Antimicrobial Delivery Systems

Colleen Rutledge, RDH and Bill Landers

Antimicrobial delivery is a relatively new paradigm in periodontics. A *paradigm* is a conceptual model; in this case, it is a model based on a microbiological concept of periodontal disease. A *paradigm shift* occurs when there is a fundamental change in the model. Paradigm shifts tend to be gradual rather than abrupt because they change the way we think about things, what we thought we knew about the subject, and how things work. Antimicrobial delivery is part of a long-term, periodontal paradigm shift from a purely mechanical concept of periodontal disease to a microbiological one.

Under the previous mechanical model, periodontal disease was attributed to calculus.[1,2] The calculus was thought to be a purely physical irritant to the gums.[1,2] In the 1970s, the paradigm began to change as more was learned about bacterial toxins.[1,2] Therapy, though, didn't change much because the toxins were merely considered to be the chemical equivalent of a physical irritant to the periodontium.[1,2] The latest paradigm recognizes that periodontal diseases are inflammations caused by microbial infections in the form of subgingival biofilms.[1,2] Under the new paradigm, calculus is still removed, not because it's an irritant, but because it's caused by and harbors complex biofilms.[1,2]

With the paradigm shift toward treating periodontal diseases as infections, new strategies have been developed to combat infections that go beyond traditional calculus removal. One of these is antimicrobial delivery. Given that periodontal diseases are infections, that complete mechanical removal is nearly impossible with some microbes always left behind to recolonize the teeth, and that some bacteria are resistant to removal by scaling, many practices now combine traditional mechanical therapy with antimicrobial agents in a *chemomechanical* approach to care.[3,4] A wide variety of antimicrobial delivery systems and agents are now available.

The Evolution of Antimicrobial Delivery Systems

Simple bactericidal mouthwashes were the earliest antimicrobial delivery systems. The first recorded mouthwashes date to the first century and often consisted of stale urine or concentrated white wine or vinegar.[5] Mouthwashes, which are still popular, became more sophisticated over the centuries with the development of herbal blends and patented antiseptic agents.[6] Mouthwashes, however, are not very effective delivery systems because they seldom penetrate more than a few tenths of a millimeter into the sulcus.[6]

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In the late 1900s, powered oral irrigators entered the marketplace. Standard models [illegible] uid antiseptic age[illegible] the depth of the s[illegible] Professional models with subgingival cannulae can irrigate to the full depth of the sulcus.

Systemic antibiotics rely on the circulatory system rather than an instrument. While systemic delivery is theoretically an ideal system, bacterial control is often difficult to achieve. Not all periodontopathogens are sensitive to the same antibiotics and only about 25% of patients are sufficiently compliant with dosage instructions to get the optimum benefit.[7] Haphazard compliance is a major factor in the rise of antibiotic-resistant bacterial species. Over the last 10 years, site-specific delivery systems have become available.[8] These implantable devices may help to solve the problem of patient compliance.

Locally Applied Antimicrobials

Many dental hygienists embrace evidence-based dentistry, using an array of locally applied, site-specific antimicrobial agents that follow generally similar protocols for risk assessment and placement[9-11]:

- Active agent is highly effective against periodontal pathogens
- Approved by the US Food and Drug Administration (FDA)
- Biodegradable and bioadhesive
- Enhances periodontal therapy
- Have a 2-year shelf-life
- Inserted subgingivally into pockets >5 mm
- No need for a follow-up visit
- No refrigeration or dressing required
- Some restrictions with daily oral [illegible]
- Sustained release

[illegible] e new, locally applied antimicrobial delivery systems are described in the next sections.

Chlorhexidine Digluconate

One method of disinfecting a periodontal pocket uses an extremely effective antimicrobial—chlorhexidine digluconate (CHX). First introduced as an antiplaque agent in 1962, CHX is substantive, allowing it to bind to tissues and not be washed away by crevicular fluids and enhancing its ability to kill periodontal pathogens.[12] Sustained release CHX, delivered subgingivally in an ethyl cellulose material, maintains effective levels for 7 days and continues to suppress subgingival flora for up to 11 weeks.[13,14] The gelatin chip can be easily inserted into the pocket with a pair of cotton pliers. CHX binds to hemoglobin, often reducing efficacy, so caution should be exercised when placing the agent in hemorrhaging pockets.

Some studies have shown the effectiveness of CHX gelatin chips as disinfectants and have cited improvement in clinical attachment levels.[12,13] Based on the author's experience, the chip can glide easily into the base of the pocket by:

1. placing the chip at the gingival margin. Wait for the body temperature to soften the gelatin.
2. gently tapping the chip against the tooth surface. This will help curve the chip to the tooth's anatomy.
3. pressing and holding the exposed portion of the chip for 1 to 2 minutes in place after inserting into the sulcus to prevent crevicular fluid from washing the chip out of the pocket.

Colleen Rutledge, RDH

Colleen is a national speaker, consultant, practicing registered dental hygienist at the periodontal therapy level, and a published author. She is a member of Speaking Consulting Network, Collagenex Pharmaceuticals Speakers' Bureau, and is an active member of the ADHA. She welcomes visitors to her Web site at www.perioandbeyond.com.

Bill Landers

Bill is president of Oratec Corporation, a dental company specializing in anti-infective periodontics. He is an expert on chairside microbiological risk assessment technologies and in-office antimicrobial delivery systems.

Comparison of Locally Applied Antimicrobial Delivery Systems[1-3]

	Chlorhexidine Digluconate	Minocycline	Doxycycline Hyclate
FDA-approved	Yes	Yes	Yes
ADA-approved	No	No	Yes
Tetracycline-derived (antibiotic)	No	Yes	Yes
Sustained release	Up to 7 days	Up to 14 days	Up to 21 days
Sites per application	Single	Single	Multiple
Reapplication	3 months after initial placement	3 months after initial placement	4 months after initial placement
Average pocket depth reduction	>2 mm	>2 mm	>2 mm
Preparation time	None	None	90-second mix

References
1. Collagenex Pharmaceuticals, Inc. Data on file.
2. Dexcel Pharma, Inc. Data on file.
3. Orapharma, Inc. Data on file.

4. cutting the chip with small sharp, surgical scissors, which may assist with placement in the lower anterior region.

The CHX gelatin chip can be efficiently placed with a relatively low learning curve. Based on the author's experience, results vary from site to site and patient to patient. Another site-specific subgingival antimicrobial is minocycline.

Minocycline

Minocycline, a derivative of tetracycline, is a potent, broad-spectrum antibiotic that aids in the destruction of subgingival microbial complexes in periodontal pockets. Composed of 1 mg minocycline powder, the antibiotic is encapsulated in a microsphere that releases the agent when it is exposed to crevicular fluid.[15] The microsphere begins to hydrolyze and continues to release the drug for more than 14 days, well above the minimum inhibitory concentration, for several periodontal pathogens including *Porphyromonas gingivalis, Prevotella intermedia, Fusobacterium nucleatum, Eikenella corrodens,* and *Actinobacillus actinomycetemcomitans.*[15]

Placing the minocycline powder using the handle/cartridge system is simple if the manufacturer's instructions are followed. Based on the author's experience, below are additional application tips:

- Use the bottom portion of the mirror handle to gently flatten the tip (2 mm to 3 mm) of the cartridge. Do not worry if some of the powder comes out.
- Bend the plastic cartridge to adapt to the area being treated.
- Don't hold the agent in the pocket too long before depressing the handle. The patient's body temperature may begin to hydrolyze the powder while it is still in the cartridge.
- Difficulty pressing the handle may indicate the powder has no room to express into the pocket. When reaching the base of the pocket, retract the cartridge slightly to avoid splitting the cartridge.

Next we'll explore a locally applied antimicrobial that can treat multiple sites.

Doxycycline Hyclate

Doxycycline hyclate is a bacteriostatic, broad-spectrum, semisynthetic tetracycline used in the treatment of chronic periodontitis. Approved by the FDA in 1998, subgingival placement of doxycycline hyclate is indicated for chronic adult periodontitis for gain in clinical attachment, reduction in probing depth, and bleeding on probing.

The doxycycline hyclate delivery system consists of a coupled syringe containing 450 mg Atrigel (Atrix Laboratories, Inc, Fort Collins, Colo, www.atrixlabs.com) for a flowable delivery system and 50 mg doxycycline hyclate powder.[9] The 2 syringes are connected and then the plungers are used to mix the contents back and forth for about 90 seconds (100 cycles), forming a homogenous, flowable gel.[9,16] After the 2 syringes are uncoupled, a [illegible] is attached, allowing the agent to flow into pockets deeper than 5 mm.[9,16]

Based on the author's experience, placing doxycycline hyclate subgingivally presents the most challenging application technique of all locally applied antimicrobials. However, easy and efficient placement can be achieved:

- If difficulty occurs in accessing a tight pocket, create a custom-made applicator tip by beveling the plas-