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*This series aims to enhance the healthcare team's awareness of the importance of early detection by recognizing signs and symptoms of orofacial cancers and their management, and of prevention. It discusses treatment complications from surgery, radiotherapy (RT) and chemotherapy (CTX), summarizing the outcomes of a meeting on 'Oral Healthcare in People Living with Cancer' held in 2010, attended by 300 delegates from 33 countries – dentists, specialists, and Dental Care Professionals (DCPs), and the cancer support team. There is a considerable body of literature on oral cancer but very little is written on healthcare aspects of people living with cancer and a particular focus of this meeting was caring for survivors. The Faculty included European leaders in the field who have authored the series. The full peer-reviewed papers from the meeting are published in Oral Oncology 2010; 46: 485–570.*

## Comprehending the Condition, Causes, Controversies, Control and Consequences

# 1. General Principles

### What is cancer?

Cancer is a genetic disease; in the case of oral cancer not because it's inherited but caused by genetic aberrations resulting from exposure to environmental carcinogens. Carcinogenesis is a multistep process and genetic aberrations acquired during evolution of this cancer include loss or gain of genetic sequences on chromosomes or acquiring DNA mutations. These specific DNA mutations, lead to altered amino acids and thus change in cell proteins. Several DNA mutations seem necessary before the cells and tissues affected change morphologically and in their behaviour to a recognizably pre- or potentially malignant cell characterized by an ability to proliferate in a less-controlled fashion than normal. If these cells totally escape growth control (they become *autonomous*), a cancer results, characterized by loss of cohesion and invasion across basement membranes into underlying tissues. Ultimately, cancer spreads (metastasises) via lymphatics to regional lymph nodes, later by the bloodstream to lung, brain, liver and elsewhere. Cancer, by local spread, may damage and cause dysfunction in vital organs, resulting in pain and other symptoms (dysarthria, dysphagia, tooth mobility and halitosis) and, in many

instances, leads ultimately to death. However, many people survive and many succumb from other diseases, or die after living with undetected (latent) cancer which has not impaired their lifespan.

Cancers can affect a range of tissues and organs, including the mouth. Of the many neoplasms that can affect the mouth, oral squamous cell carcinoma – cancer arising from the lining mucosa keratinocytes – is the most common and therefore important. Epidemiological data show that oral cancer is increasing, and in younger patients. Tobacco, alcohol and betel quid are the main risk factors (acting alone or synergistically) but certain types of human papillomaviruses (HPV) also play a role in oropharyngeal cancer. There is benefit from diets rich in fruit and vegetables (Articles 2 and 3).

Prevention of cancer is the key but involves lifestyle changes (quitting tobacco and betel quid and moderating alcohol) which afford protection not only against cancers in many sites, but also against a wide range of other conditions, many of which are equally life-threatening.

Early oral cancer may not have symptoms. For this reason and due to lack of public awareness of presenting symptoms, much cancer presents late, in the case of oral cancer, at a stage when not only is more

radical treatment necessary, but the prognosis is also less favourable.

Early detection and treatment should reduce the mortality rate and morbidity from cancers and their treatment. Earlier diagnosis is likely to be achieved reliably only with careful clinical examination and biopsy, and with advancement of techniques, in the future with molecular studies.

Multidisciplinary teams are fundamental to cancer detection and management. The basic treatment modalities remain as surgery, radiotherapy (RT) and chemotherapy (CTX). Medical, surgical and technological (imaging) management advances have significantly improved the quality of life for survivors. Nevertheless, patients are often faced with anxiety and other psychological distress, and may be faced with pain and suffer a range of untoward oral symptoms as a result of therapy, from dry mouth, to disturbed taste, eating, swallowing and speech (Table 1).

The importance of minimization of adverse treatment effects, and of good support for the oral cancer patient and family is paramount, and a major focus of this series.

### What publications are available?

The intent in this series is to

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Radiotherapy	Surgery
Mucositis Dry mouth (and caries, candidosis, sialadenitis) Disturbed taste Disturbed mastication Disturbed swallowing Disturbed speech Osteonecrosis Trismus Scarring	Disturbed sensation Disturbed mastication Disturbed swallowing Disturbed speech Scarring Deformity of jaws, face and/or neck Carotid blow-out (haemorrhage) Chyle leakage Salivary leakage Nerve damage

**Table 1.** Challenges that may be faced by the patient having cancer therapy.

Body	URL
BAHNO Cochrane CRUK NICE NIDCR  Texas Cancer Council Institut National du Cancer (in French) WHO Collaborating Centre UK	<a href="http://www.bahno.org.uk/">http://www.bahno.org.uk/</a> <a href="http://www2.cochrane.org/reviews/en/subtopics/84.html">http://www2.cochrane.org/reviews/en/subtopics/84.html</a> <a href="http://www.openuptomouthcancer.org/index.htm">http://www.openuptomouthcancer.org/index.htm</a> <a href="http://www.nice.org.uk/Guidance/CSGHN">http://www.nice.org.uk/Guidance/CSGHN</a> <a href="http://www.nidcr.nih.gov/oralhealth/topics/oralcancer/detectingoralcancer.htm">http://www.nidcr.nih.gov/oralhealth/topics/oralcancer/detectingoralcancer.htm</a> <a href="http://www.doep.org/OHCT.pdf">http://www.doep.org/OHCT.pdf</a> <a href="http://xxlplan.ovh.net/~penseetet/inca/proto_media/inca.html">http://xxlplan.ovh.net/~penseetet/inca/proto_media/inca.html</a> <a href="http://OcDeR.org">http://OcDeR.org</a>

**Table 2.** Formal guidance on cancer from various bodies.

System	Tobacco	Alcohol	Betel quid
Bladder	Cancer	Control, infections, cancer	?Cancer
Cardiovascular	Ischaemic heart disease	Arrhythmias, Cardiomyopathy, Hypertension,	Hypertension, Metabolic syndrome
CNS	Alzheimer disease, Stroke Addiction and dependency	Intoxication, Addiction and dependency, Dementia Wernicke-Korsakoff syndrome	Dependency
Gastrointestinal	Oesophageal cancer	Gastro-oesophageal reflux, Mallory-Weiss syndrome, Oesophageal carcinoma Gastritis, Gastric ulceration, Carcinoma, Glucose and vitamin malabsorption	Oesophageal cancer, submucous fibrosis
Haematological	Malignancies	Pancytopenia, Folate deficiency, Thiamine deficiency Immune defect	?
Hepatic	Abnormal liver function, Cancer?	Hepatitis, Fatty liver, Cirrhosis, Liver cancer	Cirrhosis, Cancer
Oral	Carcinoma, potentially malignant disorders, candidosis, dry mouth (xerostomia), dry socket, halitosis, implant failure, keratosis, necrotizing gingivitis, chronic periodontal disease, teeth staining	Tooth erosion, potentially malignant disorders, carcinoma	Cancer, potentially malignant disorders, periodontitis, submucous fibrosis
Musculoskeletal	Various musculoskeletal ailments, osteoporosis	Myopathy, Gout, osteoporosis	?
Pancreatic	Cancer	Pancreatitis	Cancer
Renal	Cancer	Renal tubular dysfunction	Chronic kidney disease, Urinary calculi (related to calcium hydroxide "chuna" in betel quid)
Reproductive	Infants with low birthweight, premature or stillborn, Earlier menopause	Impotence, dysmenorrhoea, low birthweight babies, foetal alcohol syndrome	Lower birth weight babies, Lower male to female sex ratio
Respiratory	Cancer, chronic obstructive pulmonary disease	Respiratory distress, infections	Breathing problems Asthma

Adapted from: Scully C. 2010. Medical Problems in Dentistry. 4th edition. Elsevier. Oxford, Edinburgh, London. (16)

**Table 3.** Possible systemic effects of main lifestyle cancer risk factors.

summarize essential points; many publications are already available (Table 2).

For example;

- **National Institute for Dental and Craniofacial Research (NIDCR)** of USA fully discusses diagnosis.
- **Texas Cancer Council** *Oral Health in Cancer Therapy* (Eds Rankin KV and Jones KL 1999) comprehensively covers oral healthcare.
- **British Association of Head and Neck Oncologists (BAHNO)** took the lead in the UK, to deliver a National Comparative Audit based upon the National Cancer Data Set module involving many centres. A minimum dataset was defined to allow a patient and groups of patients to be identified, management quantified and simple outcomes analysed. Essential outcomes were defined as:
  - survival
  - complications of treatment
  - quality of life measures.

■ **National Institute for Health and Clinical Excellence (NICE)** guidance on *Improving Outcomes in Head and Neck Cancer*, covers healthcare organization and recommends which professionals should be involved in treatment and care, and types of hospital or cancer centre best suited to provide that healthcare.

■ **Cochrane systematic reviews** published include *Interventions for the treatment of oral and oropharyngeal cancers: Surgical treatment: Radiotherapy and combinations: Interventions for treating oral candidiasis for patients with cancer receiving treatment: and Treatment of oral leukoplakia.*

■ **Cancer Research UK (CRUK)** offers guidance for patients, and for a range of health professionals.

■ **British Dental Association** – Occasional paper on oral cancer (2010)

■ **Oral Cancer Foundation** – a US based comprehensive website (<http://oralcancerfoundation.org/>)

■ **Mouth Cancer Foundation** ([www.rdoc.org.uk](http://www.rdoc.org.uk))

### What are the cancer risk factors?

DNA mutations occur spontaneously, especially via damage by oxidation and chemical free radicals but the rate of mutations is vastly increased by various risk factors. Such risk factors are mainly exogenous lifestyle factors, most of which are addictive. Tobacco and alcohol appear particularly important. In some cases, betel quid, other chemicals, radiation (eg sunlight, ionizing), infections (eg human papillomavirus [HPV], other microbes), or immuno-incompetence are relevant.

Much cancer is thus potentially

preventable by lifestyle change but environmental and genetic factors may also play a role. For example, protective mechanisms that may fail and predispose to cancer include genes for enzymes (xenobiotic metabolizing enzymes; XME) that metabolize carcinogens (eg Glutathione S-Transferases GSTs); genes that repair DNA mutations (DNA repair genes); genes that repair damaged growth control or kill cancerous cells by a process known as apoptosis (tumour suppressor genes; TSGs); and genes for immune protection as well as immortalization (telomerase). Some other genes (oncogenes) predispose to cancer.

### How does cancer develop?

The progression from a normal cell to a potentially malignant cell – and finally a cancer cell (oncogenesis – carcinogenesis) – is characterized by an ability of cells to escape normal growth control mechanisms, and to proliferate autonomously. A series of steps lead to the aberrant expression and function of molecules regulating cell signalling, growth, survival, motility, angiogenesis (blood vessel proliferation), and cell cycle control.

Cell cycle control is disturbed particularly by oncogene over-expression or over-activity (amplification) which drives cell proliferation. Oncogenes, such as the epidermal growth factor receptor (EGFR) gene, may thus be potential targets for cancer therapy.

Working more towards cell protection are tumour suppressor genes (TSGs) which, if defective, impair protection. An important TSG is P16; this acts as a growth control checkpoint. Another is P53, which will either repair a malignant cell or kill it (by apoptosis) (Figure 1). Single nucleotide polymorphisms (SNPs) are gene areas with

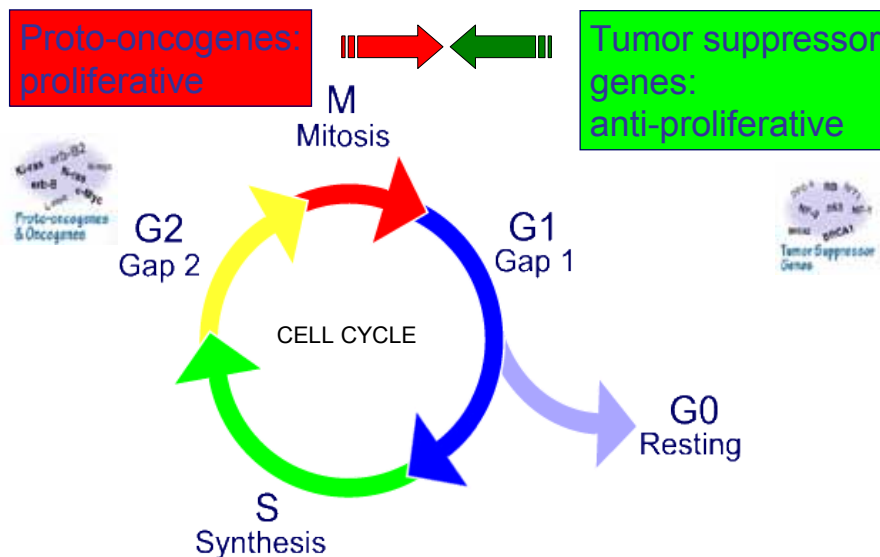


Figure 1. Cell growth cycle and influences of oncogenes and tumour suppressor genes.

altered DNA sequences which may not lead to an amino acid alteration. SNPs in various genes (TSGs, xenometabolizing enzymes, and DNA repair) may sometimes play a role in cancer.

Microarray technology has shown changes in many hundreds of genes that can be involved in oncogenesis.

### What is the importance of health promotion?

Prevention of cancer involves lifestyle changes (quitting tobacco and betel quid use and moderating alcohol consumption). A diet rich in fruits and vegetables may reduce cancer incidence. A healthy lifestyle protects not only against many cancers, but also against

many other conditions, many of which are also life-threatening (Table 3).

Health promotion for oral cancer prevention is the remit of the whole dental team, media and voluntary agencies. We propose that the dentist should take inter-professional leadership in dental-medical collaborations to reduce delays in diagnosis of oral cancer. A number of national initiatives have been brought together under the umbrella of the International Consortium on Head and Neck Cancer Awareness (ICOHANCA) whose object is to increase cancer awareness, and hopefully lead to prevention or earlier diagnosis. <http://www.ncbi.nlm.nih.gov/pubmed/17720612>

### Mouth Cancer Action Month

Early diagnosis of mouth cancer improves survival chances massively from 50% to 90%. Unfortunately, early diagnosis is rare, with over two-thirds of cases diagnosed at a late stage. This is due to a lack of awareness among the public of the early warning signs of the disease and the common risk factors. The Mouth Cancer Action Month campaign, organized by the British Dental Health Foundation, aims to change this.

Taking place annually throughout the whole of November, the campaign focuses on increasing awareness of mouth cancer, as well as promoting self-examination.

Health professionals are vital to the campaign, as their public facing roles create perfect opportunities to educate and inform the public. The Foundation encourages all health professionals to get involved in any way they can, whether it be offering free mouth cancer examinations to patients, creating an informative display or holding a sponsored event to raise money.

The facts speak for themselves – more people die from mouth cancer than from cervical and testicular cancer combined. Even more concerning, the number of annual mouth cancer cases has increased by

41% in the last decade. Action needs to be taken.

Tobacco is considered to be the main risk factor, and those who both smoke and drink in excess are up to 30 times more likely to develop the condition. A poor diet and the Human Papilloma Virus (HPV) are also risk factors.

Early warning signs include a non-healing mouth ulcer, red or white patches and any unusual swelling or lumps in the mouth.

An important part of the campaign is the Blue Ribbon Badge Appeal. Boxes of blue ribbon badges are available through the Foundation on 01788 539 793, and can be sold to members of the public to raise funds and awareness. Other Mouth Cancer Action Month resources, including the campaign's guide, can be ordered through the Foundation, and a free poster is available from Denplan (01962 827997).



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