Chapter 36: Oral Manifestations of Disease

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INTRODUCTION

As primary care physicians and consultants, internists are often asked to evaluate patients with disease of the oral soft tissues, teeth, and pharynx. Knowledge of the oral milieu and its unique structures is necessary to guide preventive services and recognize oral manifestations of local or systemic disease **(Chap. A3)**. Furthermore, internists frequently collaborate with dentists in the care of patients who have a variety of medical conditions that affect oral health or who undergo dental procedures that increase their risk of medical complications.

DISEASES OF THE TEETH AND PERIODONTAL STRUCTURES

Tooth formation begins during the sixth week of embryonic life and continues through 17 years of age. Teeth start to develop in utero and continue to develop until after the tooth erupts. Normally, all 20 deciduous teeth have erupted by age 3 and have been shed by age 13. Permanent teeth, eventually totaling 32, begin to erupt by age 6 and have completely erupted by age 14, though third molars ("wisdom teeth") may erupt later.

The erupted tooth consists of the visible *crown* covered with enamel and the root submerged below the gum line and covered with bonelike *cementum*. *Dentin*, a material that is denser than bone and exquisitely sensitive to pain, forms the majority of the tooth substance, surrounding a core of myxomatous *pulp* containing the vascular and nerve supply. The tooth is held firmly in the alveolar socket by the *periodontium*, supporting structures that consist of the gingivae, alveolar bone, cementum, and periodontal ligament. The periodontal ligament tenaciously binds the tooth's cementum to the alveolar bone. Above this ligament is a collar of attached gingiva just below the crown. A few millimeters of unattached or free gingiva (1–3 mm) overlap the base of the crown, forming a shallow sulcus along the gum-tooth margin.

Dental Caries, Pulpal and Periapical Disease, and Complications

Dental caries usually begin asymptomatically as a destructive infectious process of the enamel. Bacteria—principally *Streptococcus mutans*—colonize the organic buffering biofilm (*plaque*) on the tooth surface. If not removed by brushing or by the natural cleansing and antibacterial action of saliva, bacterial acids can demineralize the enamel. Fissures and pits on the occlusal surfaces are the most frequent sites of early decay. Surfaces between the teeth, adjacent to tooth restorations and exposed roots, are also vulnerable, particularly as individuals age. Over time, dental caries extend to the underlying dentin, leading to cavitation of the enamel. Without management, the caries will penetrate to the tooth pulp, producing *acute pulpitis*. At this stage, when the pulp infection is limited, the tooth may become sensitive to percussion and to hot or cold, and pain resolves immediately when the irritating stimulus is removed. Should the infection spread throughout the pulp, *irreversible pulpitis* occurs, leading to *pulp necrosis*. At this later stage, pain can be severe and has a sharp or throbbing visceral quality that may be worse when the patient lies down. Once pulp necrosis is complete, pain may be constant or intermittent, but cold sensitivity is lost.

Treatment of caries involves removal of the softened and infected hard tissue and restoration of the tooth structure with silver amalgam, glass ionomer, composite resin, or gold. Once irreversible pulpitis occurs, root canal therapy becomes necessary; removal of the contents of the pulp chamber and root canal is followed by thorough cleaning and filling with an inert material. Alternatively, the tooth may be extracted.

Pulpal infection leads to *periapical abscess* formation, which can produce pain on chewing. If the infection is mild and chronic, a *periapical granuloma* or eventually a *periapical cyst* forms, either of which produces radiolucency at the root apex. When unchecked, a periapical abscess can erode into the alveolar bone, producing osteomyelitis; penetrate and drain through the gingivae, producing a parulis (gumboil); or track along deep fascial planes, producing virulent cellulitis (Ludwig's angina) involving the submandibular space and floor of the mouth **(Chap. 177)**. Elderly patients, patients with diabetes mellitus, and patients taking glucocorticoids may experience little or no pain or fever as these complications develop.

Periodontal Disease

Periodontal disease and dental caries are the primary causes of tooth loss. Like dental caries, chronic infection of the gingiva and anchoring structures of the tooth begins with formation of bacterial plaque. The process begins at the gum line. Plaque and *calculus* (calcified plaque) are preventable by appropriate daily oral hygiene, including periodic professional cleaning. Left undisturbed, chronic inflammation can ensue and produce hyperemia of the free and attached gingivae (*gingivitis*), which then typically bleed with brushing. If this issue is ignored, severe *periodontitis* can develop, leading to deepening of the physiologic sulcus and destruction of the periodontal ligament. Gingival pockets develop around the teeth. As the periodontium (including the supporting bone) is destroyed, the teeth loosen. A role for chronic inflammation due to chronic periodontal disease in promoting coronary heart disease and stroke has been proposed. Epidemiologic studies have demonstrated a moderate but significant association between chronic periodontal inflammation and atherogenesis, though a causal role remains unproven.

Acute and aggressive forms of periodontal disease are less common than the chronic forms described above. However, if the host is stressed or exposed to a new pathogen, rapidly progressive and destructive disease of the periodontal tissue can occur. A virulent example is *acute necrotizing ulcerative gingivitis*. The presentation includes sudden gingival inflammation, ulceration, bleeding, interdental gingival necrosis, and fetid halitosis. *Localized juvenile periodontitis*, which is seen in adolescents, is particularly destructive and appears to be associated with impaired neutrophil chemotaxis. *AIDS-related periodontitis* resembles acute necrotizing ulcerative gingivitis in some patients and a more destructive form of adult chronic periodontitis in others. It may also produce a gangrene-like destructive process of the oral soft tissues and bone that resembles *noma*, an infectious condition seen in severely malnourished children in developing nations.

Prevention of Tooth Decay and Periodontal Infection

Despite the reduced prevalences of dental caries and periodontal disease in the United States (due in large part to water fluoridation and improved dental care, respectively), both diseases constitute a major public health problem worldwide, particularly in certain groups. The internist should promote preventive dental care and hygiene as part of health maintenance. Populations at high risk for dental caries and periodontal disease include those with hyposalivation and/or xerostomia, diabetics, alcoholics, tobacco users, persons with Down syndrome, and those with gingival hyperplasia. Furthermore, patients lacking access to dental care (e.g., as a result of low socioeconomic status) and patients with a reduced ability to provide self-care (e.g., individuals with disabilities, nursing home residents, and persons with dementia or upper-extremity disability) suffer at a disproportionate rate. It is important to provide counseling regarding regular dental hygiene and professional cleaning, use of fluoride-containing toothpaste, professional fluoride treatments, and (for patients with limited dexterity) use of electric toothbrushes and also to instruct persons caring for those who are not capable of self-care. Cost, fear of dental care, and differences in language and culture create barriers that prevent some people from seeking preventive dental services.

Developmental and Systemic Disease Affecting the Teeth and Periodontium

In addition to posing cosmetic issues, *malocclusion*, the most common developmental oral problem, can interfere with mastication unless corrected through orthodontic and surgical techniques. Impacted third molars are common and can become infected or erupt into an insufficient space. Acquired prognathism due to *acromegaly* may also lead to malocclusion, as may deformity of the maxilla and mandible due to *Paget's disease* of the bone. Delayed tooth eruption, a receding chin, and a protruding tongue are occasional features of *cretinism* and *hypopituitarism*. Congenital syphilis produces tapering, notched (*Hutchinson's*) incisors and finely nodular (*mulberry*) molar crowns. *Enamel hypoplasia* results in crown defects ranging from pits to deep fissures of primary or permanent teeth. Intrauterine infection (syphilis, rubella), vitamin deficiency (A, C, or D), disorders of calcium metabolism (malabsorption, vitamin D–resistant rickets, hypoparathyroidism), prematurity, high fever, and rare inherited defects (*amelogenesis imperfecta*) are all causes. Tetracycline, given in sufficiently high doses during the first 8 years of life, may produce enamel hypoplasia and discoloration. Doxycycline does not cause permanent tooth staining in children despite warnings included for all tetracycline-class antibiotics. Exposure to endogenous pigments can discolor developing teeth; etiologies include *erythroblastosis fetalis* (green or bluish-black), congenital liver disease (green or yellow-brown), and porphyria (red or brown that fluoresces with ultraviolet light). *Mottled enamel* occurs if excessive fluoride is ingested during development. Worn enamel is seen with age, bruxism, or excessive acid exposure (e.g., chronic gastric reflux or bulimia). Celiac disease is associated with nonspecific enamel defects in children but not in adults.

Total or partial tooth loss resulting from periodontitis is seen with cyclic neutropenia, Papillon-Lefévre syndrome, Chédiak-Higashi syndrome, and leukemia. Rapid focal tooth loosening is most often due to infection, but rarer causes include Langerhans cell histiocytosis, Ewing's sarcoma, osteosarcoma, and Burkitt's lymphoma. Early loss of primary teeth is a feature of *hypophosphatasia*, a rare congenital error of metabolism.

Pregnancy may produce gingivitis and localized *pyogenic granulomas*. Severe periodontal disease occurs in uncontrolled diabetes mellitus. *Drug-induced gingival overgrowth* may be caused by anticonvulsants, calcium channel blockers, and immunosuppressants, although excellent daily oral care can prevent or reduce its occurrence. *Idiopathic familial gingival fibromatosis* and several syndrome-related disorders cause similar conditions. Discontinuation of the medication may reverse the drug-induced form, although surgery may be needed to control both of the latter entities. *Linear gingival erythema* is variably seen in patients with advanced HIV infection and probably represents immune deficiency and decreased neutrophil activity. Diffuse or focal gingival swelling may be a feature of early or late acute myelomonocytic leukemia as well as of other lymphoproliferative disorders. A rare but pathognomonic sign of granulomatosis with polyangiitis is a red-purplish, granular gingivitis (*strawberry gums*).

DISEASES OF THE ORAL MUCOSA

Infections

Most oral mucosal diseases involve microorganisms **(Table 36-1)**.

TABLE 36-1

Vesicular, Bullous, or Ulcerative Lesions of the Oral Mucosa

CONDITION	USUAL LOCATION	CLINICAL FEATURES	COURSE
Viral Diseases			
Primary acute herpetic gingivostomatitis (HSV type 1; rarely type 2)	Lip and oral mucosa (buccal, gingival, lingual mucosa)	Labial vesicles that rupture and crust, and intraoral vesicles that quickly ulcerate; extremely painful; acute gingivitis, fever, malaise, foul odor, and cervical lymphadenopathy; occurs primarily in infants, children, and young adults	Heals spontaneously in 10–14 days; unless secondarily infected, lesions lasting >3 weeks are not due to primary HSV infection
Recurrent herpes labialis	Mucocutaneous junction of lip, perioral skin	Eruption of groups of vesicles that may coalesce, then rupture and crust; painful to pressure or spicy foods	Lasts ~1 week, but condition may be prolonged if secondarily infected; if severe, topical or oral antiviral treatment may reduce healing time
Recurrent intraoral herpes simplex	Palate and gingiva	Small vesicles on keratinized epithelium that rupture and coalesce; painful	Heals spontaneously in ~1 week; if severe, topical or oral antiviral treatment may reduce healing time
Chickenpox (VZV)	Gingiva and oral mucosa	Skin lesions may be accompanied by small vesicles on oral mucosa that rupture to form shallow ulcers; may coalesce to form large bullous lesions that ulcerate; mucosa may have generalized erythema	Lesions heal spontaneously within 2 weeks
Herpes zoster (VZV reactivation)	Cheek, tongue, gingiva, or palate	Unilateral vesicular eruptions and ulceration in linear pattern following sensory distribution of trigeminal nerve or one of its branches	Gradual healing without scarring unless secondarily infected; postherpetic neuralgia is common; oral acyclovir, famciclovir, or valacyclovir reduces healing time and postherpetic neuralgia
Infectious mononucleosis (Epstein-Barr	Oral mucosa	Fatigue, sore throat, malaise, fever, and cervical lymphadenopathy; numerous small ulcers usually appear several days before lymphadenopathy;	Oral lesions disappear during convalescence; no treatment is given, though glucocorticoids are indicated if tonsillar swelling compromises

virus)		gingival bleeding and multiple petechiae at junction of hard and soft palates	the airway
Herpangina (coxsackievirus A; also possibly coxsackievirus B and echovirus)	Oral mucosa, pharynx, tongue	Sudden onset of fever, sore throat, and oropharyngeal vesicles, usually in children <4 years old, during summer months; diffuse pharyngeal congestion and vesicles (1–2 mm), grayish-white surrounded by red areola; vesicles enlarge and ulcerate	Incubation period of 2–9 days; fever for 1–4 days; recovery uneventful
Hand-foot-and-mouth disease (most commonly coxsackievirus A16)	Oral mucosa, pharynx, palms, and soles	Fever, malaise, headache with oropharyngeal vesicles that become painful, shallow ulcers; highly infectious; usually affects children under age 10	Incubation period 2–18 days; lesions heal spontaneously in 2–4 weeks
Primary HIV infection	Gingiva, palate, and pharynx	Acute gingivitis and oropharyngeal ulceration, associated with febrile illness resembling mononucleosis and including lymphadenopathy	Followed by HIV seroconversion, asymptomatic HIV infection, and usually ultimately by HIV disease
Bacterial or Fungal Diseases			
Acute necrotizing ulcerative gingivitis (“trench mouth”)	Gingiva	Painful, bleeding gingiva characterized by necrosis and ulceration of gingival papillae and margins plus lymphadenopathy and foul breath	Debridement and diluted (1:3) peroxide lavage provide relief within 24 h; antibiotics in acutely ill patients; relapse may occur
Prenatal (congenital) syphilis	Palate, jaws, tongue, and teeth	Gummatous involvement of palate, jaws, and facial bones; Hutchinson’s incisors, mulberry molars, glossitis, mucous patches, and fissures at corner of mouth	Tooth deformities in permanent dentition irreversible
Primary syphilis (chancre)	Lesion appearing where organism enters body; may occur on lips, tongue, or tonsillar area	Small papule developing rapidly into a large, painless ulcer with indurated border; unilateral lymphadenopathy; chancre and lymph nodes containing spirochetes; serologic tests positive by third to fourth weeks	Healing of chancre in 1–2 months, followed by secondary syphilis in 6–8 weeks
Secondary syphilis	Oral mucosa frequently involved with mucous patches, which occur primarily on palate and also at commissures of mouth	Maculopapular lesions of oral mucosa, 5–10 mm in diameter with central ulceration covered by grayish membrane; eruptions occurring on various mucosal surfaces and skin, accompanied by fever, malaise, and sore throat	Lesions may persist from several weeks to a year
Tertiary syphilis	Palate and tongue	Gummatous infiltration of palate or tongue followed by ulceration and fibrosis; atrophy of tongue papillae produces characteristic bald tongue and glossitis	Gumma may destroy palate, causing complete perforation
Gonorrhea	Lesions may occur in	Most pharyngeal infection is asymptomatic; may	More difficult to eradicate than urogenital

	mouth at site of inoculation or secondarily by hematogenous spread from a primary focus	produce burning or itching sensation; oropharynx and tonsils may be ulcerated and erythematous; saliva viscous and fetid	infection, though pharyngitis usually resolves with appropriate antimicrobial treatment
Tuberculosis	Tongue, tonsillar area, soft palate	Painless, solitary, 1- to 5-cm, irregular ulcer covered with persistent exudate; ulcer has firm undermined border	Autoinoculation from pulmonary infection is usual; lesions resolve with appropriate antimicrobial therapy
Cervicofacial actinomycosis	Swellings in region of face, neck, and floor of mouth	Infection may be associated with extraction, jaw fracture, or eruption of molar tooth; in acute form, resembles acute pyogenic abscess, but contains yellow “sulfur granules” (gram-positive mycelia and their hyphae)	Typically, swelling is hard and grows painlessly; multiple abscesses with draining tracts develop; penicillin first choice; surgery usually necessary
Histoplasmosis	Any area of the mouth, particularly tongue, gingiva, or palate	Nodular, verrucous, or granulomatous lesions; ulcers are indurated and painful; usual source hematogenous or pulmonary, but may be primary	Systemic antifungal therapy necessary
Candidiasis[a]			
Dermatologic Diseases			
Mucous membrane pemphigoid	Typically produces marked gingival erythema and ulceration; other areas of oral cavity, esophagus, and vagina may be affected	Painful, grayish-white collapsed vesicles or bullae of full-thickness epithelium with peripheral erythematous zone; gingival lesions desquamate, leaving ulcerated area	Protracted course with remissions and exacerbations; involvement of different sites develops slowly; glucocorticoids may temporarily reduce symptoms but do not control disease
EM minor and EM major (Stevens-Johnson syndrome)	Primarily oral mucosa and skin of hands and feet	Intraoral ruptured bullae surrounded by inflammatory area; lips may show hemorrhagic crusts; “iris” or “target” lesion on skin is pathognomonic; patient may have severe signs of toxicity	Onset very rapid; usually idiopathic, but may be associated with trigger such as drug reaction; condition may last 3–6 weeks; mortality rate for untreated EM major is 5–15%
Pemphigus vulgaris	Oral mucosa and skin; sites of mechanical trauma (soft/hard palate, frenulum, lips, buccal mucosa)	Usually (>70%) presents with oral lesions; fragile, ruptured bullae and ulcerated oral areas; mostly in older adults	With repeated occurrence of bullae, toxicity may lead to cachexia, infection, and death within 2 years; often controllable with oral glucocorticoids
Lichen planus	Oral mucosa and skin	White striae in mouth; purplish nodules on skin at sites of friction; occasionally causes oral mucosal ulcers and erosive gingivitis	White striae alone usually asymptomatic; erosive lesions often difficult to treat, but may respond to glucocorticoids
Other Conditions			
Recurrent aphthous ulcers	Usually on nonkeratinized oral mucosa (buccal and	Single or clustered painful ulcers with surrounding erythematous border; lesions may be 1–2 mm in	Lesions heal in 1–2 weeks but may recur monthly or several times a year; protective

	labial mucosa, floor of mouth, soft palate, lateral and ventral tongue)	diameter in crops (herpetiform), 1–5 mm (minor), or 5–15 mm (major)	barrier with benzocaine and topical glucocorticoids relieve symptoms; systemic glucocorticoids may be needed in severe cases
Behçet's syndrome	Oral mucosa, eyes, genitalia, gut, and CNS	Multiple aphthous ulcers in mouth; inflammatory ocular changes, ulcerative lesions on genitalia; inflammatory bowel disease and CNS disease	Oral lesions often first manifestation; persist several weeks and heal without scarring
Traumatic ulcers	Anywhere on oral mucosa; dentures frequently responsible for ulcers in vestibule	Localized, discrete ulcerated lesions with red border; produced by accidental biting of mucosa, penetration by foreign object, or chronic irritation by dentures	Lesions usually heal in 7–10 days when irritant is removed, unless secondarily infected
Squamous cell carcinoma	Any area of mouth, most commonly on lower lip, lateral borders of tongue, and floor of mouth	Red, white, or red and white ulcer with elevated or indurated border; failure to heal; pain not prominent in early lesions	Invades and destroys underlying tissues; frequently metastasizes to regional lymph nodes
Acute myeloid leukemia (usually monocytic)	Gingiva	Gingival swelling and superficial ulceration followed by hyperplasia of gingiva with extensive necrosis and hemorrhage; deep ulcers may occur elsewhere on mucosa, complicated by secondary infection	Usually responds to systemic treatment of leukemia; occasionally requires local irradiation
Lymphoma	Gingiva, tongue, palate, and tonsillar area	Elevated, ulcerated area that may proliferate rapidly, giving appearance of traumatic inflammation	Fatal if untreated; may indicate underlying HIV infection
Chemical or thermal burns	Any area in mouth	White slough due to contact with corrosive agents (e.g., aspirin, hot cheese) applied locally; removal of slough leaves raw, painful surface	Lesion heals in several weeks if not secondarily infected

[a]See Table 36-3.

Abbreviations: CNS, central nervous system; EM, erythema multiforme; HSV, herpes simplex virus; VZV, varicella-zoster virus.

Pigmented Lesions

See **Table 36-2**.

TABLE 36-2

Pigmented Lesions of the Oral Mucosa

CONDITION	USUAL LOCATION	CLINICAL FEATURES	COURSE
Oral melanotic macule	Any area of mouth	Discrete or diffuse, localized, brown to black macule	Remains indefinitely; no growth
Diffuse melanin pigmentation	Any area of	Diffuse pale to dark-brown pigmentation; may be	Remains indefinitely

	mouth	physiologic ("racial") or due to smoking	
Nevi	Any area of mouth	Discrete, localized, brown to black pigmentation	Remains indefinitely
Malignant melanoma	Any area of mouth	Can be flat and diffuse, painless, brown to black; or can be raised and nodular	Expands and invades early; metastasis leads to death
Addison's disease	Any area of mouth, but mostly buccal mucosa	Blotches or spots of bluish-black to dark-brown pigmentation occurring early in disease, accompanied by diffuse pigmentation of skin; other symptoms of adrenal insufficiency	Condition controlled by adrenal steroid replacement
Peutz-Jeghers syndrome	Any area of mouth	Dark-brown spots on lips, buccal mucosa, with characteristic distribution of pigment around lips, nose, and eyes and on hands; concomitant intestinal polyposis	Oral pigmented lesions remain indefinitely; gastrointestinal polyps may become malignant
Drug ingestion (neuroleptics, oral contraceptives, minocycline, zidovudine, quinine derivatives)	Any area of mouth	Brown, black, or gray areas of pigmentation	Gradually disappears following cessation of drug intake
Amalgam tattoo	Gingiva and alveolar mucosa	Small blue-black pigmented areas associated with embedded amalgam particles in soft tissues; may show up on radiographs as radiopaque particles in some cases	Remains indefinitely
Heavy metal pigmentation (bismuth, mercury, lead)	Gingival margin	Thin blue-black pigmented line along gingival margin; rarely seen except in children exposed to lead-based paint	Indicative of systemic absorption; no significance for oral health
Black hairy tongue	Dorsum of tongue	Elongation of filiform papillae of tongue, which become stained by coffee, tea, tobacco, or pigmented bacteria	Improves within 1–2 weeks with gentle brushing of tongue or (if due to bacterial overgrowth) discontinuation of antibiotic
Fordyce spots	Buccal and labial mucosa	Numerous small yellowish spots just beneath mucosal surface; no symptoms; due to hyperplasia of sebaceous glands	Benign; remains without apparent change
Kaposi's sarcoma	Palate most common, but may occur at any other site	Red or blue plaques of variable size and shape; often enlarge, become nodular, and may ulcerate	Usually indicative of HIV infection or non-Hodgkin's lymphoma; rarely fatal, but may require treatment for comfort or cosmesis
Mucous retention cysts	Buccal and labial mucosa	Bluish, clear fluid–filled cyst due to extravasated mucus from injured minor salivary gland	Benign; painless unless traumatized; may be removed surgically

Dermatologic Diseases

See Tables 36-1, 36-2, and **36-3** and **Chaps. 56–61**.

TABLE 36-3

White Lesions of Oral Mucosa

CONDITION	USUAL LOCATION	CLINICAL FEATURES	COURSE
Lichen planus	Buccal mucosa, tongue, gingiva, and lips; skin	Striae, white plaques, red areas, ulcers in mouth; purplish papules on skin; may be asymptomatic, sore, or painful; lichenoid drug reactions may look similar	Protracted; responds to topical glucocorticoids
White sponge nevus	Oral mucosa, vagina, anal mucosa	Painless white thickening of epithelium; adolescence/early adulthood onset; familial	Benign and permanent
Smoker's leukoplakia and smokeless tobacco lesions	Any area of oral mucosa, sometimes related to location of habit	White patch that may become firm, rough, or red-fissured and ulcerated; may become sore and painful but is usually painless	May or may not resolve with cessation of habit; 2% of patients develop squamous cell carcinoma; early biopsy essential
Erythroplakia with or without white patches	Floor of mouth commonly affected in men; tongue and buccal mucosa in women	Velvety, reddish plaque; occasionally mixed with white patches or smooth red areas	High risk of squamous cell cancer; early biopsy essential
Candidiasis	Any area in mouth	*Pseudomembranous type* ("thrush"): creamy white curdlike patches that reveal a raw, bleeding surface when scraped; found in sick infants, debilitated elderly patients receiving high-dose glucocorticoids or broad-spectrum antibiotics, and patients with AIDS	Responds favorably to antifungal therapy and correction of predisposing causes where possible
		Erythematous type: flat, red, sometimes sore areas in same groups of patients	Course same as for pseudomembranous type
		Candidal leukoplakia: nonremovable white thickening of epithelium due to *Candida*	Responds to prolonged antifungal therapy
		Angular cheilitis: sore fissures at corner of mouth	Responds to topical antifungal therapy
Hairy leukoplakia	Usually on lateral tongue, rarely elsewhere on oral mucosa	White areas ranging from small and flat to extensive accentuation of vertical folds; found in HIV carriers (all risk groups for AIDS)	Due to Epstein-Barr virus; responds to high-dose acyclovir but recurs; rarely causes discomfort unless secondarily infected with *Candida*
Warts (human papillomavirus)	Anywhere on skin and oral mucosa	Single or multiple papillary lesions with thick, white, keratinized surfaces containing many pointed projections; cauliflower lesions covered with normal-colored mucosa or multiple pink or pale bumps (focal epithelial hyperplasia)	Lesions grow rapidly and spread; squamous cell carcinoma must be ruled out with biopsy; excision or laser therapy; may regress in HIV-infected patients receiving antiretroviral therapy

Diseases of the Tongue

See **Table 36-4**.

TABLE 36-4

Alterations of the Tongue

TYPE OF CHANGE	CLINICAL FEATURES
Size or Morphology	
Macroglossia	Enlarged tongue that may be part of a syndrome found in developmental conditions such as Down syndrome, Simpson-Golabi-Behmel syndrome, or Beckwith-Wiedemann syndrome; may be due to tumor (hemangioma or lymphangioma), metabolic disease (e.g., primary amyloidosis), or endocrine disturbance (e.g., acromegaly or cretinism); may occur when all teeth are removed
Fissured ("scrotal") tongue	Dorsal surface and sides of tongue covered by painless shallow or deep fissures that may collect debris and become irritated
Median rhomboid glossitis	Congenital abnormality with ovoid, denuded area in median posterior portion of tongue; may be associated with candidiasis and may respond to antifungal treatment
Color	
"Geographic" tongue (benign migratory glossitis)	Asymptomatic inflammatory condition of tongue, with rapid loss and regrowth of filiform papillae leading to appearance of denuded red patches "wandering" across surface
Hairy tongue	Elongation of filiform papillae of medial dorsal surface area due to failure of keratin layer of papillae to desquamate normally; brownish-black coloration may be due to staining by tobacco, food, or chromogenic organisms
"Strawberry" and "raspberry" tongue	Appearance of tongue during scarlet fever due to hypertrophy of fungiform papillae as well as changes in filiform papillae
"Bald" tongue	Atrophy may be associated with xerostomia, pernicious anemia, iron-deficiency anemia, pellagra, or syphilis; may be accompanied by painful burning sensation; may be an expression of erythematous candidiasis and respond to antifungal treatment

HIV Disease and AIDS

See Tables 36-1, 36-2, 36-3, and **36-5**; **Chap. 202**.

TABLE 36-5

Oral Lesions Associated with HIV Infection

LESION MORPHOLOGY	ETIOLOGIES
Papules, nodules, plaques	Candidiasis (hyperplastic and pseudomembranous)[a] Condyloma acuminatum (human papillomavirus infection) Squamous cell carcinoma (preinvasive and invasive) Non-Hodgkin's lymphoma[a] Hairy leukoplakia[a]
Ulcers	Recurrent aphthous ulcers[a] Angular cheilitis Squamous cell carcinoma Acute necrotizing ulcerative gingivitis[a] Necrotizing ulcerative periodontitis[a] Necrotizing ulcerative stomatitis Non-Hodgkin's lymphoma[a] Viral infection (herpes simplex, herpes zoster, cytomegalovirus infection) Infection caused by *Mycobacterium tuberculosis* or *Mycobacterium avium-intracellulare* Fungal infection (histoplasmosis, cryptococcosis, candidiasis, geotrichosis, aspergillosis) Bacterial infection (*Escherichia coli, Enterobacter cloacae, Klebsiella pneumoniae, Pseudomonas aeruginosa*) Drug reactions (single or multiple ulcers)
Pigmented lesions	Kaposi's sarcoma[a] Bacillary angiomatosis (skin and visceral lesions more common than oral) Zidovudine pigmentation (skin, nails, and occasionally oral mucosa) Addison's disease
Miscellaneous	Linear gingival erythema[a]

[a]Strongly associated with HIV infection.

Ulcers

Ulceration is the most common oral mucosal lesion. Although there are many causes, the host and the pattern of lesions, including the presence of organ system features, narrow the differential diagnosis (Table 36-1). Most acute ulcers are painful and self-limited. Recurrent aphthous ulcers and herpes simplex account for the majority. Persistent and deep aphthous ulcers can be idiopathic or can accompany HIV/AIDS. Aphthous lesions are often the presenting symptom in *Behçet's syndrome* **(Chap. 364)**. Similar-appearing, though less painful, lesions may occur in reactive arthritis, and aphthous ulcers are occasionally present during phases of *discoid* or *systemic lupus erythematosus* **(Chap. 360)**. Aphthous-like ulcers are seen in *Crohn's disease* **(Chap. 326)**, but, unlike the common aphthous variety, they may exhibit granulomatous inflammation on histologic examination. Recurrent aphthae are more prevalent in patients with *celiac disease* and have been reported to remit with elimination of gluten.

Of major concern are chronic, relatively painless ulcers and mixed red/white patches (erythroplakia and leukoplakia) of >2 weeks' duration. Squamous cell carcinoma and premalignant dysplasia should be considered early and a diagnostic biopsy performed. This awareness and this procedure are critically important because early-stage malignancy is vastly more treatable than late-stage disease. High-risk sites include the lower lip, floor of the mouth, ventral and lateral tongue, and soft palate–tonsillar pillar complex. Significant risk factors for oral cancer in Western countries include sun

exposure (lower lip), tobacco and alcohol use, and human papillomavirus infection. In India and some other Asian countries, smokeless tobacco mixed with betel nut, slaked lime, and spices is a common cause of oral cancer. Rarer causes of chronic oral ulcer, such as tuberculosis, fungal infection, granulomatosis with polyangiitis, and midline granuloma, may look identical to carcinoma. Making the correct diagnosis depends on recognizing other clinical features and performing a biopsy of the lesion. The syphilitic chancre is typically painless and therefore easily missed. Regional lymphadenopathy is invariably present. The syphilitic etiology is confirmed with appropriate bacterial and serologic tests.

Disorders of mucosal fragility often produce painful oral ulcers that fail to heal within 2 weeks. *Mucous membrane pemphigoid* and *pemphigus vulgaris* are the major acquired disorders. While their clinical features are often distinctive, a biopsy or immunohistochemical examination should be performed to diagnose these entities and to distinguish them from *lichen planus* and drug reactions.

Hematologic and Nutritional Disease

Internists are more likely to encounter patients with acquired, rather than congenital, bleeding disorders. Bleeding should stop 15 min after minor trauma and within an hour after tooth extraction if local pressure is applied. More prolonged bleeding, if not due to continued injury or rupture of a large vessel, should lead to investigation for a clotting abnormality. In addition to bleeding, petechiae and ecchymoses are prone to occur at the vibrating line between the soft and hard palates in patients with platelet dysfunction or thrombocytopenia.

All forms of leukemia, but particularly *acute myelomonocytic leukemia*, can produce gingival bleeding, ulcers, and gingival enlargement. Oral ulcers are a feature of agranulocytosis, and ulcers and mucositis are often severe complications of chemotherapy and radiation therapy for hematologic and other malignancies. *Plummer-Vinson syndrome* (iron deficiency, angular stomatitis, glossitis, and dysphagia) raises the risk of oral squamous cell cancer and esophageal cancer at the postcricoidal tissue web. Atrophic papillae and a red, burning tongue may occur with pernicious anemia. Deficiencies in B-group vitamins produce many of these same symptoms as well as oral ulceration and cheilosis. Consequences of *scurvy* include swollen, bleeding gums; ulcers; and loosening of the teeth.

NONDENTAL CAUSES OF ORAL PAIN

Most, but not all, oral pain emanates from inflamed or injured tooth pulp or periodontal tissues. Nonodontogenic causes are often overlooked. In most instances, toothache is predictable and proportional to the stimulus applied, and an identifiable condition (e.g., caries, abscess) is found. Local anesthesia eliminates pain originating from dental or periodontal structures, but not referred pains. The most common nondental source of pain is myofascial pain referred from muscles of mastication, which become tender and ache with increased use. Many sufferers exhibit *bruxism* (grinding of the teeth) secondary to stress and anxiety. *Temporomandibular joint disorder* is closely related. It affects both sexes, with a higher prevalence among women. Features include pain, limited mandibular movement, and temporomandibular joint sounds. The etiologies are complex; malocclusion does not play the primary role once attributed to it. *Osteoarthritis* is a common cause of masticatory pain. Anti-inflammatory medication, jaw rest, soft foods, and heat provide relief. The temporomandibular joint is involved in 50% of patients with *rheumatoid arthritis*, and its involvement is usually a late feature of severe disease. Bilateral preauricular pain, particularly in the morning, limits range of motion.

Migrainous neuralgia may be localized to the mouth. Episodes of pain and remission without an identifiable cause and a lack of relief with local anesthesia are important clues. *Trigeminal neuralgia* (*tic douloureux*) can involve the entire branch or part of the mandibular or maxillary branch of the fifth cranial nerve and can produce pain in one or a few teeth. Pain may occur spontaneously or may be triggered by touching the lip or gingiva, brushing the teeth, or chewing. *Glossopharyngeal neuralgia* produces similar acute neuropathic symptoms in the distribution of the ninth cranial nerve. Swallowing, sneezing, coughing, or pressure on the tragus of the ear triggers pain that is felt in the base of the tongue, pharynx, and soft palate and may be referred to the temporomandibular joint. *Neuritis* involving the maxillary and mandibular divisions of the trigeminal nerve (e.g., maxillary sinusitis, neuroma, and leukemic infiltrate) is distinguished from ordinary toothache by the neuropathic quality of the pain. Occasionally, *phantom pain* follows tooth extraction. Pain and hyperalgesia behind the ear and on the side of the face in the day or so before facial weakness develops often constitute the earliest symptom of *Bell's palsy*. Likewise, similar symptoms may precede visible lesions of herpes zoster infecting the seventh nerve (*Ramsey-Hunt syndrome*) or trigeminal nerve. *Postherpetic neuralgia* may follow either condition. *Coronary ischemia* may produce pain exclusively in the face and jaw; as in typical angina pectoris, this pain is usually reproducible with increased myocardial demand. Aching in several upper molar or premolar teeth that is unrelieved by anesthetizing the teeth may point to *maxillary sinusitis*.

Giant cell arteritis is notorious for producing headache, but it may also produce facial pain or sore throat without headache. Jaw and tongue claudication with chewing or talking is relatively common. Tongue infarction is rare. Patients with subacute thyroiditis often experience pain referred

to the face or jaw before the tenderness of the thyroid gland and transient hyperthyroidism are appreciated.

"Burning mouth syndrome" (*glossodynia*) occurs in the absence of an identifiable cause (e.g., vitamin B_{12} deficiency, iron deficiency, diabetes mellitus, low-grade *Candida* infection, food sensitivity, or subtle xerostomia) and predominantly affects postmenopausal women. The etiology may be neuropathic. Clonazepam, α-lipoic acid, and cognitive-behavioral therapy have benefited some patients. Some cases associated with an angiotensin-converting enzyme inhibitor have remitted when treatment with the drug was discontinued.

DISEASES OF THE SALIVARY GLANDS

Saliva is essential to oral health. Its absence leads to dental caries, periodontal disease, and difficulties in wearing dental prostheses, masticating, and speaking. Its major components, water and mucin, serve as a cleansing solvent and lubricating fluid. In addition, saliva contains antimicrobial factors (e.g., lysozyme, lactoperoxidase, secretory IgA), epidermal growth factor, minerals, and buffering systems. The major salivary glands secrete intermittently in response to autonomic stimulation, which is high during a meal but low otherwise. Hundreds of minor glands in the lips and cheeks secrete mucus continuously throughout the day and night. Consequently, oral function becomes impaired when salivary function is reduced. The sensation of a dry mouth (*xerostomia*) is perceived when salivary flow is reduced by 50%. The most common etiology is medication, especially drugs with anticholinergic properties but also alpha and beta blockers, calcium channel blockers, and diuretics. Other causes include Sjögren's syndrome, chronic parotitis, salivary duct obstruction, diabetes mellitus, HIV/AIDS, and radiation therapy that includes the salivary glands in the field (e.g., for Hodgkin's lymphoma and for head and neck cancer). Management involves the elimination or limitation of drying medications, preventive dental care, and supplementation with oral liquid or salivary substitutes. Sugarless mints or chewing gum may stimulate salivary secretion if dysfunction is mild. When sufficient exocrine tissue remains, pilocarpine or cevimeline has been shown to increase secretions. Commercial saliva substitutes or gels relieve dryness. Fluoride supplementation is critical to prevent caries.

Sialolithiasis presents most often as painful swelling but in some instances as only swelling or only pain. Conservative therapy consists of local heat, massage, and hydration. Promotion of salivary secretion with mints or lemon drops may flush out small stones. Antibiotic treatment is necessary when bacterial infection in suspected. In adults, *acute bacterial parotitis* is typically unilateral and most commonly affects postoperative, dehydrated, and debilitated patients. *Staphylococcus aureus* (including methicillin-resistant strains) and anaerobic bacteria are the most common pathogens. Chronic bacterial *sialadenitis* results from lowered salivary secretion and recurrent bacterial infection. When suspected bacterial infection is not responsive to therapy, the differential diagnosis should be expanded to include benign and malignant neoplasms, lymphoproliferative disorders, Sjögren's syndrome, sarcoidosis, tuberculosis, lymphadenitis, actinomycosis, and granulomatosis with polyangiitis. Bilateral nontender parotid enlargement occurs with diabetes mellitus, cirrhosis, bulimia, HIV/AIDS, and drugs (e.g., iodide, propylthiouracil).

Pleomorphic adenoma composes two-thirds of all salivary neoplasms. The parotid is the principal salivary gland affected, and the tumor presents as a firm, slow-growing mass. Although this tumor is benign, its recurrence is common if resection is incomplete. Malignant tumors such as mucoepidermoid carcinoma, adenoid cystic carcinoma, and adenocarcinoma tend to grow relatively fast, depending upon grade. They may ulcerate and invade nerves, producing numbness and facial paralysis. Surgical resection is the primary treatment. Radiation therapy (particularly neutron-beam therapy) is used when surgery is not feasible and after resection for certain histologic types with a high risk of recurrence. Malignant salivary gland tumors have a 5-year survival rate of 94% when the stage is local and 35% when distant.

Dental Care for Medically Complex Patients

Routine dental care (e.g., uncomplicated extraction, scaling and cleaning, tooth restoration, and root canal) is remarkably safe. The most common concerns regarding care of dental patients with medical disease are excessive bleeding for patients taking anticoagulants, infection of the heart valves and prosthetic devices from hematogenous seeding by the oral flora, and cardiovascular complications resulting from vasopressors used with local anesthetics during dental treatment. Experience confirms that the risk of any of these complications is very low.

Patients undergoing tooth extraction or alveolar and gingival surgery rarely experience uncontrolled bleeding when warfarin anticoagulation is maintained within the therapeutic range currently recommended for prevention of venous thrombosis, atrial fibrillation, or mechanical heart valve. Embolic complications and death, however, have been reported during subtherapeutic anticoagulation. Therapeutic anticoagulation should be confirmed before and continued through the procedure. Likewise, low-dose aspirin (e.g., 81–325 mg) can safely be continued. For patients taking aspirin and another antiplatelet medication (e.g., clopidogrel), the decision to continue the second antiplatelet medication should be based on individual consideration of the risks of thrombosis and bleeding. The newer target-specific oral anticoagulants (dabigatran, apixaban, rivaroxaban,

and edoxaban) are in increasingly common use. Simple extractions of one to three teeth, periodontal surgery, abscess drainage, and implant positioning do not typically require interruption of therapy. More extensive surgery may necessitate delaying or holding a dose of the anticoagulant or more elaborate measures to manage the risk of thrombosis and bleeding.

Patients at risk for bacterial endocarditis **(Chap. 128)** should maintain optimal oral hygiene, including flossing, and have regular professional cleanings. Currently, guidelines recommend that prophylactic antibiotics be restricted to those patients at high risk for bacterial endocarditis who undergo dental and oral procedures involving significant manipulation of gingival or periapical tissue or penetration of the oral mucosa. If unexpected bleeding occurs, antibiotics given within 2 h after the procedure provide effective prophylaxis.

Hematogenous bacterial seeding from oral infection can undoubtedly produce late prosthetic-joint infection and therefore requires removal of the infected tissue (e.g., drainage, extraction, root canal) and appropriate antibiotic therapy. However, evidence that late prosthetic-joint infection follows routine dental procedures is lacking. For this reason, antibiotic prophylaxis is generally not recommended before oral surgery or oral mucosal manipulation for patients who have undergone joint replacement surgery. Exceptions to this may be considered for patients who have experienced joint replacement complications.

Concern often arises regarding the use of vasoconstrictors to treat patients with hypertension and heart disease. Vasoconstrictors enhance the depth and duration of local anesthesia, thus reducing the anesthetic dose and potential toxicity. If intravascular injection is avoided, 2% lidocaine with 1:100,000 epinephrine (limited to a total of 0.036 mg of epinephrine) can be used safely in patients with controlled hypertension and stable coronary heart disease, arrhythmia, or congestive heart failure. Precautions should be taken with patients taking tricyclic antidepressants and nonselective beta blockers because these drugs may potentiate the effect of epinephrine.

Elective dental treatments should be postponed for at least 1 month and preferably for 6 months after myocardial infarction, after which the risk of reinfarction is low provided the patient is medically stable (e.g., stable rhythm, stable angina, and no heart failure). Patients who have suffered a stroke should have elective dental care deferred for 9 months. In both situations, effective stress reduction requires good pain control, including the use of the minimal amount of vasoconstrictor necessary to provide good hemostasis and local anesthesia.

Bisphosphonate therapy is associated with *osteonecrosis* of the jaw. However, the risk with oral bisphosphonate therapy is very low. Most patients affected have received high-dose aminobisphosphonate therapy for multiple myeloma or metastatic breast cancer and have undergone tooth extraction or dental surgery. Intraoral lesions, of which two-thirds are painful, appear as exposed yellow-white hard bone involving the mandible or maxilla. Screening tests for determining risk of osteonecrosis are unreliable. Patients slated for aminobisphosphonate therapy should receive preventive dental care that reduces the risk of infection and the need for future dentoalveolar surgery.

Halitosis

Halitosis typically emanates from the oral cavity or nasal passages. Volatile sulfur compounds resulting from bacterial decay of food and cellular debris account for the malodor. Periodontal disease, caries, acute forms of gingivitis, poorly fitting dentures, oral abscess, and tongue coating are common causes. Treatment includes correcting poor hygiene, treating infection, and tongue brushing. Hyposalivation can produce and exacerbate halitosis. Pockets of decay in the tonsillar crypts, esophageal diverticulum, esophageal stasis (e.g., achalasia, stricture), sinusitis, and lung abscess account for some instances. A few systemic diseases produce distinctive odors: renal failure (ammoniacal), hepatic (fishy), and ketoacidosis (fruity). *Helicobacter pylori* gastritis can also produce ammoniacal breath. If a patient presents because of concern about halitosis but no odor is detectable, then pseudohalitosis or halitophobia must be considered.

Aging and Oral Health

While tooth loss and dental disease are not normal consequences of aging, a complex array of structural and functional changes that occur with age can affect oral health. Subtle changes in tooth structure (e.g., diminished pulp space and volume, sclerosis of dentinal tubules, and altered proportions of nerve and vascular pulp content) result in the elimination or diminution of pain sensitivity and a reduction in the reparative capacity of the teeth. In addition, age-associated fatty replacement of salivary acini may reduce physiologic reserve, thus increasing the risk of hyposalivation. In healthy older adults, there is minimal, if any, reduction in salivary flow.

Poor oral hygiene often results when general health fails or when patients lose manual dexterity and upper-extremity flexibility. This situation is particularly common among frail older adults and nursing home residents and must be emphasized because regular oral cleaning and dental care

reduce the incidence of pneumonia and oral disease as well as the mortality risk in this population. Other risks for dental decay include limited lifetime fluoride exposure. Without assiduous care, decay can become quite advanced yet remain asymptomatic. Consequently, much of a tooth—or the entire tooth—can be destroyed before the patient is aware of the process.

Periodontal disease, a leading cause of tooth loss, is indicated by loss of alveolar bone height. More than 90% of the U.S. population has some degree of periodontal disease by age 50. Healthy adults who have not had significant alveolar bone loss by the sixth decade of life do not typically experience significant worsening with advancing age.

With the passing of those born in the first half of the twentieth century, complete edentulousness in the United States is becoming increasingly restricted to impoverished populations. When it is present, speech, mastication, and facial contours are dramatically affected. Edentulousness may also exacerbate obstructive sleep apnea, particularly in asymptomatic individuals who wear dentures. Dentures can improve verbal articulation and restore diminished facial contours. Mastication can also be restored; however, patients expecting dentures to facilitate oral intake are often disappointed. Accommodation to dentures requires a period of adjustment. Pain can result from friction or traumatic lesions produced by loose dentures. Poor fit and poor oral hygiene may permit the development of candidiasis. This fungal infection may be either asymptomatic or painful and is suggested by erythematous smooth or granular tissue conforming to an area covered by the appliance. Individuals with dentures and no natural teeth need regular (annual) professional oral examinations.

FURTHER READING

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