SCIENTIFIC MEDICAL CLINICAL AFFAIRS

NEWS & VIEWS

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Oral health

Oral health is crucial to our overall wellness and physical attractiveness and helps to prevent a number of health issues related to poor oral health. Although largely preventable, oral diseases are among the most common chronic diseases worldwide. They affect an estimated 3.5 billion people – almost every second person in the world - and impact every aspect of life from relationships and self-confidence, through to school, work and the ability to interact with others.

Oral diseases are chronic and progressive in nature. Poor dental health may for example contribute to dental caries. Globally, an estimated 2 billion people suffer from caries of the permanent teeth and about 510 million children suffer from caries of the primary teeth.

Furthermore, poor dental hygiene may contribute to gingivitis and, in the long term to periodontitis. Severe periodontal disease is estimated to affect around 19% of the global adult population, representing more than 1 billion cases worldwide.[1,2,3]

Vulnerable patients may be more susceptible to serious conditions, such as endocarditis and respiratory infection. Hence, implementation of an antiseptic oral hygiene routine is recommended in the context of infection prevention, for example in dental practice and ICU patients.[4,5]

Moreover, sustained personal oral care, which includes toothbrushing twice daily with a fluoride toothpaste, is a fundamental aspect of maintaining good oral health.[2]

Short questions & quick answers

What is the oral microbiome?

The oral microbiome consists about over 600 species of bacteria and approximately 100 species of fungi. Much of the composition seems to be similar in most people. *Streptococcus, Haemophilus, Rothia, Neisseria*, and *Veillonella* make up 85% of all adult genera. Youth oral microbiomes are more diverse, here the above-mentioned bacteria make up only 72%.[6,7]

Where do the bacteria colonize?

Numerous microorganisms can be found in the saliva. At the same time, the saliva contains numerous immunological defense proteins which in combination with physio-chemical properties of the saliva (e.g., a reduced surface tension and thus reduced adhesion) and the physical mechanism of swallowing lead to a constant clearance of microorganisms. The oral mucosal epithelial layer is shed continuously, thus limiting colonization to a certain extend through the constant renewal of the mucosal layer. The tooth surface is the only non-shedding surface in the oral cavity. Hence, the tooth surface represents an ideal environment for bacterial adhesion and growth and, thus the formation of dental plaque.[8,9]

What is a commensal microbiome?

The commensal oral bacteria play a key role in maintaining oral health, as some oral commensals (*S. sanguinis, S. cristatus, S. salivarius, S. mitis, A. naeslundii*) inhibit the growth and reduce the ability of disease-associated bacteria to adhere to oral surfaces, such as *P. gingivalis.*[10]

How do oral infections develop?

Pathogenic oral bacteria are the key factors in the development of oral diseases. However, not only a single pathogen is responsible, but a general dysbiosis of the oral microbiome.[11]
The state of the oral microbiome is influenced by a variety of endogenous and exogenous factors. In addition to genetic and geographical factors, other variables including host diet, systemic disruptions, antibiotics, stress, consumption of alcohol or tabacco, and frequencies of flossing and dentist visits determine differences in the composition of the microbiome.[7,12]

What is the relationship between oral and systemic health?

Oral infections manifest mostly locally, for example in form of dental caries or gingivitis, but can also have systemic consequences if the host has other systemic diseases. The relationship between oral and systemic health is bidirectional.[12]
The development of some types of cancer such as head and neck squamous cell cancer, pancreatic cancer and colorectal cancer, and systemic diseases, including rheumatoid arthritis, hypertension, Alzheimer's disease and systematic lupus erythematosus has been associated to a changed oral microbiome. Additionally, similarly like periodontal disease, diabetes, rheumatoid arthritis, and systemic lupus erythematosus are associated with inflammatory responses. Thus, they can play a role in the development or progression of periodontal disease.[13-20]

Oral colonization during life

In early life – The prenatal oral cavity is sterile until birth. Within 8-16 hours after birth, the colonization of the oral cavity occurs through transmission of microbes from human interactions and the diet.[12,21]

Colonization of the infant's mouth is related to the mode of delivery. In babies delivered vaginally, *Lactobacillus*, *Firmicutes, Bacteroides,* and *Actinobacteria* are the more common, while in babies delivered by caesarean section, *Bacteroides, Proteobacteria,* and *Firmicutes* are more common.[22]

Streptococci are the dominant group of bacteria in breast milk. Therefore, breast-fed-infants show a higher proportion of *Streptococcus*, whereas formula-fed infants show higher proportions of *Actinomyces* and *Prevotella*.[23]

Parallel to the eruption of deciduous teeth, there is a change in eating habits, which in turn leads to a change in the microbiome. *Streptococcus, Veillonella, Gemella* and *Granulicatella* accumulate.[12]

Although the initial colonizers remain as permanent colonizers into adulthood, the oral cavity is a dynamic microbial environment, that changes throughout life due to the influence of genetic factors, living conditions and habits.[12]

In adult life – According to the results of the NIH Human Microbiome Project, the oral microbiome shows the largest core set of microbes among unrelated individuals compared to other populated parts of the body. In more than 75% of the samples, *Streptococcus* (specifically *S. oralis, S. mitis, and S. peroris*) represented the main genus of the microbiome, with an abundance of more than 10%.[12,24]

In general, individuals from the same family show more similar oral microbiomes than individuals belonging to different families.[7]

Formation of oral biofilms – Oral microbial biofilms are complex ecological environments, in which plentiful and diverse microorganisms can be found. The hard, non-shedding enamel surface supports the growth and maturation of a biofilm.[9]

Initial colonizing bacteria include primarily the gram-positive Streptococci. With their surface adhesins, they specifically bind to the receptors of the salivary pellicle which is a thin layer of salivary proteins and glycoproteins that permanently coats the surfaces of the teeth and oral tissues.[25]

The interaction of bacteria, extracellular polymeric substances (EPS), proteins, and lipids from food and saliva creates a three-dimensional ecosystem, in which other bacteria can also settle. *Fusobacterium nucleatum* has a bridging role, facilitating the colonization of later bacterial colonizers through its strong adhesive ability.[26]

Nutritional gradients develop within the biofilm, which favors further colonization. For example, the aerobic streptococci produce, among other things, lactate and carbon dioxide through their metabolism. The carbon dioxide creates an anaerobic environment for the growth of anaerobic *Fusobacterium, Leptotrichia* and *Capnocytophaga* species. Lactate, in turn, is converted by *Veillonella, Corynebacterium* and *Eubacterium* species to weaker acids. Colonization by *Corynebacterium* creates long filaments on which other bacteria can attach themselves.[27-29]

Although streptococci remain the predominant species, the proportion of anaerobic bacteria such as *Porphyromonas, Fusbobacterium, Prevotella,* and *Capnocytophaga* is steadily increasing. At the border to the gums, immunological reactions are stimulated, further promoting dysbiosis and inflammation. The persistent inflammation leads to tissue destruction, deepening of the gingival crevice and induces the pathologic bone loss characteristic of periodontitis.[12,30]

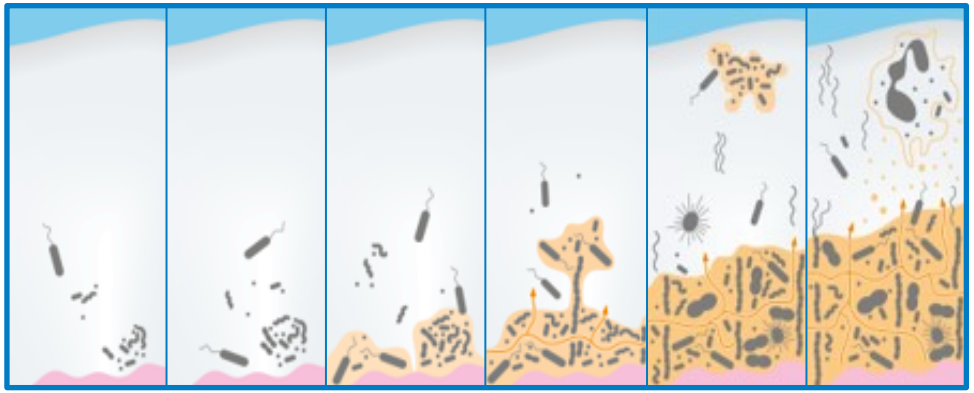


Figure adapted according to[31]: Dhir S. Biofilm and dental implant: The microbial link. J Indian Soc Periodontol. 2013 Jan;17(1):5-11

Oral infections

Dental caries – Dental caries, or tooth decay, is currently the most common health condition in the world. It is the result of breakdown of teeth due to bacterial acids.[32]

Dental caries is a dynamic process during which the demineralization of dental hard tissues outweighs the remineralization. This initially manifests in a small chalky area within a smooth surface, worsens until it damages the tooth crown and later also exposes root surfaces.[32,33]
The development of caries is biofilm-mediated and dependent on carbohydrate intake. The consumption of large amounts of sugary food provides a favorable environment for caries-associated bacteria.[26]
The increased amount of carbohydrates leads firstly to increased acid production by the microbes, which reduces the buffering capacity of the saliva, and secondly to increased production of a biofilm exopolysaccharide matrix. This induces positive feedback loops that encourage the growth of acidifying species such as *S. mutans* and *Lactobacillus* species. As a result, carious lesions and cavities increase, which come with symptoms such as discomfort, sensitivity and pain. If left untreated, complications including inflammation of the pulp or tooth surrounding tissue, acute or chronic infection, abscess formation and tooth loss can occur.[12,32,33]

Periodontal disease – Periodontal disease, also known as gum disease, is the result of an inflammatory response in the periodontal tissue, caused by localized toxic effects of oral biofilms.[34]
Gingivitis is considered an early form of periodontal disease and can be the precursor of the more severe form, periodontitis.[35]

Through the maturation of oral biofilms, the microorganisms in the local plaque environment can initiate and maintain inflammatory processes. This leads to subversion of the host's immune system and prevents tissue recovery.[36,37]
The unmitigated inflammation of the gums mediates the development of gingivitis, which is accompanied by red and swollen gums. Occasionally, bleeding can also occur.[38]
The pathology of gingivitis is reversible and can be mitigated with proper oral hygiene.[36]

With accumulation of dental plaque* there comes a shift in the periodontal microbiome that is accompanied by an increase in gram-negative anaerobic species. This dysbiosis ensures the development of periodontitis.[36]
Persistent inflammation causes the biofilm to expand into the subgingival area and promotes the proliferation of pathogenic bacteria. The irreversible and progressive degradation of periodontal tissues leads to formation of periodontal pockets, gum recession and exposure of the roots. The body's defensive response to the ongoing inflammation causes attachment loss and alveolar bone loss, which can result in the reduction of chewing function and loss of teeth.[35,36,39,40]
The oral pH also plays a role in the development of oral infectious diseases. For example, an acidic pH (≤ 5.5) favours demineralization, the proliferation of caries-causing bacteria and thus the development of caries. A pH in the more neutral range (~ 6.3) is associated with oral health, whereas the pH in periodontitis patients is slightly more increased (~ 6.8).[41,42]

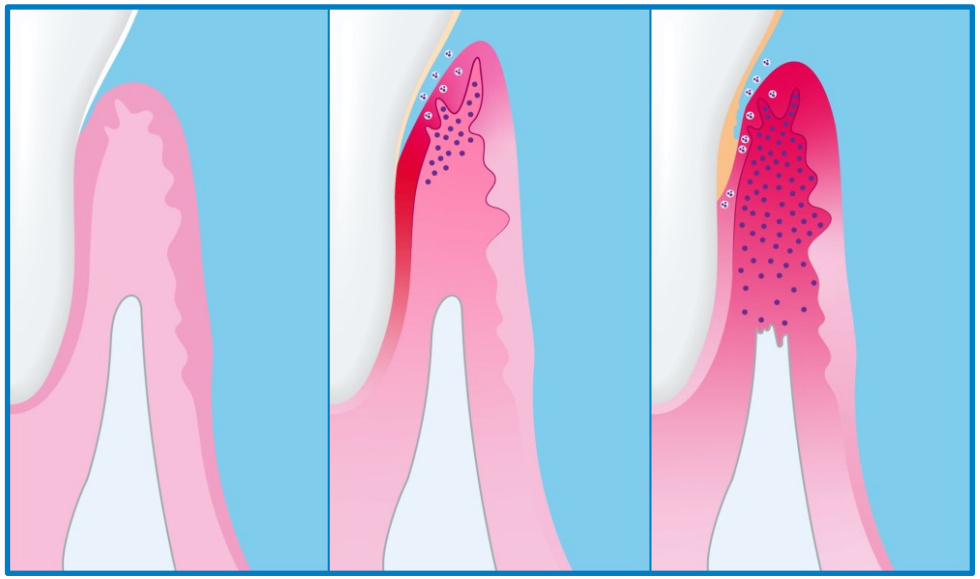


Figure adapted according to[36]: Kriebel K et al. (2018), Oral Biofilms from Symbiotic to Pathogenic Interactions and Associated Disease – Connection of Periodontitis and Rheumatic Arthritis by Peptidylarginine Deiminase. Front. Microbiol. 9:53.

*Dental plaque = polymicrobial biofilm, both terms are used synonymously in the text

Oral microbial complexes

Based on the complex theory of Socransky and Haffajee, the bacteria of the oral microbiome are classified depending on their pathogenicity and role in the development of periodontal disease. Bacteria within a complex are strongly associated with each other, and additionally the complexes themselves are also related to each other in different ways.[43]

The initial colonization of the tooth surface involves the bacteria of the yellow, blue, green and purple complexes. It seems likely that the members of the yellow and blue complexes are predominantly present at the beginning of the biofilm formation, followed by members of the green and purple complexes.[43,44]

Groups	Associated bacterial species
Blue complex	*Actinomyces species*
Yellow complex	*Streptococus sanguinis, Streptococcus oralis, Streptococcus mitis, Streptococus gordonii, Streptococcus intermedius*
Green complex	*Capnocytophaga gingivalis, Capnocytophaga sputigena, Capnocytophaga ochracea, Campylobacter concisus, Eikenella corrodens, Aggregatibacter actinomycetemcomitans* serotype a
Purple complex	*Veillonella parvula, Actinomyces odontolyticus*
Orange complex	*Fusobacterium nucleatum, Prevotella intermedia, Prevotella nigrescens, Peptostreptococcus micros, Eubacterium nodatum, Campylobacter rectus, Campylobacter showae, Campylobacter gracilis, Streptococcus constellatus*
Red complex	*Bacteroides forsythus, Porphyromonas gingivalis, Treponema denticola*
Not clustered with other species	*Aggregatibacter actinomycetemcomitans* serotype b

Figure adapted according to[43]: Socransky S S et al., J. Clin. Peridontol., 1998; 25(2):134–144. doi: 10.1111/j.1600-051x.1998.tb02419.x

The *Streptococcus* species of the yellow and *Capnocythophaga* species of the green complex are usually associated with periodontal health and therefore have a higher relative abundance within healthy people.[45,46]

However, at the same time, their growth contributes to primary changes in the host and precedes the colonization with bacteria of the orange and red complexes which are more common in patient with periodontitis.[47,48]

The bacteria of the orange complex have a bridging function as they can bind to early colonizers, create suitable metabolic growth conditions.[45,48]

As colonization progresses, the oxygen content decreases, causing the amount of anaerobic bacteria to increase.[36]

The bacteria of the orange complex also provide docking sites for the bacteria of the red complex.[53]

For this reason, the red complex is closely associated with the orange complex and rarely found in the absence of it, whereas the numbers of the red complex increase with increasing colonization of the orange complex.[43,45]

The red complex is the most virulent. It includes gram-negative, anaerobic bacteria whose high virulence can be explained due to a large number of hydrolytic, proteolytic and lipolytic enzymes, co-aggregation with each other and production of toxic metabolites.[45,47]

Compared to the other complexes, members of the red complex are mostly associated with clinical parameters of periodontal disease, e.g., they are strongly related with bleeding on probing and can be found in high numbers in advanced lesions. Additionally, the red complex is actively connected to the periodontal pocket depth. Red-complex-bacteria occur most frequently in deep pockets and, at the same time, may further contribute to the deepening of pockets. Although the orange complex and the pocket depth are also related, this is less the case for other clinical parameters.[43]

The facultative anaerobic bacterium *A. actinomycetemcomitans* serotype b does not cluster with the other complexes, rather it plays a role as an outlier. Producing potent virulence factors such as phosphatases and leukotoxin to kill leukocytes, it is highly pathogenic and may be responsible for localized aggressive periodontal disease.[45,49]

Hygiene Guideline of the German working group for hygiene in dentistry

> Prophylactic antisepsis is intended to prevent the penetration of microorganisms into primarily sterile areas of the body when the mucous membrane is transected and thus to prevent local infection or bacteremia.[5]

The Hygiene Guideline of the German working group for hygiene in dentistry (Deutscher Arbeitskreis für Hygiene in der Zahnmedizin, DAHZ) recommends the use of antiseptics in the oral cavity before dental treatment of patients with an increased risk of infection, before extensive surgical interventions with subsequent saliva-proof wound closure and as a supplementary measure in the absence of mechanical tooth cleansing.
For this purpose, the DAHZ recommends authorized medicinal products based on chlorhexidine, octenidine, povidone iodine, polyhexanide or sodium hypochlorite.
In addition, antiseptic rinsing of the oral cavity reduces the risk of pathogens being passed on via the aerosol. However, the DAHZ also points out that mucosal antisepsis does not replace antibiotic prophylaxis that may be indicated.
Multi-resistant pathogens such as MRSA, VRE, 3MRGN and 4MRGN only rarely cause infections after dental treatment, but in exceptional cases can colonize the oral cavity and cause an infection that is difficult to treat. Antiseptic mouth rinses are recommended prior to treatment in patients colonized with multi-resistant pathogens.[5]

MRSA: Methicillin-resistant *Staphylococcus aureus*
VRE: Vancomycin-resistant *Enterococcus*
3MRGN: multi-resistant gram-negative pathogens with resistance to 3 of 4 antibiotic groups
4MRGN: multi-resistant gram-negative pathogens with resistance to 4 of 4 antibiotic groups

S3 Guideline of the German working group of the scientific medical societies: Domestic chemical biofilm management in the prevention and therapy of gingivitis

> The primary goal of chemical biofilm management is the additional use of antimicrobial agents to inhibit or prevent the formation of dental biofilms and thus to prevent or combat inflammation of the gingiva.[50]

Domestic mechanical biofilm management includes tooth brushing and interdental space cleaning and forms the basis for caries prophylaxis as well as prophylaxis and therapy of periodontal diseases.
In some cases, additional or sole chemical biofilm management may be necessary to reduce the number of germs. The indications can be divided into two categories: I) the mechanical oral hygiene is limited for a short-term period due to oral surgical procedures, and II) the mechanical oral hygiene cannot be performed sufficiently during a prolonged period due to prosthetic constructions, implants, limited daily oral hygiene capacity or general deficits in oral hygiene.
For the purpose of chemical biofilm management, the guideline of the German working group of the scientific medical societies (Arbeitsgemeinschaft der wissenschaftlichen medizinischen Fachgesellschaften, AWMF) mentions mouth rinse solutions containing the active ingredients chlorhexidine, essential oils, triclosan/copolymer, amine fluoride/tin fluoride and cetylpyridinium chloride, as these have an antimicrobial and plaque-inhibiting effect.[50]
The active ingredient octenidine is not explicitly considered in the guideline as relevant studies were not available at the time of the guideline preparation. In the meantime, octenidine-containing mouthwashes have been brought onto the market that as well have been proven to be effective.

A systematic review of the effect of octenidine mouthwash on plaque, gingivitis, and oral microbial growth

> Unlike a toothpaste, mouthwash being liquid can significantly reduce total oral microbial load as it rinses the entire oral cavity including inaccessible areas and soft and hard oral surfaces.[51]

Grover et al. (2020) conducted a **systematic review** to determine the efficacy of octenidine (OCT) based mouthwash on plaque formation, gingivitis, and oral microbial growth in subjects with or without periodontal disease. For this purpose, ten randomized controlled trials and six observational studies comparing any concentration of OCT against a control mouthwash/ mouthwashes containing chlorhexidine (CHG), essential oils (EOs) or povidone-iodine (PVP-I) in healthy subjects with or without periodontal disease were examined and compared.

The primary objective was to determine the effectiveness of OCT. The endpoints of the studies included percentage reduction in plaque index (PI), gingival index (GI), absolute reduction in the mean number of colony-forming units (CFU/mL[log10]) and adverse effects. An additional purpose of this review was to compare OCT versus CHG on these outcomes.

Reduction of the plaque index – Nine studies evaluated the effect of OCT on plaque formation. In all these, OCT showed a significant reduction of the plaque formation ranging from 38.7% to 92.9% within 4 days to 3 months (depending on and the duration of application, the type of application and the evaluation).
Additionally, two studies compared the effectiveness of OCT and CHG, in which OCT had a similar or greater plaque inhibition compared with CHG.

Reduction of the gingival index (GI) – The effect of OCT on the gingival index was assessed in six studies. Every study reported a significant reduction in GI with OCT versus control mouthwash. Within 4 days to 3 months the reduction of the GI ranged from 36.4% to 68.37%.

Reduction of colony-forming units (CFU/mL[log10]) – Data regarding the effect of OCT on oral microbial growth was available for ten studies. All studies reported a significant reduction in the total oral microbial growth, ranging from 1.73 to 4.4 log units versus no change in general with the placebo.
In eight studies in which the effect of OCT was compared to the one of CHG, the reduction of the microbial growth with OCT ranged from 0.37 to 5.3 log units versus 0.4 to 4.23 log units. Seven studies reported a superior efficacy of OCT against CHG, one reported comparable efficacy.

Additional benefits – The examined studies reported additional benefits of OCT-based mouthwashes:
- significant reduction of bleeding sites after 3 months
- significant decrease in the mean papilla bleeding index (PBI) and the pocket depth score (PD) in HIV positive patients with periodontal disease after 3 months
- significant reduction of PD and sulcus bleeding index (SBI) after 21 days
- significant reduction of inflammatory exudate from periodontal tissue after 7 days
- any tooth discoloration was reversible [51]

Conclusion – There is a moderate evidence that OCT is an effective antiplaque agent. The OCT-based mouthwashes inhibited plaque formation up to 93% and gingivitis up to 68% versus placebo. This resulted in efficient elimination of different oral bacteria. Overall, OCT-based mouthwashes were either superior or comparable to CHG-based mouthwashes.[51]

0.1% octenidine mouthwash inhibits plaque formation and reduces the bacterial count over 5 days

Randomized, placebo-controlled, double-blind, parallel group, multi-center phase 3 study

201 patients
152 patients: 0.1 % octenidine mouthwash (OCT)
49 patients: 0.5 % phenoxyethanol mouthwash (placebo)

Jockel-Schneider et al. (2021) investigated the plaque inhibition of an oromucosal solution containing 0.1% octenidine in the absence of mechanical plaque control. Rinsing was conducted twice daily for 30 seconds over a course of five days. Colony forming units in saliva were assessed before and after the first rinse. Primary study outcome was the amount of plaque regrowth assessed by the plaque index (PI) after 5 days. Additionally, the gingival index (GI), tooth discoloration index (DI) and bacterial load were assessed.
Compared to placebo, octenidine significantly reduced the bacterial load in saliva (OCT vs. placebo: 2.73 vs. 0.24 log RF), inhibited plaque formation (PI OCT vs. placebo: 0.36 vs. 1.29) and reduced the gingival index (GI OCT vs. placebo: 0.25 vs. 0.38). The tooth discoloration was slightly higher with octenidine compared to the placebo (DI OCT vs. placebo: 0.25 vs 0.00).
This study shows that 0.1% OCT inhibits the plaque formation over 5 days and can therefore be recommended when regular oral hygiene is temporarily compromised.[52]

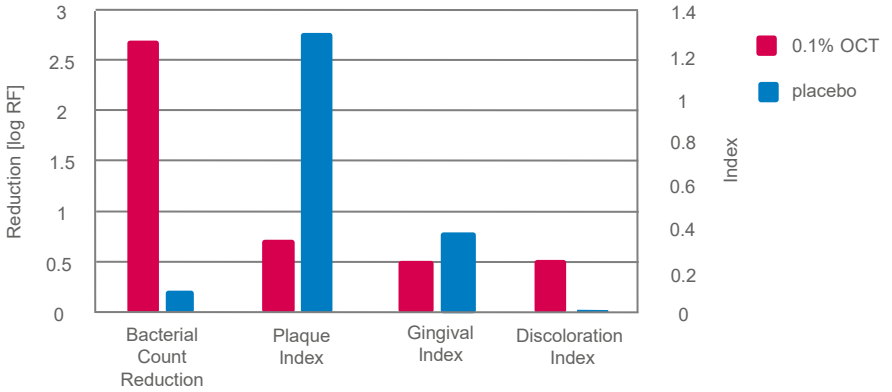


Figure adapted according to[52]: Jockel-Schneider et al., Impact of 0,1% octenidine mouthwash on plaque re-growth in healthy adults: a multi-center phase 3 randomized clinical trial, Clin Oral Investig., 25(7):4681-4689, 2021.

0.1% octenidine mouth rinse inhibits plaque formation and gingivitis more efficiently than 0.2% chlorhexidine

Double blinded, randomized case control study

45 patients
15 patients: 0.2% chlorhexidine gluconate (CHG)
15 patients: 0.1% octenidine dihydrochloride (OCT)
15 patients: distilled water (DW)

Razi et al. (2021) investigated octenidine and chlorhexidine compared to distilled water in terms of their antimicrobial and antiplaque efficacy.
The patients brushed their teeth twice daily and used mouth rinse after 30 minutes prior to brushing for a period of 15 days. The plaque index (PI), modified gingival index (MGI) and gingival bleeding index (GBI) were assessed every 5 days. Additionally, supragingival plaque samples were collected before the start of the study and on day 15 to investigate the microbial colony count (CFU/ml).
OCT compared to CHG and DW was able to cause a greater reduction of the PI (ΔPI OCT vs. CHG vs. DW: 0.81 vs. 0.66 vs. 0.20) as well as MGI (ΔMGI OCT vs. CHG vs. DW: 0.88 vs. 0.79 vs. 0.07) and GBI (ΔGBI OCT vs. CHG vs. DW: 56.56 vs. 53.21 vs. 48.51). Further, OCT reduced the microbial colony count more than CHG and DW (ΔCFU/ml OCT vs. CHG vs. DW: 236 vs. 86 vs. 16).
The antimicrobial and antiplaque efficacy of the mouth rinse containing octenidine was higher than the one with chlorhexidine and therefore, shows higher potential for controlling plaque and gingivitis.[53]

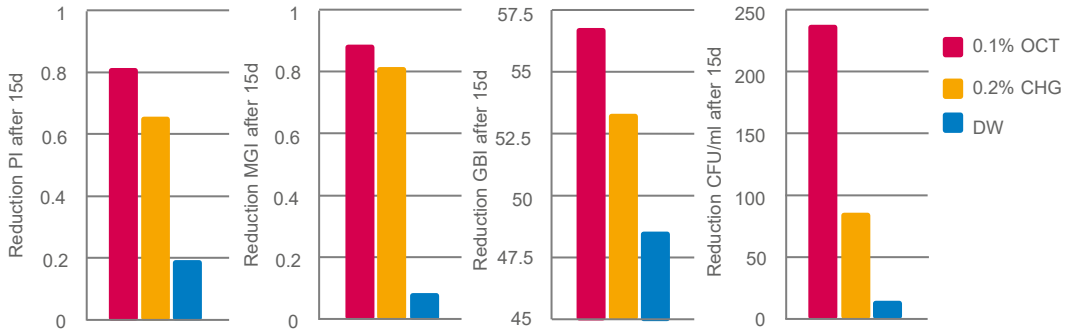


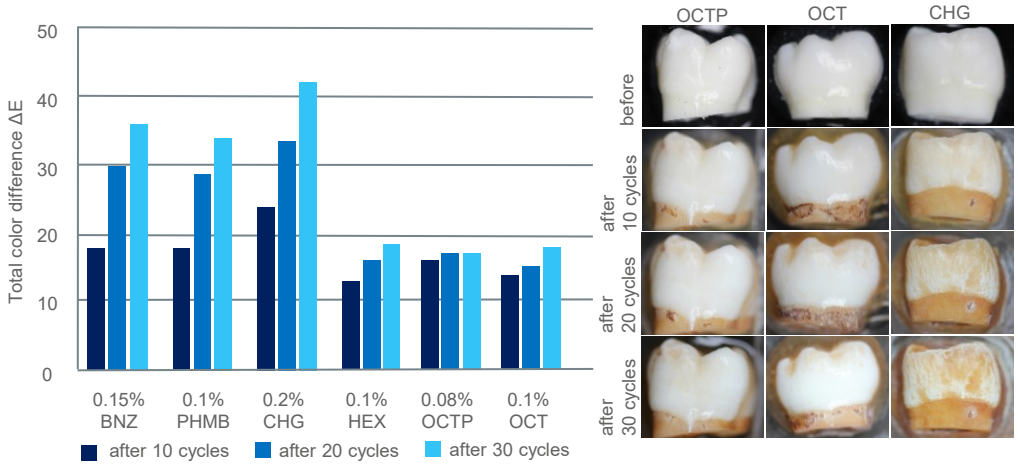
Figure adapted according to[53]: Razi et al., Efficacy of 0.2% chlorhexidine gluconate and 0.1% octenidine dihydrochloride mouth rinses in patients with plaque induced gingivitis: Double blinded randomised case control study. University Journal of Dental Sciences, 7(1):9-16, 2021.

Octenidine-based mouth rinses cause less discoloration than mouth rinses containing other active ingredients

in vitro model to evaluate tooth discoloration potential of mouth rinse solutions on human enamel (halved molar crowns)

6 different mouth rinses containing benzydamine (BNZ), polyhexanide (PHMB), chlorhexidine (CHG), hexetidine (HEX), octenidine (OCT) or octenidine/phenoxyethanol (OCTP)

Sarembe et al. (2023) investigated the staining potential of different mouth rinses on human enamel. The tooth crowns were exposed to a cyclic treatment, consisting of soaking in artificial saliva, staining with black tea, brushing with toothpaste and soaking in rinsing solution. After each step, the crowns were rinsed with distilled water. This cycle was conducted 30 times, thus mimicking a consumer behavior over 15 days, assuming two applications per day. Subsequently, color measurements were made to determine the total color difference ΔE.
After cycle 30, significantly less tooth staining was observed for OCT-containing mouth rinse solution as compared to CHG-containing mouth rinse solutions.[54]



Figures adapted according to[54]: Sarembe et al., in vitro model to evaluate the development of discolorations on human enamel caused by treatment with mouth rinses and black tea considering brushing, Fraunhofer IMWS, 2023.

Octenidine-based mouth rinses show a broad efficacy against periodontal pathogens

in vitro study, quantitative suspension test

4 mouth rinses: octenisept® (Octenidin, Phenoxyethanol), octenidol® (Octenidin), Chlorhexamed® (Chlorhexidin) und Meridol® (Amin-/Zinnfluorid)
10 periodontal pathogens

Mutters et al. (2007) investigated the microbiocidal efficacy of 4 different commercially available antiseptic mouth rinses on various anaerobic and microaerophilic pathogens commonly found in the mouth using the quantitative suspension test.
For all microorganisms except for *E. corrodens* and *P. micros*, the rinses containing octenidine showed a log reduction > 6. These results show the efficacy of octenidine against common oral pathogens and its suitability for the prevention of oral infections and pneumonia.[55]

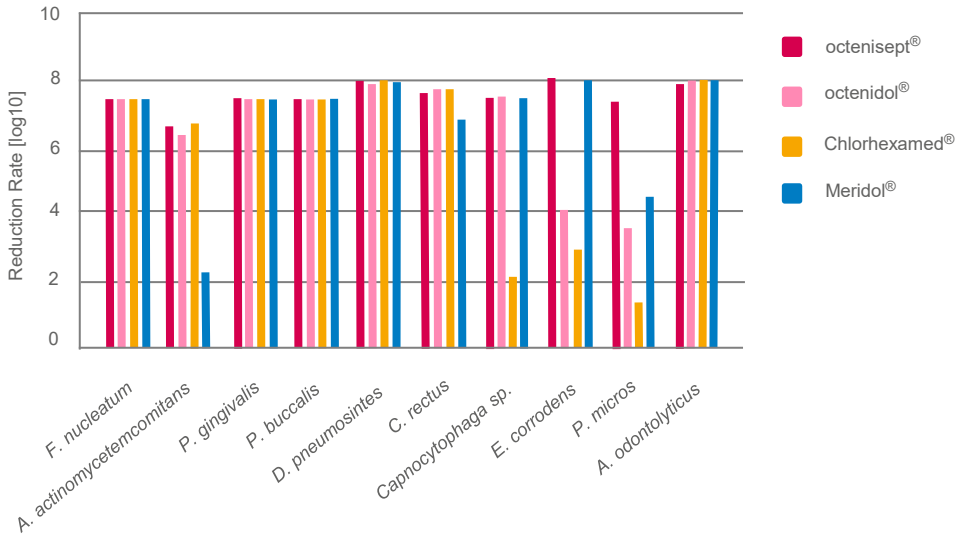


Figure adapted according to[65]: Mutters et al., Microbiocidal efficacy of antiseptic octenidine-, chlorhexidine- or amine-/tin-fluoride-based oral rinses on periodontal pathogens. GMS Krankenhaushygiene Interdisziplinär, 2007.

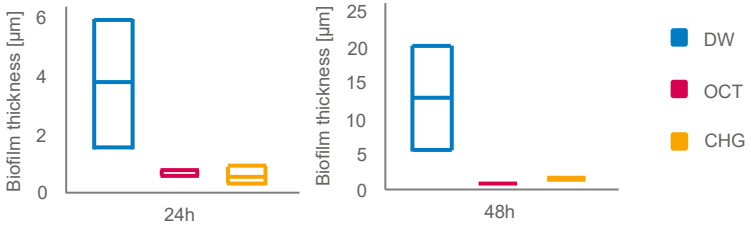
Octenidine-based mouth rinses reduce biofilm formation and disrupt mature biofilms

Cross-over *in situ* study

5 patients
0.1% octenidine (OCT), 0.1% chlorhexidine (CHG), water (DW)

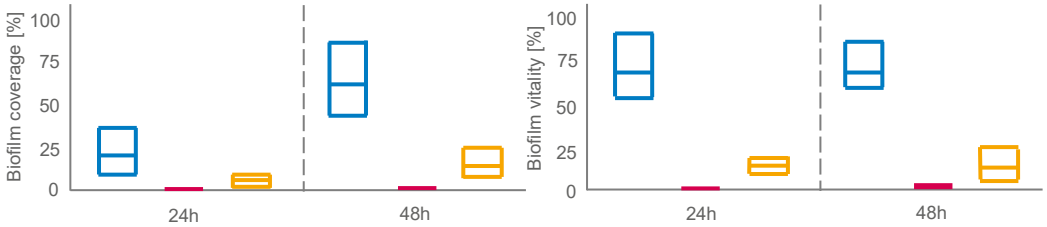
Reda et al. (2021) investigated the effects of different mouth rinses on biofilm formation and on the disruption of mature biofilms. The biofilms were formed intraorally on enamel specimens fixed to acrylic splints.
For the analysis of the biofilm formation, the rinses (OCT, CHG, DW) were applied for 30s every 12h and the samples evaluated at 24h and 48h time points. For the analysis of the disruption effect on mature biofilms, the biofilms were allowed to mature for 48h, after which samples were taken as controls. Subsequently, samples were analyzed directly after the first rinsing. After 12h, rinsing was performed once again, and after further 12h the last samples were taken. The biofilms were analyzed by fluorescence microscopy for biofilm coverage and vitality and by transmission electron microscopy for biofilm thickness.

After 24h, the biofilms rinsed with water showed a thickness of 3.62 ± 1.73 µm, and after a total of 48h a thickness of 12.32 ± 6.58 µm. A significant reduction could be achieved by rinsing with OCT and CHG (OCT vs. CHG; 48h: 0.50 ± 0.26 µm vs. 0.73 ± 0.11 µm; 72h: 0.54 ± 0.09 µm vs. 1.37 ± 0.29 µm).

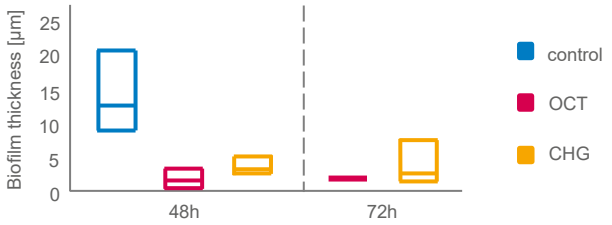


Figures adapted according to[56]: Reda et al., Effects of Octenidine on the Formation and Disruption of Dental Biofilms: An Exploratory In Situ Study in Healthy Subjects, J Dent Res., 100(9):950-959, 2021.

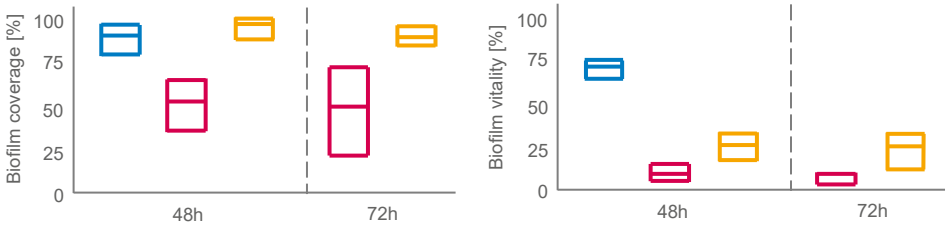
OCT and CHG both reduced the biofilm coverage, with OCT being significantly superior at 48 h (OCT vs. CHG; 48h: 0.4% vs. 4.5%; 72h: 0.5% vs. 11.3%).
Additionally, bacterial vitality decreased more in the OCT-treated samples compared to those treated with CHG (OCT vs. CHG; 48h: 1.25% vs. 12.35%; 72h: 1.9% vs. ± 11.5%).



The matured biofilms had a thickness of 12.1 ± 3.5 µm before the first rinsing. A significant reduction was achieved by rinsing with OCT and CHG (OCT vs. CHG; 48h: 1.4 ± 1 µm vs. 3.1 ± 0.6 µm; 72h: 1.6 ± 0.4 µm vs. 2.5 ± 2.4 µm).



Compared to CHG, OCT led to a significant reduction of the coverage (OCT vs. CHG; 48h: 50.6% vs. 93.4%; 72h: 50.2% vs. 88.2%).
Further, OCT was significantly more effective in reducing the bacterial vitality of mature biofilms (OCT vs. CHG; 48h: 8% vs. 2.2%; 72h: 4.9% vs. 25.1%).



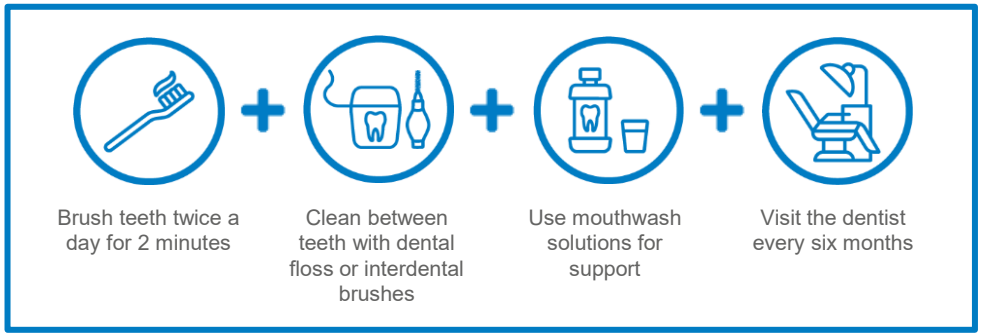
The results showed OCT significantly reducing biofilm formation and bacterial vitality *in situ*. Simultaneously, the biofilm thickness of both the new and mature biofilms was strongly decreased.[56]

The way to a good oral hygiene

Adequate oral hygiene is essential for our general well-being. Poor oral hygiene can lead – among other health-issues – to the development of gingivitis and periodontitis which, in turn, can manifest as sensitive gums and ultimately tooth loss. Periodontal disease is microbiologically characterized by the presence of pathogenic bacteria within the subgingiva. The presence of *A. actinomycetemcomitans* and bacteria from the red complex is attributed to a late and severe stage.[35,36,39,40,43]

The fact that *A. actinomycetemcomitans* and bacteria of the red complex are correlated with periodontal disease does not necessarily presupposes their absence in healthy subjects. Early colonizers such as *S. mitis* and *S. sanguinis* are part of the commensal oral microbiome and, thus, provide the basis for the colonization of other bacteria at any time without the intervention of proper oral hygiene. Late-colonizers can also be found in healthy subjects. Hence, they pose a risk for the development of periodontal disease.[12]

Mechanical measures for tooth cleaning are the basis of caries and periodontal disease prophylaxis. In some cases, additional chemical biofilm management may be necessary to reduce the number of oral bacteria.[50]
Therefore, in cases where an acute reduction of the bacterial load and inhibition of plaque formation in the oral cavity is required, e.g., before dental treatment of patients with an increased risk of infection or in the absence of mechanical tooth cleaning, a mouth rinse solution with an antimicrobial agent is recommended and, such products must be authorized as a medicinal product.[5]



The medicinal product **octenident® antiseptic** has been clinically proven and is indicated for the temporary reduction of the bacterial count in the oral cavity, for the temporary inhibition of plaque formation and, in cases of insufficient oral hygiene capacity. octenident® antiseptic is alcohol-free and also suitable for pregnant women (after the first trimenon, from the fourth month of pregnancy). Adults should rinse thoroughly with 10 ml of the solution for 30 seconds twice daily after meals and brushing teeth. After rinsing the product must be spat out. Please consider the instructions for use in the patient information leaflet.

Additionally, the cosmetic **octenident® mouthwash** is also available for daily oral care and can be used in adults and children from the age of 6 years. It inhibits bad breath-causing bacteria and leaves a fresh breath due to its mint flavor. 15 ml of the mouth rinse solution should be used for 30 seconds after brushing teeth. After rinsing the product must be spat out. Please consider the information on the product packaging.

Disclaimer:
These products are not available in every country. For more information, please contact our local subsidiary or distributor.

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octenident® antiseptic 1 mg/ml oromucosal solution. Active substance: octenidine dihydrochloride. Composition: 1 ml of solution contains 1 mg of octenidine dihydrochloride. Other ingredients: glycerol 85 per cent (E 422), sodium gluconate, citric acid, disodium phosphate dihydrate (for pH adjustment), macrogolglycerol hydroxystearate, sucralose, purified water, mint flavour (contains propylene glycol (E 1520)). Indications: octenident antiseptic has an antimicrobial effect. It is used for temporary reduction of bacterial count in the oral cavity, for temporary inhibition of plaque formation, and in cases of insufficient oral hygiene capacity (no toothbrushing possible, for example) in adults. Contraindications: Allergy to octenidine dihydrochloride or any of the other ingredients. Undesirable effects: Very common: Temporary taste disturbance, such as bitter aftertaste; Mild, reversible dental discoloration. Common: Numb sensation in the mouth, Coating of the mouth or the tongue, Temporary tongue discoloration, Sensitivity of teeth. Uncommon: Headache, Nausea, Tingling of the tongue, More saliva in the mouth than normal. Revision 03/23
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