Macedonian Journal of Medical Sciences. 2012 Jul 31; 5(2):215-221.
doi:10.3889/MJMS.1857-5773.2012.0228
Review Article

OPEN ACCESS

Modern Approach to the Identification and Elimination of Periodontal Infection

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Citation: Atanasovska-Stojanovska A. Modern Approach to the Identification and Elimination of Periodontal Infection. Maced J Med Sci. 2012 Jul 31; 5(2):215-221. http://dx.doi.org/10.3889/MJMS.1957-5773.2012.0228.

Key words: periodontitis; polymerase chain reaction; Laser therapy; Light activated disinfection; probiotics; review.

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Received: 10-Oct-2011; Revised: 27-Feb-2012; Accepted: 02-Apr-2012; Online first: 05-Jun-2012

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Competing Interests: The authors have declared that no competing interests exist.

Abstract

In global terms, periodontitis is the leading cause of tooth loss, and causes serious aesthetic and functional problems. There are numerous scientific evidence that power periopathogenic microorganisms may have influence on some systemic conditions and diseases. If we add the fact that periimplantitis are caused by identical periopathogenes, management or effective identification and elimination of periodontal inflammation set as imperative in successful periodontal treatment and possible complications locally or systemic, as well as resistance and lifetime of the implants. As a method for quantifying and classification of bacterial species are recommended monitoring of the bacterial micro flora through PCR (polymerase chain reaction) technique. Laser therapy as a supplementary method to classic treatment is strongly emphasized as a new therapeutic option that uses the photo-thermal effect to fight bacterial infection. Air flow - an original method that uses water, air and powder help to destroy the biofilm and remove plaque. Oral application of LAD (Light activated disinfection) therapy influence nascent oxygen breaks down the interaction in biofilm and makes the microorganisms more sensitive to further damage. Finally, the role and use of probiotics as a link between the beneficial oral bacteria species and inflammation.

1. Epidemiology of Periodontal Disease

Periodontal disease is a chronic bacterial infection that affects the gingiva, periodontium, alveolar bone and cementum, and starts when bacteria found in dental plaque cause inflammation of the gingiva. If this inflammation is left untreated, it penetrates the deeper periodontal tissue and causes a chronic inflammatory immunological response. Damage to the gingival sulcus and the formation of a periodontal pocket filled with various bacterial flora and bacterial toxins lead to damage to the alveolar bone and ultimately, tooth loss. In global terms, periodontitis is the leading cause of tooth loss, with an aggressive form that attacks the younger population and causes serious aesthetic and functional problems such as distorted speech and difficulty chewing being a particular problem [1].

There is much scientific evidence that periodontal microorganisms have a significant effect on certain systemic conditions and diseases, for example: by increasing the risk of myocardial infarction,

atherosclerosis, stroke, osteoporosis, premature birth and low-birth-weight babies; and by increasing the damage caused by diabetes mellitus and chronic respiratory diseases [2].

As an example, many studies concerning preterm delivery and periodontitis have suggested mandatory periodontal treatment among pregnant women in order to prevent undesirable effects on the foetus [3-6]. Individual types of periopathogens have been directly connected with atherosclerosis, and their presence has been noted in atheromatous plaques in blood vessels [7].

2. Aetiology of Periodontal Disease

The deciding factor that determines periodontal tissue destruction is the composition of the microbial ecosystem and its equilibrium. It is well known that over 1,000 different microorganisms colonise the oral cavity during our lifespan; a normal balance among these microorganisms is the key factor for oral health. These bacteria are most often found in the oral mucosa, on hard dental surfaces, in the saliva and in the gingival fluid. These bacteria also form dental plaque, which is an adherent, complex structure and functions as a multi-cellular organism with over 100 microorganisms in one cubic millimetre of plaque [8]. Healthy periodontal tissue mainly supports gram-positive microorganisms. *Streptococci* are most often involved in the initial formation of plaque, which is followed by colonisation by *Actinomyces*, *Veillonella*, *Prevotella*, *Haemophilus* and *Capnocytophagi*. In the next stage, when oxygen flow to the biofilm decreases, colonisation by anaerobic or facultative anaerobic types of *Treponema*, *Porphyromonas*, *Actinobacillus* and *Helicobacter* begins. Periopathogens cause inflammation via virulence factors (specific cell structure, aggressive enzymes, endo- and exotoxins), and demonstrate their pathogenic potential in conditions of homeostatic imbalance in the periodontal tissue. Pathogenic occurrences during this inflammatory process in the gingival tissue enhance the release of pro-inflammatory mediators, such as cytokines and prostaglandins, which damage the periodontal tissue. This biofilm is an independent entity with a strong ability to survive, and together with its bacteria and their by-products (lipopolysaccharides), results in damage to the periodontal tissue [9].

Systemic risk factors that can contribute to the development of a higher stage of periodontal disease in certain individuals are: diabetes; hormonal changes in women; genetic factors; certain medications; smoking; stress [10].

3. Treatment of Periodontal Disease

The key role in the treatment of periodontal disease lies in the reduction of inflammation, i.e. the removal of dental plaque and most of the periopathogens adhering to the tooth connective tissue and alveolar bone.

In order to deal with the invasion of microorganisms, we need a detailed plan of action:

- Periodic examination and motivation of patients in order to maintain optimal daily oral hygiene, which includes removing plaque from all surfaces of the teeth;

- Mechanical and professional plaque removal, as well as the reduction or elimination of existing periodontal pockets (using conventional or surgical methods) such as *locus minoris resistentiae*;

- Systemic or local use of antibiotics and antiseptics;

- Laser removal of necrotic and granulation tissue and disinfection of periodontal pockets;

- Use of water–powder system to mechanically remove bacteria, or UV light systems for light-activated disinfection.

All of the above methods are used to reduce or eliminate periopathogens and their by-products, and thus eliminate inflammation [11-14].

We must address the misconception that dental calculus is the aetiological cause of periodontopathy, and that its removal is the only treatment of this complex process, which occurs in all periodontal tissue. Only live bacteria pose any danger and cause an inflammatory response in tissue and its subsequent demise, so the focus of each dentist should be the removal of dental plaque and the complete elimination of inflammation and all its mediators, to the very last bacteria.

The era of implants also necessitates the fight against bacterial colonisation. The concept that microorganisms are essential to the development of infection around dental implants has been well documented in many scientific studies [15]. The microorganisms associated with periodontal implants are similar to those present in periodontitis, while periodontal pockets are reservoirs for the microorganisms

that colonise newly inserted dental implants. Peri-implant disease is associated with predominantly gram-negative bacterial types. Patients prone to periodontal disease react differently to infective agents, as a result of a genetically pre-determined susceptibility, resulting in further periodontal tissue damage. For this reason, patients with a history of periodontal disease are at greater risk of developing peri-implantitis, compared to those without periodontitis [16].

3.1. Microbiological Differentiation of Periodontal Disease – Bacterial PCR as a Method of Qualitative and Quantitative Classification of Bacterial Types

Bacteria and their metabolic by-products are the main cause of periodontal tissue loss and loss of implants. It is therefore logical to track and define specific bacteria as indicators of the initial phase and progression of the disease, its active phase, as well as clinical verification of the exacerbated state of the disease. Thus far, there is no adequate clinical or radiological indicator that shows the true activity of periodontitis and there is always a large delay between the onset of the disease and the time at which changes can be clinically detected and identified on x-ray.

Sub-gingival plaque is a biofilm that consists of more than 500 different bacterial species; however, they are not all equally as significant to the lifespan of the disease, or the progression of periodontitis, just as complications with implants (peri-implantitis) are strictly associated with specific microorganisms.

Actinobacillus actinomycetemcomitans, *Porphyromonas gingivalis*, *Prevotella intermedia*, *Tannerella forsythia* (*Bacteroides forsythus*) and *Treponema denticola* all play a key role as a result of their exotoxins and directly affect inflammation and the increased loss of supportive periodontal tissue. In order to prescribe antibiotic therapy for the remaining bacteria, aside from physical treatment, a microbiological diagnosis is necessary [17]. Until now, this has been achieved using bacterial cultures. Polymerase chain reaction (PCR) is a method that consists of taking biological material (dental plaque, inflamed gingival tissue, gingival fluid or saliva) containing DNA of the infecting microorganisms to determine the most prevalent periopathogenic bacteria (*Porphyromonas gingivalis, Aggregatibacter actinomycetemcomitans, Prevotella intermedia*).

Benefits of microbiological diagnostics:

- increased prognostic value

- aids in planning appropriate therapeutic strategy

- targeted antibiotic therapy

- monitoring of successful periodontal therapy

- allows a high level of certainty when expensive interventions such as placing dental implants and prosthetic or orthodontic rehabilitation are necessary [18].

Features of PCR diagnostic techniques

- high level of specificity and sensitivity

- possibility of quantifying bacteria

- possibility of standardisation of samples [19].

PCR diagnostic techniques are an important aspect in the treatment of periodontitis. The specific and sensitive detection of periopathogens in the sub-gingival plaque allows for quick identification of high-risk patients and offers vital information on which type of therapeutic option to choose. This method is also of value during the course of periodontal treatment and can be used to document the success of therapy during and after treatment. During visits to maintain the results achieved by treatment (which both the doctor and patient must value and respect as being crucial to the successful long-term management of periodontitis), this method may help in the early detection of repeated active inflammation. It is also important that the test is run before each major prosthetic reconstruction in the oral cavity, in order to assess any possible risk posed by the implants. Finally, the results of the PCR identification of microorganisms can increase the patient's motivation to maintain good oral hygiene.

Unlike the bacterial cultivation method, this method, which is carried out at the nucleic acid level, does not depend on the presence of living bacteria. This means simplified sample collection and transport [20,21].

3. 2. Laser Therapy for Curettage of the Soft Tissue Wall of the Periodontal Pocket and Disinfection of Periodontal Tissue

The primary goal of periodontal treatment is to eliminate inflammation through the reduction and/or complete removal of the offending microorganisms. The current approach to dealing with infection, besides mechanical removal, involves the systemic or local use of medication. There are two problems facing this approach. First, contraindications are a factor for a

certain percentage of patients, as is pregnancy among female patients. The second problem, given the chronic nature of periodontal disease, is that the repeated use of antibiotics may lead to the resistance of certain bacterial types due to mutation. For these reasons, laser therapy, which uses the photo-thermal effect to fight bacterial infection, is strongly recommended as a new therapeutic option and supplementary method to classical treatment approaches. Periodontal disease can be treated with laser therapy at any stage [22].

The use of Nd:YAG lasers in the treatment of chronic periodontitis is based on successful sub-gingival curettage, which allows the creation of a new attachment through regeneration of the cementum and periodontal ligament, and contributes to the formation of the alveolar bone [23]. These results are achieved through a reduction in the number of bacteria in the periodontal pocket and coagulation of the inflamed and necrotic tissue. This results in a biostimulatory effect that helps the tissue to heal, and reduces the need for haemotherapeutics. The bactericidal effect of the laser extends 3–4 mm into the tissue [24,25].

This gives laser therapy a great advantage over systemic antibiotic therapy, since laser radiation does not negatively affect the rest of the body and does not cause resistance. The minimal risk of creating resistant bacteria is laser therapy's greatest advantage [26]. Some studies suggest that the use of the laser as a supplement to the conventional treatment of periodontal pockets SRP (scaling and root planning) can significantly improve outcomes [27, 28].

3.3. Current Concepts on Disinfection of Periodontal Pockets

3.3.1. Air Flow Method for Removal of Biofilm

This method uses water, air and powder as an additional means of accessing periodontal pockets to help destroy the biofilm, and can be used to polish and remove plaque, even in the deepest areas of periodontal pockets exceeding 5 mm in depth, unlike conventional methods [29].

Three different powders are available: for sub-gingival use and the elimination of bacteria in deeper pockets; for regular prophylaxis and for patients with sensitive gums; and for basic polishing, whitening and removal of deposits [30]. Microorganisms colonise periodontal tissue and grow, creating a zone in which they are completely isolated and protected from external factors, i.e. the biofilm. Here, they are resistant to medication. However, the immune mechanisms of the host begin to act, and, in order to prevent bacterial invasion, release mediators that can damage the alveolar bone. This also applies to implants that are affected by biofilm, and the resulting peri-implantitis culminates in loss of the implants. We can conclude from this that implants are a poor investment without the proper prophylactic measures. Peri-implantitis is identical to periodontitis among patients with implants. The biofilm adheres to the titanium implants, causing infection, which ultimately leads to damage of the alveolar bone and implant loss. The use of this method restores the biocompatibility of the titanium implant with the alveolar bone, due to the optimal abrasion of the titanium surface [31].

The advantages of this method are as follows: simple and delicate access to tissue with controlled turbulence of the powder and water mixture, allowing the prevention of soft tissue emphysema; the gentle application of bio-kinetic energy generated by this method is not abrasive to the tooth surface; efficient removal of biofilm deep within periodontal pockets with no damage to the cementum; continuous reduction of bacterial persistence prevents loss of teeth or implants in patients with periodontopathy and peri-implantitis; effective polishing without damage to the epithelium or connective tissue; quick, stress-free treatment for maximum patient comfort [32].

3.3.2. Light-Activated Disinfection (LAD)

The principle of photo-dynamic therapy has been known for over 100 years, but has received increased interest in the past 10 years based on its use in the treatment of various microorganisms [33]. Oral bacteria are trapped in the biofilm, an extracellular matrix of microorganism polymers and self-protective host molecules, and are somehow protected from medication such as antibiotics and antiseptics as well as the immune reactions of the host, and to some degree, external factors. Nascent oxygen breaks down this interaction and makes the microorganisms more sensitive to further damage [34]. Oral LAD therapy is of particular interest because of its straightforward method of application, and is a powerful source of non-laser light that is technically uncomplicated to use as well as being relatively inexpensive [35]. The photosensitizer attaches to the surface of microorganisms, absorbs light in a specific spectrum, and receives energy. The energy received affects the O_2 molecule of nascent oxygen,

which reacts strongly and instantaneously to destroy microbial cell walls as well as their internal organelles [36].

Periodontal Treatment: After preparing the periodontal pockets, the photosensitizer is introduced into the pockets. Deep pockets are illuminated for 10 seconds with a long tip within the pocket, and then from the outside for 10 seconds with a blunt tip against the gingiva. This method is also used to treat peri-implantitis, gingivitis and pericoronitis (external application), and caries, and for endodontic treatment [37].

The advantages of LAD therapy are as follows: can be used as needed and works instantaneously; effective on all microorganisms; no resistance develops; quick and accurate results; the treatment is safe for both patient and practitioner; easy application and a powerful source of non-laser light; quick and easy to apply; low-cost treatment [38, 39].

3.3.3. Probiotic Therapy

What is probiotic therapy? Probiotics are live bacteria with a weakened structure that beneficially activate the immunity of a host and improve the microbial flora of the oral cavity [40]. These living microorganisms are administered at appropriate levels and result in sufficient benefit for the host organism. The mechanism by which probiotics work in the oral cavity is based on two separate, but complementary, pathways: exchange of supplemental pathogen flora, which is strengthened as a result of antibiotic therapy (chemical activity), and control of immunological protection (local or systemic) [41].

The benefits of probiotic therapy are: inhibition of bacterial growth; reduction of plaque accumulation; reduction of gingival bleeding; does not cause irritation of the soft tissue; does not cause discolouration of the teeth; has a pleasant flavour; probiotics are naturally found, not synthetic; can be introduced to the daily maintenance of oral hygiene; and can be used in combination with other medication. The use of probiotics is widely supported by numerous clinical studies [42].

Probiotics stimulate the systemic and oral immune system and restore the appropriate concentration of antigens. Some of these bacteria produce antimicrobial agents, while others take the place of harmful colonising bacteria. These mechanisms prevent the growth of undesirable microflora and return microbial balance to the oral cavity. Probiotics are also important, as they selectively inhibit periopathogens. In relation to antibiotic therapy, probiotics are beneficial since antibiotics act non-selectively against bacteria; they destroy the balance of an already unbalanced oral microflora and inhibit the defensive mechanisms of the host [43]. Probiotics can be administered as a supplement to periodontal therapy, in order to stabilise and minimise inflammation and to re-establish homeostasis of the oral bacteria.

Patients who are at risk for plaque accumulation for any reason, or have gingival inflammation, stomatitis or periodontitis, can be treated with oral probiotics. They can also be useful for patients with immunodeficiency disorders and acute or chronic stress, as well as for reducing side-effects among patients taking oral contraceptives, antihistamines, anti-depressives, anticancerogenic medication, steroids and other medications that lead to a dry mouth.

Probiotics are safe for use by children, pregnant women, diabetics, patients with osteoporosis, patients with orthodontic treatments, smokers and elderly patients [44].

References

1. Mcleod D. A practical approach to the diagnosis and treatment of periodontal disease. J Am Dent Assoc. 2000;131(N4):483–91.

2. Page RC. The pathobiology of periodontal diseases may affect systemic diseases: inversion of a paradigm. Ann Periodontol. 1998;1:108–20

3. Lopez NJ, Da Silva I, Ipinza J, Gutierrez J. Periodontal therapy reduces the rate of preterm low birth weight in women with pregnancy-associated gingivitis. J Periodontol. 2005;76(11 Suppl):2144–53.

4. Lopez NJ, Smith PC, Gutiererez J. Periodontal therapy may reduce the risk of preterm low birth weight in women with periodontal disease: a randomized controlled trial. J Periodontol. 2002;73(8):911–24.

5. Offenbacher S, Lin D, Strauss R, et al. Effects of periodontal therapy during pregnancy on periodontal status, biological parameters and pregnancy outcomes: a pilot study. J Periodontology. 2006;77(12):2011–24.

6. Atanasovska-Stojanovska A, Stojovski M, Popovska M. Higher risk of preterm birth and low weight in woman with periodontal disease. Balkan J Stom. 2007;11:62–8.

7. Aimetti M, Romano F, Nessi FJ. Microbiological analysis of

periodontal pockets and carotid atheromatous plaques in advanced chronic periodontitis patients. J Periodontol. 2007;78(9):1718–23.

8. Sánchez MC, Llama-Palacios A, Blanc V, et al.. Structure, viability and bacterial kinetics of an in vitro biofilm model using six bacteria from the subgingival microbiota. J Periodontal Res. 2011;46(2):252–60.

9. Hojo K, Nagaoka S, Ohshima T, Maeda N. Bacterial interactions in dental biofilm development. J Dent Res. 2009;88(11):982–90.

10. Scannapieco FA. Periodontal inflammation: from gingivitis to systemic disease? Compend Contin Educ Dent. 2004;27 (7 suppl 1):16-25.

11. Khuller N, Sharma N. Recent trends in periodontal treatment (surgical and non- surgical): A review. The Internet Journal of Dental Science. 2009;7(2).

12. Dae Hyun L. Application of laser in periodontics: A new approach in periodontal treatment. Dental Bulletin. 2007;12(10).:23-25.

13. Umeda M.,Takeuchi Y.,Noguchi K et all.Effects of nonsurgical periodontal therapy on the microbiota. Periodontol 2000. 2004;36:98-120.

14. Petersilka GJ, Ehmke B, Fleming TF. et all Antimicrobial effects of mechanical debridment. Periodontol 2000. 20002: 28:56-71.

15. Sanchez-Garces MA, Gay-Escoda C. Peri-implantitis. Med Oral Patol Oral Cir Bucal. 2004;9(Suppl. 69–74):63–9.

16. Barboza EP, Caula AL, Carvalho WR. Crestal bone loss around submerged and exposed unloaded dental implants: a radiographic and microbiological descriptive study. Implant Dent. 2002;11(2):162–9.

17. Subramani K, Jung RE, Molenberg A, Hammerle CH. Biofilm on dental implants: a review of the literature. Int J Oral Maxillofac Implants. 2009;24(4):616–26.

18. Loomer PM. Microbiological diagnostic testing in the treatment of periodontal diseases. Periodontol 2000. 2004:34:49-65

19. Masunaga H, Butae W, Oh H, Shinozuka N, Lishimoto N, Ogata Y. Use of quantitative PCR to evaluate methods of bacteria sampling in periodontal patients. J Oral Sci. 2010;52(4):615–21.

20. Jewoe-Storm PM, Koltscher M, Falk W, et al. Comparation between culture and real time PCR for detection and quantification of 5 putative periopathogenic bacteria in subgingival plaque samples. J Clin Periodontol. 2005;32:778-783.

21. Eick S, Pfister W. Comparation of microbial cultivation and a commercial nuclear acid based method for detection of periodontopathogenic species in subgingival plaque samples. J Clin Periodontol. 2002; 29:638-644.

22. Cobb CM. Laser in periodontics: A review of the literature. J Periodontol. 2006;77(4):545–64.

23. Slot DE, Kranendonk A.A., Paraskevas S. et al. The effect of a pulsed Nd:Yag laser in non surgical periodontal therapy: A systematic review. J Periodontol. 2009; 80:1041–56.

24. Schwartz F, Aoki A, Becker J, Sculean A. Laser application in non-surgical periodontal therapy: a systematic review. J Clin Periodontol. 2008;35(8 Suppl):29–44.

25. Dilsiz A, Aydin T, Canakci V, Gungorums M. Clinical evaluation of Er:Yag, Nd-Yag and diode laser therapy for desensitization of teeth with gingival recession. Photomed Laser Surg. 2010;28(Suppl 2):311–7.

26. Cobb CM, Loev SB, Coluzzi DJ. Lasers in the treatment of periodontitis. Dent Clin N Am. 2010;54(1):35–53.

27. Dilsit A, Canaki V, Ozdemir A, Kaya Y. Clinical evaluation of Nd:Yag and 685 diode laser therapy for desensitization of teeth with gingival recession. Photomed Laser Surg. 2009;27(6):843–8.

28. Atanasovska - Stojanovska A, Popovska M. Clinical evaluation of the effectiveness of the Fidelis III Nd:Yag laser as an adjunct to conventional periodontal treatment of chronic periodontitis Balkan J Stom. 2011;15:155-160.

29. Moëne R, Décaillet F, Andersen E, Mombelli A. Subgingival plaque removal using a new air-polishing device. J Periodontol. 2010;81:79–88.

30. Petersilka G, Faggion Jr. CM, Stratmann U, et al. Effect of glycine powder air-polishing on the gingiva. J Clin Periodontol. 2008;35(4):324–32.

31. Schwarz F, Ferrary D, Popovski K, Hartig B, Becker J. Influence of different air-abrasive powders on cell viability at biologically contaminated titanium dental implants surfaces. J Biomed Mat Res B Appl Biomater. 2009;88(1):83–91.

32. Schwarz F, Sculean A, Romanos G, et al. Influence of different treatment approaches on the removal of early plaque biofilms and the viability of SAOS2 osteoblasts grown on titanium implants. Clin Oral Investig. 2005;9(2):111–17. Epub 2005 Apr 20.

33. Upadya MH, Kishen A. Influence of bacterial growth modes on the susceptibility to light activated disinfection. Int Endod J. 2010;43(11):978–87.

34. Bouillaguet S, Wataha JC, Zapata O, et al. Production on reactive oxygen species from photosensitizers activated with visible light sources available in dental offices. Photomed Laser Surg. 2010;28(4):519–25.

35. Gambarini G, Plotino G, Grande NM, et al. In vitro evaluation of cytotoxicity of Foto San light activated disinfection on human

fibroblasts. Med Sci Monit. 2011;17(3):MT21–5.

36. Zazparhooh A, Shah PS, Tenebaum HC, Goldbarg MR. The effect of photodynamic therapy for periodontis: A systemic review and meta-analysis. J Periodontol. 2010;81:4–14.

37. George S, Kishen A. Augmenting the antibiofilm efficacy of advanced noninvasive light activated disinfection with emulsified oxidizer and oxygen carrier. J Endod. 2008;34(9):1119–23.

38. El Yazami H, Zeinoun T, Bou Saba S, et al. Pulp temperature increased during photo-activated disinfection (PAD) of periodontal pockets: an in vitro study. Lasers Med

Sci. 2010;25(5):655–9.

39. Bergmans L, Moisiadis P, Huybrechts B, et al. Effect of photo-activated disinfection on endodontic pathogens ex vivo. Int Endod J. 2008;41(3):227–39.

40. Alvarez-Olmos MI, Oberhelman RA. Probiotic agents and infectious disease: a modern perspective on a traditional therapy. Clin Infect Dis. 2001;32(11):1567–76.

41. Caglar E, Kavaloglu SC, Kuscu OO, et al. Effect of chewing gums containing xylitol probiotic bacteria on salivary Mutans, Streptoccoci and Lactobacilli. Clin Oral Investig. 2007;11(4):425–9.

42. Jones SE, Versalovic J. Probiotic Lactobacillus reuteri biofilms produce antimicrobial and anti-inflammatory factors. BMC Microbiol. 2009;9:35.

43. Shimauchi H., Mayanagi G., Nakaya S., et al Improvment of periodontal condition by probiotics Lactobacillus salivarius WB 21:a randomized, double-blind, placebo-controled study J Clin Periodontol. 2008;35(10):897-905.

44. Krasse P, Carlsson B, Dahl C, et al. Decreased gum bleeding and reduced gingivitis by the probiotic Lactobacillus reuteri. Swed Dent J. 2006;30(2):55–60.