Head and Neck Cancer Clinics
Series Editors: Rehan Kazi · Raghav C. Dwivedi

Peter A. Brennan
Tom Aldridge
Raghav C. Dwivedi *Editors*

Premalignant Conditions of the Oral Cavity

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Head and Neck Cancer Clinics

Series editors

Rehan Kazi
Manipal University
Manipal
India

Raghav C. Dwivedi
Department of Otolaryngology
Head Neck Surgery
Queen Elizabeth University Hospital
Glasgow
UK

Head and Neck Cancer (HNC) is a major challenge to public health. Its management involves a multidisciplinary team approach, which varies depending on the subtle differences in the location of the tumour, stage and biology of disease and availability of resources. In the wake of rapidly evolving diagnostic technologies and management techniques, and advances in basic sciences related to HNC, it is important for both clinicians and basic scientists to be up-to-date in their knowledge of new diagnostic and management protocols. This series aims to cover the entire range of HNC-related issues through independent volumes on specific topics. Each volume focuses on a single topic relevant to the current practice of HNC, and contains comprehensive chapters written by experts in the field. The reviews in each volume provide vast information on key clinical advances and novel approaches to enable a better understanding of relevant aspects of HNC. Individual volumes present different perspectives and have the potential to serve as stand-alone reference guides. We believe these volumes will prove useful to the practice of head and neck surgery and oncology, and medical students, residents, clinicians and general practitioners seeking to develop their knowledge of HNC will benefit from them.

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Editors

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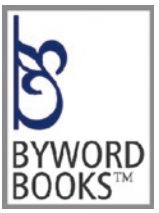

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Editors
Peter A. Brennan
Department of Oral and Maxillofacial Surgery
Queen Alexandra Hospital
Portsmouth
UK

Tom Aldridge
Department of Oral and Maxillofacial Surgery
Queen Alexandra Hospital
Portsmouth
UK

Raghav C. Dwivedi
Department of Otolaryngology
Head Neck Surgery
Queen Elizabeth University Hospital
Glasgow
UK

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Preface

Oral cancer is a global healthcare problem with an increasing incidence year on year. While there have been many advances in the diagnosis, staging, treatment and reconstruction and rehabilitation following ablative surgery, the crude 5-year survival rates still remain at approximately 50%. Systemic chemotherapy using some of the newer monoclonal antibodies as well as the prompt treatment of early stage disease are associated with increased survival. New advances in surgery and radiotherapy including for example intensity-modulated radiotherapy (IMRT) are reducing post-treatment complications.

Oral squamous cell carcinoma (OSCC) is often related to smoking, alcohol consumption and other habits including betel or areca nut chewing. p16 has been more recently implicated in the aetiology of tumours of the oropharynx including tonsil and tongue base. Some OSCCs seem to arise de novo in clinically normal looking mucosa, while others occur following a premalignant disease. Therefore, the early recognition, diagnosis and management of these pre-cancerous diseases are crucial to improve survival and reduce morbidity for patients.

Research in both pre-malignant diseases and OSCC continues at a rapid pace, and it can be difficult to keep abreast of all developments particularly with some of the new and exciting molecular pathways and understanding of pathogenesis. In this unique new book, we have brought together respected experts and colleagues from around the world to provide a contemporary overview of the common premalignant conditions affecting the oral cavity. Following an overview which includes information on epidemiology and diagnosis, we have focused on the common diseases leading to potential malignant change in the oral cavity and their management. We have included cutting-edge research and developments across the specialties of oral medicine, oral pathology and OMFS.

With such a vast and ever-increasing subject, we apologise in advance for any omissions and would be grateful to receive feedback from readers with suggestions for the next edition of this book.

Portsmouth, UK — Peter A. Brennan
Portsmouth, UK — Tom Aldridge
Glasgow, UK — Raghav C. Dwivedi

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About the Editors

Peter A. Brennan, MD, FRCS, FRCSI, Hon FRCS Professor Peter Brennan is a Consultant Oral and Maxillofacial Surgeon at the Queen Alexandra Hospital, Portsmouth, UK, with an interest in head and neck oncology and reconstruction. He has a personal chair in surgery in recognition of his research and education profile, publishing over 530 papers to date as well as editing five major textbooks (including lead editor of the two-volume *Maxillofacial Surgery*) used successfully worldwide. He is lead editor for the new *Gray's Surgical Anatomy*—sister to the famous *Gray's Anatomy* itself.

Peter is committed to teaching and education at all levels and was previous Honorary Editor of the *British Journal of Oral and Maxillofacial Surgery*. In addition to reviewing for many reputed journals, he is the current editor of the *Journal of Oral Pathology and Medicine*—one of the most well-respected journals in this specialty area. Peter has research interests in oral cancer, neck anatomy, patient safety and human factors.

Tom Aldridge, BDS, MFDS, BM, FRCS Tom Aldridge is an Oral and Maxillofacial Consultant in Queen Alexandra Hospital, Portsmouth, UK. He received his Bachelor of Dental Surgery from the University of Bristol in 2000 and Bachelor of Medicine from Southampton University in 2008. He completed specialist training in oral and maxillofacial surgery in 2015.

Tom specialises in facial trauma, orthognathic surgery, skin surgery and dentoalveolar surgery and has a keen interest in medical education and training.

He has published widely across the specialty and presented nationally and internationally.

Raghav Dwivedi, FRCS (Glas), PhD, FRCS (ORL-HNS) Raghav Dwivedi is a Consultant Head Neck Surgeon at the Queen Elizabeth University Hospital, Glasgow. He completed ENT and head neck surgery specialty training from the UK and India. He also completed head neck research fellowship at the Royal Marsden Hospital and the Institute of Cancer Research, London, and head neck surgical fellowships at Nottingham University Hospital, Cambridge University Hospitals, Portsmouth University Hospitals, and Imperial College, London. He holds an intercollegiate FRCS (ORL-HNS) from the Royal College of Surgeons of England; PhD from the Institute of Cancer Research, University of London, UK; and MS (ENT) from the King George's Medical University, India.

He is a dedicated head neck and ENT surgeon and has a unique blend of high-quality clinical and research experience. His areas of interest are minimally invasive head neck, thyroid and parathyroid surgery, HPV-related head neck cancers and outcome research. To date he has published 80 scientific papers in peer-reviewed indexed journals, 21 chapters (including one in the upcoming edition of Scott-Brown's *Otolaryngology: Head and Neck Surgery*) and edited one head neck surgery book. He has also served on the editorial board of six specialty journals and has been scientific reviewer for 35 peer-reviewed indexed journals including *BMJ*, *Cancer*, *Head and Neck*, *Oral Oncology* and *Surgical Oncology*.

Contributors

Tom Aldridge Department of Oral and Maxillofacial Surgery, Queen Alexandra Hospital, Cosham, Portsmouth, UK

Munita Bal Department of Pathology, Tata Memorial Centre, Mumbai, India

Peter A. Brennan Department of Oral and Maxillofacial Surgery, Queen Alexandra Hospital, Cosham, Portsmouth, UK

Rajiv S. Desai Department of Oral Pathology and Microbiology, Nair Hospital Dental College, Mumbai Central, Mumbai, Maharashtra, India

Marina Gonçalves Diniz Department of Oral Surgery and Pathology, School of Dentistry, Universidade Federal de Minas Gerais (UFMG), Belo Horizonte, Brazil

Raghav C. Dwivedi Department of Otolaryngology Head Neck Surgery, Queen Elizabeth University Hospital, Glasgow, UK

Camile S. Farah Australian Centre for Oral Oncology Research and Education, UWA Dental School, University of Western Australia, Perth, WA, Australia

Felipe Paiva Fonseca Department of Oral Surgery and Pathology, School of Dentistry, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil

Eduardo Rodrigues Fregnani Service of Oral Medicine, Sírio-Libanês Hospital, São Paulo, Brazil

Agnieszka Frydrych Australian Centre for Oral Oncology Research and Education, UWA Dental School, University of Western Australia, Perth, WA, Australia

Ravikant S. Ganga Department of Oral Pathology and Microbiology, Nair Hospital Dental College, Mumbai Central, Mumbai, Maharashtra, India

Carolina Cavalieri Gomes Department of Pathology, Biological Sciences Institute, Universidade Federal de Minas Gerais (UFMG), Belo Horizonte, Brazil

Ricardo Santiago Gomez Department of Oral Surgery and Pathology, School of Dentistry, Universidade Federal de Minas Gerais (UFMG), Belo Horizonte, Brazil

Michaela Goodson Newcastle University Medicine Malaysia, Iskandar Puteri, Johor, Malaysia

Esther A. Hullah Guy's and St Thomas' NHS Foundation Trust, London, UK

Omar Kujan Australian Centre for Oral Oncology Research and Education, UWA Dental School, University of Western Australia, Perth, WA, Australia

Márcio Ajudarte Lopes Department of Oral Diagnosis (Pathology and Semiology), Piracicaba Dental School, University of Campinas, Piracicaba, Brazil

Divya Mehrotra Department of Oral & Maxillofacial Surgery, Faculty of Dental Sciences, King George's Medical University, Lucknow, UP, India

Amanda Phoon Nguyen Australian Centre for Oral Oncology Research and Education, UWA Dental School, University of Western Australia, Perth, WA, Australia

Prathamesh S. Pai Department of Head and Neck Surgical Oncology, Tata Memorial Centre, Mumbai, India

Lakshminarasimman Parasuraman Department of Head and Neck Surgical Oncology, Tata Memorial Centre, Mumbai, India

Katherine Pollaers Australian Centre for Oral Oncology Research and Education, UWA Dental School, University of Western Australia, Perth, WA, Australia

Hélder Antônio Rebelo Pontes Service of Oral Pathology, João de Barros Barreto University Hospital, Federal University of Pará, Belém, Brazil

Kate Shearston Australian Centre for Oral Oncology Research and Education, UWA Dental School, University of Western Australia, Perth, WA, Australia

Martina K. Shephard Eastman Dental Hospital, University College London Hospitals NHS Trust, London, UK

Ben Tudor-Green Department of Oral and Maxillofacial Surgery, Queen Victoria Hospital, East Grinstead, UK

Pablo Agustin Vargas Department of Oral Diagnosis (Pathology and Semiology), Piracicaba Dental School, University of Campinas, Piracicaba, Brazil

Chapter 1
Introduction

Peter A. Brennan and Tom Aldridge

We have invited leading experts from around the world to contribute to this book on the management of oral premalignancy. The book includes an up-to-date and comprehensive analysis of risk factors and systemic conditions that can lead to oral squamous cell carcinoma (OSCC) as well as a description of carcinogenesis at both molecular and genetic levels. Specific premalignant conditions are discussed, and detailed management strategies are provided. In the remaining chapters, current, interesting and useful information on the various premalignant conditions are included which we hope will enhance clinical practice and patient care.

In this introduction, we provide a brief overview of the epidemiology of oral premalignant disease and the potential impact that it has on our patients. We also give an overview on the structural and mucosal anatomy of the oral cavity and lips that makes this area such a challenging and complex location to manage.

Oral Premalignancy

Oral cavity cancer accounts for approximately 3% of all cancers. Most are oral squamous cell carcinoma (OSCC), and disappointingly the 5-year survival has not significantly improved over the last few decades, despite many advances in diagnosis, imaging and treatment modalities. Quality of life following oral cancer treatment has also improved with advances in free tissue transfer and targeted therapy including intensity-modulated radiotherapy (IMRT) which can spare adjacent structures such as the salivary glands and cervical spinal cord. Many OSCC tumours develop from premalignant conditions of the oral mucosa which are sometimes not detected or diagnosed before the cancer itself. Premalignant conditions have huge

P. A. Brennan (✉) · T. Aldridge
Department of Oral and Maxillofacial Surgery, Queen Alexandra Hospital, Portsmouth, UK
e-mail: peter.brennan@porthosp.nhs.uk; Tom.aldridge@porthosp.nhs.uk

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geographical, socioeconomic and population variation with an accepted prevalence of 1–5% and are most commonly found in the buccal mucosa, lower gingivae, tongue and floor of the mouth [1].

The World Health Organization originally recommended the terms 'precancerous lesions' and 'precancerous conditions'. A precancerous lesion is a morphologically altered tissue in which oral cancer is more likely to occur than in apparently normal counterpart. A precancerous condition is a generalised state associated with significantly increased risk of cancer. However, in 2005 these terms were simplified to 'potentially malignant disorders' to eliminate confusion from the previous used terminology, definitions and classifications of oral lesions with a predisposition to malignant transformation (Fig. 1.1) [2].

Oral precancerous lesions take many forms with leukoplakia, oral submucous fibrosis (OSMF) and oral erythroplakia being the most common (Fig. 1.2). There are other presentations of systemic conditions that can also be premalignant, such as xeroderma pigmentosum and Fanconi's anaemia. The link between carcinogenesis and immunodeficiency is also well known [3].

Although our knowledge is improving, the aetiology of premalignant conditions of oral mucosa is still incompletely understood [4]. There are well-recognised risk factors such as tobacco chewing, tobacco smoking, areca nut (for OSMF) and alcohol. While tobacco chewing is a major risk factor for oral leukoplakia, OSMF and erythroplakia, tobacco smoking may be a risk factor for oral leukoplakia. Alcohol drinking may increase the risk by 1.5-fold for oral leukoplakia, by twofold for OSMF, and threefold for erythroplakia.

The risk of malignant change in the external lip can occur with use of the above agents, but actinic damage following chronic sun exposure (UVA light) is the major risk factor associated with lower lip SCC (Fig. 1.3). The lower lip is at particular risk due to its reduced keratinised mucosa, reduced melanocyte number and orientation perpendicular to the sun and lack of protection from all but the widest brimmed hats.

Fig. 1.1 Leukoplakia, left side of the tongue