Oral Signs of Systemic Disease

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To my beautiful children, Sina and Monah, who inspire me to persevere through any challenge and bring so much love and joy into my life.

Foreword

Oral Signs of Systemic Disease provides valuable insight into solving diagnostic challenges. Careful oral examination can provide such clues to the learned observer. However, the medical education and training of most physicians and other healthcare providers does not emphasize the oral cavity. This results in a lack of familiarity with normal and abnormal features and the diagnostic clues they can provide. By contrast, dental education provides the necessary skills to distinguish between normal and abnormal findings. However, the dental clinician may not be skilled in placing abnormal features in the context of a mucocutaneous or systemic condition. Thus, this contribution serves to educate both physicians and dentists.

Dr. Nasim Fazel is an eminently well-suited editor for *Oral Signs of Systemic Disease.* She is a DDS graduate of Northwestern University Dental School and an MD graduate of the University of Michigan Medical School. This education was followed by residency training in dermatology at Henry Ford Hospital in Detroit, Michigan. Dr. Fazel has been a faculty member at the University of California, Davis in the Department of Dermatology for more than a decade and a half, where she has developed an oral dermatology practice and has served as Dermatology Residency Program Director. As a dual-trained dentist and dermatologist, as well as a consummate educator, Dr. Fazel brings great knowledge and experience to bear on the topic.

The contributors to this textbook are scholars from broad areas of expertise including dentistry, pediatric dermatology, oral dermatology, oral medicine, oral pathology, microbiology, and medical genetics. Each brings a depth of knowledge and understanding of the relevance of their topics to the problem-solving algorithm for the patient with troublesome oral lesions. Dermatologists know that the skin is often a mirror of systemic diseases. Those skilled in the diagnosis of challenging oral diseases know that the mouth is, similarly, a mirror of systemic diseases.

This book will be a valuable addition to medical libraries as a reference volume and to the personal library of the clinician whose patient has a vexing oral disease.

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Preface

The conception of *Oral Signs of Systemic Disease* came about with the intention to provide a practical reference for the day-to-day practice of clinicians in the fields of dermatology, dentistry, oral medicine, and otolaryngology. In addition, the comprehensive nature of this textbook can serve as an educational tool for students, residents, and fellows in training with the goal of learning the fundamentals of oral mucosal disease.

Oral Signs of Systemic Disease provides descriptive clinical and oral manifestations and differential diagnoses, including principles of therapy of major entities, while maintaining a uniform chapter format. I am greatly appreciative of the authors for their contributions, without whom this textbook would not have been possible. I would also like to thank Portia Wong, Diane Lamsback, and Rebekah Collins at Springer Publishing for their time and support.

Sacramento, CA, USA — Nasim Fazel

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Introduction

1

Parastoo Davari and Nasim Fazel

Introduction

Oral signs and symptoms can be a presenting feature of many systemic diseases, which can aid the clinician in establishing a definitive diagnosis. Immunologic and infectious conditions, hematologic disorders, vitamin deficiencies, and endocrinopathies, in addition to psychological disorders and physiologic conditions such as pregnancy, can present with oral signs and symptoms. Oral signs such as mucosal inflammation or infection, discoloration, decreased salivary flow, dental caries, and bleeding can be indicative of a systemic condition. However, these oral signs can be overlooked without thorough examination of the oral mucosa, thus increasing the likelihood of delayed diagnosis or misdiagnosis.

Competence in the diagnosis of oral diseases and recognition of their signs and symptoms is relevant to all practitioners. However, adequate knowledge and understanding of oral diseases is particularly important for specialists such as dermatologists, dentists, and otolaryngologists. In this introductory chapter, we briefly review the anatomy, histology, physiology, and microbiology of the oral mucosa.

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Anatomy and Histology

The oral cavity includes four main components: the mucosa, tongue, dentition, and salivary glands.

Oral Mucosa

The oral cavity is lined by stratified squamous epithelium. Merkel cells and melanocytes can also be found throughout the oral mucosa [1]. The turnover time of the epithelial mucosa ranges from 14 to 24 days, for the buccal mucosa and the hard palate, respectively [2]. Various degrees of keratinization are observed in the epithelium of different regions of the oral cavity. The gingiva and hard palate are exposed to friction and mechanical stress during mastication. Hence, these areas are lined by a keratinized epithelium, which is tightly adherent to the underlying tissues. The dorsal tongue has a specialized mucosa composed of a mosaic of keratinized and nonkeratinized epithelium that is firmly attached to the underlying tongue muscles [2, 3]. The epithelium of the floor of the mouth, buccal mucosa, and the ventral tongue is nonkeratinized allowing for movements that are required for functions such as mastication, swallowing, and phonation. In addition, the underlying connective tissue is more flexible than the masticatory regions of the oral cavity. The specialized mucosa of the dorsal tongue represents approximately 15% of the surface area of the oral cavity,

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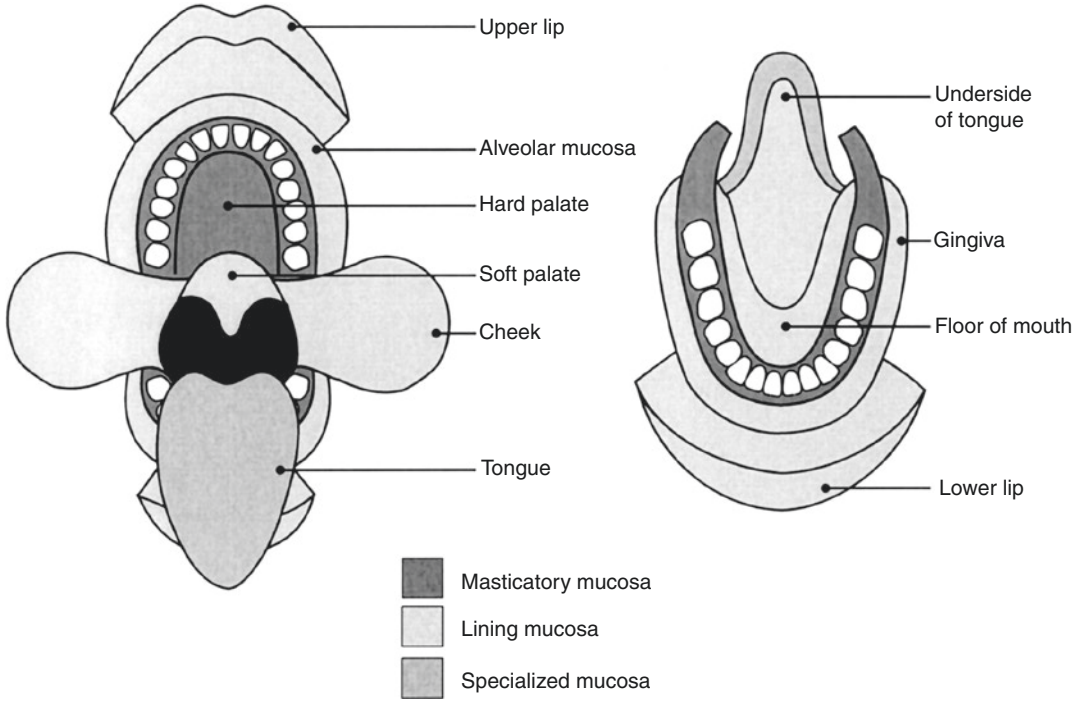

Fig. 1.1 Oral cavity regions. (Reprinted with permission from Squier and Kremer [2])

while the nonkeratinized surfaces (i.e., labial mucosa, buccal mucosa, and floor of the mouth) and masticatory mucosa cover approximately 60% and 25% of the surface area, respectively (Fig. 1.1) [2].

The Tongue

The tongue is a muscular organ that is entirely covered by a specialized mucosa, which is attached to the floor of the mouth via the lingual frenulum. A tuft of mucosa (sublingual caruncles) on either side of the lingual frenulum harbors the opening of the sublingual and submandibular salivary gland ducts. The median sulcus divides the tongue into two parts: right and left halves. Figure 1.2 demonstrates that the sulcus terminalis is a V-shaped groove that divides the tongue into the body (anterior two-thirds) and the root (posterior one-third) [4].

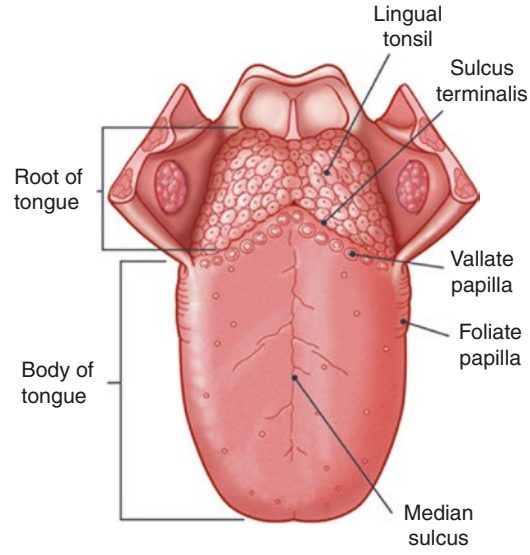

Fig. 1.2 The tongue is divided by the sulcus terminalis into two parts: the body and the root. The circumvallate papillae are located anterior to the sulcus terminalis. (Reprinted with permission from Weaker [4])

The dorsum of the tongue is lined by lingual papillae that are lamina propria projections covered by keratinized epithelium. Foliate papillae are small and found on the lateral surfaces of the tongue. Filiform papillae are the most numerous papillae of the tongue. Fungiform papillae are mushroom-shaped, fewer in number, and dispersed in between the filiform papillae. Circumvallate papillae, the most prominent and largest papillae, are located in a V-shaped configuration anterior to the sulcus terminalis. Taste buds are present in foliate, circumvallate, and fungiform papillae as well as the soft palate and pharynx [4, 5].

Dentition

The permanent dentition consists of 8 incisors, 4 canines, 8 premolars, and 12 molars (Fig. 1.3). Each tooth is divided into a root and a crown. The crown includes enamel and dentin enclosing the pulp, while the root contains only dentin surrounding the pulp and is covered by cementum. Enamel is the hard, highly mineralized outer surface of the tooth that protects the dentin and pulp and serves as the grinding surface during mastication. The interior chamber of the root contains the radicular pulp, whereas the interior chamber of the crown houses the coronal pulp. Nerves, blood vessels, and lymphatics pass through the apical foramen (Fig. 1.4). The periodontal ligament attaches the tooth to the surrounding bony structures of the maxilla and mandibular alveolar processes. The teeth are enclosed by the gingiva including the free, attached, papillary, and marginal gingiva. The interdental papilla is found between two adjacent teeth. The marginal gingiva lines the space between the teeth and the gingiva. The mucogingival line separates the gingiva from the alveolar mucosa [4].

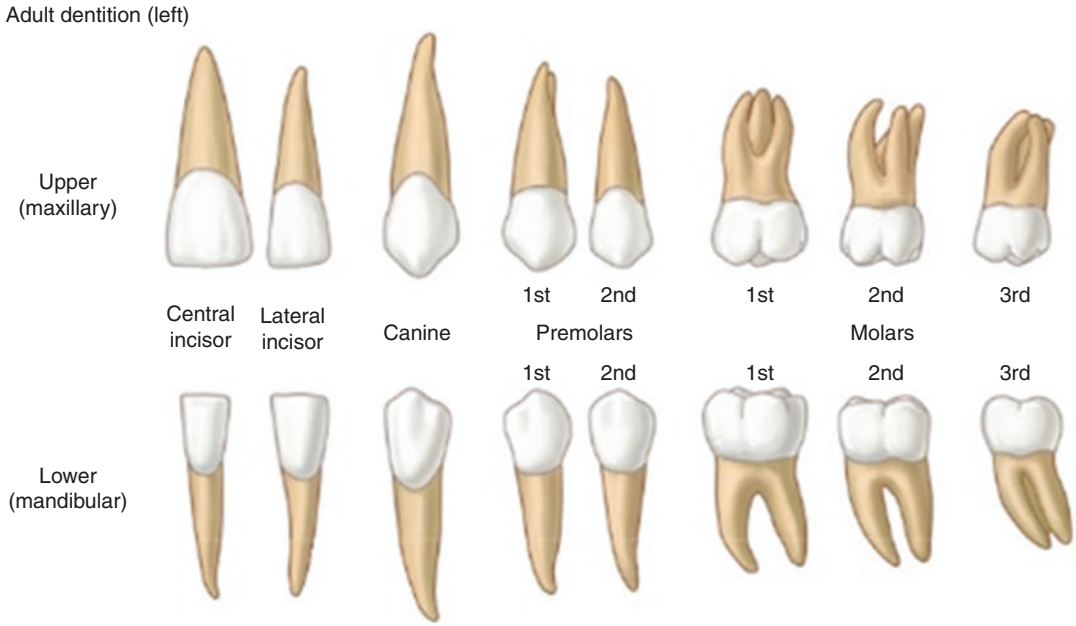

Fig. 1.3 The adult dentition is composed of two incisors, one canine, two premolars, and three molars in each quadrant. (Reprinted with permission from Weaker [4])

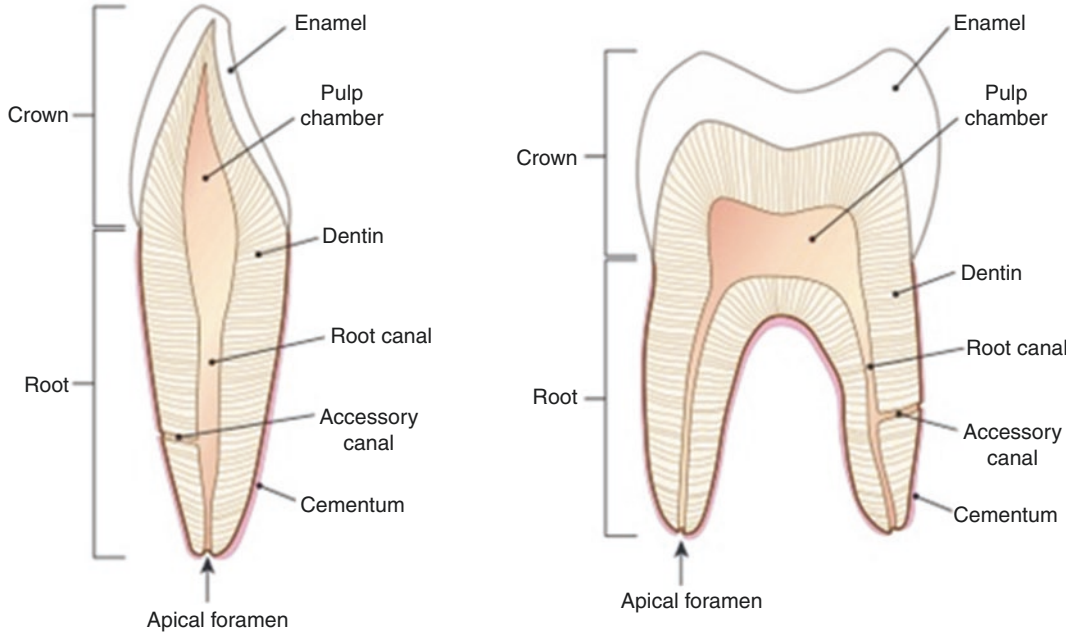

Fig. 1.4 Cross-section of a tooth showing two main parts: the crown and the root. The crown is composed of enamel, dentin, and the pulp chamber, which harbors the blood vessels, nerves, and lymphatics of the pulp. Dentin surrounds the pulp of the root and is covered by cementum. (Reprinted with permission from Weaker [4])

Salivary Glands

The parotid, submandibular, and sublingual salivary glands are the major salivary glands, which are paired and secrete 95% of the saliva. The parotid is the largest salivary gland. It is a serous gland, producing 30% of the saliva, and has a triangular shape with its base facing the zygomatic arch and its apex extending to the angle of mandible. Diseases of the parotid can affect the major anatomical structures passing through the gland: the facial nerve, retromandibular vein, and external carotid artery.

The submandibular gland is found in the submandibular triangle, which produces approximately 60%–65% of the saliva. It contains both mucous and serous fluids; however, serous secretion is more predominant. The sublingual gland, the smallest major salivary gland, is located in the floor of the mouth. It is a mixed gland with predominantly mucinous secretion. Minor salivary glands are concentrated in the submucosa throughout the walls of the oral cavity. The soft and hard palate, the labial and buccal mucosa, and the tongue contain several minor salivary glands [2, 6].

Physiology

The major functions of the oral cavity are mastication, taste, and phonation. The lips prevent the saliva from drooling and the food from spilling from the mouth. The tongue has both motor and sensory functions and plays a central role in swallowing. Molar teeth are necessary for chewing food. The lips, tongue, and palate are essential for phonation and articulation. A major function of the oral mucosa is to protect underlying structures from mechanical and chemical injuries. The epithelium also prevents fluid loss and entry of environmental toxins and microbial agents. The masticatory stratum corneum endures the mechanical forces and shearing stress. The continuous shedding of the oral mucosa also limits colonization of microbial agents [2]. Saliva lubri-

cates the oral mucosa, which facilitates the functions of phonation, mastication, food bolus formation, and swallowing. It also protects the oral mucosa from mechanical injuries such as abrasion and contains enzymes that aid in the digestion of carbohydrates. In addition to its antimicrobial properties, saliva enhances the removal of microorganisms and desquamated cells from the oral mucosa and has a protective role in the prevention of dental caries. As a buffer, it modulates the pH and protects the oral mucosa and teeth from the acidic environment caused by the ingestion of food or gastroesophageal reflux [7].

Oral Microbiome

Despite constant desquamation of the oral mucosa, the oral cavity contains a dense population of microorganisms including bacteria, viruses, protozoa, fungi, and archaea [8]. The oral cavity is a suitable environment for microbial agents to thrive due to its stable temperature, pH and the presence of saliva as a medium [9]. Carbohydrates, lipids, and proteins in dietary food and salivary glycoproteins in addition to exuded serum proteins from the gingival sulci provide nutrients for the oral microbiota [10]. The microbiome composition of the oral cavity varies in different sites. The tongue has the highest density of microorganisms containing different microbial communities such as *Veillonella atypica* and *Porphyromonas gingivalis*, while the tooth surface provides a unique microenvironment for microbial biofilms containing *Streptococcus mutans*, *Actinomyces*, *Eubacterium*, and *Peptostreptococcus*. Figure 1.5 demonstrates the heterogeneity of the oral microbiome within the different anatomical areas of the oral cavity [9]. Bacteria are frequently responsible for the major microbiome-related diseases of the oral cav-

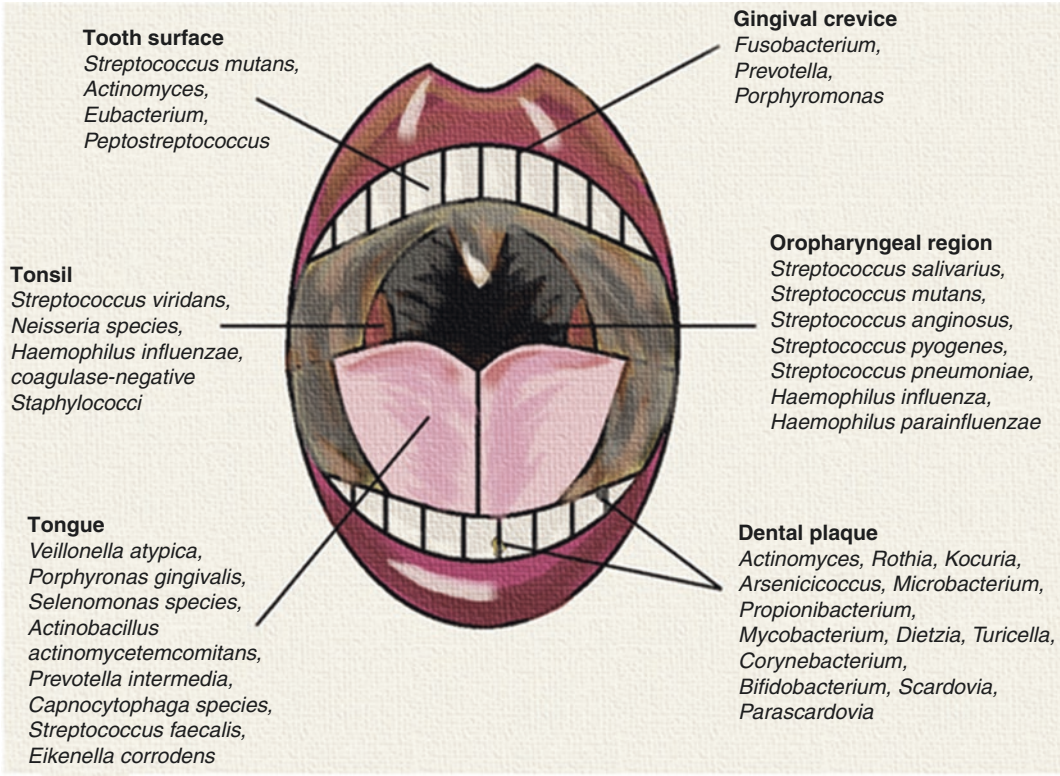

Fig. 1.5 Major microbial agents residing in the oral cavity and oropharyngeal region. (Reprinted with permission from Lim et al. [9])

ity including dental caries, endodontic infections, gingivitis, and periodontitis. The correlation between oral diseases and systemic conditions such as cardiovascular diseases, head and neck cancers, and diabetes mellitus warrants further characterization of the oral microbiome [8, 9]. The commensal microbiome provides a healthy environment in the oral cavity and prevents overgrowth of pathogens such as candida and *Staphylococcus aureus*. Some microbial species such as *Streptococcus salivarius* have shown protective effects against periodontitis and halitosis in in vitro and in vivo studies, respectively [11, 12]. Nitrate-reducing bacteria such as *Actinomyces* and *Veillonella* convert nitrates to nitrites, which may lower the risk of dental caries. Acidified nitrites may restrict the growth of cariogenic bacteria via the antimicrobial effect of oxides of nitrogen such as nitric oxide [13–15].

Principles of the Oral Examination

Comprehensive examination of the oral cavity includes visual inspection and palpation of the various anatomical structures within the oral cavity. Partial and complete removable prostheses should be removed prior to examination of the oral mucosa. Adequate lighting and proper positioning of the patient is of significant importance in conducting an oral examination. The patient's head should be stable and well positioned to allow visualization of all mucosal surfaces. A tongue blade or a cotton gauze is used to retract the tongue and allow adequate exposure to various sites within the oral cavity [16].

Inspection

The lips, dorsal and ventral tongue, hard and soft palates, buccal mucosa, gingiva, and the floor of the mouth are visually inspected for the presence of any abnormal growths, inflammation, ulceration, discoloration, or bleeding. Visual inspection is performed by using a tongue blade or dental mirror to retract the lips and cheeks and evaluate the buccal mucosa, teeth, and alveolar ridges. The patient should be asked to raise the tongue and touch the palate to adequately examine the floor of the mouth and the ventral tongue. The lateral tongue and floor of the mouth are best observed by retracting the tongue using a tongue blade or a gauze wrapped around the tip of the tongue. The posterior oropharynx can be inspected using a dental mirror. The presence of hypoglossal and glossopharyngeal nerve palsy can be assessed, if the patient's condition warrants it. To detect hypoglossal palsy, the examiner should initially look for signs of atrophy, fasciculation, or tongue deviation while the tongue is in a resting position. The tongue deviates toward the affected side when the patient protrudes the tongue. The glossopharyngeal nerve can be assessed by inducing the gag reflex. Movement of the soft palate and uvula should be also assessed; in hypoglossal nerve palsy, the soft palate and uvula deviate to the unaffected side while the patient says "Ah" [16].

Palpation

If an abnormality is noted on visual inspection, the suspected area should be palpated to assess the consistency, texture, and depth of the lesion. The face and neck should also be palpated for any abnormalities to include palpation of the anterior/posterior cervical, submandibular, and supraclavicular lymph nodes [16].

Summary

Clinical competence in detecting abnormalities within the oral cavity, familiarity with common manifestations of systemic disorders, and the pathophysiology of those conditions are important elements of the comprehensive clinical exam. A thorough history and meticulous oral exam can play a crucial role in the early diagnosis and prompt treatment of various systemic diseases.

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2 Oral Signs of Gastrointestinal Disease

John C. Steele

Inflammatory Bowel Disease

Crohn's disease and ulcerative colitis are the most commonly recognized inflammatory bowel diseases (IBD), and both can initially present with oral manifestations. It is estimated that up to 1.4 million people in the United States suffer from inflammatory bowel disease [1] with as many as 70,000 new cases being diagnosed annually [2].

Crohn's disease and orofacial granulomatosis

Crohn's disease and orofacial granulomatosis (OFG) have been grouped together in this section since there is much debate in the literature as to whether the latter is a reflection of oral Crohn's disease or indeed is an entity entirely on its own [3–5]. More recently, a systematic review of pediatric cases of OFG identified a high prevalence of Crohn's disease and concluded that OFG may be a subtype of Crohn's disease [6].

OFG was initially described in 1985 and is an uncommon, chronic inflammatory, granulomatous disorder of the orofacial region [7]. Others have used synonyms for OFG including granulomatous cheilitis, cheilitis granulomatosa, cheilitis granulomatosis, and oral granulomatosis. For the purposes of this chapter, OFG is the preferred nomenclature.

There is also speculation whether OFG without gastrointestinal signs/symptoms, Melkersson-Rosenthal syndrome (triad of facial swelling, facial palsy, and fissured tongue), and cheilitis granulomatosa are a spectrum of the same disease [4, 8, 9]. Cheilitis granulomatosa (Meischer's cheilitis) is monosymptomatic and characterized by lip swelling only.

Epidemiology

The worldwide incidence of Crohn's disease varies from 0.1 to 6/100,000 [1] with an increased incidence in smokers. There have been a few studies examining the prevalence of oral manifestations in Crohn's disease patients [8], and the presence varied from 0.5% to 60%.

Etiopathogenesis

The etiopathogenesis of OFG is uncertain with a number of postulated theories: genetic predisposition, hypersensitivity/allergy to dietary components/dental materials, microbiological agents/infection, and inflammatory/immunological factors.

Genetic

Limited small case series have suggested that there is a genetic link with OFG being seen in families and there being a human leucocyte

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antigen (HLA) association. However, there has not been enough evidence for a conclusive link to be made [8, 9].

Hypersensitivity/Allergy

A recent study [10] demonstrated that prevalence rates of allergy were significantly greater in patients with OFG (82%) than in the general population (22%). This has been supported by other studies showing OFG patients to have higher rates of atopy [8]. A number of food additives and substances have been implicated in evoking a delayed-type contact hypersensitivity. These include, among others, cinnamaldehyde (also found in toothpaste) and benzoates. Adhering to a specific cinnamon and benzoate exclusion diet has been shown to improve the clinical features of OFG [11]. Allergy to dental materials has been proposed as an etiological factor in OFG; however, there has not been any conclusive evidence to support this [9].

Microbiological/Infection

An infective etiology has been proposed based on the fact that certain microorganisms (bacteria) have been implicated in other chronic granulomatous conditions such as sarcoidosis, Crohn's disease, and tuberculosis [8, 9]. Research has focused on mycobacteria, *Saccharomyces*, spirochetes, and *Borrelia* species. There appears to be conflicting evidence from small studies as to whether there is a relationship with OFG or not, and so a recent review concludes that there is insufficient evidence to support the role of infection as a cause of OFG [9].

Inflammatory/Immunological

An immunological basis for OFG has not been supported in the literature by studies of appropriate power, and although the theory is plausible, further work is required. There is a hypothesis that OFG is not driven by a single antigen but by a random influx of inflammatory cells [9].

Clinical Manifestations

Crohn's disease can affect any part of the gastrointestinal tract from the mouth at the proximal end to the anus at the distal. The small intestine is most often involved with the terminal ileum being the commonest site. "Skip lesions" of normal non-diseased mucosa may be present. Symptoms include abdominal pain, diarrhea +/− bleeding per rectum, stricture formation, and lesions affecting the anus, perianal region, and the mouth. There is an increased risk of fistulae and abscess formation as well as hematinic deficiencies (B12 and iron). Signs of the disease can be seen clinically, radiologically, and by direct endoscopic visualization. Pathological features include transmural inflammation and the presence of noncaseating granulomas.

Oral Signs and Symptoms

The most common oral complaint is of swelling, which predominantly affects the lips, although other orofacial structures such as the buccal mucosa may also be involved. The physical disfigurement can be detrimental to the psychosocial quality of life of the individual (Fig. 2.1a, b).

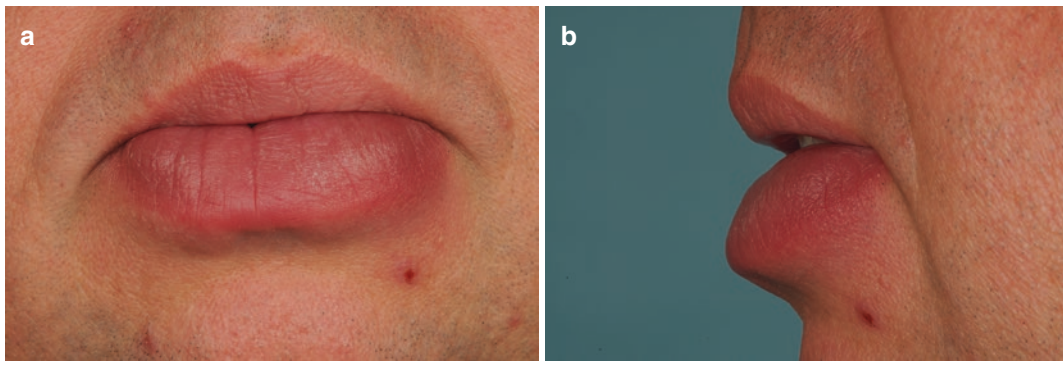

Fig. 2.1 (**a**) OFG – This figure shows swelling of the lower lip (anterior view). (**b**) OFG – This figure shows swelling of the lower lip (lateral view)

Table 2.1 Clinical features of OFG

Extraoral: lip/facial swelling (Fig. 2.1a, b)
Angular cheilitis
Lip fissuring (vertical)
Perioral erythema
Cervical lymphadenopathy
Intraoral: cobblestoning of the buccal mucosa (Fig. 2.2)
Mucosal tags (Figs. 2.3 and 2.4)
Full width gingivitis/hyperplastic gingivitis/ granulomatous gingivitis (Fig. 2.3)
Linear "slit-like" ulceration (Fig. 2.5) or aphthous-like ulcers (round/oval)
"Staghorning" of the submandibular ducts (Fig. 2.6)
Tongue fissuring
Neurological: facial palsy

There have been a few reasonably large case series of OFG patients reported in the literature (Al Johani 2009 – 49 cases [12], McCartan 2011 – 119 cases [13], Campbell 2011 – 207 cases [4]), which aimed to characterize the most common clinical features. Lip swelling was the most common feature (51%, 77%, and 91%, respectively) observed, and this can be either recurrent or persistent. Cobblestoning of the buccal mucosa ranged from 27% to 63% [4, 13]. The mucosal ulcerations associated with OFG can either be aphthous-like (shallow round ulcers with an erythematous border) in appearance or deep and linear. The latter commonly appear in the buccal sulci with hyperplastic mucosal edges and tend to be persistent [14, 15]. Swelling of the area around the submandibular/sublingual gland orifices results in a "staghorn" appearance and was noted in 10% of the largest case series [4]. Neurological manifestations have been reported including recurrent relapsing and remitting facial palsy [9, 12].

Table 2.1 summarizes the most commonly observed extra- and intraoral features associated with OFG, and Figs. 2.1, 2.2, 2.3, 2.4, 2.5, and 2.6 demonstrate some of these presentations.

Pyostomatitis vegetans can present as the sole oral manifestation of Crohn's disease. Please see the section on *Pyostomatitis vegetans* for further information.

Differential Diagnosis

The differential diagnosis for the orofacial swelling associated with OFG includes immunological conditions, infection, and inflammatory disease [9, 12]. Please see Table 2.2.

The following investigations should be considered to help ascertain a definitive diagnosis: CBC, iron studies, inflammatory markers, ACE

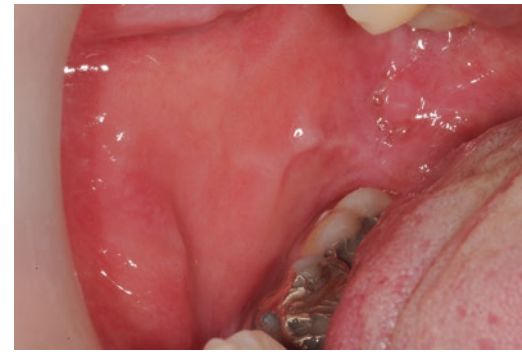

Fig. 2.2 OFG – Cobblestoning of the buccal mucosa can be seen on the anterior right buccal mucosa

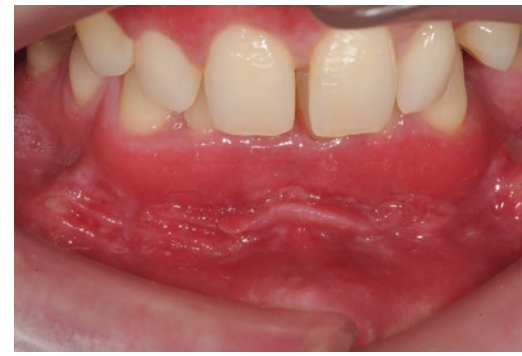

Fig. 2.3 OFG – This figure demonstrates a full-width gingivitis and mucosal tags affecting the anterior mandibular gingivae

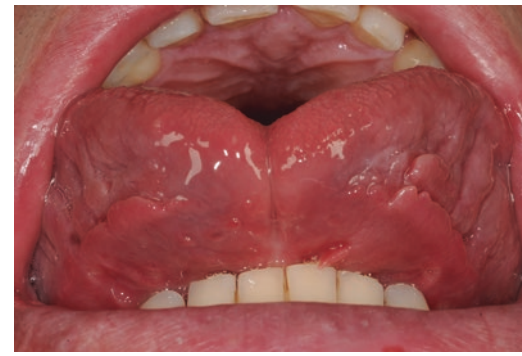

Fig. 2.4 OFG – Mucosal tags can be seen on the ventral surfaces of the tongue

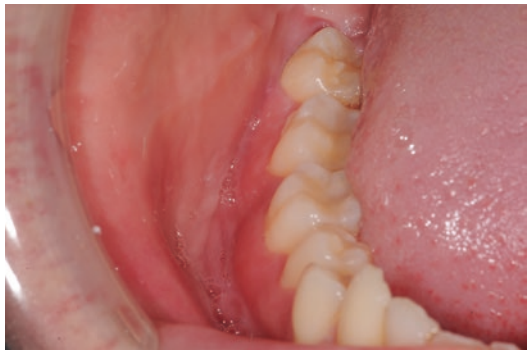

Fig. 2.5 OFG – A healing linear "slit-like" ulcer can be seen in the right buccal sulcus

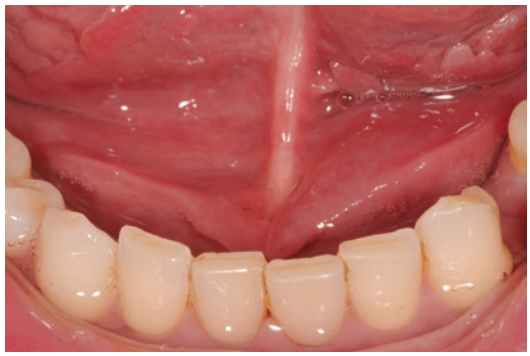

Fig. 2.6 OFG – This figure shows "staghorning" of the submandibular ducts

Table 2.2 Differential diagnosis of orofacial swelling

Immunological	Angioedema – hereditary and acquired/c1-esterase inhibitor deficiency
Infections	Tuberculosis
	Deep fungal infections
	Leprosy
Inflammatory disease	Crohn's disease
	Foreign body and delayed hypersensitivity reactions
	Cheilitis granulomatosa (Meischer's cheilitis)
	Sarcoidosis
	Melkersson-Rosenthal syndrome

levels, chest x-ray, and a deep incisional biopsy of any swollen oral mucosa.

The characteristic histopathological features of OFG [4] are of noncaseating epithelioid granulomas, lymphedema of the corium, and dilated lymphatics, which can be virtually indistinguishable from Crohn's disease or systemic sarcoidosis [9].

Table 2.3 Management/treatment options for OFG

Angular cheilitis	Topical/systemic antimicrobial agents
Diet	Cinnamon- and benzoate-free diet (low phenolic acid diet)
Lip fissure	Emollients
	Antimicrobial/combined antimicrobial and corticosteroid
Lip swelling	Local
	Intralesional corticosteroid injection
	Topical corticosteroid
	Systemic
	Dietary modification
	Immunosuppression (off-label)
Generalized inflammation	Immunosuppression (off-label)
	Azathioprine
	Anti-TNFα therapy
Oral ulceration	Topical
	Corticosteroids (various preparations)
	Analgesics
	Antiseptic mouthwash
	Systemic
	Corticosteroids (rescue therapy)
	Immunosuppression (off-label)

Treatment Recommendations

The aim of treatment for OFG depends on the presenting symptom. In the majority of cases, the patient is concerned about the cosmetic appearance of any facial swelling. Patients are also concerned about pain and impact on their quality of life from oral ulcers. Management/treatment options are listed in Table 2.3. The undertaking of much larger randomized controlled trials is needed since much of the evidence is based on small case series.

Intralesional corticosteroid injection has been shown to be effective in treating persistent lip swelling; however, multiple injections are often required [9]. The injection itself can be painful, and consideration should be given to injecting local anesthetic prior to injecting the corticosteroid.

Many different types of immunosuppressants have been used off-label to manage the clinical manifestations of OFG. These include colchicine, dapsone, hydroxychloroquine, infliximab, methotrexate, tacrolimus, and thalidomide among others

[6]. Two small case series using anti-TNFα treatment have been reported showing a good short-term response in the management of recalcitrant OFG with infliximab [16] and thalidomide [17]. Unfortunately, a significant number of those taking infliximab lost efficacy over time.

Dietary modification can be of significant benefit. An initial study published in 2006 involving 32 patients showed a statistically significant improvement in global lip and oral inflammatory scores after 8 weeks adhering to a cinnamon- and benzoate-free diet [11]. A review of the literature by the same research group in 2011 demonstrated that this diet can be beneficial in 54–78% of patients with 23% requiring no adjunctive therapies [18]. They also noted that the results of patch testing for cinnamaldehyde and benzoates did not predict success or failure in adhering to this diet. More recently, the same group has tested a low phenolic acid diet with micronutrient supplementation [19] since phenolic acids are among the constituents restricted in a cinnamon- and benzoate-free diet. The conclusion was that this new diet holds potential promise but larger-scale studies are required.

The clinician should consider referral to gastroenterology, especially in children, for a thorough work-up to rule out inflammatory bowel disease.

Ulcerative Colitis

Ulcerative colitis (UC) is a chronic inflammatory bowel disease that mainly affects the large intestine (colon) and rectum (proctitis).

Epidemiology

The worldwide incidence of UC varies from 0.5 to 24.5/100,000 [1]. There is a decreased incidence of UC in smokers. In the USA, UC affects between 250,000 and 500,000 people with an annual incidence of two to seven per 100,000 [20].

Etiopathogenesis

An inflammatory cell infiltrate affects only the mucosa and submucosa. The current theory is that the mucosal immune system becomes dysregulated, which results in normal microflora inducing an excessive immunological response [20].

Clinical Manifestations

The main symptom is of diarrhea with associated blood and mucous. Other symptoms include abdominal pain, nausea, fever, rectal urgency, and tenesmus [1, 20]. UC is associated with an increased incidence of chronic active hepatitis, primary biliary cirrhosis, sclerosing cholangitis, and colon cancer. Toxic megacolon may develop possibly necessitating an urgent colectomy.

Oral Signs and Symptoms

There are no oral signs and symptoms specific to UC. However, there can be oral signs of iron deficiency anemia if there is significant blood loss such as aphthous ulcers, angular cheilitis, and glossitis. Pyostomatitis vegetans can present as the sole oral manifestation of UC. Please see the section on *Pyostomatitis vegetans* for further information. A recent small case-control study [21] examining the oral manifestations of UC patients versus a control group without gastrointestinal disease reported that the presence of a tongue coating and the symptoms of dry mouth, halitosis, and taste changes were more common in the former group.

Differential Diagnosis

Please see the next section on *Pyostomatitis vegetans*.

Treatment Recommendations

The main medication classes used to treat UC include aminosalicylates, corticosteroids, immunosuppressants, and antibiotics. Surgery, as mentioned above, has a role and can "cure" UC following total colectomy [1].

Correction of any underlying iron deficiency can help control the symptoms of oral ulcers, angular cheilitis, or glossitis. Topical corticosteroids and analgesics can be prescribed to manage the pain and discomfort associated with ulcers. Antimicrobials can be prescribed to manage angular cheilitis depending on the implicated organism, which are usually either a *Candida* species or *Staphylococcus aureus.*

Pyostomatitis vegetans

Pyostomatitis vegetans (PV) is a rare, benign, chronic condition that is strongly associated with and considered a highly specific marker of IBD [22–24]. It is more commonly seen in UC than in Crohn's disease. It is considered the mucosal equivalent of pyodermatitis vegetans and is also associated with pyodermatitis gangrenosum. IBD commonly presents before the onset of oral lesions by a period of months to years [22].

Epidemiology

There is a male predilection [14, 22] for PV with a ratio of 2–3:1. PV can be seen in patients of any age but is most commonly seen in young-middle-aged patients between 20 and 59 years of age with a mean of 34 years [14].

Etiopathogenesis

The etiopathogenesis of PV is unknown and poorly understood. Immune dysregulation, microbial factors, or a nutritional deficiency have been implicated in the etiology [22].

Components of a complete blood count (CBC) and features seen on histopathological examination may support the immunological reaction theory. Raised lymphocyte and eosinophil counts are often seen as well as atypical immunofluorescence being observed at the basement membrane although this may be due to tissue damage [22]. A further theory concerns cross-reacting antigens of the bowel and skin [24].

Microbial factors have been considered since the cutaneous equivalent of PV, pyodermatitis vegetans, occurs in areas where microbial growth is encouraged (e.g., skin folds) and PV is a disorder included in the chronic pyodermas group. However, bacterial, fungal, and viral cultures of PV lesions are consistently negative [22, 24]. An additional hypothesis is that infections and their effect on the immune system may be implicated in the pathogenesis of IBD [22]. Interestingly, it has been noted that peripheral eosinophilia is present in 90% of reported cases [22].

Clinical Manifestations

PV usually runs in parallel with underlying IBD and has been considered a reliable marker of intestinal activity by some research groups [25]. Please see the preceding sections on Crohn's disease and ulcerative colitis for information on the clinical manifestations.

Oral Signs and Symptoms

Oral lesions present as multiple friable, gray-yellow pustules on an erythematous and thickened mucosal base. The pustules tend to rupture easily, producing erosions and fissures, and may coalesce, resulting in the appearance of "snail-track" ulceration and vegetations. All areas of the oral cavity can be affected with the most commonly affected sites being the labial and buccal mucosa, hard and soft palate, gingivae, and sulci. The tongue and floor of the mouth are least likely to be affected [23, 24].

Differential Diagnosis

The differential diagnosis [14, 22, 23] is summarized in Table 2.4. Histopathological examination including immunofluorescence studies can help differentiate immunobullous disease from PV.

Treatment Recommendations

In the absence of any underlying IBD, topical corticosteroids can successfully treat PV [22]. There are various preparations available including mouthwashes prepared by dissolving corticosteroid tablets, sprays, and ointments although many of these preparations are used off-label as they may not be indicated for oral use.

Table 2.4 Differential diagnosis of pyostomatitis vegetans

Behçet's disease
Bullous drug eruption
Bullous pemphigoid
Dermatitis herpetiformis
Erythema multiforme
Epidermolysis bullosa acquisita
Herpes simplex infection
Pemphigus vegetans/vulgaris

It would be sensible to refer a patient with PV who does not have any IBD symptoms for a gastroenterology consultation to exclude any silent disease [15, 24].

In the presence of IBD, medical or surgical interventions (total colectomy for UC) are the main management considerations.

There have been a number of case reports/small case series [22, 23] reporting that the following systemic treatments may be helpful in the management of PV: corticosteroids, dapsone, sulfasalazine, sulfamethoxypyridazine, azathioprine, cyclosporine, and isotretinoin. A single case report found success with topical tacrolimus [26].

Celiac Disease (Sprue)

Celiac disease (also known as sprue) is an autoimmune, T-cell-mediated, gluten-sensitive enteropathy seen in genetically susceptible individuals. It is the most common genetically based food intolerance worldwide [27, 28].

Gluten is a substance rich in glutamine and proline residues that is unable to be fully digested in celiac disease [27]. It is found in wheat (gliadin), barley (hordein), and rye (secalin) and seen in foods such as pasta, cereals, and grains [29]. Celiac disease often develops when solid food is introduced into the diet and therefore usually presents after the sixth month of life during transition to solid foods such as cereals [29].

There are different presentations of celiac disease: typical (with gastrointestinal symptoms), atypical (having extraintestinal manifestations), and the silent form (asymptomatic) [30].

Antibody testing is used as a screening tool with the current recommendation being to use the serum immunoglobulin A tissue transglutaminase (tTG) antibody test, which has a sensitivity and specificity >90% [28, 31]. This would identify those who would then need a diagnostic endoscopic small bowel biopsy [28].

Epidemiology

The estimated incidence of celiac disease is 3–13 cases per 1000 with an overall prevalence of 1% [28]. Only 10–15% of this population have been diagnosed and treated; therefore a large number of cases remain undiagnosed [27, 31]. There is a higher prevalence among relatives of patients with celiac disease, and this has been calculated at 1:22 for first-degree relatives and 1:39 for second-degree relatives [28, 32]. In a recently published large study, the prevalence of celiac disease in the United States was calculated at 0.71% (1 in 141), but the authors acknowledged that most cases were in fact undiagnosed [33].

Etiopathogenesis

There is a genetic and environmental basis to the development of celiac disease.

Genetic

It is acknowledged that under the influence of environmental factors, genetically susceptible individuals develop celiac disease with two HLA class II genes (HLA-DQ2 and HLA-DQ8) having been identified [27, 28].

Environmental

Celiac disease does not develop without dietary exposure to gluten. Some studies have reported that children introduced to gluten in the first 3 months of life were at greater risk of celiac disease. Interestingly, prolonged breastfeeding is associated with a smaller risk of developing the disease [27].

Clinical Manifestations

In typical celiac disease, the most common symptom is abdominal pain. Other gastrointestinal symptoms include diarrhea (chronic or intermittent), vomiting, abdominal distension, and constipation [27, 28]. Failure to thrive or weight loss can be a sign of celiac disease. Cachexia and severe malnutrition can be observed in a delayed or late diagnosis [28].

In atypical celiac disease, the most common extraintestinal sign is iron deficiency anemia [27]. Dermatitis herpetiformis, which is a symmetrical chronic, pruritic blistering rash affecting the extensor surfaces of the elbows and knees and the buttocks, is the cutaneous manifestation of

celiac disease [27]. Other signs and symptoms include deficiencies in vitamin D leading to osteoporosis, short stature, malabsorption resulting in hematinic deficiencies, extreme weakness, fatigue, myalgias, headaches, liver function abnormalities, menstrual irregularities, infertility, and adverse pregnancy outcomes [28, 29, 31].

Celiac disease is often associated with other conditions, most notably Type 1 diabetes mellitus and autoimmune thyroiditis as they have a common genetic background [30]. Other associations include selective IgA deficiency and various chromosomal disorders including Down syndrome, Turner syndrome, and Williams syndrome [27].

Oral Signs and Symptoms

Celiac disease can be suspected in individuals with both oral mucosal and dental signs and symptoms.

Aphthous ulcers (Fig. 2.7) are associated with celiac disease although the cause is unknown. The ulcers may be due to malabsorption leading to a hematinic deficiency [31]. The highest prevalence that has been observed in celiac patient subgroups has been in children, adolescents, and women and measures approximately 20% [29].

Dermatitis herpetiformis, the cutaneous manifestation of celiac disease, can present in the oral cavity in the form of erosions and desquamative gingivitis.

Another oral soft tissue sign that has been noted is papillary atrophy of the tongue, which can appear red and be painful. It is postulated that this is due to malabsorption of hematinics [29].

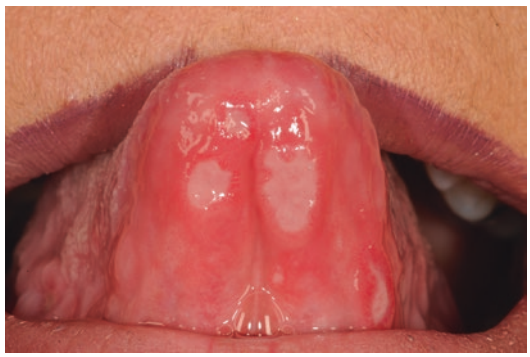

Fig. 2.7 Aphthous ulcers on the ventral surface of the tongue

Enamel defects (enamel hypoplasia, pitting, grooving, and partial/complete loss of enamel) have been observed in celiac disease patient cohorts [27, 31]. The prevalence of dental enamel hypoplasia among celiac patients is reported to be in the range 10–97% according to various studies [27, 28], although there is debate in the literature as to whether there is a true association [34]. There are two theories as to how enamel defects arise. The first concerns malabsorption of calcium and phosphorus during enamel formation, which leads to nutritional deficiencies such as hypocalcemia resulting in hypomineralization [35]. The second relates to immune disturbances against the enamel organ itself during enamel formation [28, 31, 34]. An association between delayed eruption of teeth [27] has been identified in up to 27%.

A case-control study involving 300 celiac patients reported that 33% were affected by enamel hypoplasia and 8.3% by recurrent aphthous ulcers and 20% had experienced a delay in dental eruption. The results for the control group were 11%, 3%, and 8%, respectively [34].

Differential Diagnosis

The differential diagnoses for the cause of enamel defects [29, 31] and other factors predisposing to the formation of aphthous-like ulcers [36, 37] are seen in Tables 2.5 and 2.6, respectively.

Treatment Recommendations

Adhering to a strict gluten-free diet for life is the mainstay of treatment in the management of both typical and atypical celiac disease. Compliance can be difficult especially in teenagers [28]. Aphthous ulcers often regress when patients are on a gluten-free diet [28], but topical agents (steroids, analgesics, and antiseptics) may have to be considered in the interim while a patient is adapting to a new diet.

Table 2.5 Differential diagnosis for enamel defects

Amelogenesis imperfecta
Enamel fluorosis
Localized infection
Nutritional disorders during enamel formation
Hypocalcaemia
Malnutrition
Vitamin D deficiency
Trauma

Table 2.6 Factors predisposing to the formation of aphthous-like ulcers

Behçet's disease
Cyclic neutropenia
Hematinic deficiencies
HIV disease
MAGIC syndrome (mouth and genital ulcers with inflamed cartilage)
PFAPA (periodic fever, aphthous stomatitis, pharyngitis, and cervical adenitis)
Sweet's syndrome
Trauma

Table 2.7 Orofacial signs of Gardner's syndrome

Dental	Congenitally missing teeth
	Dentigerous cysts
	Hypodontia
	Hypercementosis
	Impacted/unerupted teeth
	Odontomas
	Supernumerary teeth
Osteomas	Can affect the maxilla or mandible
Soft tissue	Epidermoid cysts
	Fibromas

Consideration should be given to referring a patient to a dentist for restorative treatment if there is a concern regarding enamel defects or missing teeth.

Gardner's syndrome

Gardner's syndrome (GS) is a rare autosomal dominant inherited disorder that is considered a subtype of familial adenomatous polyposis (FAP). GS comprises the triad of potentially malignant (high risk) intestinal adenomatous polyps, cutaneous lesions, and osteomas [38, 39].

Epidemiology

The incidence of GS ranges from 1 in 4000 to 1 in 12000 [40]. In comparison, the incidence of FAP ranges between 1 in 8300 and 1 in 14,025 live births with equal sex distribution and uniform worldwide distribution [39]. Intestinal polyps usually occur prior to puberty and become more generalized in early adulthood [39, 40]. If these polyps are not treated, all (100%) patients will develop cancer of the large intestine before the age of 40 [39].

Etiopathogenesis

GS is an autosomal dominant disorder with almost complete penetrance of 80% [41]. It is caused by a mutation in the *APC* gene located on the long arm of chromosome 5 (5q21) [39–41].

Clinical Manifestations

Polyps can develop at any site in the gastrointestinal tract but are particularly located in the distal colon [40].

Soft tissue manifestations include epidermoid, dermoid, and sebaceous cysts with the latter being present in 60% of patients with GS [38]. In 15–30% of patients, fibromas are noted.

Oral Signs and Symptoms

There are a number of dental anomalies that are associated with GS, and these can be present in 17–75% of GS patients [38, 40]. Supernumerary teeth, unerupted teeth, and odontomas (compound) usually affect the anterior parts of the jaws with the molar regions being rarely affected [15]. Osteomas affecting the mandible are more common than those affecting the maxilla and tend to be larger in size [39]. They are generally asymptomatic but can lead to facial asymmetry and therefore aesthetic concerns for the patient [40]. Soft tissue lesions, as mentioned above, can also affect the oral and maxillofacial region. The majority of soft tissue lesions are of multiple benign epidermoid cysts affecting the face, scalp, and extremities [40, 42]. Fibromas have been noted to infiltrate the masticatory and suprahyoid musculature [38]. Orofacial signs are summarized in Table 2.7.

Differential Diagnosis

Conditions that can have multiple radiopaque masses/odontomas on plain film radiographs as well as supernumerary and impacted teeth include the following rare conditions: cleidocranial dysplasia, osteo-cemental dysplasia, and periapical osteo-cemental dysplasia [38].

The differential diagnosis for intestinal polyposis includes a number of different syndromes of varying incidence, and these are listed below in Table 2.8.

Table 2.8 Differential diagnosis of intestinal polyposis syndromes

Basal cell nevus syndrome
Bannayan-Ruvalcaba-Riley syndrome
Cowden's syndrome
Cronkhite-Canada syndrome
Familial adenomatous polyposis (FAP) syndrome
Familial juvenile polyposis
Hereditary mixed polyposis
Hyperplastic polyposis syndrome
MYH-associated polyposis (MAP)
Peutz-Jeghers syndrome
Turcot's syndrome

Treatment Recommendations

The high risk of colorectal cancer developing from an intestinal polyp necessitates screening and endoscopic surveillance, but often prophylactic colectomy is required to ensure that the risk is minimized [38, 39]. Osteomas are surgically excised if they result in functional or cosmetic problems. Sebaceous cysts may be removed at the request of the patient, if they have a detrimental effect on their appearance. Fibromas/fibromatous tumors are sometimes excised, if they locally infiltrate the musculature [38].

Peutz-Jeghers syndrome

Peutz-Jeghers syndrome (PJS) is a rare condition of autosomal dominant inheritance that is associated with the development of hamartomatous polyposis mainly of the small intestine and mucocutaneous oral/perioral pigmentation. There is an associated increased cancer risk related to the polyps but also in relation to other malignancies.

The diagnosis of PJS is made clinically and is based on the presence of benign hamartomatous polyps, mucocutaneous pigmentation, and family history. The diagnostic criteria for PJS is based on any one of the following findings [43]:

- Three or more histologically confirmed benign hamartomatous polyps
- Family history of PJS and any number of hamartomatous polyps
- Family history of PJS and mucocutaneous pigmentation
- Any number of hamartomatous polyps and mucocutaneous pigmentation

Epidemiology

There are various estimates for the prevalence of PJS, which range from 1 in 8500 live births to 1 in 200,000 live births depending on the population sampled. There is no discrepancy based on sex or ethnicity [43, 44].

Etiopathogenesis

Half of all PJS cases are attributed to a mutation of a serine-threonine kinase (STK11/LKB1) gene, which is located on the short arm of chromosome 19p13.3 [43–45].

Clinical Manifestations

Seventy to 90% of patients have polyps present in the small intestine [45] with the jejunum being the most common location [43]. Colorectal polyps are present in 50% of patients and 25% have gastric polyps [45].

A significant increase in the size of a polyp can result in intussusception (especially in younger patients) as well as bowel obstruction. This can present clinically as severe abdominal pain and bleeding both from within the gastrointestinal tract and rectally, which can result in anemia [43].

There is a 2–3% incidence of gastrointestinal adenocarcinoma in PJS. There is also an increased risk of malignancies of the breast, pancreas, thyroid gland, genitourinary tract, lung, and testis. An estimated 48% of patients with PJS will succumb to malignancy by the average age of 57 [42].

Oral Signs and Symptoms

Melanotic macules classically present on or around the lips and appear in up to 95% of all PJS patients [46]. The vermillion border is also affected in 95% of patients [42]. They can vary in size from 1 to 5 mm and also in color incorporating different

Table 2.9 Differential diagnosis of mucocutaneous oral pigmentation

Becker's nevi
Carney complex
Cowden syndrome
Laugier-Hunziker syndrome
Leopard syndrome
Melanotic macules/ephelides/nevi/lentigines
Nevi of Ota

shades of brown and black [44]. They first appear in infancy and can also affect other oral sites including the buccal mucosa, labial mucosa, palate, and tongue [43, 44]. Lentigines can present periorally on the skin as well as other sites including perianally and on the fingers and toes [46].

Anemia as a result of gastrointestinal/rectal bleeding can be indicated by the presence of oral ulcers, glossitis, or angular cheilitis.

Differential Diagnosis

The differential diagnosis of intestinal polyposis [38, 43, 45] and mucocutaneous oral pigmentation [43] are summarized in Tables 2.8 (see section on Gardner's Syndrome) and 2.9, respectively.

Treatment Recommendations

There is no medically indicated requirement to remove any mucocutaneous pigmentation although the appearance may be cosmetically unappealing and, thus, has a psychosocial impact on the patient [15]. Camouflage makeup can be used to conservatively cover up any hyperpigmentation. Various modalities have been used to remove such pigmentation; however, there is no definitive treatment recommendation to be made.

Approaches utilized include filtered intense pulse light, Q-switch ruby laser, and CO_2-based lasers [46].

Surveillance is the key to managing the intestinal polyps. A recent review paper [46] acknowledges that there is no consensus as to how and when this is undertaken. The role of surveillance is to detect large polyps that may predispose to obstruction/intussusception or bleeding and also to detect any cancerous changes as early as possible [46]. The authors conclude that a baseline colonoscopy and upper gastrointestinal endoscopy are indicated at age 8 years and video capsule endoscopy should be performed every 3 years, if polyps are found at the initial examination. Polypectomy of enlarging polyps is the surgical intervention of choice.

Malabsorption Conditions

Malabsorption is a term that encompasses various processes with many causes whereby nutrients are not fully absorbed from the gastrointestinal tract. Malabsorption can arise from maldigestion, mucosal or mural problems, or microbial causes [47]. A consequence of malabsorption is malnutrition. Hematinic (ferritin, folate, and vitamin B_{12}) deficiencies caused by malabsorption can lead to oral signs and symptoms.

The most common causes of hematinic malabsorption that can present with oral manifestations include Crohn's disease, celiac disease, and pernicious anemia.

The different causes of malabsorption that can contribute to each of the aforementioned hematinic deficiencies are outlined in Table 2.10 [47–49].

The epidemiology and etiopathogenesis of Crohn's disease and celiac disease have been elaborated on earlier in this chapter. To discuss all of the other less common causes mentioned in Table 2.10 in detail would be beyond the scope of this chapter. However, a brief description of pernicious anemia follows.

Pernicious anemia is an autoimmune macrocytic anemia that is caused by vitamin B_{12} (cobalamin) deficiency. Intrinsic factor, which is produced by gastric parietal cells, is required to absorb vitamin B_{12}. Autoantibodies act against both gastric parietal cells and intrinsic factor resulting in a deficiency of B_{12} [48, 50]. Pernicious anemia is associated with the development of gastric adenocarcinoma and atrophic body gastritis [50].

Clinical Manifestations

General signs of malabsorption include unintentional weight loss or failure to thrive in

Table 2.10 Malabsorptive causes of hematinic deficiencies

B_{12}	Atrophic gastritis
	Blind loop syndrome
	Celiac disease
	Crohn's disease
	Gastrectomy – partial/total
	Ileal resection/disease
	Long-term use of acid-reducing drugs
	Parasitic/bacterial infections of the small intestine
	Bacterial overgrowth
	Fish tapeworm (diphyllobothriasis)
	Giardiasis
	Pernicious anemia
	Tropical sprue
	Zollinger-Ellison syndrome
Ferritin	Celiac disease
	Crohn's disease
Folate	Celiac disease
	Tropical sprue

children. The main clinical manifestations of malabsorption with respect to hematinics are those of anemia such as fatigue, lethargy, pallor, and breathlessness.

Oral Signs and Symptoms

Hematinic deficiencies (ferritin, folate, and vitamin B_{12}) are implicated in the development of recurrent oral ulceration (aphthous ulcers), a susceptibility to developing infection (angular cheilitis), a burning sensation of the oral mucosal tissues (stomatodynia), and the development of atrophic glossitis (beefy red tongue), which can be painful [15].

Differential Diagnosis

Please see Table 2.6 for factors predisposing to the formation of aphthous-like ulcers. Please see Table 2.11 for the differential diagnosis of an oral burning sensation.

Treatment Recommendations

Management/treatment depends primarily on addressing the underlying cause. It may also be necessary to replace deficient nutrients. Treatment for oral ulcers and angular cheilitis is outlined in the section entitled Crohn's disease and orofacial granulomatosis.

Table 2.11 Differential diagnosis for an oral burning sensation

Local causes	Allergy/contact sensitivity
	Dry mouth
	Infection (fungal/viral)
	Mucosal lesions (e.g., geographic tongue, oral lichen planus)
	Pain conditions (e.g., postherpetic neuralgia)
	Trauma (friction from grinding/clenching teeth/loose dentures)
Systemic causes	Endocrine (diabetes/hypothyroidism)
	Hematinic deficiency
	HIV disease
	Medication side effects
	Sjögren's syndrome (dry mouth)

Gastroesophageal Reflux Disease

Gastroesophageal reflux disease (GERD) is a chronic disease and occurs when there is involuntary projection of gastric acid from the stomach upwards through the esophagus. The acid can be regurgitated into the oral cavity. There are many reasons as to why this occurs, but it is more commonly seen in obesity, pregnancy, patients with a hiatal hernia, smokers, and a high-fat diet.

Epidemiology

It is estimated that seven million people in the United States have some symptoms of GERD and that 50% of those diagnosed are between the ages of 45 and 64 [51].

Etiopathogenesis

Problems with the lower esophageal sphincter such as transient relaxation or hypotonia can result in GERD. Other etiological factors include changes to the gastroesophageal anti-reflux barrier, which may occur with a slipping hiatal hernia and inadequate esophageal peristalsis [52].

Clinical Manifestations

The main clinical manifestations of GERD include dyspepsia (indigestion), heartburn, odynophagia, regurgitation of acid/foodstuffs into the pharynx/oral cavity, and a dry cough particularly at nighttime when lying flat. Complications of long-standing acid reflux into the esophagus

include metaplastic changes as seen in Barrett's esophagus, which is a potentially malignant condition and the formation of strictures.

Oral Signs and Symptoms

Acid reflux into the oral cavity can lead to erosion of the dentition [53], halitosis, and a burning sensation of the oral soft tissues through direct contact [54]. Dental erosion, which is one of the types of non-carious loss of tooth structure along with attrition and abrasion, can affect posterior teeth and the palatal surface of anterior teeth [53]. This can lead to an irreversible loss of tooth substance and increased sensitivity especially pain with consuming cold substances. The enamel can become smooth and shiny, and with significant erosion, the yellow appearance of the underlying dentin can be visualized [15].

Differential Diagnosis

The differential diagnosis for an oral burning sensation and the causes of dental erosion are outlined in Tables 2.11 and 2.12, respectively.

Treatment Recommendations

Avoiding precipitants such as alcohol or specific foodstuffs (e.g., spicy foods) should be advised.

Medical management entails the use of drugs that inhibit gastric acid secretion. Proton pump inhibitors are the most potent and effective. Histamine 2 receptor antagonists and antacids are alternatives but much less effective [55, 56]. A formal gastroenterology consultation may also need to be sought.

The surgical procedure of choice, if medical intervention fails, would be a fundoplication.

Referral for a dental consultation should be considered if there is evidence of significant dental erosion in order to facilitate restorative treatment.

Table 2.12 Differential diagnosis for causes of dental erosion

Alcoholism	Chronic vomiting
	Consuming low pH alcoholic drinks
Eating disorders	Anorexia nervosa
	Bulimia
Dietary erosion	Acidic foods (e.g., vinegars)
	Low pH carbonated drinks
	Fruit juices

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