

# Non-odontogenic infections in dentistry

GUNNAR DAHLÉN

This volume of *Periodontology 2000* is dedicated to non-odontogenic infections that may be present in patients attending dental clinics. Dentists therefore need to have a thorough understanding of infectious diseases in order to diagnose such infections correctly and to decide whether they can provide appropriate treatment or whether referral to dental or medical specialists is necessary. It is of utmost importance for dentists to be able to differentiate between infectious and noninfectious illnesses in the oral cavity and between infectious diseases having an oral or a nonoral origin. An increasing number of patients present with systemic diseases or are undergoing treatment with medications that can increase the risk for infections in the oral cavity and in the surrounding tissues. Treatment of opportunistic oral infections caused by underlying systemic or local factors often requires a close collaboration between dentists and medical specialists. Patients in many countries seek dental care at regular appointments, which provides dentists with the opportunity to diagnose illnesses not only in the oral cavity but also in the surrounding body structures. Lack of insight into infectious diseases may cause a delay in the administration of appropriate therapy. Dentists must also be able to distinguish between different types of infections. Too many viral and fungal infections are treated with common antibiotics indicated only for bacterial infections. Moreover, dentists need to be acquainted with the most common medical infections in order to undertake proper safety precautions aimed at preventing the transmission of infectious agents to the dental office personnel.

## Non-odontogenic infections

This volume of *Periodontology 2000* distinguishes between odontogenic infections, such as periodonti-

tis, dental caries, endodontic infections, pericoronitis and dental abscesses, and non-odontogenic infections where teeth are not involved. Odontogenic infections are characteristically caused by bacteria resident in the dental plaque. These bacteria are not primarily pathogenic, but may initiate and sustain infectious processes if present in high levels or at the wrong location (tissue invasion). Dental caries is caused by acid-producing gram-positive facultative bacteria, and infections of the tooth-supporting tissues (marginal and apical periodontitis) are characterized by gram-negative proteolytic and predominantly anaerobic species. Although a number of bacterial species have been specifically associated with odontogenic infections, the microbial nature of odontogenic infections is polymicrobial and may show relatively little microbial specificity.

In contrast, the non-odontogenic infections of the oral cavity and the neighboring structures and organs show a higher degree of microbiological specificity. Typically, specific microorganisms will appear in some types of oral infections, but seldom in others. Table 1 presents the most common infectious agents in non-odontogenic infections and the most common illnesses caused by these agents. Thus, *Staphylococcus aureus* is a major pathogen in skin infections, abscesses and sometimes in the oral mucosa (angular and lip cheilitis). The organism is seldom recovered from upper and lower respiratory infectious diseases, such as tonsillitis and otitis media. *Streptococcus pyogenes* is a common pathogen of skin infections and a major pathogen in tonsillitis, but is less common in infections of the oral mucosa and the rest of the respiratory system. *Streptococcus pneumoniae* and *Haemophilus influenzae* are pathogens of the respiratory system, including sinusitis and otitis media. However, the organisms are virtually never involved in infections of the oral cavity. *Helicobacter pylori* is the key organism in stomach infections and may be

**Table 1.** Major infectious agents in non-odontogenic infections in dentistry

Infectious agent groups	Individual infectious agents	Disease (reference)
Bacteria	<i>Staphylococcus aureus</i>	Oral mucosal infections (5) Abscesses (2) Skin infections (9)
	<i>Streptococcus pyogenes</i> (beta-hemolytic group A streptococci)	Pharyngotonsillitis (20) Skin infections (9)
	<i>Streptococcus pneumoniae</i> (pneumococci)	Middle ear infections (10) Sinusitis (3)
	<i>Enterococcus faecalis</i> (enterococci)	Oral mucosal infections (5)
	<i>Propionibacterium acnes</i>	Skin infections (9)
	<i>Moraxella catarrhalis</i>	Middle ear infections (10)
	<i>Haemophilus influenzae</i>	Middle ear infections (10) Sinusitis (3)
	<i>Legionella pneumoniae</i>	Respiratory infections (11)
	<i>Helicobacter pylori</i>	Stomach and esophagus infections (14)
	<i>Mycobacterium tuberculosis</i>	Tuberculosis, respiratory infections (11)
	<i>Escherichia coli</i> , <i>Klebsiella pneumoniae</i> , <i>Enterobacter</i> spp., <i>Pseudomonas</i> spp. (aerobic gram-negative bacilli)	Oral mucosal infections (5) Respiratory infections (11)
	Anaerobic species	Abscesses (2) Sinusitis (3)
	Fungi	<i>Candida</i> spp.
<i>Aspergillus</i> spp.		Respiratory infections (11)
<i>Malassezia</i> spp.		Skin infections (9)
<i>Trichophyton</i> spp.		
Viruses	Herpes simplex virus-1, mumps virus, varicella-zoster virus, morbilli virus (measles), influenza virus, Coxsackievirus A and B, respiratory syncytical viruses, human cytomegalovirus, Epstein-Barr virus, human papillomaviruses, human immunodeficiency virus (HIV)	Oral viral infections in children (17) Oral viral infections in adults (19) Respiratory infections (11)
Protozoan parasites	<i>Leishmania</i> spp.	Leishmaniasis (1)

present in the oral cavity, but it is not considered to cause infections in any part of the respiratory system. Enterococci and aerobic gram-negative bacilli, including *Escherichia coli*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*, are potential pathogens in every part of the respiratory system, especially in immunocompromised individuals, but the organisms are seldom seen on the skin. *Legionella pneumoniae* is associated only with pneumonia.

Similarly to bacterial infections, fungal infections show some degree of site-specificity. *Candida* spp. cause clinical infections in the oral cavity and in the

respiratory tract, *Aspergillus* spp. cause clinical infections in the lower respiratory system, and *Malassezia* spp. and *Trichophyton* spp. cause clinical infections exclusively on the skin. Viral infections may manifest and produce symptoms on the skin over most of the body, including the face and the oral mucosa. Examples of such viruses are measles, chickenpox and hand, foot and mouth disease. Some viruses may result in localized oral infections and ulcers, such as the herpes simplex virus-1 (herpes labialis) and the varicella-zoster virus (facial skin, lips, and oral mucosa). Other viruses target the

oropharynx (Epstein–Barr virus-related mononucleosis), the upper respiratory tract (the common cold virus and the influenza virus), or the lower part of the respiratory system [the coronavirus of severe acute respiratory syndrome (SARS)]. Finally, parasitic infections may also occur in the oral environment. Leishmaniasis is a serious disease that can affect the oropharynx and the facial skin.

## Infections of the oral mucosa

Distinction must be made among bacterial, fungal, viral and parasitic infections in the oral cavity in order to provide a precise diagnosis and to give optimal care. The diagnosis, which forms the basis for appropriate therapy, is made by the clinical appearance and symptoms of the infection and by microbiological sampling and analysis of the offending infectious agents. White mucosal lesions are often caused by yeasts, and oral ulcers often have a viral component; however, the clinical picture of a variety of oral infections is far from clear. Microbiological diagnosis of oral lesions is underemphasized in dentistry and most dentists do not use microbiological sampling in their daily practice (4). This is the result of a lack of knowledge of microbiology and because of perceived difficulties in interpreting the microbiological diagnosis and making the relevant treatment decision. Proficient oral microbiology laboratories are also absent in many countries. Even if an oral microbiology service facility actually exists, many dentists are unaware of its existence (15). Many dentists using a medical microbiology laboratory have the experience of getting the answer ‘normal oral flora’, which does not provide much useful information. Moreover, a major reason for rejection of microbiological sampling in endodontics is that dentists do not think that it offers any advantage compared with conventional treatment strategies (12). This argument for not using microbiological diagnostics can probably also be applied to other oral infections. Lack of laboratory request forms and sampling material are also barriers for using a microbiology testing service. Increased and better communication between the dentist and the oral microbiology laboratory is a prerequisite for a more successful use of microbiological diagnostic services in the treatment of oral infections.

Bacterial and fungal infections can easily be disclosed by culture on selective media and, thus, other diagnostic techniques for microbial identification

have only received limited attention. However, the introduction of modern molecular methods for the diagnosis of viral and bacterial infections calls for an increased application of such methods to all types of infections in the oral cavity and the nearby structures.

The most common non-odontogenic infections of the mouth are bacterial mucosal infections (5). Dahlén (5) has discussed whether the presence of microorganisms in an oral mucosal sample is of etiological relevance or if the bacteria only represent a carrier state, colonizing oral surfaces with little or no relation to the etiology of the diseases. Oral mucosal infections often occur during breakdown of the microbial homeostasis (balance), which allows opportunistic microorganisms to overgrow and subsequently cause disease. Common bacterial opportunists in the mouth are *S. aureus*, enterococci, beta-hemolytic streptococci and aerobic gram-negative bacilli (*E. coli*, *Enterobacter* spp., *Klebsiella* spp., *Pseudomonas* spp., and others). These organisms often exhibit a high degree of antibiotic resistance and are prone to therapeutic failures.

Fungal infections in the oral cavity are common in immunocompromised patients. Samaranayake et al. (16) have specifically detailed fungal infections in human immunodeficiency virus (HIV)-positive patients. Although *Candida albicans* is still the most frequent pathogen recovered, later studies have shown that other *Candida* spp., including *C. tropicalis*, *C. krusei* and the recently described *C. dublinensis*, are also present in oral candidiasis. The occurrence of a broad range of *Candida* spp. is partly explained by the increased antibiotic resistance that has followed a too-generous use of systemic antifungal agents, such as ketoconazole and fluconazole.

Viral infections have been largely overlooked in both the dental literature and dental practice, unless, like HIV and hepatitis B and C, they have had implications on the practice of barrier-preventive techniques and risk of disease transfer. During the past decade, the interest for mammalian viruses in oral diseases has increased considerably. This is a result of the finding that viruses may play a significant role in the oral ecosystem and in disease development, such as periodontitis (18). Slots (18) has described how periodontal sites containing Epstein–Barr virus or cytomegalovirus show more extensive tissue breakdown than herpesvirus-negative sites. However, the association between herpesviruses and destructive periodontal disease is probably not exclusively because of the virus infection. Herpesvirus-related periodontitis may result

from an ecological synergy between viruses and bacteria, where an active herpesvirus infection induces a local immunosuppression, which then leads to an overgrowth of periodontopathic bacteria. Another synergistic interaction between viruses and bacteria takes place with herpetic gingivostomatitis, which occurs in children as a primary infection or as a re-activation of herpes simplex virus-1 and a secondary bacterial infection. It is plausible that herpesviruses, including Epstein–Barr virus and cytomegalovirus, play a similar role in the development of acute necrotizing gingivitis and noma. A similar form of acute gingivostomatitis occurs in patients with acquired immunodeficiency syndrome (AIDS), in whom secondary bacterial or fungal infections are clearly the consequence of a virus-induced immunosuppression. Oral ulcers have several etiologies, including treatment with cytotoxic drugs, radiation therapy, intake of etching foods and autoimmune reactions, but viruses, most prominently herpes simplex virus and cytomegalovirus, are probably the most common causes of oral ulcers. Secondary invasion of bacteria in oral ulcers may subsequently worsen the lesions clinically and postpone healing. Also, Epstein–Barr virus, herpesvirus-8 (Kaposi's sarcoma virus) and papillomaviruses are important oncogenic agents in the oral cavity (19). As viral infections manifest quite differently in children and adults, the topic of oral viral infections is discussed in two separate chapters of this issue of *Periodontology 2000* (17, 19).

Although parasite clinical infections are rare in the oral cavity, they can be severe in affected individuals. Bergquist (1) argues that parasites in the oral cavity are more common than previously thought, and that some (for example *Trichomonas tenax*) may play a role in periodontal disease. Various parasitic diseases, and specifically leishmaniasis, are common in the tropical areas of the world. Leishmaniasis may be imported to countries of the temperate zones as a result of increased global travel of humans.

## Medical infections in the oral environment

Dentists are frequently faced with infections in the oral environment and in neighboring structures of the oral cavity. The medical profession primarily considers this type of infection. However, the symptoms may be clinically and subjectively difficult to distinguish for both the medical and the dental professionals. Patients may initially seek advice from

their dentist, which makes it important to increase the knowledge of the dental profession about these conditions, which are rarely reviewed in the dental literature.

A number of infections in the nearby structures of the oral cavity may yield symptoms that need to be distinguished from odontogenic infection in order to avoid misinterpretation. This group of infections includes sinusitis, pharyngotonsillitis and abscesses of the head and neck region. Each of these infections has been described in separate chapters of this volume of *Periodontology 2000*. These infections are important medical infections that are extremely common and are heavily resource-requiring in daily medical practice. Certain microorganisms are major pathogens in specific infections, for example *S. pyogenes* (group A streptococci) in pharyngotonsillitis (20), and *S. pneumoniae* and *H. influenzae* in sinusitis (2, 3), whereas other infections, such as abscesses, are more nonspecific and polymicrobial in nature. Anaerobic bacteria, primarily from the oro-pharyngeal resident flora, predominate in all types (odontogenic as well as non-odontogenic) of deep infections (abscesses) in the head and neck region. Anaerobes are probably underestimated in sinusitis and tonsillitis, especially if the infections are purulent and abscess-forming.

Infections in the lower respiratory tract include bronchitis and pneumonia, and some develop from the oro-pharyngeal and/or the naso-pharyngeal flora (11). An abundance of literature lists numerous infectious agents, including viruses, bacteria, mycoplasma and fungi, as potential and specific causes of pneumonia. Serious new respiratory diseases are constantly being discovered, such as SARS and 'bird flu'. Lung infections are frequently seen in patients who suffer from other systemic diseases and/or are heavily medicated. Lungs have a weak defense because the lower respiratory system has no resident flora and is a dead-end with no natural drainage. The defense is built on the adhesion of airborne infectious agents to the mucosal membranes in the nasal and oral cavity and the upper respiratory tract, preventing pathogens from reaching the lungs. Factors that interfere with this fragile system are of significance for lung infections. Some respiratory tract infections (e.g. legionellosis and tuberculosis) can potentially be transmitted by aerosols produced during high-speed drilling and ultrasonication, and this is of serious concern in dental practice. Pneumonia can develop in anyone, but is a greater risk in hospitalized and systemically diseased or immunocompromised individuals. Patients who are confined to bed and/or

who are mechanically ventilated are at serious risk for pneumonia. Pneumonia is an extremely common cause of sepsis and mortality among the old age people and hospitalized patients.

Less commonly reviewed in dentistry are infections of the esophagus and stomach, despite the fact that they are quite frequently connected with oral disease conditions (14). Bacteria-associated problems in the esophagus and stomach are mostly related to gastroesophageal reflux disease and to *H. pylori*-related gastritis/peptic ulcers. *H. pylori* may be an inhabitant of the oral cavity of some individuals, especially those suffering from gastric ulcers.

Middle ear infections are quite common in young children (10). Like many other upper respiratory tract infections, infection of the middle ear occurs as part of the immune-maturation process of the child and should not necessarily be treated with antibiotics. Otitis media is often caused by viruses in cooperation with bacteria. *S. pneumoniae* (pneumococci) seems to be the most frequent bacterial cause of otitis media, followed by *H. influenzae* and *Moraxella catarrhalis*. Vaccines are now available for *S. pneumoniae* and *H. influenzae*. It is of importance for dentists to diagnose otitis media properly, because the disease in adults may coincide with toothache and/or temporomandibular joint disorders.

Facial skin infections are another group of diseases that are seldom reviewed in dentistry (9). Facial skin infections, such as angular cheilitis, are quite common in the dental patient. The skin, and especially the nostrils, frequently harbor pathogens such as *S. aureus* and function as reservoirs for spreading organisms to the oral cavity and to other sites of the body. The need for good barrier techniques in the dental practice should be emphasized because of the high frequency of 'healthy carriers' of *S. aureus* on the skin and nose among healthcare personnel, including dentists, dental hygienists and nurses, and the potential for spreading the organism to patients. Other microorganisms causing skin infections are the bacteria *S. pyogenes* and *Propionibacterium acnes*, and a number of fungi, including *Candida*, *Malassezia* and *Trichophyton*.

## Antibiotics

Various antibiotics are frequently prescribed for infections in the oral cavity and the oral environment. At a time when medical healthcare systems have great problems with the development and spread of antibiotic resistance, it is of utmost importance that

antibiotics are prescribed restrictively and specifically. The literature contains alarming reports on poor knowledge regarding when and how to use antibiotics (6–8, 13). Many trial-and-error approaches in the treatment of infections are suspected to occur in dental practice. Both medical doctors and dentists are prescribing antibiotics 'just in case' or on patients' demand, rather than as a result of an adequate clinical and/or microbiological diagnosis. It seems important to increase the knowledge about infections and their possible treatments in order to reduce the misuse of antibiotics or, when indicated, how to use them appropriately.

In contrast to the rather poor future for using antibiotics against many multidrug-resistant bacterial pathogens, immune-prophylaxis approaches are more promising. Well-established vaccines are available against many viruses, such as measles, mumps and rubella (MMR), hepatitis B virus, pathogenic papillomaviruses and influenza viruses, and vaccines against other viruses (e.g. herpes simplex virus-1, HIV) are under development. Similarly, vaccines against bacterial pathogens (e.g. *H. influenzae* and *S. pneumoniae*), are available at least in developed countries, and additional vaccines (e.g. to *H. pylori*) will probably soon reach the market. For other specific infections (e.g. caused by *S. aureus* and aerobic gram-negative bacilli), which show an alarming development and spread of antibiotic resistance, there is an urgent need to implement alternative therapeutic strategies, including immune-prophylaxis and antimicrobial peptides.

## Conclusions

The aim of this volume of *Periodontology 2000* was to convey knowledge about non-odontogenic infections. Insights into oral mucosal infections and infections in tissues and structures surrounding the oral cavity will allow a more complete understanding of patients in health and disease and permit better patient care.

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