

Toolbox

Oral cancer

Crispian Scully, Stephen Porter, Eastman Dental Institute for Oral Health Care Sciences, University College London, University of London, 256, Gray's Inn Road, London, WC1X 8LD, UK

Correspondence to: Dr Scully c.scully@eastman.ucl.ac.uk

Competing interests: None declared

This article was published in *BMJ* 2000;321:97-100.

This article is the third in a series adapted from *The ABC of Oral Health*, edited by Crispian Scully and published by the *BMJ Publishing Group* in November 2000.

Most cancer found in the mouth is oral squamous cell carcinoma. This disease is uncommon in the developed world, except in parts of France, but it is common in the developing world, particularly Southeast Asia and Brazil. Oral cancer typically is seen in men past middle age (although it is increasingly common in younger people), tobacco users, and members of lower socioeconomic groups.

Etiologic factors (acting on a genetically susceptible individual) include tobacco use (75% of people with oral cancer smoke), betel use (betel leaf, and often tobacco, plus spices, slaked lime [calcium hydroxide], and areca [betel] nut), alcohol consumption, a diet poor in fresh fruit and vegetables, infective agents (*Candida*, viruses), immune deficiency, and, in the case of lip carcinoma, exposure to sunlight.

Additional primary neoplasms may arise in the aerodigestive tract. These lesions occur in up to 25% of people who have had oral cancer for longer than 3 years and in up to 40% of persons who continue to smoke.

Oral malignant neoplasms

Common

- Squamous cell carcinoma

Uncommon

- Malignant salivary gland tumors
- Malignant melanoma
- Lymphomas
- Neoplasms of bone and connective tissue
- Some odontogenic tumors
- Maxillary antral carcinoma (or other neoplasms)
- Metastatic neoplasms (from breast, lung, kidney, stomach, or liver cancer)
- Langerhans' cell histiocytoses
- Kaposi's sarcoma

Summary points

- Oral cancer may present as a solitary lump, ulcer, or red or white lesion
- Oral squamous cell carcinoma is mainly a disease of men over middle age, but its prevalence is increasing in other age groups
- Earlier diagnosis offers better treatment, cosmetic and functional outcome, and survival
- Any oral lesion persisting more than 3 weeks should be treated with suspicion; biopsy is mandatory
- Biopsy is also mandatory to confirm diagnosis and determine the extent of involvement and presence of any second primary neoplasms
- Dental treatment, both preventive and curative, is essential before radiotherapy to minimize oral disease and the possible adverse consequences of operative intervention

Similarly, patients with lung cancer are at risk of developing second primary oral cancers.

Potentially malignant lesions or conditions may include some erythroplasias, dysplastic leukoplakias (about one half of oral carcinomas have associated leukoplakia), lichen planus, submucous fibrosis, and chronic immunosuppression. Rare causes of oral cancer include tertiary syphilis, discoid lupus erythematosus, dyskeratosis congenita, and Plummer-Vinson syndrome (iron deficiency and dysphagia).

DIAGNOSIS

Too many patients with oral cancer seek evaluation late in the course of their disease or their disease is detected when disease it is advanced and metastasis to lymph nodes has occurred. With earlier detection, treatment is less complicated, the cosmetic and functional results are better, and survival is improved.

Carcinomas arise anywhere in the oral cavity, often on the posterolateral margin of

the tongue and floor of the mouth—the “coffin” or “graveyard” area. It is crucial, therefore, to examine the entire oral cavity both visually and manually and to inspect and palpate the posterolateral margins of the tongue and the floor of the mouth. Possible findings include a solitary chronic ulceration (figure 1), red or white lesion (figure 2), indurated lump (figure 3), fissure, or enlarged cervical lymph node. Lip carcinoma manifests as thickening, crusting, or ulceration, usually of the lower lip (figure 4).

Enlargement of an anterior cervical lymph node may be detected during palpation (figure 5). Some 30% of patients present with palpably enlarged nodes containing metastases; of those who do not, an additional 25% will develop nodal metastases within 2 years. **Molecular techniques** can reveal the presence of tumor tissue in many histologically normal nodes.

Clinicians should have a high index of suspicion of a solitary lesion present for longer than 3 weeks, particularly if it is indurated, accompanied by cervical lymphadenopathy, or found in a patient who is in a high-risk group.

Investigations

It is essential to confirm the diagnosis and to determine whether cervical lymph nodes are involved or the patient has other primary tu-



Figure 1 Carcinoma of the tongue presenting as an ulcer

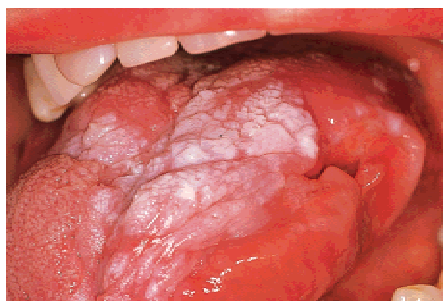


Figure 2 Carcinoma of the tongue with associated white lesions

mors or metastases. Therefore, the following are usually indicated:

- Lesional biopsy (usually an incisional biopsy, but an oral brush biopsy is now available, mainly for patients with widespread, potentially malignant lesions and for revealing malignancy in lesions that appear benign)
- Jaw and chest radiography
- Endoscopy
- Complete blood cell count and liver function tests

Computed tomography or magnetic resonance imaging can determine the extent and invasion of the tumor and if any of the cervical lymph nodes are involved. Ultrasound-guided cytologic analysis of nodes may be useful. The staging systems of tumor, nodes, metastases (TNM) classification and T and N integer score (TANIS) are often used. Molecular analysis techniques are being introduced for prognostication in potentially malignant lesions and tumors, as well as to identify nodal metastases.

MANAGEMENT

The prognosis of oral squamous cell carcinoma is site dependent. For intraoral carci-



Figure 3 Carcinoma of the tongue manifests as a lump

noma, 5-year survival may be as low as 30% for posterior lesions that often are detected late in the course of the disease. For lip carcinoma, however, 5-year survival is often greater than 70%. Important factors to consider in management are quality of life and patient education: in one study, 47% of patients still smoked and 36% drank alcohol to excess at least 6 months after the diagnosis of oral cancer. Only a third were aware that these habits were important in the development of oral cancer.

Oral squamous cell carcinoma is now treated surgically or with irradiation, although few unequivocal controlled trials of treatment methods have been conducted. Photodynamic therapy and chemotherapy have occasional applications. Clinics staffed by both surgeons and oncologists, and their support staff, usually have a consistent treatment policy and offer the best outcomes.

SURGERY

Surgical intervention allows the complete excision of a tumor and lymph nodes, followed by a full histologic examination for staging, which has implications for prognostication



Figure 4 Carcinoma of the lip

and assessing the need for adjuvant radiotherapy (figure 6). Surgery can also be used for radioresistant tumors. Disadvantages are mainly the perioperative mortality and morbidity, but modern techniques have significantly decreased these adverse outcomes as well as decreased the aesthetic and functional defects that result from surgery.

Patients who succumb to oral cancer usually die because of failure to control the primary malignancy or because of nodal metastases. Death because of distant metastasis is unusual. Ablative surgery excises the cancer with, ideally, at least a 2-cm margin of clinically normal tissue. If a node has clinical signs of invasion, it is reasonable to assume that other nodes may also be involved, and they

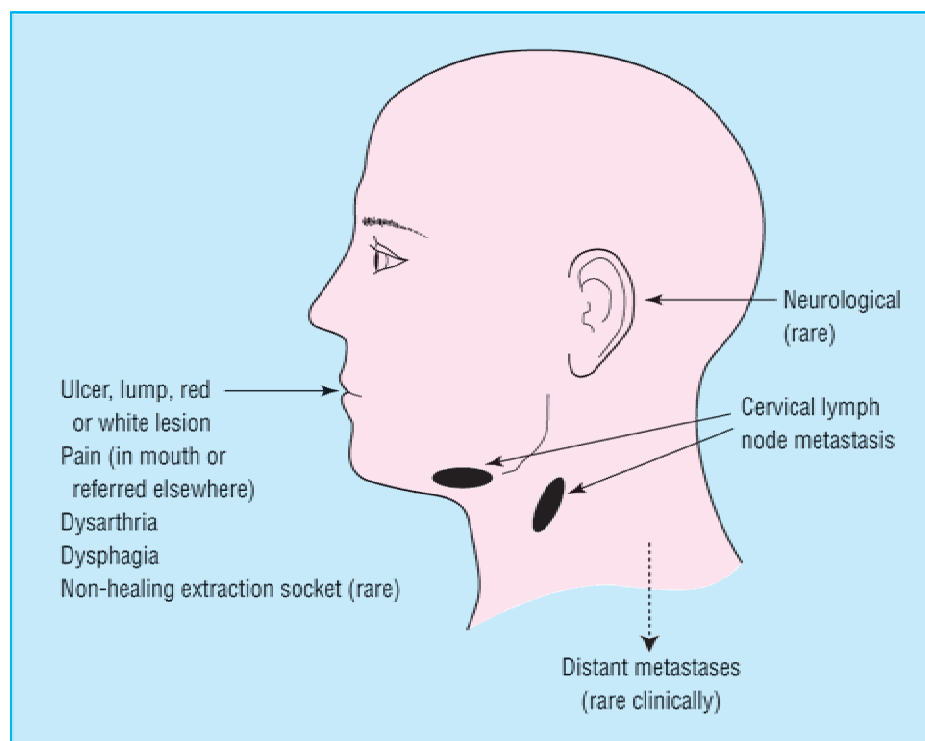


Figure 5 Possible features of oral carcinoma

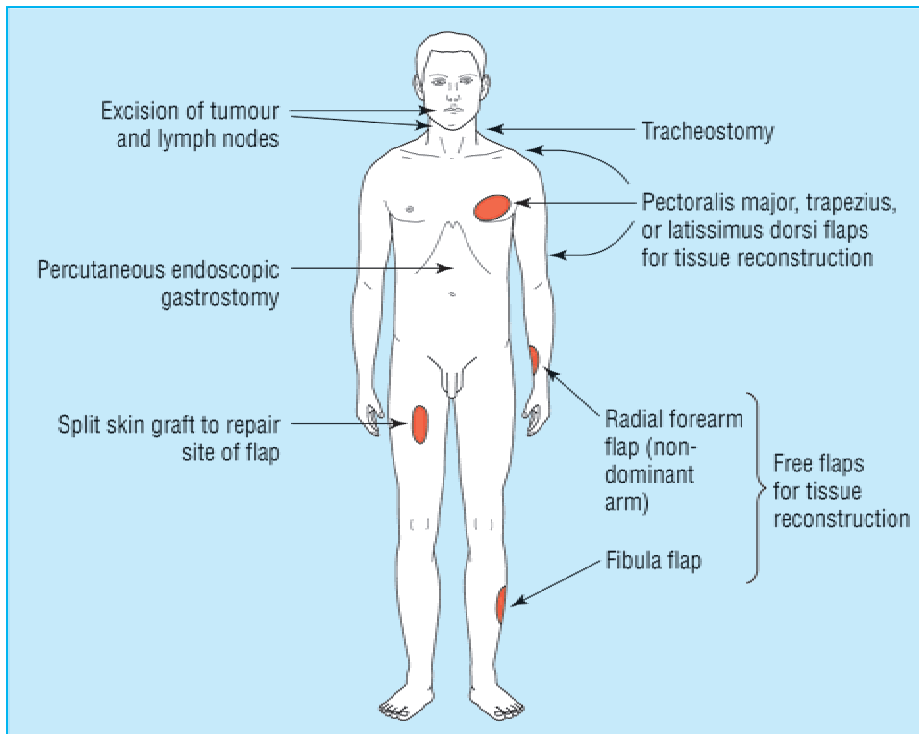


Figure 6 Surgical procedures that may be used in treating patient with oral cancer

must be removed by traditional radical neck dissection. “Functional” neck dissections, modified to preserve the jugular, sternomastoid, or accessory nerve while ensuring complete removal of involved nodes, have gained popularity. Moderate-dose radiotherapy is sometimes used to “sterilize” cervical nodes affected by metastatic disease.

Reconstruction

Reconstruction is tailored to the patient’s ability to cope with a long operation and the risk of substantial morbidity.

Soft-tissue reconstruction

Local flaps (such as nasolabial flaps) provide thin, reliable flaps suitable for repairing small defects. Often, however, tissue must be brought into the region to repair large defects. For these larger areas, split skin grafts or flaps—free or pedicle—are required.

Free flaps. Microvascular surgery facilitates excellent tissue reconstruction in a single operation by using free flaps. For example, forearm flaps based on radial vessels are particularly useful when replacing soft tissue. Flaps based on the fibula may be used if bone is also required (figure 7).

Pedicle flaps. Myocutaneous or osteomyocutaneous flaps are based on a feeding vessel to muscle and perforators to the skin paddle. These flaps may be used in a 1-stage operation to replace skin, and because they also contain muscle, they have adequate bulk to help repair defects. Pedicle flaps may also be used to import bone (usually rib). Examples

include flaps based on the pectoralis major, latissimus dorsi, or trapezius muscles. Flaps from the forehead or deltopectoral pedicle were once the mainstay for reconstruction, but they required a 2-stage operation, replaced only skin, and relied on a tenuous blood supply.

Hard-tissue reconstruction

Ideally, hard-tissue reconstruction is performed at the time of tumor resection. Dental implants can then be inserted to accommodate a dental prosthesis. Bone is traditionally in the form of free nonvascularized bone grafts taken from the iliac crest or a rib, but these grafts may survive poorly if contaminated or the vascularity is impaired after irradiation. In such cases, or when the defect is large, an osteomyocutaneous flap improves the graft’s vascular bed. True free vascularized bone grafts such as fibula grafts have great benefits, but they are time-consuming to perform and require considerable expertise.

The benefits of bone grafting for maxillary defects are less certain, and maxillary reconstruction is usually accomplished with an obturator (bung), which has the advantage that the cavity can subsequently be inspected.

Surgical complications in patients with oral cancer may include infection, carotid artery rupture, salivary fistulae, and thoracic duct leakage (chylorrhea).

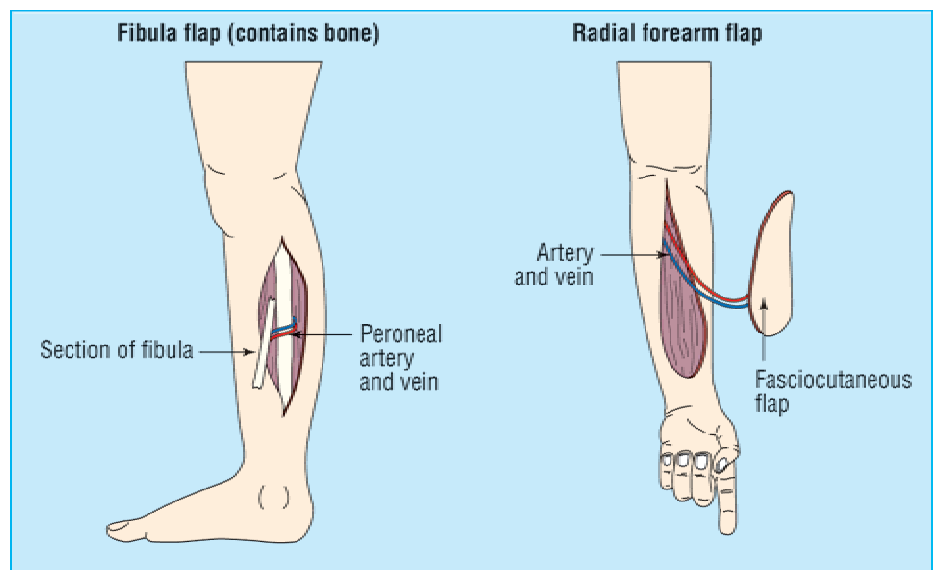


Figure 7 Free flaps that may be used for tissue reconstruction after tumor resection

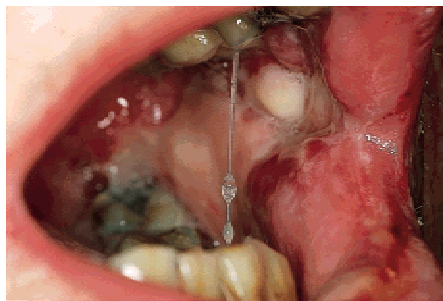


Figure 8 Radiation-induced mucositis

RADIOTHERAPY

With radiotherapy, normal anatomy and function are maintained, general anesthesia is not needed, and salvage surgery is still available if radiotherapy fails. Radiotherapy has its disadvantages: adverse effects are common, and subsequent surgery is more difficult and hazardous (with survival rates further reduced).

Methods of delivery

Radiotherapy can be delivered by external beams or by implanting a radioisotope. External beam irradiation (teletherapy) is commonly accompanied by side effects (see subsequent discussion). With interstitial therapy (brachiotherapy, plesiotherapy), implants of iridium-192 give a radiation dose equivalent to teletherapy but confined to the lesion and immediate area. Plesiotherapy thus causes fewer complications but is used mainly for tumors less than 2 cm in diameter and in selected sites.

Complications

Immediate complications include painful mucositis (figure 8). The time to healing de-

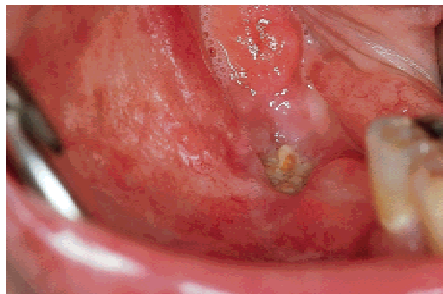


Figure 9 Osteoradionecrosis of the mandible

pends on the radiation dose but is usually complete within 3 weeks of the end of treatment. Tobacco smoking delays resolution, and mucositis can provide a portal for systemic infection. Mucositis can be reduced by minimizing doses of radiation or cytotoxic drugs, avoiding irritants (smoking, spirits, and spicy foods), maintaining good oral hygiene, cooling the mouth with ice, and using certain therapeutic agents (topical aspirin, benzydamine, lidocaine, chlorhexidine, sucralfate, or polymyxin E and tobramycin sulfate).

Osteoradionecrosis is a potentially serious complication (figure 9). With its high density and poor vascularity, the mandible is more prone to develop this complication than is the maxilla. Risk of osteoradionecrosis increases with higher radiation dose, larger radiation fraction size and number, and extraction of teeth after radiotherapy.

Complications of radiotherapy in children include enamel hypoplasia, microdontia, impaired tooth development and eruption, and alterations to the developing craniofacial skeleton.

Dry mouth (xerostomia) may cause a sub-

jective complaint of dry mouth, difficulty with speech and swallowing dry foods, a burning sensation in the mouth, dental caries, oral candidiasis, and bacterial sialadenitis. Gustatory (sugar-free chewing gum) or pharmacologic (cholinergic agents) stimuli may increase the functional activity of residual salivary tissue. Pilocarpine in doses of up to 5 mg 3 times daily can be effective. Patients with a dry mouth should avoid anything that further impairs salivation, such as drugs, tobacco, and alcohol. They may benefit from dietary control, taking frequent sips of water (particularly during eating), and using artificial saliva (such as Oralbalance) and topical fluorides.

Other complications of radiotherapy include loss of taste and cervical atherosclerosis.

Acknowledgment: The authors are grateful for the advice of Rosemary Toy, general practitioner, Rickmansworth, Hertfordshire, England, and David Cunliffe, senior registrar in maxillofacial surgery, John Radcliffe Hospital, Oxford, England.

Authors: Crispian Scully is dean and Stephen Porter is professor of oral medicine at the Eastman Dental Institute for Oral Health Care Sciences, University College London, University of London (www.eastman.ucl.ac.uk).

Causes of a complaint of dry mouth

Iatrogenic

- Drugs
- Anticholinergics (such as antidepressants, antihistamines, antihypertensives, antiretrovirals)
- Sympathomimetics (such as bronchodilators)
- Irradiation damage
- Graft versus host disease

Salivary gland disease

- Sjögren's syndrome
- Human immunodeficiency virus infection
- Hepatitis C virus
- Human T-lymphotropic virus type I infection
- Sarcoidosis
- Aplasia

Dehydration

- Uncontrolled diabetes

Psychogenic

Further reading

- Allison PJ, Locker D, Feine JS. The relationship between dental status and health-related quality of life in upper aerodigestive tract cancer patients. *Oral Oncol* 1999;35:138-143.
- Cancer Research Campaign. *Factsheet 14.1*. London: CRC; 1993.
- Prince S, Bailey BM. Squamous carcinoma of the tongue: review. *Br J Oral Maxillofac Surg* 1999;37:164-174.
- Rodrigues VC, Moss SM, Tuomainen H. Oral cancer in the UK: to screen or not to screen. *Oral Oncol* 1998;34:454-465.
- Rogers SN, Hannah L, Lowe D, Magennis P. Quality of life 5-10 years after primary surgery for oral and oro-pharyngeal cancer. *J Craniomaxillofac Surg* 1999;27:187-191.
- Schepman K, der Meij E, Smeele L, der Waal I. Concomitant leukoplakia in patients with oral squamous cell carcinoma. *Oral Dis* 1999;5:206-209.
- Sciubba JJ. Improving detection of precancerous and cancerous oral lesions. Computer-assisted analysis of the oral brush biopsy. US Collaborative Oral-Dx Study Group. *J Am Dent Assoc* 1999;130:1445-1457.
- Scully C, Ward-Booth P. Detection and treatment of early cancers of the oral cavity. *Crit Rev Oncol Haematol* 1995;21:63-75.