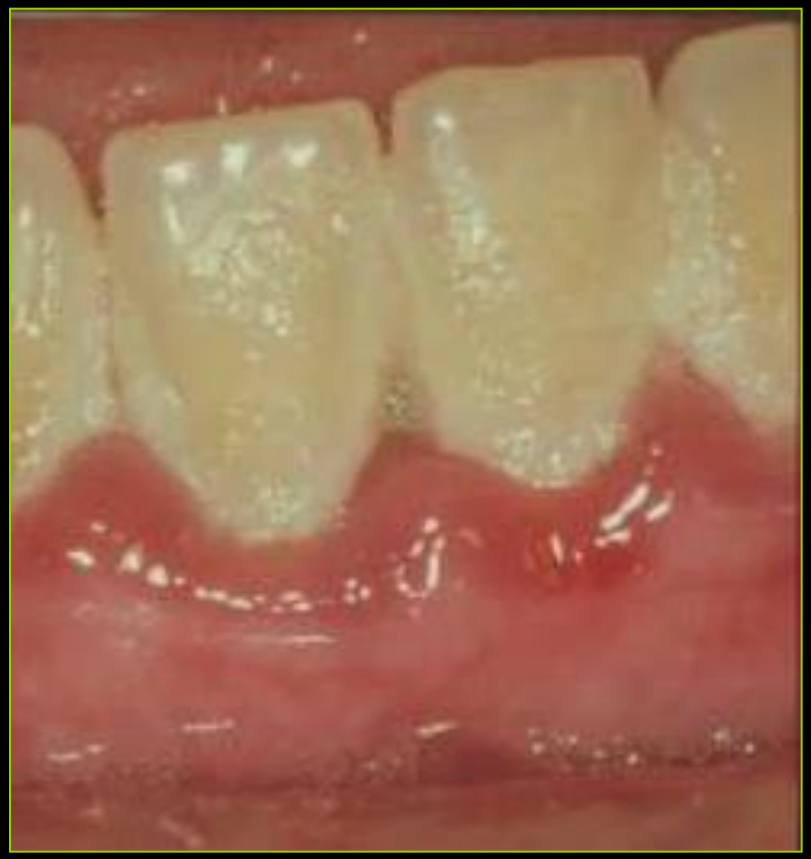
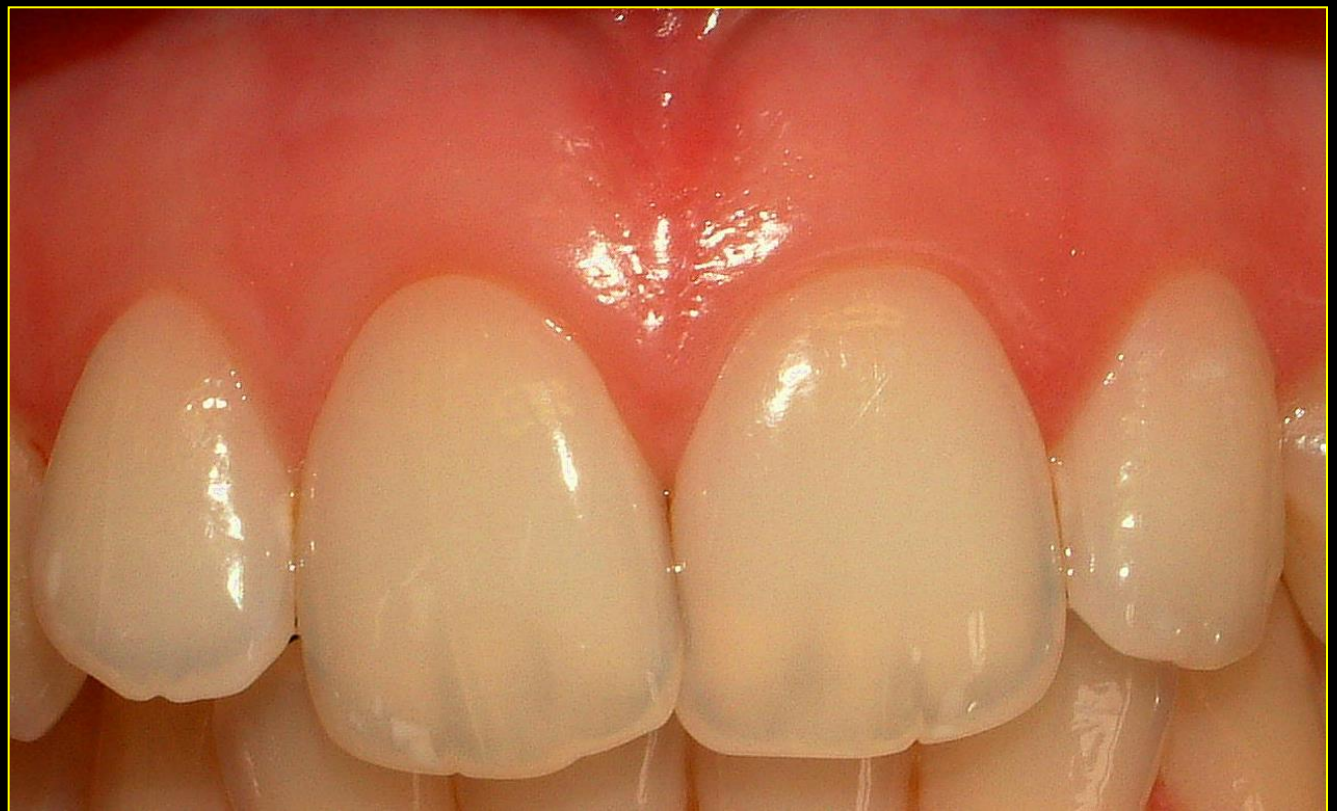
DENTAL PLAQUE AS A BIOFILM

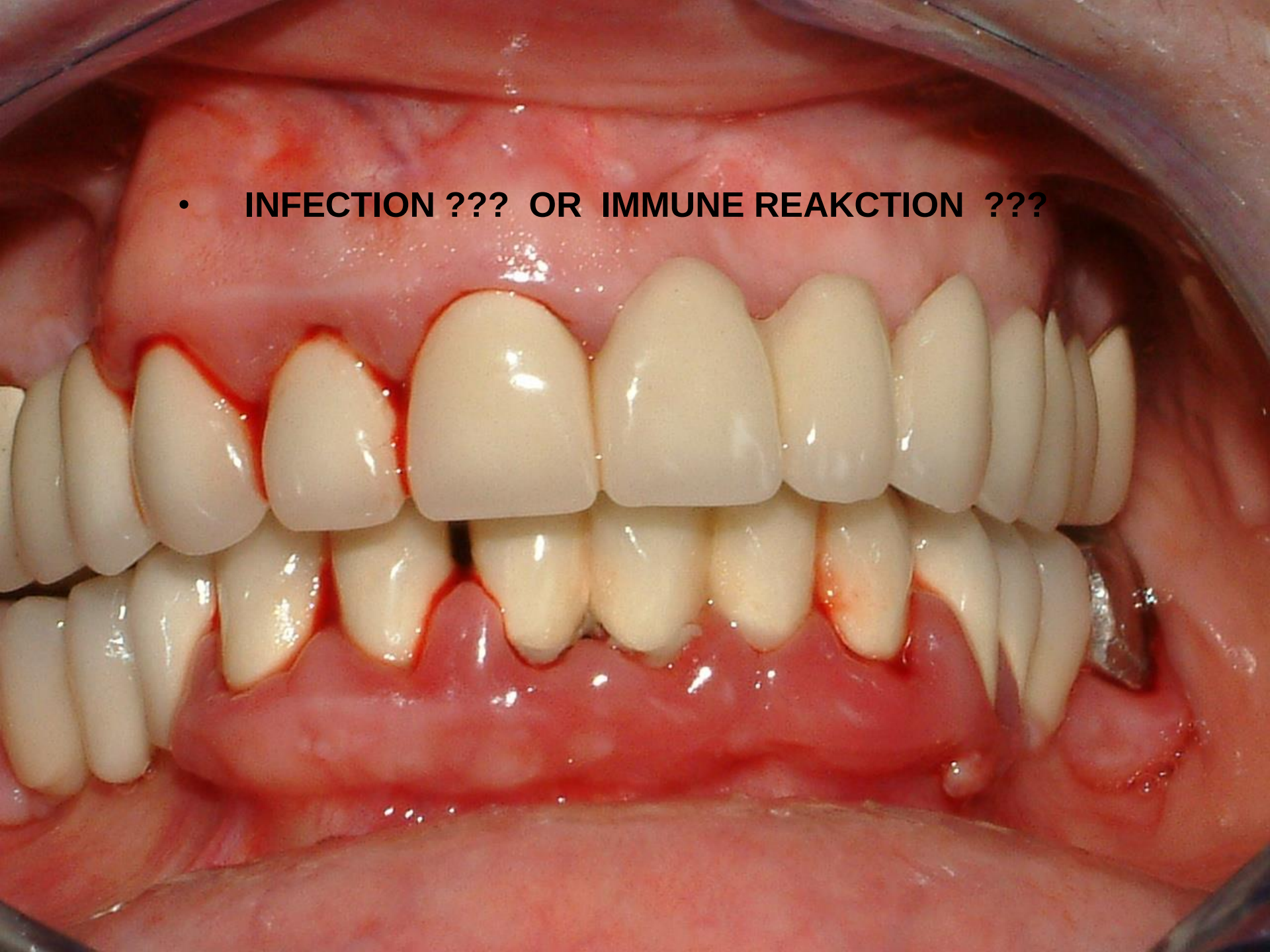
THE POSSIBILITIES OF CHEMICAL PLAQUE CONTROL

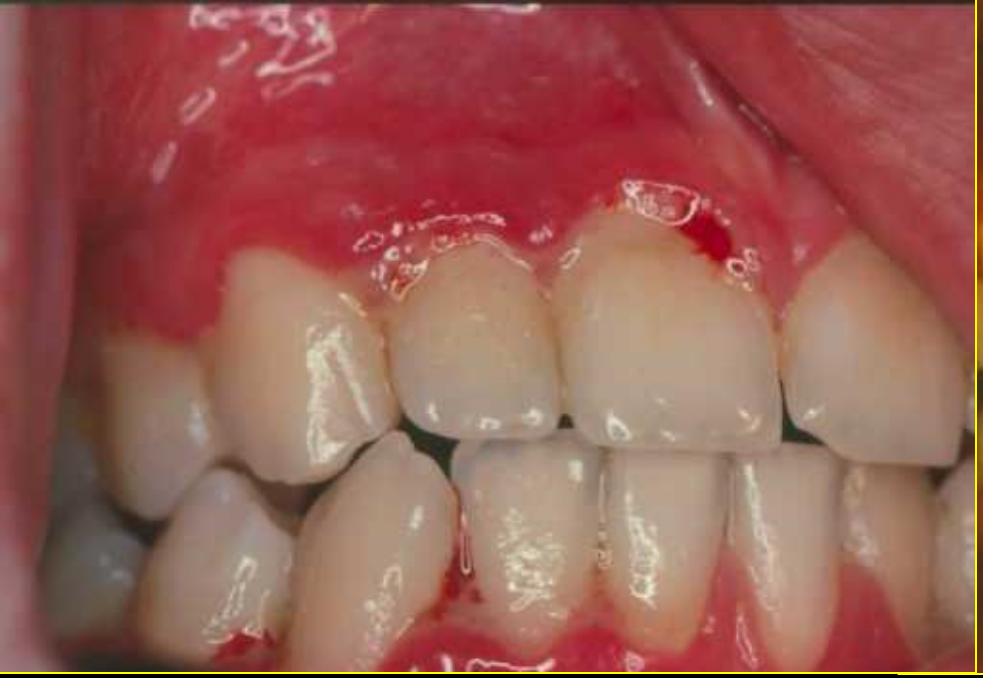


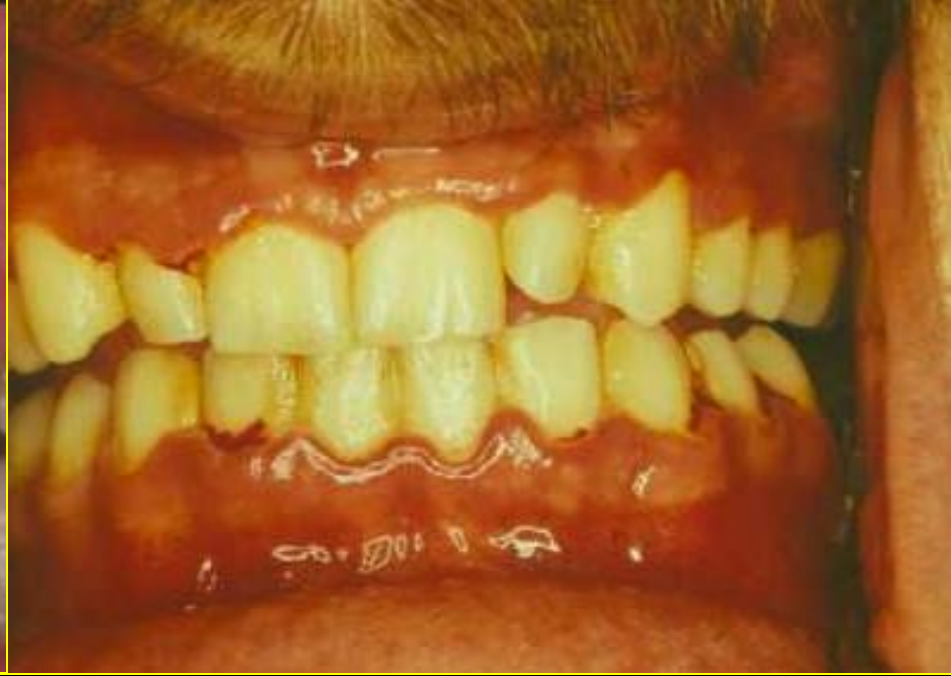
DR. GERA ISTVÁN SE DPT. PERIODONTOLOGY

THE HUMAN HOST IS HEALTHY DESPITE THAT THE 90% OF THE CELLS IN THE HUMAN BODY ARE BACTERIA (Henderson 1998)




• INFECTION ??? OR IMMUNE REAKCTION ???





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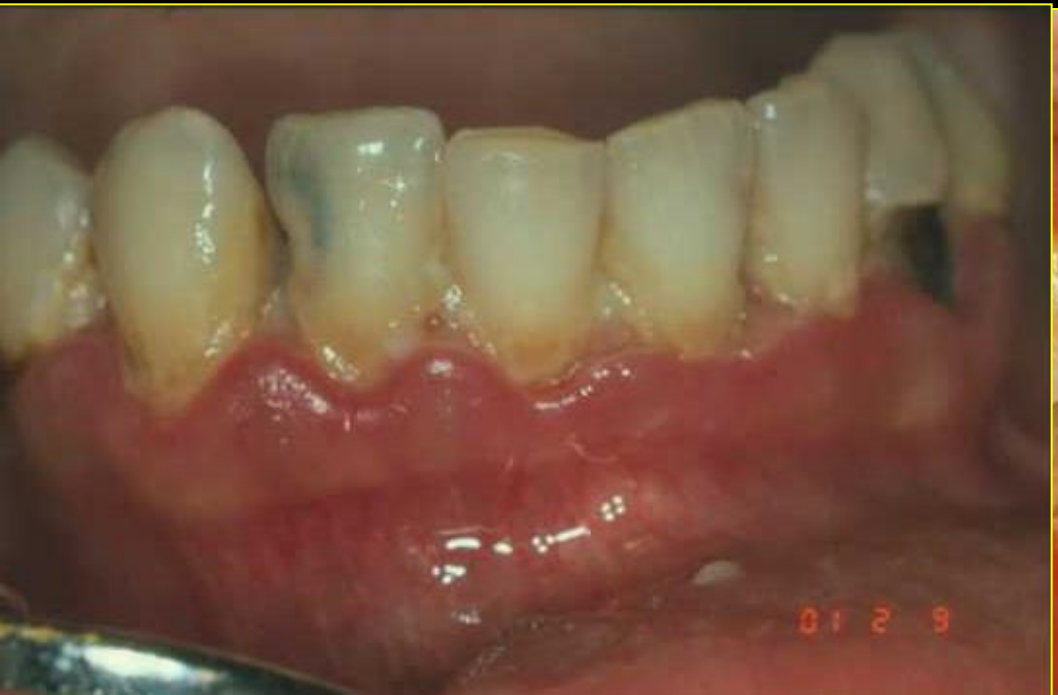

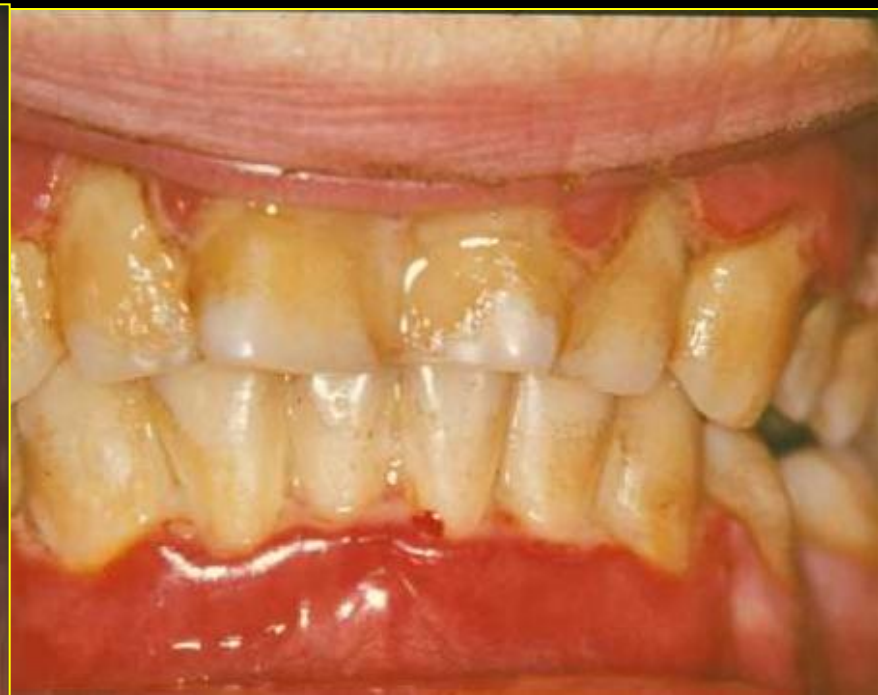

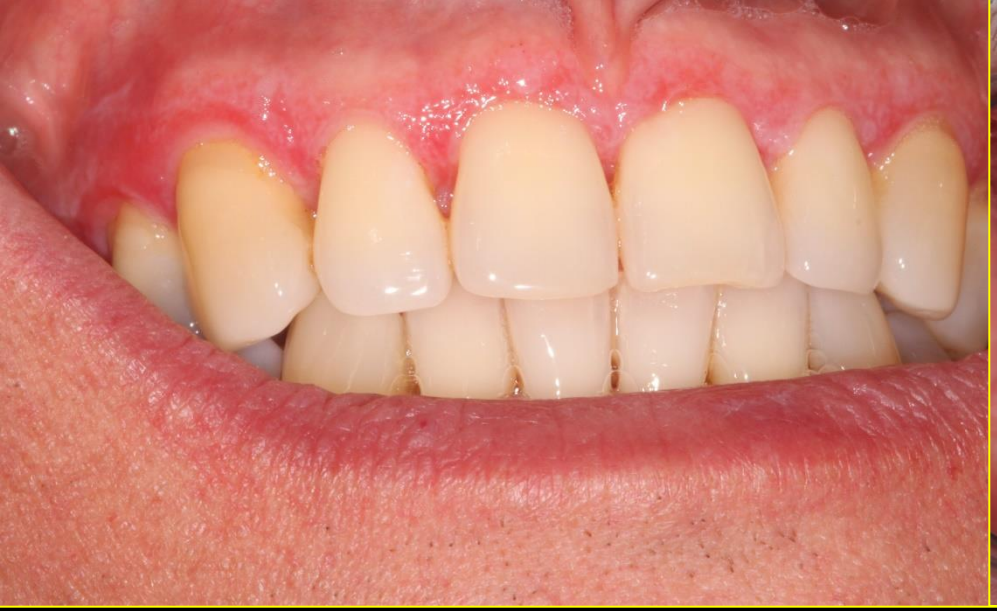

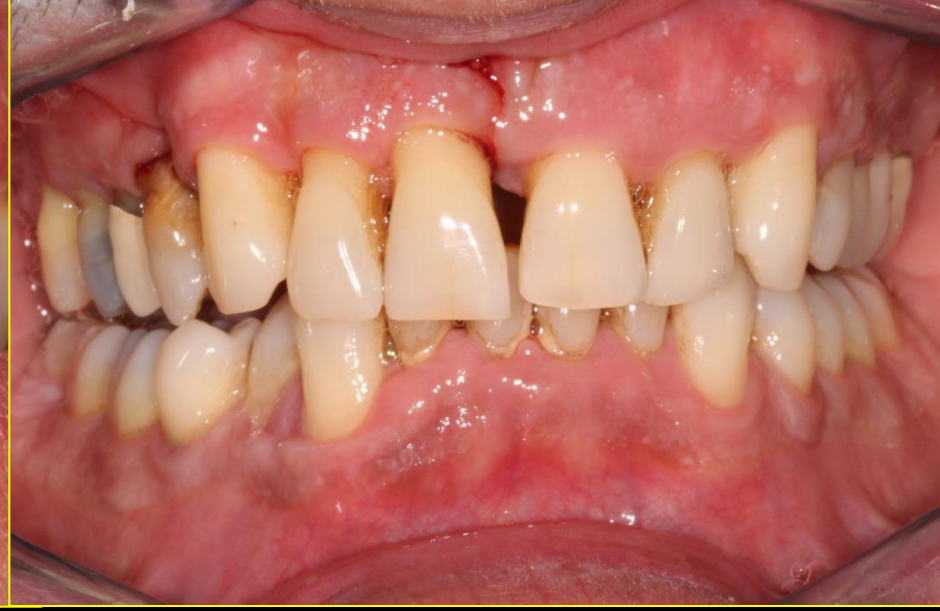

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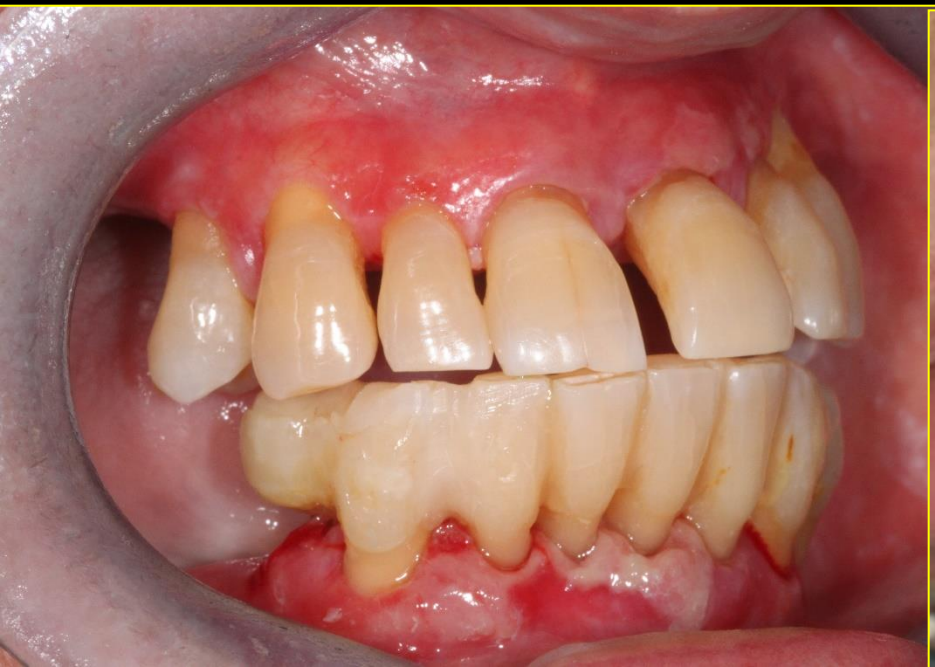

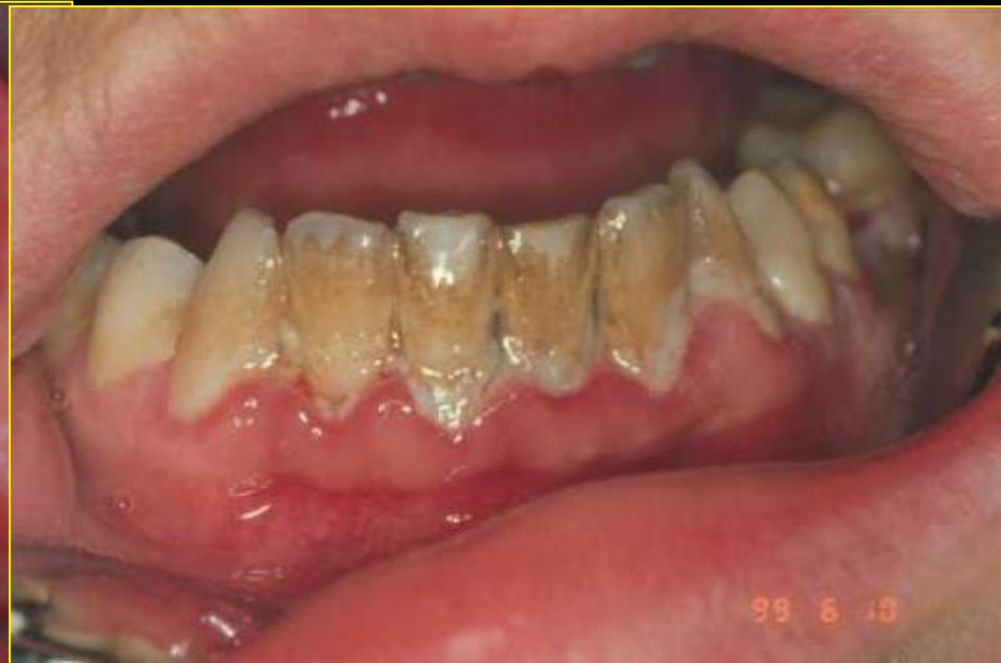

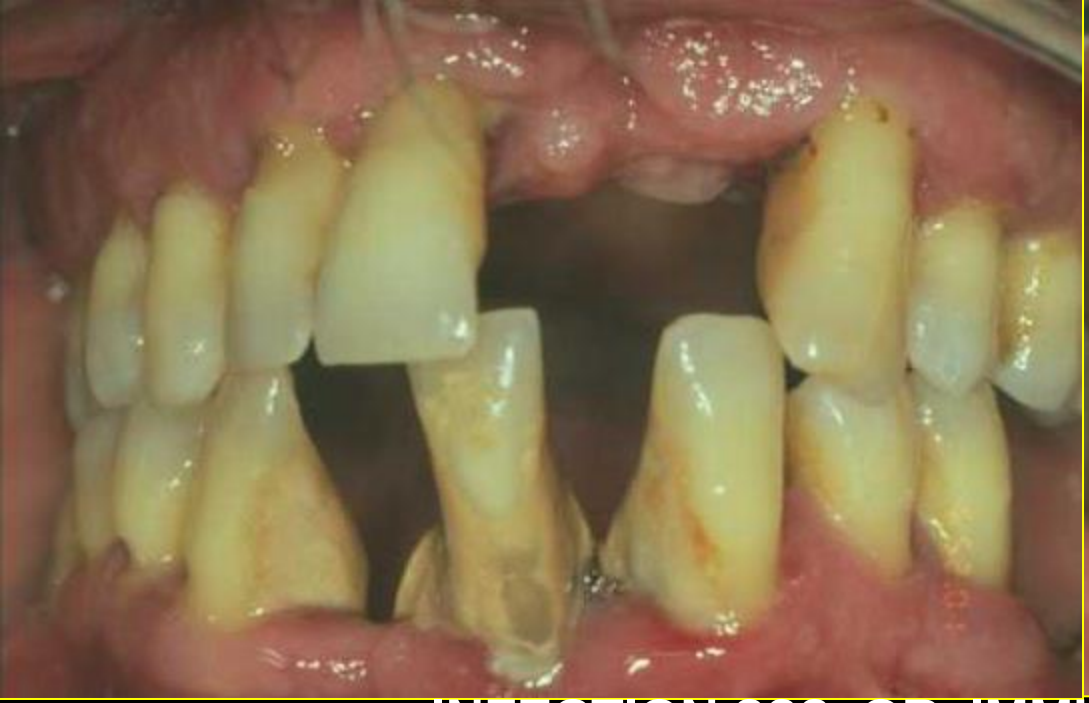

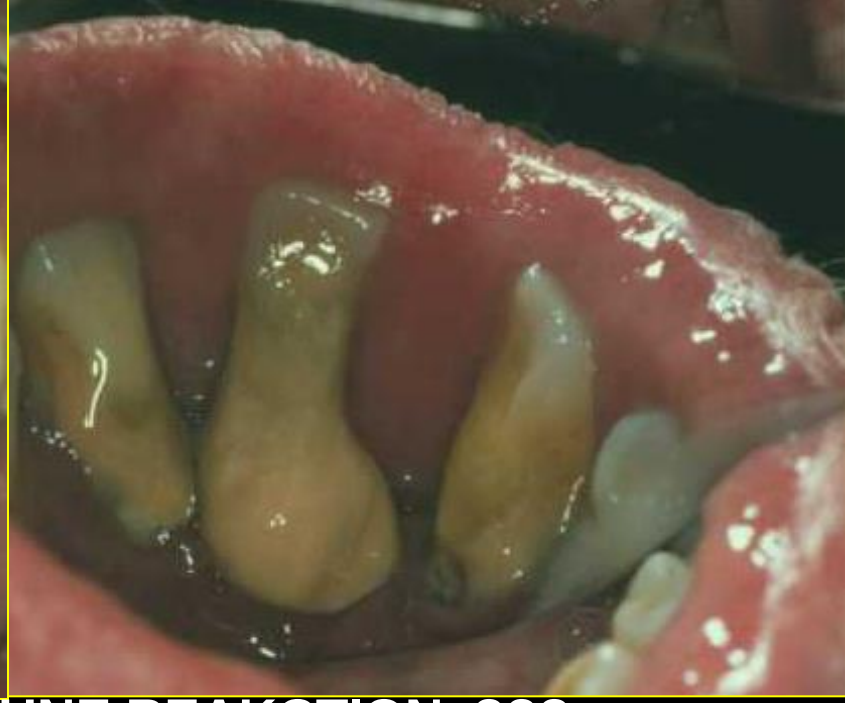

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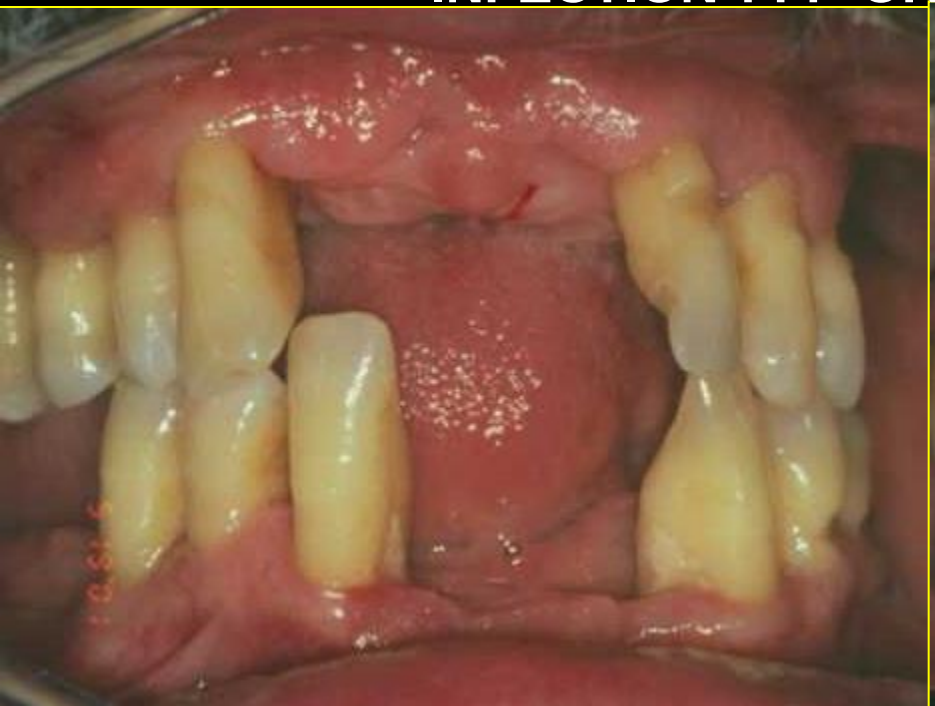
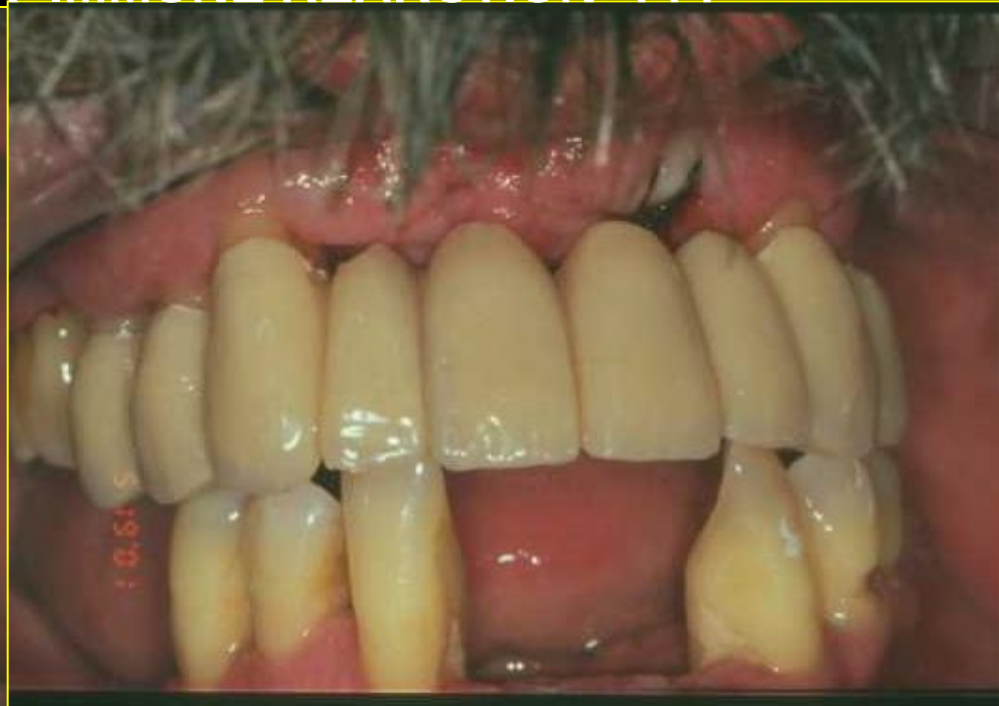
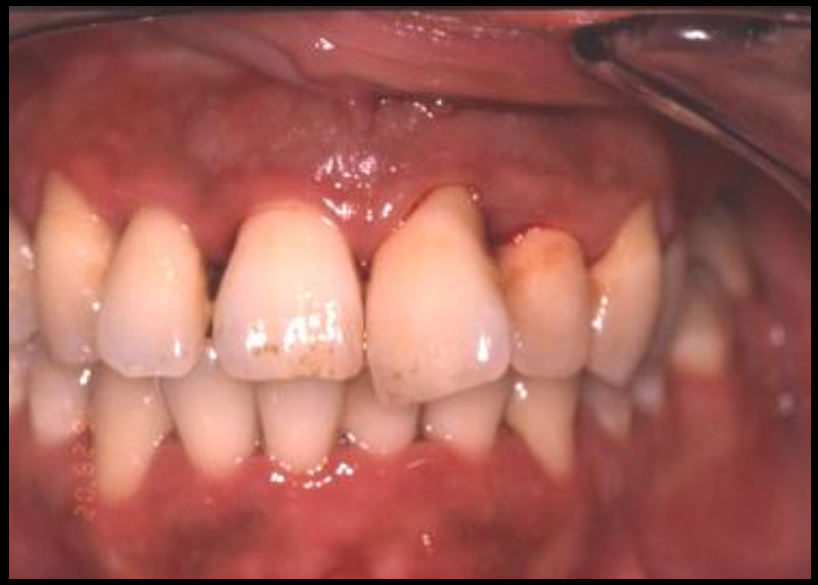




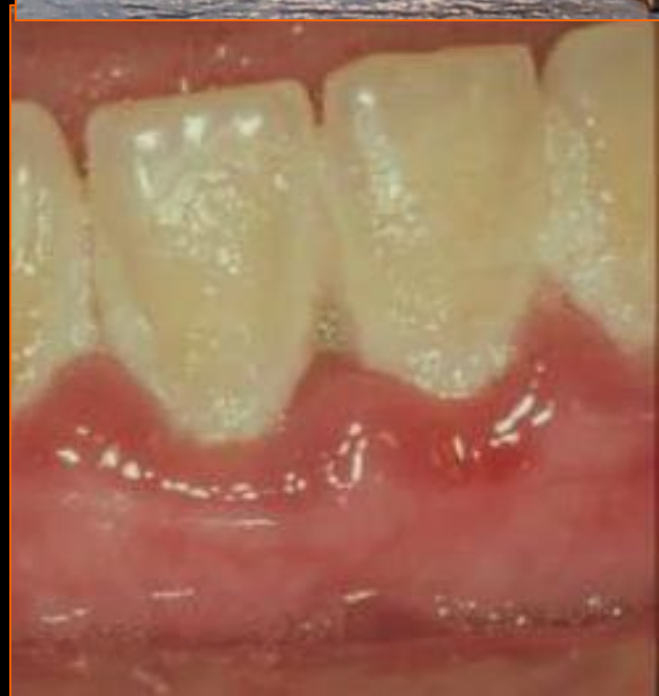
PERIODONTAL DISEASE IS A POLYMICROBIAL INFECTIOUS DISEASE

BENEFITIAL COMMENSAL AND PATHOGENIC BACTERIA PLAY AN IMPORTANT ROLE IN THE PATHOGENESISI OF PERIODONTAL DISEASE



DENTAL PLAQUE: BIOLOGICAL SIGNIFICANCE OF A BIOFILM AND COMMUNITY LIFE-STYLE

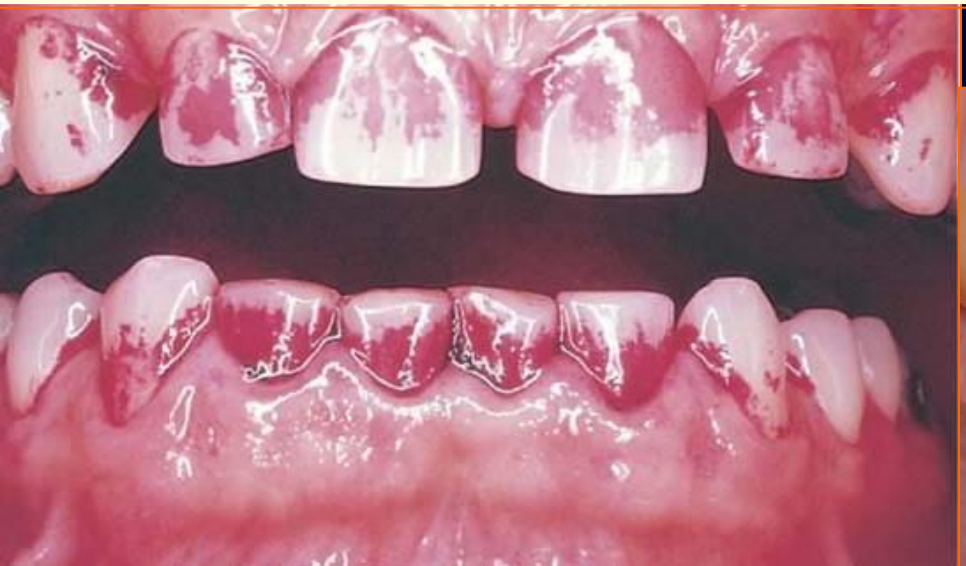
- Most microorganisms in nature attach to surfaces and form matrix-embedded biofilms.
- Biofilms are highly structured and spatially organized, and are often composed of consortia of interacting microorganisms,
- The properties of microbial communities, are more than the sum of the component species

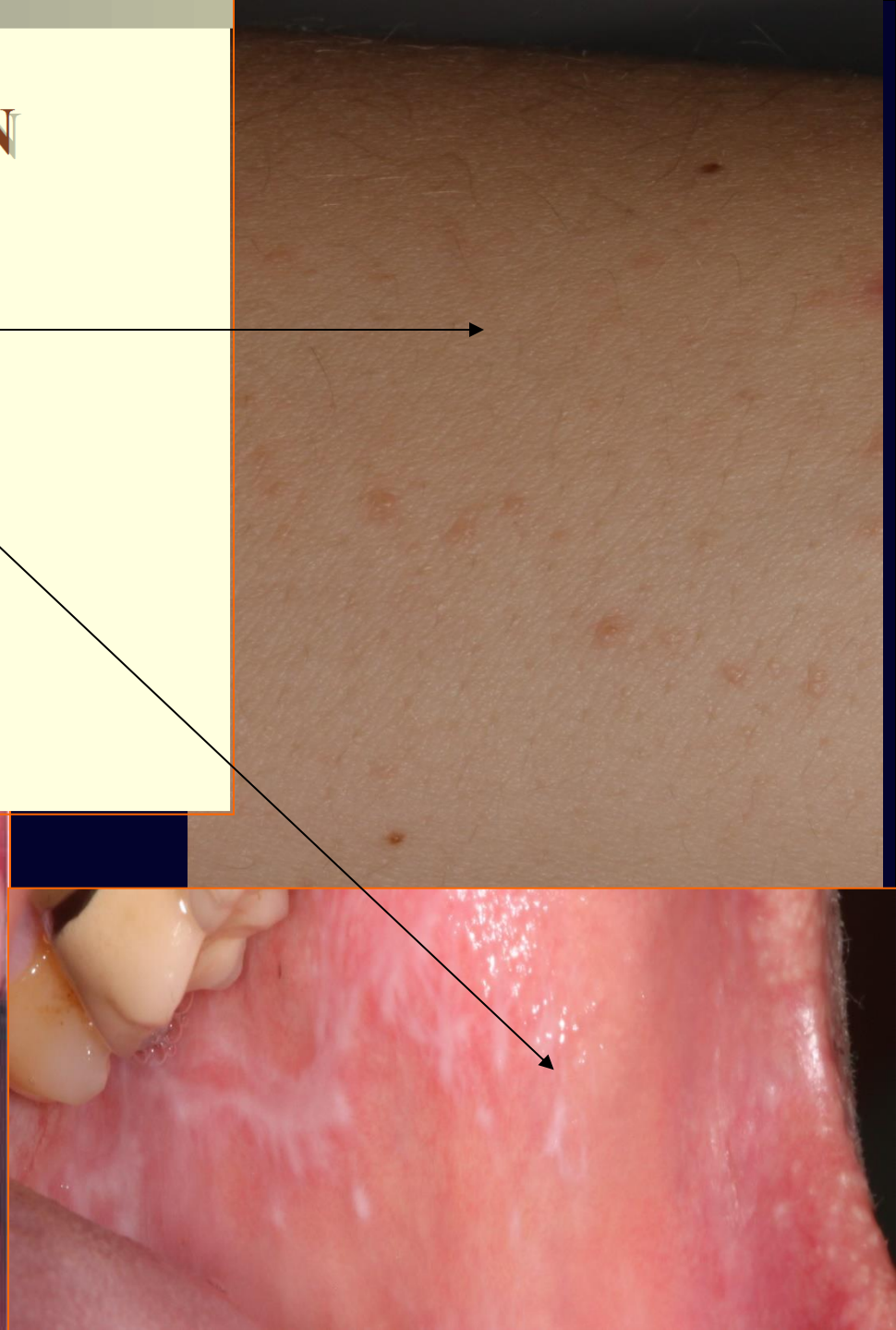


PLAQUE FORMATION

The organism enharbour many billions of bacteria on its surfaces. Nevertheless the desquamation of the epithelial cells anticipates the long lasting bacterial coexistence in the body.

In the oral cavity the non shedding surfaces, like enamel, root cementum, restorations can promote permanent, long lasting bacterial adhesion and survival on the surfaces.

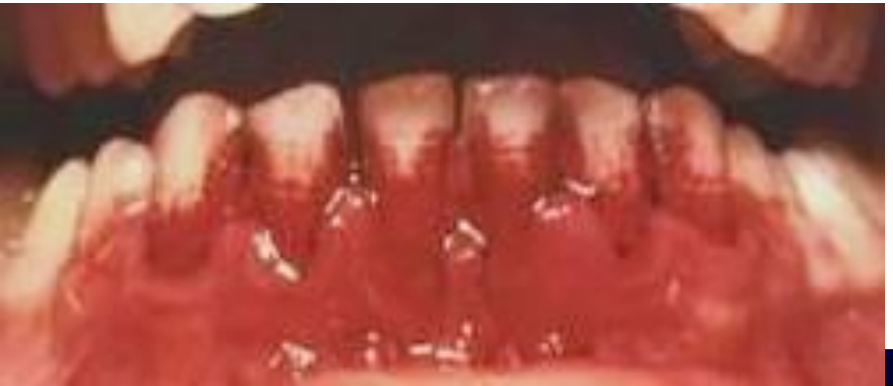




PLAQUE FORMATION

Löe - experimental gingivitis model (1965), proved that plaque accumulation can lead to gingivitis, and its removal can reverse the disease.

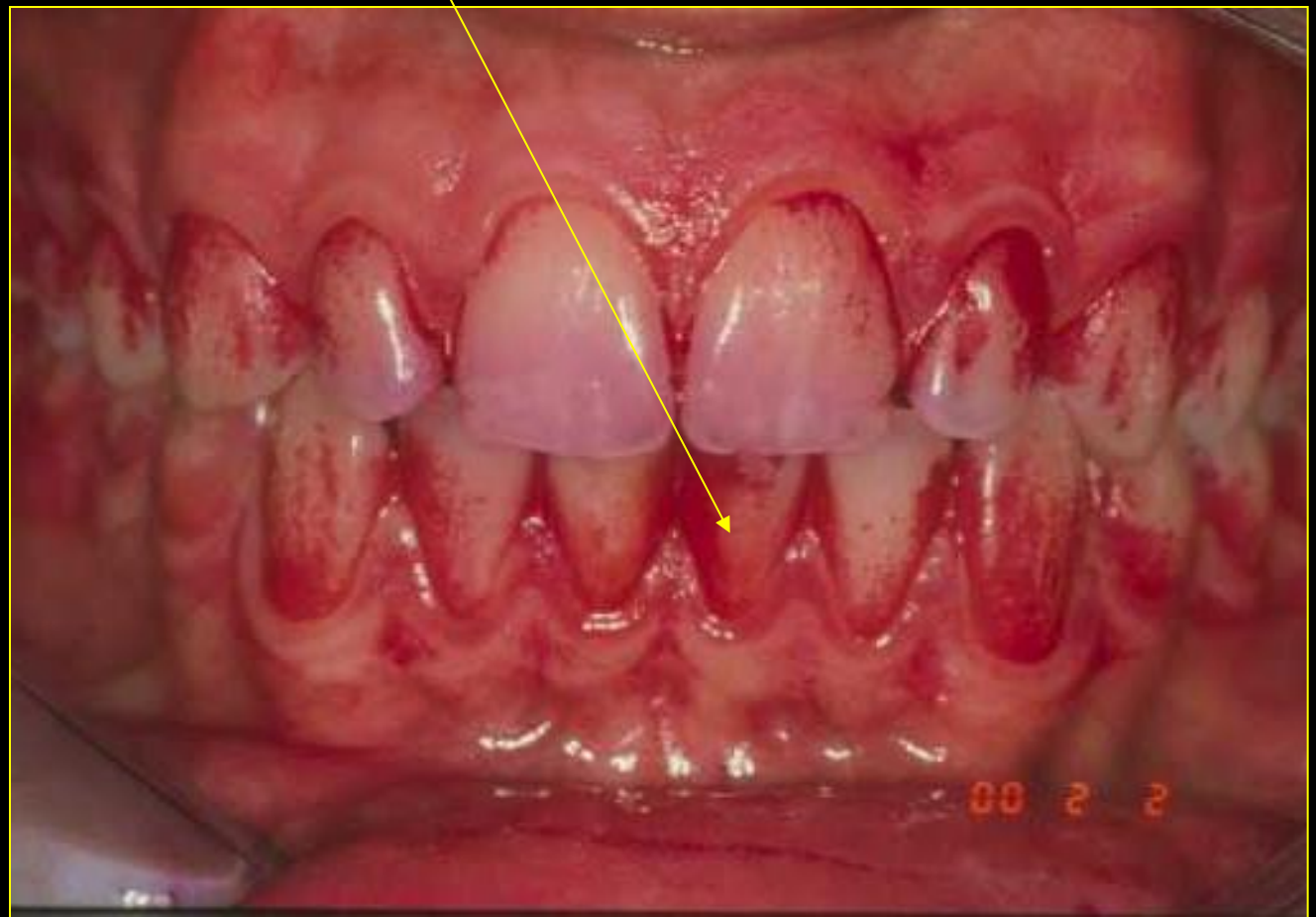
Similarly experimentally was proven that plaque accumulation can cause peri-implantalis (Pontoriero 1994).



Pontoriero R, Tonelli MP, Carnevale G, Mombelli A, Nyman SR Land NP. Experimentally induced periimplant mucositis. A clinical study in humans. *Clinical Oral Implants Research* 5 254-259. 1994.

Plaque is natural and exists in harmony with the host in health.

Maintenance of health depends on the balance of the homeostatic relationship between the bacterial challenge and the host response.



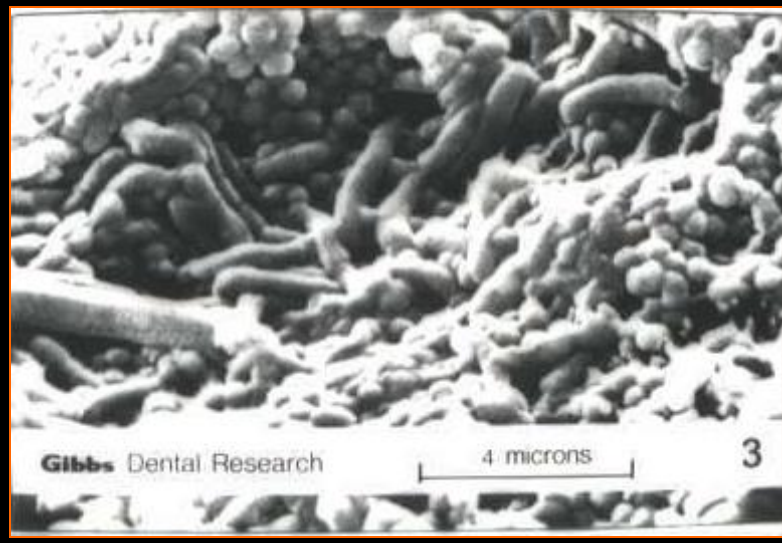
BACTERIAL BIOFILM

IS MADE UP OF

„FRIENDLY COMMENSAL BACTERIA

AND HOSTILE PERIODONTOPATHOGENIC STRAINS

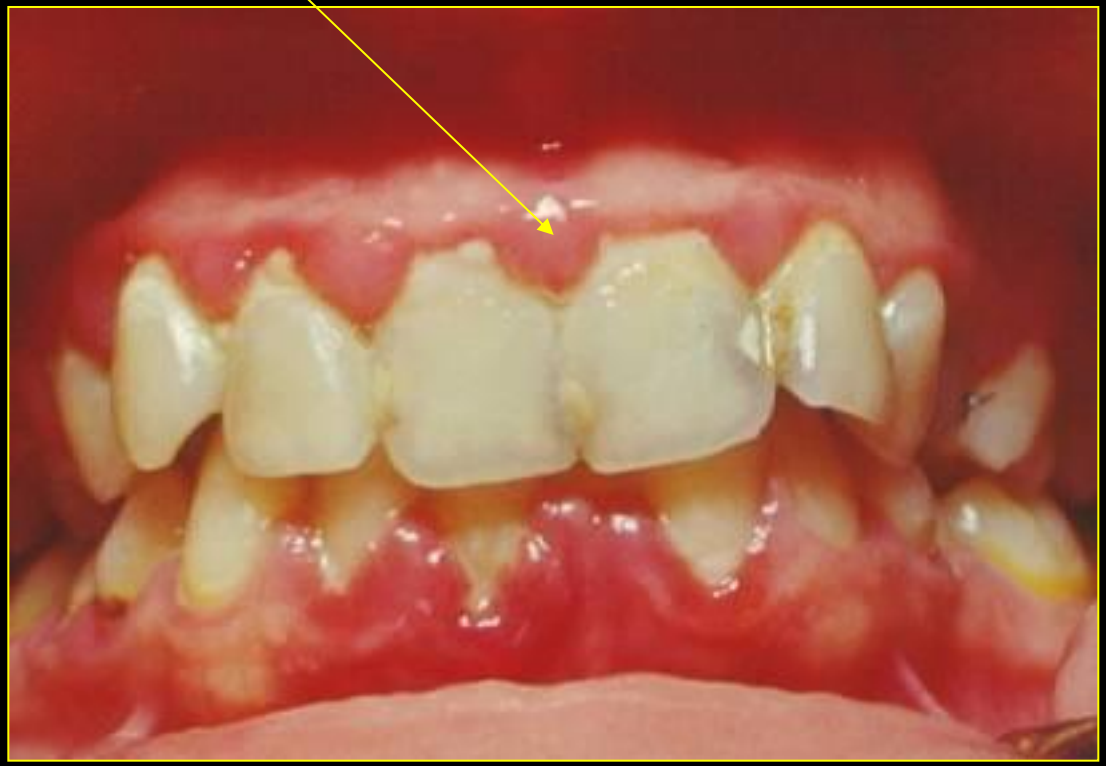
THE MANIFESTATION OF PERIODONTAL BREAKDOWN IS DEPENDENT ON THE HOST'S SUSCEPTIBILITY AND THE VIRULANCE OF THE BIOFILM



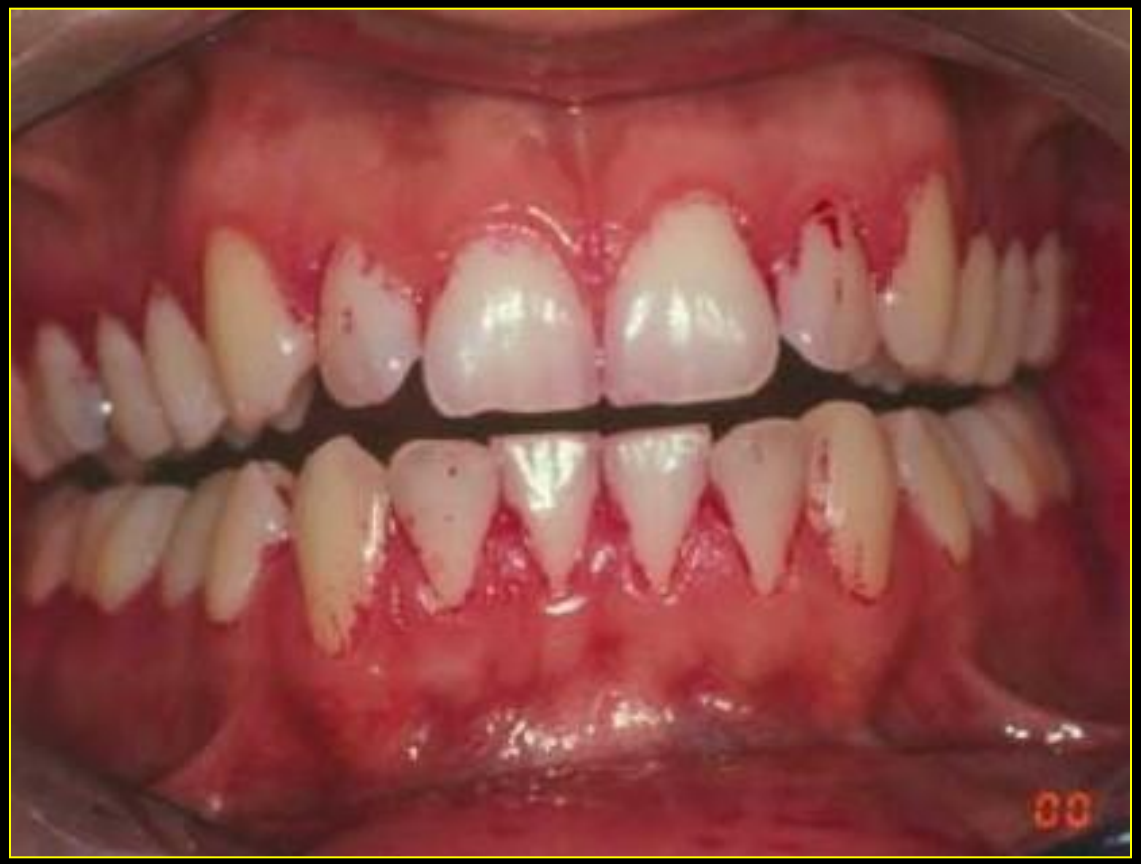
Disease is the consequence of this balanced relationship breaking down, provoked by

- **either changes to the magnitude or nature of the microbial challenge**
- ***or* the scale and appropriateness of the host response**

(Socransky et al. 1998).



Most bacterial species currently implicated in periodontitis can be found in periodontally healthy subjects in low numbers. (Van Winkelhoff et al. 2002).



CHRONIC PERIODONTITIS AND HEALTHY CONTROLS THE OCCURENCE OF PERIODONTOPATHOGENIC STRAINS

THE NUMBER OF SUBJETS AND THE PROPORTION (%)

BACTERIUM	CHRONIC PERIO (n=29)	HEALTHY (n=20)
Treponema sp.	29 (100)	8 (40)
A.A.	26 (89.7)	1 (5)
P. gingivalis	29 (100)	6 (30)
Fusobacterium sp.	29 (100)	17 (85)
T. forsythia	28 (96.9)	11 (55)
P. intermedia	26 (89.7)	1 (5)
P. micros	28 (96.6)	6 (30)

Choi BK et al. Detection of major putative periodontopathogens in Korean advanced adult periodontitis patients using a nucleic acid-based approach J. Periodontol 2000;71:1387-1394

Most bacterial species currently implicated in periodontitis can be found in periodontally healthy subjects in low numbers.

THE PREVALENCE OF PERIODONTOPATHOGEN POSITIVE AND NEGATIVE POCKETS IN CHRONIC PERIODONTITIS AND IN HEALTHY CONTROLS

THE ABSOLUTE NUMBER AND RELATIVE PROPORTION (%) OF POSITIVE POCKETS

BACTERIUM	CHRONIC PERIODONTITIS active pocket (n=116)	CHRONIC PERIODONTITIS inactive pocket (n=28)	HEALTHY CONTROLS (n=100)
Treponema sp.	114 (98.3)	13 (46.4)	22 (22)
A.A.	86 (74.1)	8 (28.6)	1 (1)
P. gingivalis	113 (97.4)	14 (50)	18 (18)
Fusobacterium sp.	116 (100)	20 (71.4)	58 (58)
B. forsythus	112 (96.6)	9 (32.1)	18 (18)
P. intermedia	82 (70.7)	5 (17.9)	2 (2)
P. micros	95 (81.9)	10 (35.7)	8 (8)

Choi BK et al. Detection of major putative periodontopathogens in Korean advanced adult periodontitis patients using a nucleic acid-based approach J. Periodontol 2000;71:1387-1394

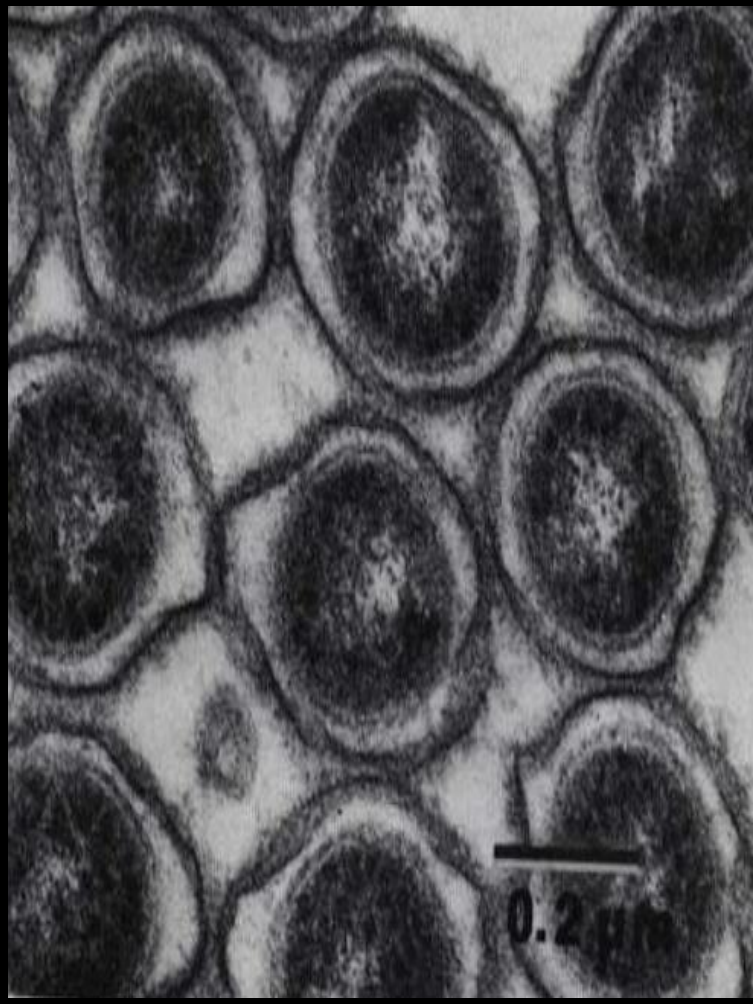
Most bacterial species currently implicated in periodontitis can be found in periodontally healthy subjects in low numbers.

•Most natural biofilms contain multiple species and are termed microbial communities.

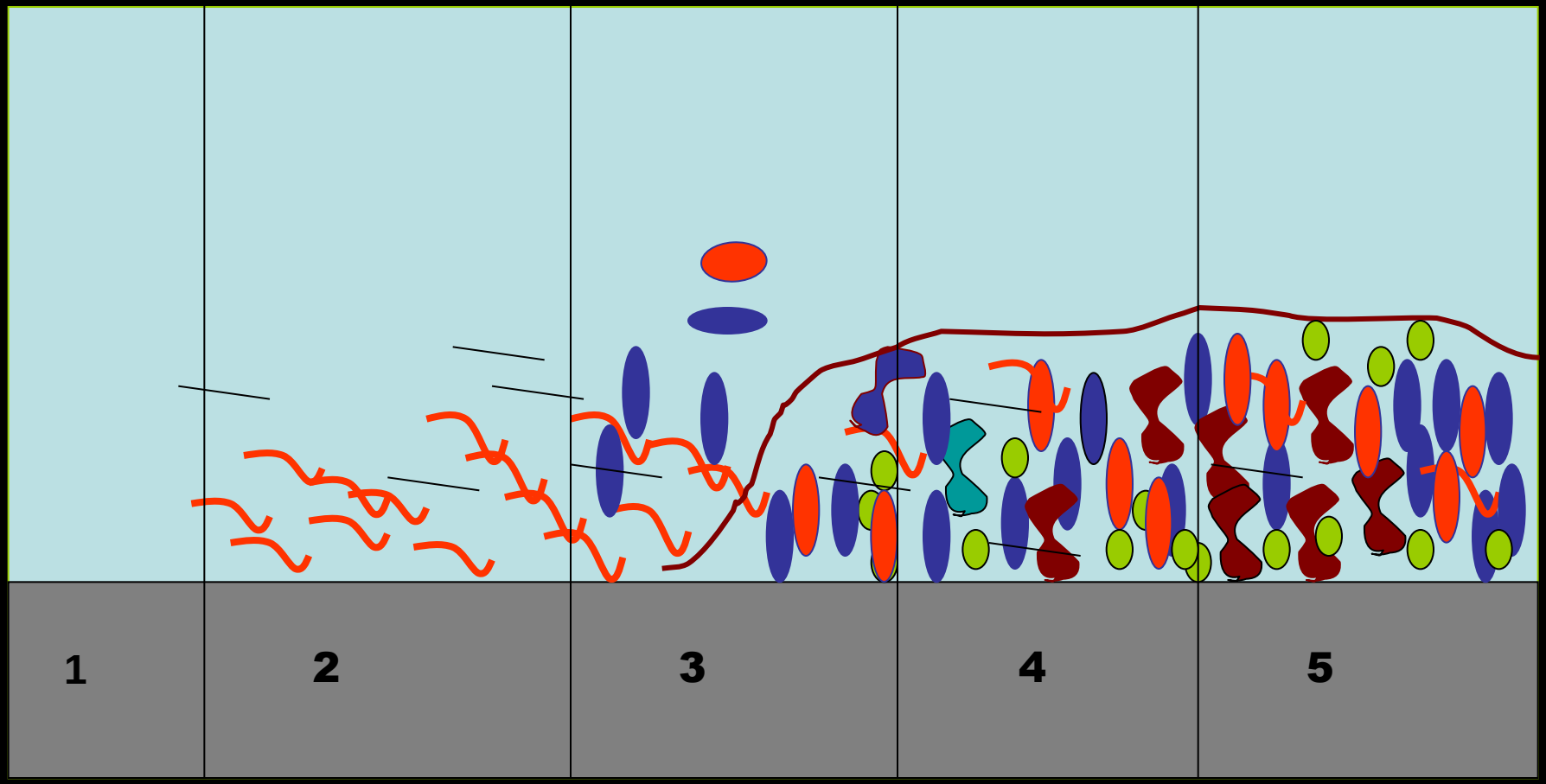
•The component organisms are not merely passive neighbors

• they are involved in a wide range of physical, metabolic and molecular interactions.

•These interactions may well be essential for the attachment, growth and survival of species at a site, enabling organisms to persist in hostile environments.



biofilm formation



THE PRINCIPLES OF MICROBIAL ECOLOGY

- MICROBIAL SUCCESSION
- Autogenic succession – the bacterial community changes the anvironment to favor the growth of other species
- Allogenic succession – the environment changes because of non microbial factors like restorations, pocket depth etc.

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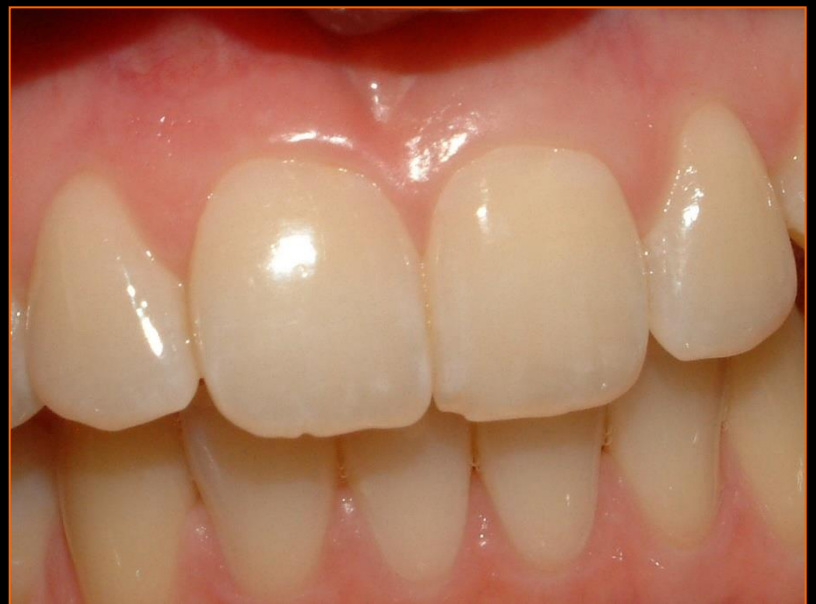
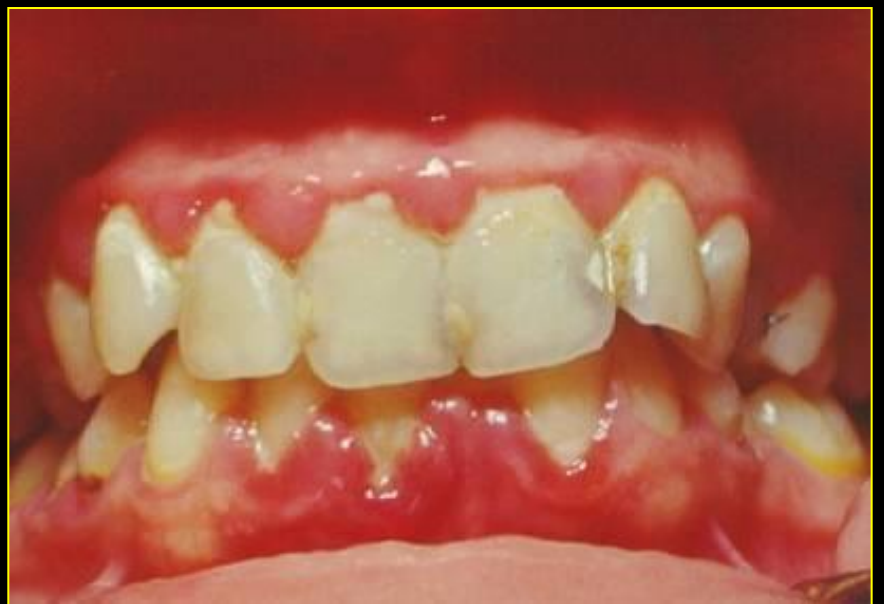
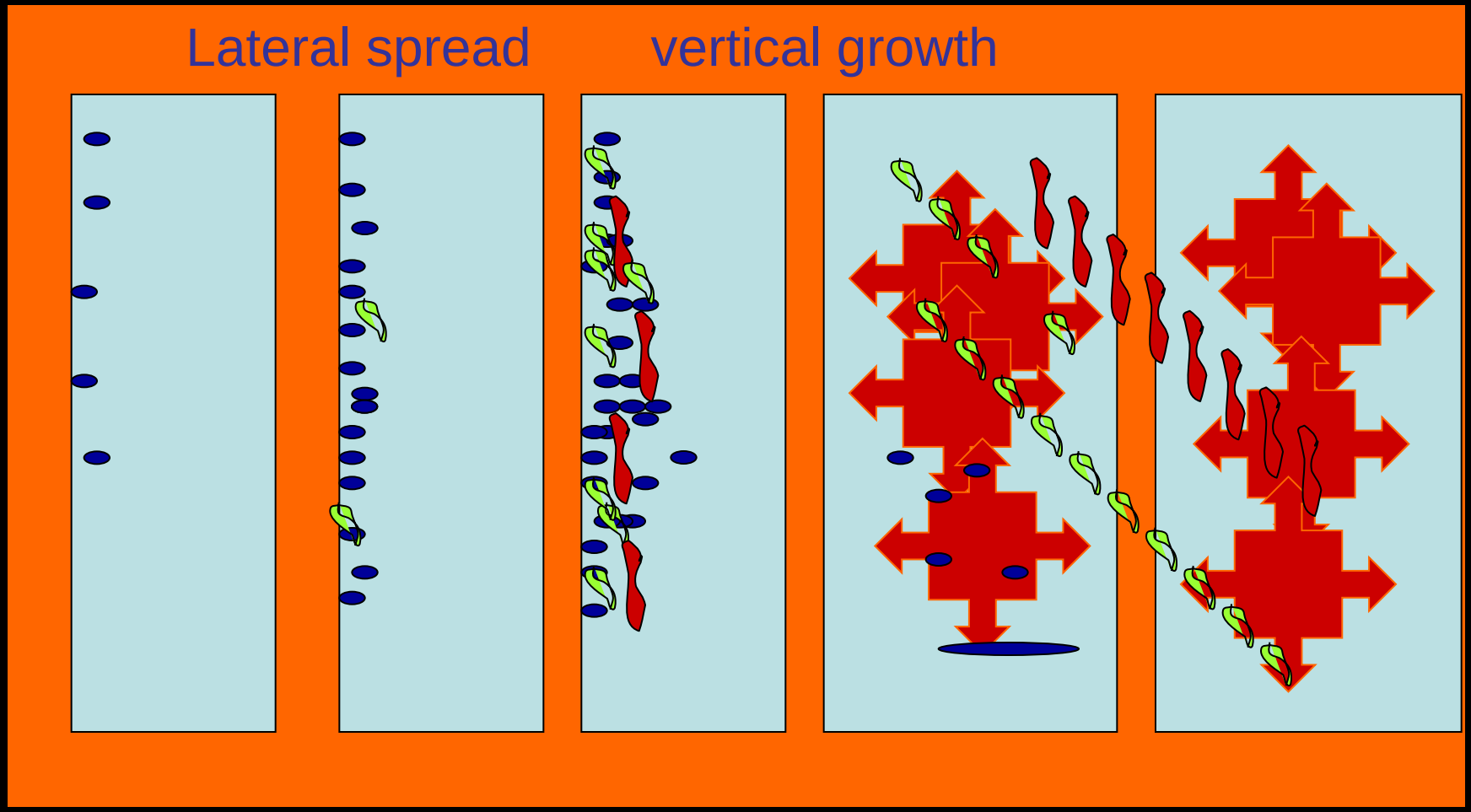




THE DEVELOPMENT OF DENTAL BIOFILM



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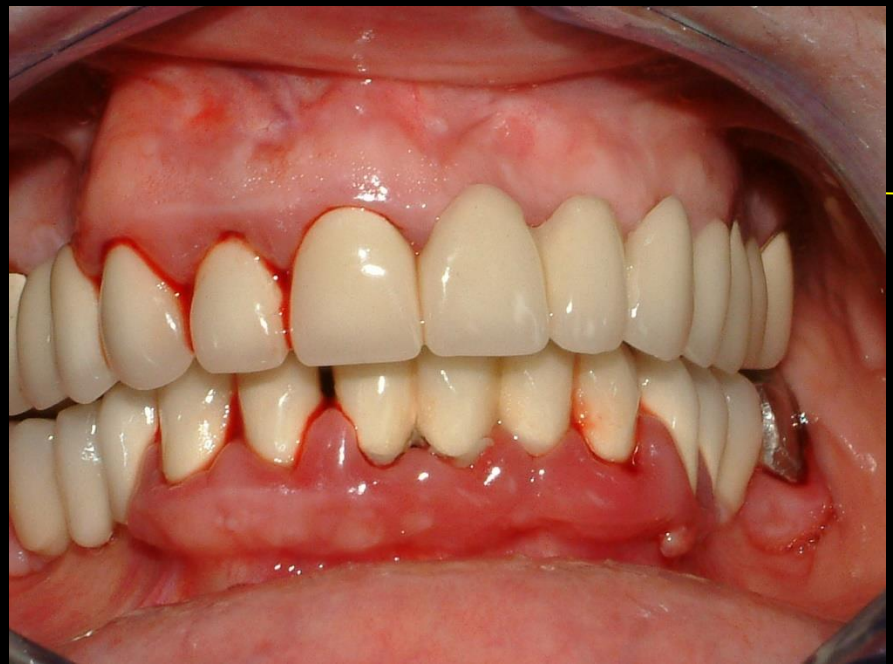


During the inflammatory response to plaque accumulation,

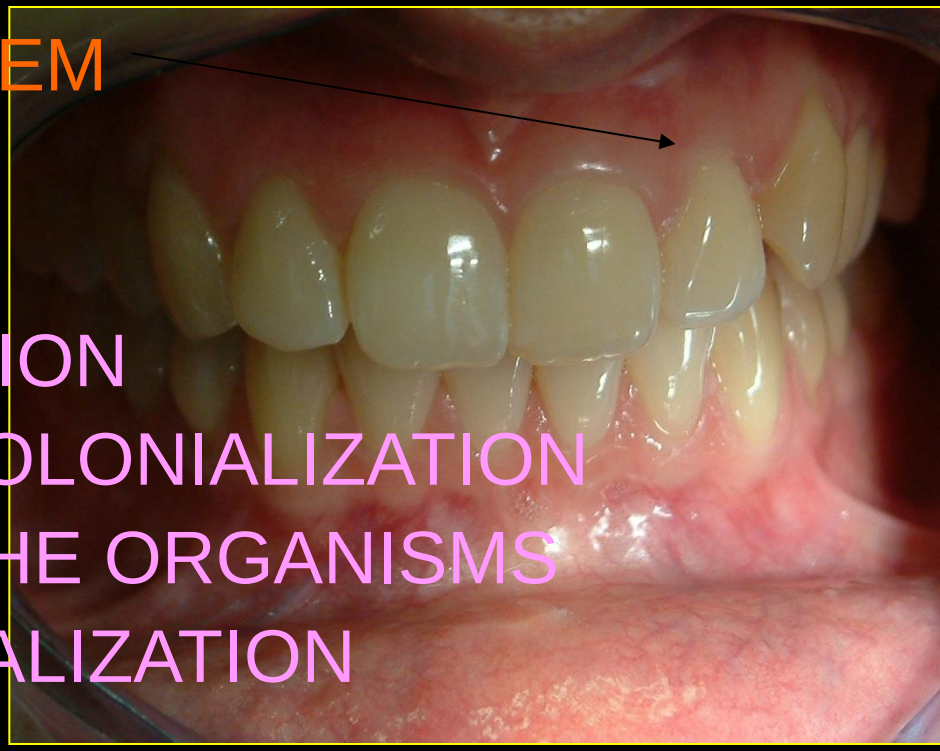
there is an increase in the flow of gingival crevicular fluid;

this not only delivers components of the host defences

but also provides more nutrients (proteins and glycoproteins) that favour the growth of organisms with an asaccharolytic metabolism

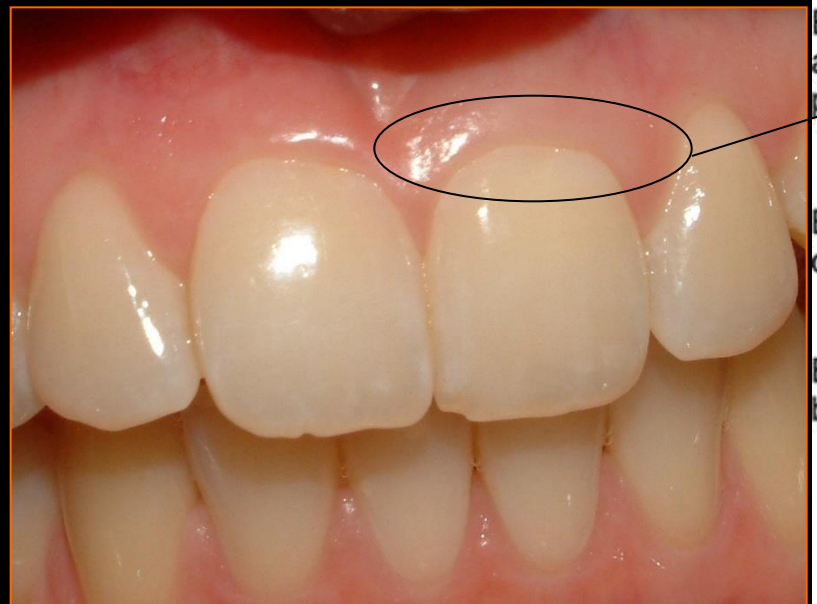
THE PRINCIPLES OF MICROBIAL ECOLOGY

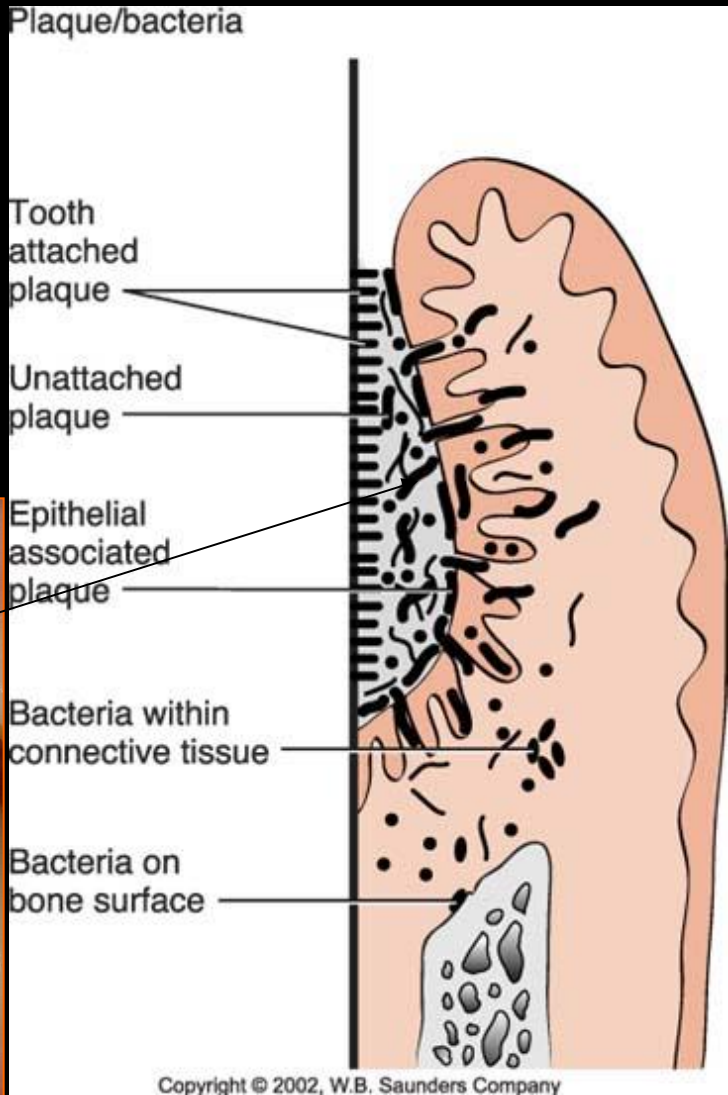
- BACTERIAL ECOSYSTEM
- HABITAT
- NICHES
- MICROBIAL SUCCESSION
- FACTORS LIMITING COLONIALIZATION
- DISSEMINATION OF THE ORGANISMS
- SUCCESSFUL COLINIALIZATION
- CLIMAX COMMUNITY



THE PRINCIPLES OF MICROBIAL ECOLOGY

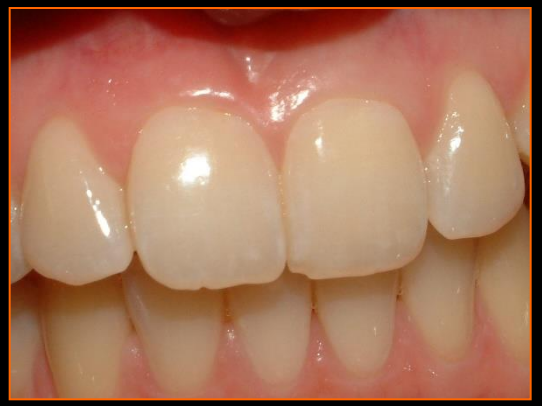
- BACTERIAL ECOSYSTEM
- **HABITAT**
  SULCUS
- is the site at which a population of bacteria grows

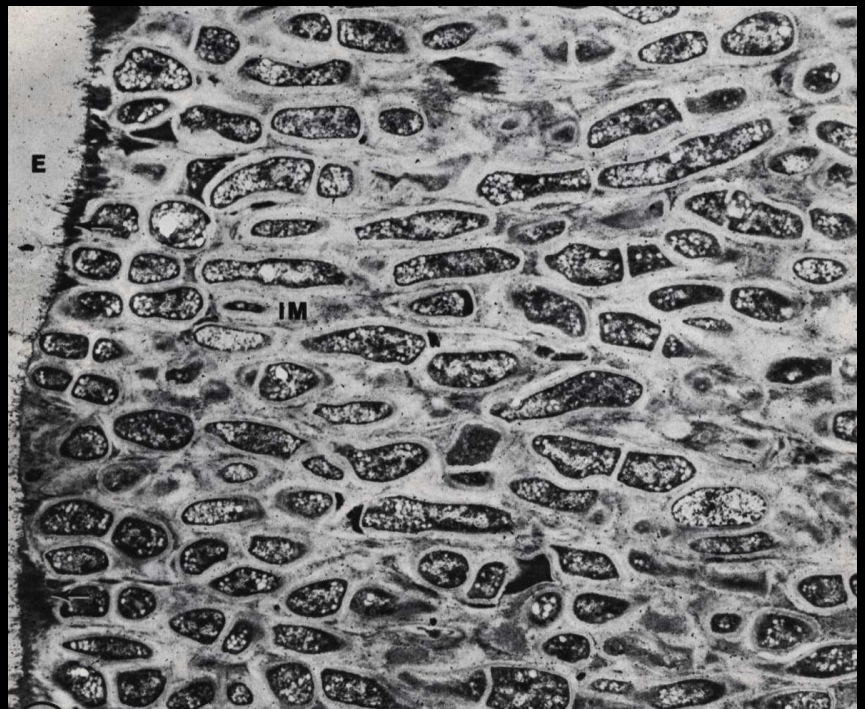


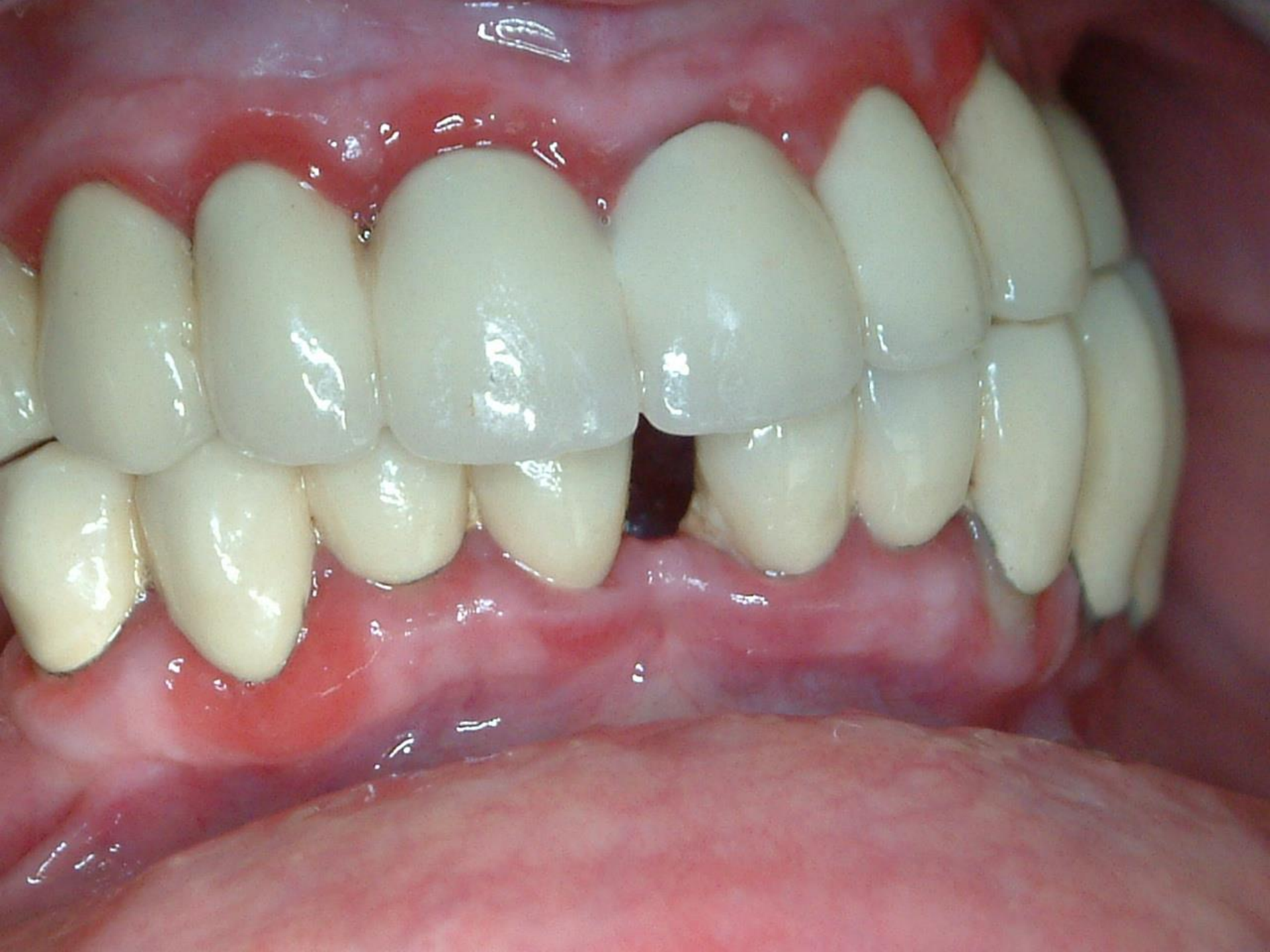


THE PRINCIPLES OF MICROBIAL ECOLOGY

- NICHES
- the function of the bacteria in a habitat is its niche
- A bacterium can have one niche in one habitat and another niche in another habitat







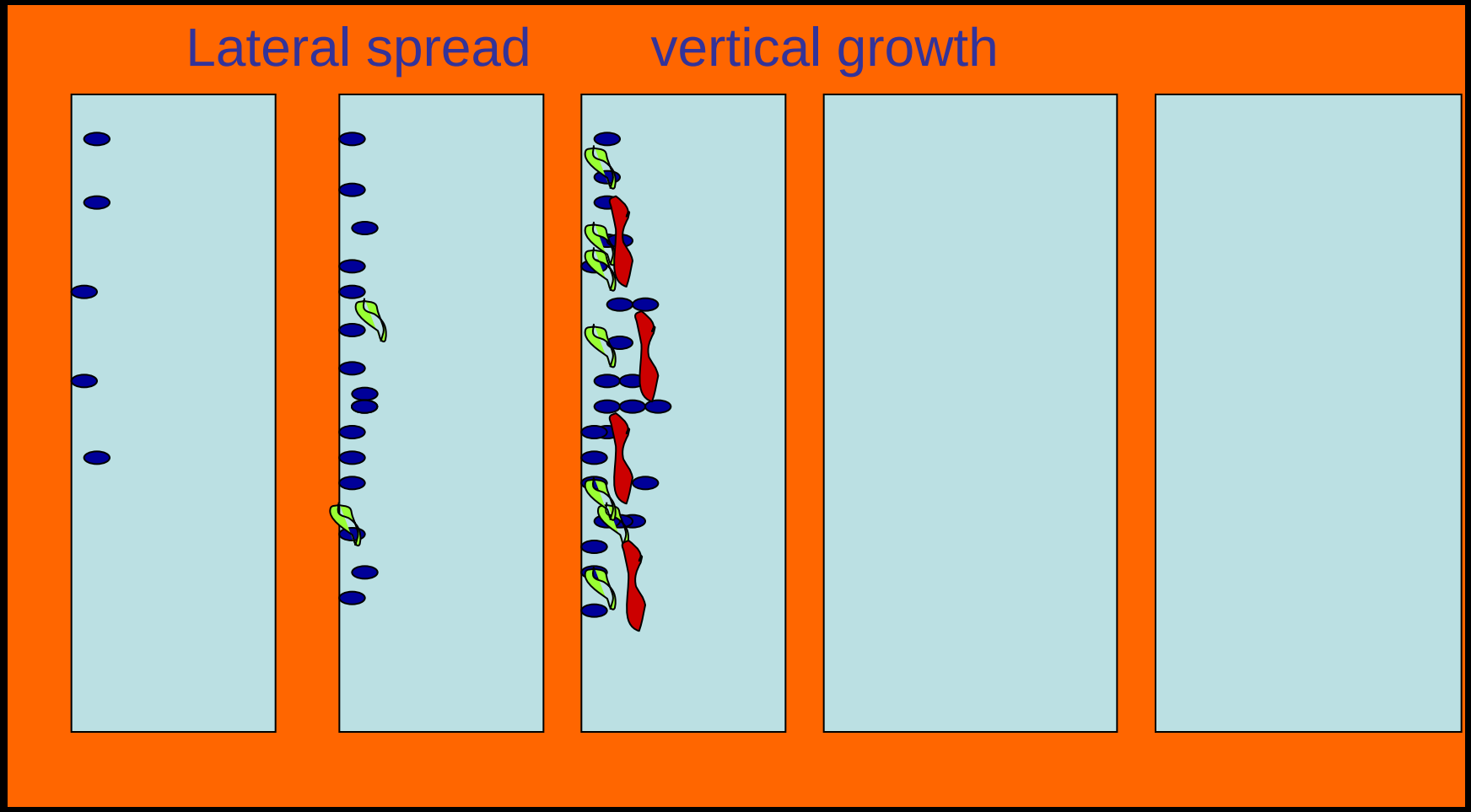
DETERMINANTS OF SUBGINGIVAL BIOFILM

- THE MICROBIAL COMPOSITION OF SUBGINGIVAL BIOFILM
- THE INFLUENCE OF SURFACE ON THE COMPOSITION
  - TOOTH, EPITHELIA, CREVICULAR FLUIS
- THE BULK FLUID
  - SALIVA OR CREVICULAR FLUID

THE PRINCIPLES OF MICROBIAL ECOLOGY

- **MICROBIAL SUCCESSION**
- Factors contributing to microbial succession:
  - Provision of nutrients
  - Altering the concentration of inorganic nutrients – like metals
  - Modifying the host tissues – like edema
  - Autointoxication
  - Elimination of organisms by physical means
  - Establishment of barriers

THE DEVELOPMENT OF DENTAL BIOFILM



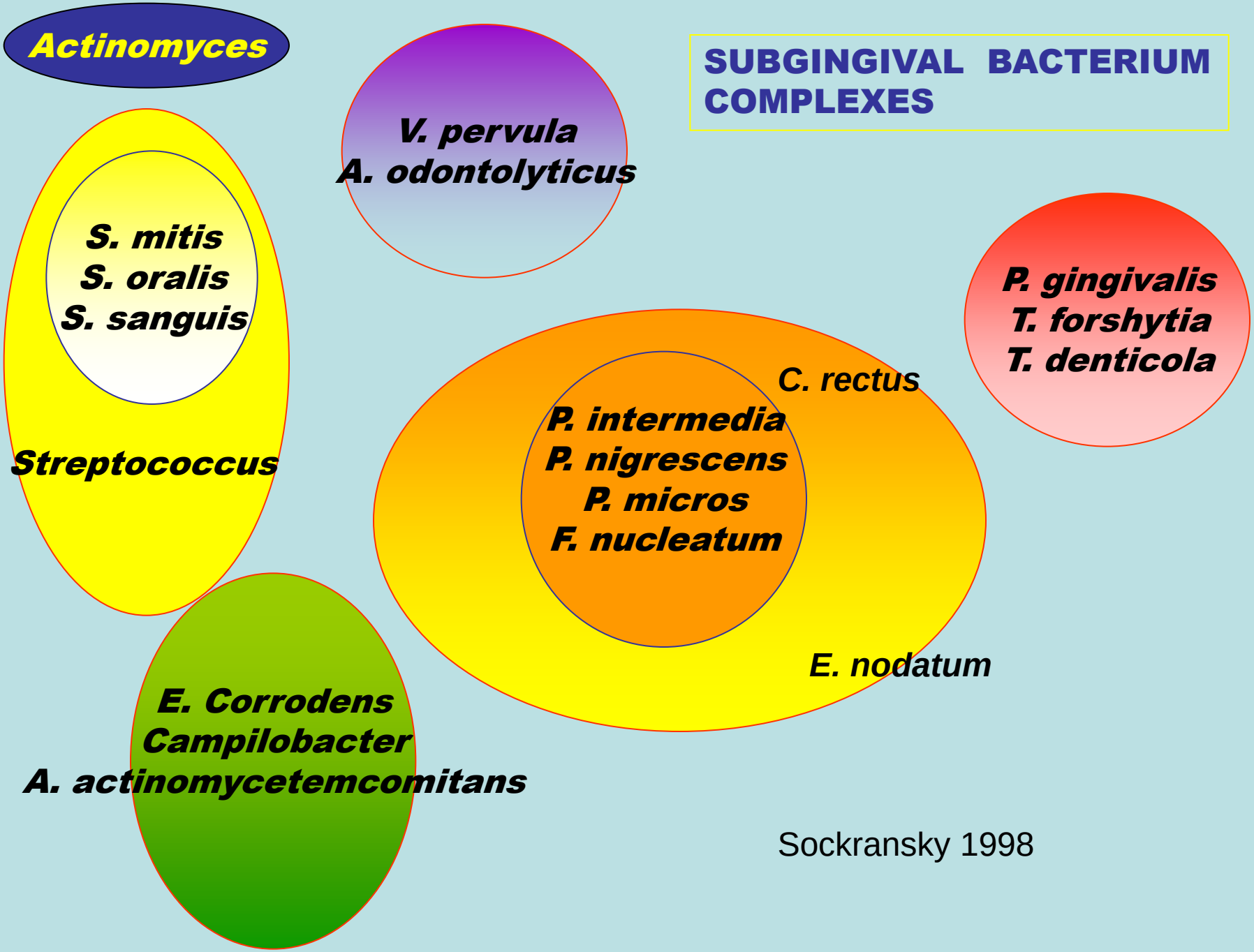
„COMPLEXES" OF BACTERIA ARE ASSOCIATED WITH EITHER HEALTH OR DISEASE

(Socransky et al. 1998, Socransky & Haffajee 2002).

Certain groups of bacteria are early colonizers of the tooth surface,

Others, such as members of the "red complex" (*Porphyromonas gingivalis*, *T. denticola*, *Tannerella forsythensis*), are associated more commonly with periodontal diseases, and are rarely detected in the absence of members of other "complexes" (e.g. the "orange complex",

(Socransky et al. 1998, Socransky & Haffajee 2002).

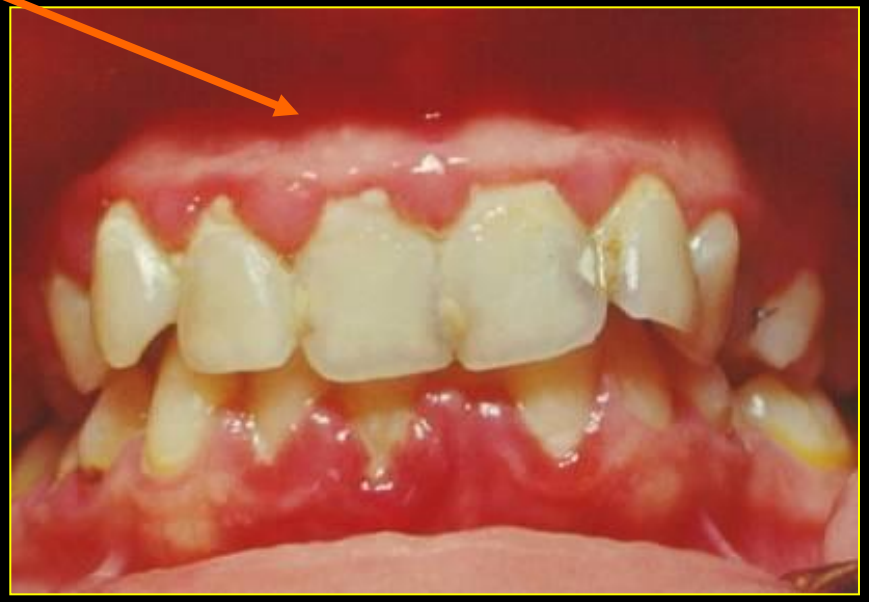


Sockransky 1998

THERE CAN BE A NULL STATE BETWEEN BIOFILM AND HOST – NO OVERT INFLAMMATORY REACTION

OR

CLINICALLY MANIFEST INFLAMMATION



PERIODONTOPATHOGENIC BATERIA IN ORAL CAVITY

PERIODONTAL DISEASE IS NOT CAUSED BY ONE SINGLE STRAIN

KOCH'S PUSTULATE IS MODIFIED BY SOKRANSKY'S POSTULATE

(Sokransky 1992)

- THE ORGANISM SHOULD BE FOUND IN HIGH NUMBERS IN THE PROXIMITY TO THE PERIODONTAL TISSUES
- THE ORGANISM SHOULD BE ABSENT OR IN SIGNIFICANTLY SMALLER NUMBER IN HELTHY PERIODONTAL TISSUES
- THE ORGANISM SHOULD HAVE HIGH TITER OF SERUM ANTIBODY
- THE ORGANISM SHOULD POSSES MANY VIRULENCE FACTORS
- THE ORGANISM SHOULR PRODUCE PERIODONTAL INFLAMMATION IN ANIMAL MODELS
- FOLLOWING ERRADICATION OF THE ORGANISM CLINICAL IMPROVENENT SHOULD OCCURE
- THE ORGANISM MUST BE OF A VIRULENT CLONAL TYPE
- THE HOST SHOULD BE SUSCEPTIBLE TO THE ORGANISMS

THE PRINCIPLES OF MICROBIAL ECOLOGY

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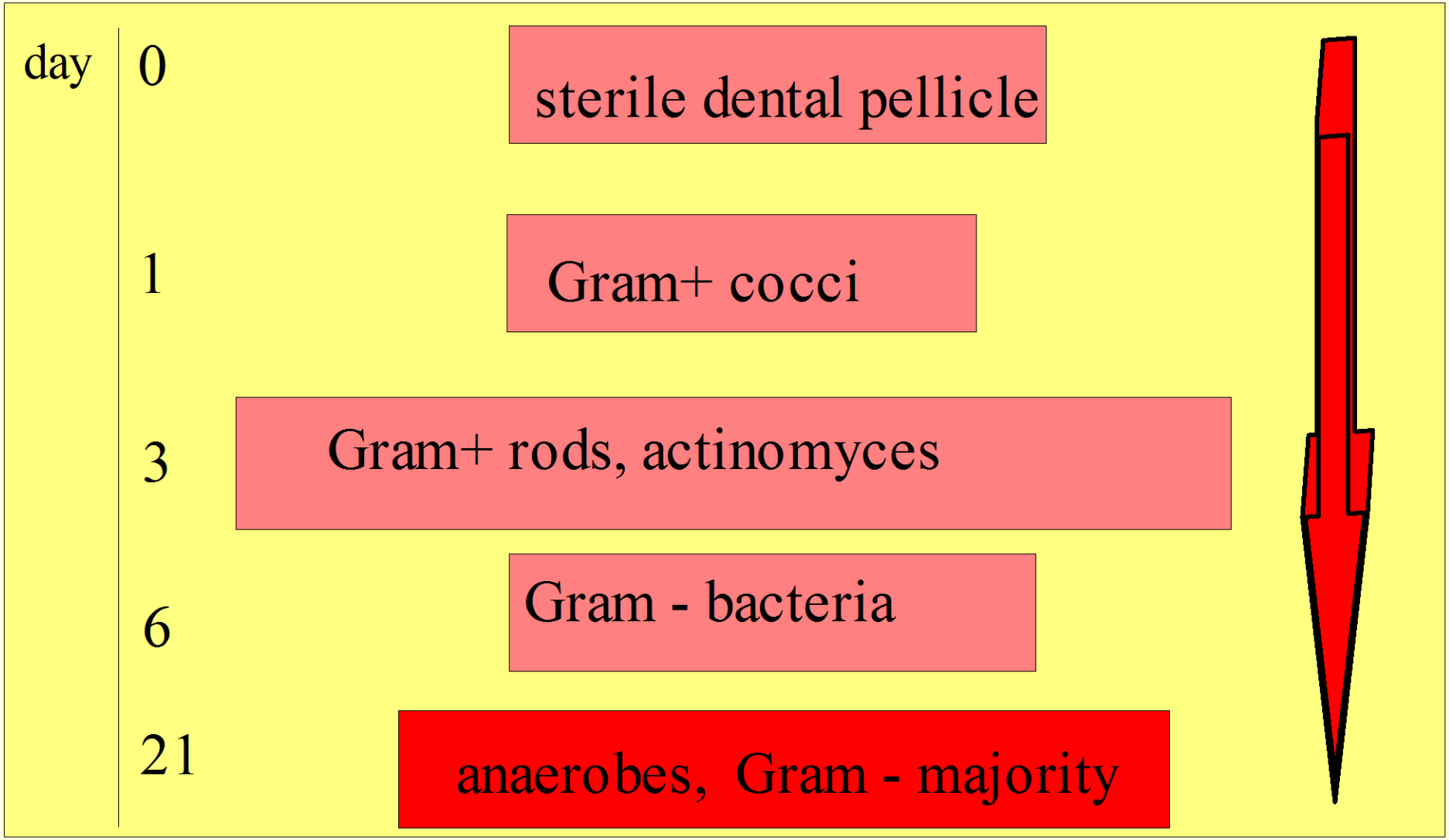
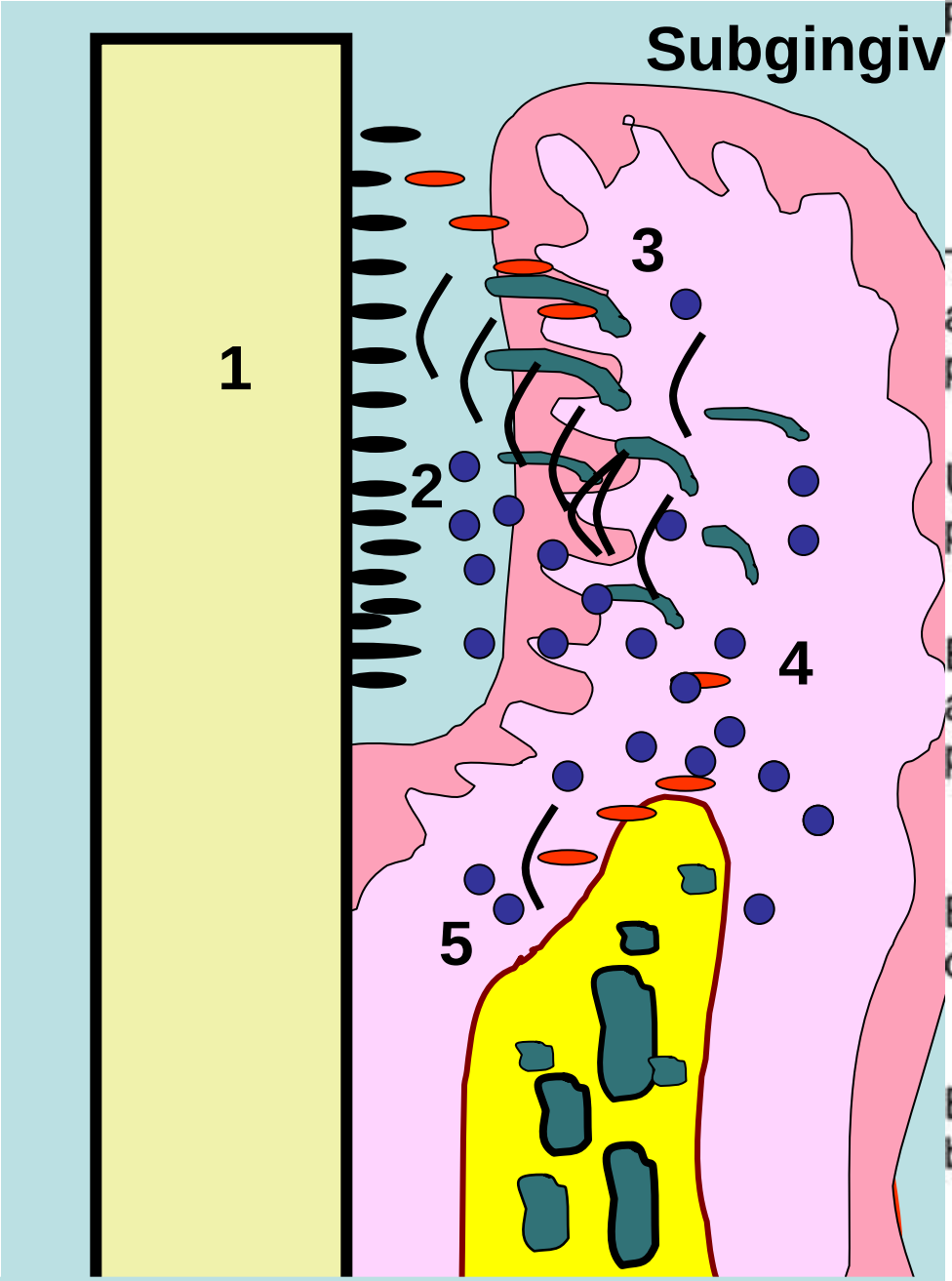
THE MECHANISM OF PLAQUE ACCUMULATION

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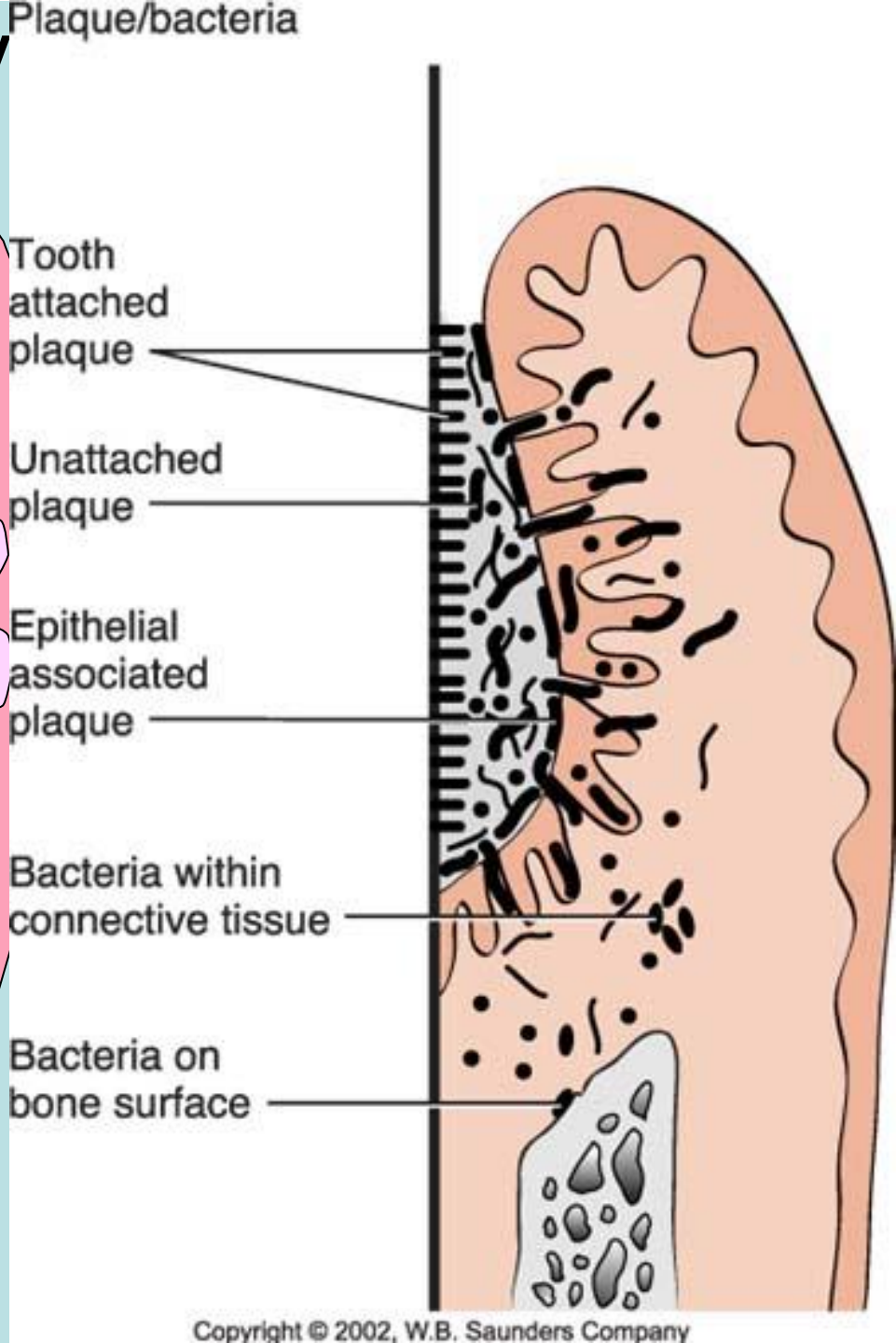
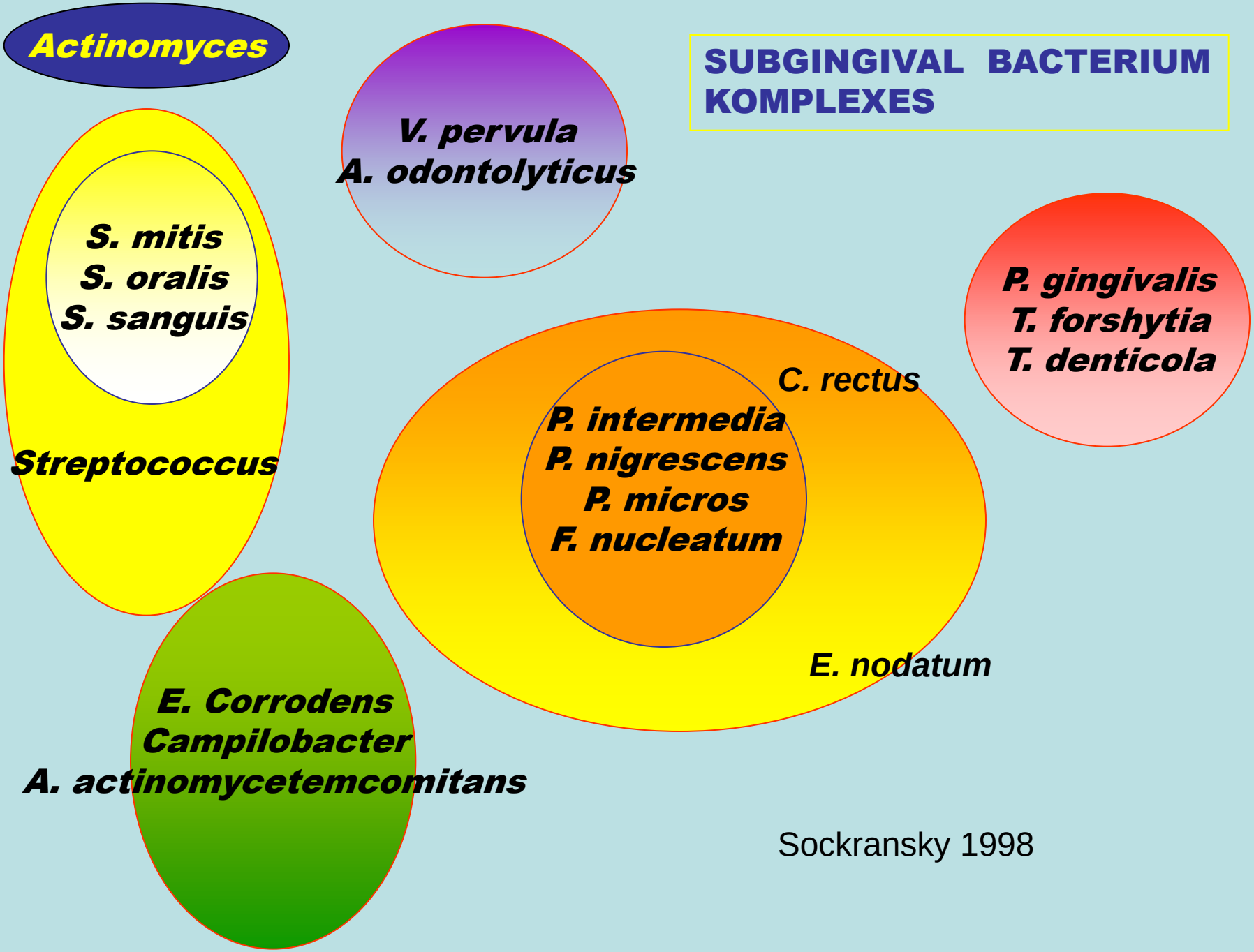
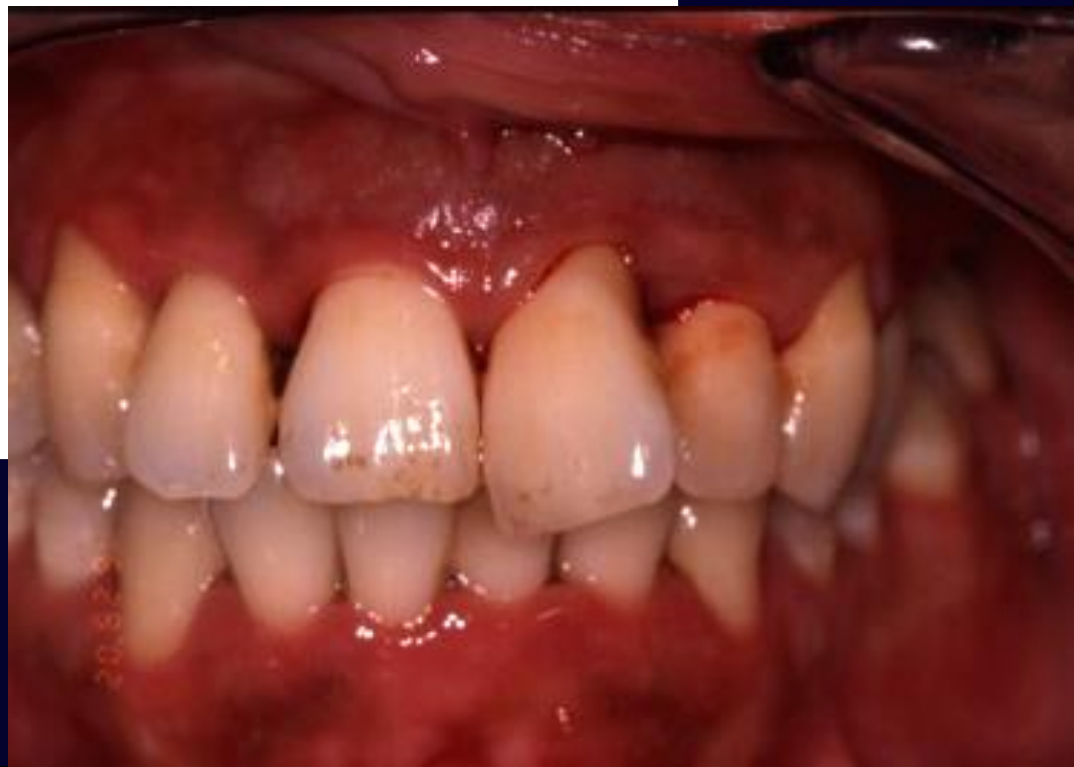

Plaque/bacteria
Tooth attached plaque
Unattached plaque
Epithelial associated plaque
Bacteria within connective tissue
Bacteria on bone surface
Copyright © 2002, W.B. Saunders Company



Sockransky 1998

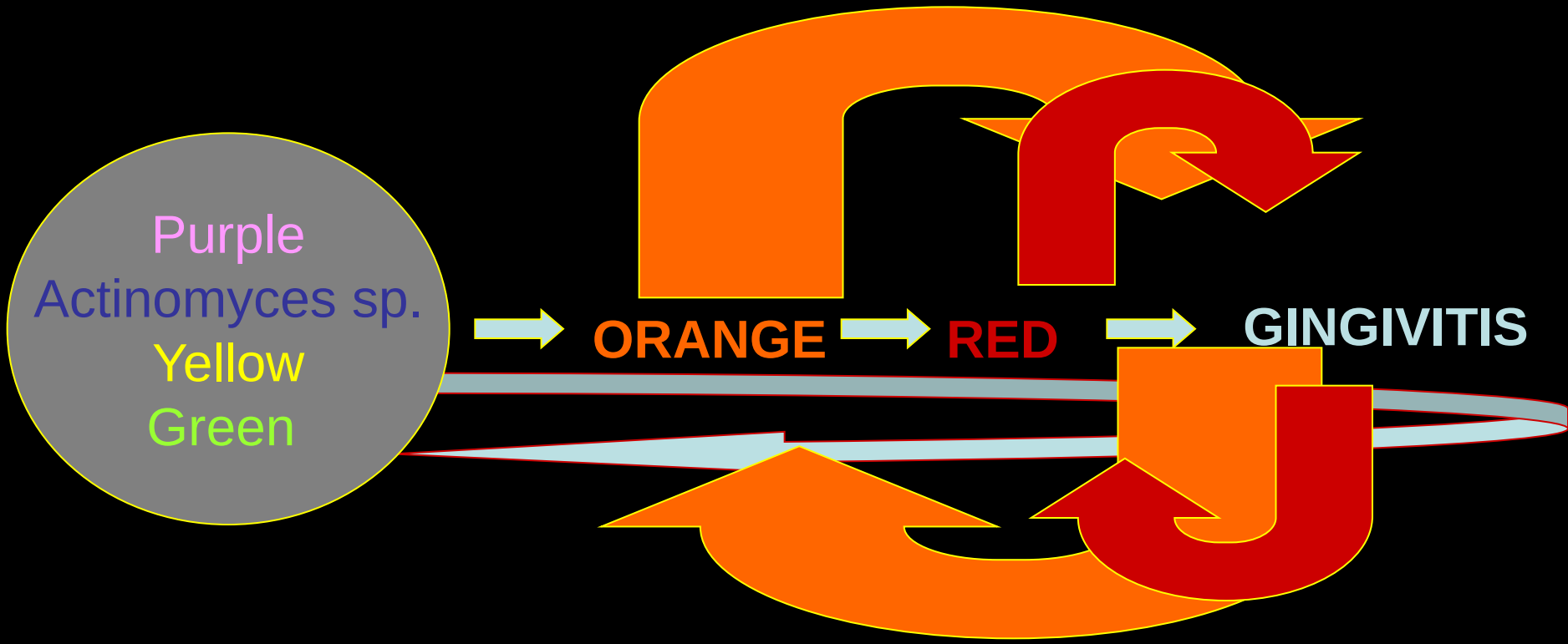
periopatogen strains :

Actinobacillus (Aggregatibacter)
actinomycetemcomitans,
Tannerella forsythia ,
Campylobacter rectus,
Eubacterium nodatum,
Fusobacterium nucleatum,
Peptostreptococcus micros,
Porphyromonas gingivalis,
Prevotella intermedia,
Prevotella nigrescans,
Streptococcus intermedius
certain Treponema species



THE PRINCIPLES OF MICROBIAL ECOLOGY

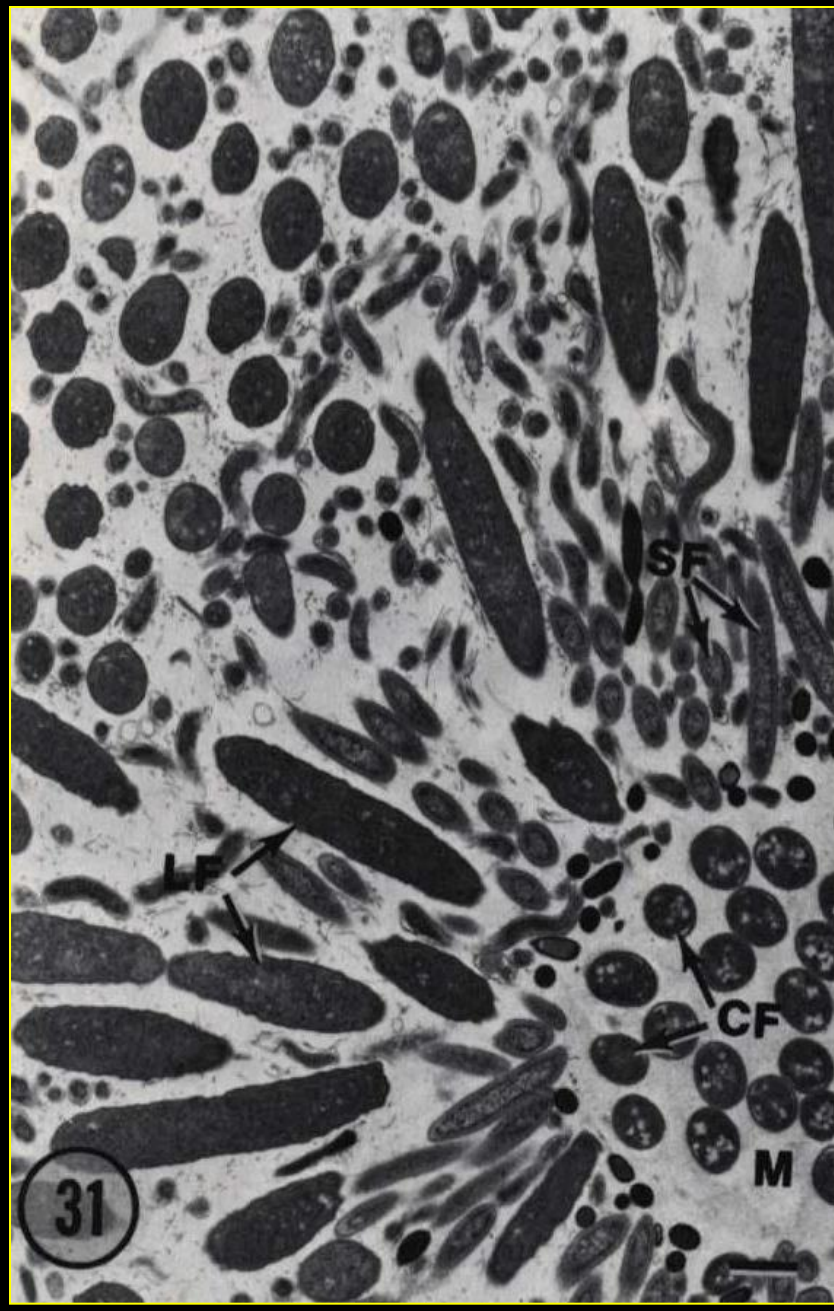
- MICROBIAL SUCCESSION



•Biofilms have been defined as matrix-embedded microbial populations, adherent to each other and/or to surfaces or interfaces (Costerton et al. 1995).

•Biofilms are usually highly structured with channels traversing the depth of the biofilm, creating primitive circulatory systems (Costerton et al. 1995).

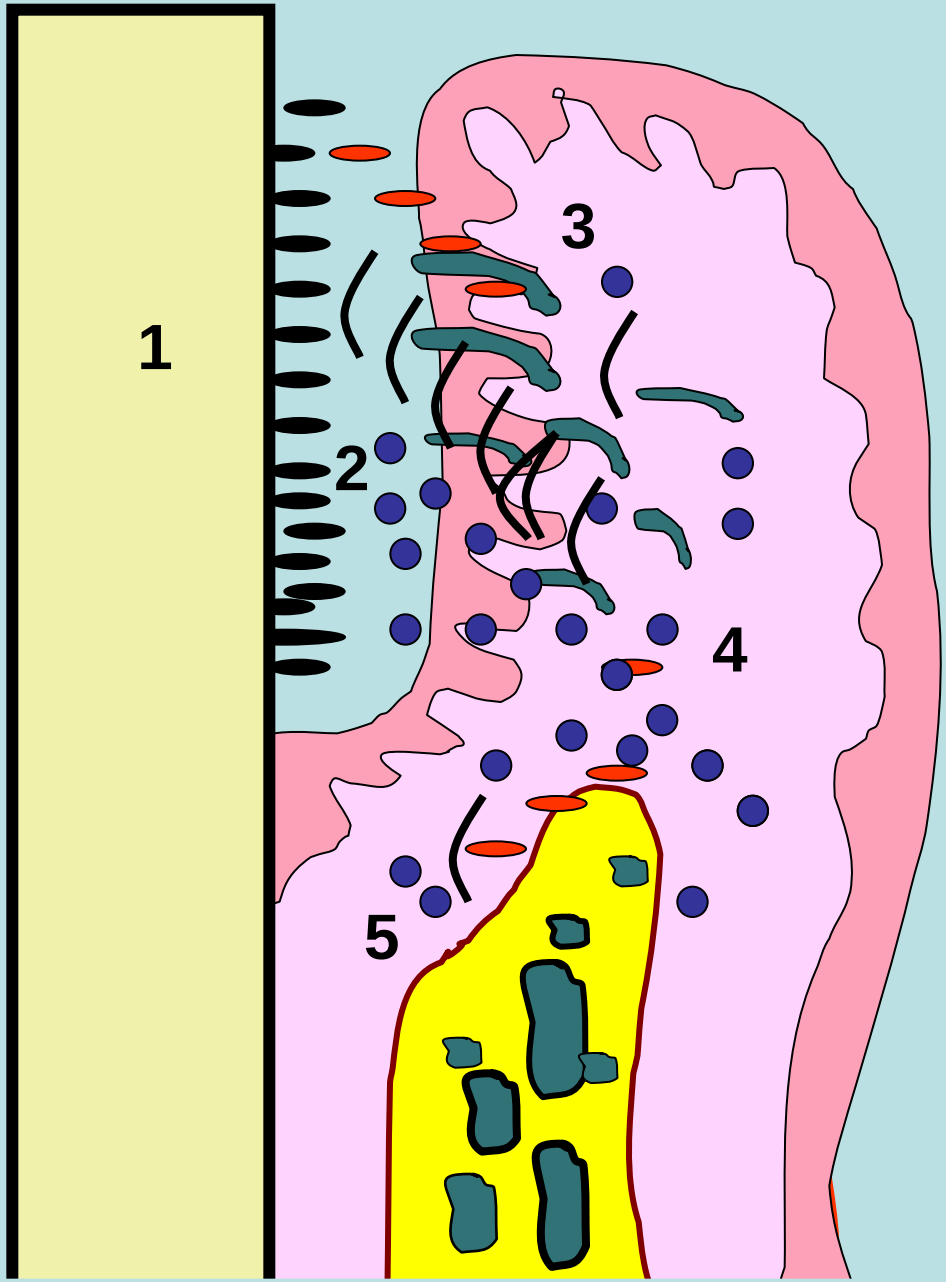
•The component species are not randomly distributed but are spatially and functionally organized, and many natural biofilms have a highly diverse microflora.



- Environmental heterogeneity in biofilms can accelerate phenotypic and genotypic diversity in bacterial populations
- Cells are better prepared to cope with adverse conditions

"biological insurance,,

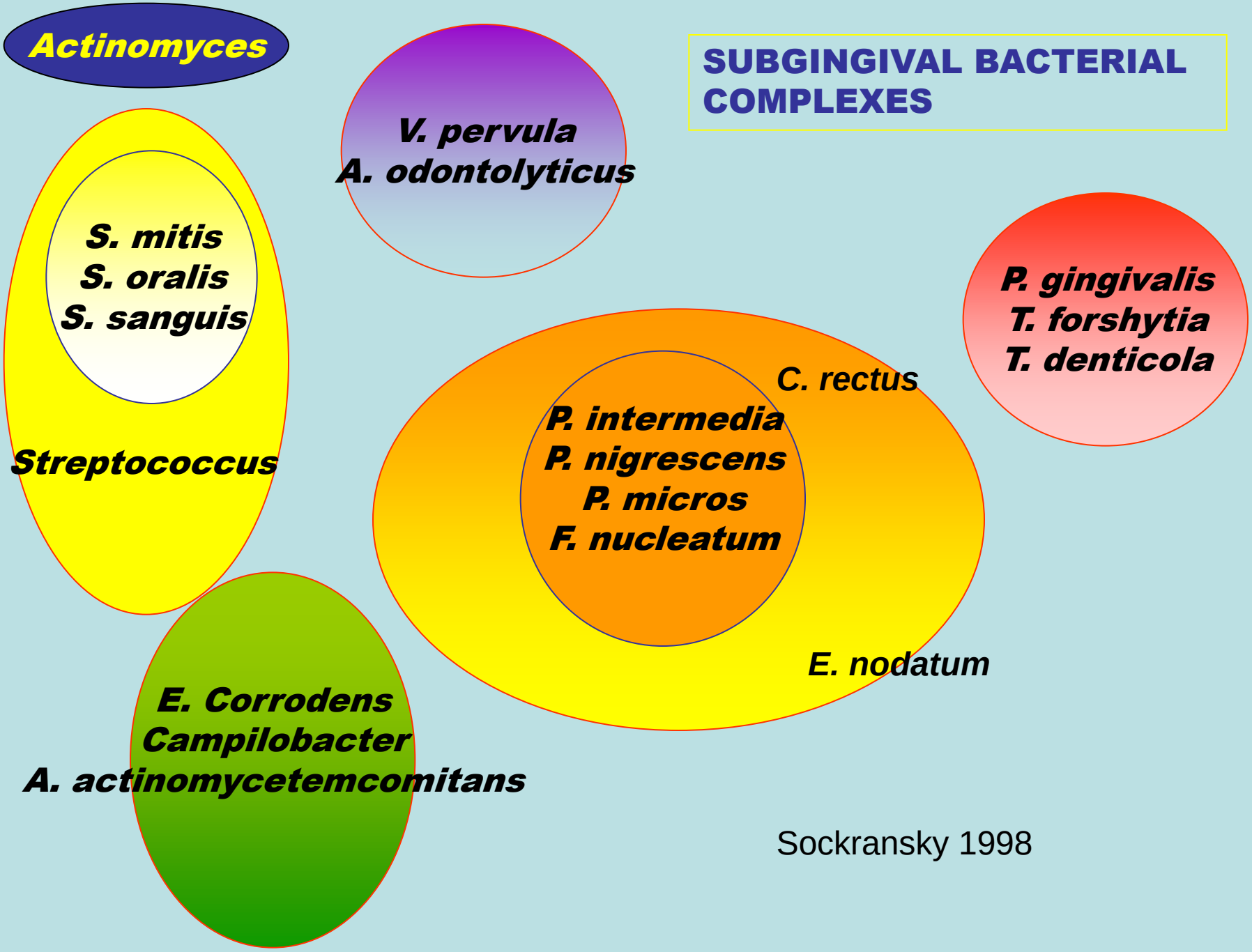
(Boles et al. 2004).



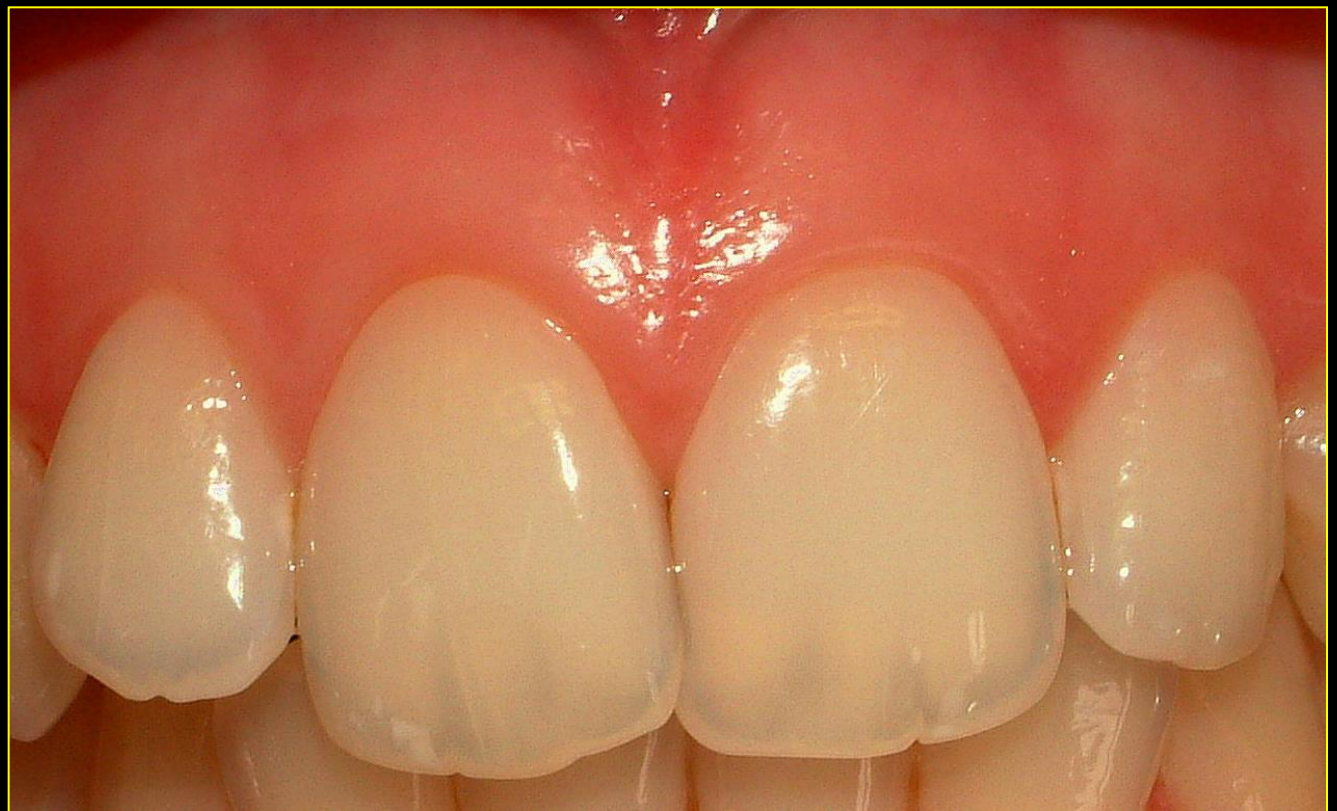
In deep periodontal pockets :

the deepest zones were colonized mainly by spirochaetles and Gram-negative anaerobic bacteria

shallow regions comprised predominantly Gram-positive cocci (Wecke et al. 2000)


Actinomyces
SUBGINGIVAL BACTERIAL COMPLEXES
V. pervula
A. odontolyticus
S. mitis
S. oralis
S. sanguis
Streptococcus
P. gingivalis
T. forshytia
T. denticola
C. rectus
P. intermedia
P. nigrescens
P. micros
F. nucleatum
E. nodatum
E. Corrodens
Campilobacter
A. actinomycetemcomitans
Sockransky 1998

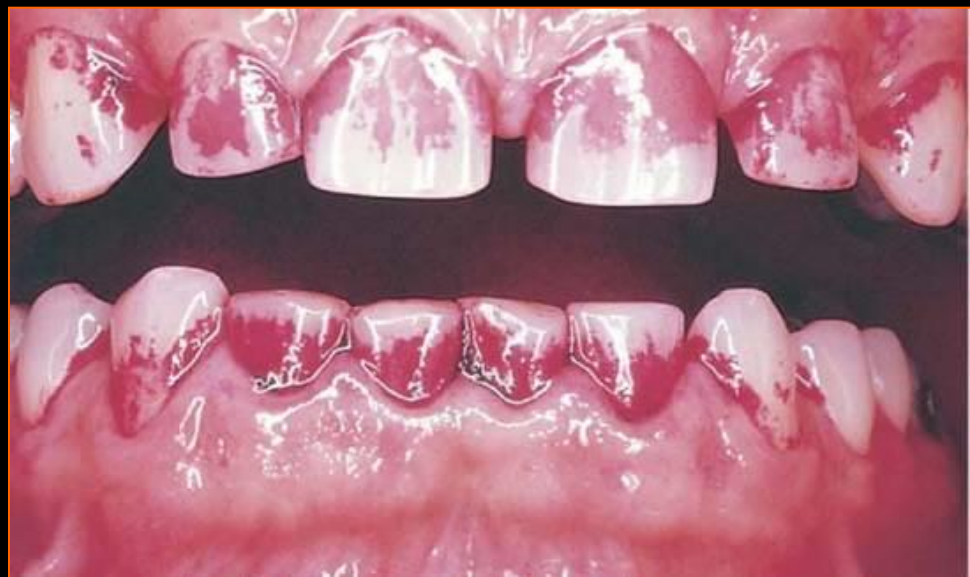
THE HUMAN HOST IS HEALTHY DESPITE THAT THE 90% OF THE CELLS IN THE HUMAN BODY ARE BACTERIA (Henderson 1998)



COMMENSAL BACTERIAL FLORA

COMMENSAL MEANS – RELATIONSHIP BETWEEN ORGANIS OF TWO DIFFERENT SPECIES IN WHICH ONE DERIVES NUTRIENTS FROM THE OTHERS WHILE THE OTHER REMAINS UNHARMED AND UNAFFECTED

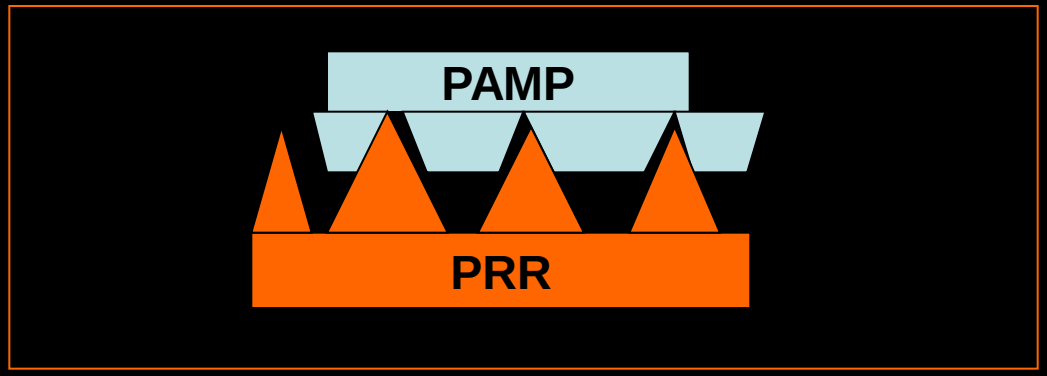
COMMENSAL BACTERIA CAN BE PATHOGENIC ON OTHER LOCATIONS, LIKE ORAL OR GUT BACTERIA IN OTHER TISSUES



TOLL LIKE RECEPTORS AND THE COMMENSAL FLORA

Toll like receptors are to recognize microbial molecular patterns

by this host can discriminate between commensal and hostile bacteria



HOW COMMENSAL FLORA CAN MAINTAIN PERIODONTAL HEALTH?

IN THE GUT THE NORMAL SALMONELLA FLORA CAN SUPRESS LOCAL INFLAMMATORY CYTOKINE PRODUCTION

•IN THE ORAL CAVITY THE COMMENSAL FLORA CAN PREVENT THE HOST TO ACIVATY THE IMMUNE SYSTEM

COMMENSAL BACTERIA AND EPITHELAIL ANTI-MICROBIAL PEPTIDES

- The harmless early colonizers of the dental pellicule (*streptococci*) keep unwanted pathogens off the plaque.

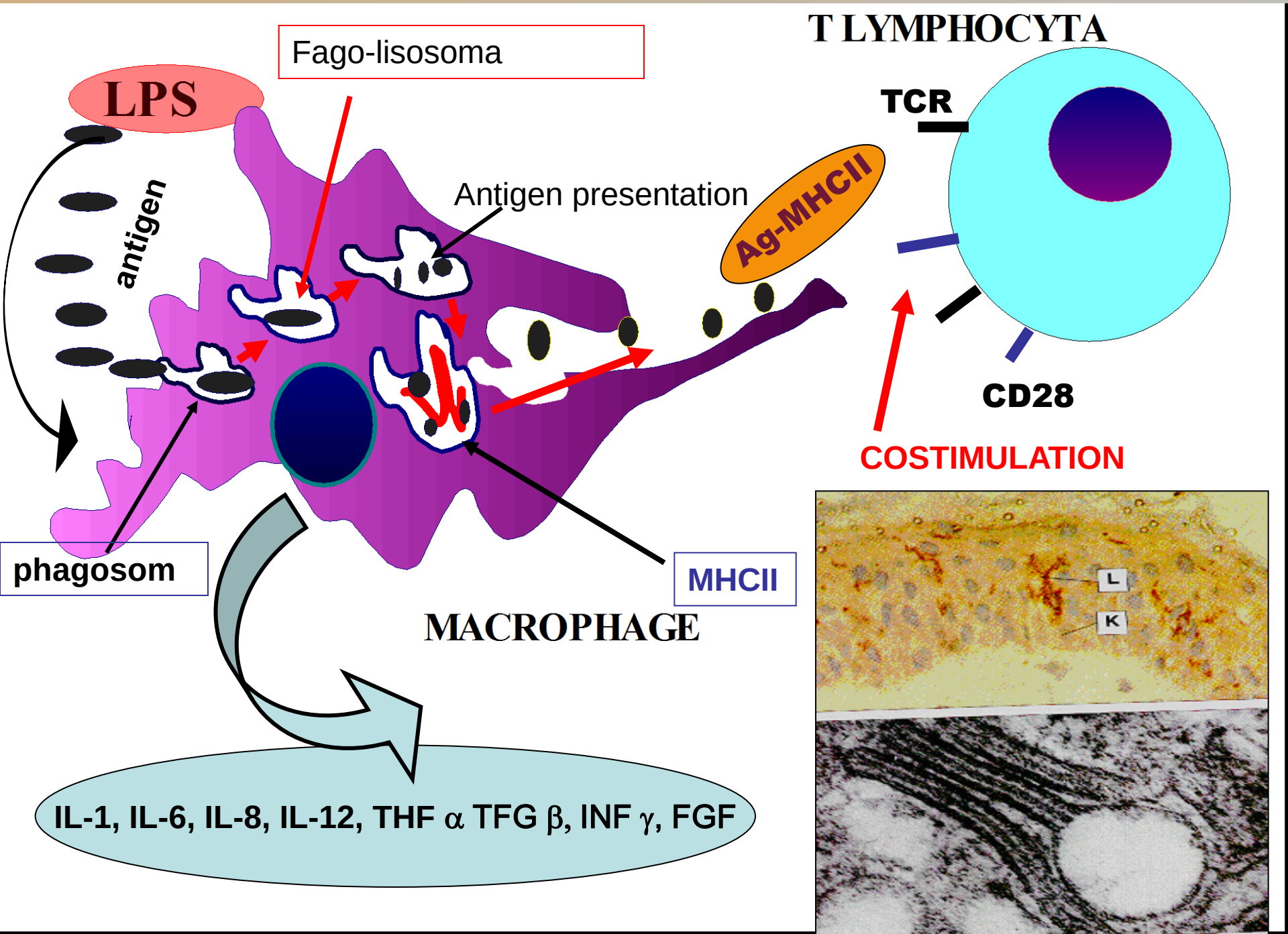
- Commensal bacteria promote the production of antimicrobial peptides than kill pathogens but has no effect on commensal bacteria

- *F. nucelatum* can protect the epithelial cells from P. gingivalis invasion by enhancing defensin-2 production

- HUMAN *F. NUCLEATUM* ITSELF IS RESISTANT TO DEFENSINS

HOW COMMENSAL FLORA CAN MAINTAIN PERIODONTAL HEALTH?

- **THE MAJOR DIFFERENCE BETWEEN COMMENSAL AND PATHOGENIC BACTERIA THAT THE ONE ELICITE IMMUNE TOLERACE THE OTHER PROVOCE ADAPTIVE IMMUNE RECATION**
- BACTERIA CAN STIMULATE SUPPRESIVE T LYMPHOCYTES TO PRODUCE INHIBITORY CYTOKINES (TGF, IL-10)
- COMMENSAL BACTERIAL ANTIGINE PRESENTATION TO DENTRITIC CELLS HAPPENS WITHOUT COSTIMULATION


T LYMPHOCYTA
Fago-lisosoma
LPS
TCR
antigen
Antigen presentation
Ag-MHCII
CD28
COSTIMULATION
phagosom
MHCII
MACROPHAGE
L
K
IL-1, IL-6, IL-8, IL-12, THF α TFG β, INF γ, FGF

In the presence of commensal bacteria the mucosal antigen presenting cells suppress inflammation by maintaining low level of costimulatory molecules and favors Th2 cytokin production

FUSOBACTERIUM NUCLEATUM CAN ENHANCE MHC II EXPRESSION BUT DECREASES THE PRODUCTION OF COSTIMULATORY MOLECULES

P. GINGIVALIS WILL ENHANCE THE PRODUCTION OF COSTIMULATORY MOLECULES

COMMENSAL BACTERIA AND CYTOKINE PRODUCTION

COMMENSAL BACTERIA CAN PRODUCE

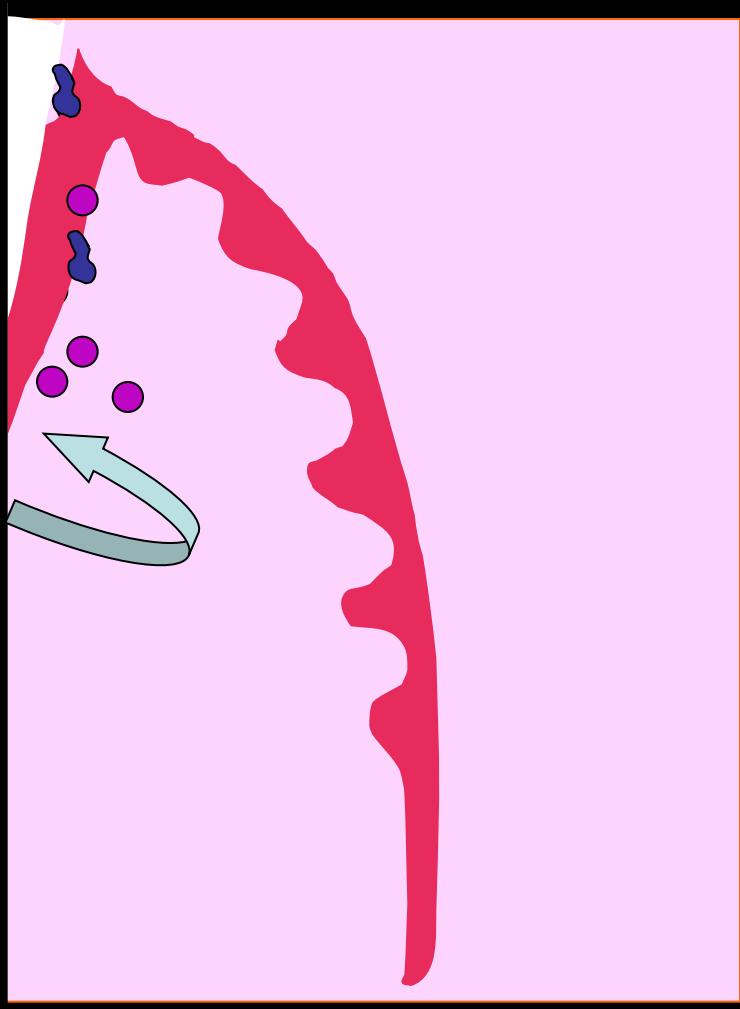
- CONSTANT IL 8 PRODUCTION → MILD PMN LEUKOCYTE EMIGRAION

- ADHESION MOLECULES - → ICAM-1, LCAM-1, PLATELET ADHESION MOLECULE 1, THAT ASSIST RECRUITING PMN LEUKOCYTES

-

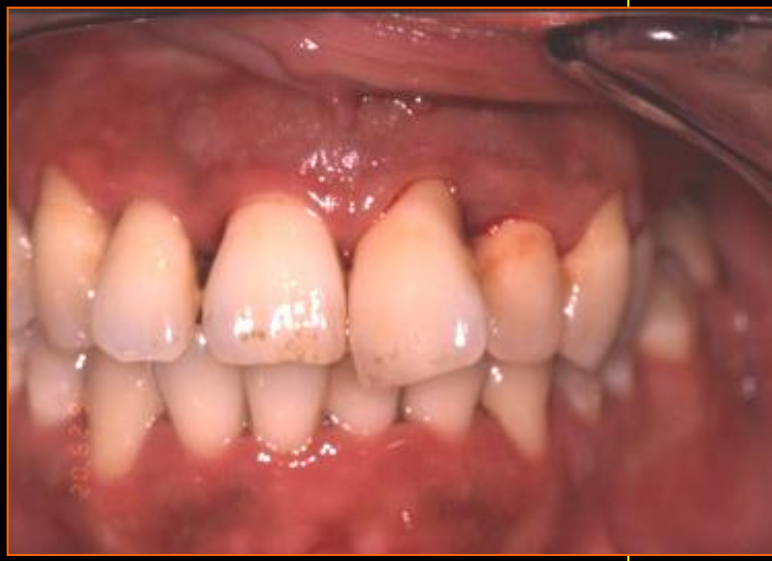
- EPITHELIAL DERIVED ANTIBACTERIAL PEPTIDES – → DEFENSINS –

•THOSE BACTERIA ARE IMMUNE TO THOSE AGENTS !!!!!



PERIOPATHOGENIC BACTERIA AND PERIODONTAL TISSUE

The composition of the dental plaque dictates the degree of which the periodontium breaks down



Red complex bacteria

- **T. denticola**
- **T. forsythia**
- **P. gingivalis**

The ability to- colonize subgingivally

The invasive capacity

Proteases and exotoxin production

To induce destructive immune reactions

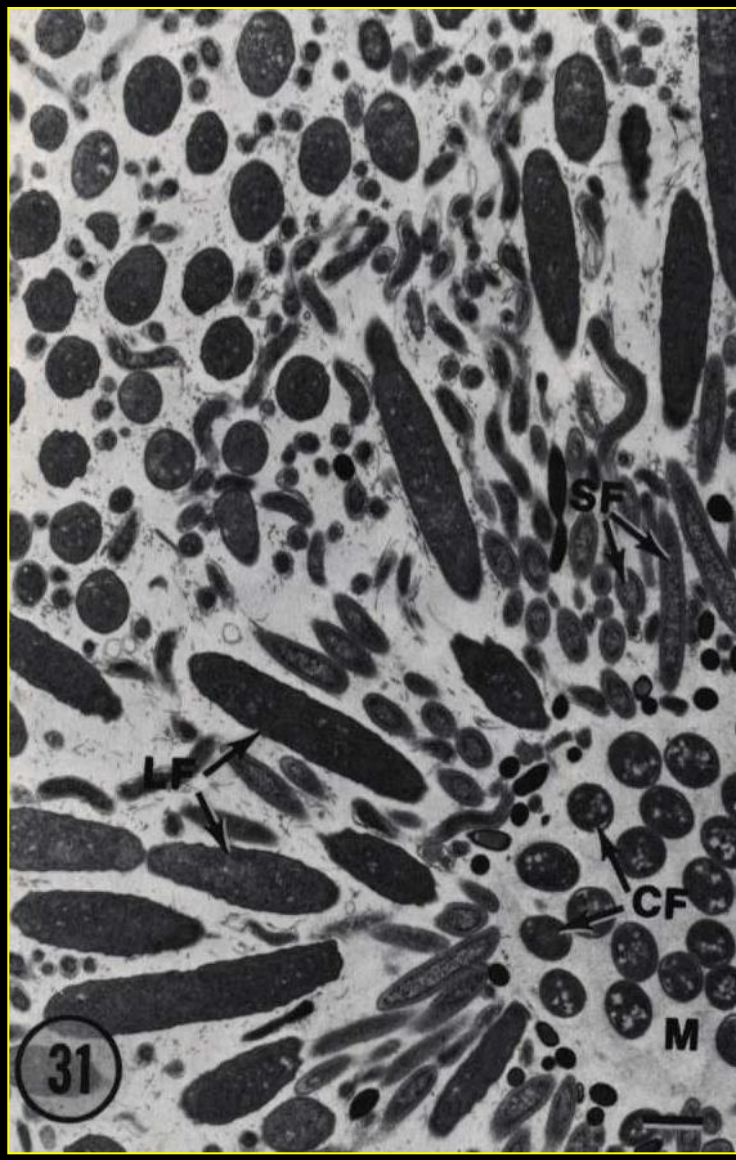
Gene expression can alter markedly when cells form a biofilm,

resulting in many organisms having a radically different phenotype following attachment to a surface

when compared with conventional liquid grown (planktonic) cells.

(Whiteley et al. 2001)

- The **matrix is** not only important physically as part of the scaffolding that determines the structure of biofilms,
- but it is also biologically active and can retain nutrients, water (thereby preventing desiccation) and key enzymes within the biofilm
- (Allison 2003, Branda et al. 2005).

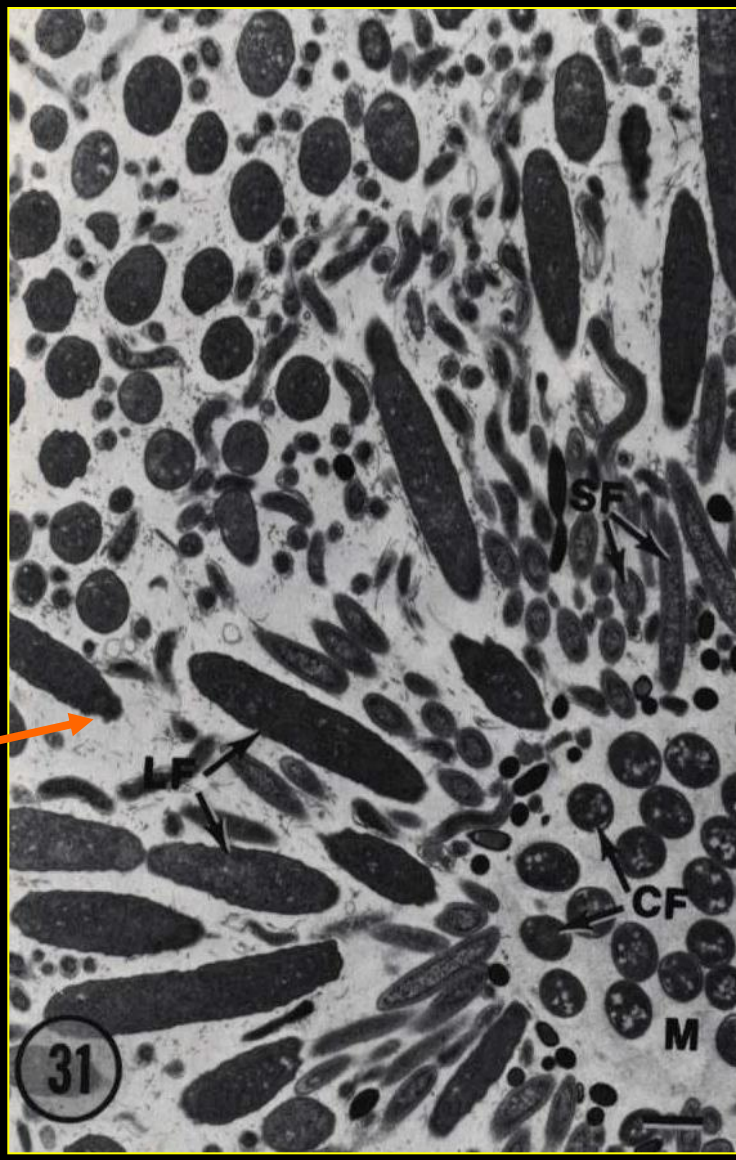


•The binding of bacteria to specific host receptors can also trigger significant changes in host cell patterns of gene expression (Abraham et al. 1998).

•As the biofilm matures, there is continued synthesis of exopolymers to form an **extracellular matrix.**

•

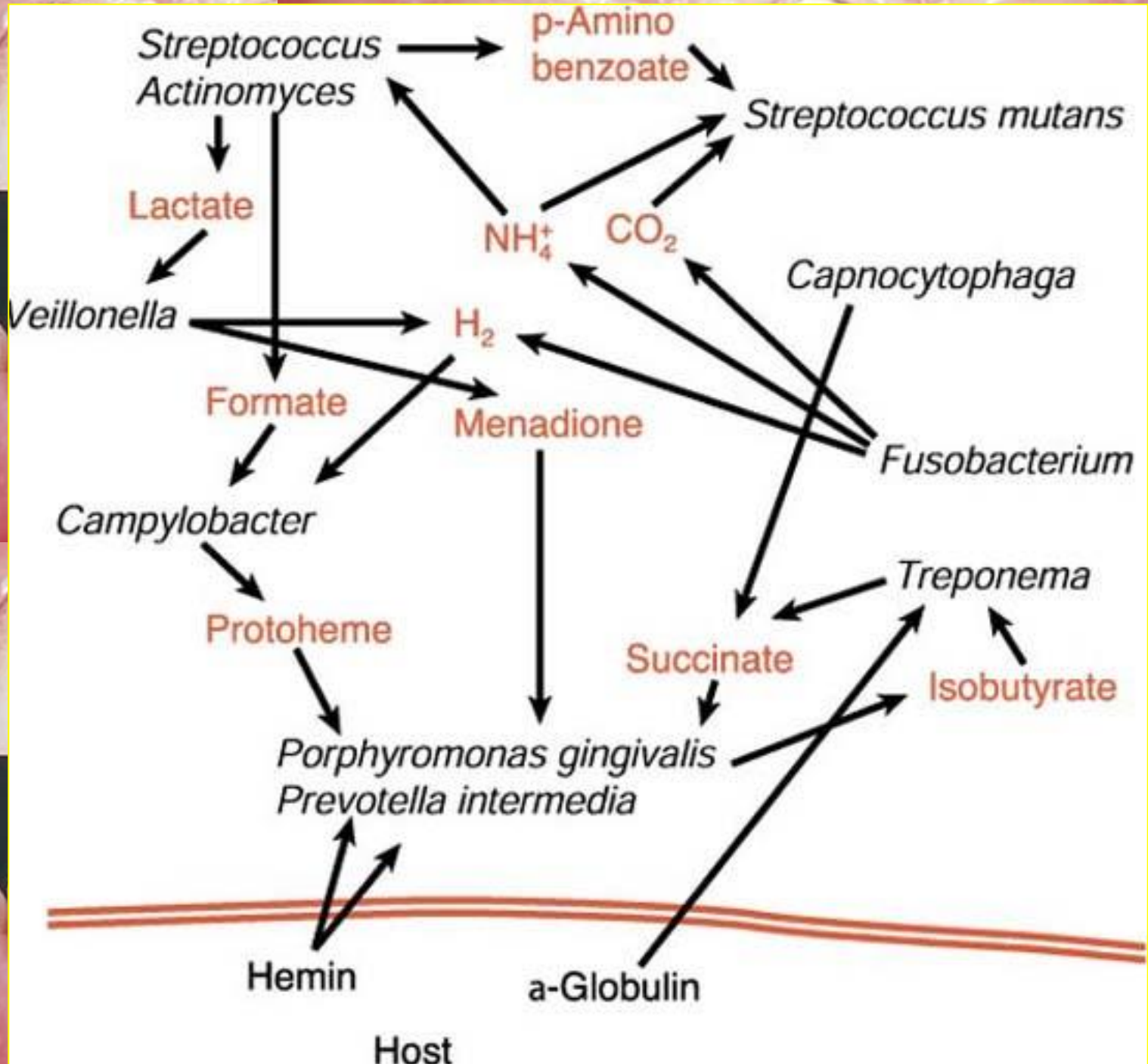
•(Allison 2003, Branda et al. 2005).



This community life-style provides enormous potential benefits to the participating organisms

(Caldwell et al. 1997, Shapiro 1998, Marsh & Bowden 2000).

- The metabolism of early colonizers alters the local environment, making conditions suitable for attachment and growth of later species.
- Thus, the diversity of the microflora increases over time because of microbial succession.

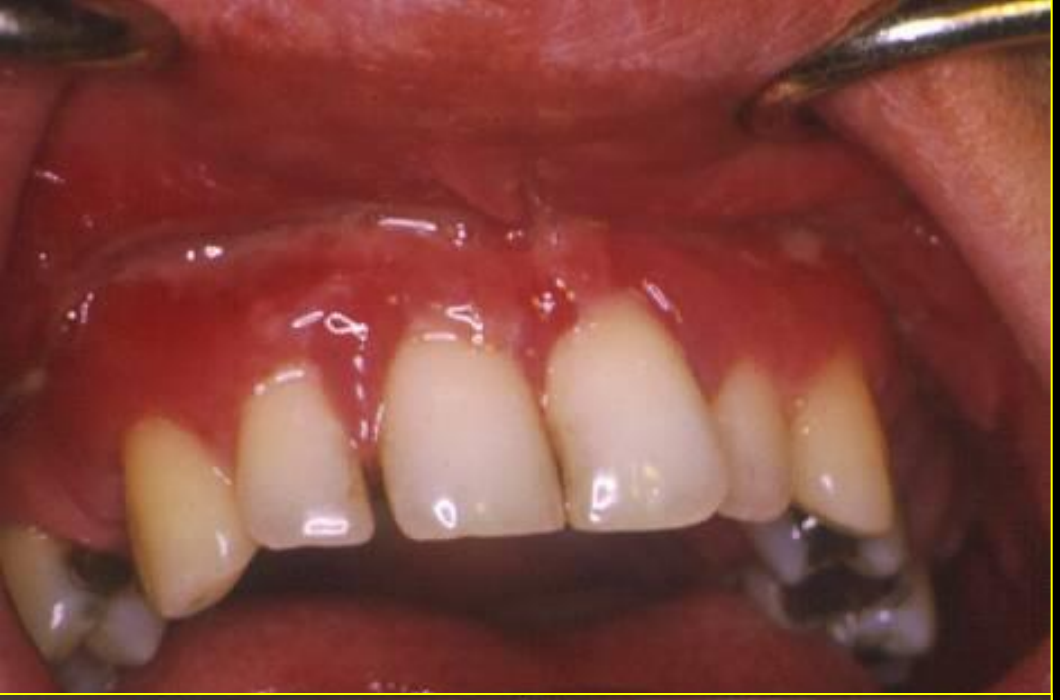

Streptococcus
Actinomyces
p-Amino
benzoate
Streptococcus mutans
Lactate
NH_4^+
CO_2
Capnocytophaga
Veillonella
H_2
Formate
Menadione
Fusobacterium
Campylobacter
Treponema
Protoheme
Succinate
Isobutyrate
Porphyromonas gingivalis
Prevotella intermedia
Hemin
a-Globulin
Host

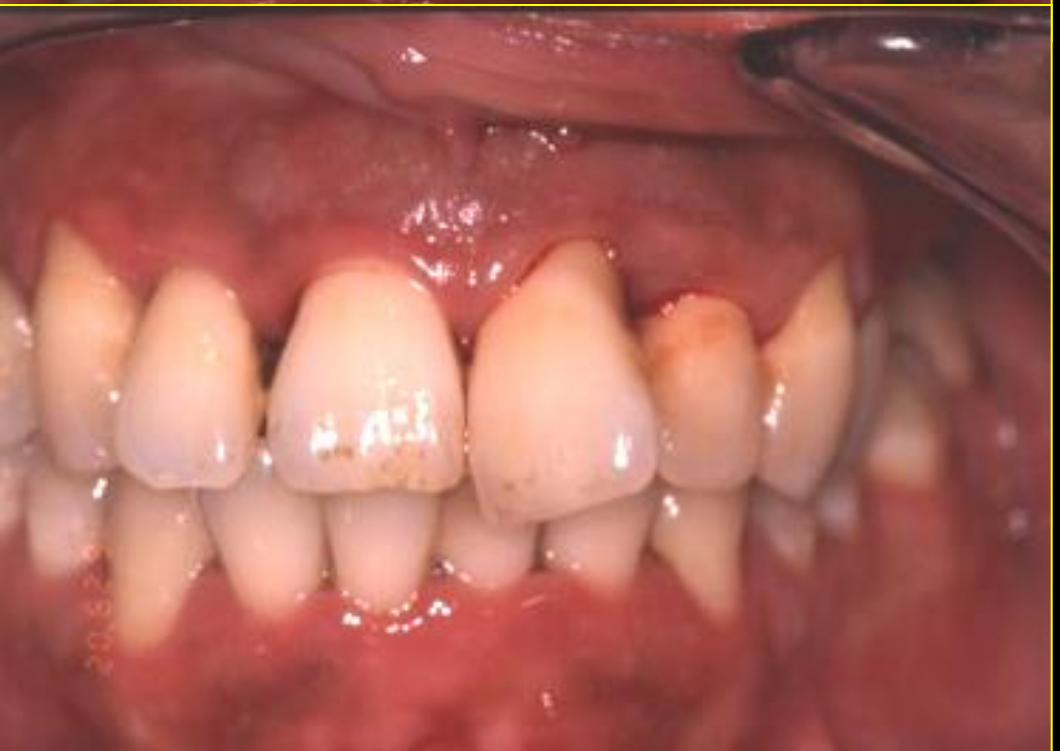
The environmental heterogeneity generated within biofilms promotes accelerated

genotypic and phenotypic diversity

"biological insurance"

that can safeguard the "microbial community" in the face of adverse conditions





This diversity can affect several key properties of cells,

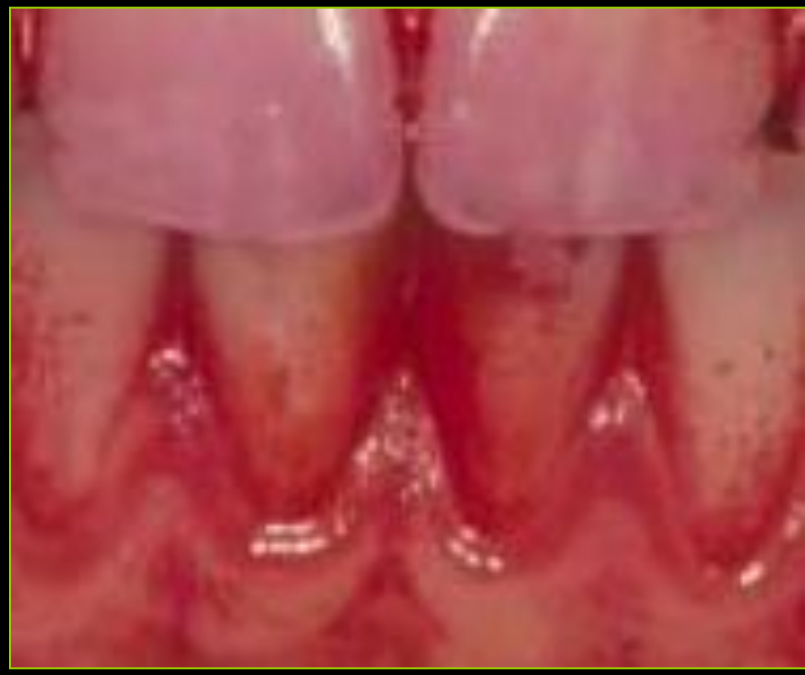
- motility,
- nutritional requirements,
- secretion of products,
- detachment,
- biofilm formation;

this diversity better equips an organism or community to survive an environmental stress.

AN IMPORTANT CLINICAL CONSEQUENCE:

structural organization of biofilms

altered pattern of gene expression



reduced susceptibility of cells to antimicrobial agents

(Gilbert et al. 1997, 2002, Ceri et al. 1999, Stewart & Costerton 2001).

- **Conventionally, the sensitivity of bacteria to antimicrobial agents is determined on cells grown in liquid culture by the measurement of the minimum inhibitory concentration (MIC) or minimum bactericidal concentration (MBC).**

- **Numerous studies have shown that the MIC of an organism growing on a surface can range from 2- to 1000-fold greater than the same cells grown planktonically**

- **(Stewart & Costerton 2001, Johnson et al. 2002).**

ANTIMICROBIAL RESISTANCE

Bacteria growing in dental plaque also display an increased tolerance to antimicrobial agents, including those used in dentifrices and mouthrinses

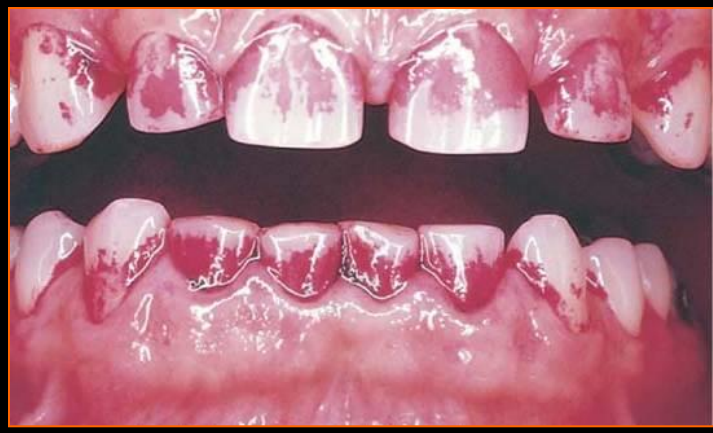
(Marsh & Bradshaw 1993, Kinniment et al. 1996, Wilson 1996, Pratten & Wilson 1999).

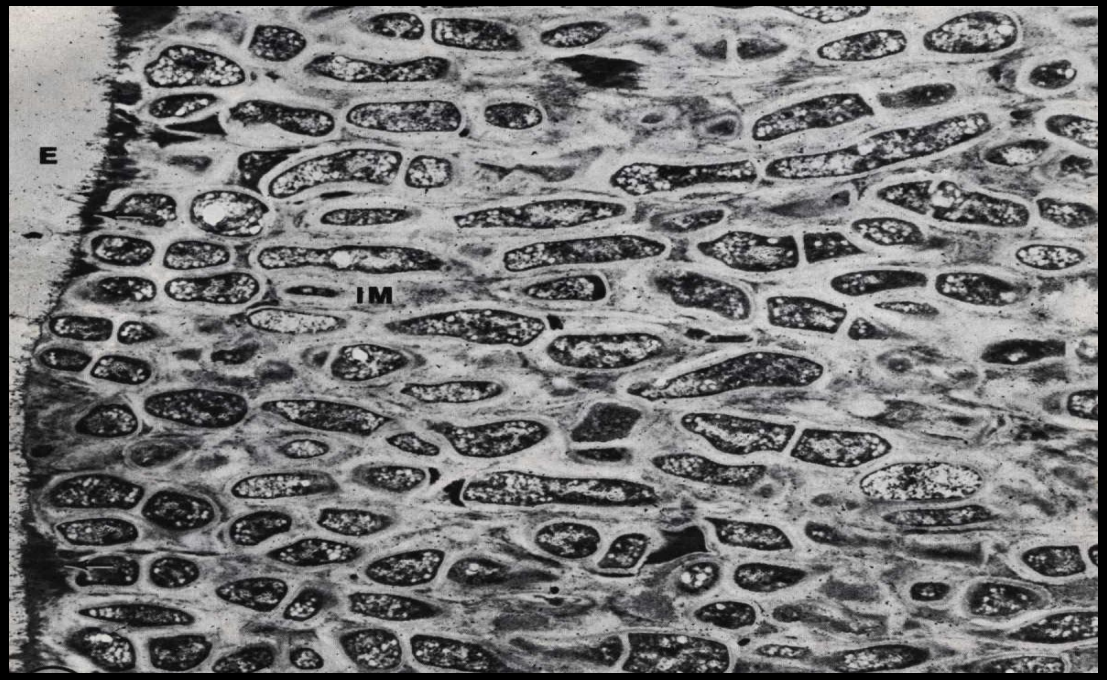
The BIC for chlorhexidine and amine fluoride was 300 times and 75 times greater, respectively, when *S. sobrinus* was grown as a biofilm compared with the MBC of planktonic cells

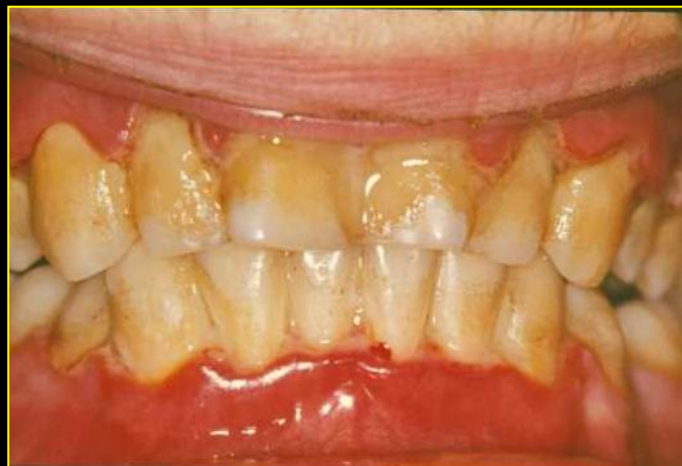
(Shani et al. 2000).

The age of the biofilm can also be a significant factor; older biofilms (72 h) of *S. sanguinis* were more resistant to chlorhexidine than younger (24 h) biofilms

(Millward & Wilson 1989).







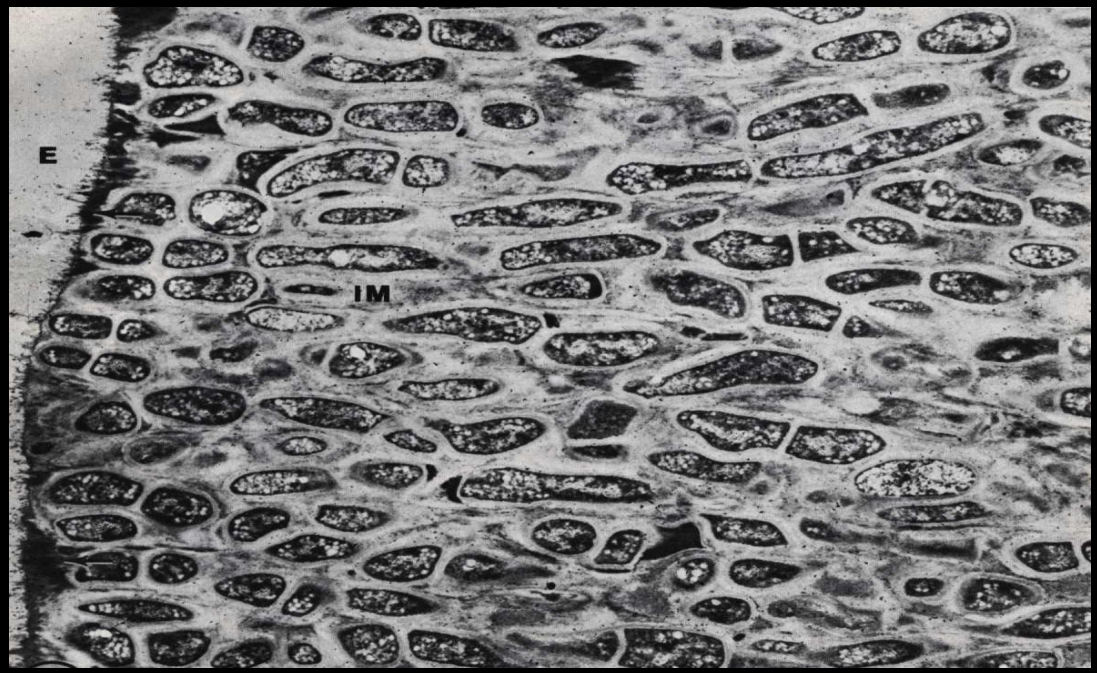
Biofilms of oral bacteria are also more tolerant of antibiotics than planktonic cells

(e.g. amoxycillin, doxycycline, minocycline, metronidazole)

(Larsen 2002, Socransky & Haffajee 2002, Noiri et al. 2003),

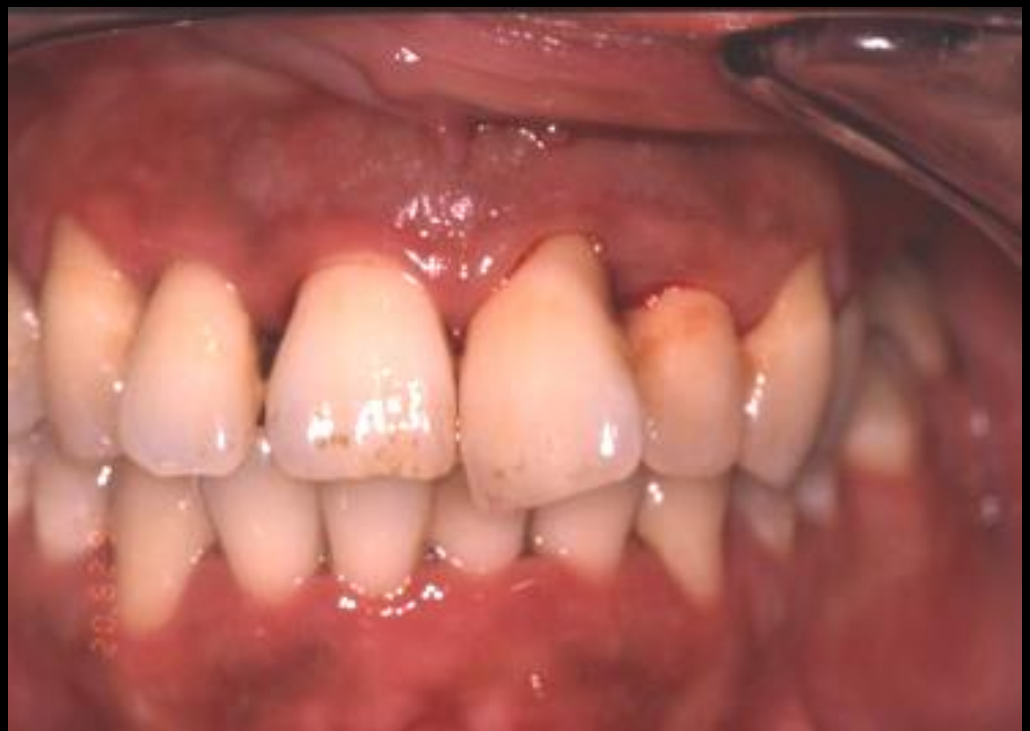
Biofilms of *P. gingivalis* tolerated 160 times the MIC of metronidazole that had been determined for planktonic cells

(Wright et al. 1997),



it would be more appropriate to determine the "biofilm inhibitory concentration" (BIC) of an agent (also described as the "biofilm eradicating concentration" or biofilm killing concentration)

(Anwar & Costerton 1990, Nichols 1994, Johnson et al. 2002).



why,???

- The structure of a biofilm may restrict the penetration of the antimicrobial agent;
- charged inhibitors can bind to oppositely charged polymers that make up the biofilm matrix (diffusionreaction theory).
- The agent may also adsorb to and inhibit the organisms at the surface of the biofilm, leaving cells in the depths of the biofilm relatively unaffected.
- The matrix in biofilms can also bind and retain neutralizing enzymes (e.g. -lactamase) at concentrations that could inactivate an antibiotic or inhibitor (Allison 2003).

SUMMARY

Plaque as a community

biofilm

Oral bacteria do not exist as independent entities but rather function as a co-ordinated, spatially organized and metabolically integrated microbial community
(Marsh & Bradshaw 1999, Marsh & Bowden 2000)

Benefits of a community life-style to plaque

(a) a broader habitat range for growth,

oxygen-consuming species create environmental conditions suitable for colonization in plaque by obligate anaerobes (Bradshaw et al. 1996).

Benefits of a community life-style to plaque

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(b) A more efficient metabolism, e.g. many complex host macromolecules, especially glycoproteins such as mucins, can only be degraded efficiently by consortia of oral bacteria (Bradshaw et al. 1994).

Benefits of a community life-style to plaque

(a) a broader habitat range for growth,
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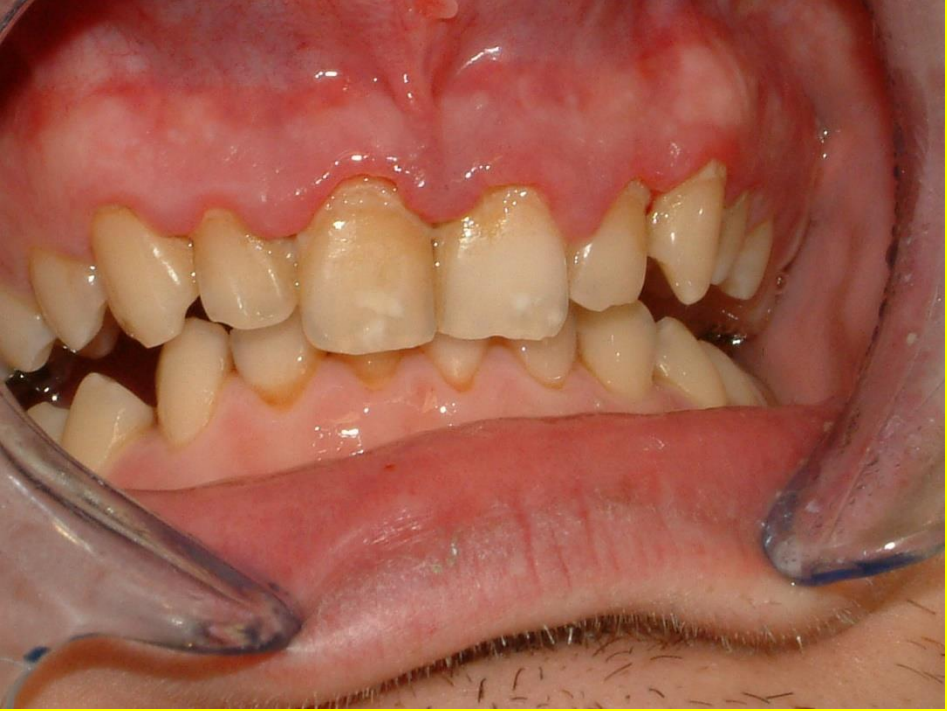
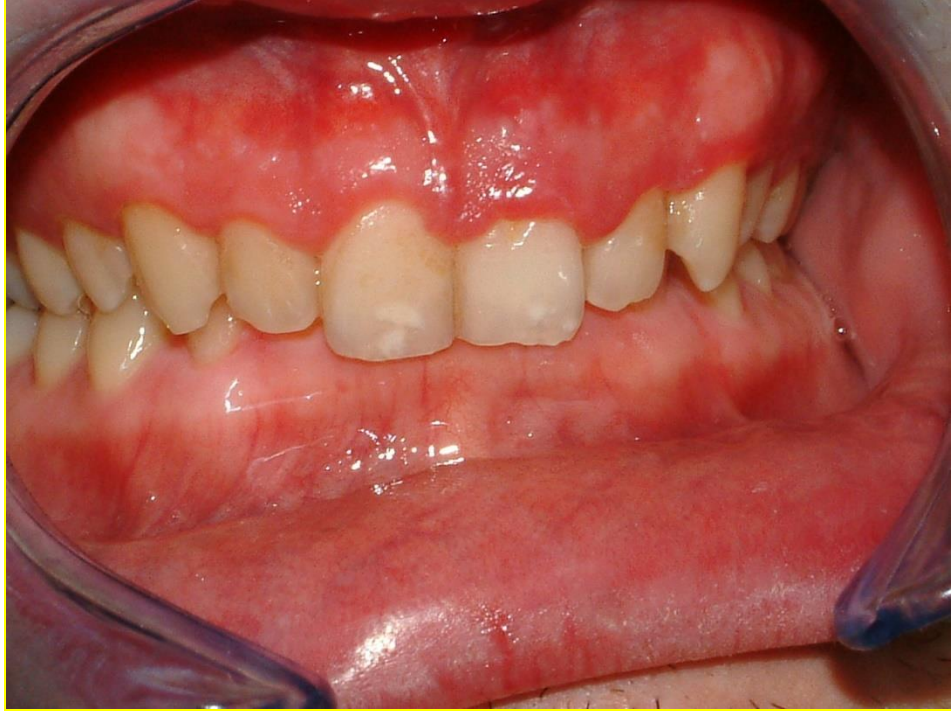
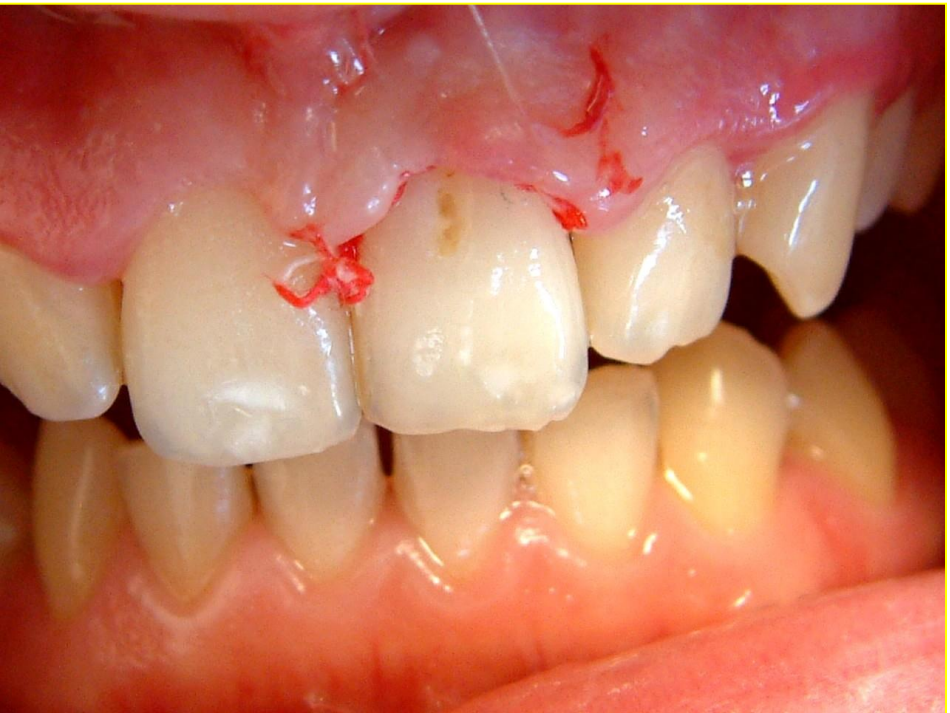
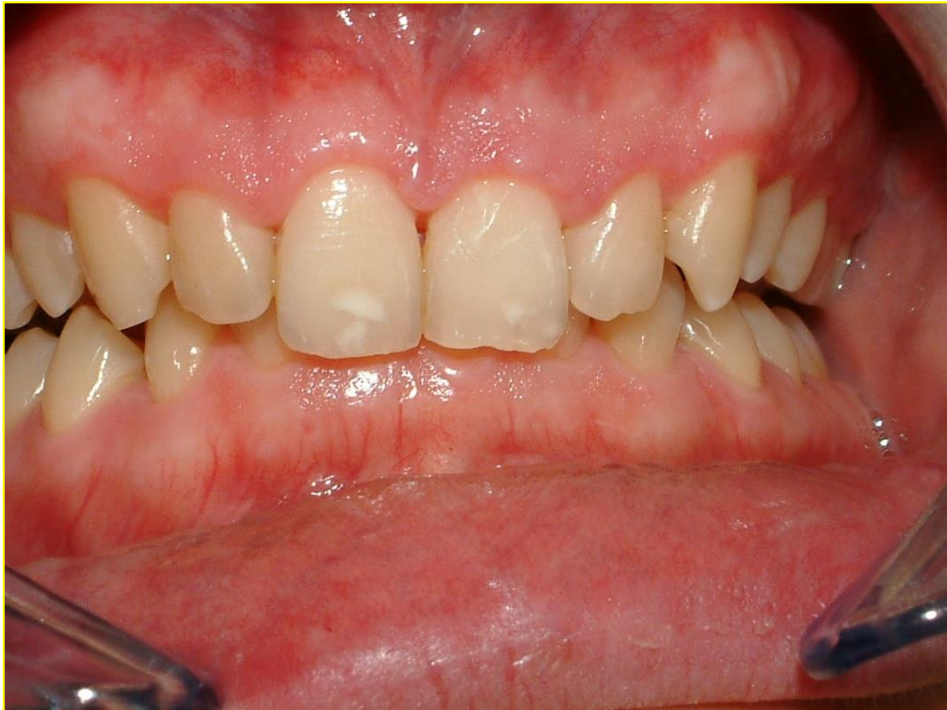
(b) A more efficient metabolism, e.g. many complex host macromolecules, especially glycoproteins such as mucins, can only be degraded efficiently by consortia of oral bacteria (Bradshaw et al. 1994).

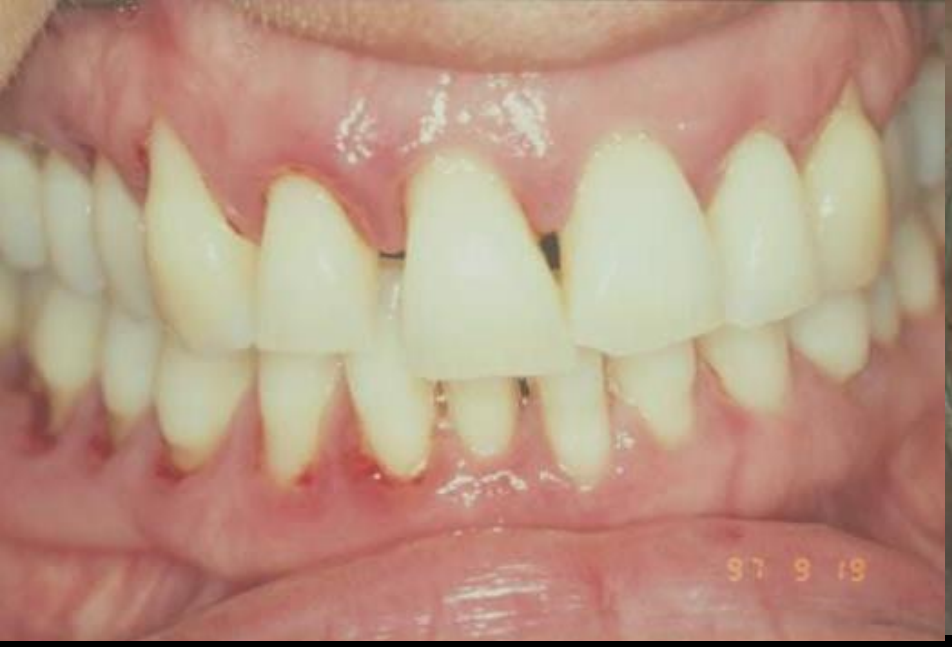
c) Increased resistance to stress and antimicrobial agents.
a sensitive organism can be rendered as being apparently "resistant" to an antibiotic if neighbouring, non-pathogenic cells produce a neutralizing or drug-degrading enzyme ("indirect pathogenicity")

Benefits of a community life-style to plaque

d) communities with varying bacterial composition have been found at sites with similar disease, and would be consistent with the concept of "complexes" associated with health and disease (Socransky & Haffajee 2002).

e)The shift towards communities containing increased proportions and numbers of anaerobic and proteolytic bacteria, as seen in periodontal disease, could be explained by the response of sub-gingival biofilms to changes in local environmental conditions and host responses. "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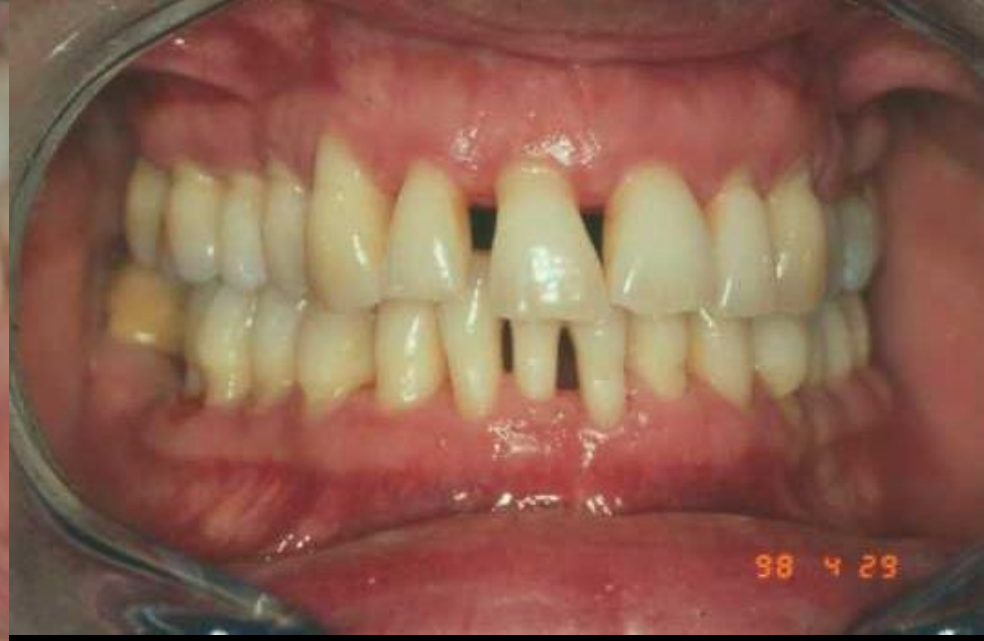
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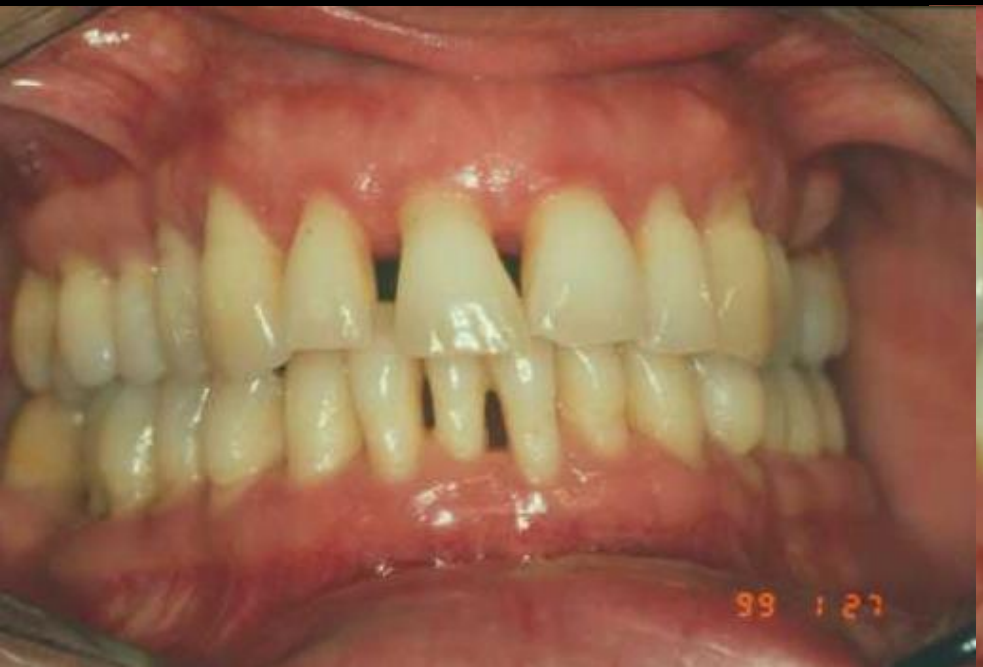
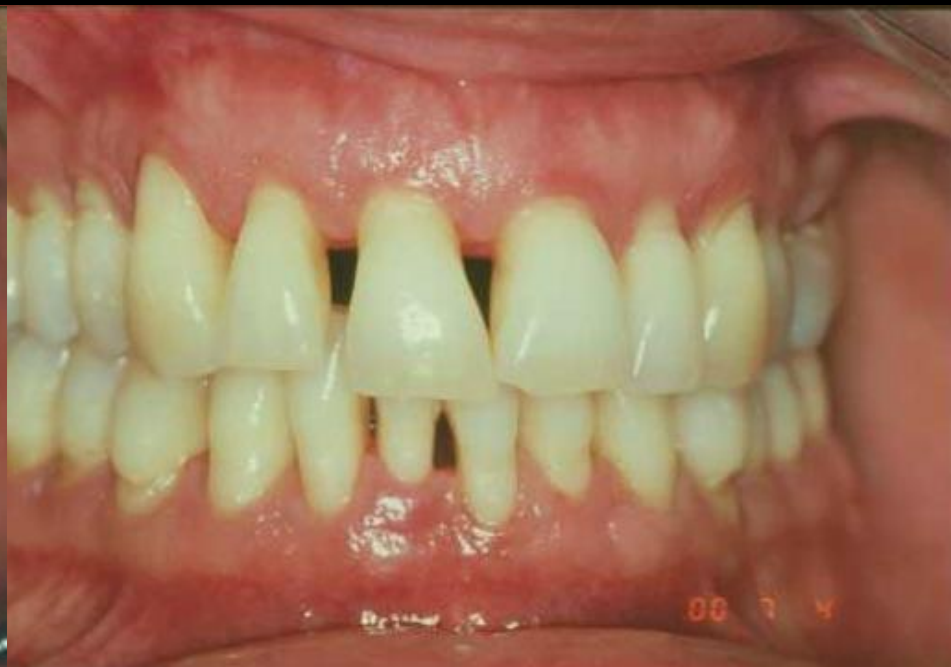
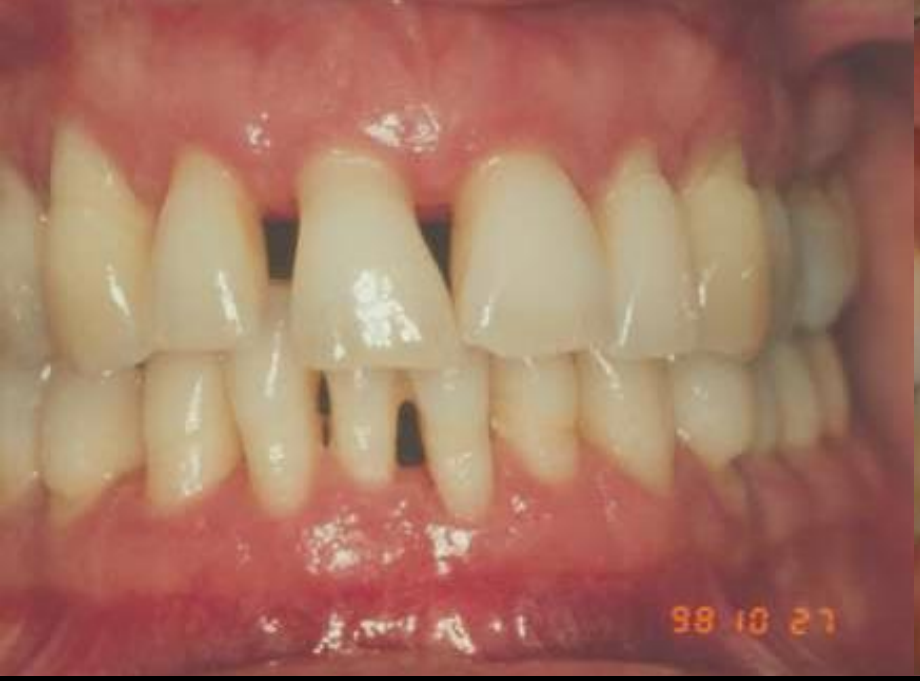

99 1 27

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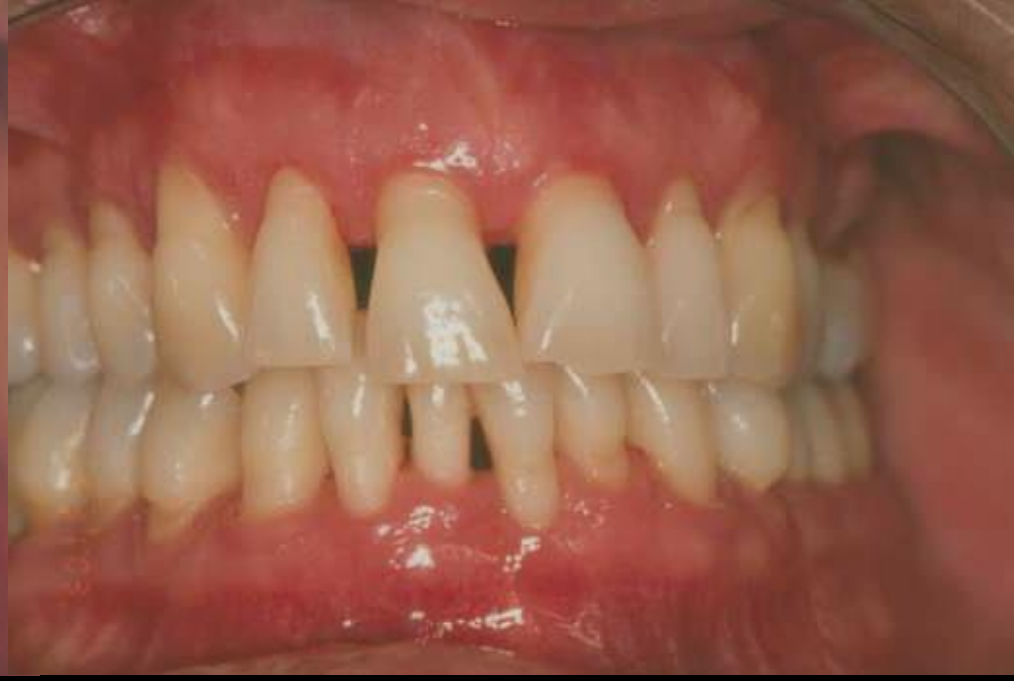

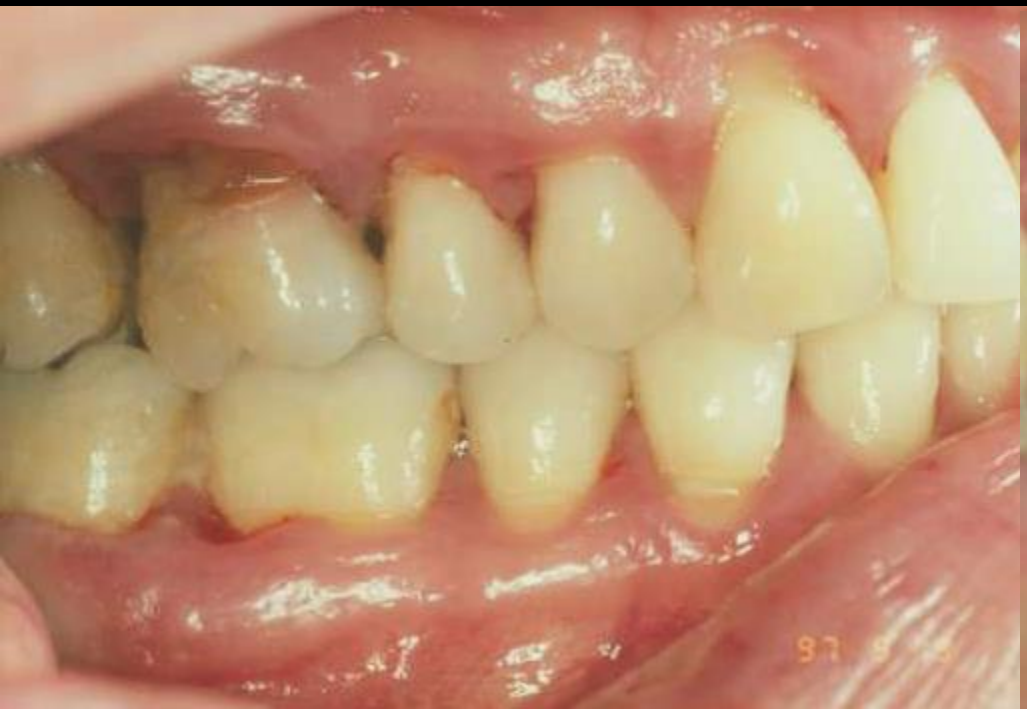

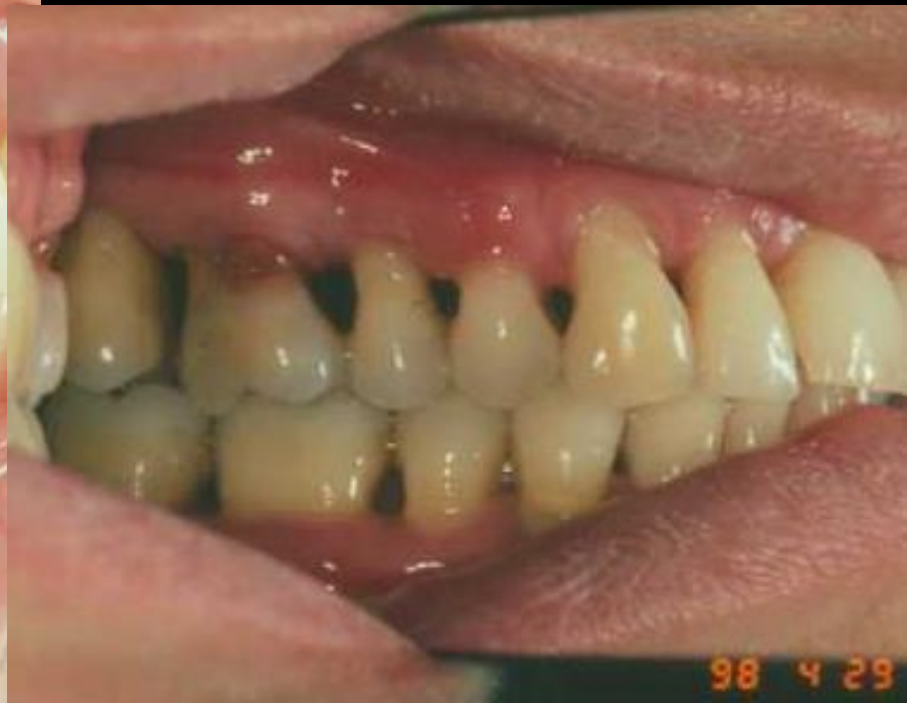
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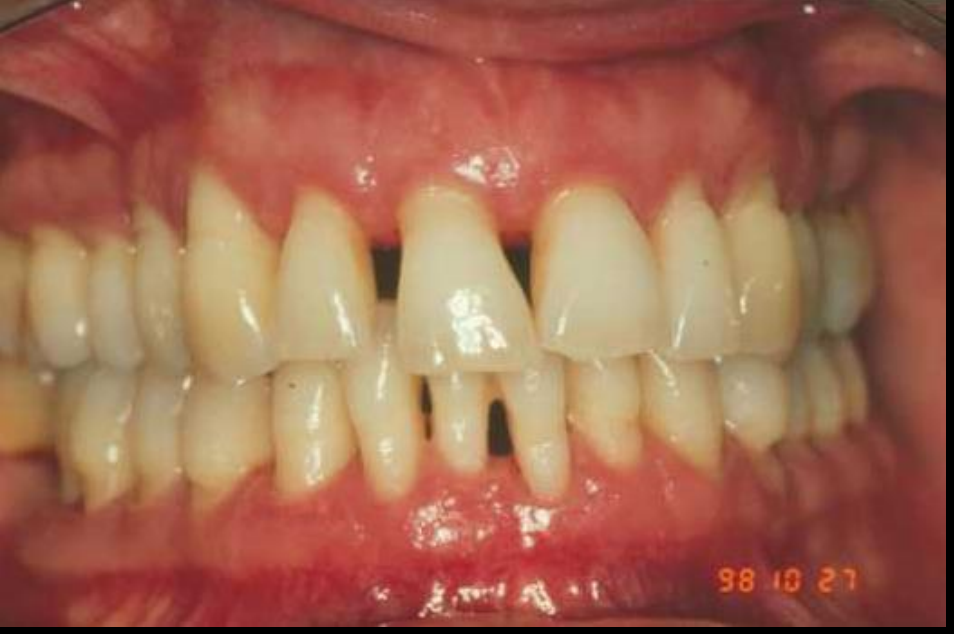
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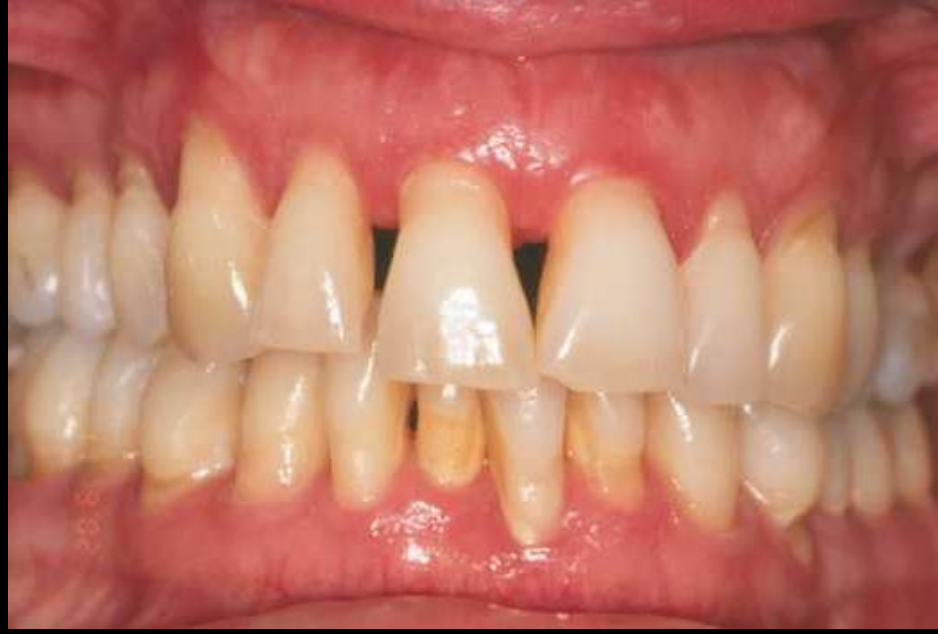

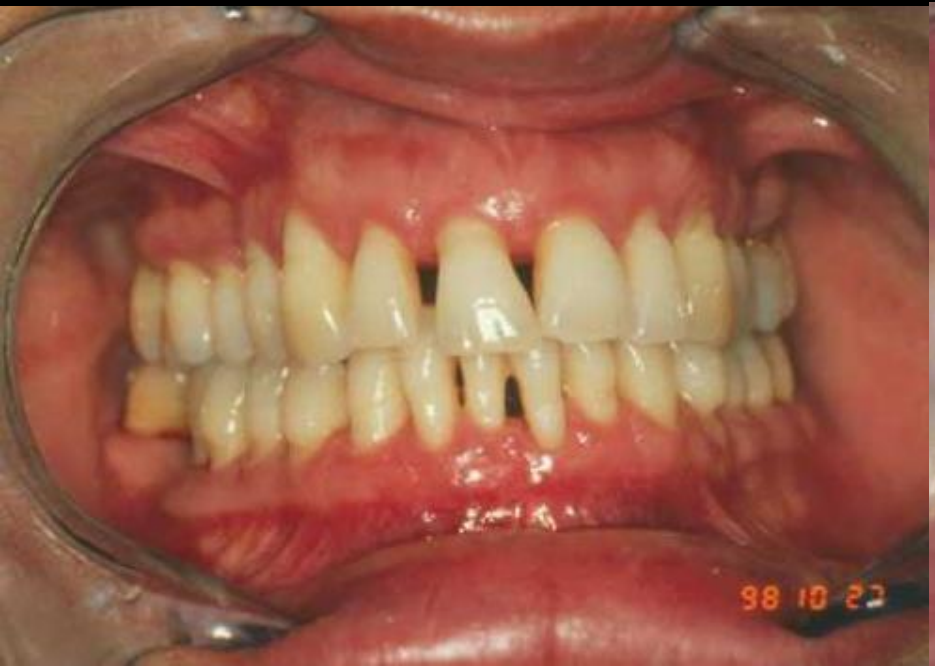
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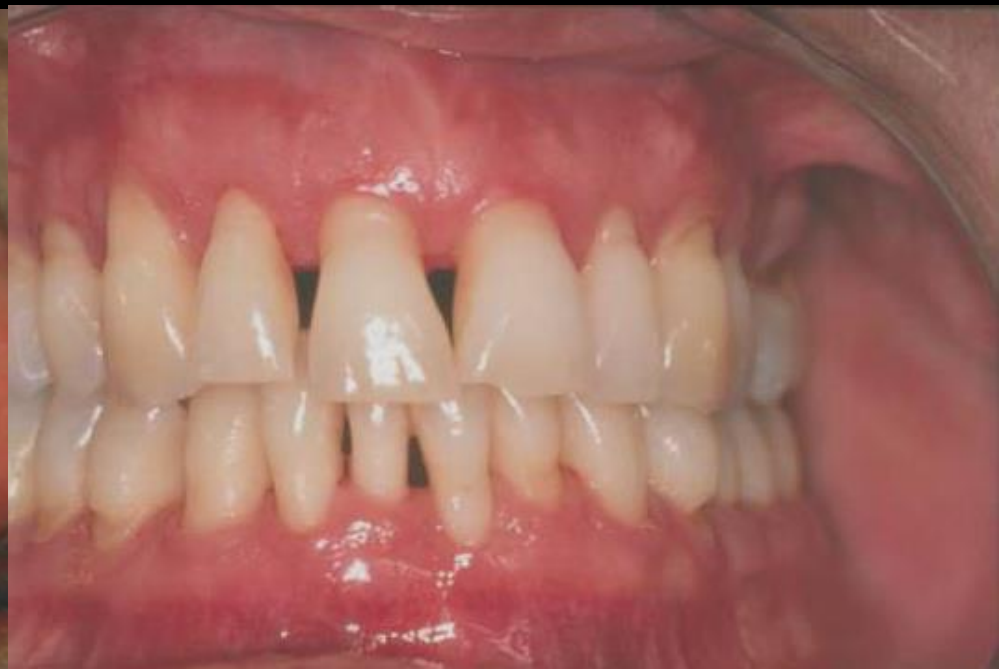
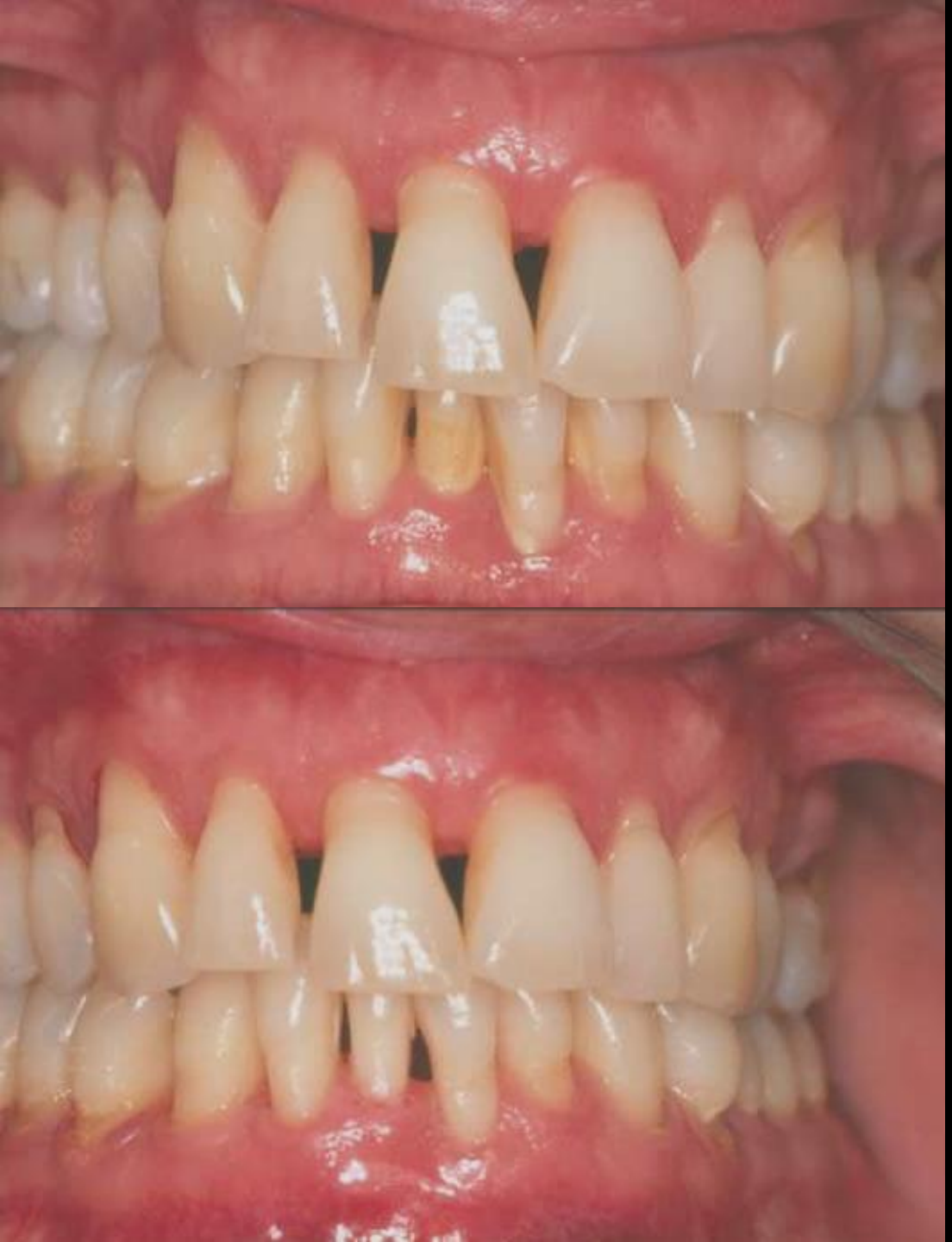
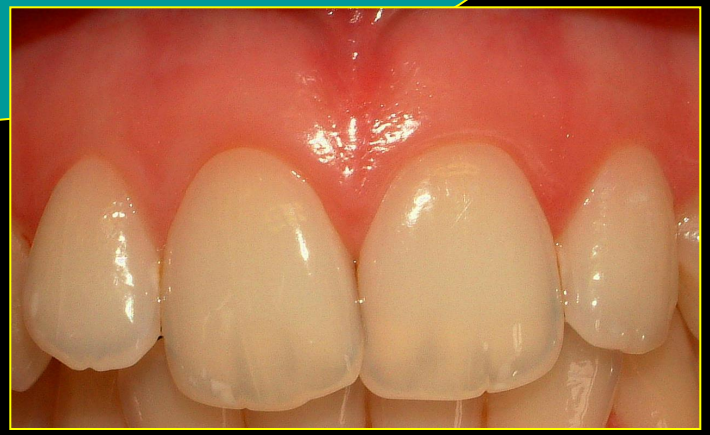


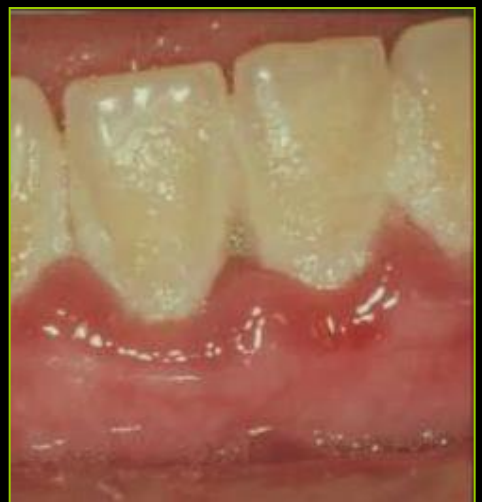


CHEMICAL PLAQUE CONTROL

- ***chemopropphylaxis***



- ***chemotherapy***



CHEMOPROPHYLAXIS

to sustain the normal ecological balace of the oral cavity and control bacterial colonization .

Chemotherapy

kill subgingival bacteria

control bacterial invasion into the deeper periodontal tissues

assist periodontal healing

Periodontal chemoprophylaxis

Non-selective with total bacterial eradication
Non-selective with marked oral bacterial reduction

.

Selective chemoprophylaxis .

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

Classification of anti-plaque agents

- **Duration of its effect**
- short, first generation
- substantive –second generation
- ***Biological effect***
- Enzymes ,
- Antibiotics
- Antiseptics

Phenol derivatives :

- **Listerin with** American Dental Association (ADA) seal
- Evidence support its anti plaque anti gingivitis effects
- Ingredients: thimol, menthol, methylsalicitate eukaliptol.
- **Triclosan** (2,4,4'-triklór-2'-hirdoxifenil-ether) chemically active ingredient in many toothpastes and mouth rinses

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***
- ***domifen-bromid***.

Halogens
iodine and fluorides .

- ***Betadin***.
- ***fluorides***
- ***Sn-fluoride and amino fluoride with strong anti-plaque effects***
- ***mild anti plaque effect comparing to Chlorhexidin***
- ***Meridol amino-fluoride + stannous fluoride .***

Bisbiguanid derivatives

second generation chemoprophylactic agents .

- **Chlorhexidin** ***1,6-di-4-klórfenil-diguanidhexan***.
- 0,2,% 0,15, % 0,05 % - rinses Corsodyl, Chlorhexamed , Curasept
- 1%-os gel Corsodyl

- **Alexidin** ***etil-hexil-biszguanidin-dihidroklorid***
- Similar effect to Chlorhexidin ,
- locally less irritation ,
- does not contain carcinogenic phenyl groups

Bisbiguanid derivatives

second generation chemoprophylactic agents .

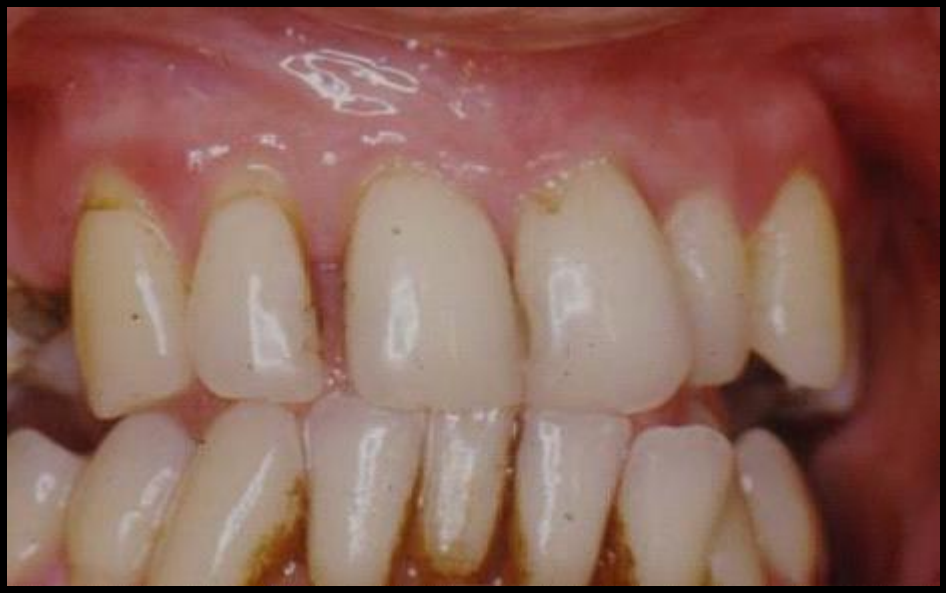
- **Chlorhexidin**
- Broad spectrum antiseptic
- Effective against Gram negative and Gram-positive microorganisms
- Proportionally decrease the whole oral bacterial count
- Effective against anaerobs and *Streptococcus mutans* ,
- Clinically improves plaque and gingivitis indices

Bisbiguanid derivatives

second generation chemoprophylactic agents.

- **Chlorhexidin**
- 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 can sustain permanent anti-plaque effect in oral cavity

Bisbiguanid derivatives
second generation chemoprophylactic agents



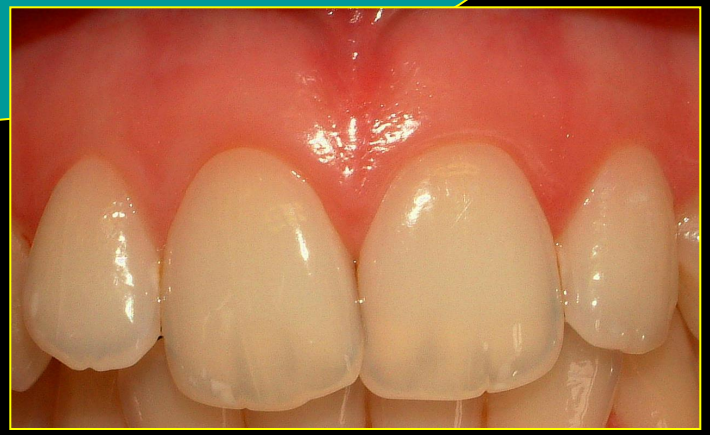
- **Chlorhexidin**
- Several side effects
- Discoloration
- Taste disturbances
- Glossitis
- After long term use, mucosal chronic irritation can occur. .

Antibiotics as chemoprophylac agents

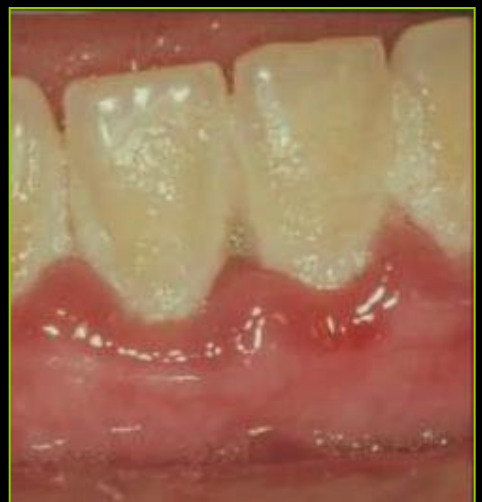
- Should be selective againts plaque bacteria
- Will not be used in other systemic disorders
- Non toxic ,
- Has no cumulative or chronic irritative effect
- Does not develop bacterial resistance
- Does not act as an allergen ,
- Has a substantive effect
- Today there is no ideal agent

CHEMICAL PLAQUE CONTROL

- ***chemopropphylaxis***



- ***chemotherapy***



Periodontal chemotherapy

- **Can be administered :**
- **Locally ,**
- **per os**
- **Parenterally**

BASIC PRINCIPLES OF PERIODONTAL ANTIBIOTIC THERAPY

- **Definitive periodontal diagnosis**
- **Only in active disease stage is to be used**
- **Preferably bacteriological testing**
- **Antibiotic therapy is not a monotherapy**
- **Systemic treatment can be completed by antiseptics (Chlorhexidine, Betadine, Tetracyclin etc.)**
- **Antibiotics can be used before surgery and postoperatively to improve periodontal wound healing**
- .

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

Metronidazol (Klion)

- Daily dose 2x250 mg, 3x250mg
- Clinical studies indicated that daily 500-750mg metronidazol combined with subgingival SRP was superior to only mechanical SRP alone .

Penicillin derivatives

- Penicillin 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 can be combined with metronidazole**

- **Infective endocarditis prophylaxis**

Amoxicillin:

- 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).
- Dose: - 3x 375mg/day – 3x625mg/day for one week .

Tetracyclin

- Bacteriostatic agent
- Effective against both Gram +, mint Gram –
- Crevicular fluid concentration is 2-10 fold higher than serum concentration
- It can inhibit *A. actinomycetemcomitans at relatively low sulcus fluid concentration* (4ug/m
- At very low concentration can inhibit bacterial and tissue collagenase enzyme activity and indirectly decrease tissue damage during inflammation.

Tetracyclin

- Semi-synthetic agents
- doxycylin,
- vibramycin
- minocyclin .

Tetracyclin

- ***Doxycyclin***
- In vivo its absorption is unpredictable
- Its great advantage that only one tablet is to be taken daily.
- Dose: as antibiotic – first day 2x100mg, and than 100mg/ day .
- Dose: as anti collagenaze : 2x 20mg/ day *doxycyclin hyclat* Periostat (USA) .

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 pseudomembranosus colitis can occur

Ciprofloxamin (Ciprobay)

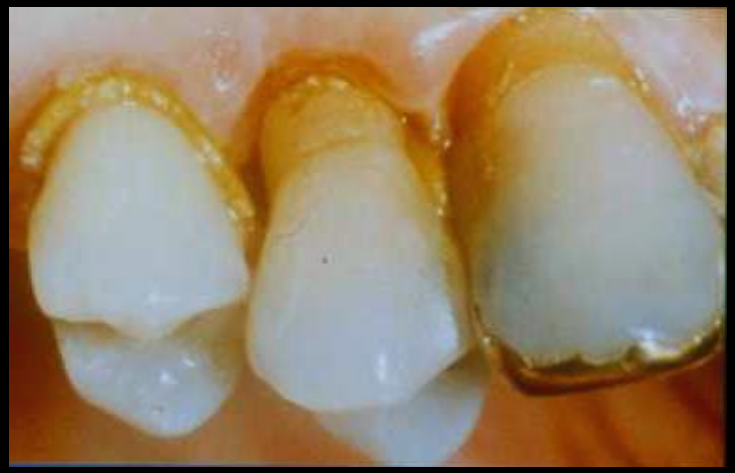
- Today all *A. actinomycetemcomitans* clonal forms are sensitive
- Strongly inhibits *A. actinomycetemcomitans* cell division but has minimal effect on commensal oral bacteria
- It is very effective to restore the normal composition of oral subgingival and supragingival bacterial flora,
- Daily dose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

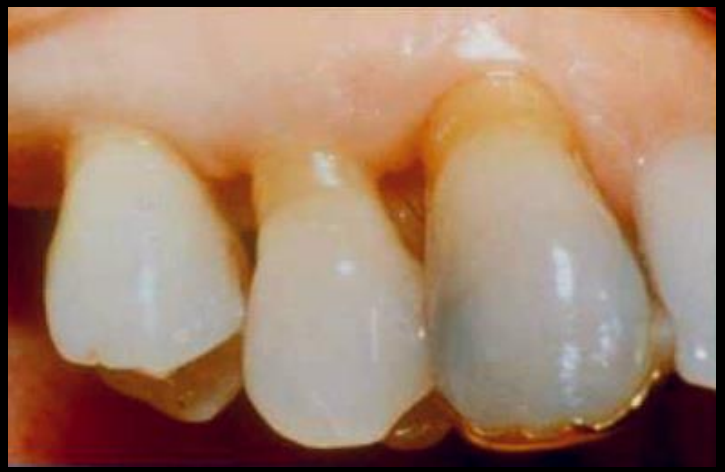
Local antibiotic therapy

- 1000 mg Tetracycline given per os can only produce 10ug/ml sulcular concentration while the minimal effective concentration should be 30ug/ml
- A microflora in deep pockets cannot be influenced with mouth rinses
- The supragingival plaque control has minimal effect on the composition of subgingival biofilm located deeper than 1-2 mm

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%.
- ***Periochips*** 2,5 mg chlorhexidin incorporated into hydrolyzed gelatin –pellets (chips)
- In deep pockets can sustain 100ug/ml concentration in crevicular fluid

Periochips