competes with bacteria for adherence (27). In nonirradiated patients, topical fluoride encourages the growth of S. sanguis over S. mutans (27,52). However, irradiation favors S. mutans over S. sanguis (4,24). In spite of this, topical fluoride tends to arrest shallow existing caries (8), while preventing caries in the postirradiation xerostomic patient (4,24).

Topical fluoride seems to have the ability to buffer the acid pH changes characteristic of the cariogenic S. mutans and A. viscosus (52,53). The fluoride ion decreases the availability of potassium and reduces the ability of S. mutans to take up the potassium that is present (53). The potassium ion is an important cofactor for proper functioning of the enzymes phosphatase and ATPase (53). In addition, potassium is necessary for S. mutans to use sucrose (25), its prime cariogenic property. Finally, fluoride inhibits the enzyme enolase, which interferes with the production of phosphoenol pyruvate (PEP), a key glycolytic pathway intermediate (25) in bacterial systems.

During irradiation

For this relatively short time, managing the symptoms of mucositis and controlling infection are the primary concerns.

All oral irradiated patients will experience some mucositis (7); approximately one half have mild to moderate reactions, while the other half may be severe (7). The common subjective symptoms of dysgeusia, dysphagia, dysorhexia, and pain (1,6,7) can be expected to last for ten days to four weeks (3,6,7). Topical pain relievers, such as viscous xylocaine or Orabase with benzocaine protective paste, are both effective at controlling acute pain in specific denuded or desquamated areas and can be applied by the patient as needed. More generalized, nonspecific pain can be controlled with dilute salt and soda solutions (1,6,7) or peroxide (3) mouth rinses. The previously mentioned Travad 1500 bag (13) or the equivalent is an excellent means of using these solutions.

If physical signs of infection are present, topical, anticandidial drugs such as Mycostatin oral suspension and systemic antimicrobials may be used.

Since topical fluoride may irritate the mucositis, its use may be delayed until symptoms subside (7). Weekly prophylaxis with fluoride polish is then recommended until topical fluoride can again be applied.

Postirradiation care

At the patient's medical follow-up examination, dental prophylaxis with fluoridated polish and a dental head and neck examination can be done. Good oral hygiene and continued use of topical fluorides should be stressed, as well as the long-term need for this type of follow-up.

Prosthetic reconstruction may begin as soon as tissues return to near normal. Management of osteoradionecrosis, from simple debridement to resection, should be done by a trained specialist.

In all of these ways, a trained dental practitioner can help the irradiated oronasopharyngeal cancer patient by preventing or alleviating some of the effects of irradiation on the oral cavity.

Acknowledgment

The author wishes to thank Dr. Frederick M. Matvias for his insight and time in many discussions on this subject.

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