

Mouthwash: A review for South African health care workers

^aVan Zyl AW, BChD, MChD (OMP)(Stell) ^bVan Heerden WFP, BChD, MChD (Oral Path)(Pret), FC Path (SA) Oral Path, PhD, DSc

^aDepartment of Periodontics and Oral Medicine, University of Pretoria, Pretoria, South Africa

^bDepartment of Oral Pathology and Oral Biology, University of Pretoria, Pretoria, South Africa

Correspondence to: Prof Andre van Zyl, e-mail: andrevanzyl@up.ac.za

Keywords: mouthwash, oral rinses, chlorhexidine

Abstract

Many conditions within the oral cavity require the use of a mouthwash. This can vary from breath fresheners to treatment of life threatening secondary infections such as oral mucositis in patients undergoing bone marrow transplant therapy. The use of mouthwashes requires a correct diagnosis of the oral condition and a thorough knowledge of the product in question to achieve effective treatment. It is the objective of this review to help health care workers in South Africa make the correct choice of treatment when dealing with diverse conditions of the oral cavity.

Peer reviewed. (Submitted:2009-10-12, Accepted:2010-03-17). © SAAFP

SA Fam Pract 2010;52(2): 121-127

Introduction

The use of mouthwash to control oral bacteria goes back almost 5000 years when the Chinese recommended the use of a child's urine for the control of gingivitis.¹ The modern era of mouthwashes was introduced by the release of Listerine® as an over-the-counter (OTC) remedy for bad breath in 1914. Mouthwash use is usually based on anecdotal evidence rather than scientific evidence. This is especially true for OTC products and there is even less data on herbal remedies.²⁻³ This often leads to the use of an inappropriate product and incorrect mode of application, with the end result a failed treatment outcome.⁴ Mouthwashes can be used for many preventative and therapeutic purposes (see discussion later).^{2-3,5-7} This review will address some of the different products currently on the market in South Africa, their uses in different clinical settings, and the correct protocols for their use. It is however important to remember that many systemic diseases may predispose patients to oral conditions, and that a thorough examination, both oral and systemic, as well as a thorough medical and dental history remain the cornerstones of good clinical practice. It is not within the scope of this article to review those systemic conditions, and for the purpose of mouthwash use, the clinical protocol remains the same, regardless of possible underlying systemic conditions.

Antibacterial rinses have many uses in the oral cavity. For antibacterial rinses to be effective in the oral cavity they need to be bactericidal or bacteriostatic and most

of all must have a degree of substantivity.⁸ Substantivity in a mouthwash is that property that ensures the effect is sustained for a longer period than just the time it is held in the mouth.³ This is especially important with mouthwashes due to the dilution effect of saliva and fluid intake, which will diminish the effect within minutes if there is no substantivity.

Of all the antimicrobial mouthwashes, chlorhexidine gluconate (CHX), a bis-biguanide, has been the most widely studied, and has consistently been shown to be the most effective in the management of oral infections.^{4,9-11}

CHX is a cationic substance that binds to all negatively charged surfaces and is then released over a period of 7–12 hours.¹² Due to its cationic nature, it can interact with anionic substances such as toothpaste and be neutralised. It has a broad spectrum antimicrobial action. CHX does not work by interaction with any microbial enzymes or receptors and therefore does not lead to resistance build-up from organisms.³ It is effective against gram-positive and -negative bacteria, yeasts (such as *Candida*) and viruses with a lipid envelope.¹³⁻¹⁴

CHX does have unwanted side effects, such as unpleasant taste, staining of teeth and tongue, gingival desquamation, taste disturbance and painful mucosa.¹⁵⁻¹⁶ There are two concentrations available in South Africa, namely 0.12% (Paroex®) and 0.2% (Corsodyl® or any generic). The rationale for using the lower concentration is to minimise the side effects whilst maintaining the benefits of the CHX. It has

been shown that the effect of CHX rinse is dose-dependent, rather than just reliant on the concentration.¹⁷ It is therefore important to inform patients in detail on the correct dosage, depending on which concentration is prescribed, namely 15 ml for the 0.12% solution and 10 ml for the 0.2% solution.¹⁷ The length of time of the rinsing seems to be less important and 30 seconds is an acceptable length of time to ensure good compliance and efficacy.¹⁸

Chlorhexidine can also be used in the management of oral candidiasis.⁷ Although it is very effective with other topical agents, patients should be advised not to use it simultaneously as the chlorhexidine may inhibit the uptake of the second topical agent (such as topical miconazole).

Patients should be advised to observe nil per mouth for 15 minutes after rinsing to prevent dilution/removal of the CHX before it can bind to oral surfaces. We advise patients that the best time for rinsing is just before going to bed and after breakfast, with at least a 30 minute interval after tooth brushing. According to some this interval should be longer if possible, or alternatively the mouth should be rinsed vigorously with water after tooth brushing and before using the CHX rinse.^{3,19}

Alternative products to CHX are cetylpyridinium chloride (Cepacol[®]) rinse (a quaternary ammonium compound) and hexetidine (Oraldine[®]). Whilst not as effective as CHX, they do have fewer side effects.²⁰⁻²¹ Another alternative to CHX is Listerine[®] (essential oils). Listerine[®] does have a beneficial effect in the treatment of gingivitis and halitosis,¹ but is not suitable for ulcerative conditions due to the alcohol content of more than 20% by volume.

Analgesic mouthwashes are generally used in cases such as ulcerative conditions. Anti-inflammatory rinses such as those containing benzydamine hydrochloride (Andolex[®]), will have analgesic effects as well.² Alternatively a topical anaesthetic rinse combined with anti-microbial substances can be used, such as benzocaine combined with CHX 0.2% (Orochlor[®]). The side effect of a numb mouth is an unpleasant sensation that may put off many patients from preparations with a topical anaesthetic.

Anti-inflammatory mouthwashes are ideal in situations where there is an element of inflammation either as the primary cause of the condition, or as a secondary complication to the condition. The best known of these rinses contain benzydamine hydrochloride alone (Andolex[®]) or in combination with CHX (Andolex-C[®]). Benzydamine hydrochloride works through stabilisation of cell membranes (preventing the release of arachidonic acid) and inhibits cyclo-oxygenase, reducing synthesis of prostaglandins and related substances which promote inflammation.²²

Breath freshening mouthwashes have been used for many years. Listerine[®] was the first to be marketed exclusively for bad breath treatment in 1914 and is still one of the most popular rinses in the United States of America. In the recent past a two-phase mouthwash (Dentyl pH[®]) has been developed for the treatment of bad breath (halitosis) and this is currently one of the most popular rinses in the western world. It combines two antibacterial substances that have a proven track record in the reduction of bacteria intra-orally (cetylpyridinium chloride and triclosan), combined with oil that binds bacteria.²³ An additional benefit is that it contains fluoride and is alcohol free.

Fluoride mouthwashes have been used for many years to prevent caries. It is a well known fact that fluoride rinses will protect the permanent dentition against caries, but the effect on the primary dentition is not that clear cut.²⁴ Many antibacterial rinses now contain fluoride in an attempt to combine the benefits of both.³ ORO-NaF[®] is an alcohol-free 0.05% sodium fluoride rinse for daily use, and is available through dentists.

Salivary substitute mouthwashes are used for the symptomatic treatment of xerostomia. The objective of these mouthwashes is to facilitate speech, eating and swallowing.⁷ There are not many mouthwashes on the market in South Africa for this purpose. Products that can be recommended are Biotène[®] and Xerostom[®] (a betaine-olive oil base alcohol-free mouthwash). Betaine has been found to alleviate xerostomia and to protect the oral mucosa against irritating substances.²⁵⁻²⁶

Covering agents are beneficial in ulcerative conditions. The idea behind a covering agent in the mouth is that it will protect the broken mucosa against further trauma and allow the ulcer to heal undisturbed. Sucralfate is a covering agent for stomach ulcers that has been tested for the mouth, but with mixed results.²⁷ Gelclair[®] is a covering agent for the mouth that has shown an improvement of more than 80% in pain management of mucositis patients.²⁸⁻²⁹ A slightly different version of it is available in South Africa as a spray or mouthwash (Alocclair[®]). It is alcohol free and is therefore also suitable for use in babies when applied with a spray nozzle.

Mouthwashes for specific conditions (See Table I)

Oral mucositis

Oral mucositis is a complication affecting many patients receiving chemotherapy, head and neck radiation and those undergoing bone marrow transplant therapies.³⁰⁻³² Oral mucositis can develop from the direct effect of cytotoxic drugs on oral mucosa due to the rapid turnover of oral epithelium, although the pathogenesis is probably more

complicated than that.³³ Should mucositis interfere with cancer therapy, the costs can be crippling, and in severe cases lead to discontinuation of cancer therapy.^{34–35} Topical pain control in oral mucositis can be problematic as topical anaesthetics have a very short duration of effectiveness (less than two hours) and most patients therefore rely on systemic opioid analgesics for effective pain control.^{30,36} Plaque control and good oral hygiene maintenance are important factors in the prevention and management of oral mucositis.³² Chlorhexidine mouthwashes can be used for this purpose, but combination rinses are more suitable as the side effects are normally less than single agent rinses. A combination rinse that is effective for mucositis is Andolex-C[®] which can be used 3–4 times per day, 15 ml per rinse delivering an effective dose. Orochlor[®] is also a good option. An alcohol free CHX 0.12% rinse for antimicrobial effect, is Paroex[®]. The correct regimen is 15 ml 2–3 times per day. Covering agents such as Aloclair[®] can be used throughout the day to help ease the discomfort and has been shown to provide a significant improvement in the pain management of these patients.^{28–29}

Halitosis

The majority (85%) of cases of halitosis are intra-oral in origin and are caused by micro-organisms.⁵ This does imply that 15% of halitosis cases can be from extra-oral causes, such as nasal. A correct diagnosis is therefore important. An accurate diagnosis of oral halitosis, evaluating all possible aetiological factors such as periodontal disease, caries, tongue coatings, peri-implant disease, food impaction and xerostomia to name a few, is important, before effective management can be achieved.⁵ Treatment is based on a multi-factorial approach directed towards reducing accumulation of food debris and oral micro-organisms.⁵ This may require periodontal therapy if periodontitis is the main cause, restorative treatment if caries is the culprit, or even extensive treatment of peri-implant disease.

A tip for diagnosing periodontal disease is to check for red or swollen gum tissues, or to ask the patient about loose teeth or bleeding gums during brushing. In severe advanced periodontitis teeth will drift and spaces will appear between incisor teeth.

Several types of mouthwashes, especially those with chlorhexidine, triclosan and cetylpyridinium as active ingredients may be useful for the chemical reduction of oral bacteria.³⁷ Masking products containing menthol or mint only is of limited use due to the short-term effect. Mouthwashes containing a combination of low concentrate of zinc with chlorhexidine, with or without cetylpyridinium have shown improved synergistic effects in clinical trials.^{38–39} Listerine[®] mouthwash can be effective against halitosis and was in

fact the first mouthwash to be used for this purpose. It can however cause burning of the oral mucosa when used, due to the high alcohol content. A recently launched product is the alcohol-free two-phase rinse, Dentyl pH[®], and this is currently one of the most popular rinses for the treatment of halitosis in the UK and USA. It also contains fluoride.

Xerostomia

Xerostomia is not a disease but a sign of an underlying condition or side effect of treatment, most notably a range of medications and radiation to the head and neck area. Radiation therapy of the head and neck area not only diminishes the volume of saliva, but changes the consistency to thick sticky saliva and reduces the pH.^{7,40}

Xerostomia is a common sign in the elderly, with the added complication that older people tend to be on more medication, which can have xerostomia as a side effect.⁷ Although there is a perception that salivary function decreases with age, there is no scientific proof that this is the case.⁷ Symptomatic treatment is based on stimulation of saliva production, avoidance strategies (dry sticky food), saliva replacement and prevention of oral disease.⁷ Excellent plaque control is imperative to prevent caries, so regular visits to an oral hygienist would be advisable.

Nonalcohol-containing chlorhexidine mouthwashes can be used for additional bacterial and fungal control while fluoride rinses should be part of a fluoride delivery system for caries control.^{7,32} This is especially important for those patients with severe xerostomia, such as in radiation therapy. Several salivary replacement products are on the South African market of which Biotène[®] and Xerostom[®] are effective. DentylpH[®] can also be of benefit. Drinking frequent small amounts of sugar free liquid can also be beneficial.

Periodontal (gum) diseases

Gingivitis and periodontitis are generally known as gum diseases and are two of the most common diseases in the world.^{41–42} Gingivitis is generally a superficial infection of the gingiva around teeth, with periodontitis a deeper infection involving the alveolar bone. This explains why gingivitis will respond to mouthwashes and periodontitis not. It is therefore important to make the correct diagnosis in order to prescribe the correct treatment. As periodontitis has implications for general health,^{43–45} it is important to refer the patient to a dentist if in doubt. For the treatment of gingivitis, CHX mouthwash at concentrations of either 0.12% or 0.2% is the most effective and can reduce the incidence up to 80%.⁴⁶ In South Africa Corsodyl[®] was the first available 0.2% commercial rinse and Paroex[®] was the first available 0.12% rinse. Andolex-C[®] is also a good option for the inflammation and bacterial control. There are many generic 0.2% rinses available.

Table I: Suggestions for product choice in different clinical conditions

| Clinical condition | Treatment | Active ingredients | Commercial product in South Africa |
|--|--|--|--|
| Oral mucositis/oral sores (alcohol free) | Covering agent | Polyvinylpyrrolidone/ various | Alclair® |
| | Anti-inflammatory | Benzydamine hydrochloride | Andolex® |
| | Antimicrobial | Chlorhexidine 0.12% Generic CHX 0.2% Povidone Iodine | Paroex® Various Betadine Oral rinse |
| | Analgesic/anti-inflammatory/ antimicrobial | Benzydamine hydrochloride/ chlorhexidine | Andolex-C® |
| | Antimicrobial/analgesic | Benzocaine/chlorhexidine | Orochlor® |
| Halitosis | Antimicrobial, without flavourings | Generic CHX 0.2% Chlorhexidine 0.12% Chlorhexidine 0.2% | Various Paroex® 0.12% Corsodyl® (original) |
| | Antimicrobial, with flavourings | Chlorhexidine 0.2% Cetylpyridinium chloride, triclosan with oil Essential oils | Corsodyl® (mint) DentylpH® Listerine® |
| Xerostomia | Saliva substitute with antimicrobial properties | Betaine/olive oil/xylitol/fluoride Various enzymes Cetylpyridinium chloride, triclosan with oil | Xerostom® Biotene® DentylpH® |
| | Tooth protection –fluoride | Sodium fluoride 0,05% | ORO-NaF® |
| Periodontal (gum) diseases | Antimicrobial with or without flavourings | Chlorhexidine 0.2% Chlorhexidine 0.12% Benzydamine hydrochloride / Chlorhexidine | Corsodyl® Generic CHX 0.2% Paroex® 0.12% Andolex-C® |

Alcohol-containing mouthwashes

A number of commercially available mouthwashes contain alcohol at between 5 and 27%. Several studies have been performed over the last few decades to determine a relationship between alcohol-containing mouthwash and the risk of developing oropharyngeal cancer. Critical reviews of the study designs and reanalysis in some cases have shown no correlation between alcohol-containing mouthwashes and an increased risk of oropharyngeal cancer.⁴⁷⁻⁴⁸ It was demonstrated in a recent German study that alcohol-containing mouthwashes lead to acetaldehyde (toxic metabolite of ethanol) concentrations in saliva similar to those found after consumption of alcoholic beverages.⁴⁹

Until there is clarity on this issue, alcohol-containing mouthwashes should be restricted to short-term therapeutic situations under supervision. The use of alcohol-containing mouthwashes over the long term should be discouraged.

Conclusion

As can be seen from the above, the use of mouthwashes can be varied, depending on the lesion/condition present in the mouth. It is the authors' view that clinicians should be aware of all the different aetiological factors

and possible predisposing systemic conditions when dealing with a particular oral lesion/condition. Systemic diseases such as diabetes mellitus and acquired immune deficiency syndrome, may predispose a patient to fungal infections as well as periodontal disease and health care workers should be aware of these and other conditions. Clinicians should also take cognisance of the possible interactions between products, such as chlorhexidine that can block the action of another topical preparation given simultaneously. In such cases the use of products can be administered with appropriate intervals. Health care workers should also be aware that many medications may have side effects on the oral cavity, such as for example psychotropic and diuretic drugs that can lower the salivary flow.⁵⁰ Alternative products can sometimes be prescribed with a lesser effect on salivary flow. When in doubt, consult with a colleague.

References

1. Mandel ID. Chemotherapeutic agents for controlling plaque and gingivitis. *J Clin Periodontol* 1988;15:488-98.
2. Scully C, Field EA, Randall C. Over-the-counter remedies for oral soreness. *Periodontol 2000* 2008;48:76-84.
3. Moran JM. Home-use oral hygiene products: mouthrinses. *Periodontol 2000* 2008;48:42-53.
4. Lang NP, Tan WC, Krahenmann MA, Zwahlen M. A systematic review

- of the effects of full-mouth debridement with and without antiseptics in patients with chronic periodontitis. *J Clin Periodontol* 2008;35:8–21.
5. Scully C, Greenman J. Halitosis (breath odor). *Periodontol* 2000 2008;48:66–75.
 6. West NX, Moran JM. Home-use preventive and therapeutic oral products. *Periodontol* 2000 2008;48:7–9.
 7. Eveson JW. Xerostomia. *Periodontol* 2000 2008;48:85–91.
 8. Grossman E, Meckel AH, Isaacs RL, Ferretti GA, Sturzenberger OP, Bollmer BW, et al. A clinical comparison of antibacterial mouthrinses: effects of chlorhexidine, phenolics, and sanguinarine on dental plaque and gingivitis. *J Periodontol* 1989;60:435–40.
 9. Milstone AM, Passaretti CL, Perl TM. Chlorhexidine: expanding the armamentarium for infection control and prevention. *Clin Infect Dis* 2008;46:274–81.
 10. Renvert S, Roos-Jansaker AM, Claffey N. Non-surgical treatment of peri-implant mucositis and peri-implantitis: a literature review. *J Clin Periodontol* 2008;35:305–15.
 11. Loe H, Schiott CR. The effect of mouthrinses and topical application of chlorhexidine on the development of dental plaque and gingivitis in man. *J Periodontal Res* 1970;5:79–83.
 12. Bonesvoll P, Lokken P, Rolla G, Paus PN. Retention of chlorhexidine in the human oral cavity after mouth rinses. *Arch Oral Biol* 1974;19:209–12.
 13. Harbison MA, Hammer SM. Inactivation of human immunodeficiency virus by Betadine products and chlorhexidine. *J Acquir Immune Defic Syndr* 1989;2:16–20.
 14. Suci PA, Tyler BJ. Action of chlorhexidine digluconate against yeast and filamentous forms in an early-stage *Candida albicans* biofilm. *Antimicrob Agents Chemother* 2002;46:3522–31.
 15. Flotra L, Gjermo P, Rolla G, Waerhaug J. Side effects of chlorhexidine mouth washes. *Scand J Dent Res* 1971;79:119–25.
 16. Lang N, Brex MC. Chlorhexidine digluconate; an agent for chemical plaque control and prevention of gingival inflammation. *Journal of Periodontal Research* 1986;21:74–89.
 17. Segreto VA, Collins EM, Beiswanger BB, Rosa M, Isaacs RL, Lang NP, et al. A comparison of mouthrinses containing two concentrations of chlorhexidine. *Journal of Periodontal Research* 1986;21:23–32.
 18. Van der Weijden GA, Timmerman MF, Novotny AG, Rosema NA, Verkerk AA. Three different rinsing times and inhibition of plaque accumulation with chlorhexidine. *J Clin Periodontol* 2005;32:89–92.
 19. Kolahi J, Soolari A. Rinsing with chlorhexidine gluconate solution after brushing and flossing teeth: a systematic review of effectiveness. *Quintessence Int* 2006;37:605–12.
 20. Haps S, Slot DE, Berchier CE, Van der Weijden GA. The effect of cetylpyridinium chloride-containing mouth rinses as adjuncts to toothbrushing on plaque and parameters of gingival inflammation: a systematic review. *Int J Dent Hyg* 2008;6:290–303.
 21. Ernst CP, Canbek K, Dillenburger A, Willershausen B. Clinical study on the effectiveness and side effects of hexetidine and chlorhexidine mouthrinses versus a negative control. *Quintessence Int* 2005;36:641–52.
 22. Quane PA, Graham GG, Ziegler JB. Pharmacology of benzydamine. *Inflammopharmacology* 1998;6:95–107.
 23. Kozlovsky A, Goldberg S, Natour I, Rogatky-Gat A, Gelernter I, Rosenberg M. Efficacy of a 2-phase oil: water mouthrinse in controlling oral malodor, gingivitis, and plaque. *J Periodontol* 1996;67:577–82.
 24. Poulsen S. Fluoride-containing gels, mouth rinses and varnishes: An update of evidence of efficacy. *Eur Arch Paediatr Dent* 2009;10:157–61.
 25. Rantanen I, Nicander I, Jutila K, Ollmar S, Tenovuo J, Soderling E. Betaine reduces the irritating effect of sodium lauryl sulfate on human oral mucosa in vivo. *Acta Odontol Scand* 2002;60:306–10.
 26. Rantanen I, Tenovuo J, Pienihakkinen K, Soderling E. Effects of a betaine-containing toothpaste on subjective symptoms of dry mouth: a randomized clinical trial. *J Contemp Dent Pract* 2003;4:11–23.
 27. Makkonen TA, Bostrom P, Vilja P, Joensuu H. Sucralfate mouth washing in the prevention of radiation-induced mucositis: a placebo-controlled double-blind randomized study. *Int J Radiat Oncol Biol Phys* 1994;30:177–82.
 28. The clinical effectiveness of Gelclair in the management of oral mucositis. *Aust Nurs J* 2009;16:30–3.
 29. Innocenti M, Moscatelli G, Lopez S. Efficacy of gelclair in reducing pain in palliative care patients with oral lesions: preliminary findings from an open pilot study. *J Pain Symptom Manage* 2002;24:456–7.
 30. Epstein JB, Epstein JD, Epstein MS, Oien H, Truelove EL. Doxepin rinse for management of mucositis pain in patients with cancer: one week follow-up of topical therapy. *Spec Care Dentist* 2008;28:73–7.
 31. Bellm LA, Epstein JB, Rose-Ped A, Martin P, Fuchs HJ. Patient reports of complications of bone marrow transplantation. *Support Care Cancer* 2000;8:33–9.
 32. Scarpace SL, Brodzik FA, Mehdi S, Belgam R. Treatment of head and neck cancers: issues for clinical pharmacists. *Pharmacotherapy* 2009;29:578–92.
 33. Scully C, Sonis S, Diz PD. Oral mucositis. *Oral Dis* 2006;12:229–41.
 34. Trotti A, Bellm LA, Epstein JB, Frame D, Fuchs HJ, Gwede CK, et al. Mucositis incidence, severity and associated outcomes in patients with head and neck cancer receiving radiotherapy with or without chemotherapy: a systematic literature review. *Radiother Oncol* 2003;66:253–62.
 35. Elting LS, Cooksley C, Chambers M, Cantor SB, Manzullo E, Rubenstein EB. The burdens of cancer therapy. Clinical and economic outcomes of chemotherapy-induced mucositis. *Cancer* 2003;98:1531–9.
 36. Rubenstein EB, Peterson DE, Schubert M, Keefe D, McGuire D, Epstein J, et al. Clinical practice guidelines for the prevention and treatment of cancer therapy-induced oral and gastrointestinal mucositis. *Cancer* 2004;100:2026–46.
 37. van den Broek AM, Feenstra L, de Baat C. A review of the current literature on management of halitosis. *Oral Dis* 2008;14:30–9.
 38. Winkel EG, Roldan S, Van Winkelhoff AJ, Herrera D, Sanz M. Clinical effects of a new mouthrinse containing chlorhexidine, cetylpyridinium chloride and zinc-lactate on oral halitosis. A dual-center, double-blind placebo-controlled study. *J Clin Periodontol* 2003;30:300–6.
 39. Thrane PS, Young A, Jonski G, Rolla G. A new mouthrinse combining zinc and chlorhexidine in low concentrations provides superior efficacy against halitosis compared to existing formulations: a double-blind clinical study. *J Clin Dent* 2007;18:82–6.
 40. Dirix P, Nuyts S, Van den Bogaert W. Radiation-induced xerostomia in patients with head and neck cancer: a literature review. *Cancer* 2006;107:2525–34.
 41. Brown LJ, Brunelle JA, Kingman A. Periodontal status in the United States, 1988–1991: prevalence, extent, and demographic variation. *J Dent Res* 1996;75 Spec No: 672–83.
 42. Oliver RC, Brown LJ, Loe H. Periodontal diseases in the United States population. *J Periodontol* 1998;69:269–78.
 43. Williams RC, Barnett AH, Claffey N, Davis M, Gadsby R, Kellett M, et al. The potential impact of periodontal disease on general health: a consensus view. *Curr Med Res Opin* 2008;24:1635–43.
 44. Niedzielska I, Janic T, Cierpka S, Swietochowska E. The effect of chronic periodontitis on the development of atherosclerosis: review of the literature. *Med Sci Monit* 2008;14:RA103–6.
 45. Agueda A, Echeverria A, Manau C. Association between periodontitis in pregnancy and preterm or low birth weight: Review of the literature. *Med Oral Patol Oral Cir Bucal* 2008;13:E609–15.
 46. Santos A. Evidence-based control of plaque and gingivitis. *J Clin Periodontol* 2003;30 Suppl 5:13–6.
 47. La Vecchia C. Mouthwash and oral cancer risk: an update. *Oral Oncol* 2009;45:198–200.
 48. Cole P, Rodu B, Mathisen A. Alcohol-containing mouthwash and oropharyngeal cancer: a review of the epidemiology. *J Am Dent Assoc* 2003;134:1079–87.
 49. Lachenmeier DW, Gumbel-Mako S, Sohnius EM, Keck-Wilhelm A, Kratz E, Mildau G. Salivary acetaldehyde increase due to alcohol-containing mouthwash use: a risk factor for oral cancer. *Int J Cancer* 2009;125:730–5.
 50. Persson RE, Izutsu KT, Truelove EL, Persson R. Differences in salivary flow rates in elderly subjects using xerostomatic medications. *Oral Surg Oral Med Oral Pathol* 1991;72:42–6.