Episode 61 – Oral Manifestations of Systemic Conditions: Part 2 – Infectious Diseases

May 27, 2022

Introduction

The head and neck, including the oral cavity can reflect signs and symptoms of both health and disease, which may help in the diagnosis of some systemic conditions. However, the clinical appearance of these oral manifestations may be similar, accordingly other ancillary procedures, such as diagnostic imaging, biopsy, and laboratory tests may be necessary to aid in diagnosis.

Numerous infectious diseases can present with oral manifestations, which are often the first sign and symptom of the disease.

Infectious diseases with oral manifestations

Bacterial	Viral	Fungal
• Cervicofacial actinomycosis • Gonorrhea • Scarlet fever • Prenatal syphilis • Primary syphilis • Tertiary syphilis • Tuberculosis	•Chickenpox •COVID-19 •Cytomegalovirus •Hand, foot, & mouth disease •Hepatitis A, B, & C •Herpangina •Lyme •Papilloma •Primary acute herpetic gingivostomatitis •Recurrent herpes labialis •Shingles •HIV disease •Measles •Monkeypox •Infectious mononucleosis •Mumps •Roseola •Rubella	• Histoplasmosis • Candidiasis

Oral manifestations of infectious diseases

Disease	Etiology	Usual location of oral signs	Clinical features	Disease course
Bacterial				
Cervicofacial actinomycosis	*Actinomyces* species Most infections are polymicrobial with other oral anaerobes e.g., streptococcus, gram-negative rods, & other fusiform bacteria.	Swellings in region of face, neck, & floor of mouth	*Actinomyces* are often present commensally in the oral cavity. Since they are nonvirulent, they require a break in the mucous membranes to invade deeper body structures to cause illness. Infection may be associated with periodontal disease (most common portal of entry) oral surgery, dental infection, poor oral hygiene. Painless or occasionally painful nodular lesion(s) of submandibular or perimandibular area (i.e., 'lumpy jaw'), which gradually increase in size & number (i.e., multiple abscesses) & form multiple sinuses that open onto cheek or submandibular area & drain pus containing sulfur granules. Tendency to remit & recur. Lymphadenopathy is typically absent; fever is variably present. Reddish or bluish discolouration of skin overlying the lesion(s). May cause chewing difficulties.	Acute form may last several weeks; chronic form lasts months or years. Prognosis is favourable with early diagnosis & treatment. Infection may extend to cranium or bloodstream if untreated. Treatment: long term antibiotics (penicillin preferred), often combined with surgical debridement. [1] [2] [3] [4] [5]
Gonorrhea Public Health reportable disease	*Neisseria gonorrhoeae*	Lesions may occur in oral cavity at inoculation site or secondarily by hematogenous spread from a primary focus elsewhere	Sexually transmitted infection (STI) or transmitted to infant during birth. Early oral symptoms: burning or itching sensation, dryness, or heat in mouth followed by acute pain on eating or speaking. Tonsils & oropharynx most frequently involved. Oral tissues may be diffusely inflamed or ulcerated. Sore, red throat.	Incubation period: ~2-7 days after exposure. *Neisseria gonorrhoeae* have developed resistance to many antibiotics. Lesions usually resolve with appropriate antibiotic therapy. [1] [6] [7] [8]

Disease	Etiology	Usual location of oral signs	Clinical features	Disease course
			Saliva develops increased viscosity & fetid odour. Submaxillary lymphadenopathy with fever in severe cases.	
Scarlet fever (Scarlatina)	*Streptococcus pyogenes* (Group A *Streptococcus*)	Tongue, throat	Transmitted via respiratory particles, sharing contaminated objects (e.g., utensils, drinking glasses, etc.), or close contact with infected household member. Scarlet fever may develop after strep throat. Bacteria release an endotoxin that produces bright red papular rash that feels like sandpaper, blanches with pressure, & begins on trunk spreading quickly outward to cover most of body, usually sparing the palms, soles, & face. Pastia lines (accentuation of the rash in skin creases e.g., neck, underarm, elbow, groin). Other symptoms: very red sore throat, high fever, dysphagia (difficulty swallowing), nausea or vomiting, headache, cervical lymphadenopathy. Oral signs: "Strawberry tongue" begins with a white coated tongue with hyperplastic papillae. As the white coating resolves, papules remain, giving the tongue the strawberry appearance. Red, edematous, exudative tonsils. Face may appear flushed with a pale ring encircling the mouth.	Incubation period: ~2-5 days Contagious during incubation period & acute illness. Common in ages 5-15 years. Rash usually appears 1-2 days after illness begins (e.g., fever, sore throat). Rash fades in ~7 days. As rash fades, skin around fingers, toes, groin area may peel. Peeling can last for several weeks. Scarlet fever was once considered a serious childhood illness, antibiotic treatment (penicillin preferred) has greatly reduced morbidity & mortality. [9] [10] [11] [12] [13] [14] [15]
Prenatal (congenital) syphilis	*Treponema pallidum*	Palate, jaws, tongue, teeth	Transmitted transplacentally to fetus.	Pregnant individuals diagnosed with syphilis should be treated immediately (penicillin preferred).

Disease	Etiology	Usual location of oral signs	Clinical features	Disease course
Public Health reportable disease			Gummatous[1] involvement of palate, jaws, & facial bones. Hutchinson's incisors (peg-shaped with crescent-shaped notch usually on permanent incisors). Mulberry molars (multiple rounded rudimentary enamel cusps usually on permanent first molars). Glossitis, mucous patches, & fissures of corners of mouth.	Tooth deformities in permanent dentition irreversible. [1] [16] [17]
Primary syphilis Public Health reportable disease	*Treponema pallidum*	Lesion appears where organism enters body (e.g., lips, tongue, tonsillar area)	STI transmitted via skin or mucous membrane contact with ulcer(s). Small papule develops rapidly into a large, painless ulcer with indurated border (i.e., chancre); usually single chancre but may be multiple. Unliteral lymphadenopathy. Chancre & lymph nodes contain spirochetes.	If untreated, syphilis progresses through 4 stages: primary, secondary, latent (no visible symptoms), & tertiary. Penicillin preferred treatment. Chancre resolves with or without treatment. Untreated, chancre heals 1-2 months, followed by secondary syphilis in 6-8 weeks. [1]
Secondary syphilis Public Health reportable disease	*Treponema pallidum*	Oral mucosa (primarily palate), labial commissures	Maculopapular lesions of oral mucosa, 5-10 mm in diameter with central ulceration covered by grayish membrane. Eruptions occur on various mucosal surfaces & skin accompanied by fever, malaise, & sore throat.	Symptoms resolve with or without treatment. Untreated lesions may persist from several weeks to 1 year. [1]
Tertiary syphilis Public Health reportable disease	*Treponema pallidum*	Palate, tongue	Gummatous infiltration of palate or tongue followed by ulceration & fibrosis. Gumma may destroy palate, causing complete perforation.	Tertiary syphilis occurs 10-30 years after infection, can damage various organs (e.g., heart, brain, etc.), & may result in death.

[1] Gumma is a granulomatous lesion characterized by a centre of necrotic tissue with a rubbery texture.

Disease	Etiology	Usual location of oral signs	Clinical features	Disease course
			Tongue papillae atrophy produces characteristic bald tongue & glossitis.	Most individuals with untreated syphilis do not develop tertiary syphilis. [1] [18] [19] [20]
Tuberculosis (TB) Vaccine preventable disease[2] Public Health reportable disease	*Mycobacterium tuberculosis*	Tongue (most commonly affected), tonsillar area, soft palate, lips, buccal mucosa, floor of mouth, salivary glands	Transmitted via inhalation of airborne particles primarily dispersed through coughing, singing, talking by individual with active disease. Symptoms may include persistent cough (2-3 weeks), coughing up blood or mucus, fatigue, fever, night sweats, weight loss. Oral lesions are rare & may be either primary or secondary. Primary lesions are uncommon, seen in younger individuals, present as single painless ulcer of long duration with regional lymph node enlargement. Secondary lesions are more common, often associated with pulmonary TB, & present as a single, indurated, irregular, painful ulcer covered by a persistent exudate, seen in any age group but more common in middle-aged & older adults. Lesions are usually secondarily inoculated with infected sputum or due to hematogenous spread.	Oral lesions are important for early diagnosis. Lesions may be of long duration. TB is usually treated with long-term antibacterial medications. [1] [21] [22] [23] [24]
Viral				
Chickenpox (Varicella)	Varicella-zoster virus (Human herpesvirus type 3)	Gingiva, oral mucosa	Transmitted via inhalation of airborne particles or direct contact with lesions. Fever, malaise, headache, 1-2 days before skin rash appears, which is generalized, pruritic, &	Highly contagious disease which can be serious in infants, adolescents, adults, pregnant individuals, immunocompromised individuals (e.g., hospitalization, death)

[2] Refer to Episode 15 for additional information on vaccine preventable diseases.

Disease	Etiology	Usual location of oral signs	Clinical features	Disease course
Vaccine preventable disease Public Health reportable disease			progresses rapidly from macular to papular to vesicular lesions before crusting. Skin lesions may be accompanied by small vesicles on oral mucosa that rupture to form shallow ulcers. Ulcers may coalesce to form large bullous lesions that ulcerate. Mucosa may have generalized erythema.	Incubation period ~10-21 days Lesions heal spontaneously within 2 weeks. Contagious 1-2 days before rash onset until all lesions have crusted. Virus stays latent in the body. Reactivation causes herpes zoster (shingles). [1] [25] [26]
COVID-19 Staying up to date with recommended COVID-19 vaccinations[3] provides best protection against severe illness, hospitalization, & death, along with following individual public health measures. [27]	SARS-CoV-2	Tongue, palate, lips, gingiva, buccal mucosa[4]	Transmitted via respiratory particles. Presents mainly with flu-like symptoms (e.g., fever, chills, cough, dyspnea (shortness of breath), fatigue, lethargy, myalgia (muscle ache) nausea, vomiting, diarrhea, ageusia (loss of taste) or anosmia (loss of smell). [28] Oral lesions reported with COVID-19 include: <u>Ulcerative lesions</u>: aphthous-like ulcers, herpetic stomatitis, nonspecific ulcers, erythema multiforme (e.g., vesicles & erosions on palate & gingiva) [29] <u>Tongue changes</u>: geographic tongue, red or swollen tongue, strawberry tongue, fissured tongue, macroglossia, coated tongue. Tongue changes led to term 'covid tongue'.	It is unclear whether oral lesions are manifestations of COVID-19 or the results of immunosuppression &/or treatment side effects. Oral mucosal lesions usually reported to disappear (6-14 days) or regress in size with time.

[3] Refer to Episodes 28, 39, 40, 56 for additional information on COVID-19 vaccines.
[4] Refer to Episode 10 for additional information on oral manifestations of COVID-19.

Disease	Etiology	Usual location of oral signs	Clinical features	Disease course
			Hemorrhagic lesions: angina bullosa (blood filled blister), petechiae, hemorrhagic ulcer, focal erythema, spontaneous oral hemorrhage. Gingival lesions: desquamative gingivitis, necrotizing gingivitis, papillary hyperplasia. Fungal lesions:	
	Candida	Tongue, soft palate, oropharynx, buccal mucosa, labial commissures	Candidosis (e.g., pseudomembranous candidiasis, angular cheilitis).	Treated with antifungals
	Aspergillus	Palate, posterior tongue	Aspergillosis (black or yellow necrotic tissue on an ulcer base).	Treatment includes antifungals & surgical management.
	Rhizopus, *Mucor*	Paranasal sinuses, nasal areas, hard palate	Mucormycosis (malaise, facial pain, swelling, irregular black eschar,[5] exudation of pus from the eye & nose, low-grade fever, infection usually begins in nasal mucosa or palate & spreads via nearby vessels to paranasal sinuses e.g., maxillary & ethmoidal sinuses). Other oral conditions: Xerostomia[6] Oral lichenoid lesions Oral enanthema Halitosis Mucositis [30] [31] [32] [33]	Treatment includes antifungals & surgical management.

[5] Eschar is a crust that covers necrotic tissue in the skin.
[6] Refer to Episode 55 for information on xerostomia.

Disease	Etiology	Usual location of oral signs	Clinical features	Disease course
Cytomegalovirus (CMV)	Cytomegalovirus (Human herpesvirus 5)	Lips, tongue, pharynx, or any mucosal site	Transmitted via blood, body fluids, transplanted organs, transplacentally, or during birth. Primary CMV infection is usually asymptomatic or produces mild flu-like symptoms in healthy individuals, with or without a morbilliform (measles-like) rash. Rarely manifests intraorally even in immunodeficient individuals. In rare cases, CMV produces deep, aphthous-like ulcers with a punched-out look & rolled erythematous borders.	Common virus in individuals of all ages. Virus remains latent throughout life. May reactivate but rarely causes disease unless individuals are immunocompromised. Antiviral treatment is used for immunocompromised individuals with life-threatening illnesses due to CMV. [34] [35] [36] [37] [38]
Hand, foot, & mouth disease	Coxsackievirus A16, also coxsackievirus A6, enterovirus 71	Oral mucosa, pharynx	Mildly contagious infection common in children. Transmitted via contact with nasal & throat secretions, saliva, fluid from blisters or feces, or respiratory particles. Characterized by mouth sores & rash on hands & feet (flat red spots, sometimes with blistering). Fever, malaise, headache with oropharyngeal vesicles that become painful, shallow ulcers.	Incubation period 2-18 days. Most contagious during 1st week of illness. Individuals may still be infectious days or weeks after symptoms resolve. Lesions heal spontaneously in 2-4 weeks. [1] [39] [40] [41] [42]
Hepatitis A Vaccine preventable disease *Public Health reportable disease	Hepatitis A virus (HAV)	Oral mucosa	Transmitted via ingestion of contaminated food & water, or direct contact with infectious individual. May be asymptomatic, especially in children. Symptoms may include jaundice of skin/sclera of eyes, poor appetite, nausea, vomiting, diarrhea, abdominal pain, low-grade fever, joint pain, fatigue, itchy skin, dark urine, light-coloured stools. Dysgeusia (altered taste), jaundice of oral mucosa. Abnormal bleeding if significant liver damage has occurred.	HAV does not cause chronic infection, usually self-resolving infection (4-6 weeks) without lasting liver damage. In rare cases liver failure & death can result (e.g., in older individuals & those with serious health issues, e.g., chronic liver disease, immunocompromised). [43] [44] [45] [46]

Disease	Etiology	Usual location of oral signs	Clinical features	Disease course
Hepatitis B[7] Vaccine preventable disease Public Health reportable disease	Hepatitis B virus (HBV)	Oral mucosa, gingival tissues, tongue	Highly infectious, transmitted via blood & body fluids, household contact between family members, or during birth. Symptoms can include jaundice of skin/sclera of eyes, poor appetite, nausea, vomiting, diarrhea, abdominal pain, fever, joint pain, fatigue, dark urine. Oral signs of liver dysfunction include mucosal membrane jaundice, bleeding disorders, petechiae, increased bruising, gingivitis, gingival bleeding, fetor hepaticus (i.e., a distinctive breath odour associated with severe liver disease & hepatic encephalopathy), cheilitis, smooth & atrophic tongue, xerostomia, crusted perioral rash.	Hepatitis B can be a short-term acute infection lasting <6 months. However, it can be chronic leading to serious life-threatening health issues (e.g., cirrhosis, liver cancer). Treatment for chronic infection may include antiviral medications, interferon injections, & possibly liver transplant if liver is severely damaged. [47] [48] [49] [50]
Hepatitis C Public Health reportable disease	Hepatitis C virus (HCV)	Oral mucosa, gingival tissues, tongue	Transmitted via infected blood & body fluids, or during birth. Symptoms can include jaundice of skin/sclera of eyes, poor appetite, nausea, vomiting, diarrhea, abdominal pain, fever, joint pain, fatigue, dark urine, light-coloured stools, ascites (fluid build up in abdomen), itchy skin. Oral signs of liver dysfunction include mucosal membrane jaundice, bleeding disorders, petechiae, increased bruising, gingivitis, gingival bleeding, fetor hepaticus, cheilitis, smooth & atrophic tongue, xerostomia, crusted perioral rash.	Hepatitis C can be a short-term acute illness but for most individuals it leads to chronic infection. Chronic infection can be lifelong if not treated, leading to serious health issues (e.g., liver damage, cirrhosis, liver cancer, death). Treated with antiviral medications. [47] [51] [52]

[7] Refer to Episode 53 for additional information on Hepatitis B.

Disease	Etiology	Usual location of oral signs	Clinical features	Disease course
			Increased likelihood of Sjögren's syndrome, sialadenitis (saliva gland infection), & oral lichen planus.	
Herpangina	Coxsackieviruses A & B, echovirus, & enterovirus A71	Oral mucosa, pharynx, tongue	Transmitted via close contact, respiratory particles, direct contact with saliva, mucus, feces. Sudden onset of fever, sore throat, & oropharyngeal vesicles, usually in children <4 years, during summer months. Vesicles: 1-2 mm, grayish-white surrounded by red areola; vesicles enlarge & ulcerate.	Incubation period 2-9 days. Fever for 1-4 days; recovery uneventful. [1] [53] [54] [55]
Lyme disease (Lyme borreliosis) Public Health reportable disease	*Borrelia burgdorferi*, rarely *Borrelia mayonii*	Head, neck	Bacteria transmitted by bite of infected black-legged tick (deer tick). Untreated disease produces range of symptoms, depending on stage of infection. Early signs: erythema migrans usually at site of tick bite (i.e., red macule or papule, erythematous, circular "bull's-eye rash"), fever, chills, fatigue, headache, myalgia, arthralgia (joint pain), lymphadenopathy. Later signs: erythema migrans on other areas of body, arthralgia, joint swelling, severe headaches, neck stiffness, impaired memory. Orofacial signs: facial palsy (Bell's palsy), TMJ arthralgia, dysgeusia, sore throat, neck pain, erythema migrans, acute parotitis, masticatory myalgia, limitation in jaw opening, dental pain.	Most symptoms appear 3-30 days after tick bite. Late symptoms may appear weeks to months after tick bite. Early antibiotic treatment helps prevent late Lyme disease. Some individuals report persistent symptoms of pain, fatigue, difficulty thinking even after treatment. Cause for persistent symptoms is unclear. [56] [57] [58] [59] [60] [61] [62] [63]

Disease	Etiology	Usual location of oral signs	Clinical features	Disease course
Papilloma Vaccine preventable disease for HPV types 6, 11, 16, 18, 31, 33, 45, 52, 58	Human papillomavirus (HPV)[8] (>40 HPV types can infect mucosa)	Oral mucosa	Transmitted via skin-to-skin contact, transplacentally, or during birth. Single or multiple papillary lesions, with white keratinized surfaces containing many pointed projections, cauliflower lesions covered with normal-coloured mucosa, or multiple pink or pale bumps (focal epithelial hyperplasia). Oropharyngeal cancer signs: sore throat, lymphadenopathy, inability to open mouth fully, trouble moving tongue, dysphagia, odynophagia (painful swallowing), swollen tonsil, orofacial numbness, indurations, unhealing sores, etc.	Lesions can grow in size & spread. Most HPV infections are cleared by the immune system within 2 years. Several HPV types have oncogenic potential, with at least 14 being high-risk types, including HPV16, 18, 31, & 33. [1] [64] [65] [66] [67]
Primary acute herpetic gingivostomatitis	Herpes simplex virus type 1 (HSV-1), rarely type 2 (HSV-2) (Human herpesviruses types 1 or 2)	Lips, oral mucosa	Virus transmitted via direct contact with lesions or infected body fluids (e.g., saliva). Occurs primarily in infants, children, & young adults. Labial vesicles rupture & crust, intraoral vesicles quickly ulcerate; extremely painful. Acute gingivitis, fever, malaise, foul breath odour, & cervical lymphadenopathy. Difficulty eating & drinking may lead to dehydration.	Ulcers heal spontaneously in 10-14 days unless secondarily infected. Oral antiviral therapy is recommended if initiated early. HSV-1 most commonly infects the trigeminal ganglia, where the virus remains latent until reactivation, most commonly in the form of herpes labialis. [1] [68] [69]
Recurrent herpes labialis	Herpes simplex virus (HSV)	Mucocutaneous junction of lip, perioral skin.	Reactivation of HSV. Extraoral lesions: eruption of groups of vesicles which may coalesce, then rupture creating painful	Lasts ~7-10 days, but may be prolonged if secondarily infected.

[8] Refer to Episode 7, 12, 53, & 58 for additional information on HPV.

Disease	Etiology	Usual location of oral signs	Clinical features	Disease course
		Intraoral lesions less common, tend to occur on keratinized mucosa (attached gingiva, hard palate)	weeping ulcerations that crust. Lesions sometimes preceded by burning or tingling sensation. Intraoral vesicles rupture to form small painful ulcers.	Ulcerations infectious for ~3-5 days, until they crust. Antivirals are well established treatment for HSV infection. [1] [34] [70]
Shingles (Herpes zoster) Vaccine preventable disease	Reactivation of varicella-zoster virus (Human herpesvirus type 3)	Cheek, tongue, gingiva, palate, side of face	Prodromal phase: ~48 hours before lesions develop & may include tooth pain, fatigue, headache. Acute eruptive phase: painful unilateral vesicular eruption & ulceration in linear pattern which follows the sensory distribution of trigeminal nerve or one of its branches.	Acute phase can last 2-4 weeks. Gradual healing without scarring. Postherpetic neuralgia is common (e.g., pain, burning, tingling, prickling) can last ≥4 weeks. Several antiviral medications are available to treat shingles, & shorten the length & severity of the illness. [1] [71] [72]
HIV disease Public Health reportable disease	Human immunodeficiency virus *Candida*	 Gingiva, palate, pharynx	Transmitted via sexual contact, blood, transplacentally, during birth, or breast feeding. Many oral signs have positive predictive value for immune decline. Oral signs may include: Oral candidiasis: often the first presenting sign of HIV infection. Candidal infections may be recurrent & severe.	Oral lesions usually associated with CD4 lymphocyte counts <400 cells/µL. CD4 T-cell count reliably reflects the current risk of acquiring opportunistic infections. [1] [74] [75] Frequency of candidal infection increases as HIV disease progresses (i.e., as viral loads increase CD4 lymphocyte counts decline). Adherence to antiretroviral therapy (ART) reduces incidence of oral candidiasis. Candidiasis treated with antifungals, but can be difficult to

Disease	Etiology	Usual location of oral signs	Clinical features	Disease course
				eliminate in immunocompromised individuals. [34]
	Herpes simplex virus (HSV)	Vermillion of lip, keratinized mucosa (e.g., dorsal tongue, gingiva, hard palate), nonkeratinized mucosa (e.g., labial mucosa, ventral tongue, floor of mouth, buccal mucosa, soft palate) & may extend to tonsillar pillars & esophagus.	Recurrent herpes simplex: immunodeficiency permits reactivation of latent herpes infections. HSV infection often more aggressive, prolonged, & diffuse.	Recurrent HSV lesions typically heal 7-10 days but in immunodeficient individuals, lesions can be more persistent. Treated with antivirals. [34]
	Epstein-Barr virus (EBV) *(Human herpesvirus 4)*	Tongue	Hairy leukoplakia (HL): usually, asymptomatic corrugated white verrucous plaques on lateral borders of the tongue. Plaques range in appearance from thin & homogenous to thickened & rough, mimicking hyperplastic candidiasis. If symptomatic, lesions may be infected with *Candida.* HL is the most specific oral sign of HIV disease. [34]	HL has prognostic implications for progression to AIDS as HL rarely manifests with CD4 counts >200 cells/µL. Biopsy should be performed to rule out candidiasis. Treatment is elective if asymptomatic (e.g., podophyllin resin with or without antiviral cream [e.g., penciclovir or acyclovir]). Antifungals if *Candida* present.

Disease	Etiology	Usual location of oral signs	Clinical features	Disease course
	Kaposi sarcoma-associated herpesvirus (KSHV), also known as Human herpesvirus-8 (HHV-8)	Hard palate, mucosa, gingiva, salivary glands	Kaposi sarcoma (KS): brown, blue, purple, or red patches & papules. Early lesions appear as flat macules or patches on the mucosal surface, over time becoming nodular, with tendency to ulcerate & bleed. Salivary glands can be affected & may cause head & neck lymphadenopathy.	KS is second most common malignancy in HIV disease; considered an AIDS-defining illness. ART has reduced incidence & clinical course of KS. KS treatment may include surgical excision, cryotherapy, sclerotherapy, radiotherapy, laser therapy, & topical or intralesional chemotherapy. [34]
	Cytomegalovirus (CMV) (Human herpesvirus 5)	Lips, tongue, pharynx, or any mucosal site	Cytomegalovirus (CMV) infection: can cause retinitis, pneumonia, & encephalitis. Rarely manifests intraorally even in immunodeficient individuals. In rare cases, CMV produces deep, aphthous-like ulcers with a punched-out look & rolled erythematous borders.	In immunodeficient individuals, CMV infection is associated with significant morbidity & mortality. Treated with intravenous antiviral agents.
	Human papillomavirus (HPV)	Oral mucosa	Human papillomavirus (HPV): higher prevalence of oral HPV infections & higher risk of developing HPV-associated malignancies. Most common oral manifestation is oral mucosal warts that appear on the gingiva, lips, & labial mucosa, usually caused by HPV 13 or 32. HPV-associated oral squamous cell carcinomas may present as a nonhealing ulcer with signs of bleeding, loosening of teeth, neck masses. Symptoms may also include dysphagia, dysarthria (difficulty speaking), & odynophagia.	Although ART has reduced incidence of many HIV-associated oral lesions, incidence of HPV-associated oral warts has increased with ART. This phenomenon is poorly understood. Treatment for HPV-associated oral warts includes excision, laser ablation, cryotherapy, or topical 5-fluorouracil or imiquimod. [34]
	Not caused by an infectious agent	Oral mucosa	Aphthous ulcers: painful yellow-gray ulcerated areas surrounded by halo of erythema, ranging in size from 1 mm to >1 cm. Forms of recurrent	Aphthous ulcers in HIV-positive individuals may have extremely

Disease	Etiology	Usual location of oral signs	Clinical features	Disease course
			aphthous ulcerations include minor, major, & herpetiform. Major aphthae are usually >1 cm, form deep crater erosions, & differ from other aphthae forms as they often heal with scarring. Major form is most common in HIV-positive individuals. Herpetiform aphthae tend to occur in clusters of 10-100 ulcers, may be localized or distributed throughout the oral mucosa, & are often mistaken for HSV lesions.	protracted healing times, up to months. Recurrent appearance of the major aphthae is a reliable indicator of severe immunodeficiency & disease progression in HIV-positive individuals. Major aphthae take 14-21 days to heal. Biopsy indicated for diagnosis of HIV-related ulcers as bacterial, viral, & fungal pathogens, as well as HIV-medications, can cause atypical oral ulcers. [76]
	Periodontal pathogens similar to periodontitis seen in non-HIV individuals, but also include Candida albicans, herpes viruses, or superinfecting bacterial species	Periodontium	Necrotizing periodontal disease (NPD): HIV infection is associated with occurrence of NPD, increased attachment loss, & gingival recession that correlate with declining CD4 counts. Necrotizing gingivitis: necrosis & ulcer of interdental papilla, gingival bleeding, pain, pseudomembrane formation, halitosis, lymphadenopathy, fever. Necrotizing periodontitis (NP): necrosis & ulcer of interdental papilla, gingival bleeding, pain, pseudomembrane formation, periodontal attachment & bone destruction, bone sequestrum may occur, halitosis, lymphadenopathy, fever.	NPD may be predictive of progression of HIV infection. NPD may be more frequent & progress faster, with higher risk of evolving into more severe lesions (i.e., NP & NS). Higher tendency for disease recurrence & poor response to therapy. [77] [78]

Disease	Etiology	Usual location of oral signs	Clinical features	Disease course
			Necrotizing stomatitis (NS): painful, destructive necrosis & ulceration in periodontal, & other oral surfaces beyond mucogingival junction. Bone denudation through the alveolar mucosa, with areas of osteitis & bone sequestrum. [73]	
Measles[9] (Rubeola) Vaccine preventable disease *Public Health reportable disease	Morbillivirus	Oral mucosa	Highly contagious virus transmitted via respiratory particles. Characterized by fever, malaise, cough, coryza (runny nose), conjunctivitis (red watery eyes), enanthem (i.e., Koplik spots), maculopapular rash. Koplik spots: tiny white spots with bluish-white centres surrounded by bright red halo (described as grains of salt on a red background). Cutaneous pruritic erythematous maculopapular rash begins in front of & below ears & side of neck. Spreads within 1-2 days in a cephalocaudal direction (head to hands & feet)	Measles spreads easily, can cause serious complications (e.g., hospitalization & death) in children <5 years, adults >20 years, pregnant individuals, individuals who are immunocompromised. Koplik spots typically occur 2-3 days after symptoms begin (e.g., high fever, cough, coryza, conjunctivitis) & 1-2 days before cutaneous lesions appear. Koplik spots resolve with cutaneous lesion onset. Cutaneous rash lasts ~7 days, gradually fading on face & lastly feet. [10] [79] [80] [81] [82]
Monkeypox On May 20, 2022 Ontario Chief Medical Officer of Health issued an Order under	Monkeypox virus (*Poxviridae* family)	Tongue, mucous membranes	Viral illness endemic to parts of Central & West Africa. Transmitted via direct contact with bodily fluids or lesions of infected animals or person; direct contact with contaminated material (e.g., linen, clothing); respiratory droplets; or transplacentally.	Rodents thought to be main sources of the virus. [90] Incubation period ~7-14 days (range 5-21 days), usually asymptomatic, noncontagious during this stage.

[9] Refer to Episode 15 for additional information on measles.
Refer to Episode 34 for information on the impact on children vaccine schedules caused by the COVID-19 pandemic.

Disease	Etiology	Usual location of oral signs	Clinical features	Disease course
section 77.6 of Health Protection & Promotion Act requiring any cases that meet the case definition to be reported to Public Health Ontario within 1 business day.[10] Individuals who develop symptoms should seek advice from their healthcare provider. [83]			Symptoms similar to but milder than smallpox symptoms, except lymphadenopathy does not occur with smallpox. Illness begins with fever, headache, malaise, myalgia, lymphadenopathy (i.e., submandibular, cervical, axillary [armpits], inguinal [groin], may be bilateral or unilateral). Enanthem (small lesions) develops on tongue & oral mucous membranes first. Lesions ulcerate & may cause difficulties with eating & drinking. Cutaneous rash begins on face & spreads in cephalocaudal direction to hands & feet (including palms & soles). Rash has a centrifugal distribution (i.e., lesions concentrated on extremities & face. Lesions progress through following stages: macules (flat lesions), papules (raised); vesicles (raised, filled with clear fluid); pustules (filled with opaque fluid) are sharply raised, round, firm to touch (like peas under the skin), & develop central depression (i.e., umbilicated). Lesions crust over forming scabs. Scabs eventually fall off & may leave scars. [84] [85] [86] [87] [88] [89]	Lymphadenopathy typically occurs with fever onset, 1-2 days before rash onset. May be contagious when symptoms begin. Contagious at enanthem onset. Cutaneous rash follows enanthem beginning ~1-3 days after fever onset. No longer contagious once scabs have fallen off. Self-limited disease typically lasting 2-4 weeks. Severe cases can occur with mortality ~3-6%. [91] Treatment is supportive as there is no proven, safe treatment for monkeypox virus infection. Certain antiviral medications may potentially be useful. [92] [93] There is global evidence that smallpox vaccines may offer

[10] Section 77.6 Health Protection & Promotions Act Chief Medical Officer of Health Order https://www.health.gov.on.ca/en/pro/programs/emb/docs/CMOH_77.6_Order_Monkeypox_HCP_PHU.pdf

Disease	Etiology	Usual location of oral signs	Clinical features	Disease course
				protection against monkeypox. Individuals who received smallpox vaccine are at reduced risk of monkeypox. Canada stopped routine immunization against smallpox in 1972. [92] [94]
Infectious mononucleosis (Kissing disease, mono)	Epstein-Barr virus (EBV) (Human herpesvirus type 4) Other infections that can cause infectious mononucleosis: • Cytomegalovirus (CMV) • Toxoplasmosis (*Toxoplasma gondii* parasite) • HIV • Rubella • Hepatitis A, B, C • Adenovirus	Oral mucosa	Transmitted mainly via bodily fluids, especially saliva (e.g., kissing, sharing utensils, etc.), blood & semen during sexual contact, or organ transplantations. Fatigue, sore throat, malaise, low-grade fever, & enlarged cervical lymph nodes, swollen tonsils, splenomegaly (swollen spleen), hepatomegaly (enlarged liver), maculopapular skin rash. Numerous small oral ulcers usually appear several days before lymphadenopathy. Gingival bleeding & multiple petechiae at junction of hard & soft palates.	Disease is common among teenagers & young adults. Symptoms appear 4-6 weeks after infected. Many signs & symptoms last 4-6 weeks. Oral lesions disappear during convalescence. After infection, EBV remains dormant in throat & blood cells for life. The virus can reactivate periodically; however, usually without symptoms & no risk for developing mononucleosis again. [1] [95] [96] [97]
Mumps (Epidemic parotitis) Vaccine preventable disease	Paramyxovirus	Parotid glands	Transmitted via respiratory particles or contact with infected saliva (e.g., sharing contaminated utensils, etc.). Fever, headache, fatigue, myalgia, loss of appetite. Oral signs: pain, tenderness, & swelling in one or both parotid salivary glands (parotitis) causing the	Incubation period ~16-18 days (range 12-25 days). Infectious period: 2 days before to 5 days after parotitis onset. On average, parotitis lasts 5 days, with most cases resolving after 10 days. Mumps can cause complications, especially in adults, such as

Disease	Etiology	Usual location of oral signs	Clinical features	Disease course
Public Health reportable disease			angle of the mandible to no longer be visible or felt. Odynophagia or pain while chewing.	orchitis (which may lead to testicular atrophy, temporary sterility, or decreased fertility); oophoritis; mastitis; pancreatitis; encephalitis; meningitis; deafness. [98] [99] [100] [101]
Roseola (Roseola infantum or sixth disease)	Human herpesvirus type 6 or 7	Soft palate, uvula	Transmitted via contact with respiratory secretions or saliva (e.g., sharing contaminated utensils, etc.). High fever (may cause febrile seizures). Nonpruritic, pink papular rash that begins on the trunk & spreads to extremities after fever resolves. Irritability, swollen glands, swollen eyelids, ear pain, decrease appetite, diarrhea, cough. Oral signs: erythematous papules on soft palate & base of uvula (i.e., uvulopalatoglossal spots or Nagayama spots).	Most commonly affects children <2 years. Fever typically lasts 3-5 days. Rash can persist for 1-2 days. [10] [102] [103] [104]
Rubella (German measles or 3-day measles) Vaccine preventable disease *Public Health reportable disease	Rubella virus	Palate	Transmitted via respiratory particles or transplacentally. Prodrome: low-grade fever, headache, sore throat, malaise, lymphadenopathy, conjunctivitis. Fine pink rash starts on the face & spreads to the rest of body, over time the spots increase in diameter & become macule papules. Post-auricular, occipital, & posterior cervical lymphadenopathy. Petechiae form on the soft palate (i.e., Forchheimer spots), later coalescing into a red	Clinical manifestations appear between 12-23 days after infection. Prodrome lasts ~1-5 days Rash lasts ~3-5 days. Infection during early pregnancy can cause spontaneous abortion, stillbirth, or congenital defects (e.g., cataracts, congenital heart disease, hearing impairment, developmental delay). [10] [105] [106] [107] [108]

Disease	Etiology	Usual location of oral signs	Clinical features	Disease course
			blush. Forchheimer spots occasionally precede skin rash.	
Fungal				
Candidiasis	*Candida* Usually *Candida albicans,* but also *Candida glabrata, Candida tropicalis, Candida krusei*	Any area of oral mucosa	*Candida* is often present in the oral cavity, an imbalance in normal flora may result in overgrowth, due to corticosteroid (e.g., inhaled for asthma) or antibiotic use; xerostomia (e.g., from medications or medical conditions); immunosuppression; etc. Common types of *candida* infections include: Pseudomembranous form (thrush) has white patches that are easily wiped off revealing erythematous or eroded mucosa. Any oral surface may be involved but commonly buccal mucosa, palate, & vestibule are affected. Erythematous form manifests as nonspecific areas of erythema & atrophy, commonly on palate or dorsum of tongue. Angular cheilitis due to *Candida* involves cracked, red, & sometimes ulcerated fissures in the labial commissures. Chronic atrophic candidiasis (denture stomatitis) presents as chronic erythema & edema of the palate in contact with the denture base. Hyperplastic form is rare & manifests as white plaques that cannot be easily removed. Often mistaken for premalignant leukoplakia.	Usually responds to antifungals. However, oral candidiasis can be difficult to eliminate in individuals who are immunocompromised. Removable dental prostheses (e.g., dentures) must also be treated to prevent reinoculation. [1] [34] [109] [110] [111]

Disease	Etiology	Usual location of oral signs	Clinical features	Disease course
Histoplasmosis	*Histoplasma capsulatum*	Any area of the oral cavity, particularly tongue, gingiva, or palate.	Numerous small intraoral nodules may ulcerate. Hoarseness & dysphagia may occur because of lesions in larynx usually associated with fever & malaise. Clinical manifestations usually seen in individuals who are immunocompromised or in individuals who are exposed to high quantity of spores.	Can be caused by breathing in fungal spores, which are often found in bird & bat droppings. Severe histoplasmosis (i.e., disseminated histoplasmosis) may be fatal if untreated. Treated with antifungal drugs. [1] [112] [113]

* Diseases marked * should be reported immediately to local Medical Officer of Health by phone (24/7) or fax (Mon-Fri, 8:30 am – 4:30 pm). Other diseases can be reported next working day by fax, phone, or mail. [114]

Glossary of terms [115] [116] [117]	
Blister – raised, fluid-filled lesion (vesicle or bulla)	**Nodule** – solid raised lesion >5 mm; extends into dermis or subcutaneous tissue
Bulla – raised, clear fluid-filled blister >1 cm	**Papule** – solid raised lesion <1 cm
Crust (scab) – consists of dried serum, blood, or pus	**Patch** – flat lesion >1 cm
Enanthem – lesion on surface of mucous membrane	**Plaque** – solid lesion >1 cm, raised or depressed compared to skin surface
Induration – localized hardening of soft tissue	**Pustule** – raised, pus-filled lesion, usually <1 cm
Macule – flat lesion <1 cm	**Verrucous** – irregular, pebbly, or rough surface
Maculopapular – consisting of both macules and papules	**Vesicle** – raised, clear fluid-filled blister <1 cm

Take home messages

- Oral healthcare clinicians should be aware and knowledgeable of oral lesions and their possible relationship with infectious diseases. Vigilant detection and appropriate referral are vital for early diagnosis, effective treatment, and favourable health outcomes.
- Educating clients on self-examination techniques to detect oral lesions and to report anything unusual or suspicious to a dental or medical professional will also aid in early diagnosis.
- Monkeypox stresses the importance of oral healthcare professionals staying current on emerging infectious diseases, including knowing their oral manifestations to be part of the interdisciplinary team to identify disease occurrence as early as possible.

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