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Unintended Consequences Trailing Cancer of the Oral Cavity: An Overview and Systematic Review

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Abstract

Oral cancer rank in the ten most common cancers worldwide, and it is especially seen in disadvantaged elderly males. Men's risk of been diagnosed with oral cancer is twice that of women. Factors that interact to increase a person's likelihood of developing oral cancer are age, genetics, nutritional status, and hormonal imbalance. This article emphasizes on the unintended consequences, and diagnostic processes of oral cancer and an overview. Detailed evidence-based literature was used in the discuss. A relevant search showed that signs and symptoms of oral cancer often resemble red or white patch or ulcer on the gums, tongue, tonsil, or lining of the mouth. The principal factors may include heavy smoking (or chewing tobacco products), heavy alcohol consumption, poor dentition, oral sex and biological factors amongst others. As patient consciousness regarding the danger of oral cancer rises, the demand for "screening" and histopathology examination is expected to increase. However, prompt referral to an appropriate specialist allows for the best management. Therefore, to develop more effective approaches to preventing oral cancer, public health professionals need a better understanding of the group at high risk of oral squamous carcinoma. Consequently, early detection and prompt treatment offer the best chance for survival.

Key word: Oral squamous carcinoma, oral cancer, oral cavity, brush cytology and biopsies

Introduction

Oral cancer is a subtype of head and neck cancer, the cancerous tissue growth located in the oral cavity (Andrews *et al.*, 2009). It may rise in any of the tissue of the mouth; it may also look like principal lesion or metastasis at a distant site of origin such as the nasal cavity. Worldwide, oral cancer is a prevalent malignancy, majorly linked with an

assortment of tobacco-related conducts and forms, including poor diets with low intake of vegetables and fruits. It is the cause of significant morbidity, suffering, and death (Andrews *et al.*, 2009). In U.S.A alone it is responsible for over 8,000 deaths each year, killing roughly one person in one hour, 24 hours per day. Of those 36,000 newly diagnosed individuals, only slightly more than half will be alive in 5 years (Ayllon *et al.*, 2008). It is one of the cancers that has not significantly improved in decades. Mortality from oral cancer is more than that associated with cervical cancer, testes, Hodgkin's lymphoma, larynx, and the endocrine systems such as thyroid, or skin cancer (Ayllon *et al.*, 2008).

Oral cancers can originate from tissues of the mouth, and may be of different histologic types such as melanoma, lymphoma, adenocarcinoma or teratoma. Though, about 90% are squamous cell carcinomas that originates from tissues, which line the lip and mouths. They are malignant tumors and are inclined to spread rapidly (Lumerman *et al.*, 1995). Also, one-third of oral cancer is diagnosed in the mouth cavity and a similar proportion on the tongue. Scully and Bagan (2009) reports that lip cancer is the least frequent type of oral cancer. Oral cavity cancer includes tumors of the following: Buccal mucosa, retromolar triangle, alveolus, hard palate, anterior two-thirds of the tongue, and mucosal surface of the lip, the floor of the mouth, tongue cancer and Carcinomas of the tongue base (Ayllon *et al.*, 2008). Oral mucosal melanomas may occur, particularly affecting the palate, alveolar gingivae, and lips. Virtually any malignancy can cause metastasis to the oral cavity, but carcinomas of the breast, lung, kidney and adrenal gland are common. Treatment and primary detection are often serious, by way of increased chances of survival considerably, and

allow for simpler treatment and result in an improved quality of life for survivors (Scully and Bagan, 2009).

Tongue cancer and Carcinomas of the tongue base are most frequent in recent years. The tongue malignancy can grow to a significant size before symptoms surface (Andrews *et al.*, 2009). Roughly 75% occur in the mobile tongue: They are often well-differentiated. Cancer may spread easily and become symptomatic only when its size interferes with movement: Squamous cell carcinoma (SCC) of the tongue may arise in the apparently normal epithelium, in areas of leukoplakia, or in an area of chronic glossitis (Andrews *et al.*, 2009). These lesions are usually bigger than 2 cm at presentation, with the lateral border being the most common site. The macroscopic appearance depends on the duration of the lesion, the amount of keratinization, and the changes in the attached mucosa. Fully developed lesions have looks of an exophytic bulky lesion, which is gray in color to greyish-red and rough, shaggy, or papillomatous surfaces. The patient may develop speech and swallow dysfunction (Brocklehurst *et al.*, 2010). Pains may occur when the tumor involves the lingual nerve, and may also extend to the ears. Meanwhile, carcinomas of the tongue base are clinically silent until they deeply infiltrate the tongue musculature. They are usually less differentiated Brocklehurst *et al.*, (2010) especially in difficulties with direct visualization, which can spread to the tongue or have clinical lymph metastases before diagnosis.

Epidemiology

Scully and Bagan (2009), revealed that the UK incidence figures (per 100,000 populations) were as follows: All oral cavity cancers: 15.5 (males 10.9; females 4.6), Mouth: 4.6 (males 3.0; females 1.6), Tongue: 4.7 (males 3.2; females 1.5), while Lips: 0.7 (males 0.5; females 0.2). People over 40 years of age are more likely to be affected by mouth cancer, though an increased amount of young people also develop the condition, particularly women (Brocklehurst *et al.*, 2010). National Cancer Institute (2011), reported that 50 years ago, mouth cancer was five times more common in men than women. However, now it is only twice as common, as more women are diagnosed. In Europe the incidence of oral cavity cancer is very low, accounting for less than 5% of all cancers. While, in France, the male incidence is around 8 per 100,000 per annum, which is the third most frequently diagnosed cancer in

males and the second regular cause of death from cancers (Shiboski *et al.*, 2005).

Incidence

Men's risk of being diagnosed with oral cancer is twice that of women, and African American men suffer disproportionately from this disease (Brocklehurst *et al.*, 2010). Whereas, oral cancer is the sixth leading cancer in U.S. men and the fourteenth most common cancer in U.S. women. It is the fourth leading cancer in African-American men, who are also more likely to be diagnosed at the early age and at a more advanced stage and are more likely to die from the disease (Shiboski *et al.*, 2005). Also, 95% of oral cancer cases are diagnosed in people older than 45 years and the median age of diagnosis is 64 years. Compared with other types of cancer, oral cancer has one of the lowest survival rates (5 years), which is around 52% of people detected with oral cancer survived after five years (Missmann, 2006). An early detection of oral cancer increases the chance that a person will be alive after 5 years following the initial diagnosis. However, the 5-year survival rate though put at 81% for those diagnosed with early-stage oral cancer, only 22% of persons diagnosed with advanced stage cancer survives (Shiboski *et al.*, 2005). Contrary to the previous report by Andrews *et al.* (2009) in a finding that just 35% of oral cancer is detectable in the earliest phase. Moreover, further indication suggests that African-American men are at a disadvantage because only 19% diagnosis are made in the first stage of cancer compared with 38% in white men. Missmann (2006), also reports that African-American men have a 5-year survival rate of 34%, compared with the 56% survival rate for the White counterparts.

Risk Factors

Brook, (2010) reported that cancer cells are categorized by damaged DNA, which causes abnormal cell development. There have two defining characteristics for an injured DNA: first, they can no longer split and segregate normally. Secondly, they may invade the surrounding tissue and travel to various sites within the body. Recall that a healthy body is well fortified to defend itself against cancer. It becomes possible only when the immune system and other defenses fail, which is when cancer prevails. Existing evidence (Muir and Weiland 1995; Andrews *et al.*, 2009) suggests that cancers develop from a complex interface of exposure to carcinogens and accrued mutations in numerous genes.

Researchers have identified more than 100 cancer genes known as oncogenes (Ali, 2016; Andrews et al. 2009). Oncogenes provide growth-promoting signals, which causes one or more characteristics of cancer cells when overexpressed or mutated. These two types of oncogenes are called proto-oncogenes and tumor suppressor genes. Both types of oncogenes remain dormant unless genetic or acquired mutation transforms them. The usual cause of acquired genetic damage is either a hormone, viral agents, environmental and dietary carcinogens, and radiation. Some factors that interact to increase a person's likelihood of developing cancer are age, genetics, nutritional status, hormonal balance, and response to stress (Brook, 2010).

Muir and Weiland (1995), earlier reported that the principal risk factor(s) in western countries have been summarized to include but not limited to the following: heavy smoking or chewing tobacco products, betel quid, heavy alcohol consumption. Others are poor dentition, oral sex, biological factors, excessive sunlight exposure, which is associated with melanoma of the lip, and Paterson-Brown-Kelly syndrome (Plummer-Vinson syndrome). Derka et al., (2006) reported that oral cancer links young men and women who indulge in the conventional "smokeless" chewing or spit tobacco habit and chewing of betel quid. Some individuals believe that spit tobacco or betel quid chewing is not harmful. However, it may take several decades of smoking, or chewing of these betel quid for instance, to precipitate the development of cancer. Tobacco use in all its forms is number one on the list of risk factors. When tobacco is combined with heavy use of alcohol, the risk is significantly increased, as the two acts synergistically. Those who smoke and drink are 15 times greater in the risk of developing oral cancer than others. Again, growing evidence showed that oral sex is an influential factor in transmitting the disease via the spread of the human papillomavirus (HPV) that initiates in the lining of the mouth, throat, cervix, and the anus. HPV has been detected in various amounts in persons with oral dysplasia, leukoplakia as well as malignancy (Glenny et al., 2010). The human papilloma virus, principally HPV16, has been definitively implicated in oral cancers, particularly those that occur in the back of the mouth. Biological factors include viruses and

fungi, which have been found to associate with oral cancers. The human papilloma virus, particularly version 16, has been shown to be sexually transmitted between partners. Moreover, is conclusively implicated in the increasing incidence of young non-smoking oral cancer patients (Derka et al., 2006). It is the same virus that is the etiologic agent, along with another version of the virus in over 90% of cervical cancers (Andrews et al., 2009).

Signs and Symptoms

United States of America National Cancer Institute (2011), issued a statement on the real dangers of oral cancer presentation in its early stages can go unnoticed. Also, it can present as a lump, or ulcer on the tongue, lip, skin lesion, or other mouth areas. Usually, the lesion is small and most often pale colored, may be dark or discolored. An early sign could be a white patch (leukoplakia) or a red patch (erythroplakia) on the soft tissues of the mouth, usually painless initially (National Cancer Institute, 2011). A burning sensation or pain may develop as the tumor advance. Also, symptoms that may be associated with this disease including tongue problems, swallowing difficulty. Mouth sores that do not resolve in 14 days and pain and paraesthesia are late symptoms. Many benign tissue changes normally occur in the mouth, and times is like a bite on the inside of the cheek, which appears as a dangerous tissue change. It is important to have any sore or discolored area of the mouth, which does not heal within 14 days, looked at by a professional. Therefore, any discussion of diagnosis must be prefaced with the issue of discovery. While an annual screening of oral cancer is necessary, it is possible that some changes will be noticed in the mouth or throat that needs examination between annual screenings. Derka et al., (2006) reports the following as symptoms of oral cancer: a sore or lesion in the mouth that does not heal even after two weeks, lump or thickening in the cheek, white or red patch on the gums, the lining of the mouth, tongue, or tonsil. A sore throat or a feeling that there is difficulty chewing or swallowing, difficulty moving the jaw or tongue, a caught in the throat, numbness of the tongue or another area of the mouth. Others are swelling of the jaw that causes dentures to fit poorly or become uncomfortable, chronic hoarseness, and speech and swallowing dysfunction (Derka et al., 2006).

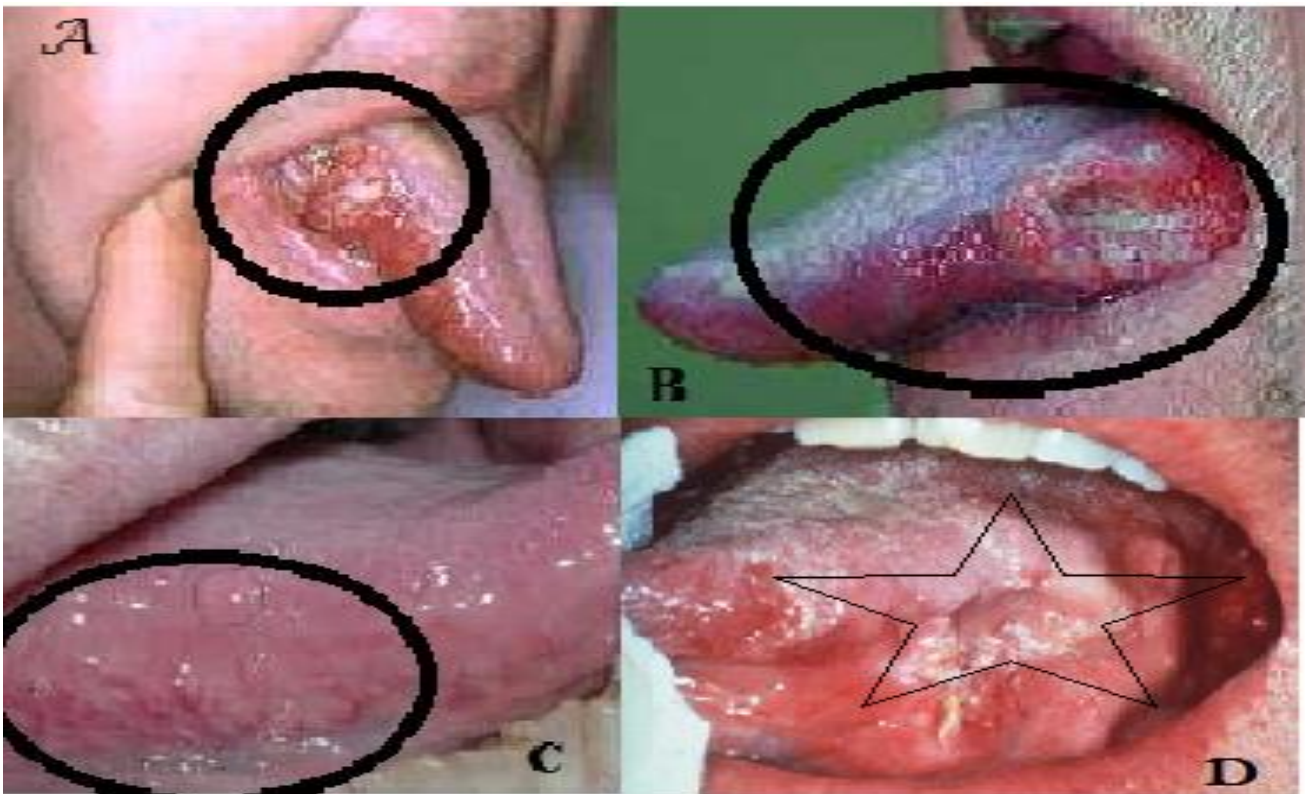


Plate 1: Showed the gross appearances of the pattern of oral cancers. (A) Showed leukoplakia with ulcerated tongue, (B) showed both leukoplakia and erythroplakia, Slide (C) Showed chronic hoarseness and lesion on the tongue, while (D) shows the different parts of oral cavity venerable to oral squamous carcinoma (National Cancer Institute, 2011).

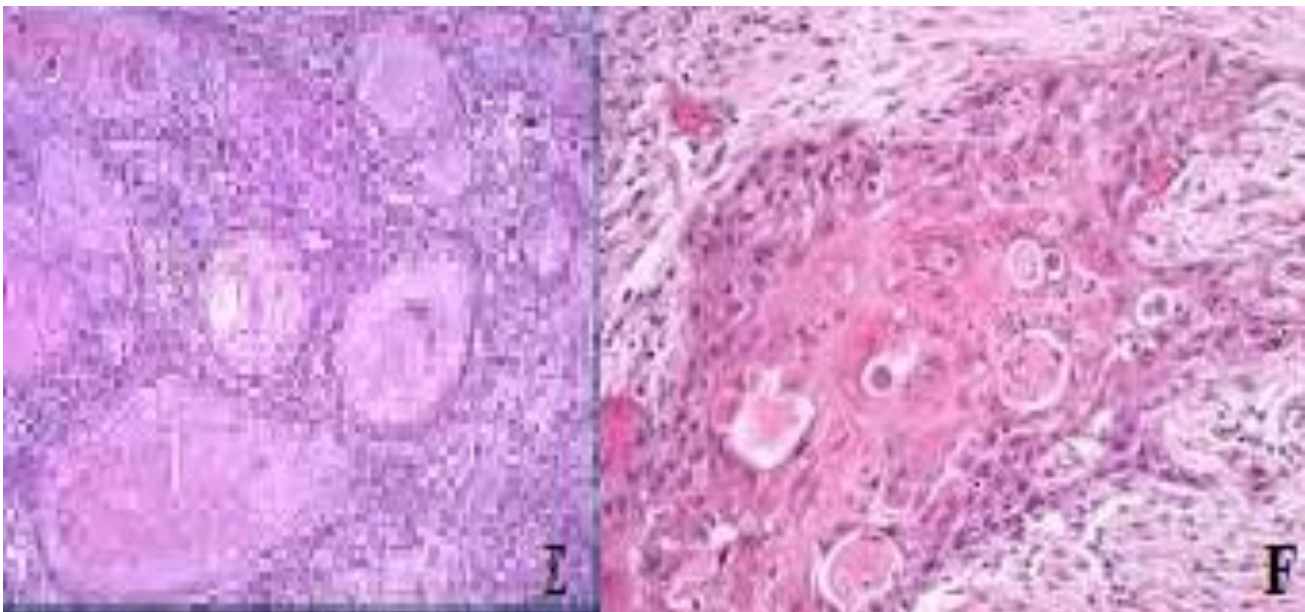


Plate. 2: Shows the histology of oral cancer. (E) Shows the metastatic stage of squamous cell carcinoma in situ, while slide (F) shows squamous cell carcinoma bounded with varying degrees of necrotic and inflammatory cells (National Cancer Institute, 2011).

Screening

National Cancer Institute-US (2011) reported the informative steps during oral cavity screening, which includes: lymph nodes check, the neck and under the lower jaw, cheeks, lips and gums. The tongue is pulled forward, palpate the cheek, check the back of the throat and check the floor of the mouth. There is evidence that a visual examination as part of a population-based screening program will reduce the mortality rate of oral cancer in high-risk persons. There is otherwise little evidence to support any screening program for early detection of oral cavity cancers. Also, Guo *et al.*, (2001) reported a major problem inherent in current oral cancer screening in the US, is that visual examinations alone, pre-cancers and early stage oral cancers are most likely be identified, and if professionals are not actively engaged in a program of opportunistic visual and tactile screening of their patient populations, lesions may easily be overlooked and neglected. It is well established that oral lesions, which appear innocuous may occasionally harbor dysplasia or cancer and that a delay in diagnosis may limit treatment options, ultimately resulting in a poor prognosis for the patient. In essence techniques such as brush, collection systems are completely dependent on professionals that are engaged in the discovery process and participate in opportunistic screening to find areas of suspicion.

Diagnosis

The ability to detect oral cancer at the earliest stages, as well as its precise location in the oral cavity, can improve the survival rate, and allow for less disfiguring ways to address the tumors and lesions associated with it (Gandolfo *et al.*, 2006). The most traditional type of biopsy is incisional in which the affected part or the entire lesion, which depend on its size and the ability to define the extent of it at the early stage are removed. The sample of tissue is then sent to the histology laboratory for tissue processing using the automatic tissue processor or manually. Sections are cut, mounted on a grease free glass slides and examined under the microscope to examine for atypical or malignant cells. When dealing with an area of significant mass, such as an enlarged lymph node, fine needle aspiration cytology (fine needle biopsy or FNB) has found an increasing role in diagnosis (Gandolfo *et al.*, 2006). The technique is reliable and relatively inexpensive, which makes use of a small needle attached to a syringe and inserted into the questionable mass. Cells are aspirated, or pulled out into the syringe as the piston of the syringe is withdrawn. The success

of this method depends on how accurately the needle is placed, and, as with all biopsies, on the skill and experience of the tissue scientist or pathologist who examine the cells. Another form of incisional biopsy is referred to as a punch biopsy. In this case, a subtle circular blade is pressed down into the suspect areas cutting a round border. The center of the suspected area is pulled, and with a scalpel or a pair of small tissue, scissors snip it free of the surrounding tissue, removing a perfect plug of cells from the sampled area. Just as the previous process, the prepared histology slide is sent to the scientist or pathologist for examination. The area where the plug was removed will not bleed much and normally heals without any stitches since it is so small. However, some dental offices do "brush biopsy" where a sampling of cells is collected by aggressively rubbing a brush against the suspect area. While this has some usefulness in the preliminary evaluation of a suspect area, it is not a stand-alone procedure, and if positive findings are achieved, it must be confirmed by a conventional incisional biopsy (Gandolfo *et al.*, 2006).

Laboratory Investigation

Brush Cytology and the Oral Brush Biopsy

The increased mortality incidence from oral cancer may be as a result of several factors. Undoubtedly the most substantial is late diagnosis. Studies have demonstrated that the survival and cure rate dramatically increase when oral cancer is detected in its precancerous stage or as an early stage disease (Epstein *et al.*, 2003, Derka *et al.*, 2006). For example, the 5-year subsistence for patients with localized disease is put at 80% compares to 20% for those with distant metastases (Epstein *et al.*, 2003). Unfortunately, roughly two-thirds of patients at the time of diagnosis are symptomatic while above 50% display evidence of spread to regional lymph nodes and metastases (Derka *et al.*, 2006). Given the significant morbidity and mortality associated with advanced oral cancer and its treatment, there is a need to providing clinicians with an accurate diagnostic technique that will increase the detection of early stage oral cancer that has been compelling.

Diniz-Freitas *et al.*, (2006) indicated that developments in the early diagnosis of oral cancer are unfolding and analogous to those made in the advances for cervical cancer. Furthermore, in the early 1950's, cervical cancer was the second leading cause of cancer deaths in American women. The disease is a biopsy, which was usually triggered by advanced symptoms such as persistent spotting and bleeding. Cervical cancer, like oral cancer, is highly

curable when detected at an early dysplastic stage and highly morbid when detected at a late, symptomatic stage (Epstein *et al.*, 2003). By the late 1960's, cervical cancer dropped to the seventh leading cause of cancer deaths among American women. The difference was due to the America female population becoming informed about cervical cancer and the opportunity for early detection, the compliance of the Gynaecology professionals community to offer screenings that were well done, and the widespread utilization of brush cytology, specifically, the cervical Papanicolaou (PAP) smear. These changes have resulted in a reduction of cervical cancer deaths in the United States by 74% (Diniz-Freitas *et al.*, 2006). Brush cytology has the potential to assist the diagnostic portion of the "screening gap" which currently challenges the early detection of many epithelial cancers, including oral cancer (Shiboski *et al.*, 2005). Brush cytology can be a non-invasive means of diagnosing dysplasia and early carcinoma in those patients who are either asymptomatic or in those with minor symptoms who do not warrant immediate biopsy (Diniz-Freitas *et al.*, 2006). The mechanism of cytology, regardless of its application to cervical, bladder or oral mucosal lining, is based on the fact that dysplastic and cancerous cells tend to have fewer and weaker connections to each other and their neighboring normal cells in the surrounding tissue. Dysplastic and cancerous cells, therefore, tend to "slough off" or exfoliate preferentially and can easily be collected from the surface of the lesion. A sample of these cells applied to a microscope slide will often contain abnormalities if harvested from a dysplastic or cancerous lesion (Shiboski *et al.*, 2005).

Derka *et al.*, (2006) revealed that the success of the Pap smear was a primary impetus for some studies conducted in the mid 1960's that examine the sensitivity and specificity of oral exfoliative cytology. Exfoliative cytology is thought of as a technique that could facilitate and accelerate clinical and histopathologic recognition of oral cancer. The use of oral cytology for large, advanced and obviously malignant lesions is not indicated since such growths always require a definitive biopsy-obtained diagnosis. In contrast, Epstein *et al.*, (2003) suggested that the value of cytology lies in the identification of early stage oral cancers and dysplasias whose clinical appearance is often innocuous or trivial. To buttress the above information (Derka *et al.*, 2006) reported that the use of oral cytology can be a means to accelerate biopsy of these clinically harmless-appearing cancers that

would have otherwise been neglected. Despite the high initial degree of interest and research, traditional, manual, oral cytology currently is not utilized as a method of diagnosing oral precancers and cancers (Shiboski *et al.*, 2005). Although many authors initially concluded from their data that oral cytology could serve as a useful adjunct to biopsy, the current general perception among both dentists and physicians is that the sensitivity of oral cytology is not sufficient to warrant its widespread use as a screening modality to triage visible lesions (Diniz-Freitas *et al.*, 2006). There are several reasons why traditional oral cytology has proven to be of little value in detecting oral dysplasias and cancers. When cytologic instruments are used in the mouth to diagnose precancers and cancers, their accuracy is relatively low (Scully *et al.*, 2003). Specifically, exfoliative cytology performed on oral cancers has high false negative rates, which can exceed 30%. Furthermore, the effectiveness of exfoliative cytology for detecting dysplasia is even more doubtful, with false negative rates reported as high as 63% (Diniz-Freitas *et al.*, 2006; Scully *et al.*, 2003).

In an earlier report (Scully *et al.*, 2003) revealed that poor results are due, in part, to the fact that cytology instruments do not sample the deepest layers of the oral lesion. This is essential, since unlike cervical cancer, the deepest layer of the lesion, the basal cell layer, is often the only layer that contains abnormal cells within an oral precancerous or cancerous lesion. The sensitivity of cytology is often dependent on a tedious visual search for a potentially rare abnormality on the microscope slide, the precancerous or cancerous cells collected on the slide may not have been detected by the histology scientist or pathologist. Although abnormal cells may preferentially exfoliate from a dysplastic lesion, they are often vastly outnumbered on the microscope slide by the enormous numbers of normal cells that exfoliate due to constant turnover. For example, Scully and Bagan (2009) revealed that a cervical Pap smear from a patient with carcinoma-in-situ may contain 300,000 normal cells with only a dozen abnormal cells scattered among them. Several studies (Scully and Bagan 2009; Shiboski *et al.*, 2005 Scully *et al.*, 2003) already demonstrated that women who develop advanced cervical cancer despite a history of "negative" Pap smear often experienced one or more false negative smears determined as such because they contained very few abnormal cells. In oral cytology, this false negative impasse is aggravated by two additional factors: the

amount of abnormal cells available for sampling, which may be limited by the keratinized nature of many oral lesions and, secondly the high level of epithelial turnover in the mouth, which may further numerically dilute the little abnormal cells obtained in the smear (Scully *et al.*, 2003).

National Cancer Institute (2011) in the United States of America informed that the oral brush biopsy was announced to the Dental Professionals in 1999. Moreover, current practice exploits the improved brush to acquire the complete transepithelial biopsy sample with cellular depiction from all of the three layers of the lesion, which includes the superficial, intermediate and basal layers. Contrasting with the preceding cytology instruments, which collect only exfoliated superficial cells, when used up evenly and rubbed against the suspected areas of tissue aggressively (to the point of minor bleeding) the biopsy brush infiltrates the basement membrane, thereby removing tissues from the three epithelial layers of the oral mucosa. As with the brush collection methods, it does not maintain the architecture of the cells relationship to each other (Kuratomi *et al.*, 2006). The oral brush biopsy does not involve topical or local anesthetic that causes negligible bleeding and pain. The brush biopsy device has two cutting surfaces, the flat portion of the brush and the circular edge of the brush. Either surface may be used to obtain the specimen. Brush biopsies are utilized routinely in the detection of precancer and cancer in other organ systems. Examples of well-known applications of brush biopsies include fiberoptic bronchoscopy (bronchial), ureteral retrograde brush biopsy (renal or ureter tissue), cholangiography (bile duct stricture), pancreatic ductal brush biopsies and others, including endometrial, nasopharynx, and GI tract applications (rectal, gastric, esophageal, colon) (Kuratomi *et al.*, 2006).

The Department of Health and Human Services-U.S.A (2000) reported the results of brush biopsy study, which demonstrates that the tool can be reliably put in use on oral lesions. It can, therefore, serve as a method of confirming the benign nature of the lesion and more importantly, reveal the precancerous and cancerous areas that are clinically assumed. The role of a sampling system such as the brush biopsy is to determine the actual category of lesions, which would not otherwise receive any further testing, i.e. lesions that are not diagnosed sufficiently upon suspicious visual inspections are examined for an instantaneous incisional biopsy. It is a method for identifying unsuspected oral cancers seen in a visual investigation, at early and curable

stages if the professional practitioner engages in a devious routine screening (visual and palpable), which will reveal suspect regions for sampling. The brush biopsy provides the dentist with a diagnostic screening test resembling a Pap smear. While the Pap smear is a procedure performed on all women and a brush biopsy is used majorly for patients with a visible mucosal spot. Both examinations are adjuncts to the clinical investigation and are used to identify a disease condition, which is still in the primary and reversible stage. They are both simple to accomplish, office-based, less-painful tests; and the two procedures can be combined to the routine daily practices (Missmann *et al.*, 2006). Given the exertion in clinically distinguishing premalignant and early malignant oral lesions from those that are benign, the brush biopsy allows specialists to test lesions that are diagnosed daily. When the brush biopsy pathology returns a positive result, it cannot be used as a decisive purpose of malignancy, and a conventional, gold standard, incisional or punch biopsy that must be performed (Missmann *et al.*, 2006).

Toluidine Blue

Toluidine blue (TB) staining is a modest and cheap diagnostic tool that makes do with a blue dye in highlighting an abnormal area in the mucosa. TB is a basic metachromatic nuclear stain which stains nuclear material of malignant lesions (Epstein *et al.*, 2003). The process includes the patient rinsing the mouth with 1% acetic acid for 20 seconds followed by the same double rinsing in water for 20 seconds. Also, rinsing the mouth with 5-10 cc. 1% toluidine blue solution; and lastly rinsing with 1% acetic acid solution (5 oz.) for about 1 minute followed by a water rinse. In the highest risk population, prior upper autodigestive tract cancer patients, TB has a higher sensitivity to detect carcinoma *in situ* (CIS) when compared to a conventional oral examination (96.7% and 40%, respectively). Epstein *et al.*, (2003) suggested that a false positive staining (when lesions stain blue, but no carcinoma is identified after a biopsy is taken) occurred in 8-10% of cases associated with keratotic lesions and the regenerating edges of ulcers and erosions. The clinical appearance of a dark royal blue stain may be significantly related to the nuclear uptake of TB, compared to pale royal blue staining which may be unrelated to any histological feature (Gandolfo *et al.*, 2006). Studies assessing TB have shown a sensitivity and specificity ranging from 93.5 to 97.8% and 73.3 to 92.9%, respectively (Gandolfo *et al.*, 2006; Zhang *et al.*, 2005). High-risk oral potentially malignant lesions (PMLs) with a poor outcome may be

identified by Toluidine blue staining. While a positive TB staining may be related to genetic changes [allelic loss or loss of heterozygosity (LOH)] associated with a progression to oral squamous cell carcinomas (OSCC) even in histologically benign lesions including lesions with a mild dysplasia (Zhang *et al.*, 2005). TB may also help pre-operatively; in one reported case of OSCC, there was malignant or pre-malignant cells more than 1 cm away, requiring a resection of a size that would not have been addressed during a conventional oral examination alone (Missmann *et al.*, 2006). From the ongoing discuss, it can be seen that even mucosa of a normal appearance may also contain molecular changes of an early carcinogenesis.

Diagnostic Staging

In much imagination, the diagnostic stage of treatment affects a throughput that determines accurately and more efficiently the malignancy and stage of cancers (Brocklehurst *et al.*, 2010). Hence, staging cancer involves trying to establish carefully the degree to which particular oral cancer has spread. Also to what extent it involves other areas of the mouth and neck or even distant locations elsewhere in the body, which may help to express how rapidly cancer has spread. A cancer violence spreading is described using terms like poorly differentiated, moderately differentiated or well differentiated. A well-differentiating cancer is not deeply aggressive while spreading; moderately differentiating cancer is aggressive intermediately whereas a poorly differentiating cancer is very much aggressive in the speed at which it spreads (Brocklehurst *et al.*, 2010).

Staging examination sometimes will include incisional biopsy while the patient is conscious. In most cases, local anesthesia may be adequate. For lesions or tumors in deeper tissues or less accessible areas, a general anesthetic can provide a better opportunity to perform the biopsy and also to make a full clinical assessment of the lesion (Kuratomi *et al.*, 2006). Following biopsy confirmation of the presence of oral cancer, a patient undergoes a thorough evaluation of their overall health and the state of their disease. The patient's overall fitness in anticipation of treatment is determined. Many patients afflicted with oral cancer, though certainly not all, are elderly. Older patients may be suffering from other illnesses, and they are also at risk of having other cancers in the respiratory or digestive tract. These "synchronous carcinomas" of the head and neck, lungs, or esophagus occur as frequently as

10 percent of the time with elderly oral cancer patients. Therefore, checking for cancer in these areas as well can be part of the diagnostic process (Kuratomi *et al.*, 2006).

Conclusion and Recommendation

The entire point, of course, is that no treatment decisions should be made before there is confirmation of malignancy. Even in the case of what would seem to be an obvious malignancy, appearances can occasionally be misleading, hence the need for a proper biopsy. Also, the degree of differentiation between healthy and malignant tissues, along with the stage of the disease will influence treatment strategy and prognosis. Therefore, we at this moment recommend the development of more effective approaches to preventing oral cancers. Also, public health professionals need a better understanding of groups at high risk for oral cancer.

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