Introduction
Recently, there has been an apparent increased interest in employing various antimicrobial agents to treat Periodontal Disease. The modes of drug delivery, suggested agents and indications for treatment have varied. This article will discuss mechanical and antimicrobial therapy, and in particular a product that is a controlled release local delivery system called "Atridox". This product has been approved in the United States and Europe, and Canadian approval is anticipated shortly.

Mechanical and Antimicrobial Therapy
Periodontal disease is an infection of the periodontium. Extensive research and clinical experience has shown that suspected periodontal pathogens are susceptible to mechanical removal. Traditional techniques of mechanical removal have included non-surgical (e.g. scaling and root planing), and surgical (e.g. open flap debridement) therapies.

The issue of "Mechanical versus Antimicrobial" therapy boils down primarily to the need for the removal of: "Calculus and Microbial Plaque versus Pathogenic Microbial Plaque" (i.e. based on their relative importance in the etiology of Periodontal Disease).

Mechanical debridement aims to remove both plaque and calculus deposits while antimicrobial therapy targets the susceptible micro-organisms.

The question then arises: If significant subgingival calculus is left on the root surfaces, what will the benefit of antibiotic therapy be? Listgarten et. al. have shown that once a systemic antibiotic regimen is discontinued, pathogenic bacteria quickly return.1 Definite calculus removal and good plaque control however can delay the return of pathogenic bacteria. As well, research indicates that it is not actually calculus, but rather microbial plaque (always present on/in the calculus) that is the source of periodontal pathogenic bacteria. Therefore if calculus remains, so does the microbial plaque. One may conclude that thorough calculus removal should be a prerequisite to the long-term control of the subgingival microbial plaque.

Additional arguments against using systemic antimicrobial therapy as an alternative to thorough mechanical therapy include: a) research showing equal or better results being achieved with conventional mechanical therapy, b) minimizing the use of antibiotics and the potential bacterial resistance that may result due to over-use, c) mechanical therapy can remove calculus which can harbor endotoxins, d) mechanical therapy can remove calculus retentive factors which can serve as a nidus for plaque accumulation and, e) mechanical therapy can disrupt and remove the biofilms which may be impervious to insufficient concentrations of antimicrobial therapy.

An additional serious concern with inadequate subgingival calculus removal, with or without antimicrobial therapy, is that this may cause "disease masking". Disease masking commonly occurs following non-surgical treatment, where there is ineffective removal of calculus in the apical aspect of the pocket, especially when combined with more complete removal of coronal calculus. The result is that the clinician and patient can be deceived into believing that the treatment was successful, possibly delaying additional needed treatment, which may lead to additional attachment loss. The astute clinician should see the signs and symptoms that indicate unresolved disease, including:

1) residual inflammation
2) marginal bleeding
3) bleeding on probing
4) suppuration on probing
5) acute periodontal exacerbation
6) absence of crestal lamina dura, and
7) loss of attachment.

The treatment of unresolved disease should primarily involve the thorough removal of residual subgingival calculus and predisposing factors. In fact, the most appropriate timing of antibiotic therapy may be following thorough removal of calculus and calculus retentive factors, and even then only in selected situations. The early diagnosis of unresolved disease and disease masking is the critical initial step which then allows the therapist to develop an appropriate treatment plan and therapy. However, diagnosis and modulation of treatment must be ongoing because of the episodic nature of periodontal disease. For example, the clinician must recognize the limits of non-surgical therapy (which may include scaling and root planing and antimicrobial therapy) and institute open flap procedures when indicated to remove significant residual calculus. The threshold level of residual subgingival calculus that would be compatible with health cannot be accurately quantified. Therefore the clinician must strive to be as thorough as necessary in order to arrest disease, and as well institute a supportive periodontal maintenance care program.

In summary, there may be a serious misconception amongst some clinicians and patients that subgingival periodontal treatment should be directed towards only the microbial plaque, even in cases where there remains significant residual subgingival calculus. Evidence based, contemporary periodontal therapy however, strongly suggests that the primary periodontal treatment be directed towards mechanical debridement techniques in order to remove calculus (and calculus retentive factors) as well as microbial plaque.

On the other hand, local antibiotic delivery has potentially positive features in that it may:

a) be technically easier to perform
b) take less time
c) be applied comfortably for patients
d) spare cementum with potential less post treatment thermal sensitivity
e) potentially reach pathogenic microorganisms that have invaded the sulcular tissues

f) deliver a very low systemic dose, minimizing the potential for bacterial resistance, and

f) achieve higher drug concentrations in the sulcus compared to systemic administration.

Local Drug Delivery: Important Characteristics

The potential success of any drug therapy is dependent upon the agents to:

1) inhibit or kill the pathogen
2) reach the targeted site (ie. base of the pocket)
3) be maintained at a sufficient concentration
4) be retained at the target site long enough (ie. substantivity) to achieve the desired effect, and
5) not do any harm.

With locally applied agents, the delivery system in particular is important because of the turnover of gingival fluid and its ability to flush the contents out of the pocket within minutes. Various local drug delivery systems and their potential beneficial characteristics are summarized in Table 1.

The potential advantages of controlled delivery systems compared to other delivery systems are:

1) better patient compliance
2) enhanced pharmo-kinetic result
3) better localization of the agent
4) better control of drug dosage, and
5) prolonged drug delivery at high concentrations (which may be especially important in the periodontal lesions because subgingival plaque tends to organize as "biofilms" which require higher antibiotic concentration in order to allow the antibiotics to penetrate).

Atridix is a subgingival controlled release product composed of a two syringe system. Syringe "A" contains 450 mg of a polylactic acid gel, which is a bio-absorbable. Syringe "B" contains Doxycycline Hyclate powder which is equivalent to 42.5 mg of Doxycycline (Atridix is a registered trademark of Block Drug Corporation). The contents of the 2 syringes are mixed together and applied subgingivally. The flowable material conforms to the anatomy of the pocket and sets to a gel-like consistency upon contact with the gingival crevicular fluid. Material absorption occurs over several weeks, however, it can be removed one week after initial placement.

<table>
<thead>
<tr>
<th>DELIVERY SYSTEM</th>
<th>Mouthrinse</th>
<th>Subgingival Irrigation</th>
<th>Systemic Delivery</th>
<th>Controlled Delivery</th>
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<td>Poor</td>
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<td>Adequate Concentration</td>
<td>Good</td>
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<td>Fair</td>
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<tr>
<td>Adequate Duration</td>
<td>Poor</td>
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Atridox Clinical Studies

Atridox was evaluated for safety and efficacy in two well-controlled, parallel-design, multicenter, 9-month clinical trials, involving a total of 831 patients with moderate to severe adult periodontitis. Patients were divided into four groups, and received either Atridox plus oral hygiene, SRP plus oral hygiene, placebo gel plus oral hygiene, or oral hygiene alone. All sites with probing depths greater than or equal to 5mm were treated at the start of the study, and then four months later. After nine months, the reductions in probing depth and increases in attachment level for Atridox and SRP were equivalent (1.2mm and 0.8mm respectively). For placebo and oral hygiene alone, the reductions in probing depth and increases in attachment level were 0.9mm and 0.3mm for placebo gel, and 0.7mm and 0.4mm for oral hygiene respectively.

Obviously, with Atridox being a newly introduced therapy, there are no long-term clinical data yet available. However, Atridox was approved for the use in the USA for the treatment of chronic adult periodontitis for a gain in clinical attachment, reduction in probing depth, and reduction in bleeding on probing. Also, Atridox is the first and only locally delivered antimicrobial to have received the Seal of Acceptance of the American Dental Association.

Potential Indication for Clinical Usage of Atridox

As with any new product, research is limited. Additional research for example is needed to determine use of Atridox as a treatment not only for Chronic Adult Periodontitis, but for situations such as; smokers, peri-implantitis and all types of periodontal disease other than chronic Adult Periodontitis.

With further research and clinical experience, additional clinical situations may be found where use of Atridox may prove to be a valuable adjunct to conventional periodontal therapy. Below is a summary of clinical situations where (strictly in the opinion of the author) Atridox may be considered in the future. Readers are reminded, however, that at the present time, the only approved indication for Atridox in the US is:

1) For use in the treatment of Chronic Adult Periodontitis for a gain in clinical attachment, reduction in probing depths, and reduction of bleeding on probing. Other potential clinical indications (though not yet substantiated with published data) may include:
2) As an initial treatment option in dental phobics, or patients who refuse mechanical therapy,
3) Medically compromised patients who cannot undergo mechanical therapy,
4) As a treatment in sites that have not responded to traditional mechanical therapy, eg. during initial and/or periodontal maintenance therapy,
5) Areas of recurrent disease,
6) In esthetically critical areas, where there is a concern that mechanical therapy would be more likely to result in unacceptable recession,
7) Areas that are inaccessible to mechanical therapy — eg. deep narrow tortuous pockets, deep furcation areas, peri-implant defects, etc.
8) As an adjunct to mechanical therapy in patients who have declined periodontal surgery that would minimize probing depth and inflammation,
9) Periodontally compromised patients where extensive inflammation may be reduced with antimicrobial therapy to facilitate the mechanical therapy that would follow after.

Conclusion

Atridox presents a user-friendly and patient friendly treatment that has many promising indications. Antimicrobial therapy, however, should not be considered as a substitute to conventional mechanical periodontal therapies.