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Jeffrey N. Myers and Erich M. Sturgis	

## **Etiology and Biology**

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Mia Hashibe and Erich M. Sturgis

Although tobacco prevalence is declining in most developed countries, less developed countries are still experiencing an increase in tobacco use. Thus the future burden of oral-cavity and oropharyngeal cancers in less developed countries is expected to be heavy. The incidence of human papillomavirus (HPV)-associated oropharyngeal cancer is dramatically increasing in the United States and other developed countries, although trends in less developed countries are not clear at present. HPV vaccine compliance in the United States is low, although it continues to increase each year. Increasing the HPV vaccination rate to control future HPV-associated cancer incidence remains a priority.

<b>Impact of Human Papillomavirus on Oropharyngeal Cancer Biology and Response to Therapy: Implications for Treatment</b>	<b>521</b>
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Juliana Bonilla-Velez, Edmund A. Mroz, Rebecca J. Hammon, and James W. Rocco

Oropharyngeal squamous cell carcinoma (OPSCC) originating from human papillomavirus infection has emerged as a new entity in head and neck cancer, defining a subset of patients with distinct carcinogenesis, risk factor profiles, and clinical presentation that show markedly improved survival than patients with classic OPSCC. De-escalation of therapy and identification of relevant biomarkers to aid in patient selection are actively being investigated. This review addresses the implications of these findings in clinical care.

<b>Oral Cavity and Oropharyngeal Squamous Cell Carcinoma Genomics</b>	<b>545</b>
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Marietta Tan, Jeffrey N. Myers, and Nishant Agrawal

Recent technological advances now permit the study of the entire cancer genome, which can elucidate complex pathway interactions that are not apparent at the level of single genes. In this review, the authors describe innovations that have allowed for whole-exome/genome analysis of genetic and epigenetic alterations and of changes in gene expression. Studies using next-generation sequencing, array comparative genomic hybridization, methylation arrays, and gene expression profiling are reviewed, with a particular focus on findings from recent whole-exome sequencing projects. A discussion of the implications of these data on treatment and future goals for cancer genomics is included.

**Why Otolaryngologists Need to be Aware of Fanconi Anemia**

567

Jiahui Lin and David I. Kutler

Fanconi anemia (FA) is a rare disorder inherited in an autosomal recessive fashion, with an estimated incidence of 1:360,000 births. Although hematologic complications are the most common manifestation of this disease, cancers, especially of the head and neck, are also prominent. The chromosomal fragility of patients with FA necessitates careful planning of therapy and monitoring, and awareness of this rare disorder is crucial to recognizing it in the clinic.

**Evaluation and Therapy****Oral Premalignancy: The Roles of Early Detection and Chemoprevention**

579

Jean-Philippe Foy, Chloé Bertolus, William N. William Jr, and Pierre Saintigny

Premalignancy and chemoprevention studies in head and neck cancer typically focus on the oral cavity. Avoiding or cessation of alcohol and smoking, early detection of potentially malignant disorders or cancer, and early detection of recurrent and/or second primary tumor form the basis of prevention of oral cancer. Analysis of tissue prospectively collected in evaluation of retinoids for chemoprevention trials allowed identification of molecular biomarkers of risk to develop oral cancer, loss of heterozygosity being the most validated one. Improving risk assessment and identification of new targets for chemoprevention represent the main challenges in this field.

**Evaluation and Staging of Squamous Cell Carcinoma of the Oral Cavity and Oropharynx: Limitations Despite Technological Breakthroughs**

599

Mark E. Zafereo

Squamous cell carcinoma of the oral cavity (SCCOC) and squamous cell carcinoma of the oropharynx (SCCOP) represent two distinct disease entities. SCCOC continues to be related to tobacco risk factors, and the current anatomic staging system provides useful prognostic value. Most patients with SCCOP in Western countries now have HPV-associated tumors, and tumor HPV status is considered the most important prognostic factor. Smoking status is emerging as an important prognostic factor for HPV-driven SCCOP, independent of tumor HPV status. Sentinel lymph node biopsy and FDG-PET/CT imaging are diagnostic staging tools useful in select patients with SCCOC and SCCOP.

**Surgical Innovations**

615

Daniel R. Clayburgh and Neil Gross

This article reviews the evidence behind surgical innovations and effect on treatment-related morbidity to examine how they may be integrated into modern management strategies for oral cavity and oropharyngeal squamous cell carcinoma (SCC). Technologic advances, including transoral laser microsurgery and transoral robotic surgery, along with the application of sentinel lymph node biopsy for oral cavity and oropharyngeal SCC are discussed.

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