AMERICAN COLLEGE OF PROSTHODONTISTS®

Oral Cancer: A Prosthodontic Diagnosis

Michael A. Siegel, DDS, MS, FDS RCS,[1] Michael A. Kahn, DDS,[2] & Mitzi J. Palazzolo, DDS, MS[3]

[1]Professor and Chair, Department of Diagnostic Sciences, Nova Southeastern University College of Dental Medicine, Fort Lauderdale, FL
[2]Professor and Chair, Department of Oral and Maxillofacial Pathology, Tufts University School of Dental Medicine, Boston, MA
[3]Assistant Professor, Department of Diagnostic Sciences, Nova Southeastern University College of Dental Medicine, Fort Lauderdale, FL

Keywords
Cancer; screen; examination; diagnostic; adjunctive techniques; carcinoma; early diagnosis; recall

Correspondence
Michael A. Siegel, Department of Diagnostic Sciences, Nova Southeastern University College of Dental Medicine, 3200 South University Drive, Fort Lauderdale, FL 33328-2018. E-mail: masiegel@nova.edu

Accepted May 14, 2008

doi: 10.1111/j.1532-849X.2008.00373.x

Abstract

The prosthodontic literature is replete with articles addressing the reconstruction, psychological adaption, prosthesis success, quality of life, need for careful follow-up, and many other issues related to the patient who has undergone surgery, radiation, and/or chemotherapy for oral malignant neoplasms. However, in the prosthodontic professional literature, there is a paucity of information related to the early diagnosis and referral of lesions that may represent premalignant or malignant neoplasia. This article will describe the rationale, epidemiology, and appearance of oral premalignant and malignant mucosal lesions as well as the state-of-the-art diagnostic tools currently available to prosthodontists to ensure that their patients are diagnosed at the earliest possible time.

In 2006, approximately 31,000 cases of oropharyngeal cancer were diagnosed in the United States, and about 25% of these patients died from their disease.[1] The preponderance of these tumors represents squamous cell carcinoma of the oral mucous membranes. The combined 5-year survival rate in the United States is approximately 57%, and it has been established that less advanced disease increases the prognosis significantly.[1-4] The axiom familiar to every dental student—*early detection and diagnosis provide the best prognosis*—remains valid.

According to Campisi, "...the development of cancer is almost inevitable as mammalian organisms age."[5] Although the need for prosthodontics was expected to decline with the promotion of preventive measures, it is actually increasing with the aging population.[6] Oral mucosal disease, including malignant neoplasms, is found in higher frequency in an elderly population.[7,8] There is also significant data showing that prosthetic patients suffer significant oral morbidity following cancer therapy that requires close medical and psychological follow-up.[9,10] There are studies suggesting that poor oral hygiene due to infrequent tooth brushing and sores caused by dentures are risk factors for oral precancer and cancer, but this remains controversial and will require larger prospective studies to validate.[11-13] It is recommended that patients at risk for oral cancer be followed carefully for the development of chronic irritation from teeth and appliances (Fig 1).[12]

The prosthodontic literature is replete with articles addressing the reconstruction, psychological adaption, prosthesis success, quality of life, need for careful follow-up, and many other issues related to the patient who has undergone surgery, radiation, and/or chemotherapy for oral malignant neoplasms.[10,14-18] However, in the professional literature available to the practicing prosthodontist, there is a paucity of information related to the early diagnosis and referral of lesions that may represent premalignant or malignant neoplasia.

Epidemiology of oral squamous cell carcinoma

Oral squamous cell carcinoma, which arises from the mucosal lining of the oral cavity, accounts for over 90% of oral cancers.[3] Worldwide, more than 500,000 new cases are diagnosed annually.[19,20] Oral cancer accounts for less than 3% of all cancers in the United States, but it is the sixth most common cancer in males and twelfth most common in females.[1] It is estimated that 34,360 new cancer cases of the oral cavity and pharynx will be diagnosed in 2007.[21] The incidence rates are more than twice as high in men as in women; however, the disparity in the male:female ratio has become less pronounced over the past half century. This may be because the exposure to alcohol and tobacco in women has also increased.[22] The incidence of cancer of the oral cavity is greatest in men who are older than 50; however, the average annual incidence and mortality rates vary considerably between different races, genders, and age groups. During the past decade, it has been noted and verified that

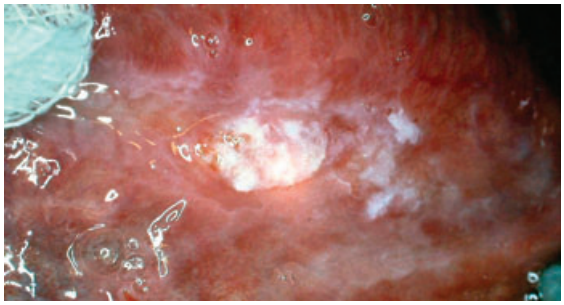

Figure 1 Squamous cell carcinoma of the left lateral tongue border in a 67-year-old man. Note the presence of *Candida albicans* on the surface of the lesion only. This is an ominous prognostic sign, as it may represent an opportunistic infection related to compromised tissue immunity at the site of a neoplasm.

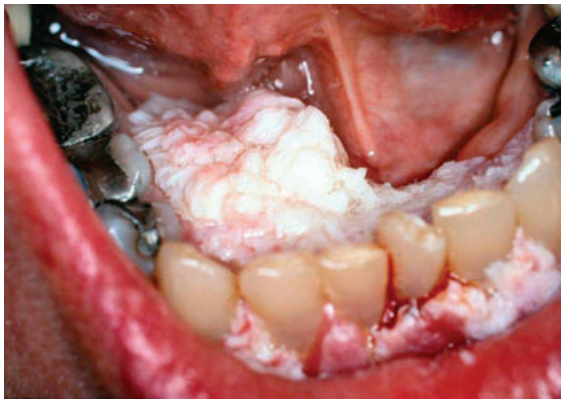

Figure 2 Cauliflower-like lesion that clinically represents human papillomavirus-induced verrucous carcinoma in a 59-year-old woman.

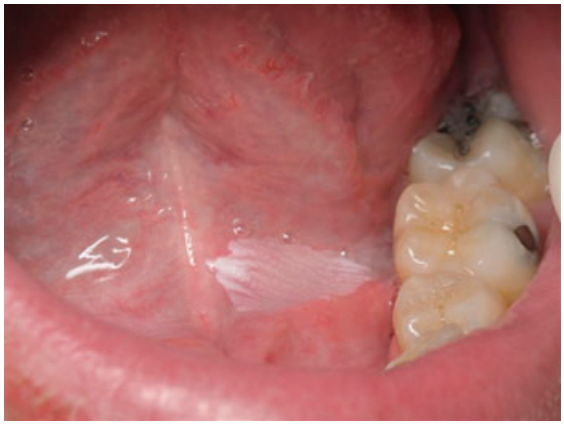

Figure 3 Homogeneous leukoplakia of the floor of the mouth in a 36-year-old male patient with a significant cigarette smoking history. Excisional biopsy provided a histopathologic diagnosis of hyperkeratosis and mild dysplasia.

the incidence rate in persons under the age of 40 is increasing. Over time, the incidence of intraoral cancer has been increasing dramatically for black men in the United States. An estimated 7,550 deaths from oral cancer are expected in 2007.[21] The 5-year relative survival rates vary by race and sex. Black men

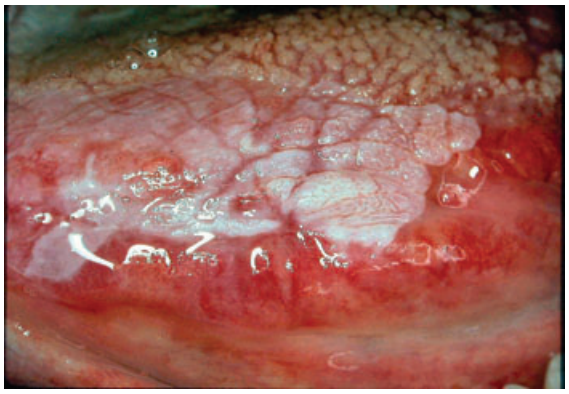

Figure 4 Erythroleukoplakia of the left lateral tongue border in a 42-year-old male patient. Biopsy of the lesion disclosed moderate epithelial dysplasia.

seem to carry a higher burden, with a survival rate of 35.5% compared to whites (62.8%).[21]

Risk factors associated with the development of oral squamous cell carcinoma

The cause of oral squamous cell carcinoma is multifactorial.[23] No single causative agent or factor has been clearly defined or accepted. It is likely that multiple factors play a role in malignant transformation.

Tobacco and alcohol

The strong association between squamous cell carcinoma of the oral cavity with tobacco use is well established.

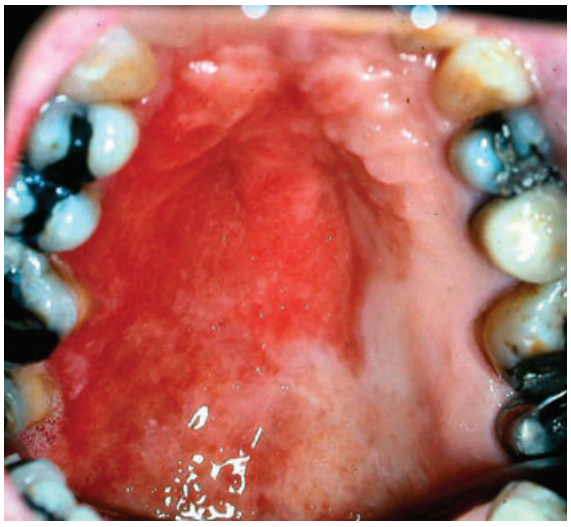

Figure 5 Erythroplakia of the right palate in a 76-year-old man; biopsy proven as well-differentiated squamous cell carcinoma.

Epidemiological studies show that the risk of developing oral cancer is 5 to 9 times greater for smokers than for nonsmokers, and this risk may increase to as much as 17 times greater for extremely heavy smokers of 80 or more cigarettes per day.[22] The risk for a second primary carcinoma of the upper aero-digestive tract is 2 to 6 times greater for treated patients with oral cancer who continue to smoke than for those who quit after diagnosis.[22]

Alcohol use has been identified as a major risk factor for cancers of the upper aero-digestive tract. In studies controlled for smoking, moderate-to-heavy drinkers have been shown to have a 3 to 9 times greater risk of developing oral cancer.[22] In addition, alcohol consumption appears to be a significant potentiator or promoter for other causative factors, especially tobacco, and its effects are significant when it is understood that most heavy drinkers are also heavy smokers. The simultaneous use of tobacco products and alcohol abuse results in a multiplicative effect of those two social habits rather than an additive one.

Oncogenic viruses

Viral agents capable of integration into the host's genetic material may inhibit the ability of the host to regulate the normal growth and proliferation of the infected cell. Recent evidence suggests that human papillomavirus (HPV) is associated with some oral and oropharyngeal cancers. HPV-16 and HPV-18 have been identified in up to 50% of the oral squamous cell carcinomas arising in Waldeyer's tonsillar ring and in 15 to 25% of those in the tongue and other parts of the oral cavity (Fig 2).[24,25]

Premalignant lesions of the oral cavity

Invasive oral squamous cell carcinoma is often preceded by the presence of clinically identifiable premalignant changes of the oral mucosa. These lesions often present as white, red, or mixed patches, known as leukoplakia, erythroplakia, or erythroleukoplakia, respectively.[22] Many cases of oral squamous cell carcinoma are preceded by recognizable premalignant epithelial changes, the most important of which is thought to be the presence of epithelial dysplasia.[26,27] Histopathologic evaluation of the epithelium adjacent to oral squamous cell carcinomas often reveals dysplastic changes, and these changes are frequently multicentric. Severe dysplasia indicates a very high risk of the subsequent development of cancer.[28]

The proportion of squamous cell carcinomas that develop through clinically recognizable precancerous stages is not known. Histopathologically, these precancerous lesions vary from mild to severe. Prediction of which precancerous lesions will develop into oral carcinoma is difficult. Overall, the proportion of dysplastic epithelial lesions that evolve into cancer is about 16%, and the time period over which this occurs varies from months to beyond 20 years.[27] The average malignant transformation rate has been reported to be 24 to 30 months. Higher grades of dysplasia are generally associated with a higher risk of development of carcinoma. Only 4 to 11% of mild to moderate dysplasia progresses to squamous cell carcinoma, whereas 35% of lesions diagnosed as severe dysplasia progress to squamous cell carcinoma. The presence of dysplasia does not always predict the development of squamous cell carcinoma, which may also develop in the absence of dysplasia.[27]

Leukoplakia

Leukoplakia, as defined by the World Health Organization, is a clinical term that describes "a white patch or plaque that cannot be characterized clinically or pathologically as any other disease" (Fig 3). Therefore, leukoplakia is a clinical term and has no specific histopathologic connotation. The majority of these lesions are detected in individuals aged 60 years or older, although patients of any age may be affected. In men over the age of 70, the prevalence of leukoplakia is 8%. The prevalence in women past the age of 70 is approximately 2%.[22] The male:female predilection is decreasing, with women being affected almost as frequently as men. About half the lesions involve the mandibular mucosa, mandibular sulcus, and buccal mucosa.[29]

The majority of leukoplakic lesions are physiologic reactions of the mucosa against chronic trauma or irritation. Ill-fitting dentures and parafunctional oral habits such as cheek or tongue chewing are common causes. Factors associated with these white mucosal lesions include, but are not limited to, mechanical and chemical irritants, chronic hyperplastic candidiasis, syphilis, and electro-galvanic reactions.[30] Leukoplakic lesions are frequently noted in patients with a history of tobacco or alcohol use. Leukoplakias may be varied in their appearance. The lesions may appear homogenous or heterogenous with a smooth, fissured, or corrugated surface and colored white, gray, or translucent. Leukoplakias are also variable with regard to size and distribution. These lesions may be barely discernable clinically or cover entire mucosal surfaces. The sites where leukoplakic lesions are commonly encountered are the floor of the mouth, lateral and ventral borders of the tongue, labial and buccal mucosae, gingivae, soft palate, and retromolar areas.

The vast majority (i.e., 80%) of leukoplakias are benign.[29] The remaining lesions are either premalignant (dysplastic or carcinoma-in-situ) or malignant. The precancerous nature of leukoplakia has been established based on several factors. In various studies, 15.6 to 39.2% of leukoplakia biopsy samples have demonstrated epithelial dysplasia or invasive carcinoma, and more than one third of oral carcinomas have areas of leukoplakia in close proximity.[31] The location of oral leukoplakia has a significant correlation with the frequency of finding dysplastic or malignant changes upon biopsy. The floor of the mouth shows the highest chance of dysplasia or carcinoma (42.9%) presence, while the lateral and ventral tongue is second highest (25%).[22]

Dysplastic lesions are multicentric and are most commonly encountered in the floor of the mouth or on the tongue.[29,32] Other risk sites for premalignant or malignant leukoplakias include the labial mucosa and vermilion lip, lateral and ventral borders of the tongue, floor of the mouth, soft palate, uvula complex, and retromolar areas. Leukoplakic lesions are prognostically ominous in a patient with a previous history of carcinoma of the tongue. Multiple carcinomas of the oral cavity and oropharynx (116 times greater than expected) have been encountered in patients with a history of tongue carcinoma.[33]

The clinician faces the problem of determining which of these lesions are premalignant or malignant and must determine the nature of the white lesion without unreasonably alarming the patient.

Erythroleukoplakia

Leukoplakia with localized speckled red areas or erythroplakia with localized speckled white areas also confer a high risk of oral cancer (Fig 4). Many terms, such as speckled erythroplakia or speckled leukoplakia, have been used to describe these mixed red and white lesions. There is a four-fold increased risk that these lesions will undergo malignant transformation when compared to homogeneous leukoplakias.[7] Erythroleukoplakia may occur in any intraoral site. It has a male predilection. Not surprisingly, these lesions are usually found in patients exhibiting poor oral hygiene who use tobacco and alcohol. *Candida albicans*, a commonly encountered intraoral fungal organism, is often found in these lesions and may have a role in the dysplastic changes;[26] however, no studies have documented a direct relationship between candidal involvement and malignant transformation.[31,34] Mixed red and white lesions that have not resolved in 7 to 14 days following removal of any local causative factors should be selected for biopsy due to their increased risk for developing into carcinoma.

Erythroplakia

Erythroplakia is a clinical term used to define a velvety red patch that cannot be characterized as any other condition (Fig 5). These lesions are often asymptomatic and are first recognized during a routine dental examination. Erythroplakias can occur anywhere in the oral cavity but are most commonly encountered in the floor of the mouth, alveolar ridge, and oropharynx. The redness is due to the thinning (erosion) of the overlying epithelium. Incidence is highest in men and women over the age of 60, and both genders are equally affected.

Biopsy of erythroplakic lesions is mandatory, because it has been shown histologically that approximately 90% of these lesions represent severe dysplasia, carcinoma in situ, or carcinoma.[35] The patient must be followed closely, as multiple sites of the oral cavity may be affected, a phenomenon referred to as "field cancerization." In patients with multiple lesions, referral should be made to ensure that representative biopsy specimens are procured from each site.

Extraoral and intraoral examination

The prosthodontist must perform a careful, organized, and reproducible visual and palpation examination of the intraoral soft tissues as well as submandibular and cervical chain lymph node palpation on all new patients as well as patients presenting for recall examination.[36,37] Edentulous patients must be specifically counseled about returning for prescribed, regular recall examinations. They may erroneously think that, as they do not have teeth, they do not need to be regularly followed by a prosthodontist.[38] Following the examination, patients should be advised that they have been examined for oral cancer. Only 28% of patients reported ever having had an oral cancer examination. Of those, 20% had had the examination in the preceding year.[39,40] Patients who use tobacco products must be encouraged to quit. The prosthodontist may be instrumental in helping a patient quit smoking either by direct counseling or by referral to a smoking cessation program.[41] Geriatric alcoholism is rising, so the prosthodontist may also be influential in advising patients of the necessity of limiting their alcohol intake, especially if there are intraoral signs of alcohol abuse.[42,43] The highest risk of developing oral cancer is in adults over the age of 40 who use both tobacco and alcohol.[34]

The initial step in the treatment of leukoplakia or erythroplakia is to eliminate any source of chronic irritation or trauma, such as a sharp tooth or denture border. Induration, rolled borders, locations such as the lateral surface of the tongue or floor of mouth, a red component to the lesion, or a nonhomogeneous granular surface may increase the suspicion of the prosthodontist performing the examination. However, it must be kept in mind that even the most innocuous-looking homogeneous leukoplakia may be histopathologically malignant, so clinical appearance alone should not be the only criterion for the decision to refer for a biopsy. Controversy exists as to whether a therapeutic trial of medication such as a topical steroid or retinoid is appropriate prior to the performance of a biopsy, which remains the "gold standard" for the diagnosis of these lesions.[44] If the leukoplakic lesion has not resolved within a reasonable time period following the removal of local etiologic factors, the prosthodontist should refer these patients to a specialist colleague for biopsy and should follow up with that colleague to ensure that the patient has been seen and managed appropriately. In the event the lesion is found to be dysplastic or malignant, for the first 2 to 3 years, the patient should be followed up four times yearly. The prosthodontist and surgeon should coordinate a recall schedule so that the patient is alternatively seen by the two treating specialists. For example, the oral and maxillofacial surgeon can evaluate the patient in January and July, while the prosthodontist alternatively evaluates the patient in April and October. In this way, there is frequent evaluation of the patient following the diagnosis of a premalignant or malignant lesion as well as continuity of care between the two treating specialists. Any suggestion of lesion recurrence, ulceration, leukoplakia, or erythroplakia should be rebiopsied at the earliest possible time.

Oral cancer screening devices and adjunctive diagnostic techniques

Recently, several companies have marketed devices [following obtainment of FDA Class I (501c) device approval] intended to aid the dentist in the early detection and diagnosis of premalignant oral lesions. Among those intended to be used as oral cancer screening devices are Vizilite Plus® (Zila Pharmaceuticals, Inc., Phoenix, AZ), MicroLux-DL® (AdDent, Inc., Danbury, CT), Orascoptic® DK (Orascoptic by the Kerr Company, Middleton, WI), and VELscope® (L.E.D. Dental, Inc., White Rock, BC, Canada). Procedures intended for adjunctive diagnosis of oral premalignancies include The BrushTest® (formerly called the brush biopsy; OralCDx, Suffern, NY) and liquid-based cytology technology, ThinPrep®

and SurePath® (TriPath, Burlington, NC, and Cytyc Corp., Boxborough, MA, respectively). It should be noted that the techniques described below have limitations, including false-positive and false-negative results, depending on the character and site of the lesion in question. Most prosthodontists do not have ready access to these tools, but should know that they are available for the care of their patients as well as to be able to interpret the results of these adjunctive techniques. A specialist such as an oral and maxillofacial surgeon is well trained in these technologies and can use them in appropriate situations when deemed necessary; however, the scalpel biopsy is still the gold standard for definitive histopathologic diagnosis, so if the prosthodontist is especially concerned with the clinical presentation of a lesion, a routine excisional or incisional biopsy should be specifically requested.

Tissue reflectance with chemiluminescence and vital dye marking

Following the conventional incandescent light soft tissue head and neck examination described above, the Vizilite Plus system (single use, disposable kit) uses a 30- to 60-second prerinse, nontoxic 1% acetic acid swish and spit mouth rinse (raspberry flavored) followed by the bending of a plastic lightstick that when shaken results in an endothermic blue-white light-producing reaction (with peak wavelength outputs near 430, 540, and 580 nm). During the ensuing 10 minutes, with the operatory ambient lights significantly dimmed, the illuminated lightstick is shined throughout the oral cavity following its placement into a two-piece plastic retractor. The mild acetic acid rinse is reported to prepare the oral mucosa by dehydration for the detection of epithelial cells with the increased nuclear/cytoplasmic ratio, including those that may be dysplastic, following the use of the diffuse blue-white light.[45,46] If the suspicious oral lesion (i.e., leukoplakia, erythroplakia, erythroleukoplakia) noted during the routine operatory white light examination becomes visibly enhanced in coloration (e.g., leukoplakic) or darkened (erythroplakic), then it is considered a positive finding. Reports in the literature indicate that premalignant lesions (verified by subsequent surgical biopsy) that were not seen by dental experts in a high-risk patient population have been discovered following use of the Vizilite Plus system.[47-51] The second step of this system includes a visual marking of the identified lesion by use of a metachromatic vital dye, toluidine blue (toloniun chloride), which has a reported affinity for DNA and, thus, binds to epithelial cells with the increased nuclear cytoplasmic ratio. Zila Pharmaceuticals, Inc., has produced a pharmaceutical grade of this vital dye and includes it in this system with the trade name TBlue^{630} (Zila tolonium chloride). Therefore, the clinician has the option of a three-step marking of the suspicious lesion with TBlue^{630} for documentation and as an aid in biopsy/cytology sampling or by referral to a dental colleague. It should be emphasized that TBlue^{630} is only FDA-approved for use in the Vizilite Plus system *after* the use of the chemiluminescent lightstick step.

Tissue reflectance with luminescence

There are two FDA-approved Class I light-emitting devices similar to the first step of the Vizilite Plus system—MicroLux-DL® and Orascoptic DK®. These oral cancer screening aids are manufactured by the same company (AdDent, Inc., Danbury, CT) but marketed by two different companies, hence their different trade names. Both devices are reusable, battery-operated light emitting diode dental transilluminators that have been adopted to emit a diffuse blue-white light (assumed to be the same wavelength as the Vizilite) by removing the transilluminator light tip and replacing it with a sterilizable, translucent glass tip. As with the Vizilite Plus system, patients prepare their oral mucosa by rinsing and spitting with the same 1% acetic acid rinse, but, unlike Vizilite, the battery-containing handle creates the diffuse blue light in a manner similar to the common flashlight. These adjunctive devices, as with the Vizilite Plus system, are to only be used following the conventional incandescent light intraoral examination with a positive finding defined as visual enhancement of a suspicious lesion.

Narrow-emission tissue fluorescence

The VELscope is an oral premalignant screening device that emits a concentrated blue light (peak wavelength outputs of 405 and 436 nm) that creates a natural fluorescence. In North America, it is powered by a 120-V AC electric current and emits a blue light by use of a replaceable metal halide bulb, a series of dichromatic mirrors, and a flexible fiber optic cable. In addition, the blue light emitter handpiece has an optical inline ocular eyepiece through which the clinician observes the oral mucosa tissue. A series of optical filters are located between the clinician's eye and the emitted light. The emitted blue light emission excites natural substances, fluorophores, within the oral epithelium and underlying lamina propria (connective tissue). When exited, fluorophores autofluoresce and emit an apple green color that can be appreciated by the clinician due to the filters contained within the eyepiece. As with other oral cancer light screening devices, the VELscope is only to be used following a conventional incandescent light intraoral examination. The clinician repeats the intraoral examination, after dimming the ambient operatory light, with the activated VELscope; normal oral mucosa will appear green. If an area of black (i.e., loss of fluorescence) is seen, it can correlate to a suspicious premalignant lesion previously appreciated during the incandescent light examination or, in some reported cases, an area of lost fluorescence is seen despite being unable to appreciate a suspicious lesion with the naked eye.[52-53] The VELscope is reported to exhibit loss of fluorescence in the presence of dysplasia due to the destruction of the naturally occurring fluorophores in the affected epithelium and/or connective tissue. Oral lesions have also been documented in which the loss of fluorescence extends beyond the clinically visible lesion, and subsequent biopsy of the extended dark areas revealed the presence of microscopic dysplasia or squamous cell carcinoma.[54]

Adjunctive diagnostic procedures

During the late 1950s and 1960s many dental investigators attempted to adopt the Pap smear, the early 1950s' highly successful adjunctive diagnostic technique for uterine cervical cancer, for use within the oral cavity. This was an exfoliative cytology procedure in which surface epithelial cells were scraped in a minimally invasive manner and immediately transferred

("smeared") to a glass microscope slide that was subsequently sprayed with an alcohol-based fixative to preserve the collected cells. The cells were then coverslipped following the use of Papanicolaou stain and examined with the light microscope. A pathology report was issued indicating that if any of the cells exhibited atypical morphological characteristics that could indicate the clinical presence of epithelial dysplasia or squamous cell carcinoma. Unfortunately, the Pap smear proved to be unreliable when used within the oral cavity, since there were numerous reports of unacceptably high incidence of false-positive and false-negative results.[55] Thus, this noninvasive potential adjunctive oral diagnostic technique was not actively pursued for nearly 30 years. In 1999, the brush biopsy technique (recently renamed the BrushTest) was introduced to dentistry. It was reported to be an efficacious, sensitive, and specific diagnostic adjunct in which a transepithelial collection (from surface to basal cell layer) of disaggregated oral mucosa epithelial cells was removed by a helical-shaped, stiff nylon bristle brush and immediately transferred ("smeared") to a clear glass microscope slide.[56] The collected cells were fixed with an alcohol solution and, following drying, were placed in a plastic protective case and sent to a central laboratory for computer-assisted analysis followed by examination of computer-selected areas by a trained cytopathologist. The cells were to be collected in a painless or mildly uncomfortable manner verifying obtainment of all epithelial levels by the clinical sight of pinpoint bleeding and redness of the upper vascular plexus with the superficial underlying connective tissue. Subsequent to the seminal report of this technique, there has been a series of case reports and investigations that either tout or dispute the technique's accuracy.[57-62] There have also been reports that all techniques that attempt to transfer collected cells from a brush device to the planar surface of a microscope slide can fail to transfer up to 80% of the cells distributed on the brush's bristles.[63,64] There has also been controversy about the cost/benefit ratio of the brush biopsy, since a positive or atypical finding of possible epithelial dysplasia would mandate a second procedure, the gold standard surgically invasive biopsy.

During the 1990s a revolutionary new Pap smear technique garnered FDA approval following several large phase-3 clinical trials.[64-67] The adjunctive diagnostic technique, known as liquid-based cytology, is reported to increase the accuracy of Pap smears.[67] The major technical improvement is that the brush-collected cells are directly transferred into a container with methanol- or ethanol-based liquid preservative/fixative; the brush's bristle head is also placed in the liquid container. Upon arrival of the solution at the pathology laboratory, a patented machine then filters, disperses, collects, and transfers the epithelial cells of the solution to a glass slide. The cells are placed in a monolayer greatly reducing overlapping epithelial cells; in addition, obscuring elements such as inflammation, debris, mucous, and blood are also removed. Lastly, the cells are stained (Papanicolaou) and coverslipped prior to microscopic examination by a boarded medical pathologist.

More recently, the liquid-based technology has been adopted for use in nongynelogical clinical settings including within the oral cavity.[64] As with cervical mucosa, this technique utilized to obtain a transepithelial sampling of oral mucosa has the same potential to result in an improved evaluation of the disaggregated cells obtained from a clinically suspicious premalignant lesion whether detected during the incandescent light examination or during one of the above-mentioned adjunctive oral cancer screening techniques.

Conclusion

Prosthodontists are in a unique position to significantly impact their patients' overall health, not only via their expertise in the art and science of prosthodontics but also by virtue of their access to patients at risk for oral cancer and the influence they may exert. The performance of careful soft tissue intraoral examination, lymph node palpation, identification of suspect lesions, use of adjunctive diagnostic techniques, and early referral for biopsy will ensure that patients are afforded state-of-the-art prosthodontic health care along with a decreased risk of morbidity and mortality.

References

1. American Cancer Society: Cancer Facts and Figures 2006. American Cancer Society, Atlanta, 2006. Available at http://www.cancer.org (accessed on June 5, 2008)
2. Shiboski CH, Shiboski SC, Silverman S Jr: Trends in oral cancer rates in the United States, 1973–1996. Community Dent Oral Epidemiol 2000;28:249-256
3. Silverman S Jr: Demographics and occurrence of oral and pharyngeal cancers: the outcomes, the trends, the challenge. J Am Dent Assoc 2001;132(suppl):7S-11S
4. National Cancer Institute: Surveillance, Epidemiology, and End Results Program Public-Use-Data, 1973–1998. Rockville, MD, National Cancer Institute, Division of Cancer Control and Population Sciences, Surveillance Research Program, Cancer Statistics Branch, 2001
5. Campisi J: Cancer, aging and cellular senescence. In Vivo 2000;14:183-188
6. Chaytor DV: Prosthodontics 1966–2042: changes in prosthodontic education, past and future. J Can Dent Assoc 2005;71:329
7. Correa L, Frigerio ML, Sousa SC, et al: Oral lesions in elderly population: a biopsy survey using 2250 histopathological records. Gerodontology 2006;23:48-54
8. Jainkittivong A, Aneksuk V, Langlais RP: Oral mucosal conditions in elderly dental patients. Oral Dis 2002;8:218-223
9. Gellrich NC, Schramm A, Bockmann R, et al: Follow-up in patients with oral cancer. J Oral Maxillofac Surg 2002;60:380-388
10. Rogers SN, McNally D, Mahmoud M, et al: Psychologic response of the edentulous patient after primary surgery for oral cancer. J Prosthet Dent 1999;82:317-321
11. Velly AM, Franco EL, Schlecht N, et al: Relationship between dental factors and risk of upper aerodigestive tract cancer. Oral Oncol 1998;34:284-291
12. Lockhart PB, Norris CM Jr, Pulliam C: Dental factors in the genesis of squamous cell carcinoma of the oral cavity. Oral Oncol 1998;34:133-139
13. Morse DE, Katz RV, Pendrys DG, et al: Mouthwash use and dentures in relation to oral epithelial dysplasia. Oral Oncol 1997;33:338-343

14. Schoen PJ, Reinsema H, Bouma J, et al: Quality of life related to oral function in edentulous head and neck cancer patients posttreatment. Int J Prosthodont 2007;20:469-477
15. Roumanas ED, Garrett N, Blackwell KE, et al: Masticatory and swallowing threshold performances with conventional and implant-supported prostheses after mandibular fibula free-flap reconstruction. J Prosthet Dent 2006;96:289-297
16. Garrett N, Roumanas ED, Blackwell KE, et al: Efficacy of conventional and implant-supported mandibular resection prostheses: study overview and treatment outcomes. J Prosthet Dent 2006;96:13-24
17. Weischer T, Mohr C: Implant-supported mandibular telescopic prostheses in oral cancer patients: an up to 9-year retrospective study. Int J Prosthodont 2001;14:329-334
18. Weischer T, Schettler D, Mohr C: Implant-supported telescopic restoration in maxillofacial prosthetics. Int J Posthodont 1997;10:287-292
19. Sanderson RJ, Ironside JA: Squamous cell carcinomas of the head and neck. BMJ 2002;325:822-827
20. Vokes EE, Weichselbaum RR, Lippman SM, et al: Head and neck cancer. N Engl J Med 1993;328:184-194
21. Ries LAG, Melbert D, Krapcho M, et al (eds): SEER Cancer Statistics Review, 1975–2004. Bethesda, MD, National Cancer Institute, http://seer.cancer.gov/csr/1975_2004/, based on November 2006 SEER data submission, posted to the SEER web site, 2007 (accessed June 5, 2008)
22. Neville BW, Day TA: Oral cancer and precancerous lesions. CA Cancer J Clin 2002;52:195-215
23. Binnie WH, Rankin KV, Mackenzie IC: Etiology of oral squamous cell carcinoma. J Oral Pathol 1983;12:11-29
24. Kreimer AR, Clifford GM, Boyle P, et al: Human papillomavirus types in head and neck squamous cell carcinomas worldwide: a systematic review. Cancer Epidemiol Biomarkers Prev 2005;14:467-475
25. Paz I, Cook N, Odom-Maryom T, et al: Human papillomavirus (HPV) in head and neck cancer. An association of HPV 16 with squamous cell carcinoma of Waldeyer's tonsillar ring. Cancer 1997;79:595-604
26. Scully C, Cawson RC: Potentially malignant lesions. K Epidemiol Biostat 1996;1:3-12
27. Lumerman H, Freedman P, Kerpel S: Oral epithelial dysplasia and the development of invasive squamous cell carcinoma. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1995; 79:321-329
28. Bouquot JE, Ephros H: Erythroplakia: the dangerous red mucosa. Pract Periodontics Aesthet Dent 1995;7:59-67
29. Waldron CA, Shaffer WG: Leukoplakia revisited: a clinical immunopathologic study of 3256 oral leukoplakias. Cancer 1975;36:1386-1392
30. Langlais RP, Miller CS: Color Atlas of Common Oral Diseases (ed 1). Philadelphia, PA, Lea and Febiger, 1992, pp. 54-55
31. Silverman S, Jr, Gorsky M, Lozada F: Oral leukoplakia and malignant transformation. A follow-up study of 257 patients. Cancer 1984;53:563-568
32. Lumerman H, Friedman P, Kerpel S: Oral epithelial dysplasia and the development of invasive squamous carcinoma. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1995; 79:321-329
33. Shibuya H, Amagasa T, Seto K, et al: Leukoplakia-associated multiple carcinomas in patients with tongue carcinoma. Cancer 1986;57:843-846
34. Silverman S Jr: Oral Cancer (ed 5). Hamilton, BC, Decker, 2003, pp. 40-42
35. Shafer WG, Hine MK, Levy BM: A Textbook of Oral Pathology (ed 4). Philadelphia, PA, Saunders, 1983, pp. 108
36. Glazer HS: Spotting trouble: without an oral cancer screening, no dental exam is complete. AGD Impact 2003;31:18-19
37. Sciubba JJ: Oral cancer ands its detection: history-taking and the diagnostic phase of management. J Am Dent Assoc 2001;132(Suppl):12S-5S
38. John MT, Szentpetery A, Steele JG: Association between factors related to the time of wearing complete dentures and oral health-related quality of life in patients who maintained a recall. Int J Prosthodont 2007;20:31-36
39. Horowitz AM, Canto MT, Child WL: Maryland adults' perspectives on oral cancer prevention and early detection. J Am Dent Assoc 2002;133:1058-1063
40. Horowitz AM, Moon HS, Goodman HS, et al: Maryland adults' knowledge of oral cancer and having oral cancer examinations. J Public Health Dent 1998;58:281-287
41. Cruz GD, Ostroff JS, Kumar JV, et al: Preventing and detecting oral cancer: oral health care providers' readiness to provide health behavior counseling and oral cancer examinations. J Am Dent Assoc 2005;136:594-601
42. Friedlander AH, Marder SR, Pisegna JR, et al: Alcohol abuse and dependence. J Am Dent Assoc 2003;134:731-740
43. Friedlander AH, Norman DC: Geriatric alcoholism. J Am Dent Assoc 2006;137:330-337
44. Brown RS, Bottomley WK, Abromovich K, et al: Immediate biopsy versus a therapeutic trial in the diagnosis of vesiculobullous/vesiculoerosive oral lesions. Oral Surg Oral Med Oral Pathol 1992;73:694-697
45. Huber MA, Bsoul SA, Terezhalmy GT: Acetic acid wash and chemiluminescent illumination as an adjunct to conventional oral soft tissue examination for the detection of dysplasia: a pilot study. Quintessence Int 2004;35:378-384
46. Lingen MW, Kalmar JR, Karrison T, et al: Critical evaluation of diagnostic aids or the detection of oral cancer. Oral Oncol 2008;44:10-12
47. Ram S, Siar CH: Chemiluminescence as a diagnostic aid in the detection of oral cancer and potentially malignant epithelial lesions. Int J Oral Maxillofac Surg 2005;34:521-527
48. Epstein JB, Gorsky M, Lonky S, et al: The efficacy of oral lumenoscopy (Vizilite) in visualizing oral mucosal lesions. Spec Care Dent 2006;26:171-174
49. Kerr AR, Sirois DA, Epstein JB: Clinical evaluation of chemiluminescent lighting: an adjunct for oral mucosal examinations. J Clin Dent 2006;17:59-63
50. Oh ES, Laskin DM: Efficacy of the ViziLite system in the identification of oral lesions. J Oral Maxillofac Surg 2007;65:424-426
51. Epstein JB, Silverman S Jr, Epstein JD, et al: Analysis of oral lesion biopsies identified and evaluated by visual examination, chemiluminescence and toluidine blue. Oral Oncol 2008;44:538-544
52. Lane PM, Gilhuly T, Whitehead P, et al: Simple device for the direct visualization of oral cavity tissue fluorescence. J Biomed Opt 2006;11:024006
53. Poh CF, Williams PM, Zhang L, et al: Direct fluorescence visualization of clinically occult high-risk oral premalignant disease using a simple hand-held device. Head Neck 2007;29:71-76
54. Poh CF, Zhang L, Anderson SW, et al: Fluorescence visualization detection of field alterations in tumor margins of oral cancer patients. Clin Cancer Res 2006;12:6716-6722
55. Kahn MA: Oral cancer screening aids. Inside Dentistry 2007;3:24-27
56. Sciubba JJ, US Collaborative OralCDx Study Group: Improving detection of precancerous and cancerous oral lesions.

Computer-assisted analysis of the oral brush biopsy. J Am Dent Assoc 1999;2130:1445-1457
57. Svirksy JS, Burns JC, Carpenter WM, et al: Comparison of computer-assisted brush biopsy results with follow up scalpel biopsy and histology. Gen Dent 2002;40:829-834
58. Poate TW, Buchanan JA, Hodgson TA, et al: An audit of the efficacy of the oral brush biopsy technique in a specialist Oral medicine unit. Oral Oncol 2004;40:829-834
59. Potter TJ, Summerlin DJ, Campbell JH: Oral malignancies associated with negative transepithelial brush biopsy. J Oral Maxillofac Surg 2003;61:674-677
60. Rick GM: Oral brush biopsy: the problem of false positives. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2003;96: 252
61. Christian DC: Computer-assisted analysis of oral brush biopsies at an oral cancer screening program. J Am Dent Assoc 2002;133:357-362
62. Scheifele C, Schmidt-Westhausen AM, Dietrich T, et al: The sensitivity and specificity of the OralCDx technique: evaluation of 103 cases. Oral Oncol 2004;40:824-828
63. Bernstein ML, Miller RL: Oral exfoliative cytology. J Am Dent Assoc 1978;96:625-629
64. Kujan O, Desai M, Sargent A, et al: Potential applications of oral brush cytology with liquid-based technology: results from a cohort of normal oral mucosa. Oral Oncol 2006;42:810-818
65. Hayama FH, Motta AC, Silva Ade P, et al: Liquid-based preparations versus conventional cytology: specimen adequacy and diagnostic agreement on oral lesions. Med Oral Pathol Oral Cir Bucal 2005;10:115-122
66. Hoelund B: Implementation of liquid-based cytology in the screening programme against cervical cancer in the county of Funen, Denmark, and status for the first year. Cytopathology 2003;14:269-274
67. Schledermann D, Ejersbo D, Hoelund B: Improvement of diagnostic accuracy and screening conditions with liquid-based cytology. Diagn Cytopathol 2006;34:780-785