

Oral manifestations of systemic disease

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On examination, the oral cavity may exhibit manifestations of underlying systemic disease and serve as an indicator of overall health. Systemic diseases with oral findings include autoimmune, hematologic, endocrine, and neoplastic processes. Autoimmune disease may manifest as oral ulcerations, changes in the salivary and parotid glands, and changes in the tongue. Patients with hematologic illnesses may present with gingival bleeding or tongue changes such as glossitis, depending on the etiology. Oral changes associated with endocrine illness are variable and depend on the underlying condition. Neoplastic changes include metastatic lesions to the bony and soft tissues of the oral cavity. Patients with chronic diseases such as gastroesophageal reflux and eating disorders may present with dental erosions that cause oral pain or halitosis. In the pediatric population, oral changes can be related to rare cancers, such as Langerhans cell histiocytosis, or infectious etiologies, such as Kawasaki disease. In both adults and pediatric patients, poor oral health has been linked to poorer health outcomes overall. Thorough history taking and physical examination by dentists may aid in determining the underlying etiology of oral changes and allow for earlier intervention by medical colleagues.

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The oral cavity can lend insight into underlying health in both adults and children. In 2000, the US Surgeon General highlighted the links between oral and general health.¹ Many systemic diseases first present as, or can be identified based on, changes within the oral cavity. This article will review select common oral cavity findings in adult and pediatric patients and the systemic diseases with which they may be associated.

Autoimmune diseases

Lupus erythematosus

Systemic lupus erythematosus (SLE) and discoid lupus erythematosus (DLE) present with oral findings in 8%-45% and 4%-25% of patients, respectively.² SLE is the most common vascular collagen disorder in the United States. Associated oral lesions can vary greatly in appearance, manifesting as ulcerations, erythema, or hyperkeratosis (Fig 1).^{3,4} Cheilitis may also be present.³ Oral lesions associated with DLE are typically ulcerated, atrophic, and erythematous; they usually demonstrate a central zone with radiating, fine, white striae.⁵ These oral lesions are identical to erosive lichen planus; however, the absence of skin findings in patients with erosive lichen planus typically excludes the diagnosis of DLE.⁴

Lesions can be treated with topical corticosteroids, systemic antimalarial drugs, or systemic immunosuppressive agents, if needed, based on severity.

Systemic sclerosis (scleroderma)

Systemic sclerosis is characterized by dense collagen deposition within the tissues and ranges from localized to systemic disease. Females are more commonly affected.⁵ Skin findings range from Raynaud phenomenon to masklike and "mouse" facies. Oral findings are variable, including changes to the lips and mouth (Fig 2). The lips appear pursed, and opening of the mouth may be limited.⁶ Xerostomia is common; the tongue appears smooth, as do the palatal rugae.⁵ On panoramic radiographs, mandibular resorption may be noted.^{6,7}

Treatment is focused on limiting further progression, although often the changes are irreversible. Range of motion exercises may be beneficial to aid in mouth opening, and oral hygiene instruction should be provided to the patient.⁶

Sjögren syndrome

Sjögren syndrome (SS) is characterized by xerostomia and xerophthalmia and more commonly affects females. It can be classified as primary or secondary, the latter if SS is associated with another autoimmune illness. Associated autoimmune conditions include rheumatoid arthritis, SLE, and scleroderma.⁸ Oral manifestations of SS include parotid enlargement and findings related to decreased saliva, such as increased risk of dental caries, infections, and dysphagia. Saliva is often thick



Fig 1. Oral ulcer in a patient with systemic lupus erythematosus. (Reprinted from Islam NM, Bhattacharyya I, Cohen DM. Common oral manifestations of systemic disease. *Otolaryngol Clin North Am.* 2011;44(1):161-182, with permission from Elsevier.⁴)

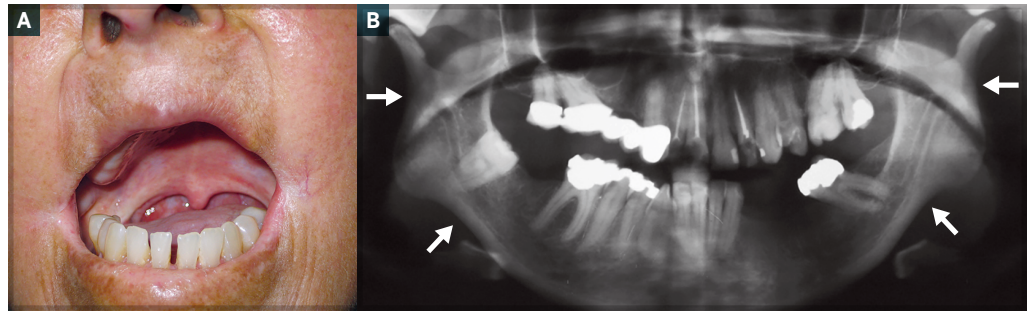


Fig 2. A. Pursed lips and masklike facies of a patient with scleroderma. B. Bone resorption (arrows) related to scleroderma. (Reprinted from Albilal et al with permission from the Canadian Dental Association.⁶)



Fig 3. Fissured tongue related to Sjögren syndrome. (Reproduced with permission from Common tongue conditions in primary care. *American Family Physician.* 2010;81(5):627-634.⁹ Copyright ©2010 American Academy of Family Physicians. All rights reserved.)

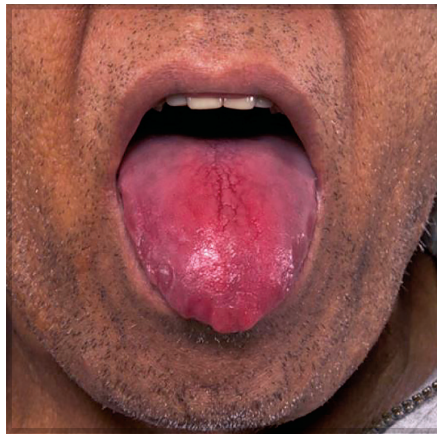


Fig 4. Amyloid deposition of the tongue in a patient with amyloidosis. (Reprinted from Mangold AR, Torgerson RR, Rogers RS 3rd. Diseases of the tongue. *Clin Dermatol.* 2016;34(4):458-469, with permission from Elsevier.¹¹)

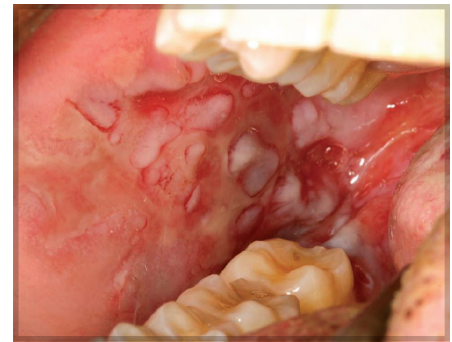


Fig 5. Ulcerations associated with pemphigus vulgaris. (Reproduced with permission from Oral manifestations of systemic disease. *American Family Physician.* 2010;82(11):1381-1388.¹⁴ Copyright ©2010 American Academy of Family Physicians. All rights reserved.)

or absent, and the oral mucosa may be dry, red, and wrinkled.⁴ The tongue may be atrophic or fissured with deep grooves and malodorous due to food trapping (Fig 3).^{4,9} Sjögren syndrome is complicated by non-Hodgkin lymphoma, primarily low-grade mucosal-associated lymphoid tissue lymphomas, with a reported incidence of 3.5%-11%.¹⁰

Treatment includes the use of sialogogues, systemic muscarinic agonists, and orosalivary gland stimulants as well as instruction in oral hygiene to protect the dentition.

Amyloidosis

Amyloidosis can be classified as 2 types: organ-limited or systemic. The oral soft tissues are rarely affected in organ-limited amyloidosis. Systemic amyloidosis can lead to macroglossia due to amyloid deposition in the tongue (Fig 4).¹¹ Tongue lesions present as nodular or diffuse enlargement with subsequent ulcerations or hemorrhages.^{12,13} Biopsy can confirm the diagnosis.

Treatment depends on the type of amyloidosis and the source of amyloid production.

Miscellaneous

Other autoimmune illnesses associated with oral findings include pemphigus vulgaris, Wegener granulomatosis, Crohn disease, Behçet syndrome, benign mucous membrane pemphigoid, sarcoidosis, and lichen planus. Painful oral ulcerations are common among all of these conditions, which may be difficult to distinguish from one another (Fig 5).¹⁴ A positive Nikolsky sign—dislodgment of the superficial epidermis with a shearing force—is consistent with pemphigus. Wegener granulomatosis often presents as “strawberry gingivitis.”¹⁴ Crohn disease is associated with diffuse swelling, localized mucogingivitis, and cobblestoned mucosa. Nodules, tissue tags, polyps, and pyostomatitis vegetans can also occur in association with Crohn disease (Fig 6).¹⁵

Hematologic diseases

Blood disorders can present differently within the oral cavity based on the underlying condition. Mucosal pallor and atrophy are common in anemia, whereas hemorrhages and gingival

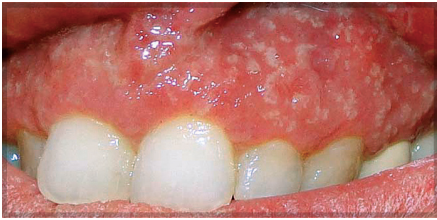


Fig 6. Pyostomatitis vegetans in a patient with Crohn disease. (Reprinted from Atarbashi-Moghadam et al with permission from JCDR Research and Publications Ltd.¹⁵)

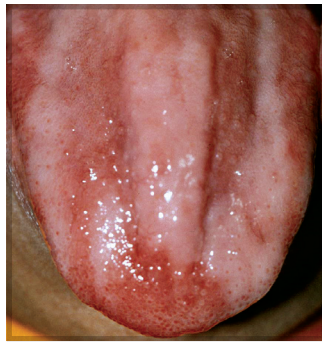


Fig 7. Atrophic glossitis. (Reproduced with permission from Oral manifestations of systemic disease. *American Family Physician*. 2010;82(11):1381-1388.¹⁴ Copyright ©2010 American Academy of Family Physicians. All rights reserved.)



Fig 8. Magenta tongue in a patient with pernicious anemia. (Reprinted from Islam NM, Bhattacharyya I, Cohen DM. Common oral manifestations of systemic disease. *Otolaryngol Clin North Am*. 2011;44(1):161-182, with permission from Elsevier.⁴)



Fig 9. Diffuse, hemorrhagic enlargement of the gingiva in a patient with leukemia. (Reproduced with permission from Oral manifestations of systemic disease. *American Family Physician*. 2010;82(11):1381-1388.¹⁴ Copyright ©2010 American Academy of Family Physicians. All rights reserved.)



Fig 10. Idiopathic purpura and hemorrhagic bullae resulting from thrombocytopenia. (Reproduced with permission from Oral manifestations of systemic disease. *American Family Physician*. 2010;82(11):1381-1388.¹⁴ Copyright ©2010 American Academy of Family Physicians. All rights reserved.)

bleeding are often associated with hematopoietic neoplasms or coagulopathies. Treatment of oral manifestations of hematologic illnesses is focused on management of the underlying disease in coordination with the patient's hematologist or oncologist.

Anemia

Iron-deficiency anemia and pernicious anemia both can present with oral findings. Iron-deficiency anemia often presents as atrophy and pallor of the mucosa and atrophic glossitis (Fig 7). Patients with pernicious anemia may present with erythema of the tongue (either focal or diffuse) along with atrophy. This condition is often referred to as *magenta tongue* (Fig 8).⁴ Burning of the lips, tongue, and buccal mucosa are common to both types of anemia, as is angular cheilitis. Overgrowth of *Candida albicans* may be a concurrent finding.¹⁴

Leukemia

Gingival enlargement, petechiae, mucosal bleeding, and ulcerations are findings within the oral cavity that are suggestive of leukemia (Fig 9).¹⁴ Hemorrhages can occur on both the hard and soft palates once the platelet counts fall below 20,000/ μ L (20×10^9 /L). Mucosal ulcers may also be present.⁴ Bony infiltration by malignant cells can lead to ulcerations of the palate and destruction of the nasal cavity and paranasal sinuses secondary to mucormycosis.¹⁶

Thrombocytopenia

Low platelet counts in patients without underlying hematologic malignancy may initially present within the oral cavity. Hemorrhages can range from petechiae to hemorrhagic bullae and hematomas (Fig 10). Bleeding can occur with minor trauma or occur spontaneously, depending on platelet counts.¹⁴

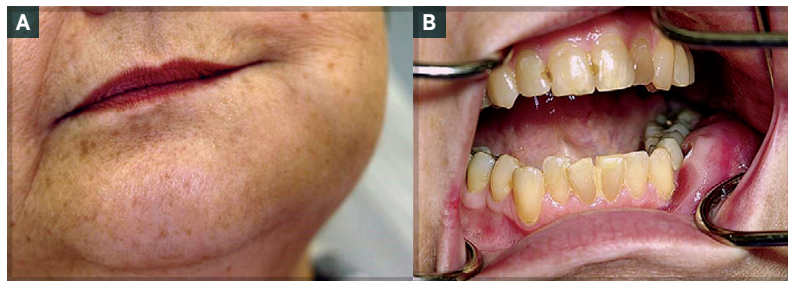


Fig 11. Oral manifestations of multiple myeloma. A. Facial asymmetry. B. Mucosal swelling. (Reprinted from Islam NM, Bhattacharyya I, Cohen DM. Common oral manifestations of systemic disease. *Otolaryngol Clin North Am.* 2011;44(1):161-182, with permission from Elsevier.⁴)



Fig 12. Periodontitis in a patient with diabetes. (Reproduced with permission from Oral manifestations of systemic disease. *American Family Physician.* 2010;82(11):1381-1388.¹⁴ Copyright ©2010 American Academy of Family Physicians. All rights reserved.)



Fig 13. Melanin pigmentation associated with Addison disease. (Reproduced with permission from Oral manifestations of systemic disease. *American Family Physician.* 2010;82(11):1381-1388.¹⁴ Copyright ©2010 American Academy of Family Physicians. All rights reserved.)

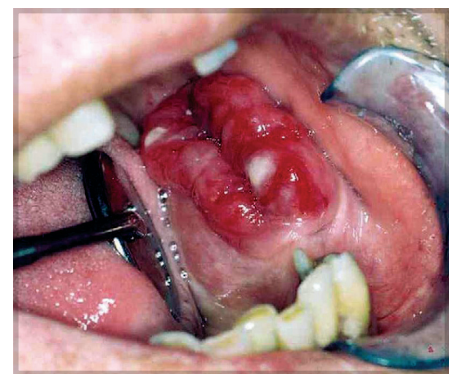


Fig 14. Tumor resulting from metastatic lung cancer. (Reprinted from Islam NM, Bhattacharyya I, Cohen DM. Common oral manifestations of systemic disease. *Otolaryngol Clin North Am.* 2011;44(1):161-182, with permission from Elsevier.⁴)

Multiple myeloma

Oral cavity involvement occurs in the later stages of multiple myeloma and often involves the mandible. Facial asymmetry and jaw or mucosal swelling can occur (Fig 11).⁴ These changes can lead to numbness, bone pain, and tooth mobility. Bony destruction can lead to pathologic fractures, which are visible on radiographs.¹⁷⁻²⁰ Rarely, deposition of amyloid that leads to macroglossia can occur.²¹

Endocrine disorders

Diabetes mellitus

In the next 20 years, up to 44 million persons in the United States may be affected by diabetes.²² Type 1 diabetes typically occurs in childhood and is related to autoimmune destruction of pancreatic islet cells. Type 2 diabetes primarily affects adults and is secondary to insulin resistance.²³ Oral manifestations of both types include periodontitis as well as gingivitis (Fig 12).¹⁴ Both oral conditions are related to higher susceptibility to infections, often secondary to poor glucose control. Patients with poorly controlled

diabetes experience greater periodontal attachment loss, and improved periodontal health may improve glycemic control.¹⁴ Other findings include diabetic sialadenosis (a diffuse, nontender enlargement of the parotid glands), fungal infections (both *C albicans* and mucormycosis), dysgeusia, and burning or dry mouth.⁴

Thyroid disease

Both hypothyroid and hyperthyroid states can cause changes that may be noted on examination. In patients with hypothyroidism, glycosaminoglycan deposition in the lips and tongue leads to associated swelling. In children, tooth eruption may be affected.^{24,25} Hyperthyroidism may lead to proptosis or exophthalmos, which may be noted when patients present for routine oral care.²⁴

Parathyroid disease

Hypoparathyroidism typically occurs secondary to surgical removal of the parathyroid gland. Reduction in parathyroid hormone results in hypocalcemia. The Chvostek sign, twitching of the upper lip after facial nerve stimulation at the zygomatic process,



Fig 15. Enamel erosion secondary to gastroesophageal reflux disease. (Reproduced with permission from Oral manifestations of systemic disease. *American Family Physician*. 2010;82(11):1381-1388.¹⁴ Copyright ©2010 American Academy of Family Physicians. All rights reserved.)



Fig 16. Bone loss in a patient with Langerhans cell histiocytosis. (Reprinted from Islam NM, Bhattacharyya I, Cohen DM. Common oral manifestations of systemic disease. *Otolaryngol Clin North Am*. 2011;44(1):161-182, with permission from Elsevier.⁴)

is a hallmark finding. In children, hypoparathyroidism may hinder tooth eruption or cause pitting and enamel hypoplasia.²⁶

Hyperparathyroidism results from excess production of parathyroid hormone. Primary hyperparathyroidism is due to parathyroid adenomas in 80%-90% of cases. Secondary hyperparathyroidism occurs due to chronic renal disease. Both manifest within the oral cavity as loss of the lamina dura of roots of teeth, leading to a “ground glass” appearance on radiographs. As disease advances, so-called brown tumors, commonly of the mandible, can develop due to hemorrhage within the bone.²⁷

Adrenal disease

Hypocortisolism either occurs secondary to chronic glucocorticoid therapy (Cushing syndrome) or results from an increase endogenous production related to pituitary or adrenal adenomas. Both types result in characteristic “moon” facies secondary to deposition of fatty tissue in the face. Bone loss also occurs and may be noted on radiographs of the mandible.²⁸

Hypoadrenocorticism (Addison disease) results from destruction of the adrenal cortex. The etiology can be variable but often is autoimmune in nature. Hyperpigmentation of the oral mucosa, although nonspecific, may be the initial presentation (Fig 13).¹⁴

Neoplastic diseases

Kaposi sarcoma

Kaposi sarcoma is a vascular malignancy occurring in 4 patterns: classic, African (endemic), immunosuppressive, and human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS). Oral Kaposi sarcoma occurs in up to 25% of HIV cases and may be the initial sign of infection.¹¹ Oral findings include nonpigmented, violet, or brown-red plaques or tumors of the tongue, palate, and gingiva.

Treatment involves focal destruction of the lesions with medications, excision, or cryotherapy as well as radiation or chemotherapy for later-stage disease.

Metastatic disease

Metastatic tumors constitute approximately 1% of oral malignant neoplasms. Tumors can occur on both the hard and soft palates

but most often affect the jaws (2:1 predilection).²⁹ When oral soft tissues are involved, the gingiva and tongue are the most commonly affected at 54% and 22.5%, respectively.²⁹ Patients typically complain of pain, tingling, or swelling. Numb chin syndrome occurs when the metastatic lesion involves the mental nerve. In women, breast cancer accounts for 65.3% of metastatic tumors of the jaw or soft tissues. In men, lung cancer is most common, at 53.3%.²⁹ Lung cancer metastasizes most often to the oral soft tissues, whereas breast cancer metastasizes to the jaw (Fig 14).^{4,30}

Chronic diseases

Gastroesophageal reflux disease

Dental erosions, water brush, and xerostomia can all occur in patients with gastroesophageal reflux disease. Burning sensations, palatal erythema, and halitosis may also be present. The occlusal surface of the mandibular posterior teeth and the lingual surface of the maxillary anterior teeth are typically affected. Dentin may become exposed and consequently sensitive to temperature changes (Fig 15).¹⁴

Eating disorders

Oral manifestations of eating disorders include xerostomia, dental erosions, sialadenosis, and dental caries. Xerostomia may be related to medications used to control weight or poor nutritional intake. Sialadenosis occurs in up to 25% of bulimia patients.³¹ Recurrent vomiting can lead to dental erosion of the lingual surface of maxillary anterior teeth and buccal surface of mandibular posterior teeth.³²

Pediatric population

Pediatric patients can present with many of the previously discussed oral findings of systemic disease, but a few diseases with oral manifestations occur primarily in children.

Langerhans cell histiocytosis

Langerhans cell histiocytosis is primarily a disease of children, involving abnormal monoclonal proliferation of antigen-presenting cells, although reports of cases in adults do exist.³³ Premature loss of primary teeth and loss of alveolar bone can



Fig 17. Lip findings in a patient with Kawasaki disease. (Reproduced with permission from Diagnosis and management of Kawasaki disease. *American Family Physician*. 2015;91(6):365-371.³⁴ Copyright ©2015 American Academy of Family Physicians. All rights reserved.)

occur. Oral findings include hard palate ulcerations, halitosis, gingival inflammation, and ulcerated nodules. On radiographs, teeth may appear to be floating in air due to periodontitis-associated bone loss (Fig 16).⁴

Kawasaki disease

Also known as *muco-cutaneous lymph node disease*, Kawasaki disease predominantly affects children younger than 5 years of age.³⁴ A systemic vasculitis, it is the leading cause of heart disease in children within the United States. Diagnosis is based on a fever of 38.5°C with a duration of 5 days along with 4 of 5 principal clinical features: oral changes, polymorphous rash, bilateral conjunctivitis, changes in the extremities, and cervical lymphadenopathy. Findings in the oral cavity include lip cracking, erythema, and “strawberry tongue” (Fig 17). The oral manifestations occur in up to 96.5% of cases.³⁴

Discussion

Many systemic diseases can have oral manifestations that may initially be observed by dental professionals. Further, periodontal disease has been linked to pregnancy complications as well as cardiovascular and pulmonary diseases.³⁵ Evidence also suggests a relationship between periodontal disease and overall health as well as systemic cancers.³⁶ These relationships are unclear and more investigation is needed. At this time, dentists should be aware of the correlations, assess patients for risk factors, and encourage patients to follow up with their physician for age-appropriate screenings.

Conclusion

Numerous systemic conditions, including some autoimmune, hematologic, endocrine, and neoplastic diseases as well as chronic illnesses, cause pathognomonic changes in the oral cavity. Dental practitioners play a vital role in preventive medicine as they work with medical colleagues to identify disease. Together, the medical and dental homes are integral to good patient health.

Author information

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