

# General medicine and surgery for dental practitioners. Part 6 – cancer, radiotherapy and chemotherapy

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## VERIFIABLE CPD PAPER

Dental practitioners will encounter patients who have been affected by cancer or who are current cancer patients. Dentists play an important role in the overall healthcare of such patients, particularly in those with head and neck malignancy. This paper gives an overview of the impact of cancer and its treatment on dental management.

### INTRODUCTION

Cancer is the term applied to malignant tumours and is essentially a genetic disease caused by somatic mutation. The multi-stage theory of carcinogenesis suggests that individual cancers arise from several sequential mutations in cellular DNA. There is a close correlation between cancer incidence and increased age, reflecting the time required to accumulate the critical number of genetic abnormalities needed for malignant change.

Improvement in cancer treatment outcomes means that in modern clinical practice, a general dental practitioner will have to advise and treat many patients requiring

### GENERAL MEDICINE AND SURGERY FOR DENTAL PRACTITIONERS

1. The older patient
2. Metabolic disorders
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oral healthcare with malignancies at various stages of the disease.

### POINTS IN THE HISTORY

As a consequence of their malignancy, patients with cancer may suffer from a number of general physical, medical and emotional problems. It is important that dental practitioners have an understanding not only of the effects of malignant disease on their patient, but also of the specific problems resulting from cancer treatments (Table 1). While the range, symptomatology and diagnosis of malignant neoplasms presenting in the head and neck region will be well known to dentists (Table 2), the effects of cancer treatment may not be and it is often this area that leads to confusion and compromised dental care.

In general, malignant neoplasms are treated using one, or some combination of the following treatment modalities:

- Surgery
- Radiotherapy
- Chemotherapy.

The patient may give a history of having experienced such treatment, may be undergoing it or waiting for it. The selection, timing and prescription of these anticancer treatments is now the remit of highly specialised multidisciplinary oncology teams and varies considerably depending upon tumour type and site. While the principles of surgical access, tumour resection with wide margins and tissue reconstruction are familiar to dentists, particularly in relation

### IN BRIEF

- Dentists will encounter patients with various types of cancer who require dental care.
- Patients may be at various stages of cancer treatment but the dentist may be involved at any stage.
- A working knowledge of the potential effects of cancer and its treatment is essential for safe practice.

Table 1 General complications of cancer

Cachexia and wasting
Anaemia and infection
Nutritional deficiencies
Cutaneous manifestations
Endocrine disorders
Rare manifestations

Table 2 Orofacial manifestations of cancer

Primary tumours in orofacial tissues
Oral squamous cell carcinoma
Salivary adenocarcinoma
Metastases in jaws or oral soft tissues
from breast, lung and prostate primaries
Effects of tumour metabolites
Facial flushing
Pigmentations
Amyloidosis
Oral erosions
Functional disturbances
Purpura
Bleeding
Infections
Anaemia

to orofacial cancers, the mechanism of action, efficacy and side-effects of radiotherapy and chemotherapy are often less well understood.

Drug classification	Examples	
Alkylating agents	Busulphan Chlorambucil Cyclophosphamide	
Cytotoxic antibiotics	Bleomycin Doxorubicin	
Antimetabolites	Fluorouracil Methotrexate	
Vinca alkaloids	Vinblastine Vincristine	
Platinum compounds	Cisplatin	
Treatment regimen	Administration	Aim
Induction	Before other treatments	Reduce tumour size
Sandwich	Between treatments	Reduce risk of metastases
Adjuvant	After treatment	Improve disease-free survival
Concurrent	With other treatments	Sensitise tumour cells
Palliative	After other treatments	Shrink residual tumours Pain relief

<b>Radiotherapy</b>
Mucositis/ulceration
Radiation caries/dental hypersensitivity/periodontal disease
Xerostomia/loss of taste
Dysphagia
Candidosis
Osteoradionecrosis
Trismus
Craniofacial defects (children)
<b>Chemotherapy</b>
Mucositis/ulceration/lip cracking
Infections
Bleeding
Orofacial pain

A patient may give a history of planned or previous radiotherapy. It is possible, but more unlikely, that they are undergoing radiotherapy at the time of attendance for dental treatment. Radiotherapy refers to the therapeutic application of localised ionising radiation (X-rays, beta rays or gamma rays) to destroy malignant cells. Cells exposed to radiation form free radicals in their intracellular water and, as a result of DNA damage, undergo death when stimulated to divide. Radiotherapy is thus particularly effective against rapidly proliferating tumour cells which are killed more efficiently than slowly growing or normal cells. While this is a considerable advantage in cancer treatment, it does not spare normal cells with high replication rates such as epithelium of skin and mucous membranes or highly specialised cells in neurological tissue, salivary gland secretory tissue or osteoblasts in bone which, when damaged, are unable to repair themselves. Other types of radiation may also be employed; for example, radioactive iodine (given orally or by intravenous injection) can be used to treat thyroid cancers. Such treatment can affect the function of the salivary glands.<sup>1</sup>

Patients may reveal a history of chemotherapy or be awaiting or undergoing this modality of treatment. The use of chemotherapeutic agents (anticancer drugs) is most often employed systemically in

the treatment of widespread malignancies such as leukaemia or lymphoma, although more recent recognition of early systemic spread of solid tumours such as breast cancer and even head and neck malignancy has resulted in greater use of chemotherapy in modern treatment protocols. Chemotherapy agents (Table 3) target actively dividing cells to eliminate tumours while allowing normal cells to recover and repair. Drugs are usually administered in high doses intermittently and often in combination to achieve synergy and overcome resistance. Newer head and neck regimens utilise chemotherapy agents administered as radiosensitisers before radiotherapy to increase treatment efficacy but this may also enhance treatment side-effects.

### EXAMINATION

The patient with cancer may look relatively well or may be cachectic. The term cachexia refers to a profound and marked state of constitutional disorder, general ill health and malnutrition. The signs and symptoms of oral cancer are well covered in relevant texts and therefore will not be covered further here.

The orofacial region contains one of the highest concentrations of specialised tissues and sensory organs in the body and it is hardly surprising that the effects of cancer treatment are particularly severe

here. The cellular damage effects of radiotherapy and chemotherapy produce similar effects on oral tissues, although more widespread and systemic complications occur following chemotherapy. Table 4 lists the oral complications of radiotherapy and chemotherapy which may be seen on examination.

Mucositis is a particularly distressing condition arising from damage to the oral mucosal lining. It presents as widespread oral erythema, pain, ulceration and bleeding. It may arise during localised head and neck radiotherapy or as a consequence of systemic chemotherapy. Although an acute and usually relatively short-lived problem, it can significantly impair quality of life and prevent oral dietary intake leading to hospitalisation. If it is particularly severe it may cause interruption to therapeutic regimens and can act as a portal for septicaemia.

Xerostomia is responsible for the most common and long-standing problems following orofacial radiotherapy. Salivary gland function rarely recovers following secretory cell damage and while newer computerised radiotherapy techniques help to spare full salivary gland irradiation, it remains difficult to avoid gland damage. As mentioned above, salivary gland damage may also occur secondary to the use of radioactive iodine for the destruction of thyroid tumours.

Permanent mouth dryness, glutinous sputum in the posterior oral cavity and pharynx, and reduction of or altered taste, together with fragile and sensitive oral mucosa, are significant post-radiotherapy sequelae impairing a patient's quality of life. Xerostomia also increases the risk of rapidly destructive dental caries ('radiation caries') and advanced periodontal disease. Artificial saliva preparations including saliva sprays, replacement gels or pastilles may be helpful. Oral administration of pilocarpine may help to increase flow in patients with residual salivary gland function.

Infections are common due to immunosuppression, especially candidal and herpetic types. Appropriate use of antifungal agents such as miconazole or systemic fluconazole may be necessary to treat severe oral candidosis.

The lesions of osteoradionecrosis, as shown in Figure 1 (non-vital bone secondary to radiotherapy), or osteonecrosis as in Figure 2 (non-vital bone secondary to bisphosphonate treatment) may be evident and should be managed as described in the next section.

## DENTAL MANAGEMENT OF HEAD AND NECK CANCER PATIENTS

The important management principles for patients undergoing radiotherapy for head and neck malignancy are summarised in Table 5. The general dental practitioner has an important role in management. It is important that the patient is rendered dentally fit before the commencement of radiotherapy treatment. This also applies to patients about to receive chemotherapy. The principles of management are summarised in Table 6.

The importance of general dental care and oral hygiene, especially for head and neck cancer patients, cannot be emphasised too strongly. A comprehensive dental assessment and proactive preventive treatment plan is mandatory before definitive head and neck cancer treatment. While this is often led by specialist restorative dentists working in multidisciplinary oncology teams, the role of the general dental practitioner remains central.

Patients undergoing radiotherapy for orofacial cancers need dental input to minimise radiation caries, the need for post-radiotherapy dental extractions and



**Fig. 1** A patient with osteoradionecrosis. The overlying skin has broken down due to its poor blood supply



**Fig. 2** Osteonecrosis in a patient who has been prescribed bisphosphonates and has had dental extractions in this area

to reduce the risk of osteoradionecrosis. Extractions are advised for grossly carious, non-vital, periodontally involved teeth or retained roots and their removal should be performed carefully before radiotherapy starts to ensure rapid healing.

Osteoradionecrosis arises due to the death of irradiated and lethally damaged bone cells stimulated to divide following traumatic stimuli such as dental extractions or localised infection (Fig. 1). Diminished vascularity of the periosteum also exists as a result of late radiation effects on endothelial lining cells, which is particularly pertinent for the dense and less vascular mandibular bone. The radionecrotic process usually starts as ulceration of the alveolar mucosa with brownish dead bone exposed at the base. Pathological fractures may occur in weakened bone and secondary infection leads to severe discomfort, trismus, foetor oris and general malaise. Radiographically, the earliest changes are a 'moth-eaten' appearance of the bone, followed by sequestration.

Treatment should be predominantly conservative, with long-term antibiotic and topical antiseptic therapy and careful local removal of sequestra when necessary. Hyperbaric oxygen and ultrasound therapy to increase tissue blood flow and

**Table 5** Management of patients receiving head and neck radiotherapy

Before radiotherapy
Oral hygiene/preventive and restorative dentistry
Risk/benefits of retaining teeth
Dental extractions
During radiotherapy
Discourage smoking and alcohol
Eliminate infections: antibiotics/antifungals/antivirals
Relieve mucositis
Saliva substitutes
TMJ physiotherapy for trismus
After radiotherapy
Oral hygiene/preventive dentistry
Specialist OMFS for dental extractions/oral surgery
Topical fluorides
Avoidance of mucosal trauma
Saliva substitutes

**Table 6** Management of patients receiving chemotherapy

Before chemotherapy
Oral/dental assessment
Oral hygiene/preventive dentistry
During chemotherapy
Folic acid to reduce ulceration
Ice to cool oral mucosa
Chlorhexidine mouthwashes
Eliminate infections: antibiotics/antifungals/antivirals
After chemotherapy
Oral hygiene/preventive dentistry
Risk of anaemia/bleeding/infection

oxygenation have also been recommended<sup>2</sup> and are used as a treatment modality in the UK.<sup>3</sup>

Osteonecrosis is a recently recognised complication of bisphosphonate treatment<sup>4</sup> (Fig. 2). This condition is defined as exposed bone in the maxillofacial region for longer than eight weeks in the absence of radiotherapy but in a patient using bisphosphonates. It is diagnosed clinically but local malignancy must be excluded.<sup>5</sup> Bisphosphonates are a group of drugs, including alendronic acid, disodium

etidronate and risedronate sodium, which are adsorbed onto hydroxyapatite crystals thus slowing their rate of growth and dissolution. They have been used in treatment of bony metastases, the hypercalcaemia of malignancy and the management of osteoporosis in post-menopausal women.

Dental extractions should be avoided wherever possible while patients are on bisphosphonate therapy to reduce the risk of necrosis. Established cases require analgesia, long-term antibiotic and topical antiseptic therapy, together with careful local debridement to remove limited bony sequestra similar to the management of osteoradionecrosis.<sup>6</sup> Risk factors that will increase the possibility of osteonecrosis developing include local infection, steroid use, trauma, chemotherapy and periodontal disease.

The mechanism by which bisphosphonates increase the risk of osteonecrosis is not fully understood. Trauma caused by dental extraction in the presence of impaired osteoclast function may cause inadequate clearance of necrotic debris. Local osteonecrosis may also occur due to secondary infection. It is also thought that bisphosphonates might have toxic effects on soft tissues around the extraction site and thereby impair the function of vascular and epithelial cells.<sup>5</sup>

Chemotherapy agents are inevitably highly toxic and risk important systemic effects such as infections and bleeding due to bone marrow involvement and resultant neutropaenia and thrombocytopaenia. It is important to liaise with an individual patient's oncologist to ensure dental or oral surgical treatments are timed to avoid periods of maximum bone marrow depression.

Management of established mucositis includes systemic analgesia, the use of intraoral ice and topical analgesics such as benzydamine hydrochloride or 2% lidocaine lollipops or mouthwash.

Subsequent to radiotherapy and chemotherapy, meticulous oral hygiene is essential, especially during treatment when the mouth is inflamed and sore. Dilute chlorhexidine mouthwashes, topical fluoride applications, saliva substitutes and active restorative care may all be needed to

preserve the remaining dentition. Should teeth have to be extracted, this is best carried out in a specialist oral and maxillofacial surgery unit and it is essential that atraumatic techniques are used, with primary closure of oral mucosa together with antibiotic therapy until healing is complete. Similar considerations apply to patients taking bisphosphonates. The timing of extractions in patients undergoing chemotherapy is critical. This should be co-ordinated with the treating oncologist so that the ideal 'window of opportunity' is used.

### EFFECTS OF DRUGS USED IN PATIENTS WITH ORAL MALIGNANCY ON DENTAL MANAGEMENT

As mentioned above, many drugs used in the management of malignant disease will affect white cell and platelet numbers. This means that bleeding and infection are risks of surgical dentistry such as extractions. A full blood count is needed to ensure that any extractions can be performed safely. Elective extractions should be carried out when the blood picture is normal, however emergency extractions may need to be performed. If the platelet count is less than  $50 \times 10^9$  per litre then intra-oral surgery is contraindicated unless a platelet transfusion can be provided; if less than  $100 \times 10^9$  per litre then sockets should be packed with a haemostatic agent such as Surgicel® and sutured. If the white cell count is less than  $2.5 \times 10^9$  per litre then prophylactic antibiotics are recommended.

It was mentioned above that xerostomia and stomatitis are side-effects of radiotherapy. These can also be unwanted effects of some drugs used to treat malignancy. Thus excellent oral hygiene and caries prevention measures such as the use of fluoride are recommended. If dentures are ill-fitting these should be removed as they may worsen drug-induced mucositis.

Some of the drugs used to treat malignancies will interfere with medications dentists might prescribe. Examples include paracetamol and metronidazole, both of which increase the toxicity of busulphan by inhibiting metabolism and increasing plasma concentration of the cytotoxic

drug. Similarly, erythromycin increases the toxicity of the chemotherapeutic drug vinblastine. The toxicity of methotrexate is increased with concomitant administration of non-steroidal anti-inflammatory drugs, penicillins and tetracyclines. These are just some examples of pertinent drug interactions. The dentist should consult a publication such as the *British National Formulary* or discuss with the patient's oncologist if there is any doubt about prescribing another medication.

Patients who have received treatment for childhood cancers may have dentofacial abnormalities as normal development may have been compromised. Problems such as poor root formation, enamel defects, prominent incremental lines in dentine and facial asymmetry may arise.<sup>7,8</sup>

### CONCLUSIONS

Many patients with cancer will present to their dental practitioner requiring routine dental care or specific attention to oral complications resulting from malignancy or radiotherapy and chemotherapy treatments. It is imperative that dental practitioners make an appropriate assessment of the patient's general medical status (including nutrition, debilitation and haematology) before embarking upon dental care. Prevention is vital throughout to avoid worsening dental disease in patients with compromised general health.

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