Oral and Maxillofacial Infections

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Faculty Disclosure

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Audience

This course is designed for all dental professionals involved in the identification and treatment of oral and maxillofacial infections.

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Course Objective

The purpose of this course is to emphasize to dental professionals the importance of quickly identifying and treating oral and maxillofacial infections.

Learning Objectives

Upon completion of this course, you should be able to:

1. Review the host response and basic components of microbiology.
2. Identify the most common odontogenic infections of various origins.
3. Analyze the available antibiotics used in the treatment of oral and maxillofacial infections.
4. Evaluate the prevalence and appropriate treatment of oral fungal infections.
5. Discuss common viral pathogens of the oral/maxillofacial complex and their treatment, with special considerations for immunocompromised patients.

INTRODUCTION

Infections involving the oral and maxillofacial complex have considerable variation in their origin, virulence, and degree of morbidity. The host response, the use of antimicrobial medications, and the definitive treatment needed to restore the affected area(s) will also vary according to the pathogen involved. This course will highlight several of the most common infections associated with the oral and maxillofacial complex and common defensive mechanisms against pathogenic microbes. Differentiation of bacterial infections of the pulp, the periodontium, and the contiguous oral structures, as well as the antibiotics used in their treatment, will be presented. In addition, the identification and treatment of oral fungal infections is discussed. Viral pathogens present unique challenges when they involve the oral tissues, as the pharmacologic treatments available can only palliate the symptoms associated with viral outbreaks, not provide a cure [1].

Oral infections of microbial origin can become a life-threatening issue for patients who are immunosuppressed. Diseases such as human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS) and pharmacologically induced immunosuppression to treat autoimmune diseases or prevent organ rejection in transplant recipients can complicate the treatment of oral/maxillofacial infections. Overall, this course will provide an appreciation for the diverse nature of oral and maxillofacial infections and the modalities available for their treatment.

HOST DEFENSE MECHANISMS

A diverse group of more than 700 different species of bacteria comprise the normal microbial community of the oral cavity [2]. In addition, fungal organisms of the *Candida* species have been isolated from the oral cavity and are considered normal inhabitants of the oral microflora. *Candida albicans* is the primary species associated with pathogenicity within the oral cavity. However, fungal infections caused by less common species, such as *Aspergillus fumigatus* or *Cryptococcus neoforman*, can develop, particularly in immunocompromised individuals [3].

The pathogenicity of any member of the oral microbial community is challenged by the local and systemic defense mechanisms the host possesses. The most basic of these defenses is intact oral mucosa. The integrity of the mucosal surface can be breached by trauma or due to ulcerations related to chemotherapy for systemic cancer or radiation therapy used in the treatment of head and neck malignancies. The long-term use of certain medications, such as methotrexate, can cause ulcerative stomatitis or mucositis, allowing for invasion of pathogens. Ulcerative lesions caused by prostheses (e.g., partial or complete dentures) disrupt the continuity of the mucosal surface, as can accidental trauma during tooth brushing, retraction, or tissue manipulation during dental procedures. Regardless of the cause, an ulcerated mucosal surface provides the oral microbial community with access for local, regional, and even systemic dissemination.

The role of saliva as a component of the host defense against oral microbial pathogenicity is often underappreciated—until the volume of the salivary flow is diminished or its quality is compromised. Saliva provides a lubricating medium to facilitate eating, speaking, and swallowing, and an adequate volume of saliva also decreases the retention of bacteria-laden plaque on the surfaces of teeth, preventing caries and periodontal disease. Some constituents of saliva inhibit microbial growth and may induce cell death. When the secreting elements of the salivary glands (acini) are destroyed by an autoimmune disease such as Sjögren syndrome or radiation therapy, the quantity and quality of saliva will be diminished permanently, resulting in an increased potential for opportunistic infections in the oral and maxillofacial complex.

Saliva also contains antibodies that target specific pathogens. Immunoglobulin A and immunoglobulin G comprise the majority of antibodies found in saliva [4]. These immunoglobulins bind to and cause agglutination of bacterial, viral, and fungal organisms in the oral cavity, preventing their adhesion and colonization on mucosal surfaces [5].

Small, positively charged peptides called histatins are also found in saliva. Histatins are drawn via electrostatic forces to negatively charged bacterial membranes, leading to membrane leakage, rupture, and destruction of bacteria [6]. A similar mechanism occurs when histatins bind to surface proteins of fungal organisms [7].

Lysozymes are small proteins found in saliva that act to break down the cell walls of gram-positive bacteria. The subsequent increase in membrane permeability leads to destruction of the bacteria. Lysozymes also exhibit some antiviral and antifungal properties [8].

These are just a few of the substances in saliva that act to provide an initial defense against potential oral pathogens. The combination of these substances and an intact oral mucosa is the foundation for a defense against microbes that have the potential to cause a wide range of infections in the oral and maxillofacial complex. However, other variables beyond the oral cavity can influence the ability of the host to maintain good oral health. Compromised host immunity, systemic illnesses, alcoholism or drug abuse, age, and genetics can result in an increase in the virulence, extent, duration, and morbidity of infections in the oral and maxillofacial complex.

MICROBIOLOGIC CONSIDERATIONS

BACTERIAL INFECTIONS

Bacterial infections in the oral and maxillofacial complex are usually polymicrobial in nature. Odontogenic infections composed solely of anaerobic bacteria comprise about 50% of all odontogenic infections, while mixed infections (both aerobic and anaerobic bacteria) account for 44%, and 6% feature only aerobic bacteria [9]. The most common bacterial species involved in odontogenic infections are anaerobic gram-positive cocci such as *Peptostreptococcus* and *Streptococcus milleri*. Gram-negative anaerobic rods such as *Bacteroides (Prevotella)* are also associated with odontogenic infections [10].

Bacterial odontogenic infections progress through several stages of development [9]. The first stage, inoculation, involves bacterial access to the facial spaces from the periapical region of necrotic teeth or from deep periodontal pockets. Aerobic bacteria predominate during this stage. The patient experiences minimal discomfort, and the overlying oral mucosa have a soft, doughy consistency on palpation.

When both aerobic and anaerobic bacteria are present, cellulitis is the next stage. Patients with cellulitis experience moderate-to-severe discomfort, and the overlying oral mucosa is firm and indurated. The boundaries of the infection lack a clear delineation. The skin in the area of the cellulitis is usually red and can feel warm to the touch.

The final stage of an odontogenic bacterial infection is an abscess. An abscess may develop one to two weeks after the inoculation stage and features localization of the infection—patient discomfort decreases, the overlying oral mucosa is fluctuant and tender, and suppuration (pus) is present. This is the period during which anaerobic organisms predominate [9; 11].

Interactions among bacterial species can also contribute to the development and the duration of an odontogenic infection. Some species manufacture nutrients that are beneficial to another microbe. For example, aerobic organisms are the early colonizers of odontogenic infections and utilize the oxygen supply during their metabolism. This creates an oxygen-depleted environment conducive to the growth of anaerobic organisms [12].

The most common treatment for odontogenic infections is antibiotics in conjunction with definitive treatment, such as endodontics or oral surgery. Beta-lactam antibiotics such as penicillin, amoxicillin, and the cephalosporins are empiric choices in the initial treatment. These agents act by inhibiting the synthesis of the cell walls of susceptible bacteria. However, an increasing number of bacterial species have become resistant to the effects of the antibiotics commonly used to treat odontogenic infections. Also, most chronic and acute endodontic infections can be successfully managed by disinfection of the root-canal system, without the need for antibiotics [13]. Many bacterial species can produce extended-spectrum beta-lactamases, which are enzymes that open the beta-lactam ring and inactivate antibiotics with this chemical structure, resulting in resistance [14]. To combat this growing problem, compounds such as clavulanate have been developed to inhibit beta-lactamase activity; clavulanate is usually combined with amoxicillin for the treatment of odontogenic infections not resolved by conventional beta-lactam antibiotics. Unfortunately, some bacteria have also become resistant to this combination [15]. Bacterial resistance to conventional antibiotics is an emerging public health crisis and has developed in part because of the imprudent use of antibiotics [13]. Clinicians should use antibiotics only when they are absolutely necessary and effective and should encourage educational initiatives that support the coherent and proper use of antibiotics [13].

FUNGAL INFECTIONS

As noted, oral fungal infections are usually associated with the fungal species *C. albicans*. This is an opportunistic pathogen that causes oral candidiasis (thrush), usually in immunosuppressed individuals, such as patients with HIV/AIDS or who are undergoing chemotherapy. Patients who have diabetes, wear dentures, use steroid inhalers, or have chronic xerostomia (dry mouth) are also at risk to develop oral candidiasis. In addition, antibiotic therapy can decrease the number of bacteria in the oral cavity that compete with *C. albicans* for available nutrients, leading to oral candidiasis, usually on the dorsal surface of the tongue or the palatal mucosa.

The transformation of C. *albicans* from a commensal organism to a pathogen is triggered by a combination of characteristics called virulence factors. Adherence of *Candida* to the epithelial cells is possible through weak interactions involving hydrophobic and electrostatic forces [16]. These forces provide resistance to the normal flushing action of saliva. Genetic factors of C. *albicans* also promote more specialized methods of binding. The genes of the agglutinin-like sequence group and the hyphal wall protein group cause the development of glycoproteins in the fungal cell wall that stimulate the adhesion of C. *albicans* to the epithelial cell surface of the oral mucosa [17; 18]. This is a critical virulence factor for C. *albicans*, as its pathogenicity requires the ability to adhere to epithelial surfaces.

High-frequency phenotypic switching (frequent switching between cell types) allows *Candida* spp. to change color and translucency in order to reproduce and elude the immune response of the host [19]. The development of tube-like structures called hyphae provides an impediment against phagocytosis by macrophages and their monocyte precursors. C. *albicans* can release hydrolytic enzymes such as aspartyl proteinases and phospholipases, which can damage host cells and the extracellular matrix in which they reside [20]. Damaged tissue offers these fungal organisms the ability to enter deeper layers of the oral mucosa and can lead to an increase in the virulence and duration of an infection. When these virulence factors are combined with an immunocompromised host, C. *albicans* infections originating in the oral and maxillofacial complex can result in significant morbidity and even death.

VIRAL INFECTIONS

There are many viral infections that can affect the oral cavity and adjacent structures. The virulence of these pathogens varies widely and can be particularly severe in the immunosuppressed patient. Unlike bacterial or fungal pathogens, viruses cannot replicate on their own and most do so within the living cells of a host organism. The entire virus particle is called a virion, which is protected by an outer protein shell called a capsid. The inner core of ribonucleic acid (RNA) or deoxyribonucleic acid (DNA) is generally the means by which host cells are infected. The type of cell the virion will infect is encoded by the capsid.

The largest viral family is *Herpesviridae*, which consists of more than 300 different types of herpes viruses capable of infecting animal species; however, only a few cause oral and maxillofacial infections in humans [21]. Only the viruses that cause influenza and the common cold are more common in humans than the herpes viruses. All members of the herpes virus family feature latency, meaning the virus lays dormant in a specific cell for periods ranging from months to decades. Subfamilies of the herpes virus group reflect the cell type in which the latency occurs. Herpes simplex virus 1 and 2 (HSV-1 and HSV-2) and the varicella zoster virus (VZV) are members of the Alphaherpesvirinae subfamily and remain in neurons during their latent period. Human herpes virus 4, also known as the Epstein-Barr virus (EBV), spends its latent period in B-lymphocytes and is a member of the Gammaherpesvirinae subfamily. Human herpes virus 5, or cytomegalovirus, is a member of the Betaherpesvirinae subfamily, as its latency period is spent in monocytes and lymphocytes [22]. The virions of the herpes virus group range from 120 to 250 nm and feature an inner core of double-stranded DNA [23].

Other viruses can cause disease in humans with oral and maxillofacial manifestations, including papillomaviruses. The double-stranded DNA family of papillomaviruses consists of more than 100 types. Several papillomaviruses (e.g., type 16) have been identified as oncogenic agents and have been implicated in the development of oropharyngeal squamous cell carcinoma [24]. Common oral manifestations of the human papillomavirus (HPV) subtypes include squamous papillomas, condyloma acuminatum (venereal warts), and oral verruca vulgaris (oral warts). The subtypes of HPV proliferate within epithelial cells, with their highest concentration in the ano-genital area, the urethra, the skin, the larynx, the trachea and bronchial areas, and the oral mucosa [25].

INFECTIONS OF ODONTOGENIC ORIGIN

ENDODONTIC (PULPAL) INFECTIONS

Dental caries remain the most common disease in adults and children in the United States [26]. The carious process begins with the microscopic demineralization of the outer layer of enamel and continues through the enamel and the dentin until the pulpal tissues are contaminated with bacteria. The initial inflammatory response is followed by necrosis of the pulpal tissues, at which point bacteria that have traversed through the pulp chamber and the root canal system can exit the apical foramen of single-rooted teeth or the apical foramina of multi-rooted teeth.

Dental caries are not the only means by which pathogenic bacteria have access to pulpal tissues. Dentinal tubules that are exposed due to gingival recession, cracks and fractures of enamel that extend into the dentin, micro-leakage around existing restorations, and traumatic injuries to teeth all provide pathogenic bacteria access to pulpal tissues. Accessory or lateral canals of the root canal system can be contaminated with bacteria when a periodontal pocket with its own pathogenic bacteria extends to their level. This can lead to pulpal necrosis of a tooth that is without caries or any prior restorations.

After pathogenic bacteria exit the apical region of the tooth, their extension into the adjacent oral tissues can lead to local, regional, or even systemic infections. The extent of odontogenic infections of pulpal origin differs based on the bacteria involved, the immunocompetence of the host, the presence of systemic diseases (especially type 1 diabetes), nutritional status, and the presence of addiction problems (i.e., alcohol and/or drug abuse). Therefore, the manifestations of odontogenic infections of pulpal origin can vary, especially the extent of swelling.

Pulpal necrosis and the presence of a periapical lesion as seen on a radiograph are not always equated with visible facial swelling. When swelling does occur subsequent to an odontogenic infection of pulpal or any other source in the oral cavity, its extent and morbidity can range from localized with minimal morbidity to regional dissemination and a compromised airway.

Bacteria that comprise the normal microflora of the mouth are usually responsible for odontogenic infections; however, non-residential bacteria can also gain access to pulpal tissues. Blunt oral and maxillofacial trauma can contaminate the oral cavity with bacteria from the skin and/or from the origin of the trauma. Dental water lines that use a municipal water supply can develop a bacterial biofilm and introduce pathogenic species into the oral environment if not properly sanitized. When high-speed hand pieces are used and a coolant spray uses water from these sources, there is a potential for contamination of the exposed dentinal tubules with bacteria from the waterline biofilm. The force from the aerosol can propel these organisms deep into the dentinal tubules and provide non-resident bacteria with a potential for pulpal contamination.

Pulpal infections vary in their bacterial composition, but some species have been more frequently associated with their development. Within the oral cavity, anaerobic bacteria predominate over aerobic bacteria, and this proportion is usually maintained in odontogenic infections involving the pulpal tissues. Although the metabolic needs for oxygen vary among the bacteria of the oral cavity, aerobic bacteria consumes the available oxygen supply and creates an environment conducive to the growth of facultative or strict anaerobes, respectively. As such, the most common microorganisms associated with endodontic infections are polymicrobial in composition and feature strict or facultative anaerobic bacteria as the majority component and aerobic bacteria in the minority. The most common gram-negative, strictly anaerobic bacteria isolated from endodontic infections are *Prevotella intermedia*, *Fusobacterium nucleatum*, *Porphyromonas endodontalis*, *P. gingivalis*, and *Selenomonas sputigena*; common facultative anaerobes include the gram-positive *Streptococcus viridans* and *S. anginosus* groups [27; 28]. Individual variances in the bacterial composition of the microflora of the oral cavity, differences in the proportions of the bacteria among pulpal infections, and the degree of immunocompetence of the host further complicate the ability to determine the specific role of isolated bacterial species in the progression of pulpal pathology. Pulpal infections should be treated promptly, as pathogenic bacteria that exit the apical foramen can then perforate the bone and extend locally, regionally, and even systemically to cause sepsis.

PERIODONTAL INFECTIONS

The development of periodontal disease is usually an insidious process, and the gradual loss of alveolar bone and attached gingiva can go unnoticed by patients for years. The deep periodontal pockets associated with intermediate and advanced stages of periodontal disease are a reservoir of diverse micro-organisms that can lead to the development of an acute infection of periodontal origin. This section will highlight oral infections that develop secondary to periodontal disease.

Periodontal Abscess

The most common acute periodontal infection is periodontal abscess. An abscess is an abrupt exacerbation and pathogenic expression of the bacteria that cause chronic periodontal disease. Periodontal abscesses are the third most common dental emergency, accounting for approximately 7% to 14% of all emergency visits [29]. These infections present as acute local inflammation with swelling in the marginal and attached gingiva that can extend into the alveolar and buccal mucosa. Examination of these lesions reveals bleeding upon probing and suppuration. The affected tissues are intensely erythematous, often with lymphadenopathy and an elevated temperature. Pain can range from mild to severe (though significant pain is rare), and the inflammation and subsequent pressure exerted

upon the periodontal ligament can produce the sensation that the tooth is mobile or that is the only tooth to be in occlusion. The affected gingival tissue is indurated (firm) in the initial stages and fluctuant in the latter stages. Spontaneous drainage can occur, after which an asymptomatic draining chronic fistula may develop. Drainage is often through the pocket. If a sinus tract is present, it should be explored.

The mandibular anterior teeth are most commonly involved in a periodontal abscess, followed by the maxillary anterior teeth and the mandibular molars [30]. A decrease in host defense or an increase in the number of pathogenic bacteria in the gingival sulcus and periodontal pocket can precipitate the development of an abscess. Other possible causes of periodontal abscess include occlusion of the gingival sulcus (preventing drainage) and root planing and scaling procedures that cause calculus to become dislodged and forced into the tissue. Periodontal abscesses that develop in patients without periodontal disease are usually the result of trauma. The introduction of a foreign body such as a popcorn kernel, a piece of a toothpick, a detached bristle of a toothbrush, or a detached piece of floss into the depth of the gingival sulcus can stimulate an inflammatory response that culminates in the formation of a periodontal abscess. Foreign materials introduced into the gingival sulcus and not removed after dental procedures, including excess dental cement, impression material, or small pieces of restorative material (e.g., amalgam or composite resin), may cause an iatrogenic periodontal abscess.

When an acute exacerbation of periodontal disease causes an abscess to develop, certain bacterial species predominate. The most common isolates include *Fusobacterium nucleatum*, *Porphyromonas gingivalis*, *Prevotella intermedia*, *Bacteroides forsythus*, and *Peptostreptococcus micros* [31].

Treatment

The goal of treatment of a periodontal abscess is to eliminate the cause of the acute infection. This is facilitated by debriding the area and creating an environment within the gingival sulcus that facilitates its cleansing, thus establishing a healthy, stable microbial community and inhibiting the development of an abscess.

If an acute exacerbation of chronic periodontal disease has caused the abscess, surgery may be required to eliminate the osseous defects and to eliminate the deep periodontal pockets that provide a favorable environment for the proliferation of the pathogens. If extensive destruction of the alveolar bone has occurred and the periodontal prognosis for the long-term retention of the tooth is poor, the tooth should be extracted to prevent recurrence of the abscess.

If the introduction of a foreign body has been the cause of the periodontal abscess, a surgical flap is usually required to obtain access and to provide adequate visualization for retrieval of the object. Radiographs should be taken to assess the alveolar bone levels and the root anatomy. Unless the foreign object is radiopaque to any degree, it will not be possible to establish its location with a standard x-ray.

Purulent material may be drained from the abscess through the gingival sulcus or by an incision into the abscessed tissue. Irrigation with sterile saline solution or an antimicrobial mouthrinse (e.g., 0.12% chlorhexidine gluconate) may be done along with the surgical procedure or curettage.

Antibiotics such as amoxicillin, clindamycin, and/or metronidazole are only used as adjuncts to definitive treatment. Antibiotic therapy alone will not eliminate the factors that precipitated the development of the abscess.

A novel treatment approach using an oral tissue decontaminant material yielded promising results in one case report study [32]. Clinical cases of acute periodontitis were treated using a mixture of hydroxybenzenesulfonic and hydroxymethoxybenzene acids and sulfuric acid. The material was positioned into the pocket on the root surface and left in the site for 30 seconds. No instrumentation was performed prior to treatment and no systemic or local antibiotics were used. All of the treated cases healed well and rapidly, and the infections were quickly resolved without complications. The pockets associated with marginal tissue recession were reduced. The brief pain felt by patients upon introduction of the material was generally well tolerated. The local application of this material avoids the use of systemic or local antibiotics [32].

PERICORONITIS

The gingival tissues of a fully erupted tooth usually extend 2–3 mm in a coronal direction and do not encroach upon or cover any part of the occlusal surface of the tooth. Of course, some teeth, most typically the third molars, become malpositioned due to space limitations and cannot erupt into normal position. The tissue that overlies these partially erupted teeth is known as the operculum. The space between the crown of the partially erupted tooth and the operculum may harbor micro-organisms that can become pathogenic and cause the acute infection pericoronitis. The space below the operculum has minimal access and limited visualization, which presents a constant challenge for the maintenance of routine oral hygiene, allowing for the accumulation of plaque and debris and providing an excellent environment for bacterial proliferation.

The clinical presentation of pericoronitis is characterized by a highly inflamed and erythematous operculum and contiguous mucosa. This can be exacerbated if the opposing tooth has drifted and traumatized the operculum. Bacterial species that have been isolated from pericoronitis include viridans streptococci, spirochetes, *Fusobacterium*, *Prevotella intermedia*, and *Peptostreptococcus micros* [33]. Pain can radiate toward the ear and the angle of the mandible. Pus may accumulate beneath the operculum and may drain spontaneously or after gentle pressure is applied. Fistulous tracts usually do not develop due to the acute nature and rapid development of the infection. Patients often have halitosis due to the presence of stagnated debris and pus. Edema in the contiguous tissues can interfere with the functional excursions of the mandible, and a soft diet may be required if the ability to masticate is compromised. Most occurrences of pericoronitis remain localized, but extension of the edema into adjacent fascial spaces, such as the masticator space or toward the pharynx, may cause a compromised airway. As such, these infections should be monitored carefully until they resolve.

Treatment of pericoronitis requires that the initial infection is controlled, and the extent of treatment necessary will depend on the extent of the infection. Pericoronitis that is well localized will differ from an infection with regional extension and lymphadenopathy. Debridement and drainage may be the only treatment necessary for well-localized pericoronitis. Infections with regional or systemic involvement will require antibiotic therapy even before debridement. Extraction of the opposing third molar may be necessary if its eruption into the operculum causes unresolved tissue trauma. Antibiotics such as amoxicillin and penicillin are appropriate choices for the treatment of more advanced pericoronitis, with

clindamycin a second-line option for patients who are not able to tolerate beta-lactam antibiotics. Impacted teeth that will never fully erupt can develop recurrent and potentially more virulent pericoronitis. Surgical removal of the operculum with or without extraction is recommended. Any tooth with a history of recurrent pericoronitis or an initial presentation with regional extension or systemic involvement should be extracted as well.

INFECTIONS IN IMMUNOCOMPROMISED PATIENTS

As noted, gingivitis usually progresses to periodontal disease gradually, with initially subtle symptoms that become more apparent over time. However, patients who are immunocompromised, particularly those with HIV, have a different progression. HIV infection causes a progressive decline in T-helper cells, also known as CD4+ cells, which leads to an increase in host immunosuppression and susceptibility to opportunistic infections. When the CD4+ count falls and the risk for infection increases, HIV infection progresses to AIDS [34]. Bacterial, fungal, and viral organisms that are not pathogenic in immunocompetent patients can cause opportunistic infections with high associated morbidity and mortality in patients with HIV/AIDS.

In immunocompromised patients, the gingival tissues are at an increased risk for infection and invasion by pathogenic bacteria. As a result, destruction of the gingival tissues and alveolar bone may progress more quickly. Periodontal infections that extend into the contiguous oral mucosa can cause the development of a necrotizing stomatitis, which can lead to extensive destruction of the oral mucosa and alveolar bone and become a life-threatening systemic infection.

There are no significant differences in the pathogens responsible for periodontal disease in patients with immunocompromising conditions compared to those without [35]. It is only the progressive immunosuppression of the host that permits a greater degree of virulence and acceleration of the involvement of the gingival tissues and of the alveolar bone.

Linear Gingival Erythema

Linear gingival erythema (LGE) is the most common periodontal disease in patients with HIV, but it can occur in any person with a compromised immune system [36]. LGE features a distinct erythematous band that involves the marginal gingiva, and it can develop without the presence of plaque or calculus and can be localized or generalized.

Unlike gingivitis in healthy patients, LGE does not respond to conventional periodontal treatment and does not improve with a meticulous at-home oral hygiene regimen. Gingival tissues affected by LGE may bleed easily and can be tender during brushing and flossing, but significant symptoms are usually absent. An increasing amount of evidence supports a fungal origin for LGE (specifically *Candida* spp.), and it has been classified as a disease of fungal etiology by the American Academy of Periodontology [37]. Treatments such as root planing and curettage do not eradicate the inflammation and erythema of LGE. Instead, treatment usually consists of the use of antimicrobial mouthrinses (e.g., one-half ounce of 0.12% chlorhexidine for two weeks) or vacuum-formed trays loaded with antifungal medication placed against the affected gingival tissues. Increasing the dose or frequency of administration may be necessary [38]. A systemic antifungal medication, such as ketoconazole, fluconazole, or itraconazole, may be used in recalcitrant cases, but it should be used with caution, as they have many potential interactions with other medications.

While mouthrinses and dental trays will decrease the intensity of the erythema and inflammation of LGE, discontinuing these regimens will result in return of the symptoms. Before any invasive treatment is started in a patient with HIV, complete blood count should be assessed to determine if the ability to achieve hemostasis will be a concern.

Necrotizing Ulcerative Periodontitis

Like LGE, acute necrotizing ulcerative periodontitis (NUP) primarily affects patients who are immunosuppressed, although it is also associated with heavy tobacco use and poor hygiene. In severely immunocompromised patients, such as those with AIDS, the development of NUP is associated with a 73% cumulative probability of death within two years of the diagnosis [38]. Compared with the slow progression of periodontal disease in immunocompetent patients, NUP features a rapid onset accompanied by severe pain. The gingival tissues necrose, followed by a rapid loss of the periodontal attachment and resorption of the alveolar bone. The destruction of the gingival tissues can lead to the exposure of the alveolar bone, which undergoes necrosis and subsequent sequestration. The formation of deep periodontal pockets characteristic of periodontal disease in healthy patients is not present in cases of NUP, as the junctional epithelium itself becomes necrotic. The necrotic tissues cause severe halitosis, and patients complain of deep, radiating jaw pain [38].

The microflora of patients with NUP consists mainly of pathogenic fusiform bacilli and spirochetes. Other bacterial, fungal, and viral opportunistic pathogens can contribute to the destructive nature of NUP. Fungal organisms of the *Candida* species and opportunistic viral pathogens of the herpes virus family, such as cytomegalovirus and the Epstein-Barr virus, have been isolated from the subgingival plaque of patients with HIV [38; 39].

Treatment for NUP depends on the pre-existing periodontal status of the patient, the virulence of the infection, and the extent to which the periodontal tissues have been affected. Patients with moderate-to-advanced periodontal disease who have compromised periodontal attachment and osseous defects before the onset of NUP have a poor prognosis for the retention of the affected teeth and will usually require extractions [38]. Patients whose initial periodontal status is more favorable can have definitive treatment designed to retain their teeth.

All patients with NUP should be prescribed an analgesic that is appropriate for their degree of pain. In addition, they may require liquid nutritional supplements, as the pressure generated on the teeth, the attached gingival tissues, and the mucosa can cause pain that interferes with the ability to chew and to eat properly [38]. The use of an antimicrobial mouthrinse can topically reduce the pathogenic microbial population. Chlorhexidine gluconate has substantivity, which promotes its retention on the teeth and soft tissues and prolongs its antimicrobial action for an extended period. Alcohol-free preparations (e.g., Paroex) are available from most manufacturers and should be used to avoid desiccation and irritation of the tissues [38]. When antibiotic treatment is used, metronidazole is the drug of choice and can be given at a dose of 250 mg four times a day or 500 mg twice daily for 7 to 10 days. Patients who cannot tolerate metronidazole may be prescribed clindamycin 150 mg four times per day or amoxicillin-clavulanate 875 mg twice daily for 7 to 10 days, if these medications are compatible with their medical history [40]. The selection and administration of any of these medications will depend on the severity of the disease and the patient's medical history. Debridement of the necrotic soft tissue and any sequestrations of bone is accomplished under local anesthesia [38].

The architecture of the alveolar bone and the gingival tissues may change drastically after treatment and healing of the tissues. The gingival tissues can become irregular and concave, which can complicate the patient's oral hygiene regimen. Clinicians should provide oral hygiene instructions and should establish a recall schedule to assist the patient to maintain optimal oral hygiene.

NUP can spread rapidly and can even lead to septicemia. Consultation with the patient's physician is advisable, as intravenous antibiotics in a hospital setting may be required. Antibiotics should be used with caution in immunocompromised patients, as their indiscriminate use can lead to the emergence of opportunistic infections, leading to serious morbidity and even death.

Occasionally, NUP will extend beyond the gingival tissues into the adjacent oral mucosa to produce necrotizing ulcerative stomatitis (NUS). NUS features a large area of ulceration, necrotic tissue, and erythema. This can extend into and cause the necrosis of the alveolar bone and lead to the sequestration of necrotic pieces of bone. Patients present with severe pain, halitosis, and signs of systemic involvement (e.g., lymphadenopathy, fever, malaise).

ANTIBIOTIC THERAPY

Endodontic (root canal) therapy or extractions are the only definitive treatments for teeth with pulpal infections. Patients should be advised that, when needed, empiric antibiotic therapy is an adjunct but not a replacement for these therapies [13]. In addition, the overuse of antibiotics has led to the development of strains of bacteria that are resistant to many commonly used agents. In an ideal situation, the bacterial species causing the odontogenic infection would be isolated and cultured to determine the antibiotic(s) to which they are susceptible. This would allow the clinician to prescribe an antibiotic with a narrow spectrum of activity and avoid the development of resistance associated with the use of broad-spectrum antibiotics. However, the time to obtain results, the cost involved, and the exacting technique required to extract and isolate the pathogenic bacteria make the routine use of cultures to drive treatment decisions impractical. Most dental infections will respond to commonly used antibiotics, but cases that are refractory to treatment require culture and/or referral to a specialist, such as an endodontist, an oral and maxillofacial surgeon, or a physician who specializes in the treatment of infectious diseases.

A thorough review of the patient's history is required before an antibiotic or any other medication can be prescribed, including age, weight, presence of any systemic disease(s), use of other prescribed or over-the-counter medications, and history of allergic reactions. When the use of an antibiotic is indicated for the treatment of a pulpal infection that has extended into the contiguous oral structures, professional experience will help guide decisions regarding the type of antibiotic to use, dose, frequency of administration, and duration of treatment. The avoidance of adverse drug reactions should also be considered before prescribing an antibiotic.

Penicillin

Penicillin V potassium remains the antibiotic of choice based on its narrow spectrum of activity against most of the gram-positive cocci and anaerobes common to odontogenic infections. This agent is well absorbed orally and maintains stability in the acidic gastric contents. Food decreases its rate of absorption, so penicillin V should be taken one hour before or two hours after meals.

Since its discovery in 1928 and patent for mass production in 1948, many bacterial species have become resistant to penicillin through the production of beta-lactamase, an enzyme that causes the breakdown and inactivation of the beta-lactam ring. Odontogenic infections that do not resolve with the administration of penicillin V should be treated with another class of antibiotics.

There are several points to consider when prescribing penicillin. First, approximately 5% to 7% of the population is allergic to penicillin and must rely on different antibiotics for the treatment of odontogenic infections [41]. In addition, drug-drug interactions are a concern. The anticoagulant effect of warfarin can be enhanced when penicillin V is used concurrently, so an alternate antibiotic or adjustment of the warfarin dose should be considered. The effectiveness of oral contraceptives can be decreased when penicillin V is used simultaneously, and another means of contraception should be used for the duration of treatment [42]. Finally, the use of penicillin V should be modified or avoided in patients with renal impairment, as all beta-lactam antibiotics are actively secreted by the renal tubules and the majority is eliminated in an unchanged form in the urine [43].

Amoxicillin

The use of amoxicillin to treat oral and maxillofacial infections has increased due to the growing bacterial resistance to penicillin. Amoxicillin was introduced in the early 1970s and is a broad-spectrum antibiotic that can be administered orally. The inclusion of a hydroxyl group within its chemical structure increases its solubility, which allows amoxicillin to be well absorbed from the gastrointestinal tract and facilitates the diffusion of the drug into organic fluids and infected tissues. It is more effective against gram-positive than gram-negative bacteria, remaining efficacious against the majority of oral anaerobic bacteria, 90% of gram-positive cocci, and about 80% of gram-negative rods [44].

Patients who are allergic to penicillin or any beta-lactam antibiotic may also be allergic to amoxicillin and should use another class of antibiotics. Adverse drug interactions parallel those of penicillin. Additionally, the medications probenecid and allopurinol, which are used to treat gout, can increase the serum levels of amoxicillin when used concurrently. A skin rash can also develop when allopurinol and amoxicillin are administered together. Coadministration of amoxicillin and methotrexate, an immunosuppressant drug used to treat rheumatic disease and cancer, can decrease the renal clearance of methotrexate and lead to an increase in the plasma levels and toxic effects, including renal failure, mucositis, myelosuppression, nausea, and vomiting [43]. As such, the simultaneous use of amoxicillin and methotrexate should be avoided. Because amoxicillin is excreted primarily by the kidneys, patients with renal disease may require a lower dose and/or longer intervals between doses to allow time for renal clearance.

Amoxicillin is often combined with clavulanic acid to extend its spectrum of activity against bacteria capable of producing beta-lactamase [43; 45]. The combination of amoxicillin and clavulanic acid (clavulanate) is often used when bacteria have proven resistance to penicillin and/or amoxicillin. However, patients may be independently allergic to the clavulanic acid portion of the medication even if they are tolerant of amoxicillin or penicillin. A dosage adjustment is required for individuals with renal impairment, and the 875-mg dose and extended-release formulations should be avoided in these patients [43].

Clindamycin

Clindamycin is classified as a macrolide antibiotic and is a semisynthetic derivative of lincomycin. While the beta-lactam antibiotics interfere with the synthesis of the bacterial cell wall, clindamycin attaches to the 50S ribosomal subunit of susceptible bacteria and inhibits protein synthesis. At lower concentrations, clindamycin is only bacteriostatic, but at higher concentrations, it can be bactericidal as well.

Clindamycin is effective against gram-positive and gram-negative anaerobic bacteria but is ineffective against most gram-negative aerobic bacteria. It is mainly used to treat odontogenic infections in patients who are allergic to penicillin or amoxicillin or who have odontogenic infections unresolved by beta-lactam antibiotics.

Clindamycin is well absorbed after oral administration and has excellent uptake into the tissues. It is actively transported into macrophages and leukocytes, cellular elements found in high concentrations in abscesses [46]. The majority of clindamycin is metabolized by the liver, so patients with hepatic disease may require an adjustment of the dosage and frequency of administration. The main route of excretion is through the bile, but some is excreted in the urine and the feces. Clindamycin should not be administered in conjunction with neuromuscular blocking agents used as adjuncts for anesthesia to induce skeletal muscle relaxation, as simultaneous use of these medications can prolong this action. Unlike the beta-lactam antibiotics, clindamycin does not enhance the anticoagulant effects of vitamin K antagonists.

The most serious adverse effects of clindamycin use are *Clostridium difficile*-associated diarrhea and pseudomembranous colitis, caused by the overgrowth of *C. difficile* in the gastrointestinal tract [47]. Therefore, patients with a history of colitis should not use clindamycin.

Erythromycin

Other macrolide antibiotics used in the treatment of infections of odontogenic origin include erythromycin and azithromycin. Systemic erythromycin has been used to treat odontogenic infections in patients with allergies to penicillin or amoxicillin and was also the medication of choice for prophylaxis against bacterial endocarditis prior to invasive dental treatment. However, increased bacterial resistance to erythromycin and common gastrointestinal side effects have widely curtailed its use for the treatment of odontogenic infections.

Azithromycin

Azithromycin is a macrolide antibiotic derived from erythromycin and has a broad-spectrum activity against both gram-positive and gram-negative bacteria. It has a better absorption profile compared to erythromycin, primarily due to its higher stability in gastric acids. After administration, azithromycin has high and prolonged tissue concentrations that provide sustained antimicrobial activity. Azithromycin is transported with the leukocytes and undergoes active intake by the phagocytes [48].

Azithromycin may be used as second-line therapy for the treatment of odontogenic infections or prophylaxis against bacterial endocarditis prior to invasive dental treatment in patients who are allergic to beta-lactam antibiotics or who cannot tolerate clindamycin. The liver is the primary site of elimination, so patients with hepatic disease may require an adjustment in the dosage. Compared to the beta-lactam antibiotics and clindamycin, azithromycin has more potential adverse interactions with other medications, including potentiation of the anticoagulant effect of warfarin and enhancement of QTc-prolonging agents [43].

Metronidazole

Occasionally, combination therapy is necessary when infections fail to resolve with initial treatment. In these cases, the addition of metronidazole, a nitroimidazole antibiotic, may be warranted. This bactericidal antibiotic interacts with bacterial DNA and causes cellular death. Metronidazole is active against gram-positive and gram-negative anaerobic bacteria but lacks any activity against aerobic bacteria [43]. It can be combined with penicillin, amoxicillin, or amoxicillin/clavulanic acid (clavulanate) for the treatment of bacterial infections in the oral cavity that have not resolved with empiric therapy.

Potential side effects include a metallic taste in the mouth, a benign darkening of the urine, and gastrointestinal disturbances. The effects of anticoagulants such as warfarin can be enhanced with the concurrent use of metronidazole. Use is contraindicated during pregnancy, as metronidazole crosses the placental barrier and may cause mutagenic effects. Consuming alcoholic beverages while taking metronidazole can cause flushing, nausea, vomiting, heart palpitations, vertigo, chest pain, and hypotension, and should be avoided [43].

ORAL FUNGAL INFECTIONS

CANDIDIASIS

As noted, most infections in the oral cavity are bacterial in origin, but the resident fungal organism *C. albicans* can become opportunistic in certain circumstances, causing localized or systemic candidiasis. Although the *Candida* genus is comprised of approximately 150 species, *C. albicans* is the etiologic agent in about half of all cases of oral candidiasis. Factors that can predispose patients to oral candidiasis include the use of dentures, reduced salivary flow or xerostomia, poorly controlled diabetes, and immunosuppression [49]. In addition, the short-term use of antibiotics can alter the oral microflora and favor the proliferation of *C. albicans* as a pathogenic organism.

The clinical presentation of oral candidiasis can vary. Acute pseudomembranous candidiasis appears as white to yellow-white plaques that are easily removed from the involved area and that leave an erythematous or bleeding surface. Acute erythematous candidiasis features painful red lesions, most frequently on the buccal mucosa, the palate, or the dorsum of the tongue that cannot be removed [49; 50]. Chronic hyperplastic candidiasis is characterized by white lesions that cannot be removed by gentle scraping. Angular cheilitis is a fungal infection localized to the radiating fissures at the corner of the mouth. Oral candidiasis is more virulent and has a higher degree of morbidity when it occurs in patients who are immunosuppressed.

Treatment of candidiasis varies according to the extent of involvement and the overall health and immunocompetence of the patient [49]. Oral candidiasis that develops due to the temporary use of antibiotics in a healthy patient may be treated and resolved with a "swish-and-swallow" regimen of an oral suspension of nystatin. Results of a 2016 study found gentian violet (GV)—a dye that is also used as an antiseptic—to be as effective as nystatin for the treatment of oral candidiasis in patients with HIV/AIDS [51]. Researchers assigned 221 patients to receive either topical GV (5 mL 0.00165% solution swish and gargle twice daily) or nystatin oral suspension (5 mL of 100,000 units/mL swish and swallow four times daily) for 14 days. Among patients eligible for analysis, 68.5% in the GV group had either cure or improvement of oral candidiasis, compared to 67.8% in the nystatin group, a non-significant difference. Cure rates were similar and both treatments were equally well tolerated. Although GV can cause bluish-purple staining of the oral mucosa, 61% of the GV group reported no staining and none stopped taking GV due to staining. The cost of GV ($2.51) is much less expensive than nystatin ($19.42) [51].

Systemic antifungal medications such as fluconazole or ketoconazole are second-line options when oral candidiasis is refractory to topical antifungal approaches [52]. Patients with refractory oral candidiasis or who are immunocompromised should be referred to their primary care physician or to a physician who specializes in the treatment of infectious disease.

As noted, systemic antifungal medications interact with many other drugs. In addition, systemic antifungal medications are infrequently associated with elevated liver enzymes and hepatotoxicity-related deaths. Patients with any form of hepatic disease should be referred to their physician to determine if these agents may be used safely.

Oral candidiasis treatment plans should address special circumstances in order to ensure a successful treatment outcome. Patients who wear partial or complete dentures should treat both the affected tissues and the surfaces of the prostheses [49]. The acrylic material of these prostheses contains numerous microscopic porosities into which the *Candida* organisms can reside and proliferate. As such, they should be treated with an antifungal preparation to prevent a cycle of re-inoculation. After a thorough manual cleaning of the prosthesis, it should be immersed in a disinfecting solution compatible with the device, and before re-insertion, it should be rinsed thoroughly [52]. A thin layer of antifungal cream should be placed on the tissue surface of the prosthesis, similar to a denture adhesive.

It is important to note that there has been an increase in antimicrobial resistance in *Candida* species, with approximately 35% of *Candida glabrata* species and 75% of *Candida krusei* species resistant to fluconazole [53]. Any fungal infection that does not resolve should be referred to a physician. This is especially true for immunocompromised patients for whom a delay in treatment can have fatal consequences.

NONCANDIDAL INFECTIONS

Although candidiasis is the most common oral fungal infection, the risk of other fungal infections appears to be growing, likely the result of a larger immunocompromised population and increased international travel and globalization [54]. Fungi that may cause disease in humans with oral manifestations include *Aspergillus* spp., *Blastomycesdermatitidis*, *Coccidioides immitis*, *Cryptococcus neoformans*, and *Histoplasma capsulatum*. In the United States, the most common sources of these mycoses are contaminated soil and decomposing plants. However, there have been reported cases of introduction of *Aspergillus* into the sinuses following perforation of the dental root cavity during a molar root canal [55].

Patients with immunosuppression (due to medications or disease), malignancy, malnutrition, or poorly controlled diabetes are at increased risk for noncandidal fungal infections [54]. These infections are usually subclinical, with few or no symptoms [54]. If untreated, the infection can spread to the lungs or heart, with more serious consequences. If present, symptoms vary based on the pathogen. Lesions can be yellow/white, ulcerative/non-healing, or black, necrotic ulcers. The location of the lesions will be indicative of the causative pathogen. For example, lesions associated with aspergillosis occur most commonly on the palate or posterior tongue [54].

It is important to note that oral manifestations of noncandidal infections are usually due to extension from a paranasal infection, meaning that considerable damage may have already been done [54]. As such, systemic treatment with an oral antifungal agent (e.g., fluconazole, ketoconazole, voriconazole) is almost always required. Antifungal prophylaxis is recommended for immunosuppressed patients [54]. In addition, surgical debridement is often necessary. Fungal destruction of the maxilla, orbit, and/or cranial base will necessitate surgical reconstruction [54]. Amphotericin B is an effective treatment for all forms of oral deep fungal infection, particularly in patients with progressive, potentially life-threatening infections [43; 54]. Flucytosine and rifampin enhance the activity of amphotericin B and may be indicated when the response to amphotericin B is inadequate. Treatment generally continues for 6 to 12 weeks after culture results are negative [43; 54].

ORAL AND MAXILLOFACIAL VIRAL INFECTIONS

As the etiologic agent of diseases ranging from the common cold to HIV/AIDS, viruses affect millions of Americans each year. Antiviral medications can alleviate the symptoms or accelerate the healing of viral diseases, but none are curative. The viral family responsible for most oral and maxillofacial manifestations is *Herpesviridae*, or the herpes viruses [35]. The oral and maxillofacial complications of these viral infections can range from inconvenient but benign to life-threatening and even fatal.

While members of the *Herpesviridae* family represent the largest viral group to have oral manifestations, numerous other viral pathogens can have oral and maxillofacial manifestations and consequences. Clinicians should remain knowledgeable regarding new and emerging trends among the various viral pathogens with effects on oral health.

HERPES SIMPLEX VIRUS-1

Herpes simplex virus-1 (HSV-1) causes the most frequently occurring oral and perioral viral infection: recurrent herpes labialis, more commonly known as "cold sores" or "fever blisters" [56]. The initial infection of HSV-1 is referred to as primary herpetic gingivostomatitis (PHG). Although the initial PHG lesions heal, the virus remains in the body, travelling along neurons to reside and remain dormant in a dorsal root ganglion until reactivated. This latency period is a common characteristic among the members of the *Herpesviridae* family. HSV-1 can be reactivated by varied stimuli, including stress, sunlight, illness, and immunosuppression [56; 57].

The classic presentation of recurrent herpes labialis is of small, fluid-filled blisters that coalesce to form larger vesicles at the junction of the skin and the lip. Patients may experience fever, anorexia, listlessness, and gingivitis, which is the most striking feature with markedly swollen, erythematous, friable gums [57]. Most patients have a prodromal sensation of burning, itching, or tingling before the emergence of the actual lesions [56]. The lesions form scabs and heal without scarring in one to two weeks in the healthy patient, but healing time can extend for several weeks in patients who are immunocompromised.

There is no cure for HSV-1 lesions, although topical or oral antiviral preparations such as acyclovir can shorten the duration of outbreaks [56]. Life-threatening HSV infections in immunocompromised patients require high-dose intravenous acyclovir. Treatment of acyclovir-resistant infections includes cidofovir and foscarnet, but both are nephrotoxic. Options for recurrent infections in immunocompetent patients include either no treatment or episodic treatment with topical agents or oral antiviral agents [57]. If topical medications are used, patients should be advised to apply the cream with a cotton-tip applicator to avoid viral contamination and inoculation of the fingertips,

referred to as herpetic whitlow [57; 58]. Patients with this form of the disease will have recurring viral outbreaks on the fingertips similar to the lesions of recurrent herpes labialis [58].

VARICELLA-ZOSTER VIRUS

Human herpesvirus 3, also known as the varicella-zoster virus (VZV), is the etiologic agent of chickenpox. In a fashion similar to HSV-1, when the chickenpox lesions heal, VZV migrates to the cranial nerve or dorsal root ganglia, where it can remain dormant for decades or the lifetime of the individual. The reactivation of VZV later in life causes shingles. Immunosuppression/compromise and older age are the leading causes of shingles reactivation, although the disease can affect individuals of any age [59].

Upon reactivation, VZV migrates from the nerve cell body within the ganglia and follows the course of the involved axon. Shingles features unilateral lesions with intense radiating pain that has been described as burning, itching, or throbbing. For some patients, significant pain will remain in the areas of the healed lesions, a phenomenon known as postherpetic neuralgia [59]. Patients with postherpetic neuralgia may require narcotic analgesics and/or antidepressant medications to alleviate the symptoms, so dental clinicians should exercise caution in prescribing sedatives or additional narcotic analgesics due to the increased risk of respiratory depression.

The treatment of shingles begins with prevention; there are now vaccines licensed for chickenpox and for shingles in adults older than 50 years of age [54]. If an outbreak does occur, antiviral medications such as acyclovir, valacyclovir, and famciclovir may be used to decrease symptoms and shorten the duration, but none are curative [59; 60].

EPSTEIN-BARR VIRUS

The human herpesvirus 4, or Epstein-Barr virus, is the causative agent of infectious mononucleosis. In the years since the emergence of HIV/AIDS, EBV has also been associated with the development of the opportunistic oral lesion oral hairy leukoplakia. Oral hairy leukoplakia is a marker of any generalized immunosuppression, but it is most closely associated with HIV/AIDS [61]. These lesions feature bilateral, nonremovable hyperplastic tissue with a corrugated texture that appears on the lateral surface of the tongue. Replication of EBV in the epithelial cells causes hyperplasia along the lateral surface of the tongue, assuming a "hair-like" appearance. These lesions are asymptomatic and usually discovered during a routine oral examination [61]. Antiviral agents such as acyclovir can cause the lesions to regress, but cessation of the antiviral therapy prompts their return. In patients with HIV/AIDS, the appearance of oral hairy leukoplakia marks a point of progressive immunosuppression and poor prognosis for the patient's long-term survival [61].

HUMAN PAPILLOMAVIRUS

There are more than 120 different genotypes that comprise the HPV family [62]. As opposed to the characteristic ballooning degeneration and cellular lysis that most viruses cause, members of the HPV family cause proliferation of the epithelial tissues that can result in a multitude of benign and malignant lesions [63]. Only a select few of the HPV genotypes have oral or facial patterns of distribution.

HPV genotypes 2 and 4 cause the common skin wart (verruca vulgaris) and may cause lesions within the oral cavity or, more frequently, near the skin of the lower lip. Nearly one-third of these intra-oral lesions occur on the hard and soft palates and the uvula [64]. The solitary lesions are usually asymptomatic, sessile, and not pedunculated.

Patients who have skin warts around nail beds or on their fingers can transmit the HPV virus to the oral tissues by parafunctional habits, such as the biting of fingernails. Conservative surgical excision with the submission of the tissue specimen for histologic analysis is required to determine if there are any malignant aspects within the lesion. Recurrences are possible.

Anogenital warts (condyloma acuminatum) are associated with the HPV-6 and HPV-11 genotypes and occur in the genital and/or anal region [65]. Oral-genital contact is the primary means by which these lesions infect the oral tissues. Unlike the lesions of verruca vulgaris or squamous papillomas, anogenital warts in the oral region develop as multiple soft, sessile lesions that are moderately infectious [66]. There is a higher degree of viral infection in the peripheral tissue adjacent to these lesions. Therefore, a wider margin of surgical excision is required when the specimens are excised and submitted for histologic analysis. This higher level of virulence also accounts for a higher recurrence rate of oral anogenital warts compared to those of verruca vulgaris [67].

The lesions of verruca vulgaris and of condyloma acuminatum do not present any specific restrictions for dental treatment. However, their discovery upon a soft-tissue examination should prompt the clinician to discuss the patient's awareness and duration of these lesions. Any lesion that has been present for more than two weeks should be excised and biopsied. Immunocompromised patients typically have higher recurrence rates after the removal of these lesions. After histologic analysis has confirmed the diagnosis of condyloma acuminatum, patients should be educated as to the means of transmission to minimize the development of new oral lesions and the transmission of the virus to others.

Genotypes HPV-6 and HPV-11 are also the cause of lesions called squamous papillomas, which are the most frequently occurring epithelial oral lesion. The morphology of these lesions can vary and may appear to have individual finger-like projections or wider sessile bases with a corrugated topography [63]. The lingual frenum, palate, buccal mucosa, and lips are the most common oral and facial areas in which these lesions develop [68]. Most lesions are solitary, pedunculated, and asymptomatic. These lesions can be excised surgically or with laser ablation, with each specimen submitted for histologic analysis. Surgical excision has the highest success rate and lowest recurrence rate. Initial cure rates are 63% to 91% [65]. Larger lesions on the buccal mucosa or the lips may be traumatized during mastication and become secondarily infected. These lesions pose no specific restrictions for dental treatment. However, due to the multitude of forms in which oral cancer can appear, clinicians should excise any lesion that involves the oral and maxillofacial complex that has not healed within two weeks of its initial presentation.

Heck Disease

Focal epithelial hyperplasia, or Heck disease, is an HPV-13 or HPV-32 infection most commonly seen among Native Americans and Alaskan Natives [69; 70]. The clinical presentation features multiple soft, dome-shaped lesions on the buccal or labial mucosa and the tongue [71]. These lesions are potentially contagious but do not interfere with routine dental treatment. Larger lesions on the buccal or labial mucosa or the lips can be traumatized during occlusion. Surgical excision can become complicated when there are multiple overlapping lesions. Excised lesions should be biopsied to determine their nature and whether they are benign or malignant, which cannot be discerned strictly from the clinical appearance. Specific immunodiagnostic techniques, such as in situ DNA hybridization, must be performed on submitted histologic samples to confirm the presence of HPV-13 and/or HPV-32 [72].

Focal epithelial hyperplasia lesions are most common among children, but adults can also be affected. The viral-induced hyperplasia of the epithelium can result in a mucosal layer that is 8–10 mm thicker than average. Some lesions will regress spontaneously as time progresses. Lesions associated with Heck disease do not develop into an oral carcinoma, but their presence can be an oral manifestation of HIV/AIDS [73].

CONCLUSION

This course has highlighted some of the most common oral and maxillofacial infections of bacterial, fungal, and viral origin. It is not an exhaustive list, but it focuses on the most common oral and maxillofacial problems that can develop when these organisms proliferate.

Oral infections of odontogenic and periodontal origin can involve regional and systemic dissemination with the potential for significant morbidity and death. Many oral infections occur more often and with greater severity among immunocompromised patients. Clinicians should be able to combine pharmacologic protocols and definitive treatment to eliminate the source of the infection and restore the patient to optimal oral and systemic health. Oral and maxillofacial infections of any microbial source that do not resolve should be referred to an oral and maxillofacial surgeon or to an infectious disease physician. The health, well-being, and life of a patient with an oral and/or maxillofacial infection will depend on the actions of the dental clinician(s). Prompt corrective action can decrease the morbidity associated with the infections and may also save a life.

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