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Reviews

Oral Health Care for the Cancer Patient

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Orofacial complications are common after radiotherapy to the head and neck, and after chemotherapy for malignant disease. Mucositis is the most frequent and often most distressing complication, but adverse reactions can affect all other orofacial tissues. This paper discusses the aetiopathogenesis and current means available for preventing, ameliorating and treating these complications, as well as indicating research directions. Copyright © 1996 Elsevier Science Ltd

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INTRODUCTION

Orofacial complications are unfortunately common with all modalities used in the management of patients with malignant disease in the head and neck. Surgery can provide a one-stage definitive procedure for local-regional malignant neoplasms, from which the patient normally recovers in large part within a few weeks. However, although modern reconstructive techniques can produce good orofacial aesthetics and function, neither can be totally assured [1]. Furthermore, many patients present with advanced tumours, and thus few operations achieve a cure, resulting in a poor outcome, and progression and/or recurrence of the tumour [1]. By contrast, radiotherapy and chemotherapy have little long-term effect on the *gross* anatomy and function of the orofacial soft tissues, but some tumours fail to respond to these modalities and adverse effects are often unpleasant.

Patients with malignant disease at other sites, such as those with lymphoproliferative disease, which may also be treated with chemo- and/or radiotherapy, often have consequent adverse effects in the orofacial region. Orofacial complications are also frequent consequences of the high-dose chemotherapy and radiotherapy used in bone marrow transplantation (BMT) as a treatment for some malignant and other diseases [2–9].

Of the early orofacial complications, the oral mucositis which invariably follows external beam radiotherapy involving the orofacial tissues, or may follow cancer chemotherapy, is by far the most common and distressing complication of treatment and may have such a significant effect on the quality of life that there is the need to interrupt or curtail the cancer therapy [6–8, 10–16]. Total body irradiation (TBI) particularly predisposes to adverse effects [9, 17]; some 40–70% of patients develop mucositis [3, 18–26]. Up to 40% of chemotherapy patients can be affected by mucositis [27–31].

Longer-term orofacial complications of radiotherapy to the head and neck region include particularly dry mouth (xerostomia), but loss of taste, limitation of jaw movement (trismus) and, less commonly, osteoradionecrosis (ORN) can be problems. Radiotherapy also complicates further surgery since the endarteritis in particular, impoverishes healing.

In children, cancer therapy may also result in long-term complications including enamel hypoplasia, microdontia, delay or failure of tooth development and eruption, and altered root formation, as well as maldevelopment in the craniofacial skeleton [32–38].

It is important to prevent and treat these orofacial complications of cancer therapy and this requires an oncological team that includes an experienced dental practitioner and hygienist. This is particularly important in children, since orofacial complications are up to three times as common as in adults having similar treatment [32, 39].

Aspects are discussed in varying depth elsewhere [40–46]: this paper reviews the current state of knowledge for the practising oncologist (Table 1).

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Table 1. Oral complications and oral healthcare for cancer patients

I.	Prevention and treatment planning before cancer therapy
II.	Oral health and disease during cancer therapy
	mucositis
	xerostomia
	alteration or loss of taste
	infection (bacterial, fungal, viral)
	pain
	bleeding risk
III.	Late/chronic complications of cancer therapy
	xerostomia
	dental demineralisation and caries
	alteration or loss of taste
	infections (e.g. candidosis)
	oral ulceration (soft tissue necrosis)
	bone necrosis
	pain
	temporomandibular disorders/trismus

PREVENTION AND TREATMENT PLANNING BEFORE CANCER THERAPY

Oral health

Most patients (97%) need some attention to oral healthcare before starting radio- or chemotherapy for cancer [47]. The establishment and maintenance of oral health, and careful dental treatment planning are essential to minimise oral disease and the need for, and possible adverse consequences of, operative intervention [21, 48, 49]. Unfortunately, however, patients with head and neck malignant disease not infrequently have poor oral hygiene and care and comply poorly with treatment [47]. Furthermore, nearly one third of patients need oral healthcare before BMT [50].

Dental and periodontal disease should therefore be treated before cancer therapy and any oral infections controlled. Patients must achieve a good level of oral hygiene before radiotherapy or chemotherapy commence. Use of chlorhexidine and fluoride are recommended [51]. Chlorhexidine may reduce oral mutans streptococci and lactobacilli [52]. Dietary control and topical fluoride therapy are essential and must be continued for life or the duration of xerostomia. Fluoride can reduce caries [53–55]. Fluoride is best applied to the whole surface of all teeth to have maximal protective effect, and this may be achieved by providing custom built carriers for each patient [56] and using a gel containing 1% sodium fluoride placed in the carriers and applied to the teeth for 5 min per day [57–60]. A 0.4% stannous fluoride gel used by patients for self-administration in customised carriers has also been recommended and may have the added advantage of reducing cariogenic bacteria [61]. Brush-on application of fluoride has also been recommended [62] as have sodium fluoride mouthrinses with chlorhexidine diacetate [63]. Further study is needed to determine the optimum form of fluoride, and the most effective method of application which gives best patient compliance.

General health

The need for psychosocial counselling of the cancer patient is extremely important, but often overlooked. The patient must be carefully prepared to be able to cope with any complications of cancer therapy [64–67] and should also be counselled to avoid the use of tobacco, alcohol and other carcinogens.

Patients undergoing head and neck cancer surgery, particularly where this involves the neck, can have life-threatening post-operative complications [68, 69]. These can often be predicted by pre-operative assessment using a specific activity scale questionnaire [70–72], assessment of alcohol abuse, and a platelet count—since thrombocytosis identifies patients at risk for wound infection [73].

It is also important to take care to exclude second primary tumours in the mouth or elsewhere. Routine panendoscopy will identify a simultaneous second primary carcinoma of the oesophagus, larynx or lung in up to 14% of oral cancer patients [74] and is widely recommended [75, 76]. Over one-third of second primaries are detectable by endoscopy at or within 1 year of diagnosis of the index tumour [76].

ORAL HEALTH AND DISEASE DURING CANCER THERAPY

The orofacial complications of cancer therapy depend mainly on the treatment modality used (agents, sequencing, rate of delivery, dosage) and to some extent also on host factors. For example, the severity of oral mucositis following radiation therapy depends upon the type of ionising radiation used, the rate at which it is delivered, the total dose given, individual response to the therapy and factors such as the use of tobacco and alcohol products.

Mucositis

As discussed above, oral mucositis is common after chemotherapy or radiotherapy to the head and neck. Mucositis appears from 3 to 15 days after cancer treatment, earlier after chemotherapy than after radiotherapy. The pain from mucositis can be so intense as to interfere with eating, and significantly affect the quality of life [6, 10, 13], frequently leading to the need for opioid analgesics and sometimes to the interruption of the planned cancer therapy [77]. In addition to causing pain, ulcerative mucositis can provide a portal for microbial entry and can thus lead to local and sometimes systemic infections [20, 24, 49, 78–80] which may even be life-threatening.

The acute oral mucosal response to radiotherapy is a result of mitotic death of epithelial cells. The cell cycle time of the basal keratinocytes is about 4 days and, as the epithelium is at least three or four cells thick, radiation changes begin to appear at about 12 days after the start of irradiation. Clinically, the buccal mucosa may initially turn whitish, but this is then followed by erythema and then after a few days more by the appearance of a patchy fibrinous exudate. If a high dose of radiation is given over a short time, ulceration may supervene early on, with a thick fibrinous membrane covering the ulcerated surface. Surviving keratinocytes respond to radiation damage by dividing more rapidly, so that spontaneous complete healing can be anticipated within 3 weeks of the end of treatment. The healing of mucositis is retarded by high-dose radiotherapy and by tobacco smoking [81].

The oral mucosal reaction to chemotherapy is due to a non-specific inhibitory effect of the agent on the mitosis of

proliferating cells, including those in the basal epithelium, causing a reduced renewal rate and thus atrophy and, eventually, ulceration [37, 82–86]. Frank oral ulceration is thus a particular problem for those on chemotherapy [78, 79, 87–90]. Up to 20% of patients on chemotherapy suffer oral ulceration [90] and this can cause pain and may be a portal for infection and septicaemia [49, 88, 91, 92]. The simultaneous use of chemotherapy and radiotherapy results in even more severe and prolonged mucositis and ulceration [85, 93].

While oral mucositis can be reduced by protecting the mucosa with midline mucosa-sparing blocks [94] or by modifying the radiation treatment or exposure to cytotoxic drugs, it cannot be avoided and therefore active measures are being sought to treat it effectively and rapidly [95].

Clinical trials of agents aimed at preventing or ameliorating mucositis have not, however, always assessed the results on strict criteria. Few mucositis rating scales have been tested for validity, and the many mucositis scales that exist deny good comparisons of products [11, 96–107].

Current management of mucositis

Although, as discussed above, there are some differences in mucositis depending on whether radio- or chemotherapy has been used, the clinical course and the treatment approaches for both types are currently broadly similar.

Avoidance of mucosal irritation. In general, mucositis should be treated conservatively to avoid further tissue irritation and damaging the remaining cells from which the epithelium will regenerate. Plaque control and oral hygiene should be maintained with aqueous chlorhexidine and tooth brushing [9] and the patient should be advised to take a soft bland diet, avoiding obvious irritants such as tobacco, alcohol or spices. Nutrition should be maintained.

Active treatment of mucositis. Of the many agents assessed for the treatment of mucositis, topical chlorhexidine gluconate and topical sucralfate have received the most attention and appear to offer the maximal benefit. The potential for aqueous chlorhexidine to control chemotherapy-associated oral mucositis has been reported in several studies [108, 109], although this finding has not been universal [22, 110, 111]. Furthermore, chlorhexidine has not been shown to control radiation mucositis [109, 112–115]. Nevertheless, although chlorhexidine has proved disappointing in some studies [110, 111, 113, 115] it still has value because of the other benefits (see below), particularly in plaque control.

Sucralfate may be of benefit both in the management of chemotherapy-induced [116–120] and of radiation-induced mucositis [121–123]. Sucralfate is a non-absorbable aluminium salt of sucrose octasulphate that, when taken by mouth, is only 3–5% systemically absorbed. It adheres to ulcer bases, thus creating a surface barrier [124], has some antibacterial activity [125] and also binds epidermal growth factor and thus might accelerate healing [126]. Even in a study that did not show sucralfate to prevent mucositis, oropharyngeal pain was decreased [127]. Others have shown the combination of sucralfate with fluconazole to be effective [128].

Chemotherapy-induced mucositis is particularly common with melphalan and 5-fluorouracil (5-Fu). Ice cold water rinses or ice pops inhibit melphalan-induced mucositis [129, 130]. Oral cooling using ice chips for 5 min prior to 5-Fu use, and then for a further 25 min, appears to reduce the mucositis [131, 132]. Promising results of a protective effect from an allopurinol mouthwash [133, 134] in 5-Fu-induced mucositis unfortunately have not been confirmed in a controlled trial [135].

Cytokines may modify the kinetics of epithelial cells and might therefore theoretically affect the development of mucositis. Granulocyte-macrophage colony-stimulating factor given subcutaneously from days 5 to 14 of chemotherapy appears to reduce the severity and duration of mucositis [136]. Further confirmatory studies are therefore indicated. Interleukin-11 [137], and transforming growth factor beta [138] have been shown to reduce the severity of mucositis in animal models, but human trials have yet to be completed. Epidermal growth factor administered at the time of chemotherapy, however, *increased* the severity of mucositis [86].

Prostaglandins have also been suggested to be able to ameliorate mucositis [139, 140] but at least one double-blind study has discounted their value [141]. Pentoxifylline also appears to be of little benefit [142–145] despite promising early results [146]. Topical vitamin E has been shown in one placebo-controlled double-blind to effectively reduce chemotherapy-induced mucositis [147]. There are many other modalities of unproven value. Topical corticosteroids have been assessed in a small number of patients [148, 149]. The potential effect of topical corticosteroids on mucositis suggests the need for further study, particularly with the availability of topical and systemic agents that may affect oral colonisation by potential pathogens which may be used in combination with topical corticosteroids. The use of soft lasers (helium–neon) may also prove of some benefit [150] but considerable more research is needed.

Control of pain. Anaesthetic agents such as lignocaine, benzydamine, dyclonine or diphenhydramine may give symptomatic relief from the pain of mucositis [112]. Benzydamine has also been shown to reduce the severity of mucositis in patients receiving radiation therapy [151, 152].

Treatment of oral infections. Homeostatic microbial communities may be protective in health by preventing or interfering with the colonisation by exogenous pathogens ("colonisation resistance") [153, 154]. When the oral tissues are irradiated, this colonisation resistance is affected and there are significant alterations in the oral microflora [155] which increase as salivary flow is disturbed. Oral levels of *Streptococcus mutans*, Lactobacillus species and Candida species typically increase significantly after radiotherapy to the head and neck [53–55, 156–159]. These changes are maximal between 3 and 6 months after radiotherapy, after which time no further deterioration occurs, and indeed there is then sometimes at least a partial return towards the baseline flora [158].

Frank oral infections may be seen after cancer therapy and are even more common and severe in patients receiving chemotherapy than after radiotherapy [1, 111, 160] particularly in terms of candidal and herpes simplex virus infections. Patients with neutropenia resulting from chemotherapy are especially at risk of septicaemia [20, 78, 79, 88, 91, 160] particularly involving alpha-haemolytic streptococci, Candida species and Gram-negative bacteria [161, 162]. Therefore, prophylactic antimicrobials can often be of use, although resistance can develop [50, 163, 164].

There has also been considerable interest in the role of yeasts in irradiation mucositis since Candida species in particular appear to increase [159, 165, 166]. Systematic trials with topical or systemic antifungals, however, have consistently failed to prevent the development of, or to cure, irradiation mucositis [109, 113, 115]. Nevertheless, candidosis is the most common oral fungal infection in cancer patients and may cause soreness as well as being occasionally responsible for disseminated infections [167]. Xerostomia, dental prostheses, antibiotics, alcohol use and tobacco smoking predispose to oral candidosis [159]. Antifungal prophylaxis is thus recommended during remission-induction chemotherapy in patients with solid tumours, lymphomas or leukaemias [168]. Meta-analysis of numerous studies has shown the prophylactic value of clotrimazole or fluconazole [168, 169] although neither topical nystatin nor amphotericin may be particularly effective [170, 171]. Chlorhexidine mouthwashes may also be of some value in reducing candidosis [4, 22, 111].

There is a significantly increased frequency and severity of oral herpesvirus infections after chemotherapy and radiochemotherapy. The main symptomatic viral infections affecting the mouth in cancer patients are herpes simplex virus (HSV) and herpes varicella-zoster virus (VZV) infections [172], although there are occasional cases reported of cytomegalovirus-induced ulceration [173]. Acyclovir remains the most useful antiviral agent for HSV or VZV infection, but brivudin and new agents such as famciclovir, penciclovir, brovavir, foscarnet and other agents may be needed where there is acyclovir-resistant HSV or other herpes viruses [174].

Radiotherapy is associated with a marked increase in oral Gram-negative enterobacteria and pseudomonads [175] which may not only contribute to the mucositis [176] but release endotoxins which can cause adverse systemic effects [177]. If Gram-negative bacilli do have a role in the aetiology of irradiation mucositis, then it should be possible to prevent, treat or ameliorate mucositis by abolishing the Gram-negative flora. Indeed, clinical trials using polymyxin E and tobramycin applied topically four times daily have given promising results [114, 177]. However, this regimen has yet to be fully evaluated for the management of irradiation mucositis, and has not been shown to be effective in the mucositis associated with chemotherapy. Furthermore, in patients receiving BMT, systemic antibiotic coverage is routinely used in most centres, yet oral mucositis remains a severe and common problem. Further study is thus needed to evaluate this bacterial hypothesis of mucositis.

Care of oral bleeding. Myelosuppression due to the primary disease or chemotherapy may result in thrombocytopenia and a bleeding tendency. Hepatotoxicity due to medical management or viral infection may also lead to coagulopathy. Surgical procedures must therefore be carried out with the care and attention given to haemostasis.

LATER POST-TREATMENT ORAL COMPLICATIONS

Xerostomia

Salivary gland tissue, especially that of the parotids, is highly susceptible to radiation damage [178–180] which affects both the acinar cells and vascular tissue, leading both to reduced resting and stimulated salivary flows [181, 182]. As little as 20 Gy can cause permanent cessation of salivary flow if given as a single dose and, with the conventional treatments for oral carcinoma (60–70 Gy), there is a rapid decrease in salivary flow during the first week of radiotherapy with eventually about a 95% reduction [181, 183, 184]. By 5 weeks of radiotherapy, the salivary flow has virtually ceased and rarely recovers [185–187]. Nevertheless, the sensation of dryness of the mouth may diminish after a few months to a year, partly as a result of compensatory hypertrophy of any unirradiated salivary glandular tissue and partly because patients may develop tolerance to the continuing sensation of mucosal dryness [188–190]. After 1 year, however, there is little further improvement in saliva production [191].

The degree of xerostomia depends also on the volume and type of salivary tissue irradiated, and xerostomia is seen particularly when the parotid glands are irradiated [13]. Fully-irradiated glands have resultant lower salivary flow rates than do partially-irradiated glands [192]: mantle field, unilateral field and bilateral fields of head and neck radiation can be associated with reduction in salivary flow of 30–40%, 50–60% and around 80%, respectively [182]. Radiotherapy to the nasopharynx damages all major and minor salivary glands, and typically causes severe and permanent xerostomia. Unilateral radiotherapy and a reduced field size is therefore delivered whenever possible in order to avoid bilateral exposure to salivary glands and to reduce the complications of treatment—including xerostomia [193].

Radiotherapy leads not only to changes in the salivary flow but also in constituents [194]. The whole saliva bicarbonate concentration is lowered with a reduction in buffering capacity and pH [195–197]. Salivary levels of sodium, chloride and other electrolytes increase, although potassium [13, 192, 195], secretory IgA and lysozyme are unchanged [13, 158, 198, 199].

Chemotherapy can also lead to decreased salivary flow, along with reduced amylase and IgA levels [200] although others have reported no change in flow rates, pH or protein content [201]. After BMT, xerostomia is significant where there is chronic graft-versus-host disease (GVHD) [19], and then a variety of qualitative salivary changes have been demonstrated [190].

Xerostomia may lead to discomfort, loss of taste and appetite [13, 188, 189, 202, 203] and especially to an increased risk of oral infections such as candidosis and caries.

Management of xerostomia

Apart from minimising unnecessary glandular irradiation, it has been suggested that stimulating the salivary glands prior to radiotherapy might be of value in reducing glandular damage [185, 204] since a high initial salivary flow rate is associated with higher flow rates after radiotherapy [185, 186, 189]. The results of a recent prospective study using pilocarpine are encouraging [205] but thorough double-blind trials have not yet been reported. Early animal studies suggest that antioxidant vitamins such as α-tocopherol and β-carotene may also reduce salivary damage [206]. Further studies are indicated.

Where there is established xerostomia, patients should be given advice to avoid any agents such as anticholinergic or sympathomimetic medications, tobacco and alcohol that

may further impair salivation. Residual salivary tissue may be able to be stimulated by gustatory or pharmacological stimuli [207–214]. Sugar-free chewing gum may be a useful gustatory stimulus [215–217]. Pharmacological stimuli may also be used but require functional salivary tissue if any benefit is to be obtained.

Drugs that may be effective at stimulating salivation may include the various cholinergic agents, notably pilocarpine. Given as ophthalmic drops placed intra-orally or as tablets, pilocarpine was effective in relieving symptoms and in improving salivation, in doses of up to 5 mg administered three times daily [210, 211, 213, 214, 218]. The tablet form of pilocarpine is, however, preferred as the dose is better controlled, and the tablet is more convenient to use. Adverse effects of pilocarpine including sweating, rhinitis, headache, nausea and urinary frequency are mild, although pilocarpine is contraindicated in asthma, chronic obstructive airways disease or any bowel obstruction.

One clinical trial of bethanechol has been reported in the management of xerostomia, and only few side effects were noted [208]. Anetholetrithione (Sialor), which acts by increasing the number and concentration of the salivary gland receptor sites for neutrostimuli can, in a dose of one to two tablets three times daily, increase saliva production in some xerostomic patients [219–222]. The use of pilocarpine with carbachol [223] or with anetholetrithione [209] may increase saliva production in individuals who fail to show improvement following the use of a single agent.

Where salivary tissue is damaged beyond repair, saliva substitutes may be helpful. Several saliva substitutes or mouth-wetting agents are now marketed [224–228]. Most contain carboxymethyl-cellulose, although others contain animal mucins, and some also contain constituents that may facilitate enamel remineralisation. Some studies have suggested that mucin-containing preparations are better accepted by patients and may also help promote the establishment of a "normal" oral flora [229–232]. Some patients find these products very useful, but clinical experience suggests that they are not always useful or well accepted [230]. When cost and convenience are taken into consideration, many patients prefer simply to frequently sip water or to use an aerosol pump of water [225, 226]. Individuals with a dry mouth will frequently sip water, particularly during eating, choose a moist diet and often keep water by their bedside for use at night.

Dental problems

Patients undergoing cancer therapy are predisposed to caries because of xerostomia, use of foods with a high sucrose content, and a shift to a more cariogenic oral microflora [191, 233–241]. Demineralisation of tooth structure and cavitation are often seen involving the incisal or cusp tips, and the cervical regions [13, 239, 242]. Periodontal disease, however, is not increased following radiation therapy [13].

It is therefore crucial that the patients follow a non-cariogenic diet, maintain oral hygiene, and use fluorides regularly [45, 57, 59, 63, 84, 233, 243–245].

Loss of taste sensation

Patients receiving radiotherapy to the mouth invariably experience disturbance or loss of taste sensation [246]. The mechanism of this loss of taste has not been elucidated: the taste receptor cells are relatively radioresistant. Xerostomia probably contributes, since disturbance of taste is particularly frequent after irradiation of the parotid glands.

Taste loss can be distressing, and contributes to poor nutrition but fortunately, taste perception usually partly recovers slowly within a few months after the end of radiotherapy. Zinc sulphate may help improve the taste sensation in some patients [237, 247].

Temporomandibular joint disorders and trismus

Temporomandibular joint disorders (TMD) may develop due to anxiety, depression or the stress associated with cancer or because of disordered sleep patterns. Fibrosis following radiation and surgery, and loss of continuity of the mandible due to surgery or pathological fracture may also result in temporomandibular disorders. Approaches to the management of TMD have not been studied specifically in cancer patients and therefore guidelines from the general literature relating to TMD must be relied upon [248]. These include the use of oral appliances, physical therapy and appropriate medications. A range of movement exercises and other physical therapy may be helpful to reduce the possible restriction of movement but, once fibrosis has been established, physical therapy can only limit further deterioration in function.

Osteoradionecrosis

Osteoradionecrosis (ORN), although uncommon, is the most serious orofacial complication of radiation therapy. Radiation of bone leads to endarteritis obliterans with thrombosis of small blood vessels, fibrosis of the periosteum and mucosa, and damage to osteocytes, osteoblasts and fibroblasts. The damaged osteocysts and osteoblasts may survive until they attempt to divide—when mitotic death occurs. An individual bone cell may not divide for months or years after irradiation, or it may divide only when stimulated by trauma. There is therefore a slow protracted loss of osteocytes and osteoblasts after radiotherapy with a consequent slowing of remodelling, which leads to the risk of bone necrosis. The mandible is at greater risk of ORN due to it containing more compact bone with a higher density than does the maxilla: the mandible absorbs more radiation, and has a poorer blood supply. The maxilla, with its lower density and rich vasculature is a much less common site of osteoradionecrosis.

Various factors predispose to ORN but, in general, the risk is greater the higher the radiation dose, fraction size and number of fractions, and when there is local trauma [249], immune defect or malnutrition. Nevertheless, ORN may also sometimes occur spontaneously, unrelated to trauma [249, 250]. Many patients with oral cancer also abuse alcohol and tobacco and are in poor general medical condition [251] which, together with poor nutritional status and oral hygiene, may place these patients at higher risk of ORN.

Prevention of ORN

Minimising radiation dose. ORN is most unlikely with radiation doses below 60 Gy delivered with standard fractionation. The incidence of ORN is only 1.8% in those receiving up to 70 Gy, but above 70 Gy it is about 9%

[252]. In modern series, some 5–15% of patients having radiotherapy to the head and neck region have suffered ORN [249, 253–257].

Multiple fields, reduced total radiation dose, smaller fraction size, devices to move the mandible or maxilla out of the radiation field and radiation shields may be used to decrease the effect of radiation therapy on the bone [258] and minimise the risk of ORN.

Minimising infection and trauma. The incidence of ORN is three times higher in dentate than in edentulous patients, mainly as a result of trauma from tooth extraction and infection from periodontal disease [255, 256]. Oral infections and trauma, including surgical intervention should therefore be kept to a minimum [259, 260].

It is now generally accepted that teeth in the high-dose irradiation field by no means inevitably need to be extracted. The only teeth that really need to be extracted before radiotherapy are those teeth within the high-dose field that are unrestorable or that have advanced periodontal involvement, and those in patients who are unwilling or unable to maintain oral care. Extractions of these teeth should be performed atraumatically, the tissues sutured and antimicrobial cover given. All other teeth should be cleaned and restored before radiotherapy begins [250, 251].

The highest incidence of mandibular ORN is seen in those patients having extractions immediately prior to, or immediately after radiotherapy [249]. Therefore extractions should be avoided if possible at these times [255, 256, 258]. In general, extractions are best carried out at least 2–3 weeks before the commencement of radiotherapy [258], although ORN is still possible, as bone remodelling proceeds for some months after extractions. If surgery becomes necessary after radiotherapy, irradiated tissue must be handled as gently as possible and, if the patient is felt to be at high risk of ORN, for example if multiple teeth are to be extracted, hyperbaric oxygen therapy should be considered as prophylaxis against ORN [258, 261].

Treatment of ORN. The initial approach to the treatment of ORN should be conservative, since up to about 60% of cases of ORN thereby resolve [252, 254–256, 258, 262, 263]. Local wound care, plus topical or systemic antibiotics may be indicated. Meticulous oral hygiene is essential, including the use of 0.02% aqueous chlorhexidine mouthwashes after meals. Debris should be irrigated away and sequestra should be allowed to separate spontaneously or gently removed, since any surgical interference may encourage extension of the necrotic process. ORN is not primarily an *infectious* process and the tissues are avascular, so systemic antimicrobial agents are of limited benefit but, despite this, tetracyclines have been recommended because of their selective uptake by bone. A regimen of 250 mg tetracycline four times daily for 10 days, followed by 250 mg twice daily continued for several months is recommended, although metronidazole, 200 mg, three times a day or other broad spectrum antimicrobials, could be added in cases of severe infection or where anaerobes are implicated [250, 263].

Hyperbaric oxyen and minor to extended surgery with reconstruction procedures may also be needed [249, 258, 261, 264, 265]. Hyperbaric oxygen therapy (HBO) has been shown to promote healing in ORN [249, 266–276]. HBO given at 2 to 2.5 atmospheres pressure for 1.5–2 h per day for up to 84 sessions is recommended [266, 275]. Untreated pneumothorax is the only absolute contraindication. Side effects of HBO are uncommon but include transient myopia, seizures, and otic or pulmonary barotrauma, the latter potentially leading to air embolism. Concern has been expressed that hyperbaric oxygen may exacerbate a variety of autoimmune and immunosuppressive disorders, and viraemia [277] but there is little supporting evidence. Relative contraindications to HBO include upper respiratory tract infection, chronic sinusitis, epilepsy, chronic obstructive airways disease, high fevers, a history of spontaneous pneumothorax or thoracic or ear surgery, viral infections, congenital spherocytosis, a history of optic neuritis and claustrophobia. The risk from HBO may be minimised by a careful pretreatment assessment including chest radiography and electrocardiography; some advise also an otolaryngological and ophthalmological assessment [277].

Surgery may also play a role in the treatment of ORN. Sequestrectomy, alveolectomy with primary closure, closure of orocutaneous fistulae, or hemimandibulectomy may be indicated.

Therapeutic ultrasound at a frequency of 3 mHz pulsed one in four at an intensity of 1 W/cm^2 applied to the mandible for 10 min daily for 50 days has also been suggested to effectively improve ORN [278] but further study is needed. Early reports on the benefits of other modalities such as pentoxifylline [279] or electrotherapy [280] have yet to be confirmed.

MANAGEMENT OF PAIN IN CANCER PATIENTS

Pain may be present due to the tumour itself, to a management complication, or to some cause unrelated to the cancer. Whether pain is related to the cancer or not, the development of pain has a considerable emotional impact upon the individual and may increase the complexity of management. Management of pain in cancer patients has been recently reviewed [248, 281]: apart from the management of mucositis discussed above, new modalities such as topical capsaicin [282] are under trial.

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