Role of Oral Microbial Infections in Oral Cancer

Brett L. Ferguson, DDS[a,b,*], Scott Barber, DDS[c], Imani H. Asher, DDS[c], Chalmers R. Wood, DDS[c]

KEYWORDS

• Viral • Microbial • Carcinogenesis

KEY POINTS

- The role of bacterial and viral carcinogenesis in the oral cavity is becoming increasingly a subject of interest, as a means to provide more methods of cancer prevention.
- There have been suggestions of relationships between bacteria and multiple strains of viruses in the progression of malignancy in some studies.
- Cancer cause is closely related to the type of carcinogen, as well as the synergistic or additive actions of combined risk factors, the susceptibility of the host, and the duration of interaction between host and exposure to risk factors.
- Different bacterial species are reviewed in detail, as well as the main viruses identified as contributive factors in carcinogenesis, including human immunodeficiency virus, human papilloma virus, Epstein-Barr virus, and human herpesvirus.
- Because most of the current studies maintain a contributive relationship and very few legitimize a definitive causal relationship, much research is being done to further define the role that these microbial and bacterial agents play in the progression of malignancy.

INTRODUCTION

Head and neck cancer refers to a group of biologically similar cancers that start in the lip, oral cavity, nasal cavity, paranasal sinuses, nasopharynx, and larynx. About 40% of head and neck cancers occur in the oral cavity, 15% in the pharynx, 25% in the larynx, and the remaining 20% are in the salivary glands and thyroid. Overall, they account for more than 500,000 cases annually worldwide. They account for 3% of all

Disclosure: The authors have nothing to disclose.

[a] University of Missouri-Kansas City, Kansas City, MO, USA; [b] Oral and Maxillofacial Surgery, Head and Neck Clinic, University Health, Truman Medical Center, American Association of Oral and Maxillofacial Surgery, 2101 Charlotte Street, Suite 310, Kansas City, MO 64108, USA; [c] Department of Oral and Maxillofacial Surgery, University Health Oral and Maxillofacial Surgery Clinic, 2101 Charlotte Street, Suite 310, Kansas City, MO 64108, USA

* Corresponding author. Oral and Maxillofacial Surgery, Head and Neck Clinic, University Health, Truman Medical Center, American Association of Oral and Maxillofacial Surgery, 2101 Charlotte Street, Suite 310, Kansas City, MO 64108.

E-mail address: brett.ferguson@tmcmed.org

Dent Clin N Am 61 (2017) 425–434

http://dx.doi.org/10.1016/j.cden.2016.12.009

dental.theclinics.com

cancers in the United States. In 2015, it was estimated to affect 61,760 people (45,330 men and 16,430 women). Men are affected significantly more often, ranging from 2:1 to 4:1. It is estimated that more than 13,000 people will die from head and neck cancer. Most of these cancers are squamous cell carcinoma (**Fig. 1**).

Risk factors for head and neck cancer include smoking, alcohol consumption, ultraviolet light, viral infections, and possibly even bacterial infections. Human papillomavirus (HPV) and Epstein-Barr virus (EBV), herpes simplex virus, and human immunodeficiency virus (HIV) have been identified as significant risk factors. Cancer cause is closely related to the type of carcinogen, as well as the synergistic or additive actions of combined risk factors, the susceptibility of the host, and the duration of interaction between host and exposure to the risk factor.[1] The possible involvement of oncogenic viruses and bacteria in oral and oropharyngeal cancers has become a field of increasing interest.

The oral cavity contains a delicate balance of microbial flora. Studies have shown that the human oral carcinoma surface biofilms harbor significantly increased levels of both aerobes and anaerobes. They have also shown that the tumor microenvironment is suitable for bacteria to thrive. Strains such as *Escherichia coli* and facultative oral streptococci are among those that have been noted to highly colonize sites of oral squamous cell cancer (OSCC).

The role of bacterial carcinogenesis in the oral cavity is becoming increasingly a subject of interest, as a means to provide more methods of cancer prevention. There have been some suggestions of a relationship between bacteria and progression of malignancy in certain studies. Some of the bacterial causes include streptococci, *Helicobacter pylori*, and *Salmonella typhi*. However, the relationship between some of these, namely *H pylori* and *S typhi*, is complex. Some species are carcinogenic, whereas the presence of others is required to prevent carcinogenesis, depending on location. For example, research has shown that *H pylori* can cause gastric cancer or mucosa-associated lymphoid tumors in some individuals. In contrast, exposure to *H pylori* seems to reduce risk of esophageal cancer in other individuals. It is now recognized that bacteria bind to and colonize the mucosal surfaces in a highly selective manner via a lock-and-key mechanism. Bacterial infections have been linked to malignancies because of their ability to induce chronic inflammation. They can also produce cell toxins that disturb cell cycles and lead to altered cell growth. Another mechanism that has been of interest in recent research studies is the ability to facilitate tumorigenesis by converting ethanol into its carcinogenic derivative, acetaldehyde, to levels capable of inducing DNA damage, mutagenesis, and secondary hyperproliferation of the epithelium. This ability is especially evident in the streptococci species in

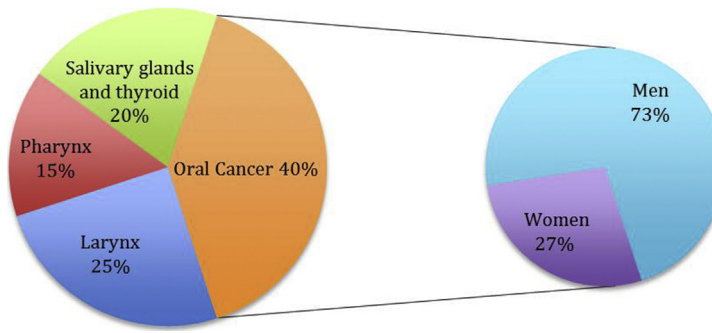

Fig. 1. Incidence of head and neck cancer.