

Denture Plaque Management of Denture-Related Stomatitis

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Abstract

The regular use of a removable prosthesis, in particular in fully edentulous aging subjects, constitutes, within the oral cavity, support for Denture Plaque (DP), promoting the growth of a candidosic population that often leads to Denture Stomatitis (DS).

This pathology is an infectious disease of multifactorial etiology. The purpose of this article is to review management approaches for DS at different levels: (1) lifestyle, (2) drug addiction, and (3) several general diseases such as diabetes mellitus, cardiovascular, respiratory and digestive diseases, and immune deficiencies that favor the development of DS.

Moreover, caries, periodontal diseases, a removable prosthesis that is poorly adapted or worn continuously, poor oral hygiene, and reduced salivary flow can promote *Candida's* ability to colonize removable dentures. In the presence of a removable prosthesis, these parameters can influence homeostasis between the host and yeast, promoting the transition of *Candida* spp. from commensal to pathogenic.

The objectives of this review are, therefore, to analyze the influence of these different parameters on the balance of DP in oral ecology, and to explore the mechanisms and means for limiting its drift toward dysbiosis.

Keywords: Bacteria; *Candida albicans*; Dental plaque biofilm; Denture management; Denture hygiene; Denture-related stomatitis; Microbiome; Oral hygiene; Prevention; Systemic disorders

Introduction

A removable denture residing in the oral cavity being bathed in saliva is the ideal platform for dynamic Denture Plaque (DP) development [1-3]. The planktonic microbiota (bacteria, archaea, viruses and eukaryotic organisms) exposed to stress and flow can quickly create favorable conditions for DP growth [4-7] (Figure 1). This biofilm is defined as a community of over 10^{11} microorganisms per gram of dry weight [1,8,9] attached to the extrados and intrados of the denture surface and surrounded by an Extracellular Matrix (ECM) produced by the bacteria and *Candida* themselves [10,11]. This matrix is composed of macromolecules such as exopolysaccharides, proteins, and DNA [12], confers structural integrity to the biofilm, and constitutes a physical barrier that can be impenetrable to drugs [13-16].

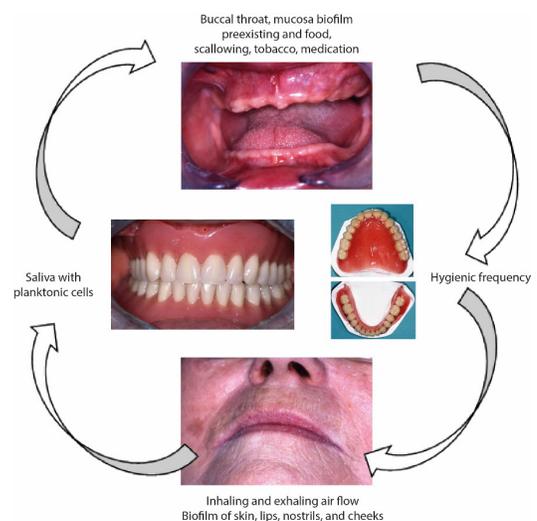


Figure 1: Relationship between dentures and different environments and conditions.

Moreover, under the denture, the contact between soft living tissue and an inert material provides another favorable environment within the oral cavity for microbial colonization [5,17-19]. This reduced space beneath the dentures leads to a decrease in oxygenation, salivary flow, and pH that promotes the activity of Secreted Aspartyl Proteinases (SAP) from the matrix, which play a central role in *Candida* pathogenicity [20]. It seems that *C. albicans* biofilm maturation occurs in the same stages but more slowly (Figure 2) than bacterial biofilm (Figure 3). The presence of hyphae and pseudohyphae is the primary difference between the two biofilms. Recent targeted studies have explained the initial adhesion to the solid surface, secondly the subsequent development of mature biofilms [21], thirdly the formation of the extracellular matrix, and finally the mechanism of dispersion and identified numerous gene products required for each of these steps [9,22-24] (Figure 4).

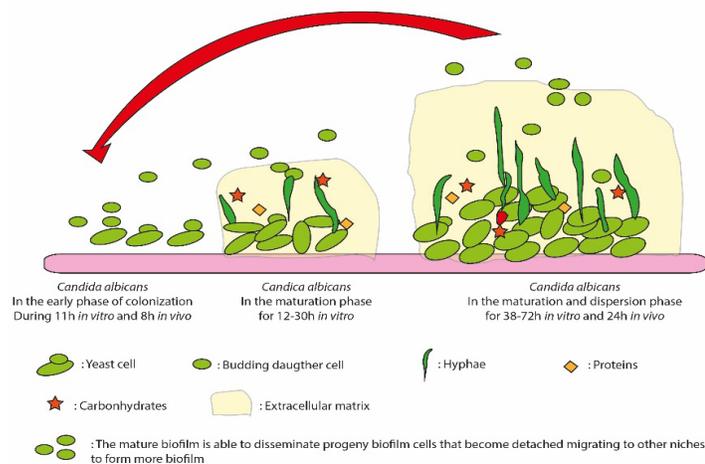


Figure 2: Three chronological stages of biofilm formation by *Candida albicans*, highlighting the ability to exhibit different cell morphologies and the capacity to produce an extracellular matrix (271) [25]. Recent targeted studies have explained the initial adhesion to the solid surface, secondly the subsequent development of mature biofilms, thirdly the formation of the extracellular matrix and finally the mechanism of dispersion and identified numerous gene products required for each of these steps [26-28].

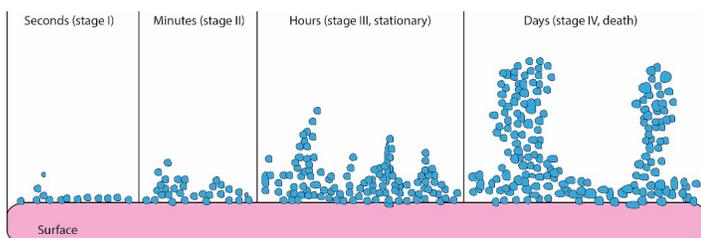


Figure 3: The four chronological stages of the onset of maturation and the decline of the microbial cycle of a biofilm on the abiotic surface of a removable prosthesis: stage I, attachment; stage II, growth; stage III, stationary; stage IV, death.

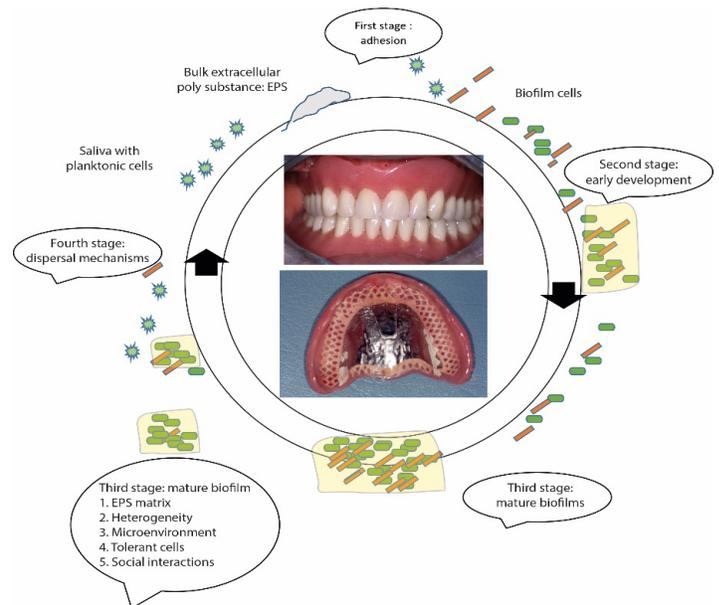


Figure 4: Biofilm envelops the dentures. Biofilm formation proceeds in distinct stages. First stage: adhesion; second stage: early development; third stage: mature biofilm; fourth stage: dispersal mechanisms. In the transition from the planktonic, free-floating state to the sessile state, attached microorganisms begin radically changing their gene and protein expression profiles [29].

The presence of a removable prosthesis in the oral cavity of 15% to 70% of patients is the cause of Denture Stomatitis (DS) [5]. This pathology is characterized by an imbalance of the microbial flora or dysbiosis resulting in, simultaneously:

- 1) The abundance of opportunistic pathogens like *C. albicans* [30,31];
- 2) The differential proliferation of certain bacterial species determined using Next-Generation Sequencing (NGS) [32-41] (Table 1). For example, natural water *Pseudomonas fluorescens* colonize the palatal mucosa of patients with DS with an abundance of 20% compared with only 2.3% in their non-DS counterparts [32];
- 3) A decrease in microbial diversity [33-35].

Autors	Denture wearer with DS or NoDS	NGS : Platform of 16S r RNA gene pyrose-quencing	Hypervariable regions of the 16S rRNA genes	Samples	Diversity and stability of microbiome	Genus level	Specie level
Shi B et al. 2016. [41]	9 DS versus 10 NoDS. All with a complete removable denture and with a minimum of four remaining teeth.(China)	454 FLX titanium platform. detection of <i>Candida</i> via PCR.	V1-V3 26 genus (25 on the denture, and 24 on the teeth) 136 species / phylotypes	2 samples -denture - teeth For the 2 groups with DS and No DS.	Data show, stability and similarity of the microbiome on the denture and on the teeth of the same person. Significantly difference exist between DS and NoDS at the species level.	Genus level the microbiota is similar on the denture and on the teeth with or without DS.	<i>Fusobacterium nucleatum sbsp animalis</i> is always present on the intrados of the denture with DS.
O' Donnell 2015 [33]	123 denture wearers with partial or complete maxillary denture and at least one tooth. (Glasgow) 45 DS et 78 No DS	Illumina Miseq detection of <i>Candida</i> by culture 72% prevalence of <i>Candida</i> species on dentures, At the denture and mucosal microbiome, there was a positive correlation with the class Bacilli and a negative correlation with <i>Fusobacteria</i> at the denture.	V4 OTU, Genus uniquely	Samples , on the mucosa, on the denture and the mucosa supra-gingival.	Patients with teeth shown microbiota diversity > Edentulous patients. No difference between microbiota of the denture and the teeth. Shannon index.	Precece of natural teeth with periodontal diseases can increase DS more than an totally edentulous patients.	Not specified-
Campos et al . 2008 [19]	10 healthy denture wearers/ 10 denture wearers with denture stomatitis (United States of America)	Culture- Cloning and sequencing And detection of <i>Candida</i> by ITS	Genus only	Samples on the denture -	32 phylotypes on the denture	DS with the genera <i>Atopobium</i> (16%) and <i>Prevotella</i> (11%), both of which fall into the classes <i>Actinobacteria</i> and <i>Bacteroidia</i> , respectively -	Not specified

Morse D J. et al. 2019. [32]	8 DS versus 11 NoDS Complete unimaxillary prosthesis (England)	Illumina Miseq + détection of <i>Candida</i> by culture and by PCR.	V1-V3 Genus and species	3 samples by patient (tongue, palate, intrados of the denture)	Decrease of the OTU and the biodiversity of microbiota of the tongue with DS versus the healthy of palate mucosa.	At the level of the genus the microbiota is similiary on the palate mucosa and on the intrados of the denture with and without DS..(Shannon index)	<i>Pseudomonas fluorescens</i> Is present (7%) on the intrados of the denture with DS(<i>Pseudomonas fluorescens</i> is most commonly found in natural water systems).
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Table 1: Analysis of denture-related stomatitis microbiota with Next-Generation Sequencing (NGS); DS: Denture Stomatitis. PCR: Polymerase Chain Reaction. ITS: Internal Transcribed Space. OTU: Operational Taxonomic Unit.

Clinically, there are three main types of DS: (I) pinpoint erythema, (II) diffuse erythema, and (III) granular-type inflammatory papillary hyperplasia of the soft palate in close contact with the denture surface [36]. The severity of DS is linked to the mixed *Candida* species biofilm, which confers an approximate five-fold increased risk of severe disease (Newton’s type III DS) compared with denture wearers colonized solely by *C. albicans* (Newton’s type I DS) [37]. Notably, *C. albicans* is a frequent commensal colonizer of the oral mucosa, susceptible to highly adaptable microbial species and capable of causing infection at various anatomical sites [38]. In this way, mature natural and denture teeth biofilms have similar total numbers of bacteria but different proportions of species, especially *Candida* spp. [34]. Furthermore, the bacterial communities residing on the teeth and dentures of a single person are similar to each other independent of the surface material; therefore, denture health could impact the maintenance of the remaining teeth and vice-versa [6].

The epidemiology of the removable prosthesis wearers, while improving the health and quality of life of edentulous patients, corresponds primarily to elderly people; for example, 70% of UK adults older than 75 years wear dentures [39]. Under healthy conditions, these DPs are tolerated by patients [40]. However, in nearly three-quarters of patients, dentures are associated with stomatitis [31,36,41,42]. DS is considered a polymicrobial biofilm-mediated oral disease that is more common among elderly denture wearers and particularly among women [5,43]. A particularity of denture-induced stomatitis is the constant increase of *C. albicans* with the severity of the disease [44-51]. The etiology of DS is multifactorial, depending on age, lifestyle, and the use of tobacco and alcohol. It is reciprocally influenced by the presence of diabetes and cardiovascular, pulmonary, and digestive diseases. Locally, the lack of good hygiene practices and prosthetic trauma contribute to an environment favorable to the proliferation of *C. albicans* [52-55]. Generally speaking, wearers of prostheses suffering from candidiasis may present various asymptomatic signs such as a sensation perceived as burning, discomfort, difficulty swallowing, and a change in taste. However,

elderly immunocompromised patients present *Candida* species in the oral cavity that can colonize the upper aero-digestive tract, causing sepsis, requiring hospitalization in 40 to 79% of cases [52,56]. Therefore, it is important for dental surgeons to be aware of the additional risk incurred by these patients and to promptly diagnose and treat oral thrush in the elderly with removable dentures. Although DP cannot be eradicated, it can be well-controlled by oral hygiene practices that include a daily regimen of brushing the mucosa and denture, followed by rinsing with an antiseptic mouthwash (MoW) [57-59]. Maintaining a healthy state is preferable for preventing the transition from harmless commensal to pathogenic. An effective oral hygiene regimen can help control DP biofilm formation and is a practical approach to preventing DS; in addition, it accrues benefits in certain systemic diseases [60]. The objective of this review is to understand, in the user of a removable prosthesis, the role that the host factors (general and local) played in maintaining a healthy oral ecology. Then grasp the current mechanisms and means that limit the drift of the oral microbiota toward dysbiosis. To do this, this article first presents the circumstances and mechanisms underlying the oral microbiota’s shift towards dysbiosis, followed by current approaches to limiting this pathological drift.

Material and Methods

A literature search for articles published through August 31, 2020, was performed using the following keywords: “Denture plaque,” “Removable prosthesis,” “Influence factor,” “Removable denture,” “Interactions,” “Denture stomatitis,” “Denture biofilm,” “General pathologies,” “Microbiome,” “Denture management,” “Denture cleaning,” “Hygiene protocols,” “Treatment of denture-related stomatitis,” “Systemic disorders,” “Oral Hygiene,” “Prevention,” and “Microbiota.” Combinations of the keywords were also used. A total of 3700 articles were extracted from PubMed/MEDLINE. Article titles and abstracts were examined to exclude irrelevant and previously identified articles. Then, the abstracts of the selected articles were read to identify studies that met the inclusion criteria. Finally, additional articles were obtained

by reviewing the references of the selected articles. Original articles written in English were included in this review if they met one of the following criteria:

Inclusion criteria

- Articles on the relationship of the denture with different environments and conditions
- Articles on the relationship between a removable denture and some species
- Articles on the relationship between a removable denture and some systemic disorders
- Articles on the biofilms under and above the removable denture
- Articles on the characterization the DP biofilms
- Articles on the denture wearer’s management

Exclusion criteria

- Clinical case reports
- Articles written in languages other than English
- Articles on the study of dentures other than the removable denture

The articles were divided into five thematic categories for this review.

The following themes were analyzed:

- Lifestyle
- General pathologies
- Local pathologies
- Maladaptive removable denture and DS
- Hygienic maintenance procedures
- Improvement of an effective solution against DP

The selection procedure for articles included in the literature review (Figure 5).

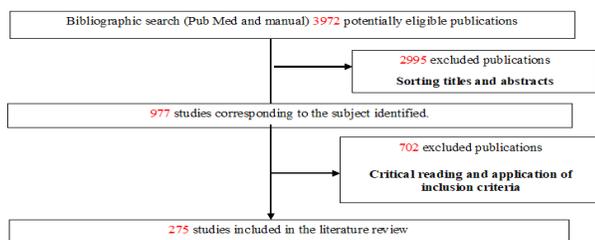


Figure 5: Selection procedure for articles included in the literature review.

Results and Discussion

Denture plaque in oral environments

Remarks

During the use of a removable denture, the DP is subjected to many mechanical and chemical constraints such as variations of the composition and flow of saliva, a variety of food toughness, temperature fluctuations, masticatory forces, and appliance loading [61,62]. Poor oral hygiene is frequently observed in denture wearers, which increases the microbial load of DP [63,34]. In this situation, the presence of the denture establishes an acidic salivary pH [65]; smoking, sugar consumption, commensal oral *Candida*, age of the denture, and choice of cleanliness influence DS [66].

Patients and denture hygiene control may present small variations of several microbial genera, which can initiate dysbiosis. Thus, depending on the site, *Scardovia* and *Lactobacillus* are found in significantly higher abundance on the dental surface, while *Fusobacterium* and *Schwartzia* are found on the surface of dental prostheses [67]. These same authors studied the influence of *Candida* on the biofilm of prostheses, mucous membranes, and teeth. They note that the candidosic load does not influence bacterial diversity, but can, on the contrary, impact their relative abundance. Thus, this incriminates the presence of *Candida* within the biofilm in terms of abundance rather than hygiene. An illustration of this phenomenon is provided by the relationship between the *Lactobacillus* species and the *Candida* load. Depending on the load of *Candida* and the location, there is a shift from antagonism (small load) to synergism (large load) between *Candida* and *Lactobacillus* [68,69]. The design of the biofilm brings together bacterial and fungal species, which illustrates the scaffolding role played by *Candida* [70] (Figure 6). The bacteria using this support for their colonization are more abundant [71] (Figure 7). Therefore, any hygienic strategy must be both antifungal and antibacterial. Clinically, good oral hygiene practices aim to stabilize and maintain a balance over time in the oral microbiome, without seeking to modify it. The development of an individualized strategy concerning biofilm formation based on the interactions between the fungal and bacterial domains must be considered.

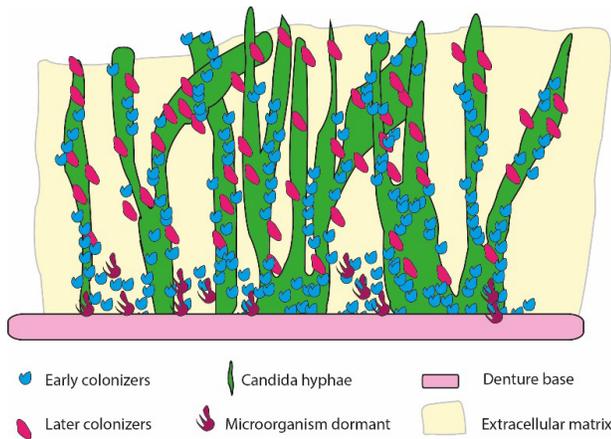


Figure 6: Schematic development of specific multi-species biofilms in DS (extrados). Early colonizers bind to the conditioning film (pellicle), start to grow, divide, and form microcolonies. Then, quickly, the production of EPS (extracellular polysubstance) starts with the co-adhesion of single cells, followed by co-aggregate groups of cells on the denture base. After about eight hours (*in vitro*) of maturation of the DP, *Candida hyphae* growth occurs.

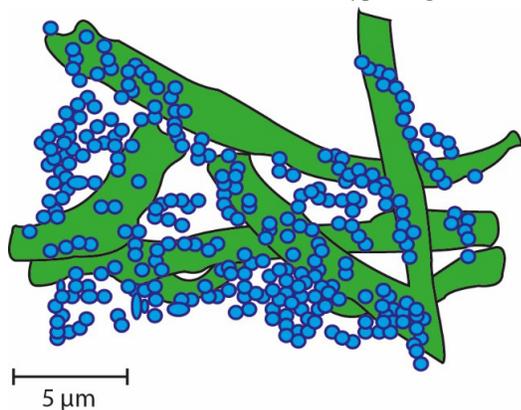


Figure 7: Schematic reproduction of a scanning electron micrograph of mixed *C. albicans* hyphal (green) and *S. aureus* (blue) cells.

Prolonged removable denture wearing day and night, with or without hygiene defects, contributes to DP development [72]. Additionally, at least 40% of elderly denture wearers do not adequately disinfect or remove their dentures at night (68). Under this condition, the risk of pneumonia [73,74] and cardiovascular diseases [75] doubles. Moreover, systemic factors are associated with the appearance of DS including deficient immune response [76], vitamin deficiency [77,78], diabetes [79], and the consumption of immunosuppressors [80], antibiotics [81], or addictive drugs [4,79,80,82-84]. However, locally, other parameters are involved in DP microbial composition, such as tooth extraction, sampling times during the day, oral health status, prosthetic restorations, dental and periodontal diseases, and dental treatment [61,62].

Denture plaque management and treatment

Generalities

The prosthetic base acts as a support for the oral microbiota at the epithelial surface and is externally in contact with the planktonic flora. With time, some organisms can penetrate the resin [7,15,85]. The maxillary and mandibular mucosa, alternatively in contact with the removable prosthesis during the day and then released at night, represents an ecosystem. Under these conditions, the complexity of the denture-associated biofilm increases, with contact between the layer of epithelial cells and the intrados of the denture base (metallic or plastic biomaterials) (Figure 8). These two dynamic biofilms coexist for hours every day and are separated at night, following recommendations regarding the wearing and cleaning of removable prostheses [67,86-91]. The treatment differs between DP maintenance (essentially preventive) and DS treatment, in which an effective curative solution might be applied. The difficulty is relevant to ascertaining the differences between DP formed by commensal microorganisms and DS including pathogens that increase the pathogenesis. Common clinical examination and treatment based exclusively on Newton mucosal classification are inadequate [19]. Maintaining *C. albicans* at a tolerable level in denture wearers involves the interaction with commensal bacterial flora and host components [92]. Today, DS treatment and DP maintenance must be viewed from a holistic, global perspective and consider:

- 1- Lifestyle,
- 2- Tooth loss and general pathologies,
- 3- Local pathologies,
- 4- Removable dentures and DS, rehabilitation, and renewal,
- 5- Hygienic maintenance and medication,
- 6- Effective solutions for DP.

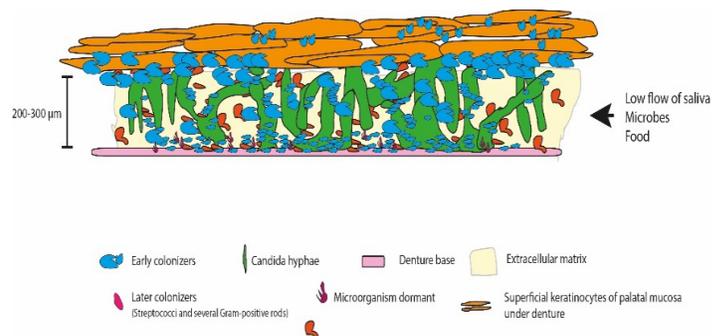


Figure 8: Schematic view of denture-induced stomatitis. Mature salivary conditioning film between biomaterial surfaces (denture base resin) is in contact with the mucosa. Bacterial species most frequently isolated with *Candida albicans* from these specific niches of the oral cavity include Streptococcus spp.: *S. gordonii*, *S. mutans*, and *S. salivaris*. Saliva, moisture, nutrient availability, hyphal *Candida* morphotype, and the presence of commensal bacteria influence the architecture and virulence characteristics of mucosal fungal biofilms.

1. Lifestyle and denture wearers in the world

The Horizon 2050 suggests that there will be two billion elderly people worldwide, which will likely correspond to a significant increase in the number of users of removable prostheses [93,94]. With great geographic diversity, this last segment of the population is often the victim of socio-economic deprivation, explaining the renunciation of an implant solution and the need to use a removable prosthesis [95]. Food habits vary around the world, but the use of removable dentures affects the choice of food and can influence a patient's health [96]. In general, these patients tend to give up hard-to-chew foods such as stringy meats, vegetables, and raw fruits [97]. A high proportion of these people have DS [5,98] due mostly to poor oral and prosthetic hygiene [99]. The patient's lifestyle, such as sleeping with their prostheses at night, impacts the oral microbiome. Patients who keep their removable prosthesis in at night have an abundantly unchanged dental microbiome but at the level of the mucous microbiome, one genus (*Dialaster*) is significantly increased. Moreover, concerning the prosthetic intrados microbiome, several genera (*Leptotrichia*, *Selenomonas*, *Moryella*, and *Prevotella*) are significantly increased [67]. Only *Prevotella* increases in the presence of DS [41,99].

Around the world, the practice of prosthetic hygiene is often empirical. However, the treatment of prosthetic microbial plaque requires a hygienic methodology adapted to the complexity of the relationship between the microbiome and the oral mycobiome [29,41,66,67,100]. Much advice on the presence of prosthetic stomatitis is given to the patient. Smoking cessation in addition to the usual therapeutic measures is recommended [101-103]. Indeed, the adhesion of *Streptococcus mutans* and *Candida albicans* in the form of a biofilm to dental plaque is favored in cigarette smokers [104,105].

Drugs predisposing to oral candidiasis, such as broad-spectrum antibiotics and immunomodulatory and xerogenic drugs, must be identified. The strong interaction between bacteria and commensal yeasts confers resistance to the colonization of pathogenic microorganisms. The prescription of a broad-spectrum antibiotic in the long-term can disturb the relationship between the commensal bacterial and fungal flora [106,107]. The cessation of antibiotics promotes a return to typical levels of bacteria and can resolve candidiasis without further intervention [101,102,108]. Other aspects of a patient's lifestyle and eating habits affect their defenses. For example, in the presence of high cholesterol content [109] or nutritional deficiencies (iron folate, vitamin C, vitamin B12, vitamin A), damage to the integrity of the oral mucosa can promote invasion and proliferation of Candidosic hyphae [8,101,110-114]. Another aspect of malnutrition is the increase in sugar consumption among prosthetic wearers. The consumption of sugar promotes the proliferation of fungi (*Candida*) on acrylic surfaces and the biofilm's resistance to antifungals, thanks to the activity of phospholipase and increased production of the extracellular matrix [103]. Compared with glucose, fructose can inhibit *C. albicans*. Therefore, foods containing fructose can

slow down the progression of candidiasis. The recommendation to consume fructose (xylitol) rather than glucose is particularly interesting for fitted patients with a biofilm containing *Candida* spp. [115].

2. Tooth loss and general pathologies

The quantitative and qualitative balance between microbes within the oral microbiota is fundamental to maintaining oral homeostasis; the presence of teeth influences this balance [116-118]. At the end of life, the oral microbiota of an elderly patient (> 65 y) who is toothless, fitted or not, is frequently associated with several general pathologies, such as ischemic heart disease [119], heart failure [119], stroke [120], peripheral vascular disease [121], and cancer [122,123]. Other characteristics, in the presence of a removable prosthesis, are the loss of teeth and the aging of patients, which accelerate the reduction of the function of Polymorphonuclear (PMN) neutrophils (oral and circulatory PMNs). This has the effect of promoting the appearance and maintenance of DS. Oral PMNs (salivary) are functionally impaired in edentulous participants; only the cPMN (circulatory) numbers were higher in the edentulous participants. This finding shows that this particular change of immunity in the oral cavities of edentulous patients leads to decreased resistance and, consequently, favors dysbiotic conditions like *Candida* infections [124]. Another characteristic site in the mouth is the surface of the mucous membrane of the tongue. It is the most populated microbial reservoir, carried by saliva; these microorganisms are capable of dispersing and colonizing other sites in the oral cavity [3,125].

Periodontal disease can spread microbes from periodontal infection via blood or saliva to target organs. Thus, a microbial relationship exists between several infectious diseases distant from the oral cavity and periodontal diseases, such as rheumatoid arthritis [126-128], cardiovascular disease [129,130], pneumonia, cystic fibrosis [131,132], hepatic or brain abscesses [133], endocarditis [134], and diseases of mental impairment [135]. Among these general diseases, some can interfere with the removable prosthesis if untreated for a long period.

21-General pathologies and DS

1-Systemic immune response on the DS:

Comparison of the profiles of lymphocytes and monocytes in the peripheral blood of two groups of elderly patients, one with DS (n = 20) associated with a fungal infection and the other free of DS (n = 24), does not show any significant difference. Only the number of CD 25+ T lymphocytes is significantly lower in DS patients. The researchers hypothesize that these aging patients with a hearing aid have a reduced potential to eliminate the infection [84]. Moreover, DS is notably more prevalent among HIV-infected female denture wearers compared to seronegative female denture wearers [136,137], and taking medication that can disrupt salivary secretion [138].

Immunosuppressive treatment in patients who have had a kidney transplant and removable dentures seems to increase the risk of *C. albicans* infection and, therefore, also of DS. *C. albicans* positive cultures of the oral mucosa were observed in 73.3% of transplant patients compared to 28% of the control group. Yeast was isolated from the surface of the denture in 83.3% of grafted patients compared to only 38% of the control group [139].

2-Cancer and DS:

A multivariate analysis of 390 sick patients, recruited from a hospice in England, identified the poor performance of the Eastern Cooperative Oncology Group. The presence of dentures, poor oral hygiene, and xerostomia is independently associated with oral thrush in community patients with advanced cancer [140]. Concerning patients with cancer receiving palliative care, the use of a removable denture in this context increases the risk of developing oral candidiasis. [136].

3-Cardiac risks influence endothelial function in older people with DS:

Comparing two groups of patients over the age of 64 years, one with DS and one without DS, revealed that the groups did not differ in ambulatory blood pressure, total cholesterol, and C-reactive protein. However, the dilation induced by blood flow was dramatically lower in patients with DS than in the control patients, whereas nitroglycerin-induced vaso-relaxation and their carotid intima-media thickness were similar. To summarize, DS is associated with endothelial dysfunction in terms of the aging of patients with removable dentures [109]. DS treatment can locally improve endothelial function assessed by flow-mediated vascular dilation [141-144].

4-Pulmonary infection, pneumonia, and dentures:

Lung infections are related to bacteria of oral origin by air [145,146]. Conversely, there are respiratory pathogens capable of colonizing the surface of removable prostheses [147]. Wearing prostheses at night promotes inflammation of the oral mucosa, increases the prosthetic microbial load, and can exacerbate pneumonia [73]. The establishment and maintenance of proper oral care in the elderly have been effective in preventing lung disease. In Japan, for two years, 163 elderly people living in institutions and benefiting from oral hygiene care and prosthetics, experienced a regression of pneumonia and consecutive deaths [148]. However, the assumption of the responsibility for oral care by the nursing staff is likely critical to effectively prevent pulmonary pathologies [149]. The removable prosthesis in the presence of poor oral hygiene can be colonized by microorganisms of periodontal disease and caries as well as those of respiratory origin [147]. Therefore, microbial sanitation of the oral cavity, especially in vulnerable patients, may decrease the risk of developing respiratory diseases [150]. Thus, the establishment of oral hygiene becomes necessary in patients at risk to ward off pulmonary infections [150,151]. Moreover, a study concerning fitted patients with pulmonary diseases with bacteria in

the upper airways found that they had an increased frequency of chronic prosthetic stomatitis compared to healthy subjects [152].

5-The link between gastric *Helicobacter pylori* and denture-related inflammation:

Inflammation of the oral cavity caused by bacteria or fungi can be accompanied by gastric inflammation, particularly in the presence of DS [153,154]. *H. pylori* eradication from the oral cavity is more difficult than from the stomach. If the bacterium survives the antibacterial therapy in the oral cavity, it can re-infect the stomach in a few weeks. Oral health and hygiene practices seem unlikely to increase the efficacy of *H. pylori* eradication from the stomach. In contrast, long-term professional dental plaque control is associated with less gastric re-infection by *H. pylori*, suggesting that DP control may help to prevent *H. pylori*-induced gastric disease or re-infection. However, after antibiotic therapy, *H. pylori* in dental plaque may represent a risk factor for gastrointestinal re-infection and ulcer relapse [155-157].

6-The influence of glucosidic metabolic endocrine disorders (diabetes) on DS:

DS associated with *C. albicans* is notably more frequent and severe in denture wearers with insulin-dependent diabetes mellitus compared to denture wearers with balanced glucose metabolisms [158,159]. A large epidemiological study on oral health confirms that subjects with insulin-dependent diabetes mellitus and removable denture wearers are more likely to have clinical signs of DS than non-diabetic control subjects with removable dentures [160,161]. Diabetes mellitus is a major risk factor for DS [162-164]. In an elderly and diabetic patient, the presence of a removable denture in the oral cavity contributes to a favorable environment for candidiasis development [78].

7- Influence of drugs and medicines on DS:

The use of drugs with the presence of dentures greatly increases the likelihood that a person over 60 will have oral mucosal lesions [165]. Treatment with parenteral antibiotics has emerged as the overriding risk factor for oral candidiasis in the presence of a removable denture [81]. The use of oral antibiotics may be involved in the onset of DS [166]. When incorporated in a biofilm, *C. albicans* is more resistant to the antifungals used to treat DS (e.g., amphotericin B, nystatin, chlorhexidine, and fluconazole) [167] than when in its planktonic form.

8- Nutritional deficiency and prosthetic stomatitis:

Vitamins C, B12, and A deficiencies appear to reduce mucosal resistance to infection: Vitamin C deficiency in patients aged 82 years on average with removable denture increases their susceptibility to candidiasis [816]. The correlation between vitamin B12 deficiency and DS in the presence of strong *Candida* colonization is also established [77]. This vitamin B12 deficiency weakens the mucous membrane and promotes inflammation. A relationship has also been found between vitamin A deficiency and

the prevalence of DS [83]. In addition, this vitamin A deficiency is associated with a five-fold increased risk of having DS [168]. The restoration of these deficiencies is an integral part of the management of prosthetic stomatitis.

3. Local pathologies (caries, periodontal diseases) and DS

The level of *Candida* appears to be a reliable indicator of microbial risk factors in caries [169,170]. This is the case for patients wearing overdentures or partial dentures, which increase the risk of caries [171]. Indeed, *Candida albicans* is highly acidogenic *in vitro*. Under this condition, DP-DS can cause the demineralization of the root or tooth. A more recent study compares the microbiota of the fitting surface of dentures in edentulous subjects with healthy palates (n = 20) and the DP in patients with DS (n = 20). The proportions of *S. mutans*, *Lactobacilli*, *Bifidobacteria*, and yeast in the DP biofilm of subjects with DS were greater (p < 0.05) and similar to those found in carious lesions, indicating that this is a low-pH environment. The interdependence between prosthetic, dental and gingival biofilms via saliva implies overall oral hygiene. Controlling all of these biofilms can have beneficial consequences for both DS, caries and periodontal disease [41,172].

Periodontal diseases and denture wearers

Wearing overdentures, partial and complete dentures, is often associated with periodontal disease adjacent to the abutment teeth [173-175]. Naturally, *C. albicans* is an aerobic fungus that has been isolated in periodontal pockets in 15% to 17% of patients [176]. Moreover, anaerobic conditions within the periodontal pockets of patients with diabetes favor the phospholipase activity of *C. albicans* [177]. Furthermore, the amount of *C. albicans* is twenty-fold higher on the denture surfaces in DS versus non-DS (45). Under the denture, the decrease in pH caused by *C. albicans* relies on the production cytotoxic acetate, pyruvate, and propionate, which promote tissue damage [178,179]. Under these conditions, it is possible considering removable denture like a reservoir of micro-organisms capable with fluids (planktonic form) of diffusion in the oral cavity. The microbial communities residing on the denture and periodontal tissues of the same person are like each other, so denture health and periodontal diseases are subordinate [41].

4. Maladaptive removable denture and DS

Risk factors underlying DS must be identified and treated; accordingly, some prostheses need to be redone [180]. Clinical examination may reveal a defective removable prosthesis, which requires verifications of the vertical occlusion dimension [181], the level of the occlusal plane, and the position of the mandible relative to the base of the skull. All of these defects can cause prosthetic instability and worsen DS; in which case, prosthesis renewal is often necessary [182]. Another important factor is the age of the prosthesis. The accumulation of plaque increases with poor hygiene aggravated by the roughness of the surface of the prosthesis [110,114,183] moreover, this accumulation increases

proportionally with the age of the prosthesis; beyond five years, 84% of patients have DS [184]. This justifies the need to regularly renew the removable prosthesis.

5. Procedure of maintenance for preventive strategies

First, inhibiting microbial adhesion, based on the fact that without initial adhesion we limit or slow down the development of DP. Three levels can be envisaged: 5.1-material optimization, 5.2-surface modifications, and 5.3-sequences for the maintenance of the denture.

5.1-Material optimization

Biofilm development on an acrylic denture increases the risk of DS five-fold compared with a metallic denture [185]. To prevent *Candida* infection in oral mucosa, some researchers have proposed using microbial molecules in the composition of denture materials [186-190]. Another domain of research involves nanoparticles. The effect of adding zirconia nanoparticles to cold-cured acrylic resin on *C. albicans* adhesion has been evaluated. Zirconium oxide nanoparticles possess antifungal properties against *C. albicans* and *Aspergillus niger* and could be used to prevent DS [191,192]. Among products of plant origin, incorporating neem powder (*Azadirachta indica*), which fights bacteria and fungi, into the acrylic base of the prostheses reduces the adhesion of *C. albicans*. So, this powder could be an effective means of preventing DS. While an *in vitro* assessment of the antifungal effects of neem powder added to polymethyl methacrylate denture base material has been published [193]. these antimicrobial macromolecules require further *in vivo* testing before the products are brought to the market.

5.2-Surface modifications

Initially, to thwart the adherence of *C. albicans*, the dentures are polished and coated with hydrophilic materials to decrease the adhesion of *C. albicans* [5,194]. *Candida* and bacterial plaque adhesion to denture materials depend on both the surface roughness and contact angle. For the former, after polishing, the resin must be below 0.09 μm (clearly under the threshold of 0.2- μm surface roughness needed for plaque accumulation) [195,196]. The contact angle of a sample not coated in saliva is around 90°, while one with a salivary coating is reduced to 35° [197]. These two parameters indicate that a denture resin coated in saliva displays almost hydrophilic properties [198]. Recent research efforts consider these factors. For example, mannan, a hydrophilic polysaccharide coating on the acrylic surfaces of the denture base, inhibits the adhesion of *C. albicans* [199]. Specifically, overnight treatment with mannan (0.1 mg/mL) inhibits the adhesion of the hyphal form of *C. albicans*. Another polysaccharide chitosan with a similar process using, inhibit *C. albicans* adhesion, but also to slow down the formation and co-aggregation biofilm [199]. Otherwise, the salivary protein components in contact with the surface of different materials are directly transformed by adsorption, as seen in the pellicle. Therefore, it seems warranted to analyze the composition

of the amount of salivary protein attached to each denture.

5.3-Sequences for the hygienic maintenance of the denture and the oral mucosa

The placement of the biofilm obeys different sequences that can affect the maintenance of the prosthesis. Effectively maintaining the oral health and hygiene of denture wearers requires a combination of mechanical and chemical measures [200,201].

Concerning the denture, the pathogen management process consists of meticulously brushing the prosthesis every day to reduce the pathogenic burden [202]. In concrete hygienic terms, the abiotic acrylic material acts as a reservoir for the *Candida* population near to the palatal tissue, with the consequence of inducing a local inflammatory response detectable clinically as erythema, edema, and hyperplasia [203,204]. The denture surface is colonized more by *C. albicans* than by the associated palatal mucosa; consequently, clinical treatment is essentially turned toward eliminating the biofilm on the denture. The goal is to avoid new colonization with relapse [91,205].

Hygienic oral preventive strategies are based on fundamental knowledge of the mechanisms involved in dental plaque formation concerning bacterial and fungal adherence. All denture wearers receive verbal and written instructions for effective hygiene protocols.

- First, the recommendation is to brush the palate region, dorsal tongue, and mucosa under the denture with a soft toothbrush and water for 2 min once per day.
- Second, the recommendation is to immerse the denture in a specific product once per day during the time proposed by the manufacturer and then brush for 2 min with a neutral soap three times per day. The use of antiseptics to inhibit or eliminate microorganisms and immersion in a chemical solution are recommended for 8 hours. Sodium hypochlorite, chlorhexidine digluconate, and alcohol disinfect or reduce the DP on prostheses [206, 207] without being cytotoxic [208].
- Third, the recommendation is to remove the denture at night and put it in a box.
- Fourth, the recommendation is to rinse the denture and put it back in the mouth every morning [86,87,143,209, 210].

Curative strategy

In the presence of chronic prosthetic stomatitis, the practitioner may suspect a particular form of *Candida*, which is often confirmed by laboratory tests [102,211]. Several methods are used to confirm the presence of *Candida* spp., such as a swab, imprint culture, whole saliva, and oral rinse [212]. The clinical diagnosis of chronic stomatitis supplemented by a culture swab (incubated for 48 hours with Sabouraud's agar) was combined with a direct examination under the microscope [103]. Targeting the candidotic species is essential for rapid treatment [213].

The choice of antifungal drug depends on the patient's general pathologies, the state of the oral cavity, and possible complications [102].

The three main classes of antifungals include polyenes (amphotericin B), azoles (fluconazole), and echinocandins (caspofungin) [214]. Amphotericin B is considered the "gold standard" of antifungal therapy but is toxic because there is no selectivity between fungal and mammalian cells [215]. However, fungal biofilms that mature on denture material become resistant to antifungals [216].

Treatment follows the chronology of *Candida* colonization

From the early stage of *C. albicans* biofilm formation, Chandra et al. showed *in vitro* that the minimum inhibitory concentrations (MICs) effectiveness of amphotericin B, fluconazole, nystatin, and chlorhexidine are 0.5, 1, 8, and 16 µg/mL, respectively, on polymethylmethacrylate strips [217]. These results suggest using these antifungal drugs during the early phase of biofilm formation related to adherence, instead of later [218].

Concerning the next stage, according to the co-aggregation of microorganisms, another mechanism is the involvement of antifungal drug resistance, linked to ECM surrounding the microorganisms in DS. In agreement, the extracellular β -1,3-glucan matrix attaches to amphotericin B, while its absence from ECM increases *C. albicans*' vulnerability to amphotericin B4, 15. Furthermore, chlorhexidine reduces the adhesion capacity of the *Candida* spp. on the denture surface [219].

Another strategy geared against the opportunistic *C. albicans* targets the two properties (filamentation and biofilm formation) of this pathogen [220]. Some small molecules (20,000 compounds from the NOVA Core library-quorum-sensing molecules) can modulate the switch from yeast to hypha form and biofilm formation of *C. albicans* [221]. Using a murine model *in vivo*, some of these compounds (SAP5, ECE1 [candidalysin], ALS3) have shown potential for efficacy with inhibitory activity against *C. albicans* biofilm formation, with no effect on overall growth [222,223]. However, *in vivo*, the prosthetic biofilm exists only in a mixed "Bacteria-*Candida*" or mycofilm concept [70].

Treatment of mixed biofilms in DS

Other treatments of DS concern the mixed biofilms composed of multiple species, with different combinations of *Candida* and/or with *Candida* and bacteria, which interact as a community in synergistic and antagonistic relationships [224] (Tables 2 and 3). The pathogenicity of *C. albicans* increases in the presence of *S. mutans*, *S. sanguinis*, and *Actinomyces viscosus* [225], which justifies the use of antibacterial agents that could also serve to decrease fungal proliferation [189]. Thus, there is widespread use of recently developed therapies (probiotics) to prevent, disrupt, and otherwise render harmless the peculiar ability of *C. albicans* to form biofilms on almost any surface in the mouth.

Interactions between... 	<i>Streptococcus mutans</i> (favored)	<i>Streptococcus Gordonii</i> (favored)	<i>Streptococcus Oralis</i> (favored)	<i>Streptococcus Sanguinis</i> , <i>S. parasanguinis</i> , <i>S. mitis</i> (favored)	<i>Streptococcus Salivarius</i> (inhibe)	<i>Staphylococcus Aureus</i> (favored)
<i>C. albicans</i>	Biofilm adhesion on acrylic surface [226-228]	Biofilm on titanium surface [229] and on mucosal tissue analog –[230]	Stronger biofilm in a mucosal tissue analog [231] and <i>in vivo</i> [191,192]	Promote biofilm of <i>C. albicans</i> on acrylic surfaces [192]and titanium [232]	Inhibits adherence and filamentation of <i>C. albicans</i> [233]	Biofilms of denture stomatitis associated <i>C. albicans</i> and <i>S. aureus</i> [202,234, 235,70]
Factors: -temperature -diet -smoking -pH-carries-periodontal diseases Resin: surface free energy, hydrophobicity, and surface-coating	Favored by high level of sucrose and lowering pH [236]	<i>C. albicans</i> utilizes amino acids to promote neutralization of the phagosomal pH, hyphal morphogenesis, and escape from macrophages. [237]	Immunocompromised patient Moist environment, <i>C. albicans</i> with hyphae increase interaction with <i>S.oralis</i> [238]	<i>Streptococcus sanguis</i> was unaffected by sucrose-rich diet [236]	Protected mice from severe candidiasis [233]	Removable denture increased pathogenicity potential of the <i>S. aureus</i> biofilm .[239] Hyphal adhesin Als3p mediate adherence between <i>S aureus</i> adhere and <i>C albicans</i> hyphae [202]
In multispecies biofilms: newly form or mature biofilm	Addition of <i>Lactobacillus salivarius</i> inhibits <i>in vitro</i> formation of biofilm of both (<i>C.albicans</i> and <i>S.mutans</i>) [240]	Mature natural and denture teeth biofilms have similar total numbers of bacteria but different species proportions. [34]	Synergistic interaction between <i>C albicans</i> and commensal oral <i>Streptococci oralis</i> [231]	Interaction between <i>C. albicans</i> and <i>S.mitis</i> , <i>S. sanguinis</i> . <i>S. parasanguinis</i> . [192,241,242]	Antagonist effect of <i>S Salivarius</i> in <i>vitro</i> growth of <i>C albicans</i> [233]	<i>C. albicans</i> support commensal protection of <i>Staphylococcus aureus</i> and both enhanced Miconazole resistance in dual-species. [235,70]

Table 2: *C. albicans* interactions with oral *Streptococci mutans* Group, mitis Group (13 species), *Salivarius* Group, and *Staphylococcus aureus* in biofilm matrices *in vitro* and *in vivo*.

Interactions between...	<i>Porphyromonas gingivalis</i> (inhibe)	<i>Actinomyces</i> spp (favored)	<i>Fusobacterium</i> spp (commensalism)	<i>Rothia dentocariosa</i> (favored)	<i>Aggregatibacter actinomycetemcomitans</i> (inhibe)	<i>Enterococcus faecalis</i> (inhibe)
 <i>Candida</i> spp: <i>albicans</i> , <i>Keftyr</i> , <i>glabrata</i> , <i>dubliniensis</i> , <i>Tropicalis</i> [238]	Detection of this periodontal pathogen in the edentulous subjects [3]	Biofilm growth on acrylic resin [243]	Co-aggregation between <i>C. albicans</i> and <i>F. nucleatum</i> [244] and with <i>C. dubliniensis</i> [245]	Biofilm formation on silicone rubber voice prostheses [246,247]	Detection of this periodontal pathogen, in the edentulous subjects [3] <i>Aggregatibacter actinomycetemcomitans</i> interacts with <i>C. albicans</i> [248]	<i>E. faecalis</i> and <i>C. albicans</i> , were isolated in approximately 40 % of oral mucosal lesions [249]
Influenced by...	Hyphal-specific adhesion Als3 on the fungal surface [250]	Co-aggregation between <i>C. albicans</i> , <i>A. viscosus</i> , [241,192] <i>A. (naeshlundii)</i> [225] <i>A. odontolyticus</i> , [251] (<i>A. oris</i>) [252,225].	Favored by arginine or mannose. [244]	Hyphal-specific adhesion Als3 play important role for the adhesion with <i>Rothia dentocariosa</i> [253]	<i>A. actinomycetemcomitans</i> produces a quorum-sensing molecule called autoinducer-2 (AI-2) significantly inhibited hypha formation of <i>C. albicans</i> [248]	<i>E. faecalis</i> can inhibit <i>C. albicans</i> filamentation, biofilm formation [254,255]
In multispecies	<i>P. gingivalis</i> can delay oral epithelium cell migration when interacting with <i>C. keftyr</i> and <i>C. glabrata</i> . [256] <i>P. gingivalis</i> in biofilm inhibe production <i>C. albicans</i> hyphae [251]	Synergism in the triad mixed biofilms on denture materials (<i>A. oris</i> , <i>S. oralis</i> , <i>C. albicans</i>) [252] Increased <i>C. albicans</i> hyphal production with <i>Streptococcus sanguinis</i> <i>S. gordonii</i> <i>Actinomyces</i> , <i>A viscosus</i> biofilm [251]	Virulence of one-another (<i>C. albicans</i> and <i>F. nucleatum</i>) mutually may benefit from promoting long-term commensalism. [257]	<i>R. dentocariosa</i> , <i>S. aureus</i> , <i>S. mitis</i> , aided colonization of <i>C. albicans</i> and <i>C. tropicalis</i> on silicone rubber surface [247]	<i>A. actinomycetemcomitans</i> is able to inhibit biofilm formation by <i>C. albicans</i> in co-cultures; this effect is rescued using a <i>luS</i> mutant strain that cannot produce AI-2 [248]	Biofilms of <i>C. albicans sap9Δ</i> with <i>S. oralis</i> , <i>S. sanguinis</i> , <i>S. parasanguinis</i> , <i>S. mutans</i> and <i>Enterococcus faecalis</i> contained more matted hyphae and more bacteria bound to substratum compared to <i>C. albicans</i> wild type [258]

Table 3: Interactions between *Candida* spp. and *Porphyromonas gingivalis*, *Actinomyces* spp., *Fusobacterium* spp., *Rothia dentocariosa*, *Aggregatibacter actinomycetemcomitans*, and *Enterococcus*.

Probiotics

Commercially available probiotics (Accuflo[®] and Culturelle[®]) that contain *Lactobacillus* species associated with mechanistic cleaning interfere with the *in vitro* ability of *C. albicans* to form biofilms on dentures [229,230]. Through the phenomenon of co-aggregation, the *lactobacilli* may secrete an adequate mass to be able to maintain a hostile micro-environment around *Candida* species through high concentrations of acids, H₂O₂, and bacteriocins, thereby possibly inhibiting the pathogen's growth. Daily use of probiotic lozenges may reduce the prevalence of high oral *Candida* counts in elderly nursing home residents [231,259]. Recently, a probiotic, the bacterium *Lactobacillus reuteri* (DSM 17938 and ATCC PTA 5289) was tested against six oral *Candida* species (*C. albicans*, *C. glabrata*, *C. krusei*, *C. tropicalis*, *C. dubliniensis*, and *C. parapsilosis*) for the ability to co-aggregate and inhibit the growth of the yeasts. The *Lactobacilli* almost completely inhibited the growth of *C. albicans* and *C. parapsilosis* but did not affect *C. krusei*, which is known

to resist the acids produced by the *Lactobacilli* [63,260]. The effectiveness of another probiotic *Lactobacillus rhamnosus* SP1 requires careful oral hygiene. This remains essential to reduce the severity of DS among the elderly population [261].

Another interesting *in vivo* finding is the efficacy of methylene blue-mediated photodynamic inactivation of *C. albicans* on the oral mucosa and prostheses of patients with DS [232,262]. An *in vitro* experiment found that irradiation with 405-nm blue LED light causes the degradation of *C. albicans* and *C. glabrata* biofilms on the surface of polymethyl methacrylate resins. The effectiveness of 405-nm blue LED light on the degradation of *Candida* biofilms formed on PMMA denture base resin has recently been confirmed without resin degradation [263].

Mouthwashes

The second stage of antimicrobial therapy, including the use of MoWs, is intended to impede the transition of stage I biofilms (adhesion) to stage II by combatting the attachment and maturation of the biofilm [264]. Many recommended chemotherapeutic products and interventions are effective against planktonic oral bacteria; however, unfortunately, live intact biofilms can persist even after treatment with many products (e.g., sodium hypochlorite) [86]. Because of the complexity of the denture environment, an appropriate MoW can avoid or at least ameliorate oral infections, such as dental caries, gingivitis, periodontitis, and DS. Both prevention and/or treatment of bacteria (oral *Streptococci*) and fungi (*C. albicans*) may play a relevant role in the onset of these oral pathologies [59,192]. In *in vitro* studies, CHX MoWs free of alcohol (e.g., Curasept, Meridol, Dentosan, Parodontax) exhibit the strongest effects against *Candida* biofilm formation at different levels (adhesion, elicitation of pro-inflammatory responses, and avoiding phagocytosis), but *viridans Streptococci* can also form biofilms. Given the side effects of CHX (e.g., staining, altered taste and feeling) MoWs with Cetylperpyridinium Chloride (CPC) does not present these same drawbacks, are an attractive alternative, all the more for impairing early biofilm formation by *S. salivarius* more effectively than of CHX. Other, MoWs, (Listerine) including essential oils after treated *S. salivarius* to be revealed susceptible to delays *Candida* biofilm formation. Moreover, MoWs such as Elmex that include fluorine molecules contribute to caries prevention [59] (Table 4). Finally, these *in vitro* studies show that MoWs containing CHX or CPC may be favorable for oral health in terms of microbial balance. However, these data must be confirmed by comparative in-depth *in vivo* studies.

Effects of MoWs	Impair <i>C.albicans</i> adhesion/ resine (5mn)	Impair <i>C.albicans</i> adhesion/ Epithel (5mn)	Elicit Cytokines Secret by epithel	Capacity to develop <i>C.albicans</i> hyphal form	Capacity of 5 oral streptococci to produce biofilm	Mixed biofilm <i>S. salivarius</i> and <i>C. albicans</i> (pretreat with MoWs).
1-Curasept 0,20% CHX	+	+	+	+(Could develop hyphal form)	Reduce biofilm production/ control (<i>inhibeS sanguinis</i>)	Impair <i>C albicans</i> biofilm formation at early stage (24 hours)
2-Dentosan Collutorio CHX	+	+	+	_ (no hyphal-form)	Reduce (inhibe <i>S. mitis/ oralis</i>) (<i>inhibeS sanguinis</i>)	No effect
3-Meridol col-lutorio 0,20 % CHX	+	+	+	_	Reduce (inhibe <i>S. mitis/ oralis</i>) (<i>inhibe S sanguinis</i>)	No effect
4-Parodontax 0,06 % CHX	+	+	+	_	Reduce (inhibe <i>S. mitis/ oralis</i>)	No effect
5-Elmex sensitive professional Fluorine molecules	+/- (without blocking completely)	+/- (leaving fungus the ability to adhere to oral epithelial cells)	-/+ fast	+	No reduction of biofilm production/ control	Noeffect
6-Listerine total care zero Essential oils	+	+	+	_	Reduce (lower effect) [265-267] (<i>inhibeS sanguinis</i>)	Impair <i>C albicans</i> biofilm formation at early stage (24 hours, but not after 48h)

7-Oral B 0,05% CPC	+impair adhesion. (more effective on planktonic rather than the sessile form of <i>C. albicans</i>) [59]	+(impair adhesion)	+	no information	Reduce (inhibe bio-film formation with <i>S. salivarius</i>) <i>Anti plaque and gingivitis</i> [268,269]	Impair biofilm formation by <i>S. salivarius</i> more effectively of CHX.
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Table 4: *In vitro* analysis of the effects of mouthwashes on the early binding of *C. albicans* and *Streptococci* colonizing dentures and epithelial cells [59]. MoWs: mouthwashes; CHX: chlorhexidine digluconate; CPC: cetylpyridinium chloride. Cytokines/chemokines: Interleukin 1-alpha and -beta (IL-1 α , IL-1 β), Interleukin-4 (IL-4); Interleukin-6 (IL-6), Interleukin-8 (IL-8), Interleukin-10 (IL-10); Interleukin-13 (IL-13); Monocyte chemoattractant protein-1 (MCP-1), Interferon-gamma (IFN- γ); Tumor necrosis factor-alpha (TNF- α)
+ : positive effect. - : negative effect. +/- : incomplete blocking effect.

In vitro, MoWs do not alter the way phagocytes perceive fungus in their surrounding environment, since their phagocytic activity remains almost unaffected.

- In MoWs Elmex and Curasept-pretreated *C. albicans*, the acidic phagolysosomes % remain unchanged relative to a PBS control. This phenomenon can be ascribed to the inhibition of a fungal dimorphic transition. Fungi treated with MoWs including Dentosan, Meridol, Listerine, and Parodontax remain in yeast form.
- MoWs capable of impairing dimorphic transitions and in turn intracellular compartment acidification contain either CHX or essential oils in their formulations
- The presence of an anti-discoloration system (ADS) in MoWs 1 (as for 2 and 3) may partially interfere with its CHX-mediated anti-fungal effects.
- With MoWs 1 (Curcept), only *Candida*'s capacity to form a biofilm is impaired [270]. Its susceptibility to phagocytes remains unchanged, while other virulence traits, such as adhesion and elicitation of proinflammatory cytokines, are affected.
- *S. salivarius* treated with MoWs Curcept and Listerine has delayed *Candida* biofilm formation, but these fail to stop it completely.

6. Improvement of an effective solution against DP

Although there is no consensus regarding how to best maintain prosthetic hygiene compatible with the patient's state of health [87,234], the disadvantages of many procedures are thoroughly evidenced [86,202]. Several habits should be avoided, such as rinsing with boiling water and prolonged maintenance in a dry atmosphere or water because these alter the qualities of some materials or promote microbial colonization. Both bleach and isopropyl alcohol (IPA) are highly antimicrobial, but bleach is incompatible with metal dental prosthesis components, and IPA MoWs damage polymethyl methacrylate [88,235]. Concerning denture cleaning tablets, the polarity of the resins, the concentrations of tablets, and the chemical content of the cleanser may directly affect *C. albicans* biofilm formation and provide

both anti-microbial efficacy and greater material compatibility [70,271]. Thus, the dosage and prescription of disinfecting tablets can vary depending on the resin used to make the prosthetic base. The use of microwave disinfection in combination with denture cleansers and brushing has also been shown to effectively disinfect dentures *in vivo* [236,272], though microwaves may also physically distort denture acrylics [240,273]. There are several unconventional approaches to denture care, including soaking in vinegar, baking soda, sodium chloride, and liquid soaps [208,241]. Though these practices aim to control the prosthetic biofilm, they may be insufficient. In-depth examinations are usually required to gain deeper understanding of the etiology and implementation of the most appropriate therapy [87,264].

In summary, prosthetic oral hygiene requires daily control of the microbial plaque. The personalized implementation of the means at our disposal is informed by the general condition of the patient, the material composition of the prosthetic base, and the presence or absence of DS. *C. albicans*, a frequent commensal member of well-balanced oral microbiota, influences the treatment [39]. The daily maintenance of prostheses has little influence on the microbiome but helps stabilize the microbial balance [67].

Conclusion

The simple presence of a removable prosthesis in the oral cavity can upset the balance of the oral microbiota.

The reciprocal relationship between the host and their prosthetic microbiome is both fragile and constantly dynamic. In addition, several general and local parameters contribute to this balance. These parameters can be specific to the host (heredity and general pathologies) but also dependent on their level of oral hygiene and their lifestyle, which makes it difficult to manage DS.

DP biofilms cannot be eliminated, especially because they are invisible to the naked eye. In addition, it is essential to differentiate between tolerance of DP and persistent infections such as DS. Despite recent advances, we still lack a comprehensive understanding of many characteristics of DP biofilms. Their tolerance of existing antifungal drugs, their ability to evade components of the host immune system, their resistance to mechanical forces under the denture, and their capacity to seed

new infections make them the central targets of a more effective strategic plan in the fight against persistent oral infections such as DS.

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