# Oral Cancer At A Glance

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**Citation**

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**Abstract**

The term oral cancer encompasses all malignancies that originate in the oral tissues. Squamous cell carcinoma of the oral mucosa and lips, however, comprises 90-95 percent of all oral malignancies. The term "oral cancer" is used in the restricted sense to describe squamous cell carcinoma and its variant, verrucous carcinoma. The incidence of oral cancer is high in several countries. Furthermore, the intraoral location differs in different population groups. These observations in turn provide pointers towards the aetiological agents involved. As the oral cavity is easily accessible for visual examination, oral cancer can be detected at an early stage. Nevertheless, in many tropical countries, in most instance patients with this disease seek medical attention only at an advanced stage thereby leading to poor prognosis and postoperative disfigurement. Many studies, especially in Southeast Asia, have established a causal relationship between tobacco and oral cancer. In this article, an attempt has been made to discuss the epidemiology, aetiology, pathology, precancerous lesions, principles of diagnosis, staging, metastasis and survival, individual cancers with treatment modalities, current concepts in management, rehabilitation and prevention of oral cancers.

## INTRODUCTION

Oral cavity is a part of the upper aerodigestive tract that begins at the lips and ends at the anterior surface of the faucial arch. Primary tumours of the oral cavity may arise from epithelium, minor salivary glands or submucous tissues. Tumours of dental origin, bone tumours and tumours of neurovascular origin are also common. The tongue, alveolus, gingivo-buccal sulcus, buccal mucosa are some of the common subsites of carcinoma. It is estimated that thousands of people die daily due to oro-pharyngeal malignancy[1]. Oral cancers are one of the commonest cancers constituting almost 50 percent of all cancers diagnosed in males. Its incidence is 3.8 to 11 per 100,000 population. The disease usually presents in advanced stages. It is surprising that a site, which is most accessible for daily self-examination, can become a leading cause of cancer death. Oral cancer is a preventable disease, which can be greatly controlled by tobacco cessation and health education.

## EPIDEMIOLOGY

The incidence rates of oral cancer differ from region to region. The annual age-adjusted incidence rates per 100 000 in several European countries vary from 2.0 (UK, south Thames Region) to 9.4 in France. In the Americas the incidence rates vary from 4.4 (Cali, Colombia) to 13.4 in Canada. In Asia, it ranges from 1.6 (Japan) to 13.5 (India). In Australia and New Zealand, it varies from 2.6 (New Zealand - Maori) to 7.5 in South Australia. In Papua New Guinea, in the Lowlands and the Highlands the incidence per 100 000 among men was 6.8 and 1.0 and among women 3 and 0.4, respectively. In Iran the incidence was reported to be 1.1 per 100 000 per year [2,3].

The prevalence rates of oral cancer available from Burma and India indicate that in Burma, among 600 villagers aged 15 years and above, the prevalence was 0.03 per cent[4]. In a study of 150 000 villagers aged 15 years and above in six districts of India, the prevalence rate of 0.1 per cent was the highest reported[5,6]. The relative frequency of oral cancer in several countries compiled from several reports published over a 25-year period varies from 2 to 48 per cent.

## SEX AND AGE DISTRIBUTION

Oral cancer predominantly affects men. This is borne out by the sex distribution of the patients in some of the large series and also from the higher incidence rates among men[3,7]. The sex differences in some population groups could be a direct consequence of the sex distribution of tobacco habits. For instance, in an epidemiological study in India, it was found that the male: female ratio of oral cancer patients was proportional to the prevalence of tobacco habits among men and women in the general population[6]. In a study of 498 oral cancers among South African Blacks, Fleming[7] et al observed a high male:female ratio (7:1) which they related to

the differences in tobacco usage between the sexes. Oral cancer, like most other cancers, affects the individuals in the higher age group, most of the patients being over the age of 40. The peak occurrence, however, varies in different population groups. In Western countries the peak occurrence is in the sixth and seventh decade, whereas in Asia it is generally earlier[8]. In Iran and India, the peak occurrence appears to be in the fifth and sixth decades[3]. There are some variations in the age distribution with regard to race and sex. In South Africa, the peak occurrence of oral cancer for two races combined was in the sixth and seventh decades. However, the disease occurred in the lower age groups among Blacks. In India, 1977 oral cancers were recorded in six registry areas and the peak occurrence for men was in the 50-59 year age group while for women it was In the 60-69 year age group[9].

## AETIOLOGY

The literature on the aetiology of oral cancer is voluminous, but few firm conclusions can be drawn, except for the role of some forms of tobacco usage. The evidence for this and other possible aetiological agents, namely, alcohol, syphilis, orodental factors, dietary deficiencies, chronic candidiasis, viruses and sunlight, is reviewed below.

## TOBACCO

Tobacco is chiefly used for smoking, commonly in the form of cigarettes, cigars and pipe. In some tropical areas locally made cigars are smoked, often keeping the burning end inside the mouth. In India, there are several other forms of smoking such as the hookah, chilum, and clay pipe. Tobacco is also chewed, often with other ingredients (‘smokeless tobacco').

## A) SMOKING

The evaluation of the relationship between smoking and oral cancer is available from several reports. The most comprehensive among them is the Report of the Surgeon General (US Public Health Service 1982). In this, the aetiological role of smoking was assessed using epidemiological parameters such as consistency of the association, strength of the association, specificity of the association, temporal relationship of the association and coherence of the association. The causality was implied when all epidemiological criteria were judged to be satisfied and pathological and experimental data were supportive. It was concluded that cigarette smoking was a major cause of cancers of the oral cavity in the United States; individuals who smoke pipes or cigars experience a risk for oral cancer similar to that of the cigarette smokers, mortality ratios for oral cancer increase with the number of cigarettes smoked daily and diminish with the cessation of smoking and cigarette smoking and alcohol use acts synergistically to increase the risk of oral cancers.

In SouthEast Asia, in addition to Western forms of smoking, bidi, hookah, and reverse smoking are also practiced. The relative risk estimates for some of these forms of smoking and oral cancer are available from Pakistan, India and Sri Lanka. In a study of 1192 oropharyngeal cancers in Pakistan, the relative risk for smoking was 5.7 for men and 12.9 for women[10]. Among different smoking habits, as compared to those with no smoking and chewing habits, cigarette or cigar smoking increased the risk by 6 times, hookah and pipe by 16 times and bidi smoking by 36 times. In India and Sri Lanka, in a study of 725 cases, the relative risk for smoking was 2.1 for men and 11.5 for women[11]. In this study the locations showing the highest risk for smoking were the oropharynx, the posterior tongue and to a lesser extent, the anterior tongue. Several investigators have mentioned the relationship between reverse smoking and palatal cancer. In this regard convincing evidence is available from a prospective study of a random sample of 10 000 villagers (India) in which, over a 10-year period, all 11 oral cancers had developed exclusively among reverse smokers (37 per 100 000 per year)[12]. In a comprehensive evaluation of the carcinogenic risk of tobacco smoking, tobacco smoking was identified as an important cause of oral cancer.

## B) CHEWING

The observation of a high frequency of oral use of snuff or tobacco chewing or both among oral cancer patients points out the possible relationship between oral cancer and smokeless tobacco use. Strong evidences for this association is available from several case control studies. Wynder[13] et al in a study of 659 cases of lip and oropharyngeal cancers found that 17 per cent of the cases chewed tobacco in contrast to 8 per cent of the controls, indicating a moderate association between tobacco chewing and the lip and oropharyngeal cancers. Further, there are several studies in which the relative risk estimates for smokeless tobacco are available or can be computed. In a case control study of 93 women with oral, pharyngeal and laryngeal cancers, the crude relative risk estimate for smokeless tobacco users was 36.5 and in another study of 33 oral cancers the relative risk was 7.1. In Puerto Rico, the relative risk for 115 oral cancers among men who chewed tobacco compared to non-tobacco users was found to be 11.9[14]. In regard to oral use of snuff, in

a study of 255 oropharyngeal cancers, the relative risk for cancer in the gingiva and the buccal mucosa was 13.8 when the duration of oral use of snuff was 1 to 24 years and it increased to 48.0 when the duration was 50 years or over[15]. The occurrence of oral cancer at the site of placement of the quid was observed by several investigators[16]. Such an observation also points to a close link between smokeless tobacco use and oral cancer.

### C) ALCOHOL

Several investigators have suggested alcohol as a risk factor in oral cancer. The problem, however, is that most heavy alcohol drinkers are heavy smokers and therefore, it is difficult to assess the independent role of alcohol. Pure ethanol does not seem to be carcinogenic. Nevertheless, the possible significance of contaminants in illicitly or home distilled liquor has been mentioned[17]. Oral cancer patients are often reported to be heavy alcohol users. For instance, in Australia there was a higher percentage (80 g/day in 63 per cent) of heavy alcohol users among 146 oral cancer patients as compared to the general population. Most of the oral cancer patients with excessive alcohol intake in this study were also tobacco smokers[18]. Wynder[13] et al found that individuals who consume more than 170 g of whisky daily, showed a risk of oral cancer 10 times more than light drinkers. In a Japanese study of oropharyngeal and laryngeal cancers in which the mortality ratios were compared, there were excesses of cancers at each site among daily cigarette smokers and the excesses of oral, pharyngeal and oesophageal cancers were higher among those who consumed alcohol compared to those who did not. The mortality ratio for buccal cancers was 2.46 for smokers and 5.26 for those who smoked and consumed alcohol compared to those who did not smoke or drink.

McCoy[19] suggested that alcohol facilitate the entry of carcinogens into the exposed cells, altering the metabolism of oral and oesophageal epithelium. In several countries, alcohol drinking is either a religious taboo, socially unacceptable or prohibited by the government. Accordingly, it is difficult to obtain reliable data on alcohol drinking. In conclusion, although pure ethanol is not carcinogenic, alcohol appears to increase the risk for oral cancer, especially in association with tobacco smoking.

## OTHER CONTRIBUTING FACTORS

### A) SYPHILIS

The aetiological role of syphilis was given recognition in the literature essentially on the basis of positive serological reaction in oral cancer patients and also on the observation of cancer development from the syphilitically altered tongue. Trieger[20] et al found 19 per cent and Deckers[21] et al six per cent of serologically positive tongue cancer patients in their series.

### B) ORODENTAL FACTORS

Poor oral hygiene, faulty restorations, sharp teeth and ill-fitting dentures have often been incriminated as possible etiological factors for oral cancer. Shanta[22] et al felt that the carcinogenic action of tobacco seems to be promoted by dental sepsis. Wahi[23] et al suggested that poor oral hygiene is a contributory factor in the causation of oral cancer. Graham[24] et al reported an increased risk for oral cancer with a decrease in the adequacy of dentition as measured by an index consisting of number of missing, infected and decayed teeth; condition of the dentures; oral hygiene and a synergistic action with heavy smoking and drinking. Although there may be isolated observations relating to orodental factors, especially irritation from sharp teeth to oral cancer, the aetiological role of these has not been substantiated.

### C) DIET AND DEFICIENCY STATES

Dietary deficiencies are sometimes considered to play a contributory role in the development of oral cancer. The relationship between sideropenic dysphagia and oral cancer is well recognised. Several investigators, however, failed to find any etiological role of diet and other deficiency states[24]. The roles of vegetarian versus non-vegetarian diet and vitamin A deficiency were investigated and these were not found to play any role in oral cancer[23]. It needs to be pointed out, however, that certain dietary deficiencies may cause epithelial atrophy, which renders the epithelium vulnerable to the action of carcinogens.

### D) CANDIDA

These opportunistic organisms in the oral cavity have been implicated in the pathogenesis of oral cancer. This arises from observations that high proportions of nodular leucoplakias are infected by these organisms and nodular leucoplakias show higher rates of epithelial dysplasia and malignant transformation. Further, there is some experimental evidence demonstrating squamous metaplasia and a proliferative tendency of the epithelium of the chick embryo when infected with Candida albicans[25]. There is however, no direct evidence so far, linking Candida and oral cancer.

## E) VIRUSES

The role of oncogenic viruses in certain human cancers is well known. Viruses are believed to induce cancers by altering the DNA and the chromosomal structures of the cells and by inducing proliferative changes of the cells. Herpes simplex virus type 1 (HSV-1) and more recently human immunodeficiency virus (HIV) have been suggested to play a role in the pathogenesis of oral squamous cell carcinoma. Shillitoe[26] et al investigated the role of HSV-1 using several immunological parameters and suggested that the tumour results from the interactions between the virus and tobacco smoke. On the strength of animal experiments, Hirsch[27] et al stated that HSV-1 with snuff exposure may be associated with oral squamous cell carcinoma. The recent observation of oral squamous cell carcinomas among patients with AIDS and AIDS-related complex (ARC) suggests a link between HIV and oral squamous cell carcinoma[28]. Nevertheless, a direct relationship between the viruses and oral cancer is yet to be demonstrated.

More than 70 types of human papilloma viruses (HPV) are suspected to have an important role in the aetiology of oral cancers. The high-risk subtypes HPV-16 and HPV-18, are associated with cervical and upper aero-digestive tract carcinoma (up to 90% and 54% of cases, respectively). HPV E6 protein is known to bind to and inactivate the p53 tumour suppressor gene, possibly allowing chromosomal instability and subsequent neoplastic growth. HPV-16 has also been shown to produce obviously dysplastic epithelial cells in differentiating tissue cultures, which are otherwise sterile. HPV-31, HPV-33 and HPV-35 have also been associated with oral precancers and cancers. High risk HPVs are found in upto 10% of normal oral mucosa, 15-42% of leukoplakias, in 50% of erythroplakias and in 50-100% of oral squamous cell carcinomas. The prognostic significance of HPV presence in oral precancers is yet to be determined by large follow up investigations. Survival from oral carcinoma does not appear to be associated with the presence or lack of HPV.

Herpes simplex virus (HSV) has been suggested to play a causative role in oral carcinoma. Epidemiological evidence now suggests that it may be no more than a common companion infection in persons with HPV infections and that the latter virus plays a much more important carcinogenic role. Currently, the evidence to prove a causal relationship between HSV and oral precancers or cancers is insufficient.

## F) SUNLIGHT

Sunlight (ultraviolet radiation) is believed to be responsible for cancer of the vermilion border of the lip on the basis of observation of lip cancer more often in fair skinned people who are generally engaged in outdoor occupations. Some investigators, however, question the independent causal hypothesis of sunlight for cancer of the vermilion border[29]. Lip cancer is uncommon among people with dark or yellow skin. It is believed that melanin pigment acts as a protective agent against actinic radiation. In Finland, however, an inverse relationship between the mean amount of annual solar radiation and the risk of lip cancer was found[29]. It was suggested that the synergistic action of some factors such as smoking and genetic factors might be decisive in the pathogenesis of lip cancer.

## G) GENETICS

The suppressor gene most frequently altered in carcinomas of the upper aerodigestive tract is the p53 gene, located on chromosome 17p. p53 mutation or over-expression has been demonstrated in 43%-93% of cases of oral carcinoma cells than in any other human cancer. Its occurrence in oral dysplasias and microscopically normal mucosa adjacent to head and neck carcinomas suggest that its alteration is an event, which occurs early in carcinogenesis. Some investigators have evaluated the next step in the process, i.e., the interaction of p53 proteins with various other cellular proteins and viral oncoproteins, for example, finding that 36% of oral carcinomas and 19% of oral dysplasias demonstrate complexes formed by the binding of p53 with heat shock proteins[30]. There is a correlation of p53-positive immunostaining with increasing severity of dysplasia (10% of control cases were positive, as were 50% of hyperkeratoses without dysplasia, 67% of low-grade dysplasias, 85% of high-grade lesions and 89% of invasive carcinomas).

In cancers of the head and neck region, over-expression of the p21 ras oncoprotein has been observed more frequently than any other, but this has not been evaluated in precancers of that region, nor is there any apparent prognostic significance to its presence.

## H) GROWTH FACTORS

Fibroblast growth factors (FGF) are widely distributed in normal and neoplastic tissues. Almost all oral carcinomas are immunoreactive to FGF and oral carcinoma cells in culture are capable of expressing FGF. Biopsy samples of oral dysplastic lesions have also demonstrated positive focal

staining which becomes stronger with increasing immaturity or severity of the dysplastic cells. Epidermal growth factors receptor (EGFR) is the protein of the proto-oncogene c-erb. Its expression has been correlated somewhat with an increased rate of recurrence in some cancers of the head and neck region, but study results vary and the final significance of EGFR has yet to be determined[31].

## PATHOLOGY

It has been demonstrated that oral carcinogenesis in a normal epithelium passes through stages of more and more severe dysplasia prior to the onset of invasive cancer. Cells and nuclei take on a more primitive appearance, similar to those of basal cells with enlarged nuclei (called nuclear hyperplasia), enlarged, often eosinophilic nucleoli (prominent nucleoli) and with an increased nuclear-cytoplasmic ratio dark-staining nuclei (hyperchromatism). These cells also appear to be crowded more closely together than normal keratinocytes. There is increased mitotic activity in dysplastic epithelium. Enlarged, tripolar or star-shaped mitotic figures are much more indicative of precancerous changes. Premature production of keratin below the surface layer is another important alteration, but is much more commonly seen in oral carcinomas than in oral premalignancies. This dyskeratosis may be represented by individually keratinised cells or by tight concentric rings of flattened keratinocytes (epithelial pearls). Cellular necrosis and loss of cellular cohesiveness (acantholysis) are major signs of poorly differentiated carcinoma but are extremely rare in the epithelial dysplasia of oral precancer[32].

The most common cancer within the oral cavity is squamous cell carcinoma. Other pathological types e.g., adenocarcinoma, adenoid cystic carcinoma and mucoepidermoid carcinoma arise from the minor salivary gland. Melanoma, plasmacytoma, soft tissue sarcoma, bone tumor etc. are uncommon neoplasms of the oral cavity.

## PRECANCEROUS LESIONS OF ORAL CAVITY

Most of the oral cancers are preceded by premalignant lesions e.g., leukoplakia, erythroplakia, submucosal fibrosis (SMF) which can be detected early and treated[33,34]. SMF is a collagen disorder that is characterised by extreme sensitivity to temperature/spices, whitening of mucosa, progressive trismus and bleeding. Usual presentation is marble like blanching of mucosa, submucosal, palpable fibrotic bands, white and raised patches with areas of ulceration or erythema. It is usually associated with habit of areca chewing in tropical countries like India, but in the west 90% have association with HPV and 50% with Candida albicans[33]. It is commonly seen in Indian subcontinent and 50-70% develops cancer in a decade. Erythroplakia is a chronic red mucosal macule 80% of which may harbour microinvasive carcinoma. Without therapy 60-90% of erythroplakia may turn into cancer in 5-10 years[33].

Leukoplakia is a whitish patch or plaque that cannot be charecterised clinically or pathologically as any other disease and which is not associated with any physical or chemical causative agent except the use of tobacco. Pindborg[34] studied the natural history of leukoplakia. He reported that 20% disappear, 18% decrease in size without treatment, 46% increase in size and 4% show malignant transformation. 12% underwent excision of which, two recurred[35]. Leukoplakia of lateral border of tongue is the worst lesion (44% malignant conversion). Excision biopsy is advised if leukoplakia is suspicious. If the histopathology report (HPR) indicates mild to moderate dysplasia, then, one needs to observe and regularly follow up the patient, but if severe dysplasia is present then wide excision is indicated with a close follow up. Severe dysplasia should be clubbed with carcinoma-in-situ (CIS) because 30-50% of severe dysplasia develops into cancer[36].

## PRINCIPLES OF DIAGNOSIS

### A) CLINICAL EXAMINATION

The emphasis is to examine the accessible oral tissues, posterior 1/3 of tongue and indirect examination of the nasopharynx and larynx. Persistent white and red patches, ulcers, lumps, loose teeth, and bony abnormalities all require investigation. Palpation of the neck should be performed. Cervical lymphadenopathy may indicate malignant disease and should always be further investigated.

### B) BIOPSY

No treatment of a lesion should proceed before histological confirmation of malignancy. Even in cases of clinically obvious malignant lesions, the tissue of origin may not be as expected. The degree of differentiation also needs to be established. Both of these factors will influence the prognosis and treatment strategy. The biopsy specimen should include the pathological lesion with a margin of normal tissue. Areas of necrosis must be avoided, as they may not be diagnostic. It must also be of sufficient depth to reveal any invasion of deeper tissues. In areas of mixed appearance the sampling of tissue from more than one site is necessary to minimize the chance of a false negative report. An excision biopsy should not be attempted. Oral

carcinomas are often found to be deeply infiltrating and an attempt at excision biopsy will often fail and more often, provide inadequate margins of clear tissue. Subsequent surgical treatment can be difficult, as the area has been mutilated. Manipulation and instrumentation of the area also need to be avoided and this principle continues to apply until the tumour is removed. Most oral lesions are sufficiently accessible to allow biopsy while the patient is conscious. Topical anaesthesia may be adequate in some cases or nerve blocks can be employed. Infiltration adjacent to the lesion should be avoided. For masses in deeper tissues or less accessible areas, general anaesthesia provides an opportunity to perform the biopsy and for a good clinical assessment of the lesion. The tissues are gently palpated to gauge the extent of infiltration present and the involvement of adjacent structures.

## C) FINE NEEDLE ASPIRATION CYTOLOGY (FNAC)

FNAC has found an increasing role in the diagnosis of head and neck malignancy. The technique is reliable, inexpensive and well tolerated by patients. It finds particular application for the diagnosis of deeply situated masses, in the confirmation of tumour in suspiciously enlarged neck nodes and in the assessment of areas of possible recurrent disease. The diagnosis of salivary gland malignancies using needle aspiration was shown by Frable[37] et al to be 92 per cent accurate for the presence of tumour and 99 per cent correct for the absence of malignant cells. The possibility of tumour cell seeding via the needle tract has received wide investigation. Also they found no confirmed cases of tumour dissemination following this technique and experimental evidence is in agreement that such an occurrence is unlikely.

## STAGING (TNM SYSTEM)

The clinical staging of oral cancer is of paramount importance as it helps the clinician to plan treatment, to evaluate various treatment modalities and to make international comparisons on various aspects of this disease. The system of staging suggested here has three parameters (UICC 1974): T, the extent of the primary tumour; N, the condition of regional lymph nodes; and M, the absence or presence of distant metastasis. Two more parameters - S, site and P, pathology of tumour have been added subsequently.

Hibbert[38] et al classified 103 patients with oral squamous cell carcinoma according to the TNM system and found that the most significant factor, which affects survival is the presence of palpable lymph nodes. They suggested that more weight should be given to the N status than is given in the present staging system. Evans[39] et al applied regression analysis to assess the STNMP system for the grading and staging of 170 oral cancers and concluded that the, TNMP system represents a considerable improvement in prognostic differentiation over the TNM system. These investigators assessed another variable, velocity of tumour growth and found it useful in predicting the survival of the patients.

## METASTASIS AND SURVIVAL

Most oral squamous cell carcinomas are well differentiated. Unfortunately, however, with the exception of lip cancer the prognosis of cancer in intraoral locations is rather poor. In most instances the poor prognosis is attributable to the late diagnosis and late initiation of treatment. The survival rates for oral cancer depend essentially on the clinical stage of the disease and the specific intraoral site involved. Lymph node involvement is generally high at first diagnosis among oral cancer patients. In one study of 1069 patients with oropharyngeal cancers, 63 per cent had clinical evidence of lymph node metastasis[40]. In this study, when the clinical diagnosis of lymph node involvement was compared with the histological examination, absence of enlarged nodes gave an erroneous impression of unaffected nodes in 15 percent of the cases. In 10 per cent, palpable nodes considered to be clinically significant did not contain metastatic deposits. Bilateral involvement is uncommon unless the tumour is large or crosses the midline. Bilateral regional lymph node involvement was observed in 13 per cent of the patients in this same study. Lymph node involvement in oral cancer below the level of the clavicle is uncommon. Evans[39] et al in a study of 170 patients found that the 5-year survival rates for stage I tumours was 78 per cent, for stage II, 67 per cent, for stage III 36 per cent and 20 per cent for stage IV. The 5-year survival rates also vary between the sexes and among different intraoral locations. In one report the survival rates among men and women were more or less equal for lip cancer but better for women for other intraoral locations, especially for localised lesions.

## INDIVIDUAL CANCERS WITH TREATMENT MODALITIES

Surgery, radiotherapy (RT) and chemotherapy are the three modalities of treatment in oral cancers either for cure or palliation. They can be used singly or in combination. A multimodality approach is required in advanced cases.

## A) LIP CANCER

Ninety five percent of the patients are males and it mostly

involves the lower lip[1]. Tobacco and ultraviolet exposure[29,42] are some of the possible causative agents. Lymphatic spread occurs relatively infrequently (5 to 10%) that too in submandibular or submental nodes. Dysplasia and carcinoma in situ (CIS) can be treated by 'Lip Shave'. Those lesions that involve less than 30% can be resected with a 'V' excision and primary closure of resulting defect. Larger lesions need transposition flap e.g., Abbe Eastlander flap, Kerapandzic flap, Abbes flap, Nasolabial flap, Gillies flap[43]. T1 lesions have 95% 5-year survival, T2 lesions have 84% and once the lymph nodes are involved then 5-year survival drops to 50%[44]. Brachytherapy alone can be used to treat T1-T2 lesions, with temporary implantation with iridium-192. For T3 lesions implantation along with external RT alone is curative. Stage III and Stage IV patients are treated by combined modality (surgery as well as RT).

## B) ALVEOLAR AND RETROMOLAR TRIGONE CANCER

These comprise of 10% of all oral cancers[1]. Usually these tumors tend to involve the bone in around 50% patients[45]. Delay in diagnosis is because of confusion with common dental conditions like gingivitis and periodontitis. These lesions have higher propensity to metastasise to lymph nodes mostly level I and II. The 5-year survival for T1 lesion is 85%, T2 lesion is 80%, T3 lesion is 60% and 20% for T4 lesion[45]. For early lesions confined to the mucoperiosteum, resection may require a marginal mandibulectomy preserving the structural integrity of the mandible. This may not be possible in elderly and edentulous people. All large or infiltrative lesions need neck dissection (at least supra-omohyoid neck dissection) even when N0 because of high incidence of micro metastasis. Larger lesions involving skin, floor of mouth (FOM) and large areas of buccal mucosa need extensive resection with reconstruction e.g., pectoralis major myocutaneous flap (PMMC), deltopectoral flap (DP), tongue flap, forehead flap or a free flap. All such lesions will need adjuvant RT.

## C) FLOOR OF MOUTH CANCER

These constitute 10% to 15% of the oral cavity tumours[1]. They present as painful infiltrative ulcers that may involve the muscles of the FOM, middle of the mandible or tongue. Sometimes it may grow to massive size without metastasising into lymph nodes. Submandibular and submental lymph nodes are the first to be affected. The overall 5-year survival rate is 85-90% for stage I, 80% for stage II, 60% for stage III and 32% for stage IV patients. Perineural invasion, depth of primary tumour invasion and poor tumour differentiation are some of the bad prognostic factors[46]. Early disease can be treated by surgery or RT alone. Radiotherapy usually involves external RT in conjunction with implant. Tumours abutting the mandible are not good cases for RT because it may cause osteoradionecrosis. Advanced lesions need surgical resection with reconstruction and adjuvant RT.

## D) BUCCAL MUCOSA CANCER

Buccal mucosa is one of the common sites of involvement either primarily or secondarily to involvement of alveolus/gingivo-buccal sulcus, owing to the tobacco eating habits. Pain, ulcer, bleeding and trismus might be the presenting symptoms. Small lesions can be widely excised intraorally but larger lesions may require supra-omohyoid dissection (SOHD) and composite resections. Surgery and RT have equivalent results in T1-T3 lesions but T4 lesions need combined modality treatment. Lymph node metastasis occurs in 10% of the T1/T2 lesions. Tumour depth is an important prognostic marker. Five-year survival ranges from 77% for T1 lesions, 65% for T2 lesions, 27% for T3 lesions and 18% for stage IV lesions[47].

## E) TONGUE CANCER

It is the commonest tumour of oral cavity after lip[1]. Incidence of this cancer is increasing in young people[48]. Lymphatic drainage is to level II, III, I in decreasing order. Primary presenting symptom is pain, difficulty in deglutition and phonation. This tumour has the highest propensity for lymph node metastasis (15% to 75% depending on the extent of primary) and incidence of bilateral metastasis is about 25%. Prognosis depends upon extent of nodal disease ranging from 75% in early stage node negative disease to 30% with multiple lymph node involvement. Perineural invasion, tumour depth, vascular invasion are some other important prognostic factors. For early disease, surgery or RT has equivalent curative rates. Excision usually entails a hemiglossectomy with special attention to surgical margins because this tumour can spread along the muscle bundles beyond the clinical margin. Most T1 lesions can be managed by iridium implant alone inserted via loading catheters under general anaesthesia. Some radiotherapists prefer to use external RT also along with interstitial RT to cover the primary as well as the neck nodes[49]. For patients who are clinically N0, their neck node treatment depends on their histopathological parameters. In a patient with very infiltrative disease, adjuvant RT to the neck and elective neck dissection are the two options. When the disease is superficial the neck can be observed. There is no role of

SOHD in tongue cancer because this can have skip metastasis to level IV directly. Very advanced lesion may require composite resection with reconstruction along with postoperative RT. Local control can be achieved in 85% T1, 70% in T2 and in only 50% of the T3[50]. Failure is most commonly in regional lymphatics and leads to 5-year survival of 35% in stage III and IV[18].

## F) HARD PLATE CANCER

Constitutes 5% of oral cancers and is seen predominantly in males[1]. In contrast to other sites, squamous carcinoma comprises only 50% of the neoplasms. Adenocarcinoma, adenoid cystic carcinoma may have equal incidence in this subsite. Lymph node metastasis is uncommon (6-29%) and is a sign of aggressive disease. The 5-year survival is 75% for stage I, 46% for stage II, 36% for stage III and 11% for stage IV[51]. Surgical treatment of early disease may involve infrastructure maxillectomy or near total palatectomy (if the disease is large) with immediate prosthetic obturator. Adjuvant radiotherapy is planned on the clinico-pathologically aggressive disease.

## CURRENT CONCEPTS IN THE MANAGEMENT OF ORAL CANCERS

Recently a technique (oral CDx study group) has been tried wherein 'Brush biopsy' specimens were obtained from lesions from all regions of the oral cavity. The brush biopsy resulted in minimal or no bleeding and required no topical or local anaesthetic. A computer, programmed to read the slide identified the most suspicious cells to be evaluated by a pathologist. The results of multi-center trials have demonstrated the potential value of computer-assisted image analysis an adjunct to the oral cavity examination in identifying pre-cancerous and cancerous lesions at early stages, when curative therapies are most effective[52].

Oral test is a patented 5-minute mouth rinse sequence with toluidine blue, used by dentists and physicians to detect early stage, asymptomatic lesions and to define margins of lesions for biopsy and surgery. It has been shown to be 100% sensitive for squamous cell carcinoma, the commonest form of oral cancer[53].

Several chemotherapy agents e.g., bleomycin, hydroxyurea, methotrexate, cisplatin, 5-fluorouracil have a high activity in squamous cell carcinoma of the head and neck. Combination of chemotherapy with RT for advanced tumors has been practiced for many years. Recently, a better understanding is being gained of the optimal schedule for combined modality treatments and their benefits compared with radiation alone[54,55]. Chemotherapy can be delivered before radiation, achieving a high response rate (40 to 90%). A meta-analysis of 11 studies of concurrent radiation and chemotherapy showed that combined treatment has reduced mortality rate by 22%[54]. Reasons for the advantage of simultaneous chemotherapy over up-front chemotherapy or RT alone stems from sensitisation of tumour cells to RT by the simultaneous delivery of drugs[55].

Recently, it was found that the delivery of two daily treatments, each delivering a relatively small dose (1.15 to 1.25 Gy) allows for some repair of radiation induced damage by the normal tissue[54]. These treatment schemes (called hyperfractionation) allow increasing the total radiation dose to about 80 Gy without increased rate of complications. Four randomised studies comparing hyperfractionated to standard radiation for advanced head and neck tumours have been conducted and published to date. All the studies reported significantly improved local and regional tumour control, and three of the four reported improved survival using hyperfractionation compared with standard radiation[55].

More recent studies have shown that it is possible to avoid mutilating surgery using a similar concept in other tumour sites in the head and neck. Efforts at organ preservation concentrate on delivering a short course of chemotherapy (neo-adjuvant chemotherapy) and selecting the patients whose tumours respond to chemotherapy. These selected patients are treated with concurrent RT and chemotherapy, while patients whose tumours do not respond to chemotherapy undergo surgery and postoperative radiation[54].

## REHABILITATION

Head and neck cancer is the commonest cancer in developing and tropical countries with thousands dying of this disease everyday and those who could be treated live in misery with a number of functional problems in respiration, speech and swallowing[56]. More than 50% of cases in cancer hospitals are head and neck cancers and of these, 2/3$^{rd}$ are advanced cases. Though many centers have the infrastructure to effectively treat head and neck cancers, the quality of life (QOL) of patients is poor. Head and neck cancer team comprises of surgeon, radiation oncologist, medical oncologist, social worker, professional counselor, speech and language pathologist, maxillofacial prosthodontist, nurses and pharmacist[56]. The dismal scenario can be improved by providing basic training and knowledge of speech and swallowing to the treating surgeon,

radiotherapist and medical oncologist.

Most of the tumours in developing countries present in advanced stages necessitating an extensive surgery and adjuvant RT. Both these therapies lead to massive deterioration in speech and swallowing[57]. Lack of knowledge of various interventions e.g., jaw/tongue exercises, thermal stimulation, augmentation prosthesis, speech exercises[58] compels a treating consultant to accept these disorders as non remediable sequels to treatment. Not only surgery but radiation too affects the physiology of swallowing. Loss of sensation, xerostomia, post RT fibrosis, mucositis, oedema are some of the causative factors. All these can be effectively handled by proper pretreatment counseling and post treatment rehabilitation. There is a need to identify speech and swallowing rehabilitation as an essential part of head and neck cancer treatment[56]. An effective treatment does not mean disappearance of tumour following surgery/RT/chemotherapy, but restoration of altered functions as well.

## PREVENTION

The oral cavity is easily accessible for visual examination and therefore, without the aid of any sophisticated methods, oral cancer can be detected in its early stages. The detection of this disease in its early stages constitutes an important facet of prevention. Oral cancer prevention can be attempted at a primary as well as a secondary level, in clinics, at hospitals and in large population groups. In primary prevention avoiding the exposure to tobacco reduces the risk for cancer development. This can be implemented in the form of a community approach where the risk to the entire community is eliminated without the individual's direct participation. Some of these measures could include curbing tobacco usage by higher taxation, changes in the manufacturing process of tobacco products and genetic changes in the tobacco plant. The problem can also be addressed through an individual approach designed to motivate the people with tobacco habits to quit their habits, or discourage people, especially vulnerable adolescents, from acquiring such habits. The implementation of primary prevention requires media inputs like films, television, radio, newspapers, posters and also intensive personal communication by doctors and social workers. There is some evidence from India that such an approach can be effective[5,6]. While the advantage of primary prevention lies in tackling the problem at a grass-roots level, it has its limitations. One of them is that it requires long sustained efforts under close monitoring. Second, the achievement of a drop in the incidence rates of oral cancer requires a long time. These limitations point to the importance of secondary prevention. This form of prevention consists of early diagnosis of oral cancer and management of suspected precancerous lesions. The treatment of early cancers will lead to better prognosis and the management of the precancerous lesions and conditions will prevent their progression to cancer. Erythroplakia, non-homogeneous leucoplakia, SMF and palatal changes among reverse smokers could be considered as high risk and oral lichen planus and preleucoplakia as low risk precancerous lesions and conditions. As the aim of the secondary prevention is to improve the prognosis, this approach entails periodic re-examination of high risk group populations. From epidemiological characteristics and known aetiological associations of oral cancer, high risk individuals are those aged 35 years and above whom use tobacco regularly in any form. In areas where the incidence of oral cancer is high the secondary prevention may appear as an immediate necessity. The practical difficulty in implementing this form of prevention, however, is the lack of sufficient trained professionals and limited resources in developing countries.

Proper education, community based early detection programmes coupled with proper treatment can be expected to be more efficient than the current treatment programmes alone.

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