Current Chemotherapeutic Modalities Available in the Treatment of Periodontal Disease

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The Changing Views of Plaque and Periodontal Diseases

1880            1900            1930            1960            1990            Present

Specific pathogens identified for many diseases
Search begins for oral pathogens in plaque

Non-specific plaque hypothesis
Diseases linked to constitutional defects

Specific plaque hypothesis
Treatment aimed at BIOFILM causative agents

Golden Age of Microbiology
Plaque Control
Biofilm
General Consensus

“Not just one bacterial species causes periodontal disease in a given host; rather, it is many species acting in concert which brings damage to the gingival tissue and bone loss.

In addition, the tissue damage and bone loss are likely the result of the immunological reaction of the host to the invading microorganisms, and not so much due to the factors elaborated by the bacteria...”
Dental Plaque

Dr Charles Cobb, University of Missouri
“Imagine a dark, hot swamp-like world. The stench of sulfur compounds permeating the environment. Somewhere in the distance is heard rumbling as methane bubbles churn. The stagnant fluid is rich in complex organic molecules. To survive in this hostile environment, primitive single celled organisms somehow learn to act in concert. Different species congregate and attach to surfaces forming mushroom-like colonies known as the biofilm…..”

Larry Burnett, DDS
What is a Biofilm?

- Biofilm is a well organized, cooperating community of microorganisms
- Microorganisms are arranged in microcolonies
- Microcolonies are surrounded by a protective matrix
- Within the microcolonies are differing environments
- Microorganisms have primitive communication system
- Microorganisms in biofilm are resistant to antibiotics, antimicrobials, and host response

How Does the Biofilm Become a Biofilm?

Shortly after a meticulous periodontal prophylaxis the following occurs... within minutes!

- Tooth surface begins to absorb a molecular layer of proteins and glycoproteins from the saliva.

- First colonizers (primarily streptococci and actinomyces) connect to the protein pellicle and form the “roots” that will anchor the biofilm to the tooth.
Artistic Depiction of Plaque Biofilm

- Bacterial Microcolonies
- Intermicrobial Matrix
- Fluid Channels
- Pellicle
- Tooth Surface
Illustration of Biofilm

Outer layers of biofilm cells absorb damage and impair diffusion

Outer layers may even inactivate antimicrobials

Inner layers of biofilm cells have more time to initiate stress response

“Persistor” cells may be present in higher numbers
Host Pathway to Periodontal Disease

Microbial Challenge
- Bio-film / Plaque / Calculus
  - Antibody
  - PMN
  - Antigens
  - LPS
  - Other Virulence Factors

Host Immuno-inflammatory Response
- Genetic Risk Factors
- Cytokines
- Prostanoids
- MMPs

Connective Tissue and Bone Metabolism

Clinical Signs of Disease

Environmental & Acquired Risk Factors

Tissue Breakdown Products & Ecological Factors

Periodontal Breakdown Cascade

Bacterial Products (Biofilm) → Host Cells

- PGE₂
- IL-1β, IL-6
- Osteoclasts
- MMPs

Bone Resorption
Connective Tissue Breakdown

Pocket Formation
Loss of Attachment
Tooth Mobility
Tooth Loss

Bacterial Component + Host Response Component = Clinical Sequelae

Possible Strategies to Control Oral Biofilm

Control of nutrients
- Addition of base-generating nutrients (arginine)
- Reduction of GCF flow through anti-inflammatory agents
- Inhibition of key microbial enzymes

Control of biofilm pH
- Sugar substitutes
- Antimicrobial agents
- Fluoride
- Stimulate base production

Control of redox potential
- Redox agents
- Oxygenating agents
How do treat / prevent periodontal disease?

• Antibiotics
• Mechanical Debridement
• Combination Therapy
Antibiotics

• Criteria of Effective Agents
  – Reach intended site of action
  – Sustain adequate concentration
  – Remain for adequate duration
  – Inhibit or kill putative pathogens
  – Do little or no harm to host
Efficacy of Antibiotic Therapy

• Depends on:
  – Anti-microbial spectrum and drug characteristics
  – Drug binding to tissues
  – Protection of pathogens by non-target organisms
  – Biofilm phenomena
  – Total bacterial load vs. max antibiotic concentration
  – Effectiveness of host defenses
  – Pathogens in sites not affected by therapy
Objectives

• Broader delivery of antimicrobial agent to the gingival sulcus

• “Assist” natural immune / systemic response to infection

• Reduce levels of pathogenic bacteria

• Maintain therapeutic levels over time
Systemic Antibiotics

- Tetracyclines
- **Doxycycline**
- Minocycline
- Metronidazole
- Ciprofloxacin
- Penicillin
- Amoxicillin
- Amoxicillin / Clavulanate
- Clindamycin

- Erythromycin
- Spiramycin
- Ofloacin
- **Combination Therapy**
- **Metronidazole + Amoxicillin**
- Metronidazole + Tetracycline
- Metronidazole + Spiramycin
- Amoxicillin + Doxycycline
Low Dose Doxycycline

- PERIOSTAT®
  (doxycycline hyclate 20 mg capsules)

No longer available
Low Dose Doxycycline (LDD)

- Periostat™ acts as an Enzyme Suppressor
  - Studies show that doxycycline hyclate 20 mg bid has no antimicrobial action
  - No change in bacterial flora after 18 months
  - No induction of resistance after 18 months
Summary

Pocket Depth Reduction
• 0.48mm improvement with SRP and Periostat vs. 0.26mm improvement with SRP alone

Attachment Level Gain
• 0.38mm improvement with SRP and Periostat vs. 0.17mm improvement with SRP alone
Effects of Systemic Antibiotics

- PD decreases from 0 to 8 weeks
- PD remains stable or decreases slightly thereafter
- Effects not as long as SRP, initially the same
- No effect on biofilm
Objectives

• Deliver antimicrobial agent directly to site of infection

• Achieve adequate therapeutic concentration; therefore, reducing levels of pathogenic bacteria

• Maintain therapeutic levels over time
Locally Delivered Antimicrobials

**Indications** -

- When localized recurrent and/or residual PD ≥5m with inflammation is still present following conventional therapies
Locally Delivered Antimicrobials

Not indicated-

- Multiple sites with PD ≥5 mm exist in the same quadrant
- The use of LDAs has failed to control periodontitis (e.g., reduction of PD)
- Anatomical defects are present (e.g., intrabony defects)
Localized Antimicrobial Therapy

• Deliver antimicrobial agent directly to site of infection

• Achieve adequate therapeutic concentration; therefore, reducing levels of pathogenic bacteria

• Maintain therapeutic levels over time
An “Ideal” Locally-Delivered Antibacterial Therapy

“Poor response to antibacterial therapy has been attributed to failure to reach the site of action at adequate concentration or the inability to maintain adequate drug levels for a sufficient time.”

– Kills or inhibits putative pathogens
– Reaches the site to be treated
– Reaches site at an adequate concentration
– Remains at the site long enough to be effective
– Low incidence of adverse events
Intracrevicular Irrigation

• Medicaments can be added to irrigant

• Irrigation at margin ~ 1.8mm

• Reached 95% of pocket depth with irrigation tip placed 3mm subgingivally (mean 5mm)

• Lack of an adjunctive benefit
  – Biofilm disruption
Actisite

12.7 mg Tetracycline
Periochip

Chx Chip
“Atridox® has been shown to help arrest periodontitis when used as directed, in a conscientiously applied program of oral hygiene and regular professional care.”

Council on Scientific Affairs, American Dental Association (ADA)
NEW Arestin
minocycline HCl 1mg
Microspheres

SHRINKS PERIODONTITIS DOWN TO SIZE
Arestin Microspheres

Characteristics

- Sustained Release
- Administered as a Powder
- Easy to Use
  - No reconstitution
  - No refrigeration
- 2 Year Stability
Minocycline Eradicates The Pathogens

**Concentrations of minocycline in gingival crevicular fluid (GCF) at site of administration**

![Graph showing the concentration of minocycline in GCF over time.](image)

**Mean GCF minocycline concentration (µg/mL)**

- **Sampling time (days)**
- **MIC = 2 µg/mL**
Chair-side Preparation
Placement of Arestin
What is the Perio Protect Method?

The Perio Protect Method uses an FDA-cleared medical device that directs antimicrobial agents of the doctor's choice into the gingival sulcus and helps maintain it at the source of the gum infections. These medications:

- may be delivered to the source of the infection
- aid in reducing the bacteria
- help to decrease the host inflammation when reducing the bacteria
- help promote healing
- decrease the bacteria which may help improve bad breath
- have been reported in professional journals to modify the plaque and biofilm
- are bleaching agents and may whiten the teeth
- may provide long-lasting results and reduce the need for surgery
What We Know

- The Perio Protect® tray was cleared for marketing by the Food and Drug Administration (FDA) on grounds that it is substantially equivalent to a previously marketed disposable fluoride tray. This type of tray is traditionally used to prevent tooth decay.

- The FDA clearance process did not determine that the Perio Protect® tray has been proven to be a safe or effective modality for the treatment of gum disease.

- To date, the Academy is not aware of any published, peer-reviewed* clinical trials that establish the effectiveness, reliability, or potential complications of this therapy.

- Numerous clinical studies have suggested that topically applied medicines do not reach the source of periodontal infections.
Localized Antimicrobial Therapy

• Uses: Localized sites refractory to mechanical surgery and / or maintenance therapy

• Not a replacement for SRP; some questions on use as adjunct to SRP in some cases

• Can help to stabilize alveolar bone and stop disease progression when definitive therapy is not an option.
Biofilm vs. Antibiotics

• The multi-layered and multi-bacterial biofilm is persistent

• The presence of antibiotics is time-limited

• Antibiotics require high concentration and sufficient length of time to yield an affect.
What is the exact role antibiotics can play in the treatment of periodontal disease?
Certain patients possess non-microbial risk factors which are difficult to reduce or eliminate (e.g., smoking, diabetes) or are beyond the clinician’s ability to control (e.g., genetic predisposition)

The use of host modulation therapy in conjunction with scaling and root planing may prove to be advantageous.
Mechanical Debridement

Primary Periodontal Instrumentation
Hand Instrument vs. Ultrasonic

Disruption of Biofilm

Approximate Position Of Scaler Tip

(Efficiency in Biofilm Disruption)
What is The Extent of Subgingival Scaling and Root Planing?
SRP is still the “Gold Standard”

“Studies show that 10-20 % of the bacteria remain at the base of the pocket even with the best SRP”

Roy Page, D.D.S, PhD
Effects of SRP

• PD decreases from 0 to 8 weeks
  — ~1mm in medium pockets
  — ~2mm in deep pockets
• PD remain stable from 8 – 24 weeks
• Disrupts the biofilm
• Removes plaque and calculus
SRP and Systemic Antibiotics

- Chronic Periodontitis
  - At best, a slight short term benefit
  - Refractory patients
  - Clindamycin: Dose

- Aggressive Periodontitis
  - Better clinical response due to host modulation
  - Amoxicillin / Metronidazole: Dose
It has been estimated that 95% of all bacteria on earth exist as biofilms. These bacteria in this protective biofilm become highly resistant to antimicrobial agents. Whether it is in your unit’s waterline or in a 6mm pocket, bacteria in a biofilm will withstand high pH levels, antibiotics or antimicrobials that would otherwise be 100% lethal if the bacteria were exposed on their own.

In fact, studies have found that some antibiotics that kill free-floating bacteria must be increased from 50 to 1500 times to be effective against the same pathogens hunkered in a biofilm.

Nield-Gehrig
Periodontal diseases should be considered infections and principles of treating infections should be employed. These principles include:

1) Elimination or suppression of the infectious organism
2) Elimination or control of the source of the infection to prevent reinfection
3) Establishment of an environment which promotes resolution of inflammation
4) Consideration of host factors
5) Adjunctive use of antibacterial agents

World Workshop in Clinical Periodontics, 1989
So Where Do We Stand?

Bacterial microcolonies that makeup the biofilm are extremely resistant to chemicals and medicaments.

That’s why mechanical debridement remains the basis of effective periodontal therapy. Everything else (surgery, irrigation, systemic and locally administered antibiotics) is and should always be considered adjunctive.....!
“As health care providers, it is important for all dentists to consider antibiotic usage guidelines in treatment planning, so that the effectiveness of their use is preserved for patients who do not initially respond to therapy; and to avoid contributing to one of the world’s most pressing public health problems namely, antibiotic resistance of bacteria.”
Questions

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QR Code link to Dental Hygiene webpage
THANK YOU