Chapter 2

Influence of the Oral Microbiome on General Health

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Abstract

The prevalence of edentulism is common worldwide. While improvements in access to healthcare and dental care are reducing the prevalence rate of edentulism, the rapidly growing number of elderly as a percent of the global population will sustain a need for denture therapy for the foreseeable future. While denture use has positive impacts on the quality of life, their use is associated with some problems and risks. Denture stomatitis, a chronic infection-related inflammatory disorder of the oral mucosa, is extremely common and has been reported to occur in up to two-thirds of denture wearers. Importantly, epidemiology studies have shown edentulism and denture wearing, while not proven as causative factors, to be associated with significant increases in risk for serious systemic diseases, such as chronic obstructive pulmonary disease (COPD), cardiovascular diseases, diabetes, and arthritic disorders. A common linkage across these diseases is an association between increased risk for the disease and chronic inflammation. The nature of surface properties and porosity of denture materials contributes to the attachment of microorganisms and the establishment and growth of the adherent biofilm. Hence, proper denture cleansing is critical in maintaining oral hygiene and general health and perhaps to reduce the risk factors for systemic disease.

Keywords: *Candida*, biofilm, stomatitis, chronic obstructive pulmonary disease, edentulism

1. Introduction

Loss of natural dentition and use of removable dental prostheses is extremely common worldwide. While improved global access to oral care is decreasing the incidence of partial and complete edentulism, the prevalence of edentulism remains high and, among the elderly, can

exceed 50% in many countries. Furthermore, over the next few years, the global population of elderly individuals will dramatically increase, and this will require the ongoing management of edentulism, at least for the foreseeable future. Edentulism adversely impacts nutrition and quality of life. For example, edentulism is associated with decreased masticatory performance, and this limits the types of food which individuals can chew and eat; furthermore, edentulous individuals report limiting their social function due to negative perceptions related to self-appearance and/or embarrassment and discomfort when eating in social settings.

Restoring dentition by use of an appropriate prosthesis is the treatment approach to edentulism. Denture prostheses can significantly improve masticatory performance, but their impact on changing and improving dietary habits is much less clear. Similarly, dentures can positively impact quality of life regarding appearance and social function, but limitations related to functional improvement often remain. Finally, denture wearing can uniquely impact oral health. Denture surfaces rapidly develop a complex biofilm of bacteria, yeasts and other microorganisms, which can contribute to oral mucosal pathologies. For example, denture stomatitis, a chronic inflammatory disorder, is one of the most common adverse conditions associated with denture use and is associated with contamination of denture surfaces and the underlying oral mucosa by *Candida albicans*, an opportunistic yeast pathogen. Hence, appropriate denture hygiene is beginning to be recognized as critical for maintenance of oral health and perhaps has a role in reducing risk of systemic disease as well. More recently, the potential that denture contamination may also impact systemic disease has been hypothesized and is an ongoing area of research.

This review provides an update of recent developments related to edentulism and denture use. The summary initially focuses on the demographics of edentulism and denture use and potential relationships between edentulism and increased risk of comorbid disease. Current understanding of the role of the denture biofilm as a contributory factor to disease risk is discussed, as are the relationships between biofilm formation and denture materials. Finally, the critical importance of denture cleansing to control the formation of the denture biofilm is summarized with a focus on approaches which can help maintain oral health and potentially reduce risk for systemic disease.

2. Results and discussion

2.1. Demographics and risk of comorbidities

Edentulism and use of dentures is very common among the elderly. This is of critical importance, as the elderly represent a dramatically increasing segment of the world population. In 2000, only 6% of the global population was estimated to be 65 years of age or older. In contrast, by 2030, the percentage of the world population who are at least 65 years of age is estimated to double to 12%, with the largest increases occurring in North America, Europe, Asia and South America [1]. Similarly, in 1998, the World Health Organization reported 390 million people worldwide to be >65 years of age and estimated that this would double by 2025 [2]. Hence, the rapid growth of the elderly as a percentage of the world population will

outpace changes in oral health management designed to reduce edentulism and will sustain a significant incidence of edentulism, the need for denture prostheses, and the requirement to manage the oral and systemic health of denture wearers.

The global prevalence of edentulism varies widely across countries. Current estimates range from 12 to 15% in Hong Kong, India, and several European countries to >60% reported in a survey of residents from Botucatu, Brazil [3, 4]. In the USA, the prevalence of edentulism is estimated to be 36% based on a national population-based survey (NHANEs III) [5]. This survey also reported that the prevalence of edentulism increased with age. In a separate population-based study, Felton reported that 26% of the US population between the ages of 65 and 74 are completely edentulous [6]. A report summarizing data from a 2003 population-based survey conducted in Canada illustrated the dramatic association between increased denture usage with increasing age among both men and women [7]. Similarly, 32 and 59% of residents of Botucatu, Brazil, aged 60–64 are reported to use complete lower and upper dentures, respectively. This increases to 52 and 82%, among those ≥75 years of age [3]. In general, the prevalence of edentulism is generally shown to be positively associated with having lower income or socio-economic status, lower education, and in some countries living in rural areas [8–14].

There are also well-demonstrated relationships between edentulism, denture wearing, poor oral health and increased risk of systemic disease. While associations between denture use and some oral diseases, such as denture stomatitis, are well known and have been widely reported and reviewed in the literature, associations between edentulism, denture use, and their potential to increase the risk for non-oral systemic diseases are less well understood. In a review, Felton reported increased risk for several systemic diseases, including asthma (odds ratio [OR] was 10.52), coronary arterial plaque (OR was 2.32), rheumatoid arthritis (OR was 2.27), diabetes (OR was 1.82), and various cancers (OR was 1.54–2.85) to be associated with edentulism [6]. A study conducted in Thailand among patients wearing either removable complete or removable partial dentures demonstrated a correlation between the presence of oral mucosal lesions or denture-related lesions with several different systemic conditions. In this study, denture patients were found to have significant comorbidities, including bone and joint disorders (26.5% of complete denture wearers), hypertension (23.2%), diabetes (19.4%), cardiovascular disease (8.4%), as well as other illnesses [15]. The study did not, however, include a reference or control group of dentate individuals. Thus, odds ratios for any increase in risk among denture users cannot be determined. Overall, there appears to be an association for significant increases of risk of comorbid disease among denture wearers; however, whether these relationships are causal or casual remains unknown.

2.2. Structure/function relationships between denture material and microbial adhesion

Two factors associated with denture structure and material, surface roughness and the presence of surface pores within the material matrices appear to be the major material-related factors which are associated with microbial adhesion. Both surface roughness and porosity provide mechanisms for the attachment of various microorganisms, and this can promote their colonization within the denture biofilm, which develops on the denture surface. The biofilm

is a complex matrix of various microorganisms [16]. In addition, some of the biofilm microorganisms can colonize within pores which open on the denture surface and hence penetrate into the material matrix. Colonization of these microscopic pores is of critical importance, as common denture cleaning approaches, such as brushing or the use of various antimicrobial rinse products, may be less able to access these sites and remove or kill these organisms. Hence, the microbes which reside within the pore structures may serve as a reservoir of residual organisms which can lead to rapid regeneration of the biofilm following surface cleaning.

2.3. Early colonizer: *Streptococcus oralis*

Different dental materials, such as acrylic, porcelain, and hydroxyapatite, have differing surface roughness; however, denture acrylic, which is the most commonly used denture material, has the highest level of surface roughness. Even smooth acrylic has a surface roughness approximately fourfold greater than that of smooth porcelain [17]. Charman et al. demonstrated more extensive in vitro colonization by *Streptococcus oralis*, an early colonizer which initiates the formation of denture biofilm, on rough (surface Ra 1.14 μm) versus smooth surface (Ra 0.07 μm) denture acrylic [18]. This supports the concept that an increase in roughness of the acrylic surface or other denture materials would promote more rapid establishment of the biofilm.

2.4. Denture biofilm composition

Denture biofilms are complex matrices containing many microorganisms. Using molecular biology approaches, Sachdeo et al. and Campos et al. characterized the microbiota in the oral cavities of healthy denture wearers as well as in denture stomatitis populations [19, 20]. As reported by Campos et al., a total of 82 bacterial species were identified in both the healthy subjects and the patients with denture stomatitis. Twenty-nine bacterial species were present exclusively in patients with denture stomatitis, and 26 species were detected only in the healthy subjects.

Using scanning electron microscopy, Glass et al. recently published images which exemplify the microbial complexity of these biofilms [21]. These images show a range of different microorganisms inhabiting the biofilm matrix and even penetrating into the pores of the denture acrylic [21]. In what may be the first study of its kind, these authors further characterized the biofilm population, identifying potential pathogens and disease-causing microorganisms. Biofilm samples isolated from the dentures of 51 individuals living in different regions of the USA were obtained. Techniques allowing the differential growth of specific microorganisms identified 916 unique microbial isolates from these dentures, of which 711, 67, 125, and 13 were aerobic bacteria, anaerobic bacteria, yeasts, and amoebae, respectively. Interestingly, no two dentures harbored the same microbiota; in addition, no association between biofilm composition and denture cleanliness could be demonstrated [21]. Hence, the microbiology of denture biofilms is complex. Biofilms occur on both complete dentures and partial dentures. Since the potential involvement of the biofilm in the disease is determined by the composition of the organisms contained within the biofilm, controlling and limiting the growth of this matrix by stringent and appropriate cleaning of dentures are critical.

2.5. Oral microbiome and systemic disease

Oral bacteria have been implicated in bacterial endocarditis, aspiration pneumonia, gastrointestinal infection, and chronic obstructive pulmonary disease. Dentures provide a reservoir for microorganisms associated with these infections, in particular respiratory and systemic opportunistic pathogens. As such, they may present an environment for antibiotic-resistant bacteria [22]. Because dentures on occasion may spend time in non-hygienic environmental conditions, non-resident oral microorganisms including *Streptococcus pneumoniae, Haemophilus influenzae, Klebsiella* spp., *Pseudomonas* spp., and *Staphylococci* including MRSA strains have been isolated [23, 24]. The continuous aspiration of microorganisms from denture plaque exposes patients to the risks of infection and the role of dentures may be significant [25].

It is not our purpose in this chapter to provide an extensive review of our knowledge and understanding of denture stomatitis, which has been broadly and extensively reviewed by others [26–36]. Denture stomatitis is a common disorder, occurring in up to 65% of denture wearers. It is characterized by a chronic inflammation of the oral mucosa, most often on mucosal areas which lie beneath the denture base. While denture stomatitis was originally considered to be, at least in part, a traumatic disorder due to poorly fitting dentures, it is now recognized as an inflammatory disorder. If there is any causative role of traumatic injury from poor-fitting dentures in denture stomatitis, it is minor. Emerging evidence suggests that ill-fitting may be a risk factor for the development of oral cancer [37]. The degree of inflammation varies and for diagnostic purposes is graded by using the well-established three-point Newton score [38]. Importantly, regardless of the severity of the inflammatory score, patients with denture stomatitis may be symptomatic or asymptomatic.

2.6. *Candida albicans* association with denture stomatitis

Denture biofilm has a role in denture stomatitis as there is a clear association between the occurrence of denture stomatitis and the presence of *Candida albicans* colonizing both denture materials and the oral mucosa. Indeed, *C. albicans* has been reported to have a selective affinity for colonizing biofilms formed on denture acrylic, with about fourfold greater biomass within biofilms on this substrate as compared to hydroxyapatite [17]. In the pathogenesis of denture stomatitis, *C. albicans* is considered an opportunistic pathogen. While *C. albicans* manifests a significantly greater presence on denture surfaces of patients with denture stomatitis, a clear causal relationship for *C. albicans* as the primary infectious agent responsible for development of this disorder has not been demonstrated. Hence, our current understanding is that *C. albicans* infection is not the single cause of denture stomatitis but has an association with the disorder and may have a role in increasing the likelihood of, or sustaining the associated, oral mucosal inflammation. Denture-related factors associated with denture stomatitis include poor denture cleanliness and hygiene, age of dentures, and continual denture wearing [28, 34, 39–41]. All of these have been reported to significantly increase the risk of denture stomatitis. All of these factors also promote formation of the adherent biofilm on the denture surfaces and hence provide conditions which increase the likelihood of the presence of *C. albicans*. Typical treatment strategies include efforts to improve denture cleanliness and oral hygiene among patients, which can also include replacing old dentures with new prosthetic

devices as well as treatment with topical or oral antifungal agents. In general, treatments can eradicate fungal infection and reduce inflammation, but stomatitis rapidly recurs once treatment is halted unless there has been a successful concomitant effort to clean and subsequently maintain the cleanliness of patients' dentures.

2.7. The importance of denture cleansing in reducing microbial biofilms and disease risk

The development of denture adherent biofilm provides the opportunity for colonization of a wide range of pathogenic and opportunistic pathogenic microbial organisms. Since the microbiota may contribute to both oral and systemic infectious disease, maximizing their eradication from the denture surfaces during routine denture cleansing could be of critical importance in improving the health of denture wearers. A number of studies evaluating different denture cleanser methods on bacterial survival have been reported [42]. These studies suggest that differences between denture cleaning methods exist and that there are simple approaches which can potentially maximize eradication of contaminating pathogens from denture surfaces.

Brushing dentures with standard toothpastes remains the most common approach to denture cleaning; however, this is inadequate. Combining brushing and use of a soaking cleanser is superior for killing bacteria and removing the adherent biofilm and plaque [30, 31, 33]. Furthermore, toothpastes generally contain abrasive components, and cleaning dentures by brushing with dentifrices has been shown to increase surface roughness [43]. Increased roughness of denture surfaces has been shown to increase adherence of microorganisms and development of the adherent biofilm. In addition, others have reported a positive correlation between denture surface roughness and colonization with *C. albicans* [44, 45]. Hence, the method used to clean dentures may be important in controlling future microbial adherence. Use of denture cleansers which can effectively eradicate or remove microbial contaminants and disrupt the denture biofilm without the use of abrasive cleansers may offer significant benefits for denture wearers.

A study by Li et al. reported differences in eradication of *C. albicans* biofilms when evaluated by different denture cleansing methods [46]. The study compared several popular denture cleansing products used in China including (a) soaking with Kyoshin denture cleanser tablet (Kyoshin Company Ltd., Japan); (b) brushing with Colgate Cavity Protection toothpaste (Colgate, NY, USA); (c) brushing with Bamboo Salt & UDCA toothpaste (LG, Beijing, China); (d) brushing with Yunnan Baiyao toothpaste (Yunnan Baiyao Group Co., Kumming, Yunnan, China); (e) brushing with Zhonghua Aloe toothpaste (Unilever, Heifei, Anhui, China); (f) soaking with Polident denture cleanser (GSK, Brentford, UK); and (g) soaking with sodium bicarbonate (0.5 g, Neptunus, Fuzhou, Fujian, China). Compared to the control (PBS) and all other treatments, only Polident, which combined soaking with a commercial denture cleanser and brushing using the same solution, resulted in almost complete removal, or eradication, of *C. albicans* from the denture acrylic disks. Furthermore, no significant regrowth of *C. albicans* was noted over a subsequent 24-h incubation following treatment with Polident. In comparison, the other procedures resulted in some reduction in *C. albicans*; however, rapid regrowth and reestablishment of *C. albicans* and the denture biofilm were observed within 6–24 h.

Lee et al. evaluated six different cleaning methods for dentures including (a) mechanical—brushing with Colgate Extra Clean toothpaste (Colgate-Palmolive, Guangzhou, China); (b) chemical—soaking with a Polident denture cleanser (GSK, Dublin, Ireland); (c) combined chemical and mechanical; (d) chemical—soaking in a commercial chlorhexidine gluconate mouthwash (Parmason Shining, Taipei, Taiwan); (e) UV irradiation (ADH Health Products, Seoul, Korea); and (f) soaking in water [47]. Compared to the control (water), brushing, soaking with a denture cleanser, and the combination mechanical-chemical method were found to be superior to soaking in a commercial mouthwash or irradiation with UV light [47].

In 2009, the American College of Prosthodontists convened a task force to establish evidence-based guidelines for the care and maintenance of dentures. Based upon a review of several hundred abstracts and articles, the recommendation put forth by the task force for effective denture cleaning was daily soaking and brushing with an effective, non-abrasive denture cleanser [48].

3. Conclusions

The relationships between oral and systemic health are complex. As illustrated in **Figure 1**, various societal factors, such as attitudes, beliefs, education and income, and behavioral factors such as oral hygiene, diet, general health maintenance, and engaging in high-risk activities, contribute to oral health. Specifically, these factors will impact dental caries and the development of periodontal disease. While not addressed specifically in this review, periodontal disease is associated with a chronic inflammatory condition and has been shown to have a relationship for increasing risk and contributing to the development of chronic systemic disorders, including cardiovascular disease, stroke, diabetes, renal disease, and respiratory diseases. This review has focused on the health impacts of edentulism and denture wearing and how we can control and improve adverse risks associated with denture wearing. Eventual tooth loss and the requirement for denture prostheses are generally considered an outcome of dental caries. The use of removable dentures, whether complete or partial dentures, is associated with changes in eating and social habits and alterations in the microbiota (or oral ecology). It is well established that the sustained presence of novel pathogenic and opportunistic pathogens in the denture biofilm, especially *C. albicans*, clearly contributes to an increased risk for denture wearers to develop denture stomatitis. In addition, the range of pathogens which colonizes denture surfaces also appears to contribute to increasing the risk for several systemic diseases. The risk potential appears to be related to the potential for these pathogens to support chronic systemic inflammation.

Hence, there is a critical need for the education of both professionals and denture patients on the importance of maintaining denture hygiene and the most appropriate and effective means for doing so. Recent studies have demonstrated differences between denture cleansing methods on removal of surface-contaminating microorganisms. In general, the use of a commercial denture cleanser appears to provide better removal and eradication of microorganisms from the denture surface and also slows the rate for regrowth of specific organisms on the dentures. The effects of denture cleansers combined with brushing using the cleaning solution appear to exceed that of brushing with an abrasive dentifrice alone.

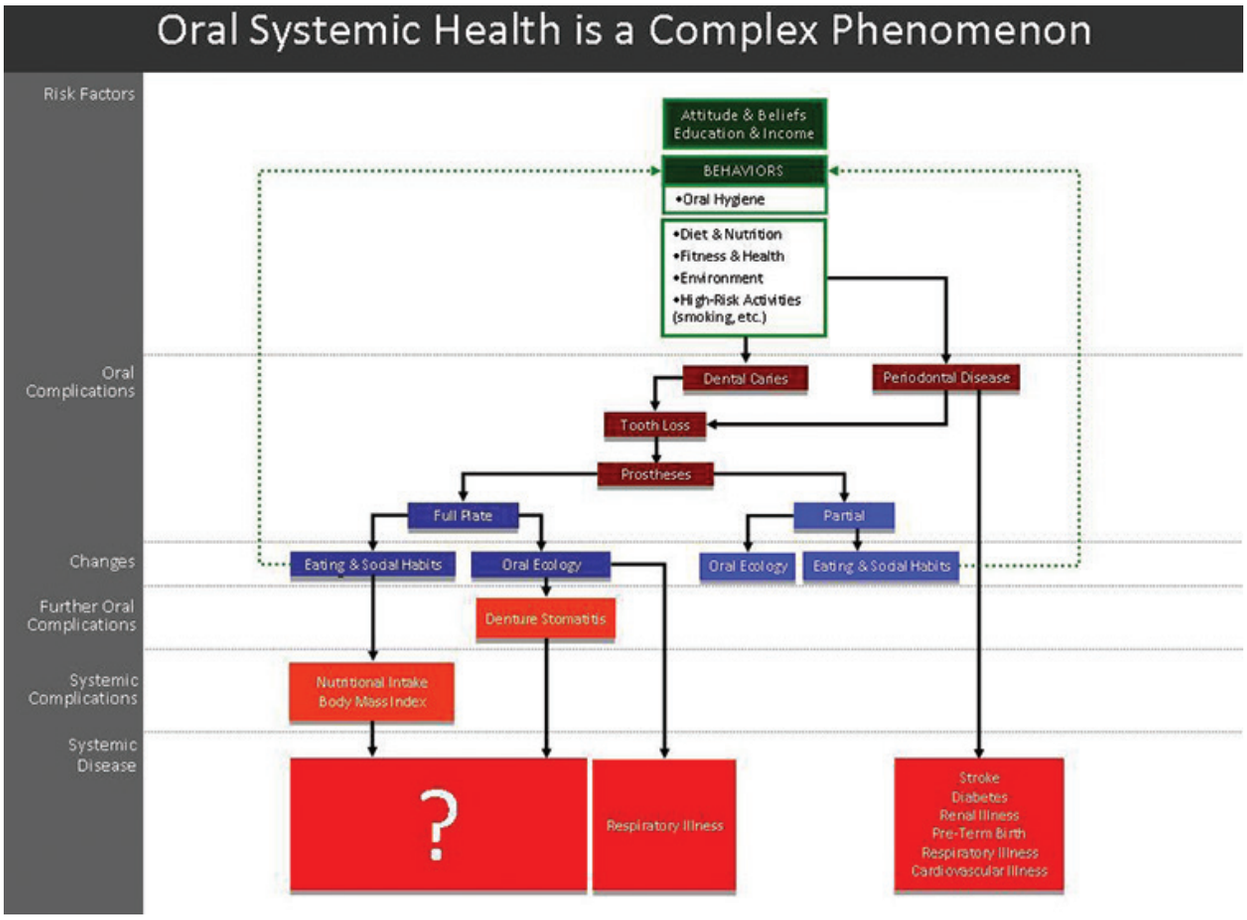

Figure 1. The oral and systemic health linkage has been pioneered by evaluating the relationship between periodontal disease and systemic diseases including diabetes, cardiovascular and stroke as summarized on the right side of this chart. Oral and systemic health as it relates specifically to the denture wearer is summarized on the left side of the chart. Initial systemic targets have included stomatitis and respiratory disease.

In summary, the age distribution of the world population is changing. Over the next 1–2 decades, there will be a significant increase in the number of elderly individuals worldwide. In many countries, this will be associated with a significant increase in the percent of their respective populations who are edentulous and who will rely on denture prostheses. There is an association between denture wearing and adverse impact on systemic health. This may become more profound with the ongoing demographic population shift we are experiencing. Improving hygienic maintenance of dentures, especially among the growing population of elderly, may reduce their risk of developing systemic disease. Furthermore, relatively simple approaches, such as the regular use of denture cleansers to clean dentures, may greatly improve denture hygiene, reduce accumulation of denture biofilm and plaque, and reduce chronic inflammatory conditions which can contribute to oral disorders, such as denture stomatitis and various systemic diseases.

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Conflict of interest

The authors of this manuscript have no conflict of interest with the subject matter of this chapter.

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