Chemical plaque control, antibiotics

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PATHOLOGY

PERIODONTAL DISEASES

could be all disorders of the periodontium, BUT the terminology of "periodontal disease" is usually utilized for the **dental plaque related** infectious/inflammatory diseases of the periodontal tissues.

ETIOLOGY

DENTAL PLAQUE IS THE PRIMARY COUSE OF ALMOST ALL CLINICAL FORMS OF PERIODONTAL DISEASE!

CONSEQUENTLY THE PREVENTION AND THERAPY OF PERIODONTAL DISEASE IS BASED ON THE ELIMINATION OF DENTAL PLAQUE!

DIFFERENCES IN THE BACTERIAL FLORA

healthy	caries	gingivitis	parodontitis
Gr +	S. mutans	Gr- facultative anaerobe	Gr- obligate anaerobe
cocci	S.sobrinus	Actinobacillus	capnophilic bacilli
S. salivaris	Veillonella	Capnocytophaga	Actinobacillus
S. mitis	Lactobacillus sp.	Eikenella	actinomycetemcomitans
A. naeslundii	...	A. israelii	Porphyromonas gingivalis
Neisseria		A. viscosus	Prevotella intermedia / nigrescens
Veillonella		Bacteroides gingivalis	Bacteroides forsythus
Haemophilus		Treponema spp	Peptostreptococcus micros
B. melaninogenicus		...	Fusobacterium nucleatum
B. intermedius			Campylobacter (Wolinella) rectus
Fusobacterium			Capnocytophaga
Eubacterium			Eikenella corrodens
Bifidobacterium			Spirochetes
...			...

Biofilms have been defined as matrix-embedded microbial populations, **adherent** to each other and/or to surfaces or interfaces

Biofilms are usually **highly structured** with channels traversing the depth of the biofilm, creating primitive circulatory systems

The **component species** are not randomly distributed but are spatially and **functionally organized**, and many natural biofilms have a highly diverse microflora.

(Costerton et al. 1995).

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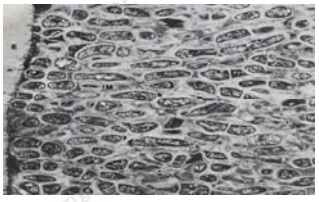
PLANCTONIC FORM VS. BIOFILM

Bacterial biofilm: protective biological formation!

- Resistant bacteria (part of the biofilm) can protect others from the effect of AB (β-lactamase)
- Formation of extracellular matrix: limited diffusion/penetration
- The bacteria in the basic layer have reduced metabolic activity – multiplication, which are the target processes of AB-s
- Unequal distribution of electrical charge
- synergistic/antagonistic microbial interactions



Antimicrobial resistance

Bacteria growing in dental plaque also display an increased tolerance to antimicrobial agents, including those used in dentifrices and mouthrinses
(Marsh & Bradshaw 1993, Kinniment et al. 1996, Wilson 1996, Pratten & Wilson 1999).

For example, the BIC (biofilm inhibitory concentration) for chlorhexidine was **300 times greater**, when *S. sobrinus* was grown as a biofilm compared with the BIC of planktonic cells.
(Shani et al. 2000).

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PERIODONTITIS – SPECIAL AREA

Anatomical consequences: pocket formation –:

- Unique inflammation: lack of massive bacterial invasion to the surrounding soft tissues
- infected tooth surface has no individual blood flow/ not easy accessible for the immun system
- Distribution of several ABs is different in the human body/tissues/fluids:
  - E.g.: crevicular fluid
  - Sufficiently high concentration for enough time

Periodontal Therapy

Mechanical plaque control

•**THE standard periodontal care**

- Individual plaque control (OH)
- Professional plaque control (S&P, RSD)

Chemical plaque control

•**For individuals with compromised immun response** even the most sophisticated tooth brushing is not effective enough

•The mechanical plaque control meets objective diffuculties by **physically** or **mentally handicapped patients**

•**Postop** cleansing, when brushing is suspended

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Periodontal chemoprophylaxis

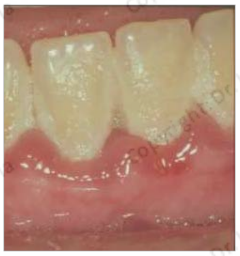
Chemical plaque control

The efficacy of any antiseptical mouth rinses depends not only on their bactericid influence, but also on their diffusive ability **through the matured biofilm**

Tooth paste

Pocket irrigation agents

Mouth rinses



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IDEAL ANTI-PLAQUE CHEMICAL OR BIOLOGICAL AGENT

- **Can permanently inhibit bacterial adhesion**
- **The agent can penetrate and reach plaque bacteria**
- **Substantive**
- **Do not alter normal oral bacterial ecology**
- **Do not have cumulative or chronic irritative effects**

BISBIGUANID DERIVATIVES

SECOND GENERATION CHEMOPROPHYLACTIC AGENTS

Chlorhexidin ***1,6-di-4-chlorphenil-diguanidhexane***

0,2% 0,12% (0,05 %) - mouthrinses

1-2%-os gel

Alexidin ***etil-hexil-bisguanidine-dihydrochlorid***

Similar effect to Chlorhexidin

locally less irritation

does not contain carcinogenic phenyl groups

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BISBIGUANID DERIVATIVES

SECOND GENERATION CHEMOPROPHYLACTIC AGENTS

Chlorhexidin

- **Broad spectrum antiseptic**
- **Effective against Gram negative and Gram-positive microorganisms**
- **Proportionally decrease the whole oral bacterial count**
- **Effective against anaerobs and *Streptococcus mutans***
- **Clinically improves plaque and gingivitis indices**
- **Molecules attach to the negatively charged surfaces –hidroxyapatite, acquvired dental pellicle, mucosa**
- **from this bond the active molecules slowly released**
- **After a single rinse approx. 30% of molecules adhere to the surfaces and can sustain inhibitory concentration for at least over 12 hours**
- **Chlorhexidin rinsing twice a day may sustain permanent anti-plaque effect in oral cavity**

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Chlorhexidin

is accepted by the Food and Drug Administration (FDA) and American Dental Association (ADA) as proved anti plaque and gingivitis agent.

PLAQUE REDUCTION CAPACITY

- 0,2% Chlorhexidine digluconate - 75-80%
- Listerin 25%
- Sanguinarin 30%
- Hydrogen-hyperoxid 30%

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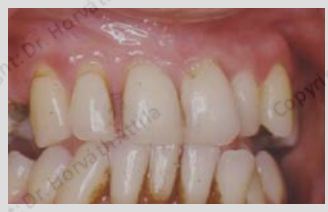
BISBIGUANID DERIVATIVES

SECOND GENERATION CHEMOPROPHYLACTIC AGENTS

Chlorhexidine



Several side effects

Discoloration

Taste disturbances

Glossitis

After long term use, mucosal chronic irritation may occur.

Periodontal chemoprophylaxis

Chemical plaque control

Effects of chlorhexidine on matured biofilm

The inhibition concentration of:

the clorhexidine was 300 times

the amino fluoride was 75 times higher

against Streptococcus sobrinus forming biofilm, than being planctonic state

Shani, S., Friedman, M. & Steinberg, D. (2000)
The anticariogenic effect of amine fluorides on *Streptococcus sobrinus* and glucosyltransferase in biofilms. *Caries Research* **34**, 260- 267.

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Periodontal chemoprophylaxis

Chemical plaque control

Effects of chlorhexidine on matured biofilm

The chlorhexidine has better penetration potential than Listerin or Meridol

Netuschil, L., Weiger, R., Preisler, R. & Brecx, M. (1995)
Plaque bacteria counts and vitality during chlorhexidine, meridol and listerine mouthrinses.
European Journal of Oral Science 103, 355- 361.

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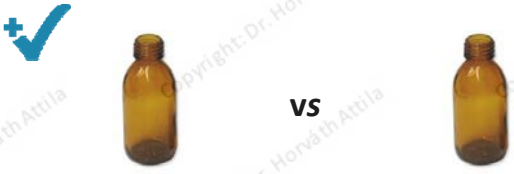
Concentration issues



CHX 0,12% **VS** **CHX 0,2%**

CHX in 0.12% is similar effective as in 0.2%

Lang et al. (1982)

CHLORHEXIDINE: Gold Standard

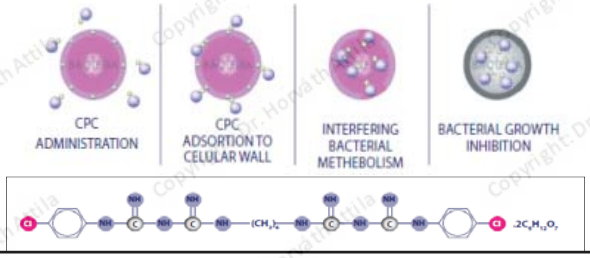
- ✓Potent antiseptic
- ✓Wide efficacy scale
- ✓High substantivity

CETYLPYRIDINIUM CHLORIDE

Mechanism of action

1) The hydrophobic part of the molecule penetrates through the cell membrane causing cell death.

2) Neutralises bacterial toxins.



PHENOL DERIVATIVES

Listerin

with American Dental Association (ADA) seal

Evidence support its anti plaque anti-gingivitis effects

Ingredients: thimol, menthol, methylsalicitate eukaliptol.

Daily and/or long term usage is not recommended

TRICLOSAN

- Has only mild anti-plaque effect
- Zink citrate or polyvinilmethyl ether –maleic acid can potentiate its effect and increase substativity
- Several clinical tirals proved the anti gingivitis effect by toothpastes containing triclosan/zink citrat or co-polymer.

QUATERNERY AMMONIUM COMPOUNDS

- In vitro strong antibacterial effect
- in vivo, mind anti plaque effect due to low substantivity
- *cetilpirimidinumklorid* (CPC)
- *benzylconium-chloride*
- *domiphen-bromid.*

HALOGENS

IODINE AND FLUORIDES

Betadine

fluorides

Sn-fluoride and amino fluoride milder anti-plaque effect comparing to Chlorhexidin

Meridol *amino-fluoride + stannous fluoride*

Summary of chemical plaque control

antiseptics

Chemical plaque control does not replace mechanical plaque control

Even Chlorhexidin do not substitutes regular SPT

In case of impairment of mechanical plaque control (disability, hospitalised patient, supressed immunity, following periodontal surgery) ADDITIONAL chemoprofilaxis is indicated. Merely for a certain period of time (i.e. 3 weeks)

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PERIODONTAL CHEMOTHERAPY

ANTIBIOTICS

Can be administered

- Locally
- Orally
- Parenterally

ANTIBIOTICS

- **Should be selective againts plaque bacteria**
- **Will not be used in other systemic disorders**
- **Non toxic**
- **Has no cumulative or chronic irritative effect**
- **Does not develop bacterial resistance**
- **Does not act as an allergen**
- **Has a substantive effect**

There is no ideal agent for the time being

BASIC PRINCIPLES OF PERIODONTAL ANTIBIOTIC THERAPY

- Definitive periodontal diagnosis is needed
- Only in active disease stage is to be used
- Bacteriological testing is usually not required
- Antibiotic tx is not a monotherapy, a broad spectrum tx, instead
- Systemic treatment can be completed by antiseptics (Chlorhexidine, Betadine, Tetracyclin etc.)
- Antibiotics can be used alongside RSD, before surgery and postoperatively to improve periodontal wound healing

PENICILLIN DERIVATIVES

Penicillin per se is not indicated against periodontal infections

Only synthetic amoxicillin or clavunated amoxicillin (Augmentin) are effective

AMOXICILLIN

- Broad spectrum semi-synthetic penicillin
- Effective against both Gram – and Gram + bacteria
- Penicillinaze , beta-lactamase producing bacteria inactivates its effect
- Indication: aggressive periodontitis and refractory periodontitis with deep pockets
- Can be combined with metronidazole
- Infective endocarditis prophylaxis

CLAVUNATED AMOXICILLIN
E.G. AUGMENTIN

- Amoxicillin + acidum clavulanicum penicillinaze resistant
- Broader spectrum
- Indication: aggressive periodontitis and refractory periodontitis can be combined with metronidazole
- Infective endocarditis prophylaxis (2 g one hour before invasive procedures)
- Dosage: 500-1000mg TID for 5-7 days

METRONIDAZOL
KLION

- It is not a real antibiotic.
- *Nitroimidazol* derivative originally was used against protozoa
- It is effective against the most obligatory anaerobic microorganisms,
- It ha a bactericide effect - blocks DNA synthesis
- Effective against most periodontopathogenic organisms *(P. gingivalis, P. intermedia, T. forsythia*),
- It does not kill *A. actinomycetemcomitans* and other facultative anaerobic bacteria
- In this cases it should be given in combination with others
- Should not be given alongside anticoag med e.g. warfarin
- Dosage: 250-400mg TID for 5-7 days

CLINDAMYCIN
DALACIN C

- Effective against the most periodontopathogenic microorganisms
- Concentrated in the bone
- Higher than serum concentration in periodontal tissue and sulcus
- Strong gastrointestinal side effects e.g. pseudomembranosus colitis may occur
- Dosage: 300mg TID for 5-7 days

CIPROFLOXACIN
CIPROBAY

- Today all *A. actinomycetemcomitans* clonal forms are sensitive
- Strongly inhibits *A. actinomycetemcomitans* cell division but has minimal effect on commensal oral bacteria
- It is very effective to restore the normal composition of oral subgingival and supragingival bacterial flora,
- Daily dose 2x 250-500 mg.

IS THE MECHANICAL DEBRIDEMENT MORE SUCCESSFUL WITH THE ADJUNCT OF SYSTEMIC ANTIBIOTICS?

Slightly better values

- **PPD reduction**
- **CAL gain**

Herrera D, Sanz M, Jepsen S, Needleman I, Roldan S. A systematic review on the effect of systemic antimicrobials as an adjunct to scaling and root planing in periodontitis patients. J Clin Periodontol 2002: 29 (Suppl 3): 136-159, discussion 160-132.

Haffajee PJ, Socransky SS, Gunsolley JC. Systemic antiinfective periodontal therapy. A systematic review. Ann Periodontol 2003: 8: 115-181.

Hatóanyag	Vizsgált paraméter	Átlagos értéke	95%-os konfidencia intervallum
Spiramycin	PPD reduction	0.41 mm	0.08-0.73
Amoxicillin / metronidazole	CAL gain	0.45 mm	0.19-0.71

Herrera D, Sanz M, Jepsen S, Needleman I, Roldan S. A systematic review on the effect of systemic antimicrobials as an adjunct to scaling and root planing in periodontitis patients. J Clin Periodontol 2002:? 29 (Suppl 3): 136-159, discussion 160-132.

ChP vs. AgP
do we need AB Tx?

Difference is not clinically significant.

	Mean difference	95% CI
	Chronic periodontitis	
PPD reduction	0.43 mm	0.24-0.63
CAL gain	0.21 mm	0.02-0.4
	Aggressive periodontitis	
PPD reduction	0.58 mm	0.39-0.77
CAL gain	0.42 mm	0.23-0.61

Sgolastra F, Gatto R, Petrucci A, Monaco A. Effectiveness of systemic amoxicillin / metronidazole as adjunctive therapy to scaling and root planing in the treatment of chronic periodontitis: a systematic review and meta-analysis. *J Periodontol 2012*: 10: 1257-1269.

Sgolastra F, Petrucci A, Gatto R, Monaco A. Effectiveness of systemic amoxicillin / metronidazole as adjunctive therapy to scaling and root planing in the treatment of aggressive periodontitis: a systematic review and meta-analysis. *J Periodontol 2012*: 83: 731-743.

SO WHEN AND WHAT TO ADMINISTER?

Possible indications -

- **A.a. – penetrates through pocket's epithelial wall**
  cumbersome to eliminate mechanically
  Refracter cases
- **Aggressive periodontitis**
- **Chronic periodontitis >6 mm** baseline PPD

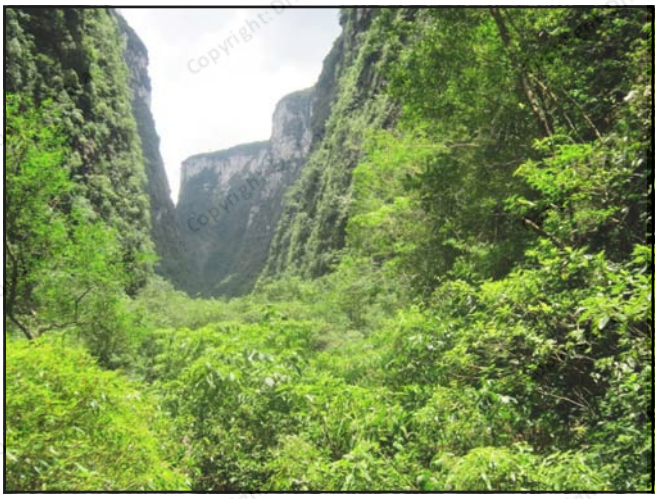
Post RSD 7-14 days

3 x 250-500 mg amoxicillin + 3 x 250-400 mg metronidazole / day (TID) for 5-7 days

Due to resistence, side effects, allergies it sould only be prescribed on a selective, individual basis!!!!

SIDE/ADVERSE EFFECTS

- **Allergy**
- **Development of microbial AB resistance** (the frequency of the usage is too high, lower dosage or for shorter period than it is necessary; patients cooperation)
- **Suppression of the normal flora – increased number of pathogenic bacteria** (destroyed biological balance) : Clostridium difficile – pseudomembranous colitis after prolonged clindamycin therapy
- **Overgrowth of non-bacterial microbes** – e.g. Candida albicans
- **Direct toxicity (e.g. overdose)**



LOCAL ANTIBIOTICS

Is the mechanical debridement more successful with the adjunct of local antibiotics?

First used in the Seventies as gels, chips

Most common :

- **Minocycline**
- **CHX**
- **Tetracycline**
- **Doxycycline**
- **Metronidalzole**

High local concentration

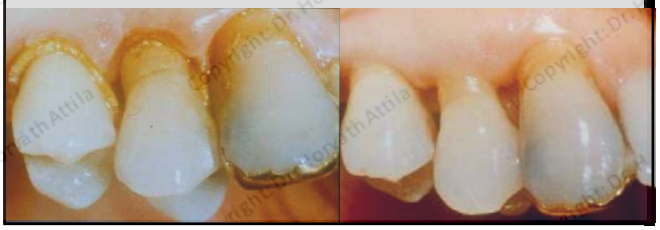
Short effect

Haneś PJ, Purvis JP. Local anti-infective therapy: pharmacological agents. A systematic review. Ann Periodontol 2003: 8: 79-98.

Bonito AJ, Lux L, Lohr KN. Impact of local adjuncts to scaling and root planing in periodontal desease therapy,: a systematic review. J Periodontol 2005: 76: 122-1236

ACTISITE

Tetracycline incorporated into etilen-vinil-copolimer fiber .
A 250 mm cord contains 12,7mg tetracycline
The Actisite fiber can be applied like the gingival retraction cords .
Treatment last for 8-10 days.
The local TCL concentration achieved is 1000-1200ug/ml in the sulcus



SLOWLY ABSORBED ANTIBIOTIC GELS

Doxycyclin gel (Atridox 10% doxycyclin),

Metronidazol gel (Elyzol 25% metronidazol),

They are not available in Hungary .

Ebrimycin gel (primicynum sulfuricum) had been successfully used for topical pocket therapy

LOCAL ANTISEPTICS IN THE POCKET

Corsodyl gel 1-5%.

Periochips 2,5 mg chlorhexidin incorporated into hydrolyzed gelatin – pellets (chips)

In deep pockets can sustain 100ug/ml concentration in crevicular fluid

Periodontal pocket irrigation with antiseptics

In order to supress biofilm

- **Antiseptics: povidone-iodine, sodium-hypochlorid, chlorhexidin digluconate** (pocket irrigation following S&P or RSD)
- **Some more PPD reduction (as an adjunct to RSD)** - *Rams & Slots, Periodontol 2000, 1996, 10: 139-159*
- **No additional benefit over mechanical instrumentation** (Sanz &Teughels, J Clin Periodontol, 2008,35: 3-7).

Full-mouth disinfection

1) '90-es, **RSD Q by Q on a weekly basis** (1 to 2 hét)

2) Full-mouth disinfection (FMD) in order to prevent reinfection from a contralateral pocket (<24 h) (*Quirynen et al, J Dent Res,1995, 74:1459-1467*

3) Full-mouth debridement: one session but without antiseptics

Conclusion: Any of the Tx above is equally effective

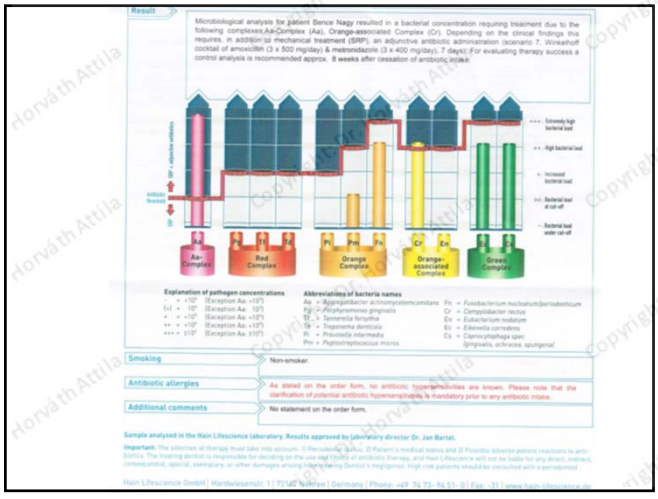
(Eberhard et al, J Clin Periodontol, 2008, 35: 591-604; Lang et al, J Clin Periodontol, 2008, 35:8-21)

Diagnostic

(Lab)

- Bacterial sampling
- DNS hibridizáció
- PCR

Parodontológia korszerűen



KEY TO SUCCESS

•Thorough RSD
•Good OH
•SPT
•Local AB Tx alone is not effective
•Systemic AB strictly when needed as a adjunctive Tx to RSD and surgeries