

## Oral Cancer- A Real Threat to Society

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### Abstract

Oral cancers often occurs out of long standing potentially malignant lesions and conditions so called premalignant lesions and conditions. Oral precancer is an intermediate state with increased cancer rate which can be recognized and treated obviously with much better prognosis than a full blown malignancy. Oral cancer risk can be lowered or even prevented by simply understanding basic oral hygiene, different bacteria found in the mouth, and how diet influences oral cancers. Currently, research is being done on the relationship between diet and oral cancer. Oral cancer is a very serious disease that can be prevented. Practicing good oral hygiene is key to help keep the oral cavity clean. Limiting the use of tobacco and alcohol products is also important because these are the causes of most oral cancers. Lastly, eating a well-balanced diet that has protective effects can reduce the risk of oral cancer. This includes a diet high in fruits, vegetables, and fish and low in high fat and cholesterol meats, rice, and refined grains.

**Key words:** Dentist, Oral cancer, Smoking, Tobacco

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### Introduction

The study of the oral cavity is important to identify the pathologies associated with it.<sup>[1]</sup> Tumor in Latin means lump.<sup>[2]</sup> The tumor or neoplasm serves no useful purpose. Fundamental to its origin, there is loss of responsiveness to the normal growth control. Epidemiological studies have shown that in the United States, over 500,000 deaths are caused every year because of malignant neoplasms. India, which occupies 2.4% of the world's land mass, accommodating about 16.5% of the world population, is estimated to have 6 million cancer patients at any point of time and nearly 2 million new cases every year, which is a major cause of death.<sup>[3]</sup> Even more anguishing than the mortality is the physical and the emotional trauma caused by these neoplasms.

Controlling this dreadful surge is based on learning more about the origin and vulnerabilities of neoplasms. It has led to a great progress in this field.<sup>[4]</sup>

The ninth version of the international classification of diseases by the World Health Organization (WHO) classifies oral cancer under lip, tongue, gingiva, floor of the mouth, and other parts of mouth.<sup>[5,6]</sup> It was Christopher Columbus who first found tobacco in San Salvador. He saw that these strange leaves were traded and used for ceremonial and medicinal purposes. They were powdered and inhaled by native Indians in a "Y" shaped piece of cone or pipe. These strange leaves later came to be known as tobacco. Tobacco was introduced to India in the late 16th and early 17th century. Here, tobacco smoking became a symbol of aristocracy with the introduction of hooka. Tobacco belongs to the

potato family genus *Nicotiana*. Linnaeus named it in 1753 after French ambassador John Nicot. It is chewed, smoked, sniffed, or sucked. The carcinogenic role of tobacco varies depending upon the tobacco product, the way in which it is used, and its combination with other substances.

In India tobacco is used in various ways that include smoked tobacco and smokeless tobacco, which is used for chewing. These substances are either used alone or in unison with other products also. A large percentage of populations have used both smoked and smokeless tobacco together.<sup>7,8</sup>

In a study conducted by Vora et al. about alcohol, tobacco, and paan use and its relation to oral cancer threat among Asian males in Leicester, it was found that 7% of first-generation Hindu males chewed paan containing tobacco that is strongly associated with oral cancer.<sup>[9]</sup>

**Education, Employment and Oral Cancer:** Many studies have showed considerable influence of education and employment on oral cancer.<sup>10</sup>

**Neoplastic Progression:** Neoplastic progression ensuing from initial clonal expansion, invasion of the basement membrane culminating in a condition of extensive bulk, invasiveness, disseminated metastasis, and death has properties defined by both rate and extent.<sup>[11]</sup> Thus, the magnitude of neoplastic progression can be estimated from the following:

1. The clinical level
2. The tissue level, by assessing the breadth of invasion and nodal metastasis; and

### 3. The cytonuclear level<sup>12</sup>

Invasive carcinoma is characterized by the cytologic changes previously described, with the hallmark being the escape of cells from the epithelial compartment through the basement membrane and allelic loss commonly observed at 5p and 4q.

An important consideration regarding the pathogenesis and progression of oral cancer, particularly neoplasms derived from stratified squamous epithelium is the terminology used to describe various diagnostic features of intraepithelial lesions prior to invasion. Boone et al, in a treatise on chemoprevention, make a strong argument that “terms such as severe atypia, dysplasia, and severe dysplasia describe epithelial cells that imperceptibly differ from the morphology of cells at the time of invasion”.

The development and progression of oral cancer have at least two antecedent controlling factors. The first is hyper- proliferation, which may not be obligatory. Oral cancer, like many other forms of cancer, is multifocal, demonstrating clonal evolution with intralesional generation of genomic structural variant cells and enhanced phenotypic heterogeneity.

#### Evaluation of Oral Cancer

The history and physical examination at the initial consultation establish a foundation for subsequent laboratory and radiographic evaluation and treatment planning. Psychosocial and nutritional assessment, followed by intervention when required is vital in achieving optimal outcome<sup>13,14</sup>.

**History:** A careful history taking helps to generate a complete differential diagnosis and all diagnostic possibilities are considered prior to establishing a definitive diagnosis. In addition, history also provides estimates of prognosis and aids in the treatment selection. The extent and severity of the disease process are assessed by determining the duration, type, and rate of progression of symptoms, and the functional impairment experienced by the patient also helps us in identifying specific co-morbidity.

**Physical Examination:** The examiner should correlate physical findings with the patient’s clinical presentation. A careful inspection and palpation of the area involved should be carried on and notice the pathological changes and special attention to abnormalities in the texture and color should be noticed. Assessment of nodal diseases is recorded according to the staging and grading followed. The fiberoptic techniques and video examination is beneficiary in educating the patients.

**Medical Examination:** A review of the medical records, past medical history, results of laboratory tests and communicating with the patient’s primary care

physician helps the examiner to identify medical co-morbidity. The severity of the co-morbidity is determined by the subjective complaints of the patients and objective findings from examination and diagnostic testing.

**Metastasis Record:** Head and neck cancer is considered a regional disease owing to tendency of metastatic spread to be restricted to the regional lymphatics. However, the possibility of systemic metastasis should not be overlooked.

**Psychosocial Assessment:** Oral cancer patients suffer a trouble of life frightening illness unlike other cancer patients; they can rarely conceal their affliction from public view as the treatment of these oral cancer results in dysfunction and disfigurement of the head and neck structures.

Patients undergoing management for oral cancer frequently have shown problems with low self-esteem due to a change in self-image. The majority oral cancer patients are associated with tobacco and alcohol abuse. Alcohol abuse can create patients many medical and psychological problems during treatment. Patients actively abusing alcohol should undergo detoxification to avoid withdrawal reaction during therapy. Nicotine withdrawal leads to anxiety, sleep disturbances and headache. Appropriate pre-treatment counselling helps to encourage patients to participate actively in the further treatment planned.

**Radiographic examinations:** CT effectively demonstrates bony changes such as erosive lesions at the skull base or mandible. MRI has multiplanar imaging capacity and can show subtle variations in soft tissue distinguishing inflammatory changes from fibrosis or recurrent tumour.

**Cytology:** In patients with unknown etiology, Fine Needle Aspiration Biopsy (FNAB) can save time and expense of an extensive work up for malignant disease and the potential complications of open biopsy. Several studies have shown that FNAB has an excellent diagnostic accuracy.

**Endoscopy:** Usually used in post-operative cases to detect presence of any synchronous lesions. The incorporation of the findings of molecular biology into the clinical practice of head and neck oncology is yet to become reality. However a new tumor antigen A9/ $\alpha$ 6 $\beta$ 4 integrin has recently been shown to have prognostic value. Assays for mutations in the p53 gene have also shown promise in screening cancer. Application of molecular biology in future will add up to refinement in oral cancer screening techniques.<sup>15</sup>

Premature recognition of oral cancer allows for a 90% increase in 5-year survival rate. Unfortunately, nowadays, 60% of these tumors are detected in

advanced stages with a 5-year survival of about 20%. Therefore, early detection is of greatest importance to both the general public (GP) and the dentist, who have primary role in early diagnosis and are also responsible for improving the population's health regarding the risk factors in oral cancer. GP and dentist should systematically check the oral cavity and mucus membrane in heavy smokers and/or drinkers above 40 years of age. Lesions become suspicious when they persist for more than 2 weeks after detection. The high-risk patients and suspicious lesions should undergo diagnostic procedures to improve the prognosis.<sup>16</sup>

Researchers of oral cancer agree that early diagnosis of oral carcinoma greatly increases the probability of cure with minimum impairment and deformity. Primary prevention, which involves reducing the exposure to tobacco, alcohol, and betel quid, has been shown to be effective in reducing the incidence of oral cancer. Secondary prevention involves screening for early detection of oral cancer; irrespective of the screening method used, a positive screening result must be confirmed by a biopsy. A public awareness program that stresses the importance of at least one annual dental examination, identification of warning signs of oral cancer, and recognition of hazards of tobacco and alcohol use is necessary to reverse the high morbidity and mortality rates associated with this disease.<sup>17,18</sup>

**Scope for Primary Prevention:** As described previously, tobacco use has a deleterious effect on oral cavity. Approximately 630,000 deaths occur every year in India and risk of mortality is invariably higher in tobacco users than among non-users. These observations through numerous studies conducted in this regard show that there is a strong need for all the dental health professionals to join hands in connection to prevent oral cancer and also other diseases caused by tobacco<sup>19</sup>.

**Effects of Primary Prevention:** Primary prevention aims at avoiding or reducing risk factors. The rural population of India has been resource for various studies conducted in this regard. Motivation by various communications imparts such as personal communications, films newspaper articles, radio programs, folk-art, and posters, a great amount of population approximating to 15% of the tobacco users have quit the use and substantial amount of people showed reduction appreciably. As most of oral cancers arise from precancerous lesion, the relative reduction in these lesions have an indirect effect on reduction of oral cancer.

**Primary prevention in day-to-day clinical practice:** Some simple clinical practices can be followed in day-to-day practice, which encourage the tobacco users to quit tobacco, like the absence of ash trays and any book

of advertisement on any tobacco product in the clinic. The other practices are: Using routine questionnaire about the use of tobacco; complimenting those who do not use tobacco of any kind; encouraging the tobacco users to stop it; display of suitable educational materials in the waiting room and also distribution of such material to the patients. Regular follow-up examination of precancerous and other tobacco-related oral lesions will greatly assist the people who are using tobacco and intend to quit. Studies have shown that these simple methods in clinical practice take an extra 2–3 min of time with the patient, but have a great impact on the knowledge, attitude, and behaviors of the individual toward tobacco use and its counter effects, and have proven to help them in a stopping and reducing the tobacco use to a great extent.

**Secondary prevention:** Secondary prevention aims at early detection of cancer of easily accessible sites and oral cavity in one such site, prompt treatment is most essential for a successful secondary prevention, secondary prevention is also called cancer control. This collaborative effort is most required because the elders, make less dental visits than those of physician visits. Which is most common in regions of low literacy and limited access.<sup>20</sup> The ideal time to detect cancer is when it is small and has not spread. In general the greatest chances of cure and prolonged survival exists when such small cancers are detected and treated. In this context dentists have prime responsibility in detecting cancer by screening oral cavity which should be performed on every new patient and at all recalls.<sup>21</sup>

**Tertiary prevention:** Tertiary prevention aims at the terminal stages. Over 70% of cancers have severe pain and other distressing symptoms in the advanced stages. Pain control and palliative care are major strategies of tertiary prevention.

#### **Tobacco Cessation: The Dentist's Challenge<sup>22</sup>**

Despite the fact that the American public is inundated with information stating the ill effects of tobacco use, approximately 25% of the population continues to smoke cigarettes.

Tomar SL, Husten CG, Manehy MW reported that fewer than one fourth of smokers had been educate by dentists to stop smoking during previous year, while 51% claimed to have been so advised by their physicians. Clinical trials have shown that dentists can be highly effective in delivering brief yet effective tobacco intervention messages, and 1 year unit rates as high as 15% have been reported in dentist-initiated endeavours.

Messages may be reinforced and patients observed. Oral health care practitioners also are provided "the teachable moment", oral effects of tobacco use are visible in the patient's mouth, so the ramifications of

tobacco use can be shown to the patient and can serve as a strong impetus to cessation.

Dentists possess an arsenal of information related to health behaviors, oral pathosis, and patient compliance, just to name a few. Dentists also know their patients well, are trusted by them, and have their respect. These combined strengths automatically give dentists an advantage in their assumption of tobacco intervention roles. Prevention and education are hallmarks of successful dental practices. Practices with a holistic bent that are concerned with the overall well-being of the patient represent the highest level of professional ethics dentistry can offer.

Dentists have key responsibilities as role models, authorities, and educators in informing the public about the dangers of tobacco use. They must personally aid their patients in cessation efforts.

The framework for the following text is based on the **Agency for Health Care Policy and Research** clinical practice guideline for smoking cessation and is supported by the documents developed by the National Cancer Institute (NCI). The AHCPR clinical strategies embody the NCI 4 as protocol of ask, advise, assist, and arrange.

**The Clinic/ Practice Environment:** For a tobacco use intervention program to be successful, the total dental practice environment must convey an atmosphere of commitment and support. In their interactions with patients, the dentist and all team members must be knowledgeable about the tobacco intervention process and supportive for patient efforts. The more reinforcement patients receive, the greater their chances for success.

The dentist also should designate a team coordinator (e.g., the dental hygienist or dental assistant) to oversee program activities. This individual should be committed, enthusiastic, and organized.

As key leaders of the practice, dentists need to convey strong statements of support for tobacco use intervention, in turn, the rest of the team will more readily claim ownership of an endeavor that can bring new life and challenge to a practice.

## Step-by-Step Strategies

### Strategy 1: Ask

The dental provider needs to be aware of the patient's tobacco use status and any other deleterious contributing factors. First strategy in any tobacco use intervention is identifying the tobacco using patient. The patient needs to be asked questions addressing the use status, extent and duration of use, type of tobacco used, and previous quit attempts in all queries, whether obtained verbally or through health history questionnaires. Other relevant information about a patient's social history should be obtained during the Ask phase relating to alcohol consumption and

exposure to sun. Why individuals initiate tobacco use? What drives their decision?

### Strategy 2: Advise:

The second strategy in the intervention process is to advise the patient to stop. The most critical step in promoting patient receptivity. The advice message must be clear, strong, and personalized. It is a challenge to advise skillfully. This message of abstinence must be stated firmly and unequivocally, yet caringly. Many practitioners fear offending their patients during the advice phase. The key to success is ensuring that warmth and caring are implicit in the message.

The oral effects of tobacco use must be shown to the patient. Related systemic issues also should be correlated with tobacco use. Radiographs that reveal extensive bone loss due to periodontal disease also personalize the message.

### Strategy 3: Identify the smokers who are ready to generate a relinquish effort

Patient's desire to abstain must be ascertained before appropriate assistance can be offered. For patients not willing to commit, the clinician should provide a brief motivational intervention. These patients need supportive messages and systematic follow up.

To help motivate patients, the dentist's message should include four key elements; relevance, risk, rewards and repetition. The practitioner's motivational message may activate a series of thought processes in the patient that will result in the decision to abstain.

### Strategy 4: Assist:

For patients ready to abstain, a formalized game plan needs to be developed. This includes setting a "quit" date, preferably within the following 2 weeks. The practitioner fosters success by giving key advice, reinforcing total abstinence, suggesting ways to deal with users living in the household, and providing supplemental patient specific literature.

Another component of the Assist strategy is the use of FDA-approved pharmacologic adjuncts, both nicotine and nonnicotine.

**Table 1: FDA Approved Pharmaceutical Agents**

<b>Replacement Agent</b>
<b>Nicotine transdermal patch:</b>
14.7-21- mg
14.721- mg
11-22 mg
15 mg
<b>Nicoderm CQ (OTC)</b>
<b>Habitrol</b>
<b>Prostep</b>
<b>Icotrol (OTC)</b>
<b>SmithKline</b>
<b>Beecham</b>
<b>Ciba</b>
<b>Lederle</b>
<b>McNeil</b>
<b>Nicotine polacrilex (gum) ;</b>
2-4 mg
<b>Nicorette (OTC)</b>
<b>SmithKline</b>
<b>Beecham</b>
<b>Nicotine nasal spray:</b>
0.5 mg per squirt
<b>Nicotrol NS</b>
<b>McNeil</b>
<b>Nicotine oral inhaler:</b>
2-2.5 mg in vapor
<b>Nicotrol inhaler</b>
<b>McNeil</b>

The use of any tobacco product is prohibited when patients are on nicotine replacement therapy. The most researched nicotine replacement therapies are nicotine transdermal patches and nicotine gum. Due to its ease of use and high level of patient compliance, the nicotine patch may be the most acceptable modality across diverse populations.

Other nicotine – containing adjuncts that recently have received FDA approval include the nicotine nasal spray and the nicotine inhaler. Patient success rests with careful decision making, instruction, and monitoring.

#### **Strategy 5: Arrange:**

Patients must be contacted either by phone or in person, preferably during the first week after their quit date. A second follow up should occur within the first month. During follow-up, a patient's successes are congratulated and reinforced, the use of FDA-approved pharmacologic adjuncts is monitored, and patient concerns and struggles are addressed. Four key issues that arise include weight gain, negative mood or depression, prolonged withdrawal symptoms, and the need for additional support.

Throughout follow-up the benefits of cessation must be reinforced and any success must be congratulated. Most relapse occurs within the first 3 months after quitting; therefore, close monitoring during this time is critical.

As with any protocol, individualization is essential. Special considerations should be followed for adolescents and geriatric and pregnant patients regarding prescribing. The dentist must be aware of any adverse effects, precautions, and contraindications for any pharmacologic adjuncts. Close monitoring of patients ensures sound risk management.

Oral cancer can be a devastating and disfiguring disease; the efforts of the dentist and the oral health team can help minimize its incidence and effects. A few minutes spent in questioning, advising, assisting and monitoring tobacco using patients can promote practice satisfaction and patient well-being.

#### **New Ways to Prevent Oral Cancer are Being Studied in Clinical Trials**

**Chemoprevention:** Chemoprevention refers to the administration of an agent to prevent a cancer from occurring. The agent can be a drug or a natural product. Candidate agents for chemoprevention should have certain characteristics. The agent must be easy to administer, cause little or no toxicity, cause no long term adverse sequelae, be affordable, and ideally, need to be administered only for a short time.

#### **Promising Agents for Chemoprevention of Oral Cancer**

**Retinoids:** Mechanism of action of these compounds for chemoprevention is not well understood. Studies have documented lower carotene (a precursor of vitamin A) serum concentrations in patients who develop cancer of the head and neck, than in patients who do not develop these cancerous tumours. Retinoids can act through induction of differentiation and can inhibit proliferation, as well as cause programmed cell death.

**Carotene:** Carotene is one of several carotenoids in the body and is a precursor of vitamin A. It is found in leafy green vegetables and yellow and orange fruits and vegetables, and it is also available in tablet form. To some extent it is converted to vitamin A in the body and is not associated with hypervitaminosis A syndrome. Several studies have noted lower blood levels of carotene in patients who develop aero digestive tract cancers compared to patients who do not develop cancer. These findings led to a hypothesis that a carotene deficiency may predispose cancer formation. The mechanism of action of carotene as a chemopreventive agent may involve antioxidant mechanisms as well as inhibition of free radical reactions.

**N-Acetylcysteine:** N-Acetylcysteine is an antioxidant and free-radical scavenger that has shown chemopreventive activity in lung and tracheal tumors in animals.

**Non-Steroidal Anti-inflammatory Agents:** In animal studies, nonsteroidal anti-inflammatory agents (NSAIDs) have chemopreventive activity in several tissues and have shown activity in tumour inhibition in preclinical head and neck cancer models. Because these compounds may be inhibitors of proliferation, they may be useful as chemopreventive agents.

**Vitamin E:** Epidemiologic studies have noted an inverse relationship between serum vitamin E levels and oral cancer. Its mechanism of action postulated to be as an antioxidant agent.

**Interferons:** Interferons have shown additive or synergistic antitumor effects in combination with retinoids.

**Curcumin:** Curcumin is the major component of turmeric, which is widely used in curry. Curcumin has inhibited carcinogen-induced tumorigenesis in an oral cancer model and is nontoxic. This agent is under consideration as cancer preventive.

### What's New in Oral Cavity and Oropharyngeal Cancer Research and Treatment?

Important research into oral and oropharyngeal cancers is taking place in many university hospitals, medical centers, and other institutions around the country. Each year, scientists find out more about what causes the disease, how to prevent it, and how to improve treatment.

**DNA changes:** A great deal of research is being done to learn what DNA changes cause the cells of the oral cavity and oropharynx to become cancerous.

One of the changes often found in DNA of oral cancer cells is a mutation of the TP53 gene. The protein produced by this gene (called p53) normally works to prevent cells from growing too much and helps to destroy cells. Changes in the TP53 gene can lead to increased growth of abnormal cells and formation of cancers. Some studies suggest that tests to detect these gene changes may allow oral and oropharyngeal tumors to be found early. These tests may also be used to better find cancer cells that may have been left behind after the tumor is removed and to determine which tumors are most likely to respond to surgery or radiation therapy.<sup>23</sup>

**Vaccines:** Most people think of vaccines as a way to prevent infectious diseases such as polio or measles. As mentioned earlier, vaccines against human papilloma virus (HPV) infection are already being used to help prevent cervical cancer. They may have the added benefit of preventing some oral cancers as well, although they won't help treat the disease.

However, some vaccines are being studied as a way to treat people with cancer by helping their

immune system recognize and attack the cancer cells. Many of these vaccines use dendritic cells (cells of the immune system), which are removed from the patient's blood and exposed in the lab to something that makes them attack tumor cells. The dendritic cells are then injected back into the body, where they should induce other immune system cells to attack the patient's cancer.<sup>23</sup>

**Gene therapy:** New discoveries about how changes in the DNA of cells in the mouth and throat cause these cells to become cancerous are being applied to experimental treatments intended to reverse these changes. Gene therapies that interfere with the growth-stimulating effect of certain HPVs are also being developed. Another type of gene therapy adds new genes to the cancer cells to make them more susceptible to being killed by certain drugs. These forms of treatment are still in the earliest stages of study, so it will probably be several years before we know if any of them are effective.<sup>23</sup>

### Conclusion

Despite advances in cancer treatment, the survival rates of patients suffering from head and neck cancer has not improved substantially. The data emphasizes the necessity of early detection of the disease as survival is influenced by the extent of the disease at the time of diagnosis. More emphasis should be placed on education programmes to the public so that they don't adopt the habit of smoking.

These findings suggest that the key to prevent oral cancer is to educate the mass in the primary level to quit the etiological factors. Mortality and morbidity of oral cancer can be significantly reduced if detected in early stages. Dentists and dental hygienists are critical players for tobacco cessation methods.

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