



Squamous cell carcinoma accounts for about 90% of cancers of the mouth.

Oral Pathology

Denise Rizzolo, PhD, PA-C, Mona M. Sedrak, PhD, PA-C

Primary care clinicians widely agree on the importance of good oral health and helping their patients maintain it—but how many feel sufficiently knowledgeable and experienced to perform a skillful oral examination?

Denise Rizzolo is a PA at the Care Station in Springfield, New Jersey, and Assistant Professor in the Physician Assistant Program at Seton Hall University in South Orange, New Jersey. **Mona M. Sedrak** is Associate Professor in the Seton Hall University PA Program.

CONTINUING EDUCATION INFORMATION

TARGET AUDIENCE: This activity has been designed to meet the educational needs of physicians, physician assistants, and nurse practitioners committed to maintaining their patient's oral health.

- **Original Release Date:** June 2009
- **Expiration Date:** June 30, 2010
- **Estimated Time to Complete This Activity:** 1 hour
- **Medium:** Printed journal and online CME
- **Sponsored by** Postgraduate Institute for Medicine

PROGRAM OVERVIEW: The primary objective of this educational initiative is to provide clinicians in primary care with the most up-to-date information regarding the presentation, diagnosis, and treatment of common oral pathologies.

EDUCATIONAL OBJECTIVES: After completing this activity, the participant should be better able to:

- Differentiate among the most common red oral lesions and white oral lesions.
- Specify oral pathologies for which biopsy and excision are recommended.
- Describe the pathologies most closely associated with oral carcinoma, including their etiologies.
- Describe the clinical manifestations and disease courses of two common herpetic oral infections.
- Review treatment strategies for common oral pathologies.

FACULTY: **Denise Rizzolo, PhD, PA-C**, is a physician assistant at the Care Station in Springfield, New Jersey, and Assistant Professor in the Physician Assistant Program at Seton Hall University, South Orange, New Jersey. **Mona M. Sedrak** is Associate Professor in the Seton Hall University PA Program.

PHYSICIANS

Accreditation Statement: This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint sponsorship of Postgraduate Institute for Medicine (PIM) and Quadrant HealthCom Inc. PIM

is accredited by the ACCME to provide continuing medical education for physicians.

Credit Designation: Postgraduate Institute for Medicine designates this educational activity for a maximum of 1.0 *AMA PRA Category 1 Credit*[™]. Physicians should only claim credit commensurate with the extent of their participation in the activity.

PHYSICIAN ASSISTANTS

The American Academy of Physician Assistants accepts AMA category 1 credit for the PRA from organizations accredited by ACCME.

NURSE PRACTITIONERS

This program has been approved by the Nurse Practitioner Association New York State (The NPA) for 1.0 contact hour.

DISCLOSURE OF CONFLICTS OF INTEREST:

Postgraduate Institute for Medicine (PIM) assesses conflict of interest with its instructors, planners, and managers, and other individuals who are in a position to control the content of CME activities. All relevant conflicts of interest that are identified are thoroughly vetted by PIM for fair balance, scientific objectivity of studies utilized in this activity, and patient care recommendations. PIM is committed to providing its learners with high-quality CME activities and related materials that promote improvements or quality in health care and not a specific proprietary business interest of a commercial interest.

The faculty reported the following financial relationships or relationships to products or devices they or their spouse/life partner have with commercial interests related to the content of this CME activity: **Denise Rizzolo, PhD, PA-C**, and **Mona Sedrak, PhD, PA-C**, reported no significant financial relationship with any commercial entity related to this activity.

The planners and managers reported the following financial relationships or relationships to products or devices they or their spouse/life partner have with commercial interests related to the content of this CME activity: **Jan Hixon, RN, BSN, MA**, **Linda Graham, RN, BSN, BA**, and **Trace Hutchison, PharmD**, reported no significant financial relationship with any commercial entity related to this activity.

METHOD OF PARTICIPATION: The fee for participating and receiving CME credit for this activity is \$10.00. During the period **June 2009** through **June 30, 2010**, participants must 1) read the learning objectives and faculty disclosures; 2) study the educational activity; 3) go to www.clinicianreviews.com, follow links to the posttest for this activity, and provide payment information via our secure server; 4) complete the 10-question posttest by recording the best answer to each question; and 5) record their response to each of the additional evaluation questions. If you have any questions, call (800) 423-3576 or e-mail evaluations@pimed.com. Only upon completion of an activity evaluation and a posttest with a minimum score of 70% will a statement of credit become accessible electronically to the participant.

DISCLOSURE OF UNLABELED USE: This educational activity may contain discussion of published and/or investigational uses of agents that are not indicated by the FDA. Postgraduate Institute for Medicine (PIM), The NPA, and Quadrant HealthCom Inc. do not recommend the use of any agent outside of the labeled indications.

The opinions expressed in this educational activity are those of the faculty and do not necessarily represent the views of PIM, The NPA, or Quadrant HealthCom Inc. Please refer to the official prescribing information for each product for discussion of approved indications, contraindications, and warnings.

DISCLAIMER: Participants have an implied responsibility to use the newly acquired information to enhance patient outcomes and their own professional development. The information presented in this activity is not meant to serve as a guideline for patient management. Any procedures, medications, or other courses of diagnosis or treatment discussed or suggested in this activity should not be used by clinicians without evaluation of their patient's conditions and the possible contraindications or dangers in use, review of any applicable manufacturer's product information, and comparison with recommendations of other authorities.

According to a 2000 report from then-Surgeon General David Satcher, MD,¹ great strides have been made to improve oral health in the United States, but a “silent epidemic” of dental and oral diseases continues to affect those with limited or no access to dental care. Fewer than two-thirds of US adults report having visited a dentist in the past 12 months; for every adult 19 years or older without medical insurance, three lack dental insurance.¹ Amid a shortage of dental professionals and significant barriers to dental care for many patients, primary care providers are often required to evaluate and treat a variety of dental and oral diseases.²

A thorough physical examination of the mouth and face can reveal signs of an underlying systemic disease, drug use, physical abuse, harmful habits or addictions, and general health status.¹ However, examination of the oral cavity is often overlooked or poorly performed, with many missed opportunities to diagnose various oral pathologies.

In a 2000 survey of 70 physicians, for example, Morgan et al³ found that 84% of respondents considered it important to conduct oral examinations, but only 19% did so routinely; 56% lacked confidence in their oral examination skills, and 77% felt their training was insufficient. In the physicians’ attempts to identify 12 oral pathology photographs, 80% misdiagnosed early squamous cell carcinoma (SCC).³

More recently, Danielsen et al⁴ identified eight oral health competencies for PAs and NPs (see table,⁴ above) and investigated these clinicians’ self-perceived skill levels in performing them. While 82% of survey respondents agreed on the importance of mastering these competencies, fewer than half expressed confidence in their skills.

General Oral Health Competencies for Physician Assistants and Nurse Practitioners

The clinician should be able and prepared to:

- Perform a thorough and competent oral examination
- Distinguish between normal and abnormal structures
- Identify obvious pathology and conditions of the oral cavity (eg, oral cancers, fungal infections, traumatic conditions, dental diseases, and congenital conditions)
- Inform adults and parents of young children what to expect in eruption patterns of primary and permanent teeth
- Recognize symptoms and manifestations of common diseases of the oral cavity
- Recognize oral symptoms of systemic diseases (eg, anemia, syphilis, tuberculosis, thyroid dysfunction, Sjögren’s disease, xerostomia)
- Explain to patients what various dental specialties can do for them
- Improve PA/NP–dentist interface and referral practices

Data extracted from: Danielsen et al. *J Physician Assistant Education*. 2006.⁴

Meanwhile, the *Healthy People 2010* objectives for oral health include reduction in the incidence of periodontal disease and increased early detection of oral and pharyngeal cancers.⁵ The importance of good oral health and its impact on the general health and well-being of patients is acknowledged and understood among primary care clinicians.^{3,4} Yet limitations in training and experience, compounded by a heavy clinical load, may hinder them from identifying common oral pathologies.

This review of oral pathologies commonly seen in primary care is intended to help clinicians form a better understanding of their presentation, diagnosis, and treatment, leading to improved oral health for their patients.

RED LESIONS

Erythroplakia

This asymptomatic red patch of the oral cavity most commonly presents on the floor of the mouth, then in the retromolar area. The lesion’s cause is unknown, but its etiologic factors are believed to be similar to those for oral carcinoma: tobacco and alcohol use, nutritional deficien-

cies, and chronic irritations.⁶

Erythroplakia occurs in patients between ages 50 and 70 and most frequently in older men.⁷ Though less common than leukoplakia (described below), erythroplakia is considered more serious: approximately 90% of lesions demonstrate dysplasia on histologic examination, with a high rate of transformation to SCC.^{7,8}

Diagnosis is made by incisional biopsy. Treatment consists of surgical excision with margins that ensure complete removal. Frequent follow-up is necessary, as any recurrence may suggest early carcinoma. In such cases, immediate referral should be made to an oral and maxillofacial surgeon or a head and neck surgeon for evaluation and management.

Pyogenic Granuloma

Despite its name, a pyogenic granuloma contains neither pus nor granulomatous tissue.⁹ It is a benign red mass composed of hyperplastic tissue, most commonly presenting on the gingiva¹⁰ (see Figure 1, page 28).

Common causes are trauma, tartar buildup, and irritation caused by such foreign objects as

dentures or dental crowns. Hormonal changes during pregnancy may increase the risk of gingival hyperplasia—hence the term *pregnancy tumor*.

Diagnosis is made by biopsy, and treatment is full excision of the lesion. Recurrence is rare unless the lesion or offending stimulus has not been completely removed.⁹

WHITE LESIONS

Lichen Planus

This common, chronic mucocutaneous disease affects more women than men.^{11,12} It is usually seen in middle-aged persons, rarely affecting children.

Several subtypes of lichen planus exist. Most common is the *reticular form*, which is characterized by numerous interlacing lines called *Wickham’s striae*, usually seen on the buccal mucosa. Next most common is the *plaque form*. Unlike leukoplakia, the plaque form of lichen planus has a multifocal distribution, with appearances ranging from a smooth, slightly elevated plaque to an irregularly shaped lesion. Primary sites are the buccal mucosa and the tongue.¹¹

The *atrophic form* of lichen planus is usually erythematous and found on the buccal and gingival mucosa. Unlike patients with the reticular or plaque subtypes, those with the atrophic form are likely to complain of pain and burning. Finally, the *erosive form* of lichen planus is usually erythematous with central ulcerations. It commonly presents on the buccal mucosa and is painful.¹¹

Diagnosis of any form of lichen planus is made by biopsy. In severe cases, topical or systemic corticosteroids will control but not cure the disease. Since the condition is chronic with a waxing and waning course, patients should be examined periodically.

continued on next page >>

FIGURE 1



Pyogenic granuloma of the buccal and lingual papillary gingiva.

FIGURE 2



Generalized leukoplakia of the buccal mucosa.

FIGURE 3



Actinic (solar) cheilitis of the lower vermilion border with ulceration.

A low incidence of malignant transformation has been documented in the atrophic and erosive forms; patients with these subtypes should be referred to an oral and maxillofacial surgeon for follow-up.^{12,13}

Idiopathic Leukoplakia

The term *leukoplakia* is used to describe a white patch or plaque on the oral mucosa that is not attributable to any other disease

(eg, lichen planus, candidiasis, leukoedema, white sponge nevus⁷; see Figure 2). Leukoplakia is generally seen in patients older than 40, but it can present at any age.⁷ One of its most common causes is use of tobacco, smoked or smokeless. Other possible etiologic factors are alcohol abuse, trauma, and iron deficiency anemia.⁷

Most leukoplakias are asymptomatic and present on the mandibular mucosa, buccal mucosa, and tongue. Clinical appearance can range from an inconspicuous, relatively normal vague whiteness to definitively white, thickened, leathery fissured, or verrucous plaque.^{7,14} Biopsy is mandatory, since some leukoplakias develop into oral SCC. Referral to an oral and maxillofacial surgeon is recommended, since treatment requires complete removal of the lesion via excision or laser ablation. Patients should be counseled to discontinue tobacco and alcohol use. Close follow-up is necessary to examine for recurrence or new lesions.

Candidiasis

Oral candidiasis is a common oral mycotic infection. The most frequently reported etiologic agent is the *Candida* genus of fungi (with *Candida albicans* the most common species).^{14,15} Typically a benign superficial infection, candidiasis has many predisposing factors, including diabetes mellitus, pregnancy, systemic steroid therapy, topical corticosteroid therapy, poor oral hygiene, malabsorption or malnutrition, systemic antibiotic therapy, cancer chemotherapy and radiation, and other causes of immunosuppression.¹⁴ It affects men and women equally and has no age predilection. In immunocompromised patients, including those with AIDS, infection may extend to the alimentary tract.

While presentation may vary,

the acute pseudomembranous form also known as *thrush* is most common. Patients are usually asymptomatic but notice white plaques on the tongue and buccal mucosa.¹⁴ Lesions become atrophic and painful, with a redder, more irritated appearance.¹⁵

Diagnosis is made by taking an intraoral scraping and examining the stained specimen for the presence of hyphae.^{14,15}

An isolated candidiasis is treated by topical applications of antifungals (eg, clotrimazole, ketoconazole, nystatin),^{16,17} continued for at least one week beyond the lesions' disappearance.

Nicotine Stomatitis

Nicotine stomatitis is a tobacco-related lesion commonly seen in middle-aged men who smoke pipes or cigars.^{7,6} It has also been reported in individuals who drink extremely hot beverages and in those who engage in "reverse smoking" (ie, with the lit end of the cigarette placed in the mouth).^{7,18,19} The lesion, found on the palate mucosa, has a white cobblestone appearance with red punctate spots marking the inflamed openings of the minor salivary gland ducts.⁷

Isolated nicotine stomatitis is benign; however, the practice of reverse smoking increases the risk of oral carcinoma.¹⁸ Therefore, if dysplasia or oral carcinoma is suspected, a biopsy should be performed. With smoking cessation, lesions usually resolve in four to six weeks.¹³

Solar Cheilitis

Actinic or solar cheilitis is a condition caused by chronic sun exposure affecting the vermilion border of the lips (especially the lower lip). The extent of damage is directly related to the patient's total cumulative exposure to sunlight. White, fair individuals are predominately affected.²⁰

The affected portion of the lip appears atrophic, pale to silvery

gray, and glossy; the lower lip can become slightly firm and swollen²¹ (see Figure 3). Fissuring and wrinkling at the angles of the lips are often seen. In severe cases of actinic cheilitis, scaling, cracking, erosion, and ulceration can occur.

There is no specific treatment for mild cases of this condition, but all patients should be urged to use sun-blocking lip balm. Because chronic sun exposure and damage often lead to carcinoma, biopsy and referral are indicated in severe cases. In these cases, the vermilion border can be removed (a procedure called a *lip shave*).²⁰

Hairy Tongue

This benign condition involves elongation of the filiform papillae on the dorsal surface of the tongue. While hairy tongue is generally idiopathic, several possibly associated substances include broad-spectrum antibiotics, systemic steroids, mouth rinses containing hydrogen peroxide, and tobacco⁶; radiotherapy for cancers of the head and neck may also be implicated.²² Bacteria, fungi, and debris can become trapped in the elongated papillae. Patients are usually asymptomatic, but severely elongated papillae may trigger a gagging sensation.

On inspection, the papillae may be several millimeters long, and color may range from tan to deep brown (see Figure 4, page 29). These characteristics are influenced by the patient's diet and oral hygiene, and the composition of the bacteria that inhabit the papillary surface.²³

Diagnosis is made clinically. Biopsy is not indicated except to identify excessive candida on the tissue surface. Treatment comprises improved oral hygiene, smoking cessation, and elimination of exposure to any other substances that may be contributing to the condition.²³

Geographic Tongue

Also known as *erythema migrans* or *benign migratory glossitis*, geographic tongue is a benign condition affecting 1.0% to 2.5% of the population; it appears to occur more commonly in children and young adults than in older individuals.^{24,25} In the United States, white and black patients appear more susceptible than Mexican-Americans, and nonsmokers more susceptible than smokers.²⁶ The lesions may change in location, pattern, and size within minutes to hours.

Patients usually present with white, annular lesions that have atrophic red centers varying in intensity along the dorsal tongue. The lesions may spontaneously disappear and occasionally can be painful, particularly if the patient eats hot or spicy foods.²⁵

Diagnosis is made on clinical appearance, and biopsy is rarely indicated. Geographic tongue is self-limiting and usually asymptomatic, and treatment is generally not required. Patients may need reassurance that the condition is benign.

ULCERATIVE LESIONS

Squamous Cell Carcinoma

Oral and pharyngeal cancers account for the fourth most common cancers among black men in the US, the seventh most common among white men, and the 14th most common among women.^{5,27} SCC represents 90% of cancers of the mouth.^{7,8,28} Alcohol use and tobacco use are two of the most common causes of oral carcinoma; other implicated factors include presence of human papillomavirus and certain other viruses, age greater than 45, black race, male gender, and marijuana use.⁸

SCC typically manifests as a white plaque (*leukoplakia*), with or without reddish reticulation (*erythroplakia*).¹³ The most common location of SCC is the lateral surface of the tongue, followed by the anterior floor of the

mouth, then the buccal vestibule^{29,30} (see Figure 5).

Lesions can vary in appearance, depending on the location and degree of dysplasia, with colors ranging from red to white. Biopsy is mandatory for all suspicious lesions, and prompt referral to an oral maxillofacial surgeon or a head and neck surgeon is essential. Treatment of resectable SCC of the oral cavity depends on the location and stage of the primary tumor; local surgery of the tumor and regional surgery of the neck nodes are considered and planned according to the patient's unique circumstances. Nonsurgical options for the treatment of cutaneous SCC include topical chemotherapy, topical immune response modifiers, photodynamic therapy, radiotherapy, and systemic chemotherapy.

By the time of diagnosis, nearly 50% of oral and pharyngeal carcinomas have metastasized.⁸ If they are detected when the tumor is still localized, the five-year survival rate is 82% for white patients and 72% for black patients; in cases in which distant metastasis has already occurred, survival falls to 21% among whites and 18% among blacks.⁸

Aphthous Ulcer

Aphthous ulcers or *canker sores* are the most common nontraumatic ulceration to affect the oral mucosa. Although their cause is unknown, they have been linked to a focal immune dysfunction.^{31,32} These painful recurrent lesions are classified according to size, which varies. They may appear on the vestibular and buccal mucosa, tongue, soft palate, and floor of the mouth. Patients occasionally report prodromal symptoms of tingling or burning.

Typically, the more common *minor* aphthous ulcers appear as a single oval lesion measuring less than 0.5 cm in diameter, with pain often disproportionate to

their size. They are covered by a yellow fibrinous membrane and surrounded by an erythematous halo.³² These lesions generally last seven to 10 days. *Major* aphthous ulcers, considered the most severe expression of aphthous stomatitis, are larger than 0.5 cm and more painful, and they may take as long as six weeks to heal with scar formation.

In patients with minor aphthous ulcers in limited numbers, no treatment is necessary other than a bland mouthwash, such as sodium bicarbonate dissolved in warm water. For those who are more severely affected, a topical steroid, a steroid rinse (for less accessible lesions), or an oral corticosteroid may be prescribed.^{30,32} Patients should be advised that recurrence is common.

Contact Allergy

Any lesion triggered by a foreign substance can be considered a contact allergy–reactive lesion. Though more common on the skin, such reactions can also occur intraorally. Common offending substances include toothpaste, mouthwash, candy, chewing gum, cinnamon, topical antimicrobials, iodine, essential oils, aspirin, and denture base material.³³ Lesions appear adjacent to the offending antigen and may be erythematous, vesicular, and even ulcerative, depending on the degree of insult to the mucosal tissue.

A careful, detailed history is key to diagnosis. While biopsy is not necessarily indicated, it may confirm the suspected diagnosis. Treatment consists of discontinuing the offending agent; topical steroids may facilitate resolution of the lesion.³³

VIRAL LESIONS

Herpes Simplex 1 Virus and Herpetic Gingivostomatitis

The soft tissue of the mouth, oral pharynx, and salivary glands is

FIGURE 4



Hairy tongue with elongated, darkened papillae.

FIGURE 5



Oral squamous cell carcinoma of the buccal vestibule, extending to the alveolar ridge.

FIGURE 6



On the soft palate, multiple vesicles representing herpetic stomatitis.

susceptible to various viral infections. Herpes viruses represent the largest family of viruses with oral manifestations; the most common type is *human herpesvirus 1* or *herpes simplex virus type 1* (HSV-1).³⁴ HSV-1 inoculation occurs through physical contact with an infected individual and has a two- to 12-day incubation period.³⁵ Most individuals are exposed to HSV-1 during childhood but cannot recall an outbreak.^{34,35}

continued on next page >>

Typically, patients present with painful oral lesions within several days after exposure. Many, however, have subclinical infections with symptoms so subtle as to go unnoticed.

In children, herpes virus commonly manifests as *primary herpetic gingivostomatitis*.³⁵ This disease is extremely contagious, especially in day care facilities and other situations involving close contact. During an outbreak, most children ages 1 to 3 become infected, often with severe illness that manifests as numerous painful lesions on the buccal and gingival mucosa.³⁵ These lesions begin as vesicles that unroof and coalesce to form superficial ulcers (see Figure 6, page 29). Patients may experience fever, arthralgia, malaise, anorexia, headache, and cervical lymphadenopathy.^{34,35}

Once the primary infection is resolved, HSV-1 migrates to regional nerve ganglia, remaining dormant until the virus is reactivated. The virus then travels distantly down the nerve tracts to nerve cells in the epithelium, where it replicates in the form of small, painful vesicles that appear within 24 hours of reactivation; the vesicles erupt to form shallow ulcers that subsequently scab and crust.³⁶ The lesions, often described as tingling, burning, or itching, recur at or near the same site with each episode, usually on the vermilion and surrounding skin.^{34,35} Secondary infections are limited in scope, resolving in 10 to 12 days, and rarely have systemic manifestations.³⁴

More than 90% of the US population has serum antibodies against HSV-1 but fewer than half of those affected ever experience recurrent herpetic lesions.³⁴ The virus may be reactivated by exposure to sunlight (“fever blisters”) or to cold (“cold sores”), trauma, stress, or immunosuppression.³⁴ Recurrences may develop as seldom as once per year

or as often as monthly.

The diagnoses of HSV-1 and herpetic gingivostomatitis are usually made clinically. Diagnosis can be confirmed by viral culture (which requires two to four days for positive identification).³⁵

For herpetic gingivostomatitis, early treatment with acyclovir suspension, administered by swish-and-swallow, is reported effective in shortening the duration of symptoms.^{35,37,38}

Recurrent HSV-1 lesions of the vermilion borders of the lip and perioral skin are primarily a cosmetic problem that can be attenuated by a number of OTC topical anesthetic agents. To prevent development of herpetic whitlow, these preparations should be applied with a cotton swab rather than the fingertip.³⁴

During the prodromal stage of HSV-1, topical acyclovir ointment can be used successfully to resolve mucosal lesions. Because it is poorly absorbed through the vermilion border and perioral skin, however, it should not be considered a first-line treatment. Systemic acyclovir has also been used to treat recurrent HSV-1.³⁴ Medications must be started within 72 hours of symptom onset. Fluids, rest, oral lavage, analgesics, and antipyretics are also essential components of treatment.³⁸

CONCLUSION

Healthy dentition is just one component of good oral health. Eating, speaking, and facial communication all require healthy oral, dental, and craniofacial tissue. Primary care clinicians who are well versed and experienced in examination of the oral cavity can help keep their patients free of chronic oral-facial pain conditions, oral and pharyngeal cancers, oral soft-tissue lesions, and other diseases and disorders—and, when such conditions are present, provide accurate, timely diagnosis and effective treatment. **CR**

Beginning with this issue of *Clinician Reviews*, readers can view or take the continuing education posttest by going to www.ClinicianReviews.com and following the link to the current CE activity.

REFERENCES

1. National Institute of Dental and Craniofacial Research, National Institutes of Health. *Oral Health in America: A Report of the Surgeon General—Executive Summary*. Rockville, MD: US Dept of Health and Human Services; 2000:1,5-6.
2. Berg P, Coniglio D. Oral health in children overlooked and undertreated. *JAAPA*. 2006;19(4):40, 42, 44 passim.
3. Morgan R, Tsang J, Harrington N, Fook L. Survey of hospital doctors' attitudes and knowledge of oral conditions in older patients. *Postgrad Med J*. 2001;77(908):392-394.
4. Danielsen R, Dillenberg J, Bay C. Oral health competencies for physician assistants and nurse practitioners. *J Physician Assistant Education*. 2006; 17(4):12-16.
5. US Department of Health and Human Services. *Healthy People 2010: Understanding and Improving Health* (2000). 21. Oral health. www.healthypeople.gov/document/HTML/Volume2/21Oral.htm. Accessed May 21, 2009.
6. Taybos G. Oral changes associated with tobacco use. *Am J Med Sci*. 2003;326(4):179-182.
7. Neville BW, Day TA. Oral cancer and precancerous lesions. *CA Cancer J Clin*. 2002;52(4):195-215.
8. Silverman S Jr. Demographics and occurrence of oral and pharyngeal cancers: the outcomes, the trends, the challenge. *J Am Dent Assoc*. 2001;132 suppl:75-115.
9. Al-Khateeb T, Ababneh K. Oral pyogenic granuloma in Jordanians: a retrospective analysis of 108 cases. *J Oral Maxillofac Surg*. 2003;61(11): 1285-1288.
10. Saravana GH. Oral pyogenic granuloma: a review of 137 cases. *Br J Oral Maxillofac Surg*. 2009 Feb 7. [Epub ahead of print]
11. Eisen D. The clinical features, malignant potential, and systemic associations of oral lichen planus: a study of 723 patients. *J Am Acad Dermatol*. 2002;46(2):207-214.
12. Rajenthiran R, McLean NR, Kelly CG, et al. Malignant transformation of oral lichen planus. *Eur J Surg Oncol*. 1999;25(5):520-523.
13. Bsoul SA, Huber MA, Terezhalmay GT. Squamous cell carcinoma of the oral tissues: a comprehensive review for oral healthcare providers. *J Contemp Dent Pract*. 2005;6(4):1-16.
14. Scardina GA, Fucà G, Ruggieri A, et al. Oral candidiasis and oral hyperplastic candidiasis: clinical presentation. *Res J Biol Sci*. 2007;2(4):408-412.
15. Lynch DP. Oral candidiasis: history, classification, and clinical presentation. *Oral Surg Oral Med Oral Pathol*. 1994;78(2):189-193.
16. Worthington HV, Clarkson JE, Eden TOB. Interventions for treating oral candidiasis for patients with cancer receiving treatment. *Cochrane Database Syst Rev*. 2007;(2):CD001972.
17. Albougy HA, Naidoo S. A systematic review of the management of oral candidiasis associated with HIV/AIDS. *SADJ*. 2002;57(11):457-466.
18. Mercado-Ortiz G, Wilson D, Jiang DJ. Reverse smoking and palatal mucosal changes in Filipino women: epidemiological features. *Aust Dent J*. 1966;41(5):300-303.
19. Rossie KM, Guggenheimer J. Thermally induced 'nicotine' stomatitis: a case report. *Oral Surg Oral Med Oral Pathol*. 1990;70(5):597-599.
20. Regezi JA, Sciubba JJ, Jordan RCK. *Oral Pathology: Clinical Pathologic Correlations*. 4th ed. St. Louis, MO: WB Saunders; 2002.
21. Markopoulos A, Albanidou-Farmaki E, Kayavis I. Actinic cheilitis: clinical and pathologic characteristics in 65 cases. *Oral Dis*. 2004;10(4):212-216.
22. Yuca K, Calka O, Kiroglu AF, et al. Hairy tongue: a case report. *Acta Otorhinolaryngol Belg*. 2004;58(4):161-163.
23. Sarti GM, Haddy RI, Schaffer D, Kihm J. Black hairy tongue. *Am Fam Physician*. 1990;41(6): 1751-1755.
24. Jankittivong A, Langlais RP. Geographic tongue: clinical characteristics of 188 cases. *J Contemp Dent Pract*. 2005;6(1):123-135.
25. Assimakopoulos D, Patrikakos G, Fotika C, Elisaf M. Benign migratory glossitis or geographic tongue: an enigmatic oral lesion. *Am J Med*. 2002;113(9): 751-755.
26. Shulman JD, Carpenter WM. Prevalence and risk factors associated with geographic tongue among US adults. *Oral Dis*. 2006;12(4):381-386.
27. Greenlee RT, Murray T, Bolden S, Wingo PA. Cancer statistics, 2000. *CA Cancer J Clin*. 2000; 50(1):7-33.
28. Oral Cancer Foundation. Oral cancer facts. www.oralcancerfoundation.org/facts. Accessed May 21, 2009.
29. Rizzolo D, Hanifin C, Chiodo TA. Oral cancer: how to find a hidden killer in 2 minutes. *JAAPA*. 2007;20(10):42-47.
30. Cuffari L, Tesseroli de Siquiera JT, Nemr K, Rapa-port A. Pain complaint as the first symptom of oral cancer: a descriptive study. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2006;102(1):56-61.
31. Woo SB, Stonis ST. Recurrent aphthous ulcers: a review of diagnosis and treatment. *J Am Dent Assoc*. 1996;127(8):1202-1213.
32. Tillis TS, McDowell JD. Differential diagnosis: is it herpes or aphthous? *J Contemp Dent Pract*. 2002; 3(1):1-15.
33. De Rossi SS, Greenberg MS. Intraoral contact allergy: a literature review and case reports. *J Am Dental Assoc*. 1998;129(10):1435-1441.
34. Lynch DP. Oral viral infections. *Clin Dermatol*. 2000;18(5):619-628.
35. Amir J. Clinical aspects and antiviral therapy in primary herpetic gingivostomatitis. *Paediatr Drugs*. 2001;3(8):593-597.
36. Kolokotronis A, Doulmas S. Herpes simplex virus infection, with particular reference to the progression and complications of primary herpetic gingivostomatitis. *Clin Microbiol Infect*. 2006; 12(3): 202-211.
37. Nasser M, Federowicz Z, Koshnevisan MH, et al. Acyclovir for treating primary herpetic gingivostomatitis. *Cochrane Database Syst Rev*. 2008;(4): CD006700.
38. Faden H. Management of primary herpetic gingivostomatitis in young children. *Pediatr Emerg Care*. 2006;22(4):268-269.