Enabling patients to achieve optimal periodontal health is a fundamental goal of the oral care provider. Periodontal disease is a complex multifactorial process with a bacterial etiology and an inflammatory progression. A large part of periodontal disease is the result of the host response causing breakdown of surrounding structures. Pathogenic bacteria initiate the inflammatory response while chronic inflammation supports these bacteria through the production of tissue breakdown products that they use as a food source. Effective elimination of periodontal pathogens can resolve inflammation. Concurrently curtailing the host inflammatory response can eliminate periodontal pathogens from the pocket due to a decreased pathogen-friendly food supply. This is a cyclical process. Once it has begun, the host response must be stopped or there will be a continued downward spiral.

The cyclic timeline of periodontal disease begins with bacterial colonization, biofilm formation, attachment, inflammation, and host response. Therapies to stop the cascade are effective at different stages of the process. They can be anti-adhesive, anti-septic, and/or anti-inflammatory. Oral rinses are the least invasive of all these therapies. They are an effective method of proactive intervention to help break the microbiologic and inflammatory cascade that often progresses to periodontal disease.

**WHY ORAL RINSES?**
Oral rinses provide chemotherapeutic agents that compensate for the difficulty in accessing hard-to-reach-areas, poor manual dexterity, and lack of compliance to regular mechanical plaque removal. Furthermore, only 20 percent of the oral environment is tooth structure. The saliva, tongue and mucosa can serve as reservoirs of periopathogenic bacteria that are routinely missed by mechanical oral hygiene tools. Mouth rinsing is preferred by the public because of its ease of use and breath-freshening effect. Oral rinses are effective on the three mechanisms of controlling periodontal inflammation, as anti-adhesive, antiseptic and anti-inflammatory agents (Table 1).

The original concept in the etiology of periodontal disease was the “non-specific” plaque hypothesis: all plaque is harmful to periodontal health and it is important to curtail the amount of plaque. The currently held view is the “specific plaque” hypothesis: specific microbial species create a toxic periodontal environment among otherwise harmless bacteria.

Dental Plaque formation progresses as follows:

1. Pellicle—when the clean tooth contacts saliva, it is quickly covered by pellicle (glycoproteins and polysaccharides). This surface enhances the attachment of microorganisms to the tooth, and if left undisturbed allows for the formation of mature dental plaque.
2. Initial colonizers are mostly non-periopathogenic gram positive sugar metabolizing bacteria.
3. The late colonizers are protein metabolizing anaerobes (P gingivalis, T forsythensis, T denticola). They have been implicated in periodontal disease and breath malodor.
4. Disrupting the biofilm frequently through various oral hygiene approaches keeps the biofilm in its early stage with non-periopathogenic bacteria (since the colonizers always appear in the same sequence).
5. Dental plaque biofilm starts supragingivally. If it is not adequately controlled at this point, it progresses into the sulcus.

Anti-adhesive and anti-septic oral rinses stop the attachment and maturation of pathogenic biofilm that can progress to periodontal disease

**ANTI-ADHESIVE AGENTS**
*Delmopinol Hydrochloride*
A recent chemotherapeutic approach for controlling plaque is
an agent that inhibits the formation of plaque while having little effect on bacteria or the balance of healthy bacteria in the oral cavity.

Delmopinol hydrochloride in PerioShield (Sunstar USA only, not in Canada at present) is a surface-active agent with low antimicrobial potency. It interferes with biofilm matrix formation by preventing synthesis of glucan polysaccharide, the substance that keeps biofilm together and attached to oral surfaces. The adherence of primary plaque forming bacteria is reduced and the emerging biofilm mass is loosely adherent. The plaque can then be easily removed by the patient (Fig. 1).

Delmopinol hydrochloride (0.2 percent) mouth rinse (Fig. 2) has shown statistically significant efficacy for reducing plaque and gingivitis. There is some staining, but less than with chlorhexidine and it is easier to remove. Delmopinol hydrochloride is indicated for long term daily use since it has few side effects and maintains the equilibrium of the oral ecosystem.

**Antiseptic Rinses**

Oral antiseptics work by causing cell death, inhibiting reproduction, or inhibiting the metabolism of microorganisms. They are formulated to penetrate the plaque matrix to gain access to the pathogens.

Effective antiseptic mouthrinse must have:
1. Non-toxicity to oral tissues and minimal side effects.
2. Efficacy against specific pathogens.
3. Adequate bioavailability of active ingredients.
5. Substantivity—ability to bind to tissue surfaces and be released slowly for continued therapeutic effect and be resistant to dilution by saliva.
6. The ability to maintain ecological balance—no overgrowth of microorganisms or bacterial resistance.

Three categories of antiseptic ingredients predominate in the oral rinse market: essential oils, chlorhexidine and cetyl pyridinium chloride.

**Fixed Combination Of Essential Oils (EO)**

Essential oils are obtained by the steam distillation of the odoriferous oily portions of plant matter. They can be derived from flowers, leaves, bark, woods, roots, rhizomes, fruits and seeds. Due to the bactericidal properties of essential oils, they are increasingly popular alternatives to synthetic chemical products.

Listerine (Johnson & Johnson), a fixed combination of four essential oils (thymol, menthol, eucalyptol and methyl salicylate), has been in clinical use since the late 19th century (Fig. 3). It has the longest clinical history of the antiseptic agents and minimal reported adverse effects.

A 30-second rinse penetrates biofilm and provides a significant antimicrobial effect on the embedded bacteria including periopathogens.

**Mechanism of action:**
1. Morphological alteration to the cell surface after a 30-second exposure leads to cell death for specific periopathogens such as *A. actinomycetemcomitans*.
2. Denatures protein.
3. Alters bacterial enzyme activity.
4. Extracts bacterial endotoxins from gram negative pathogens.
5. Affects growth rate of early plaque forming bacteria as well as disrupting the formation of biofilm.
EO also has anti-inflammatory effects:\[^16\]
1. Inhibits prostaglandin formation.
2. Scavenges free radicals generated by neutrophils in inflammation.

Unlike chlorhexidine and cetyl pyridinium chloride, EO has a neutral electrical change, which decreases undesirable side effects so that it:
1. Does not interact with charged ions found in dentifrices and mouth rinses to decrease efficacy.\[^17\]
2. Is not inhibited by proteins in blood serum that may inactivate antimicrobial agents.\[^18\]
3. Does not precipitate dietary chromogens that lead to tooth staining.\[^19\]

However, EO has no substantivity. The effect stops when the rinse is removed. Since its action is rapid, this may not be clinically significant.

EO has been shown to effectively penetrate biofilm to kill bacteria, comparable to the action of chlorhexidine.\[^20\]

Systematic review studies on EO with or without alcohol showed no significant difference in efficacy. Alcohol contributed no added therapeutic value.\[^21\] Listerine is now available in non-alcohol based formulations.

**Chlorhexidine (CHX)**
Chlorhexidine gluconate has been both a medical and surgical disinfectant since the 1950s. It has been used in the oral cavity since the 1970s.

CHX binds via adsorption to surfaces in the mouth as well as the pellicle and saliva achieving high substantivity. It is both bacteriostatic and bactericidal, depending on concentration.

Mechanism of action (Fig. 4):

The positively charged (cationic) CHX molecule binds strongly to the negatively charged bacterial cell surface, altering the integrity of the cell wall. CHX then binds to the inner cell membrane leading to increased permeability and cell damage, rupture of the cell membrane, leakage of cell contents and eventual bacterial cell death.\[^22\]

CHX has a double positive charge and is therefore extremely interactive with anions. This helps efficacy but also produces unfa-
vorable side effects:
1. Precipitation of negatively charged dietary chromogens from food and drinks (such as tea) causing staining.\(^{23}\)
2. Its efficacy may be compromised by cationic detergents (sodium lauryl sulfate) and anionic fluoride ions found in toothpaste.\(^{17}\) There must be a 30 minute window between using toothpaste and rinsing with CHX.
3. Taste alterations and nausea.
4. Enhanced supragingival calculus formation.\(^{24}\)

For the above reasons, CHX rinses are prescribed for short duration therapy only to control acute or severe bouts of periodontal disease.

CHX has a broad spectrum effect against gram-positive and gram-negative bacteria (including many periopathogens), some fungi and yeasts (including Candida) and some viruses (including HIV). No bacterial resistance with long-term use has been reported. 0.2 percent CHX rinse was previously popular in Europe. Less concentrated formula-
CHX is especially appropriate for specific populations whose oral hygiene is compromised, such as the elderly, physically-limited and mentally handicapped. Long-term use may be appropriate in these instances. Formulation without alcohol has been shown to be as clinically effective in controlling plaque and gingival inflammation as the alcohol based product. GUM PAROEX, Chlorhexidine gluconate 0.12 percent (SUNSTAR Canada), is now available in an alcohol free formulation (Fig. 5).

**Cetyl Pyridinium Chloride (CPC)**

Cetyl pyridinium chloride is a cationic, surface-active agent with bactericidal and bacteriostatic activity against bacterial pathogens and yeast. While it is bactericidal to both gram positive and gram negative bacteria, it is more effective against the former. CPC has a significant inhibitory effect on plaque and gingival inflammation.

Mechanism of action (Fig. 6):

The cationic CPC molecule binds to teeth and bacterial cell walls. Binding interferes with bacterial colonization on the tooth surface. CPC is effective against early colonizers in immature dental plaque, reducing the formation of mature biofilm. Binding to the bacterial surface causes disruption of bacterial cell membrane function, leakage of cytoplasmic material, and collapse of the intracellular equilibrium leading to death of the microorganism.

The formulation of vehicle ingredients, preservatives, stabilizers, colors, etc may impact on the bioavailability of CPC. The unique vehicle found in Crest Pro Health (Procter & Gamble)
(Fig. 7) has been shown to increase the product’s bioavailability when compared with other CPC containing mouth rinses. This product delivers 0.07 percent CPC in a high-bioavailable, alcohol-free formulation. Several studies have shown this product to provide significant antiplaque and antigingivitis benefits.

Side effects are due to its cationic structure:
1. Staining has a similar dietary etiology to CHX but it is less severe.
2. CPC can adversely interact with other charged ions in dentifrices and rinses (like CHX).

This produces an environment that exudes a rich source of nutrients such as degraded host proteins that are specifically what pathogenic bacteria need for survival and growth. Bacterial pathogens continue to exploit this environmental change, leading to more bacteria, more inflammation, bone resorption and a perfect niche space (deeper periodontal pockets) where everything can continue undisturbed.

The implication is that the pathologic biofilm is a result of periodontal inflammation, as well being the cause of periodontal inflammation. It is the proverbial chicken and egg scenario.

CPC binds strongly to tooth structure and biofilm giving it good substantivity, although not as good as CHX.

Efficacy Of Antiseptic Rinses
In a systematic literature review CHX, CPC and EO were all determined to have beneficial antiplaque and antigingivitis effects when used long-term in conjunction with mechanical oral hygiene tools. CHX had the most consistent results. CHX has been shown to be more effective than EO in plaque reduction but is comparable in anti-gingivitis properties.

ANTI-INFLAMMATORY PRO-HEALING RINSES
In the healthy periodontium, the innate response attempts to eliminate foreign bodies and is protective against injury or infection. Periodontal disease results from the body’s failure to turn off its inflammatory response to infection. The result is chronic maladaptive inflammation.

This produces an environment that exudes a rich source of nutrients such as degraded host proteins that are specifically what pathogenic bacteria need for survival and growth. Bacterial pathogens continue to exploit this environmental change, leading to more bacteria, more inflammation, bone resorption and a perfect niche space (deeper periodontal pockets) where everything can continue undisturbed.

The implication is that the pathologic biofilm is a result of periodontal inflammation, as well being the cause of periodontal inflammation. It is the proverbial chicken and egg scenario.

6. Prostaglandin production plays a role in alveolar bone resorption.

The inappropriate host response is the major contributing factor for chronic maladaptive periodontal disease. A deficient host response initiates the chronic condition and a too vigorous response leads to further tissue breakdown.

Emerging data suggests that periodontal pathogens that are present in low numbers use inflammation to provide an environment to foster their growth. Control of inflammation may actually return the composition of a pathologic biofilm to a healthy one. The implication is that the pathologic biofilm is a result of periodontal inflammation, as well being the cause of periodontal inflammation. It is the proverbial chicken and egg scenario.

Anti-inflammatory rinses attempt to break this pathologic cycle. They are recent arrivals on the oral rinse scene. They are marketed under two major classifications of ingredients: antioxidants and botanicals (essential oils). There is some overlap, but they will be discussed separately for clarity.

Anti-Oxidants
A free radical is an atom or group of highly reactive atoms that have one or more unpaired electrons. They are formed as intermediates during normal biochemical reactions. When they are generated in excess or not controlled, radicals can damage cells. Radicals of most concern in biological systems are derived from oxygen and are known as reactive oxygen species (ROS). ROS are generated by...
neutrophils in host defense to kill invading pathogens, thus raising the level of ROS during inflammation. Antioxidants neutralize damaging free radicals that produce disease states.

There is promising new research on topical application of anti-oxidants on oral tissue to promote gingival healing. Dental manufacturers such as PeriSciences (https://www.periosciences.com), have incorporated antioxidants into toothpastes, mouth rinses/mouthwashes, lozenges, gels, oral sprays, breath fresheners, and other dental products for the control of gingival and periodontal diseases (Fig. 9). There are potential beneficial clinical effects but due to the inherent unstable nature of antioxidants, simply adding an antioxidant to an oral preparation may not produce an effective agent.

Patients with periodontal disease have a reduced level of gingival and serum antioxidants. It is not yet clear whether the lower level of antioxidants contributes to the cause of periodontitis or whether the antioxidant level is reduced as a result of increased action in neutralizing free radicals.

In vitro studies have shown anti-oxidants to have a beneficial effect on fibroblast migration and proliferation during gingival healing or periodontal repair. Fibroblasts are critical in the healing process. Their collagen deposition restores tissue strength, integrity and structure.

Botanicals (Essential Oils)
Harnessing the antimicrobial properties of plant matter is not new. Listerine, a fixed combination of essential oils, has been in clinical use for over a hundred and fifty years. However, the concept of using the anti-inflammatory and healing (not only the antimicrobial) properties of botanicals is now being explored in new oral rinses. The ideal anti-inflammatory rinse is one that targets pro-inflammatory cytokines and enzymes involved in oral inflammation and tissue destruction.

PeriActive botanical rinse (http://izunpharma.com/) (Fig. 10) has been formulated with three botanical extracts at specific ratios that are antimicrobial, anti-inflammatory, and promote tissue repair. The concept is to help modulate the host inflammatory response and break the inflammatory cycle. The anti-inflammatory and tissue repair properties of the botanical extracts have been demonstrated in multiple bioassays during product development. The bioassays showed inhibition of inflammatory cytokines and their tissue destructive products (prostaglandin, MMPs); tissue healing products were increased.

The three herbs are:
1. Centella asiatica (gotu kola), which has been shown to increase effective collagen and is used in wound healing.
2. Sambucus nigra, which inhibits pro-inflammatory properties of two periodontal pathogens (P. gingivalis and A. actinomycetemcomitans).
3. Echinichia purpurea, which has antiviral, antibacterial and anti-cytotoxic effects.

The botanical rinse has demonstrated an ability to reduce gingival inflammation. A study on managing post surgical inflammation around implants found the rinse clinically equivalent to 0.12 percent CHX in controlling plaque but more effective than CHX in reducing inflammation at implant sites and areas of surgical incision.

Xylitol
Xylitol is a well researched anti-caries agent. Recently, it has also been shown to act as an anti-inflammatory agent, by decreasing the production of inflammatory cytokines in periodontal infections. These finding bring to light the potential use of xylitol in periodontal as well as anti-caries rinses. X-PUR OptiRinse (Oral Science) is a NaF anti-caries rinse containing 10 percent xylitol (Fig. 11).

CONCLUSION
There are many tools available, both mechanical and chemotherapeutic, to maintain periodontal health. Oral rinsing is a patient-friendly, minimally invasive way to proactively control the complex inflammatory cycle. The oral care provider must understand the pathogenic cycle, the needs of the patient and the specifics of the oral rinses. With this knowledge, the clinician is in a position to counsel the patient on maintaining good periodontal health for a lifetime.

Dr. Fay Goldstep has been a featured speaker in the ADA Seminar Series and has lectured at the American Dental Association, Yankee, American Academy
of Cosmetic Dentistry, Academy of General Dentistry, and the Big Apple Dental Conferences. She has lectured nationally and internationally on Proactive/Minimal Intervention Dentistry, Soft-Tissue Lasers, Electronic Caries Detection, Healing Dentistry and Innovations in Hygiene. She has served on the teaching faculties of the postgraduate programmes in Aesthetic Dentistry at SUNY Buffalo, University of Florida, University of Minnesota and University of Missouri-Kansas City. She is a Fellow of the American College of Dentists, International Academy for Dental-Facial Esthetics, American Society for Dental Aesthetics and the Academy of Dentistry International. She has been listed as one of the leaders in continuing education by Dentistry Today since 2002. She sits on the editorial board of Oral Health (healing/preventive dentistry). Dr. Goldstep is a consultant to a number of dental companies, and maintains a private practice in Markham, Canada, and can be reached at goldstep@epdot.com.

Oral Health welcomes this original article.

REFERENCES
3. Selvare. The rinse cycle. RDH 2002; Sept: 82-83,93
6. Nageleberg, R. Understanding advances in oral rinse technologies. Compendium 2011; October:3-7
16. JETPack Educational Course. Myth Busting– All antimicrobial mouthrines are the same. Instructional text