




SYSTEMIC AND LOCAL ANTIBIOTICS

Inland Empire Perio Study Club

1/11/2020






Objectives

- Understand the rationale for systemic antibiotic use in periodontal therapy
- Understand the rationale for local antibiotic use in periodontal therapy
- Understand the effects of local antibiotics in periodontal therapy
- Understand the effects of systemic antibiotics in periodontal therapy
- Understand the various options for host modulation and their use in clinical practice




PERIODONTAL DISEASE ETIOLOGY

- Bacteria
 - Biofilms
 - Tissue
 - Immune response
 - Is periodontal disease destructive or protective in nature?
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BACTERIA ASSOCIATED WITH PERIODONTAL DISEASE

- Gram Negative
 - Anaerobic
 - Rods
- 

BIOFILMS

- Matrix-enclosed Bacterial Populations
- Adherent to Each Other and/or Surfaces
- Highly Organized Aggregates of Adherent Bacteria
- Resistant to Host Defenses
- May Impair Diffusion or Inactivate Pharmacologic Agents (Costerton JW, J. Bacteriol, 1994)

CURRENT GOAL OF THERAPY

- Disruption of Plaque Biofilm to a Level Compatible With Health
- Glassy smooth root surfaces?
- But is mechanical disruption of biofilm and bacteria enough?

Chemotherapeutics

A chemotherapeutic agent is a chemical substance that provides a clinical therapeutic benefit

Two approaches:

- To reduce the bacterial load, or
- To enhance the hosts immune response

The two approaches

- Antimicrobial therapy
 - Local delivery of an antiseptic agent
 - Local antimicrobial therapy
 - Systemic antimicrobial therapy
- Host modulation therapy

Local antiseptic

- Chlorhexidine Gluconate 0.12%
 - Inhibits development of plaque, calculus and gingivitis (30 – 65% over controls)
 - Does not produce microbial resistance
 - Local reversible side effects:
 - Brown staining of teeth, tongue & resin restorations
 - Transient impairment of taste perception
 - Contains 12% alcohol
 - Substantivity

Local antiseptic

- Essential Oil mouthrinse (Listerine):
 - Contain thymol, eucalyptol, menthol, & methyl salicylate.
 - Demonstrate reduction in plaque & gingivitis (20 – 35% over controls)
 - Long history of daily use and safety
 - High alcohol content – up to 24%

Local Antimicrobial Delivery

- Drug Needs to Reach Intended Site
- Remains at Adequate Concentration
- Lasts for a Sufficient Duration
- Inhibits or Kills Pathogens
- Does No Harm (Goodson J, J Dent Res, 1989)

What complicates local delivery?


- Fluid Present in a 5 mm Pocket is Replaced 40x per Hour (Goodson J, J Dent Res, 1989)

Local Antibiotic Options

- Atridox - doxycycline in a syringable gel
- PerioChip-Chlorhexidine
- Arestin - minocycline microspheres
- Use:
 - localized pockets during maintenance
- Limitations
 - Difficult to place
 - May fall out
 - Steady rate of drug release
 - Controversy regarding clinically significant improvements.




DOXYCYCLINE POLYMER (ATRIDOX)[®]

- Released in 1999
 - Contains 10% Doxycycline
 - Derivative of Tetracycline
 - Biodegradable Formulation
 - Dissolves Over Time
- 



Doxycycline

- Flows freely and easily
 - Controlled release of doxycycline for a period of 21 days¹
 - Bioabsorbability eliminates need for removal
 - Single syringe effectively treats multiple pockets/sites
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TWO SYRINGE MIXING SYSTEM

- 450 mg Biodegradable Vehicle
- 50 mg Doxycycline Hyclate



TWO LARGE RANDOMIZED TRIALS

- Compared S/RP vs Atridox Alone
- No Differences in PD and Attachment Level (as Compared With S/RP)
- Significant Reductions in Anaerobic Bacteria



Problems with Atridox

- Allergies
 - Pregnancy
- 




ARESTINTM

- Released in 2001
- Active Ingredient-Minocycline
- Broad-Spectrum Semisynthetic Tetracycline Derivative
- 1 mg Dose-Minocycline Hydrochloride
- Affects bacteria and collagenase




ARESTIN™

- Incorporated into a Polymer of Microspheres
 - Activates and Adheres to Moisture
 - Bacteriostatic
- 



Advantages

- Premeasured and Premixed
 - Easily Placed-in seconds
 - Stays in Place
 - Nothing to Remove
 - No Refrigeration Needed
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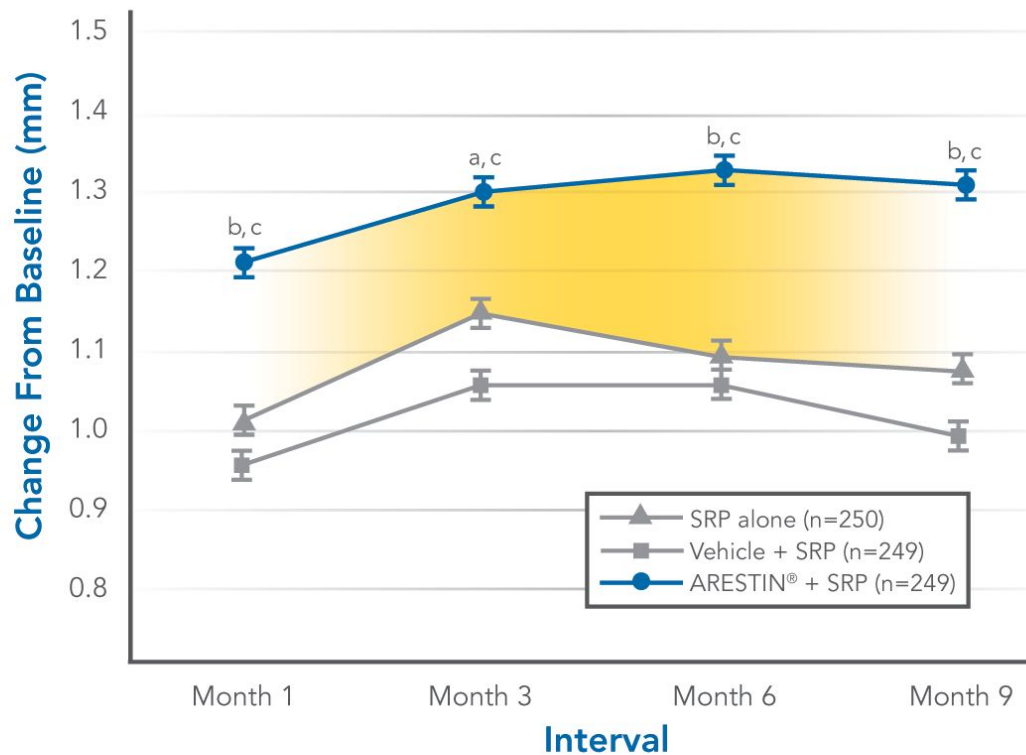


Disadvantages

- Minocycline allergies
 - Pregnancy
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Arestin study (Williams)

Statistically significant results achieved after 1 month and maintained through 9 months^{2*}



^aP<0.01, ARESTIN® vs SRP alone ^bP<0.001, ARESTIN® vs SRP alone ^cP<0.001, ARESTIN® vs vehicle

Systematic Review

- Bonito 2005 (Journal of Perio)
 - Compared SRP to SRP + local delivery
 - Look at Tetra/Minocycline/CHX/Metronidazole
 - Meta-analysis on PD/CAL improvement
 - PD improvement 0.1-0.5mm
 - CAL improvements less modest

AAP Position Statement


- Local Delivery
- Indications
 - LOCALIZED residual or recurrent PD ≥ 5 mm exist with inflammation
- Contraindications
 - GENERALIZED residual or recurrent PD ≥ 5 mm exist
 - When local delivery agents have failed (Don't retreat with locals)
 - Anatomical defects (intrabony defects)

Take home message on local delivery antibiotics

- Modest PD reduction
- Modest CAL gain
- May decrease inflammation over short term
- Tooth loss and retention?
- Effective only with mechanical disruption of biofilm



Systemic Antibiotics

- What are the limitations of systemic antibiotic use?
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Systemic Antibiotics

- Indications:
 - Aggressive forms of disease
 - Localized aggressive periodontitis
 - Generalized aggressive periodontitis
 - Necrotizing ulcerative gingivitis/periodontitis with systemic involvement
 - Periodontal abscesses
 - Periodontitis associated with systemic disease
 - Refractory periodontitis cases

Systemic Antibiotics

- Contraindications
 - Gingivitis
 - Chronic periodontitis
 - ANUG without systemic involvement



Systemic antibiotics

- Why utilize systemic antibiotics in aggressive periodontitis cases?
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Systemic Antibiotics

Choice of antibiotic ideally based on microbial culture and sensitivity testing.

The pathogens:

- *Porphyromonas gingivalis*
- *Actinobacillus actinomycetemcomitans*
- *Tannerella forsythensis*
- *Spirochetes of acute necrotizing gingivitis*
- *Prevotella intermedia*
- *Treponema denticola*

Commonly used antibiotic regimens

■ Tetracycline

- Effective against A.a.
- Concentrate in periodontal tissues
- Anticollagenase effect

■ Metronidazole

- Effective against anaerobes
- Not for A.a.
- Used in combo drugs

■ Amoxicillin

- Susceptible to beta-lactamase
- Often used as drug combo (Augmentin)

■ Clindamycin

- Effective against anaerobic bacteria
- Refractory cases shown to respond

Prescribing Antibiotics

- Metronidazole 500mg/tid/8days
 - Clindamycin 300mg/tid/8 days
 - Doxycycline 100-200mg/qid/21 days
 - Metronidazole + amoxicillin 250mg/tid/8 days of each drug
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- American Academy of Periodontology Position Paper

When to prescribe?


- Ideally prior to instrumentation (at least 48-72 hours prior to treatment)
- Periodontal abscess (drainage must be established)
- Aggressive periodontitis
- Not for chronic PD: most studies will show modest reduction in PD/BOP/Bacterial populations with effects being lost as early as 3-6 months

Systemic Antibiotics

- Administration of antibiotics must be weighed against possible adverse reactions:
 - Allergic/anaphylactic reactions
 - Opportunistic infections
 - Nausea/vomiting
 - Interactions with other medications
 - Development of resistant strains



Host Modulation

- Agents used to downregulate destructive mechanisms and upregulate protective mechanisms in the periodontal pocket
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Host Modulation

- Low dose doxycycline
 - Reduces tissue break-down in the face of a bacterial challenge through suppression of collagenase
- NSAIDs (flurbiprofen)
 - Inhibit prostaglandin & PMN migration
 - Reduce inflammation, host collagenase
- Bisphosphonates
 - Inhibit bone resorption, osteoclastic activity

Periostat 20mg

- Doxycycline 20mg
 - Subantimicrobial dose
 - Affects collagenase
 - Does not cause bacterial resistance
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- Rx: Periostat 20mg, Dispense: 180 tabs, Take 1 tab bid X 3 months, 1 refill.

Systematic Review/Meta-analysis on

▪ Sgolastra 2014 Periostat

- Systematic Review/Meta analysis
- Compared SRP alone vs. SRP + Periostat
- Found statistically significant differences favoring use of periostat in chronic periodontitis patients
- Evaluated BOP/CAL/PD




NSAIDS/Bisphosphonates

- Good clinical outcomes noted with use, but what are the problems with these agents?
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Who should be prescribed Periostat?

- Chronic periodontitis with uncontrolled inflammation
 - Refractory periodontitis
 - Osteopenic women (Golub/Reinhardt et al)
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Bottom Line


- Local delivery of antibiotics may be used during initial therapy and throughout the maintenance phase (refer to AAP statement)
- Systemic antibiotics should be used only in conjunction with mechanical therapy and only used in cases of aggressive or refractory periodontitis
- Host modulation may be used during initial therapy and maintenance therapy

American Assoc. of Endo

- Indications for ABX prescribing
 - Acute Apical Abscess with systemic involvement (fever, lymphadenopathy, malaise, etc)
- Contraindications
 - Irreversible pulpitis
 - Necrotic pulp without acute swelling/systemic involvement
 - Sinus tracts




Case Review

- 33 year old Hawaiian/Pacific Islander
 - Nonsmoker
 - No current meds
 - No known allergies
 - Systemically healthy
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Dental History

- Severe attrition
 - Acid erosion due to pop consumption
 - 3rd molars extracted
 - Minimal caries history
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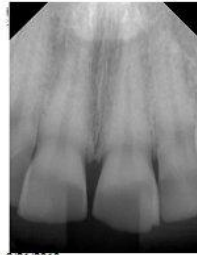
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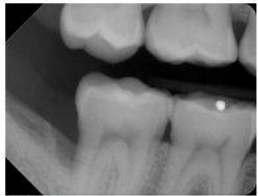
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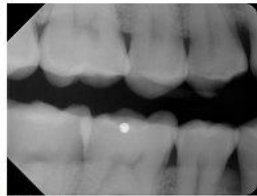
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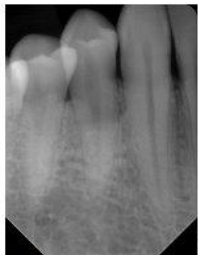
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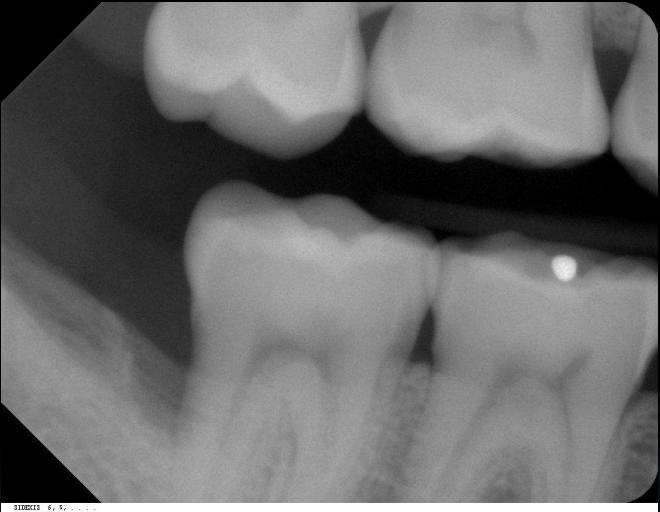


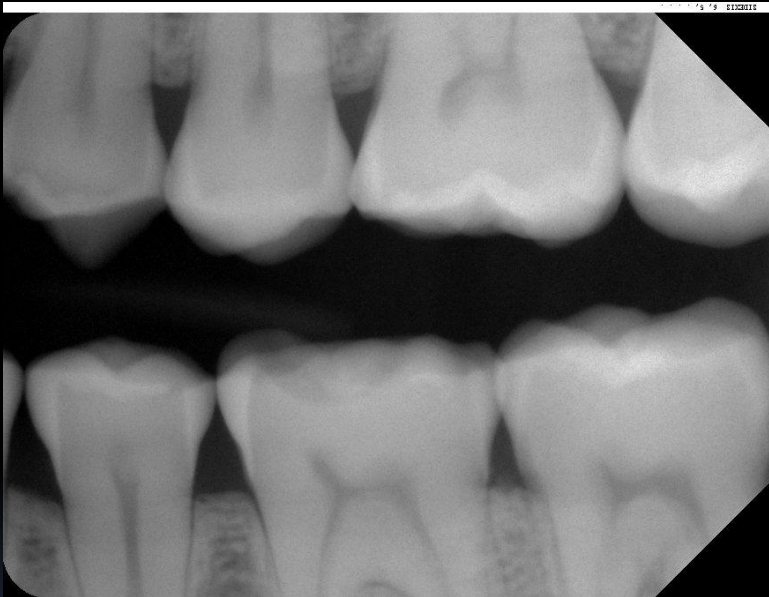
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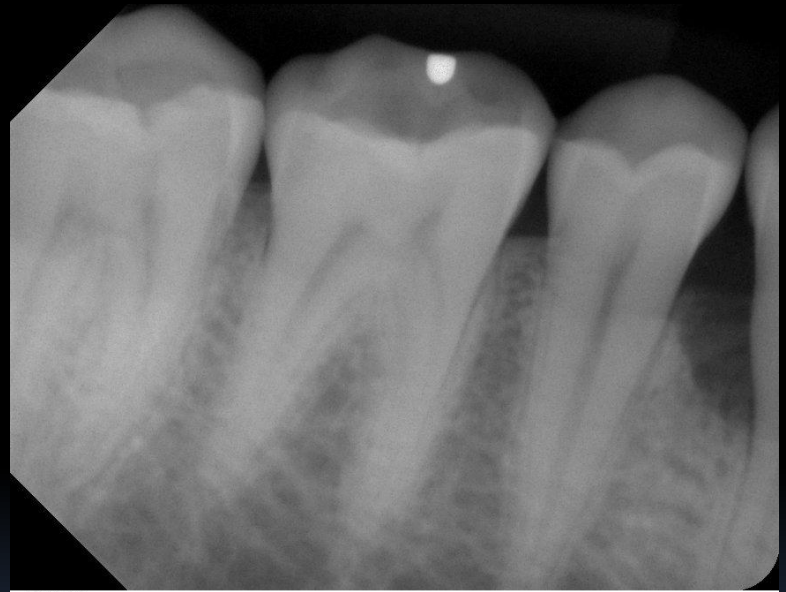
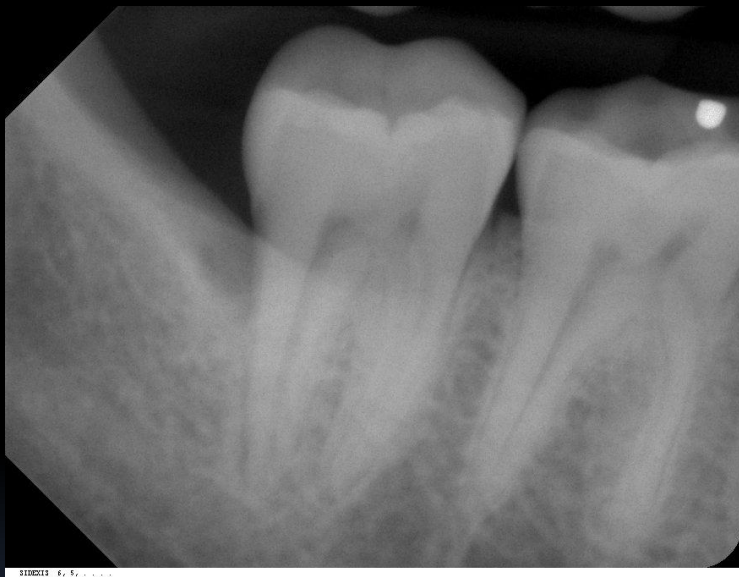






FIGURE 6.5.






Discussion

- Diagnosis
 - Periodontally susceptible?
 - Treatment recommendations?
 - Antibiotics?
 - Surgery?
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Case #2

Medical History

- 20 y.o. Caucasian male
 - Childhood diseases
 - Smoker – 1/2 pack/day
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Clinical Presentation

12/10/07



Clinical Presentation

12/12/07



Clinical Presentation

12/14/07



Clinical Presentation

12/19/07





Discussion

- Diagnosis?
 - Treatment recommendations?
 - Antibiotics?
 - Surgery?
- 