

Oral Lesions You Can't Afford to Miss

Being able to promptly recognize and diagnose oral lesions is critical to heading off several potentially serious conditions. This article and photo guide can help.

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PRACTICE RECOMMENDATIONS

- Perform a biopsy and carefully monitor all potentially malignant oral lesions, including leukoplakia and erythroplakia. **A**
- Consider evaluation for human immunodeficiency virus infection for any patient who has acute necrotizing ulcerative gingivitis/acute necrotizing ulcerative periodontitis, recurrent candidiasis, or oral hairy leukoplakia. **A**
- Include melanoma in the differential diagnosis of oral pigmented lesions that have any features of cutaneous melanoma (eg, asymmetry, irregular borders, or variable or changing color). **A**

Strength of recommendation (SOR)

- A** Good-quality patient-oriented evidence
- B** Inconsistent or limited-quality patient-oriented evidence
- C** Consensus, usual practice, opinion, disease-oriented evidence, case series

Family practice clinicians can play an essential role in managing their patients' oral health by promptly recognizing and diagnosing conditions that demand further medical attention, including nonodontogenic and odontogenic infections, primary oral mucosal diseases, oral manifestations of systemic disease, and malignancy. Many conditions are amenable to treatment by the primary care provider, while others will require referral to a specialist.

This article and accompanying photo guide describe the types of lesions you may encounter during examinations of the oral cavity and the corresponding diagnoses.

BE VIGILANT FOR NONODONTOGENIC CONDITIONS THAT MAY REQUIRE URGENT TREATMENT

There are several uncommon, acute nonodontogenic conditions that affect the oral cavity; when severe, they may require urgent medical attention and possible hospitalization.

Primary herpes simplex virus 1 (HSV-1) infection is generally subclinical, but some patients develop significant oral disease—called primary herpetic gingivostomatitis—that is characterized by painful, diffuse, irregular, croplike ulcerations throughout the oral cavity and lips (see Figure 1).¹ The gingiva is nearly universally affected, which distinguishes this condition from erythema multiforme and aphthous stomatitis (described later in this article). The incidence is highest in children, followed by adolescents and young adults.²

Erythema multiforme. This mucocutaneous hyper-

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URGENT TREATMENT

1 HSV-1 infection



Primary herpes simplex virus 1 infection characterized by painful, diffuse, irregular, croplike ulcerations throughout the oral cavity and lips, with focal ulceration of the gingiva.

2 Erythema multiforme



Erythema multiforme limited to the oral mucosa, with diffuse, extensive ulceration of the entire lower labial mucosa and patchy ulceration of the floor of the mouth. Note that the gingiva is spared.

3 Minor aphthous ulcers



Multiple minor aphthous ulcers of the ventrolateral tongue in a patient with complex aphthous stomatitis.

4 Major aphthous ulcer



Major aphthous ulcer of the maxillary right labial mucosa, with slightly irregular borders.

sensitivity reaction can be limited to the oral cavity and lips, without accompanying skin lesions. Flu-like symptoms, including fever and chills, are followed by acute onset of diffuse oral ulcerations that are generally limited to nonkeratinized mucosa and spare the gingiva (see Figure 2).³ Ulceration and crusting of the lips are common.

Aphthous stomatitis. Recurrent aphthous stomatitis (RAS) is a common immune-mediated inflammatory condition characterized by “canker sores,” or small round/ovoid ulcers with a well-defined erythematous halo (see Figure 3). Lesions

almost exclusively affect nonkeratinized mucosa (and never the lip vermilion) and heal within seven to 10 days, although “major” (> 0.5 cm) lesions may persist much longer (see Figure 4). A herpetiform pattern with multiple coalescing ulcers closely mimics HSV.

Small subsets of patients develop “complex” RAS, which is characterized by continuous and often multiple ulcerations that may extend into the esophagus, with associated chronic pain and compromised intake.² RAS associated with systemic conditions is reviewed below.

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COMMON DENTAL DISEASES

5 Dental abscess



Left-sided extraoral and submandibular swelling secondary to an abscessed left mandibular molar.

6 Parulis



Multiple decayed and broken-down teeth with an associated gingival swelling that represents a draining sinus tract.

7 Pericoronitis



Pericoronitis associated with a partially erupted left mandibular third molar, with gingival swelling and erythema.

8 Ulcerative periodontitis



Acute necrotizing ulcerative periodontitis in a patient with advanced human immunodeficiency virus infection. Note the crater-like gingival defects with complete loss of interdental papillae.

9 Dentoalveolar trauma



Dentoalveolar trauma of the anterior mandible with an alveolar process fracture involving 3 teeth. The right lateral incisor is completely avulsed and missing.

HOW TO SPOT SIGNS OF COMMON DENTAL DISEASES

In 2010 in the United States, close to 1.4 million emergency department visits and about \$1 billion in hospital charges were due to dental problems.⁴ Approximately 40% of these visits were made by individuals without insurance.⁴ Due to a lack of dental insurance, patients may present to a medical professional rather than a dental professional. Additionally, uninsured individuals may neglect their dental problem until it becomes a medical emergency. Family practice clinicians need to recognize dental disease and be able to provide basic management of emergencies.⁵

Dental abscess. A dental abscess can arise from pulpal infection (due to progression of caries) or periodontal infection (due to progression of periodontal disease). Pain symptoms are variable; however, intense, spontaneous cyclical pain is generally characteristic of a dental abscess of pulpal etiology, whereas a periodontal abscess can have less obvious symptoms. Swelling intraorally or extraorally indicates the spread of a localized infection (see Figure 5).

Severe infection and swelling can limit mouth opening and function and in extreme cases may obstruct swallowing and even breathing (eg, Ludwig's angina). Affected teeth may or may not demonstrate obvious findings of advanced dental disease, such as gross caries, fracture, heavy calculus deposits, or marked periodontal attachment loss. Oral examination may reveal a parulis (focal erythematous swelling of the adjacent gingiva with a central draining sinus tract) (see Figure 6) and percussion of the affected tooth is generally painful.

Pericoronitis is infection and swelling of the gingival tissues that surround a tooth, typically in association with a partially erupted third molar. Signs and symptoms include pain, discomfort with eating

and swallowing, and limited mouth opening. Examination demonstrates gingival inflammation around a tooth, with or without purulence (see Figure 7).

Acute necrotizing ulcerative gingivitis (ANUG) and periodontitis (ANUP) are severe conditions that are typically associated with psychological stress, severe malnutrition, and immunosuppression in patients with preexisting gingivitis or periodontitis.⁶ ANUG is associated with intense gingival pain, halitosis, generalized erythema, and destruction of the gingival papilla, often with bleeding.⁷ ANUP is a more advanced condition associated with damage and loss of the periodontium (including bone), often with loose teeth (see Figure 8).⁸

Trauma. Dental trauma can be limited to the teeth and soft tissues, while more severe injuries can also affect the jaw bone.⁹ Accidental falls, assault, and motor vehicle traffic accidents are the most common causes of facial fractures in the United States and are often associated with dentoalveolar trauma (see Figure 9). The most commonly fractured facial bone is the mandible, characterized by painful opening and closing and an incomplete or altered bite.¹⁰

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Which of the following is a definition of acute kidney injury?

- a. Decrease in urine output to < 0.5 mL/kg/h for 6 h
- b. Rise in serum creatinine of ≥ 0.3 mg/dL w/in 48 h
- c. Increase in creatinine of $\geq 50\%$ w/in 1 wk
- d. All of the above

For more on this topic, turn to page 31

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SIGNS OF SYSTEMIC DISEASE

10 Crohn's disease



Oral Crohn's disease showing fissure-like ulcerations of the mandibular buccal vestibule.

11 Crohn's disease



Oral Crohn's disease characterized by angular cheilitis and marked fissuring and erythema of the labial mucosa and maxillary gingiva.

12 Pyostomatitis vegetans



Pyostomatitis vegetans in a patient with ulcerative colitis, characterized by typical serpentine pustules that coalesce in a "snail track" pattern.

13 Pemphigus vulgaris



Erosion of the lower lip in a patient with pemphigus vulgaris.

14 Mucous membrane pemphigoid



Ulceration of the buccal mucosa with an intact bulla in a patient with mucous membrane pemphigoid.

15 Lichen planus



Oral lichen planus with characteristic radiating white striations and associated erythema of the buccal mucosa.

SIGNS OF SYSTEMIC DISEASE (cont'd)

16 Systemic lupus erythematosus



Characteristic lichenoid inflammation of the buccal mucosa in a patient with systemic lupus erythematosus.

17 Enamel erosion



Erosion of the palatal aspects of the anterior maxillary teeth secondary to severe and uncontrolled gastroesophageal reflux disease. Note that the teeth restored with full crowns are unaffected due to the porcelain material.

18 Candidiasis



Pseudomembranous candidiasis of the buccal mucosa in an immunosuppressed patient.

19 Oral hairy leukoplakia



Oral hairy leukoplakia characterized by asymptomatic corrugated white plaques of the lateral tongue.

20 Thrombocytopenia purpura



Multiple ecchymoses and thrombus formation in a patient with idiopathic thrombocytopenia purpura.

ORAL SYMPTOMS MAY BE THE FIRST SIGN OF SYSTEMIC DISEASE

Inflammatory bowel disease. Crohn's disease may affect the gastrointestinal tract anywhere from the mouth to the anus and may initially present with oral findings that may not correlate with abdominal symptoms. Oral Crohn's disease may present as mucosal cobblestoning, mucosal tags, deep linear ulcerations, gingival hyperplasia, lip fissuring, aphthous ulcers, and angular cheilitis (see Figures 10 and 11). Other features may include diffuse, painless swelling of the lips and mucosal erythema.

Pyostomatitis vegetans is an uncommon condition typically associated with ulcerative colitis that is characterized by serpentine pustules that coalesce in a "snail track" pattern (see Figure 12).¹¹

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Dermatologic/vesiculobullous diseases. Vesiculobullous lesions in the mouth may be seen in pemphigus vulgaris or bullous pemphigoid. Pemphigus vulgaris is an autoimmune intraepithelial blistering disease that often first presents in the oral cavity as flaccid bullae or painful ulcerations, prior to the onset of skin lesions (see Figure 13).

Mucous membrane pemphigoid is an autoimmune subepithelial disease that affects mucous membranes and the skin. Characteristic oral mucosal blisters quickly rupture and form ulcerations, which may occur in the absence of other mucosal involvement (eg, anus, genitalia, nose or throat) (see Figure 14).¹²

Painful aphthous ulcers are common. When oral ulcerations are diffuse and recurrent, they may be the first sign of Behçet's disease, a multisystem autoimmune vasculitis.¹³

Oral lichen planus is a chronic immune-mediated mucocutaneous disease that is often limited to the oral cavity. It presents with characteristic radiating white striations of the buccal mucosa and tongue, often with associated erythema and ulcerations (see Figure 15).¹⁴

Rheumatologic conditions. Systemic or discoid lupus erythematosus may present with oral findings that largely resemble those of oral lichen planus (see Figure 16).¹⁵ Sjögren's syndrome is an autoimmune disease with characteristic xerostomia, which can lead to oral discomfort, dysphagia, recurrent candidiasis, and rampant dental caries.

Other conditions to watch for. Erosion of the enamel on the lingual surface of the teeth may be a sign of gastroesophageal reflux disease or bulimia (see Figure 17). Examination of the oral mucosa can reveal typical white plaques of oral candidiasis (see Figure 18), which may be associated with systemic immune suppression as well as salivary gland dysfunction.

Oral conditions that have been associated with HIV infection include ANUG/ANUP, recurrent candidiasis, and oral hairy leukoplakia (see Figure 19). In the absence of known HIV infection, patients who present with any of these oral conditions should be evaluated for HIV infection.¹³

Atrophic glossitis may indicate a vitamin B deficiency. Thrombocytopenia and leukemia may present with oral petechiae, purpura, oral hematomas, or hemorrhagic bullae (see Figure 20).¹³ Painless pseudomembranous mucosal erosions may be a presentation for secondary syphilis.¹⁶

LOOK FOR SIGNS THAT SUGGEST MALIGNANCY

In the United States, oral and pharyngeal cancers account for approximately 40,000 cases of cancer and 8,000 deaths each year.¹⁷ More than 90% of these are squamous cell carcinomas (SCCs); the remainder are mainly salivary gland tumors, lymphoma, and other infrequent cancers.¹⁸

SCC of the oral cavity most commonly occurs on the tongue but can develop in any site, presenting as mucosal ulcers, plaques, or masses that do not heal (see Figure 21). Tobacco and alcohol use are associated with up to 80% of cases of SCC of the head and neck.¹⁸ Some oropharyngeal SCCs are associated with human papillomavirus infection type 16.¹⁹

Potentially malignant oral lesions include leukoplakia and erythroplakia. Leukoplakia is a white patch or plaque of the oral mucosa that can't be explained by any other clinical diagnosis (see Figure 22). These lesions are at risk for malignant transformation and may demonstrate dysplasia or frank SCC on biopsy.²⁰ Proliferative verrucous leukoplakia is a unique form of leukoplakia that is characterized by a wrinkled appearance that is often multifocal; the condition is associated with a higher risk for malignant transformation.

Erythroplakia is a red patch that similarly can't be explained by another diagnosis. It has a very high risk for malignant transformation over time. All potentially malignant oral lesions, including leukoplakia and erythroplakia, require biopsy and careful monitoring.

Non-SCC cancers. Salivary gland tumors are rare and most commonly occur in patients ages 55 to 65. Most neoplasms (70%-85%) occur in the parotid gland, while 8% to 15% develop in the submandibular salivary gland and less than 1% involve the sublingual gland.²¹ Minor salivary gland tissue, especially in the lips and palate, may also be affected (see Figure 23). Patients present with circumscribed, fixed or movable, painless, soft or firm masses in a salivary gland.

Melanoma should be included in the differential diagnosis of oral pigmented lesions that have any features of cutaneous melanoma, such as asymmetry, irregular borders, or variable or changing color.²²

Hematologic malignancies may initially present (or demonstrate evidence of relapse) in the oral cavity. Leukemia typically presents with sheet-like overgrowth and swelling of the gingiva, with associated erythema and bleeding (see Figure 24), whereas lymphoma typically presents as a solitary mass or

MALIGNANCIES

21 Squamous cell carcinoma



Squamous cell carcinoma of the posterior buccal mucosa, with well-defined, raised borders and a central area of irregular ulceration.

22 Leukoplakia



Oral leukoplakia with well-defined borders and an exophytic verrucous growth pattern. A healing punch biopsy site is evident at the anterior aspect of the lesion.

23 Mucoepidermoid carcinoma



Mucoepidermoid carcinoma of the minor salivary glands within the maxillary labial mucosa. Note the erythematous, swollen area of the upper lip.

24 Acute myelogenous leukemia



Acute myelogenous leukemia with characteristic erythematous overgrowth of the gingiva, with focal hemorrhage.

ulceration. Solid tumors that metastasize to the oral cavity may present with localized unexplained soft or hard tissue growths, with or without associated neurologic symptoms (eg, paresthesia). **CR**

REFERENCES

1. Spruance SL. The natural history of recurrent oral-facial herpes simplex virus infection. *Semin Dermatol.* 1992;11:200-206.
2. Balasubramaniam R, Kuperstein AS, Stoopler ET. Update on oral herpes virus infections. *Dent Clin North Am.* 2014;58:265-280.
3. Lozada-Nur F, Gorsky M, Silverman S Jr. Oral erythema multiforme: clinical observations and treatment of 95 patients. *Oral Surg Oral Med Oral Pathol.* 1989;67:36-40.
4. Allareddy V, Rampa S, Lee MK, et al. Hospital-based emergency department visits involving dental conditions: profile and predictors of poor outcomes and resource utilization. *J Am Dent Assoc.* 2014;145:331-337.
5. Allareddy V, Lin CY, Shah A, et al. Outcomes in patients hospitalized for periapical abscess in the United States: an analysis involving the use of a nationwide inpatient sample. *J Am Dent Assoc.* 2010;141:1107-1116.
6. Folan MO. The epidemiology, etiology, and pathophysiology of acute necrotizing ulcerative gingivitis associated with malnutrition. *J Contemp Dent Pract.* 2004;5:28-41.
7. Atout RN, Todescan S. Managing patients with necrotizing ulcerative gingivitis. *J Can Dent Assoc.* 2013;79:d46.
8. Todescan S, Nizar R. Managing patients with necrotizing ulcerative periodontitis. *J Can Dent Assoc.* 2013;79:d44.
9. Allareddy V, Allareddy V, Nalliah RP. Epidemiology of facial fracture

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- injuries. *J Oral Maxillofac Surg.* 2011;69:2613-2618.
10. Nalliah RP, Allareddy V, Kim MK, et al. Economics of facial fracture reductions in the United States over 12 months. *Dent Traumatol.* 2013;29:115-120.
 11. Padmavathi B, Sharma S, Astekar M, et al. Oral Crohn's disease. *J Oral Maxillofac Pathol.* 2014;18(suppl 1):S139-S142.
 12. Xu HH, Werth VP, Parisi E, et al. Mucous membrane pemphigoid. *Dent Clin North Am.* 2013;57:611-630.
 13. Chi AC, Neville BW, Krayer JW, et al. Oral manifestations of systemic disease. *Am Fam Physician.* 2010;82:1381-1388.
 14. Lavanya N, Jayanthi P, Rao UK, et al. Oral lichen planus: An update on pathogenesis and treatment. *J Oral Maxillofac Pathol.* 2011;15:127-132.
 15. Uva L, Miguel D, Pinheiro C, et al. Cutaneous manifestations of systemic lupus erythematosus. *Autoimmune Dis.* 2012;2012:834291.
 16. Ficarra G, Carlos R. Syphilis: The renaissance of an old disease with oral implications. *Head Neck Pathol.* 2009;3:195-206.
 17. Siegel R, Ward E, Brawley O, et al. Cancer statistics, 2011: the impact of eliminating socioeconomic and racial disparities on premature cancer deaths. *CA Cancer J Clin.* 2011;61:212-236.
 18. Licitra L, Locati LD, Bossi P, et al. Head and neck tumors other than squamous cell carcinoma. *Curr Opin Oncol.* 2004;16:236-241.
 19. Gillison ML, Broutian T, Pickard RK, et al. Prevalence of oral HPV infection in the United States, 2009-2010. *JAMA.* 2012;307:693-703.
 20. Silverman S Jr, Gorsky M, Lozada F. Oral leukoplakia and malignant transformation: a follow-up study of 257 patients. *Cancer.* 1984;53:563-568.
 21. Spiro RH. Salivary neoplasms: overview of a 35-year experience with 2807 patients. *Head Neck Surg.* 1986;8:177-184.
 22. DeMatos P, Tyler DS, Seigler HF. Malignant melanoma of the mucous membranes: a review of 119 cases. *Ann Surg Oncol.* 1998;5:733-742.