Study Questions:

1. Amoxicillin and metronidazole are the most commonly prescribed for selective periodontitis patients. What are their major features?

2. Mechanical removal of etiologic and local factors is the gold standard of anti-infective therapy in periodontics. Who could be the candidates for systemic antibiotic therapy as an adjunct to scaling and root planing?

3. Tetracycline tablets (for PO) are not currently available in the market. However, Aresin as a local delivery agent is available.

4. Local delivery agents are placed into periodontal pockets directly. What are the available local delivery agents and their active ingredients?

5. Antibiotic treatment alone is not a sufficient treatment for periodontitis. How does a systemic antibiotic affect the bacteria involved in initiation and progression of periodontal disease when it is used as an adjunct to scaling and root planing?

6. What are the different features between periodontal and pulpal abscess?

7. What are the oral rinses currently available for chemical plaque control? What are their major features?

8. What is the concept of Host Modulation Therapy in periodontics?

9. What are the major features of Sub-antimicrobial Dose Doxycycline?
Antiinfective Therapy

- Etiology of periodontal disease?

**Bacterial plaque**
- Bacteria begin reattaching to the crowns soon after the cleaning.
- Supragingival plaque biofilm becomes more complex, grows in an apical direction, and becomes subgingival.
- The bacterial biofilm extends so far subgingivally that the patient cannot reach.
- The complex biofilm may offer some protection from the host’s immunologic mechanisms in the pocket, as well as from antibiotics used for treatment.

How does a systemic antibiotic affect the bacteria involved in initiation and progression of periodontal disease?

- Antibiotic treatment alone was not a sufficient treatment for periodontitis due to the fact that the penetration of the antibiotics into the biofilm was low and that there is higher resistance in the biofilm.
- Disrupting the biofilm mechanically is the gold standard for reducing disease.
- Systemic antibiotics help prevent recolonization and reorganization of the biofilm after the biofilm has been disrupted.

Systemic antibiotics may help

After the cleaning = after instrumentation

Supragingival plaque -> becomes subgingival plaque

Antibiotic strength needed might need to be 5 times greater against bacteria arranged in biofilm
Antiinfective therapy = means disruption of subgingival biofilm. Includes: mechanical (scaling, root planing) and antibiotics.

Removal of biofilm is the gold standard.

Definitions

- **Antiinfective agents:**
  A chemotherapeutic agent acting by reducing the number of bacteria present.

- **An antibiotic:**
  A type of antiinfective agent that destroys or inhibits the growth of selective microorganisms, generally at low concentrations.

- **An antiseptic:**
  A chemical antimicrobial agent applied topically or subgingivally to mucous membranes, wounds, or intact dental surfaces to destroy microorganisms and inhibit their reproduction or metabolism.

- **A disinfectant:**
  A spectrum of antiseptics that are generally applied to inanimate surfaces to destroy microorganisms.
Not every patient needs systemic antibiotics

Candidates for systemic antibiotic therapy

- Patients who exhibit continuing loss of periodontal attachment despite diligent mechanical periodontal therapy
- Recurrent or refractory periodontitis
- Aggressive periodontitis
- Patients with medical conditions predisposing to periodontitis
- Patients with acute or severe periodontal infections

What would be the ideal qualities of antibiotics in "treating" periodontal disease?

The ideal antibiotic for treating periodontal disease would specifically target periopathogenic microorganisms to reduce their numbers sufficiently so that continued mechanical periodontal therapy is effective.

There is no single antibiotic that fulfills this requirement
There is always a potential risk with administration of systemic antibiotics. Must consider adverse reaction and risk of developing bacterial resistance.

Amoxicillin and metronidazole are most common in periodontal conditions. Combination of the two is the first choice of many clinicians in many cases.
Characteristics of the antibiotics

We are focusing on tetracycline, amoxicillin, metronidazole, and clindamycin.

Effective in treating periodontal diseases

Traditionally used to treat refractory periodontitis including localized aggressive periodontitis, but now use is limited due to side effects.
Not shown to be effective in treating periodontal diseases

Amoxicillin and Augmentin in combination therapy is used

Disrupts the DNA synthesis of bacteria

Not the drug of choice for treating Aa (due to side effects and interaction with Barbiturates and Warfarin) but is used in combination with amoxicillin
Drug of choice when allergy to penicillin

Clindamycin

**Pharmacology**
- Effective against anaerobic bacteria
- A strong affinity for mucous tissue
- Effective in patients with penicillin allergy

**Clinical Use**
- Patients with periodontal refractory to metronidazole therapy

**Side Effects**
- Diarrhea (pseudomembranous colitis)

Serial and Combination Antibiotic Therapy

**Rationale**
1. Because periodontal infections may contain a wide diversity of bacteria, no single antibiotic is effective against all putative pathogens.
2. Before combination of antibiotics are used, antibiotic-susceptibility test must be performed.

Amoxicillin and Metronidazole often prescribed
Prior to prescribing antibiotics, need to consider information on the slide.

Information in red is the gold standard for periodontal therapy in every case.

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**Pharmacologic Implications**

- The clinical diagnosis and situation dictate the need for possible antibiotic therapy.
- Disease activity may be an indication for periodontal intervention and possible microbial analysis through plaque sampling.
- Microbiologic plaque sampling may be performed according to the instruction of the reference laboratory.
- Root planning, optimal oral hygiene, and periodontal maintenance are important parts of comprehensive periodontal therapy.
- There are limited data to identify which antibiotics are suitable for periodontal treatment.

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**The concept of Local Delivery of Antibiotics**

Local delivery of antibiotics involves placing the antibiotic directly where it is intended to work— in this case, the periodontal pocket.
Most important reason for local delivery is for high gingival crevice fluid concentration.
Local delivery agents available listed on slide.
Agents available in US: Periochip, Atridox, and Arestin

Picture on slide = Arestin placement in patients mouth

Clear indication for antibiotics is periodontal abscess
Localized purulent inflammation of periodontial tissue
Gingival abscess vs. periodontal abscess based on the extent
Periodontal or anatomic origin

Huge difference: periodontal vs. pulp = pulp vitality

Not all endodontic involvements are non-vital (example: partial pulp necrosis)

Therefore, thorough clinical evaluation is needed to distinguish

Chronic = minimal symptoms, no systemic involvement

Acute = symptoms, may need systemic antibiotics
Pictures of clinical manifestations of periodontal abscess

Treatment options for periodontal abscess

- **Drainage** through pocket retraction or incision
- **Scaling and root planing**
- **Periodontal surgery**
- **Systemic antibiotics**
- **Tooth removal**

First choice = drainage. Either pocket scaling and root planing or incision through periodontal surgery.

Tooth extraction option if hopeless prognosis.
Indications for antibiotic therapy in patients with acute abscess

- Cellulitis (nonlocalized, spreading infection)
- Deep, inaccessible pocket
- Fever
- Regional lymphadenopathy
- Immunocompromised patient

Antibiotic options for periodontal infections

**Antibiotic of Choice**

- A) Metronidazole, 500 mg twice a day for 3 days
- B) Clindamycin after 3 days to determine need for continued or adjusted antibiotic therapy

**Possible Allergy**

- C) Doxycycline
- D) Amoxicillin

Data from American Academy of Periodontology, JADP, 12(3), 2006

Slide shows regimens for treatment of active periodontal abscess
Improved understanding of infectious nature of dental disease has led to an increased interested in chemical plaque control mechanisms.

The agents have to demonstrate significant improvement in gingival health compared to control.

To date, ADA has only accepted two agents approved: prescription chlorhexidine rinse and nonprescription essential oil rinse.

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**Chemical Plaque Control With Oral Rinses**

- The agents must be evaluated in placebo-controlled clinical trials of 6 months or longer
  1) Chlorhexidine Rinse
  2) Nonprescription Essential Oil Rinse

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**Prescription Chlorhexidine Rinse**

- Antiseptic properties
- The most positive antibacterial results
- Clinical studies of several months’ duration have reported plaque reductions of 45% to 65% and more importantly, gingivitis reductions of 27% to 67%.
- The 0.12% chlorhexidine digluconate preparation available in the United States for reducing plaque and gingivitis has been shown to be equally effective as the higher-concentration product.

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2 daily rinses of 0.2 chlorhexidine almost completely inhibited plaque, calculus, and gingivitis development.
Both of these are reversible localized side effects: brown staining and transient impairment of taste perception.

Non-alcohol version may be preferred by patients.

Low toxicity to humans.

Long-term clinical studies have shown plaque reduction.
Recommendations

- Chlorhexidine rinses can be used to augment plaque control curing Phase 1 therapy for patients with recurrent disease, and for use after periodontal or oral surgery.
- Essential oil rinses are effective to a lesser degree than chlorhexidine, have fewer side effects, and are available without prescriptions.
- Oral rinse preparations are also available with no alcohol content, which may be preferable to some clinicians and patients.
- The use of cosmetic oral rinses and prebrushing rinses should not be used to replace proven mechanical and chemical means of plaque removal but can be useful if patients perceive benefits from them.

Host Modulation

- Host: the individual who harbors periodontal pathogens
- Modulation: alteration of the host response to periodontal pathogens

Host modulation is a relatively new term.
Concept of HMT is new to field of dentistry

HMT used to reduce excessive levels of enzymes, cytokines, and prostaglandins. It should not be used to reduce those below essential levels.
Reduce excessive enzymes, cytokines, and prostaglandins, osteoclast and osteoblast function.

But, should not affect normal tissue turnover.

HMT key to address risk factors with adverse effect on host response: not easily managed (smoking and diabetes) or can't be changed (genetics).

Outline

- Systemically administered agents
  1. Nonsteroidal Anti-inflammatory Drugs
  2. Bisphosphonates
  3. Sub-Antimicrobial-Dose Doxycycline

- Locally administered agents
  1. NSAIDs
  2. Enamel Matrix Proteins, Growth Factors, and Bone Morphogenetic Proteins
PGE2 extensively studied in periodontal disease because it up-regulates bone resorption by osteoclasts.

NSAIDS inhibit PGE so decreases inflammation.

Systemic NSAIDS daily up to 3 years shows significant slowing of the rate of bone loss compared to placebo.

But, disadvantages when considering it as HMT in periodontal disease: daily extended use needed for benefits to be apparent. NSAIDS have side effects (GI issues, hemorrhage, and renal & hepatic impairment).

- Also, periodontal benefits are lost after administration of the NSAIDS is stopped or acceleration of bone loss seen before occurs ("rebound effect").

Therefore, long term use of NSAIDS as adjunctive treatment never developed beyond research.

Evidence suggests it is also useful as an anti-collagenase.

Modulates osteoclasts -> useful in periodontal disease.

Research demonstrated:
- Natural periodontal cases in Beagles - increased bone density compared to placebo.
- Animal models - decrease alveolar bone resorption.
- Humans - enhanced alveolar bone status and density.
  - However, unwanted effects: inhibiting bone calcification and inducing changes in white blood cell counts, as well as reports of vascular necrosis of the jaws.
  - Necrosis of the jaws risks bone necrosis after extraction.
  - ONJ hindered development of bisphosphonates as HMT to manage periodontal disease.
  - As with NSAIDS, no bisphosphonate drugs approved nor indicated for treatment of periodontal disease.
AKA Periostat
Approved and indicated as adjunct to scaling and root planing in treatment of chronic periodontitis.
Studies found no detectable antimicrobial effect when adjunct to scaling and root planing.
At present, only systemically administered HMT for chronic periodontitis approved by FDA and accepted by ADA.

Sub-Antimicrobial-Dose Doxycycline_1
- A 20-mg dose of doxycycline (Periostat)
- The only systemically administered HMT
- Taken twice daily for 3 months, up to a maximum of 5 months of continuous dosing
- Exerts its therapeutic effect by enzyme, cytokine, and osteoclast inhibition rather than by antibiotic effect.

Sub-Antimicrobial-Dose Doxycycline_2
- Indication
  1. Aggressive and chronic periodontitis
  2. The management of patients with systemic diseases such as diabetes and rosacea.
- Mechanism of action
  1. To downregulate MMPs
  2. To stimulate osteoblastic activity and new bone formation by upregulating collagen production.

MMPs = Matrix metalloproteinase
Number of agents investigated as potential adjuncts to surgery

They improve wound healing and stimulate regeneration of lost bone, periodontal ligament, and cementum

FDA approved adjuncts to surgical procedures: enamel matrix proteins, recombinant human platelet-derived growth factor-IBB, and bone morphogenetic proteins.