Periodontitis as a Contagious Infection: Contemporary Use of Antimicrobial Agents. Part II

Ulrich Saxer, Thomas Hassell

Part I of this comprehensive review article dealt exclusively with the use of chlorhexidine in the practice of dentistry and dental hygiene. While it is universally accepted that chlorhexidine is one of the most effective antimicrobial agents for intraoral application, many other substances have also been proven to be effective when applied topically. Thus, Part II of this article provides in-depth descriptions of alternative agents for antimicrobial use in dentistry, by both the patient at home and the professional in the dental office.

Key words: halogens, quaternary ammonium bases, sanguinarin, sodium hypochlorite, providone iodine, heavy metal salts, phenols, triclosan

Halogens

Iodine: Betadine (providone iodine, PVP-I) is a potent antiseptic that is widely used in medicine and dentistry. It is bactericidal on contact, and is also effective against fungi, viruses and protozoa. PVP-I does not disturb wound healing (as CHX can), nor does it elicit the evolution of resistant bacterial strains. True allergy to providone iodine is exceptionally rare; reactions that were feared in early years have now been attributed to substances in the delivery solution and not to the elemental iodine (Kozuka, 2002). The addition of a 3% hydrogen peroxide solution can greatly enhance the effectiveness of iodine in the oral cavity, significantly reducing plaque and gingivitis (Rams and Slots, 1996; Greenstein, 1999). With direct contact (i.e., microorganisms NOT embedded within a dental biofilm aggregate), PVP-I is even more effective than CHX at low concentrations (0.1–0.5%) on most common subgingival pathogenic microorganisms such as *P. gingivalis* and *A. actinomycetemcomitans* (Kligerman and Bissada, 1975; Caulfield et al, 1987; Maruniak et al, 1992; Slots, 2000). Rosling et al (2001) reported 20 years of clinical use of PVP-I, with universally favorable results. The dentist or dental hygienist can use subgingival irrigation with PVP-I prior to scaling and root planing to reduce the danger of bacteremia, but this approach should be preceded by systemic antibiotic coverage in at-risk patients. Disadvantages of PVP-I, whether used clinically or at-home, include tooth discoloration and that some patients perceive intraoral sprays as uncomfortable or otherwise unpleasant to use.

Both PVP-I and CHX are used routinely in hospital settings, where they are viewed as practically equal in efficacy (Block et al, 2000; Humar et al, 2000; Traore et al, 2000). Although the early medical literature proclaims CHX to be more effective than PVP-I for disinfection, clinical studies have shown that PVP-I may be more effective when applied subgingivally (Caufield et al, 1987).

Chlorides: Sodium hypochlorite (NaClO), commonly known as "bleach," is an acceptable oral rinsing solution when diluted (0.05 – 0.5%; (Lobene, 1972)), according to the Council on Dental Therapeutics of the American Dental Association (1992). It is inexpensive and can be used in water spray devices (Rams and Slots, 1996; Slots, 2000). Very recent studies have demonstrated that a 0.1% chlorodioxide solution can have a significant influence on halitosis and dental plaque (Frascella et al, 2000); however, effective killing of microorganisms within mature biofilms requires at least a 10% concentration, which is generally unpalatable.

Fluorides: Stannous fluoride (SnF_2, the therapeutic ingredient in the very first fluoride toothpaste in the 1960s) must actually be categorized as a metal salt compound, because its effectiveness against plaque bacteria is due to its tin (Sn) content and not to the fluoride alone (Bay and Roella, 1980; Ogaard et al, 1980; Tinanoff et al, 1980; Leverett et al, 1981; Wieder et al, 1983; Tinanoff, 1995). In Europe and Japan, SnF_2 is available over-the-counter as an effervescent tablet ("ParoCare"®) and as such can be used in water spray devices or as a 0.02% oral rinse at home, or in the dental operatory for rapid and practical disinfection, plaque reduction and simultaneous dental fluoridation (Mazza et al, 1981; Wolff et al, 1989; Oosterwaal et al, 1991). When applied as a gel, stannous fluoride significantly reduces plaque accumulation around bridge abutment teeth (Tinanoff et al,1989).
Regular and continued use of stannous fluoride preparations will result in a light yellowish discoloration of teeth unless the teeth are also routinely cleaned with an abrasive dentifrice (Ciancio, 1985, 1995).

Heavy Metal Salts

Zinc salts are effective plaque-inhibiting agents (Skjörland et al, 1978; Harrap et al, 1983; Jones et al, 1988). Zinc also reduces the acidogenic potential of dental plaque (Oppermann et al, 1980). Combinations of zinc salts with hexetidine (see below) or other substances have led to additive and synergistic effects (Saxer and Mühlemann, 1983; Giertsen et al, 1987; Günbay et al, 1992; Jackson, 1997). With 3x daily rinsing, plaque inhibition similar to that achieved with CHX was observed using a combination of zinc and hexetidine (Saxer and Hug, 1984). A rinsing solution containing 0.4% zinc sulfate and 0.15% triclosan (see below) was shown to significantly reduce dental plaque, calculus formation and gingival inflammation (Schaeken et al, 1996). When incorporated as the single active ingredient in dentifrices, zinc has been associated with an approximate 20% reduction of dental plaque (Williams et al, 1998). In combination with triclosan (see below), pronounced reductions in plaque, calculus and gingival inflammation have been reported (Saxton et al, 987; Svatun et al, 1993).

Phenols

Listerine: This venerable and world-wide recognized OTC mouthwash contains menthol and various "essential oils." It binds well to bacterial cell surfaces, and is bactericidal for many microorganisms. It is for this reason that Listerine elicits significant plaque reduction, especially after long-term and regular use. Furthermore, it appears that the lipopolysaccharides from gram-negative bacteria are bound by the constituents in Listerine, and this could explain why Listerine is also used effectively to reduce halitosis (Fine, 1995; Fine et al, 1985, 2000; Jackson, 1997).

Triclosan: Triclosan accumulates on the cytoplasmic membranes of microorganisms, and is bactericidal. Triclosan possesses a broad spectrum of effectiveness, and it is an ingredient in several international dentifrices and mouthwashes, most notably Colgate's "Total"® tooth paste (Mankoti et al, 1992). As a single ingredient, triclosan has only minimal effect in plaque reduction (Addy and Bates, 1997), but in combination with a copolymer (Lindhe et al, 1993; Rosling et al, 1997) or with zinc (Svatun et al, 1993) there appears to be a significant synergistic effect. Triclosan is not a charged molecule, thus it is bound with polymers that improve its substantivity (Ciancio, 1985, 1995). The best results with such combinations have been observed following 3–6 months of regular use (Renton-Harper et al, 1996; Roella et al, 1997; Rosling et al, 1997). Very recently on the Internet (Gee, 2000), triclosan was reportedly detected in breast milk, but other authors dispute this finding (Lindhe, 2000).

Hexetidine: In comparison to mouthwashes containing CHX, hexetidine has a rather small plaque-inhibiting effect; chemically, hexetidine is unrelated to CHX. The oral retention time for hexetidine is only 1–3 hours, and it is this fact that determines its minimal plaque-reducing effect (Roberts and Addy, 1981). In concentrations higher than 0.1%, hexetidine may elicit oral ulcerations (Bergenholz and Hanstrom, 1974). Improved clinical results with hexetidine have been reported when it is combined with zinc (Saxer, 1978; Giertsen et al, 1987; Eley, 1999).
As a constituent in mouthwash, hexetidine possesses high efficacy against streptococci in the pharynx and on the tonsils (Saxer and Mühlemann, 1983; Kühr et al, 1969). However, as a pure plaque-inhibiting agent, its role is small (Mühlemann, 1984); nevertheless, a report by Bokor (1996) showed sig-

nificant plaque reduction after direct topical application of 0.2% hexetidine spray.

Quaternary Ammonium Bases

The antibacterial effects of quaternary ammonium bases were first described in 1935 by Dogmagk. Various mouthwashes incorporating quaternary ammonium bases such as cetylpyridium chloride are commercially available OTC in the USA and elsewhere around the world, e.g., "Cepacol"® (Lobene et al, 1979; Renton-Harper et al, 1996; Allen et al, 1998; Yates et al, 1998; Ciancio, 2000). The basic quaternary ammonium compounds bind to negatively charged surfaces in the oral cavity, but this binding is not as strong as CHX, and the resultant effect is therefore measurably smaller (Ciancio, 1995). The quaternary ammonium bases have been used in combination with zinc (Ritchey et al, 1982) and with various essential oils and CHX. Reports have emerged that such combinations are effective against halitosis (Kozlovsky et al, 1996).

Natural Products

Sanguinarin/herbal extracts: Sanguinarin is an extract from the root of the Sanguinaria candanensis. The effect of sanguinarin alone on plaque and inflammation is actually quite low, and even difficult to demonstrate clinically. Thus, in most commercially available products, sanguinarin has been combined with zinc, which enhances its efficacy (Klewansky and Vernier, 1984; Wennström and Lindhe, 1985; Mandel, 1988; Kopczyk et al, 1991). As a result of a potentially serious adverse side effect – leukoplakia (Agarwal et al, 1997; Allen, 1999; Damm et al, 1999) – most products containing sanguinarin were recently removed from the market. Since the market withdrawal, however, further studies have called into question the side effect of leukoplakia (Munro et al, 1999; Tennenbaum et al, 1999). Only further research will determine whether sanguinarin-containing oral care products will return to the OTC market.

Numerous other herbal extracts have been investigated. Slight plaque reductions have been reported, but combinations of ingredients have always been shown to be more effective in vivo (Otake et al, 1991; Saxer et al, 1994; Guggenheim et al, 1997; Yankell et al, 1998). The OTC product "Parodontax"®, available in Europe but not yet in the USA, contains sodium bicarbonate and plant-derived substances such as chamomile (an antiphlogistic), myrrh (mildly astringent), sage (a tannin), ratanhia (an astringent), and echinacea (an elevator of resistance to infection). Sodium bicarbonate buffers acids and has been shown to reduce bacterial growth in animal studies (Yankell et al, 1988). The inflammation-reducing effects appear to be significant, and it is also available (in Europe) as an OTC mouthwash and as a concentrate.

CONSEQUENCES FOR PERIODONTAL THERAPY – WHERE IS THE FUTURE?

In view of the new and emerging knowledge about the various dangers and ramifications of periodontal infections, their contagious nature, and the likelihood of systemic consequences, the oral health care team is obligated to carefully re-consider the modalities of therapy that have heretofore represented the "gold standard." The routine and aggressive use of antimicrobial agents may become part of the "treatment of choice," and traditional "quadrant-by-quadrant" scaling and root planing may wane, replaced, perhaps, by the technique of "full mouth disinfection" (Quirynen et al, 2000) (see also Table 2). Further, it is becoming clear that all infected sites in a mouth must be treated simultaneously, and that the spouse and perhaps even other family members must also be clinically evaluated and/or treated within a 24-hour period of time. This aggressive approach was pioneered in 1995 by Quirynen and co-workers (Quirynen et al, 1995), and has been substantiated by subsequent clinical studies. It is a 5-step procedure:

1. Following thorough scaling and root planing under local anesthesia, during one or two appointments within a 24-hour window, first in the maxilla and then in the mandible, all periodontal pockets are thoroughly irrigated with an antibacterial solution (chlorhexidine digluconate is the apparent drug of choice, the 0.12% commercially available prescription-only products in the USA)
2. The surface of the tongue is cleaned using a toothbrush and chlorhexidine solution
3. All periodontal pockets are re-irrigated using CHX solution during a 10-minute time period, to eliminate resistant bacteria

4. The tonsils, vestibules, uvula, sublingual area, as well as any other potential harbors for bacteria are treated using CHX spray
5. The patient is instructed to rinse twice daily with CHX solution for the next 12 weeks.

Clinical studies have shown that this therapeutic regimen, in contrast to the traditionally performed quadrant-by-quadrant treatment, reduces probing depths in periodontitis patients by an additional 1.5 – 2.0 mm. Although another study showed that full-mouth therapy within a short period of time (e.g., 24 hr) was effective even without the antibacterial irrigation and subsequent rinses, Quirynen et al (1999) continue to recommend the entire procedure, including antibacterial irrigation and rinsing, stating that home care by patients after extensive periodontal debridement procedures is often inadequate. Finally, the pioneering research by Quirynen et al has recently been corroborated by Wennström (2000), who also incorporated ultrasonic devices into the therapeutic regimen.

CONCLUSION

There is a rapidly-increasing knowledge base concerning the role of bacteremia originating from the oral cavity, and it is now known that pre-treatment topical antimicrobial rinses can significantly reduce such bacteremia, which in turn also should help to prevent cardiac, circulatory and pulmonary consequences.

These facts will enhance the importance of comprehensive dental and dental hygiene care. Treatment for periodontitis patients will expand, to include more intense antimicrobial regimens, and the combination of full-mouth debridement with therapeutic antibacterial disinfection of pockets may preclude the necessity of intervention by a periodontist. For post-operative care following surgical intervention, antimicrobial agents will insure significantly better results, particularly in patients who are highly genetically susceptible to periodontits (Hassell and Harris, 1995), and "refractory" periodontal patients, who can be protected from re-infection and recurrence through targeted use of antimicrobials.

The dental team has at its disposal a potent larder of effective antimicrobial agents. It will become incumbent upon all practitioners to remain abreast of the latest research studies, in order to make appropriate decisions about which antimicrobial to use for each patient, and how the animicrobial should be employed.

REFERENCES

Addy M, Bates J: The effect of partial dentures and chlorhexidine gluconate gel on plaque accumulation in the absence of oral hygiene. J Clin Periodontol 1997; 4: 41–47.

Agarwal S, Piesco N, Peterson D, Charon J, Suzuki, Godowski K, et al: Effects of sanguinariun, chlorhexidine and tetracycline on neutrophil viability and functions in vitro. J Periodont Res 1997; 32: 335–344.

Allen C: Vivadent-related leukoplakia – The tip of the iceberg? Oral Surg Oral Med Oral Pathol 1999; 87: 393–394.

Allen D, Davies R, Bradshaw B, Ellwood R, Simone A, Robinson R, et al: Efficacy of a mouthrinse containing 0.05% cetylpyridium chloride for the control of plaque and gingivitis: a 6-month clinical study in adults. Compend Cont Educ Dent 1998; 19: 20–26.

Bay I, Roella G: Plaque inhibition and improved gingival condition by use of stannous fluoride toothpaste. Scand J Dent Res 1980; 88: 313–315.

Bergenholz A, Hanstrom L: The plaque inhibiting effect of hexetidine (Oraldene) mouthwash compared to that of chlorhexidine. Comm Dent Oral Epidemiol 1974; 2: 70–74.

Block C, Robinschtok E, Simhon A, Shapiro M: Evaluation of chlorhexidine and providone iodine activity against methicillin-resistant Staphylococcus aureus and vancomycin-resistant Enterococcsu faecalis using a surface test. J Hosp Infect 2000; 46: 147–152.

Bokor M: The effect of hexetidine spray on dental plaque following periodontal surgery. J Clin Periodontol 1996; 23: 1080–1083.

Caulfield P, Allen D, Childers N: In vitro susceptibilities of suspected periodontopathic anaerobes as determined by membrane transfer assay. Antimocrob Agents Chemother 1987; 31: 1989–1993.

Ciancio S: Antiseptics and antibiotics as chemotherapeutic agents for periodontitis management. Compend Cont Educ Dent 2000; 21: 59–76.

Ciancio S: Chemical agents: Plaque control, calculus reduction and treatment of dentinal sensitivity. Periodontology 2000 1995; 8: 75–86.

Ciancio S: Mechanical and chemical supragingival plaque control. Introduction. Periodontology 2000 1985; 8:7–10.

Damm D, Curran A, White D, Drummond J: Leukoplakia of the maxillary vestibule – an association with Viadent? Oral Surg Oral Med Oral Pathol 1999; 87: 61–66.

Dogmagk G: Eine neue Klasse von Desinfektionsmittel. Dtsch med Wochenschr 1935; 61: 829–832.

Eley B: Antibacterial agents in the control of supragingival plaque: A review. Brit Dent J 1999; 186: 286–296.

Fine D, Furgang D, Barnett M, Drew C, Steinberg L, Charles C, Vincent J: Effect of an essential oil-containing antiseptic mouthrinse on plaque and salivary Streptococcus mutans levels. J Clin Periodontal 2000; 27: 157–161.

Fine D, Letizia J, Mandel I: The effect of rinsing with Listerine antiseptic on the properties of developing dental plaque. J Clin Periodontol 1985; 12: 660–666.
Fine D: Chemical agents to prevent and regulate plaque development. Periodontology 2000 1995; 8: 87–107.
Frascella J, Gilbert R, Fernandez P, Hendler J: Efficacy of a chlorhexidine dioxide-containing mouthrinse in oral malodor. Compend Cont Educ Dent 2000; 21: 241–255.
Gee, H: The trials of triclosan. Nature Science Update, 2000. http://helix.nature.com
Giertsen E, Svatun B, Saxton C: Plaque inhibition by hexetidine and zinc. Scand J Dent Res 1987; 95: 49–54.
Greenstein G: Rovidone-iodine's effect and role in the management of periodontal disease: A review. J Periodontol 1999; 70: 1397–1405.
Guggenheim B, Lutz F, Schmid R: Caries and plaque inhibition in rats by five topically applied commercially available dentifrices. Eur J Oral Sci 1997; 105: 258–263.
Günbay S, Bicakci N, Parlak H, Güneri T, Kirilmmaz L: The effect of zinc chloride dentifrices on plaque growth and oral zinc levels. Quint Internat 1992; 23; 6619–6624.
Harrap G, Saxton C, Best J: Inhibition of plaque growth by zinc salts. J Periodont Res 1983; 18: 634–642.
Hassell T, Harris E: Genetic influences in caries and periodontal diseases. Crit Rev Oral Brol Med 1995; 6: 319–342.
Humar A, Ostromecki A, Direnfeld J, Marshall J, Lazar N, Houtsoton P, et al: Prospective randomized trial of 10% providone iodine verus 0.5% tincture of chlorhexidine as cutaneous antisepsis for prevention of central venus catheter infection. Clin Infect Dis 2000; 31: 1001–1007.
Jackson R: Metal salts, essential oils and phenols – old or new? Periodontology 2000 1997; 15: 63–73.
Jones C, Stephen K, Richie J, Huntington E, Saxton C, van der Ouderaa F: Long-term exposure of plaque to citrate. Caries Res 1988; 22: 84–90.
Klewansky P, Vernier D: Étude clinique d'une pâte gingive dentaire sur la gingive. Info Dentaire 1984; 66: 4277–4305.
Kligerman B, Bissada N: Clinical study of iodine as a chemotherapeutic agent for the control of dental plaque and gingivitis in man. J Periodontol 1975; 46: 478–487.
Kozuka T: Patch testing to exclude allergic contact dermatitis caused by povidone-iodine. Dermatology 2002; 204(suppl.1) : 96–98.
Kopczyk R, Abrams H, Brown A, Matheny J, Kaplan A:Clinical and microbiological effects of a sanguinaria containing mouthrinse and dentifrice with and without fluoride during 6 months of use. J Periodontol 1991; 62: 617–622.
Kozlovsky A, Goldberg S, Nator 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: 577–582.
Kühr H, Schmidt H, Schwalber J: Die Anwendung von Hexetidin in der Behandlung von entzündlichen Affektionen der Mundhöhle. Zahnärztl Welt Rundschau 1969; 78:560–564.
Leverett D, McHugh W, Jensen O: Effect of daily stannous fluoride rinsing on plaque, gingivitis, extrinsic staining. J Dent Res 1981; 60A: 364 (abs).
Lindhe J, Rosling B, Socransky S, Volpe A: The effect of a triclosan containing dentifrice on established plaque and gingivitis. J Clin Periodontol 1993; 20: 327–334.
Lindhe J: Personal communication, 2000.
Lobene R, Kashket S, Sopokar P, Shloss B, Sabine Z: The effect of cetylpyridium chloride on human plaque bacteria and gingivitis. Pharm Therap Dent 1979; 4: 33–47.
Lobene R: A study of the effects of antiseptic agents and a pulsating device on plaque and gingivitis. J Periodontol 1972; 43: 564.
Mankodi S, Walker C, Conforti N, DeVisio W, McCool J, Volpe A: Clinical effect of a triclosan-containing dentifrice on plaque and gingivitis: a 6-month study. Clin Prev Dent 1992; 14: 4–10.
Maruniak J, Clark W, Walker C, Magnusson I, Marks R, Taylor M, Clouser B: The effect of 3 mouthrinses on plaque and gingivitis development. J Clin Periodontol 1992; 19: 19–32.
Mazza J, Newman M, Simons T: Clinical and antimicrobial effect of stannous fluoride on periodontitis. J Clin Peiodontol 1981; 8: 203–212.
Munro I, Delzell E, Nestmann E, Lynch B: Viadent usage and oral leukoplakia: A spurious association. Regul Toxicol Pharmacol 1999; 30: 182–196.
Ogaard B, Gjermo P, Rölla G: Plaque inhibiting effect in orthodontic patients of a dentifrice containing stannous fluoride. Amer J Orthodont 1980; 78: 266–272.
Oosterwaal P, Mikx F, Van t'Hof, M, Renggli H: Short term bactericidal activity of chlorhexidine gel, amine fluoride gel and stannous fluoride gel in periodontal pockets. J Clin Periodontol 1991; 18: 97–100.
Oppermann R, Rölla G, Johansen J: Thiol groups and reduced acidogenicity of dental plaque in the presence of metal ions in vivo. Scand J Dent Res 1980; 88:389–396.
Otake S, Makimra M, Kuroki T, Hirasawa M: Anticaries effects of polyphenolic compounds from Japanese green tea. Caries Res 1991; 25: 438–443.
Quirynen M, Mongardini C, Pauweis M, Bollen C, Van Eldere J, Van Steenberghe D: One stage full versus partial mouth disinfection in the treatment of chronic adult or generalized early onset periodontitis. I. Long-term impact on microbial load. J Periodontol 1999; 70: 646–656.
Rams E, Slots J: Local delivery of antimicrobial agents in the periodontal pocket. Periodontology 2000 1996; 10: 139–159.
Renton-Harper P, Addy M, Moran J, Doherty F, Newcombe R: A comparison of chloride, triclosan and C31G mouthrinse products for plaque inhibition. J Periodontol 1996; 67: 486–489.
Ritchey T, Lamster L, Mann P, Alfana M: The effect of zinc chloride on the development of gingivitis in Beagle dogs treated with cetylpyridium chloride. J Dent Res 1982; 61: 1217–1220.
Roberts W, Addy M: Comparison of the in vivo and the in vitro antibacterial properties of antiseptic mouthrinses containing chlorhexidine, alexidine, cetylpyridium chloride and hexetidine. Relevance to mode of action. J Clin Periodontol 1981; 8: 295–310.
Rosling B, Dahlen G, Volpe A, Furuichi Y, Ramberg P, Lindhe J: Effect of triclosan on the subgingival microbiota of periodontitis-susceptible subjects. J Clin Periodont 1997; 24: 881–887.
Rosling B, Serino G, Hellström M, Socransky S, Lindhe J: Longitudinal tissue alterations during supportive therapy. Findings from subjects with normal and high susceptibility to periodontal disease. J Clin Periodont 2001; 28: 241–249.

Saxer U, Hug V: Inhibition of plaque formation after rinsing with different concentrations of zinc and hexetidine. Caries Res 1984; 18: 190 (abs).
Saxer U, Jaschouz V, Ley F: The effect of Parodontax dentifrice on gingival bleeding. J Clin Dent 1994.
Saxer U, Jaschouz V, Ley F: The effect of Parodontax dentifrice on gingival bleeding. J Clin Dent 1994; 5:63–64.
Saxer U, Mühlemann H: Synergistic antiplaque effects of a zinc fluoride-hexetidine containing mouthwash. A review. Schweiz Monatsschr Zahnheilk 1983; 93: 689–704.
Saxton C, Lane R, Van der Ouderaa F: The effects of a dentifrice containing a zinc salt and a non-cationic antimicrobial agent on plaque and gingivitis. J Clin Periodont 1987; 14: 144–148.
Schaeken M, Van der Hoeven J, Saxton C, Cummins D: The effect of mouthrinses containing zinc and triclosan on plaque accumulation, development of gingivitis and formation of calculus in a 28-week clinical test. J Clin Periodontol 1996; 23: 465–470.
Svatun B, Saxton C, Huntington E, Cummins D: The effects of a silicil dentifrice containing triclosan and zinc citrate on supragingival plaque and calculus formation and the control of gingivitis. Int Dent J 1993; 43: 431–439.
Tennenbaum H, Dahan M, Soell M: Effectiveness of a sanguinarine regimen after scaling and root planing. J Periodontol 1999; 70: 307–311.
Tinanoff N, Hock J, Camosci P, Hellden L: Effect of stannous fluoride mouthrinse on dental plaque formation. J Clin Periodontol 1980; 7: 232–241.
Tinanoff N, Manwell M, Zamerck R, Grasso J: Clinical and microbiological effects of daily brushing with either NaF or SnF_2 gels in subjects with fixed or removable dental prostheses. J Clin Periodontol 1989; 16: 284–290.
Tinanoff N: Progress regarding the use of stannous fluoride in clinical dentistry. J Clin Dent 1995; 6 (spec issue): 37–40.
Traore O, Allaert F, Fournet-Favard S, Verriere J, Laveran H: Comparison of in vivo antibacterial activity of skin disinfection procedures for insertion of peripheral catheters: Providone iodine versus chlorhexidine. J Hosp Infect 2000; 44: 147–150.
Wennström J, Lindhe J: Some effects of a sanguinarine-containing mouthrinse on developing plaque and gingivitis. J Clin Periodont 1985; 12: 867–872.
Wennström J: A randomized trial of two approaches to nonsurgical therapy using the full mouth concept. DGP Tagung, Frankfurt, Germany, 2000.
Wieder S, Newman H, Strahan J: Stannous fluoride and subgingival chlorhexidine irrigation in control of plaque and chronic periodontitis. J Clin Periodontol 1983; 10: 172–181.
Williams C, McBride S, Mostler K, Petrone D, Alexander J, Crawford R, et al: Efficacy of a dentifrice containing zinc citrate for the control of plaque and gingivitis: a 6-month clinical study in adults. Compend Cont Educ Dent 1998; 19: 4–15.
Wolff L, Backdash M, Pihlstrom B, Band C, Aeppli D: The effect of professional and home subgingival irrigation with antimicrobial agents on gingivitis and early periodontitis. J Dent Hyg 1989; 63: 224–241.
Yankell S, Dolan M, Emling R: Laboratory evaluation of an herbal sodium bicarbonate dentifrice. J Clin Dent 1988; 1 (suppl A): 6–8.
Yates R, Moran J, Addy M, Mullan P, Wade W, Newcombe R: The comparative effect of acidified sodium chlorite and chlorhexidine mouthrinses on plaque regrowth and salivary bacterial counts. J Clin Periodontol 1998; 24: 603–609.

ADDITIONAL READING

Bonesvoll P, Gjermo P: A comparison between chlorhexidine and some quaternary ammonium compounds with regard to retention, salivary concentration and plaque-inhibiting effect in the human mouth after mouth rinses. Archs Oral Biol 1978; 23: 289–294.
Caton J, Ciancio S, Tomothy M, Blieden M, Bradshaw M, Richard J, et al: Treatment with subantimicrobial dose of doxycycline improves the efficacy of scaling and root planning in patients with adult periodontitis. J Periodontol 2000; 71: 521–532.
Garrett S, Johnson L, Drisko C, Adams D, Brandt C, Beiswanger B, et al: Two multi-center clinical studies evaluating locally delivered doxycycline, placebo control, oral hygiene, and scaling and root planning in the treatment of periodontitis. J Periodontol 1999; 70: 490–503.
Garrett S, Adams D, Bogle G, Donly K, Drisko C, Hallmon W, et al: The effect of locally delivered controlled-release doxycycline or scaling and root planning on periodontal maintenance patients over 9 months. J Periodontol 2000; 71: 22–30.
Lie T, Bruun G, Böe O: Effects of topical metronidazole and tetracycline in treatment of adult periodontitis. J Periodontol 1998; 69: 819–927.
Riep B, Purucker P, Bernimoulin J-P: Repeated local metronidazole therapy as adjunct to scaling and root planning in maintenance patients. J Clin Periodont 1999; 26: 710–715.
Stelzel M, Flores-de-Jacoby L: Topical metronidazole application compared with subgingival scaling. J Clin Periodont 1996; 23: 24–29.
Stelzel M, Flores-de-Jacoby L: Topical metronidazole application as an adjunct to scaling and root planning. J Clin Periodontal 2000; 27: 447–452.
Steenberghe D, Bercy P, Kohl J, DeBoever J, Adriaens P, Van der Faeillie A, et al: Subgingival minocycline hydrochloride ointment in moderate to severe chronic adult periodontitis: a randomized, double-blind, vehicle-controlled, multi-center study. J Periodontol 1993; 64: 637–644.
Van Steenberghe D, Rosling B, Söder P, Landry R, van der Velden U, Timmerman M, et al: A 15-month evaluation of repeated subgingival minocycline in chronic adult periodontitis. J Periodontol 1999; 70: 657–667.

Reprint requests:
Ulrich P. Saxer
Dr.med.dent., Ph.D., Professor and Director
Zürich-North Dental Hygiene and Prophylaxis Center
Herzogenmuhlestrasse 148051 Zürich, Switzerland
Fax: +41 1 325 1502
E-mail: u.p.saxer.pszn@bluewin.ch