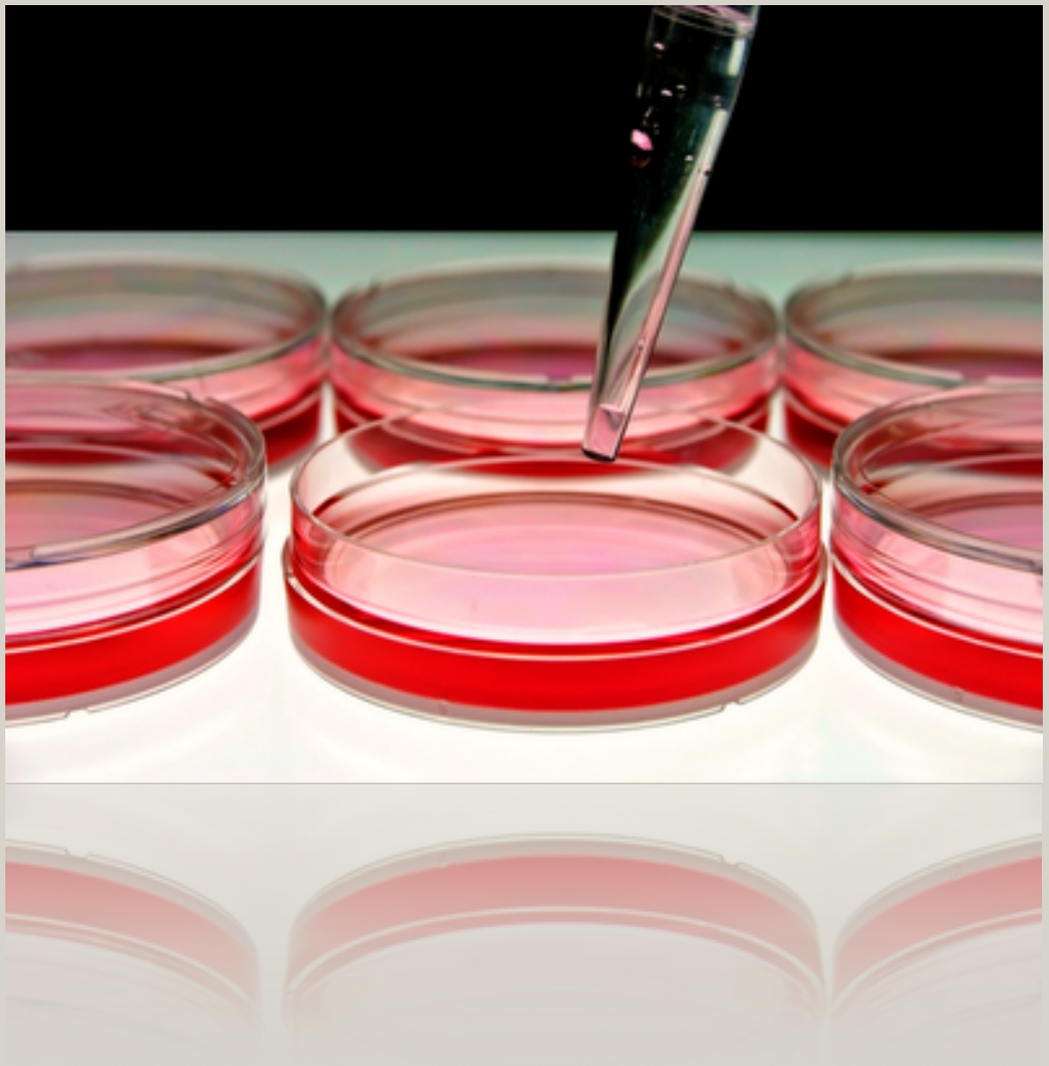

Periodontal Microbiology

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Topics

- introduction, historical perspective
- pathogens of destructive periodontal diseases
- microbial complexes
- mechanisms of pathogenicity
- therapy

Introduction

- periodontal diseases are infections that are caused by microorganisms that colonize the tooth surface at or below the gingival margin

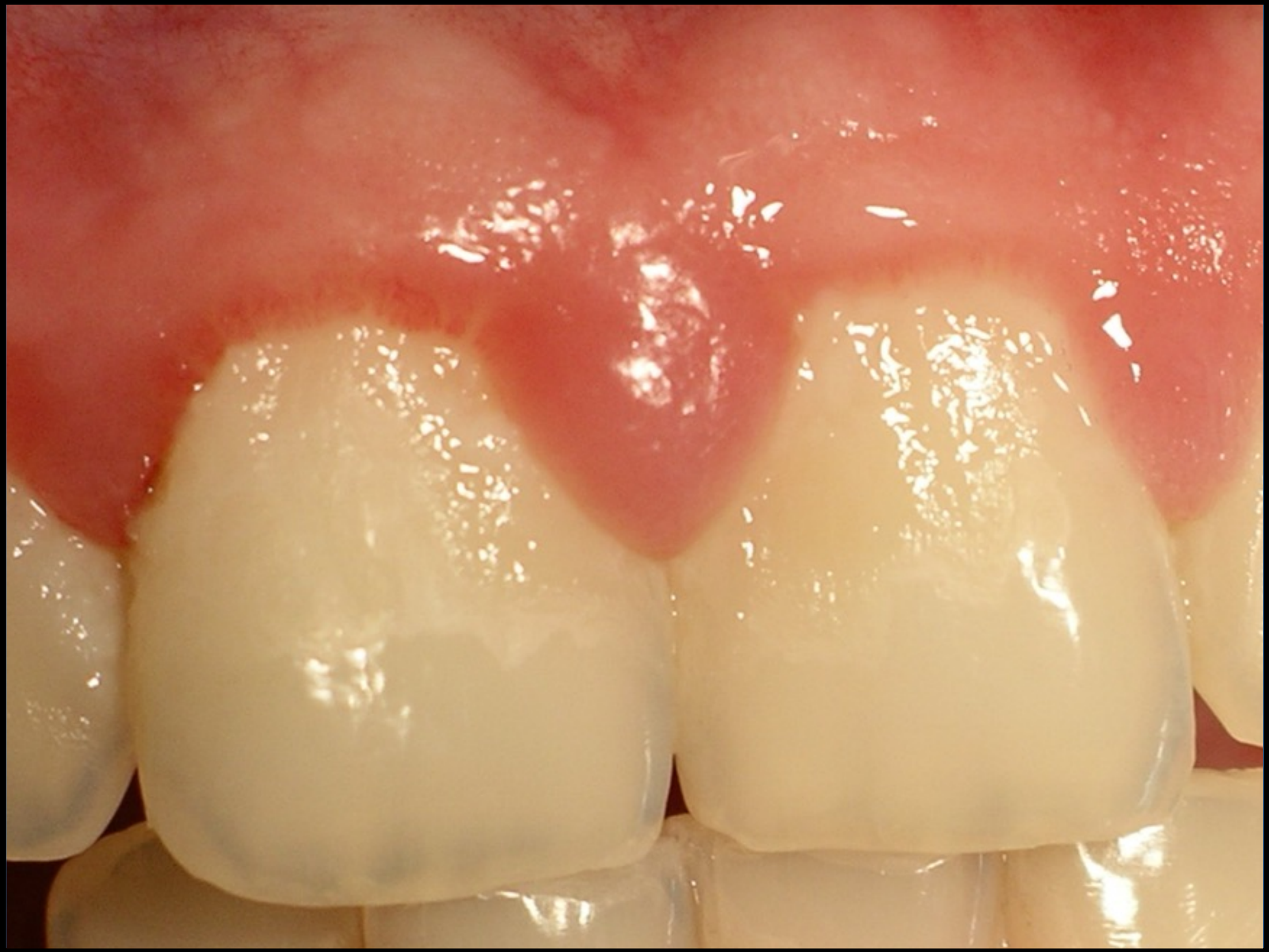
- about 700 species are able to colonize

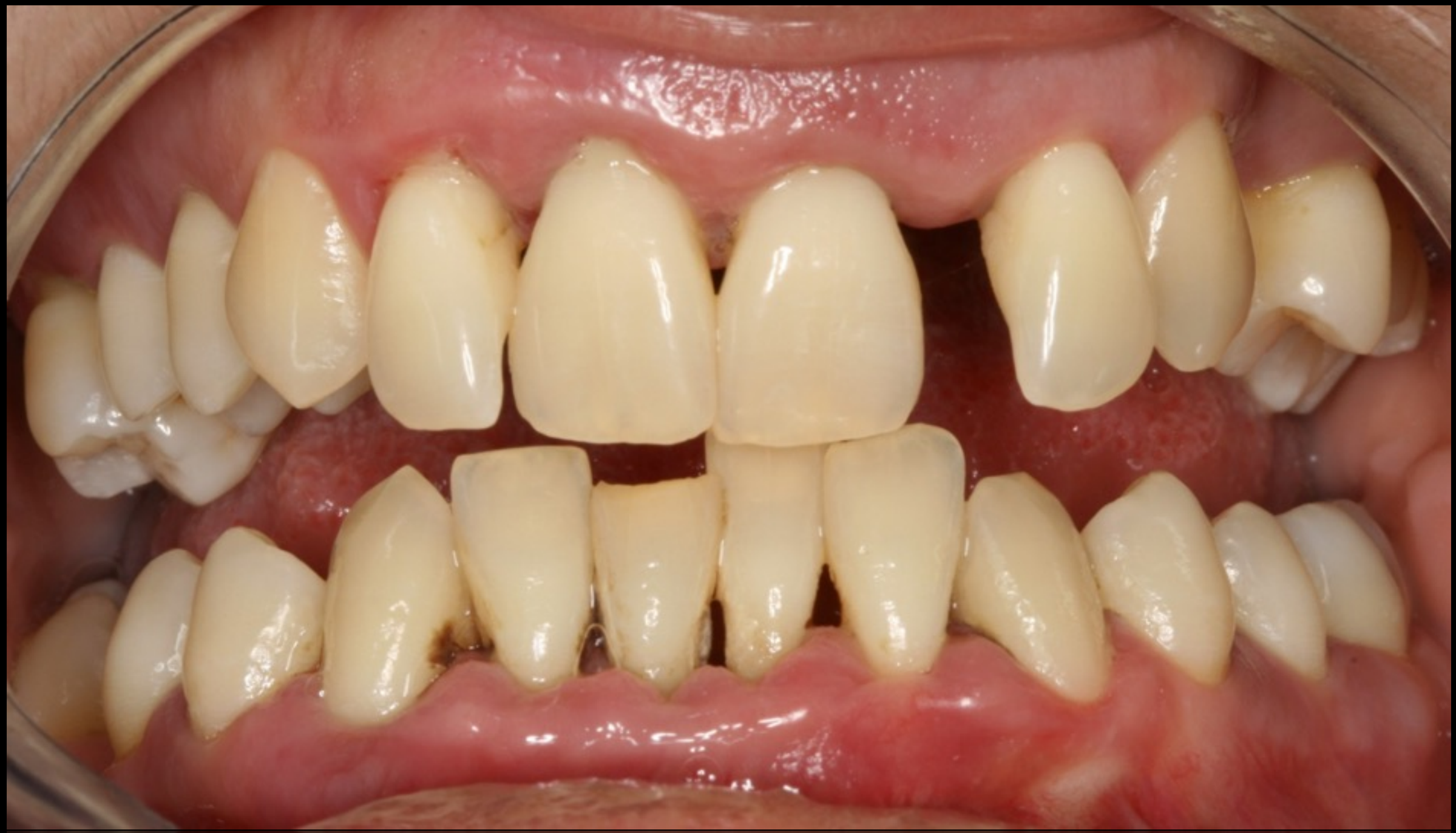
- the sulcus gingivae is never sterile

- healthy teeth and gums through a lifetime ?

- “peaceful” equilibrium - in general, the establishing microbiota live in harmony with the host

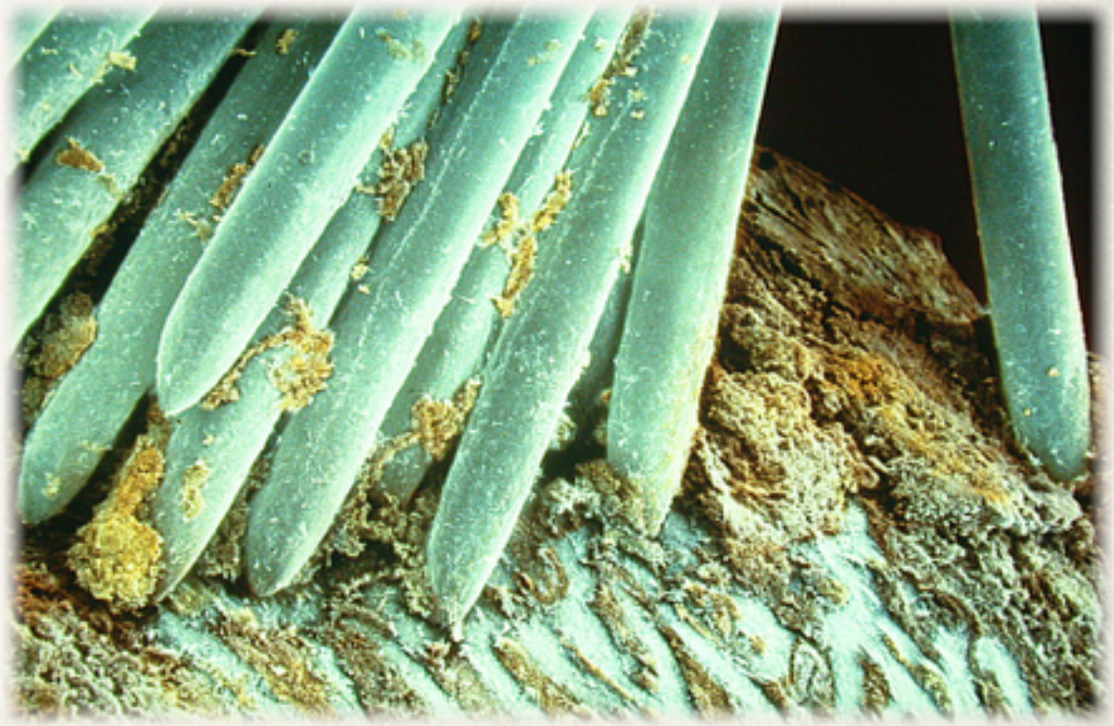
- inflammation leads to the destrucion of the periodontium





Periodontitis as an infection

- one of the most unusual infections of the human body
- the tooth is a special surface - one part of it is exposed to the environment, while the other part is within the connective tissue
- non-shedding outer layer - microbial colonization is facilitated
- the bacteria colonizing the tooth are outside the body, where they are less able to be controlled
- in the oral cavity, the bacterial deposits have been termed: **dental plaque** or **bacterial plaque**
- biofilm, dental plaque must be removed mechanically



Historical perspective

- A.van Leeuwenhoek (1683) - the dental plaque contains “small, moving” animals
- the search for the etiologic agents of periodontal diseases has been in progress for over a century
- Miller (1890)
- Löe (1965), Theilade (1966) - experimental gingivitis model - demonstrated that plaque accumulation directly preceded and initiated gingivitis
- periodontal disease are the result of an infection
- periodontal infections and dental caries, are arguably the most common infectious diseases affecting the human body

Historical perspectives

- classical "Koch's postulates" (1876) have been used to define a casual relationship between an infectious agent and disease

1. the agent must be isolated from every case of the disease

2. it must not be recovered from cases of other forms of disease

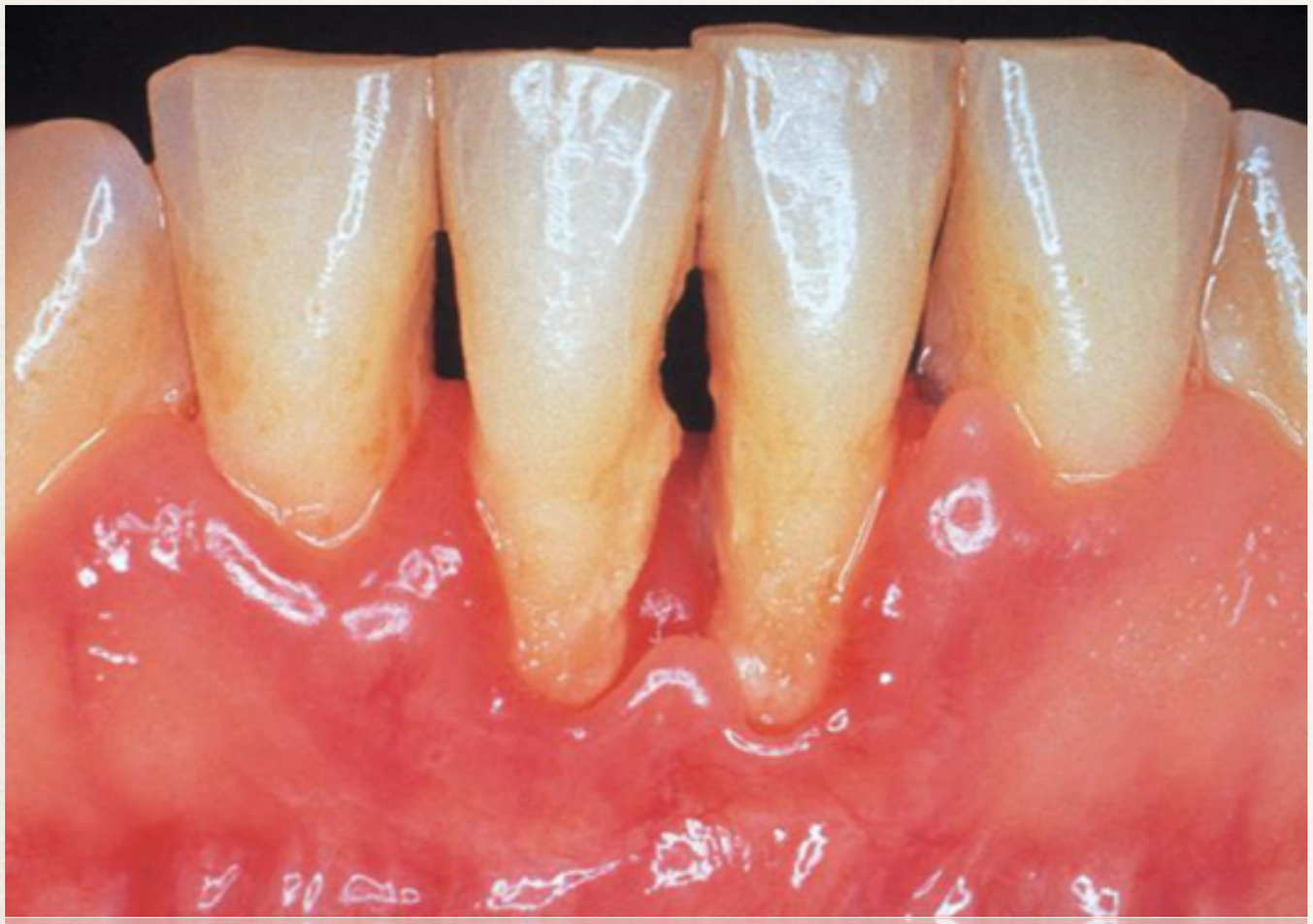
3. after isolation and growth, the pathogen must induce disease in experimental animals

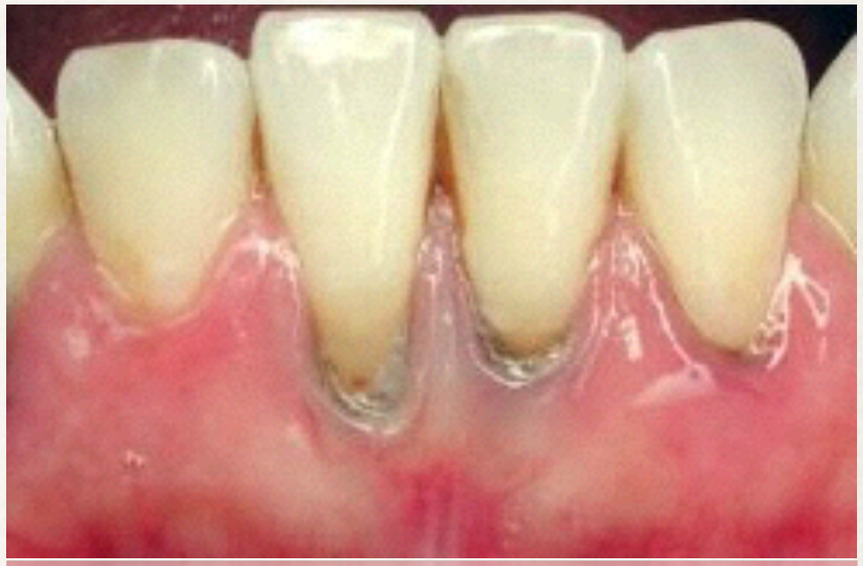
Historical perspectives

- the criteria for defining pathogens of destructive periodontal diseases are based on Koch's postulates, but have been amended and extended in the recent years (Socransky, 1979)
- associaton, elimination
- host response, virulence factors
- animal studies, risk assessments

Epidemilogical evidence

- positive correlation between plaque accumulation and gingivitis
- experimental gingivitis-model (Löe, 1965)
- acute periodontal infections and acute ulcerative gingivitis can be successfully treated by antibiotics
- mechanical plaque control is working
- topical and systemic antibiotic therapy has beneficial effect on chronic periodontitis





Prerequisites for periodontal disease initiation and progression

- plaque bacteria are necessary but not sufficient prerequisite for periodontal disease

- the pathogens should be present in a certain concentration

- the host should be locally and systematically susceptible for pathogenic microorganisms

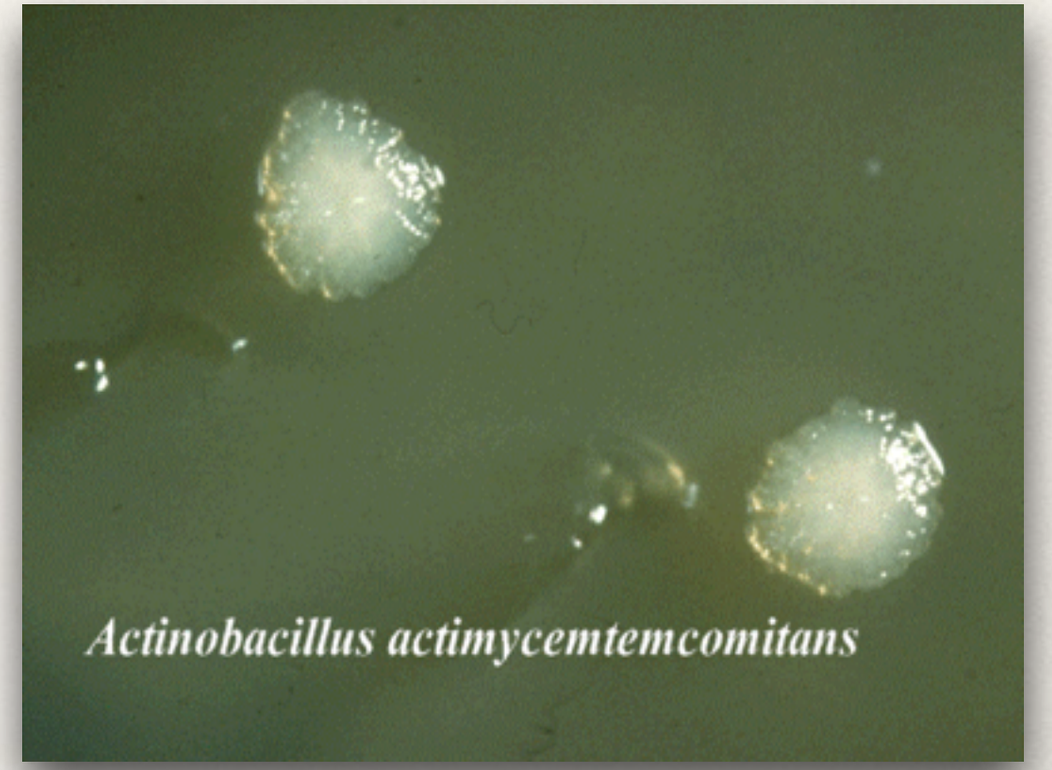
- the virulence factors should reach the target cells, and ignite reactions that finally leads to tissue destructions

Pathogenes of destructive periodontal diseases

- periodontitis is a mixed infection
- World Workshop in Periodontology (1996) designated A.actinomycetemcommitans, P.gingivalis, T.forsythia as periodontal pathogenes
- microbial complexes

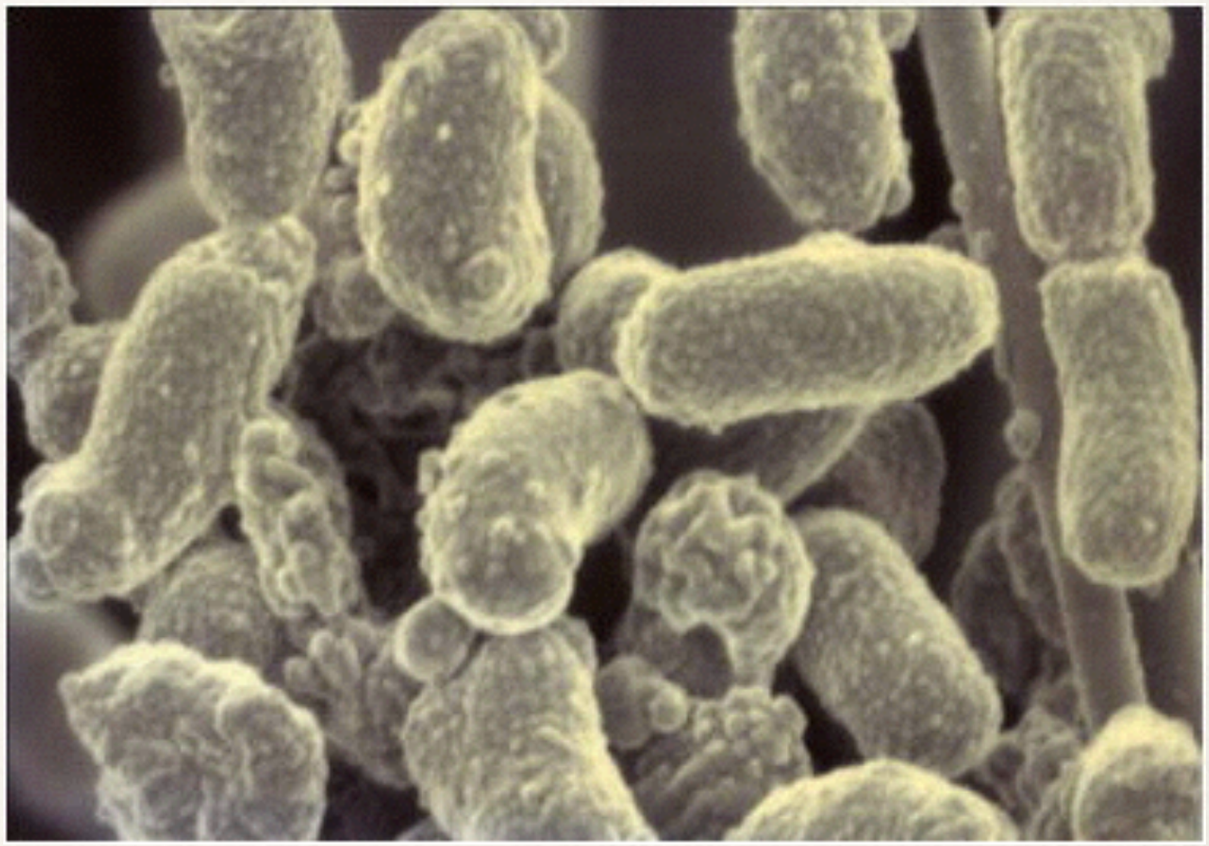
Actinobacillus actinomycetemcomitans

- has recently been renamed - Aggregatibacter actinomycetemcomitans
- first isolated from actinomycosis
- small, non-motile Gram-negative, saccharolitic, capnophilic, round-ended rod
- forms small “star-shaped” center colonies on blood agar plates



Actinobacillus actinomycetemcomitans

- subjects with LAP had an enormously elevated serum antibody response
- six serotypes (a,b,c,d,e,f)
- serotype-b for LAP
- serotype-a for chronic periodontitis



Actinobacillus actinomycetemcomitans

- virulence factors

- leukotoxin - can destroy PMN leukocytes and monocytes

- endotoxin - direct effect on endothelial cells, adverse effects on pocket epithelia, liberates cytokines, it is a strong antigen to provoke immune reactions

- bacteriocin - antibacterial substance can depress the multiplication of streptococci

Actinobacillus actinomycetemcomitans

- collagenase
- fibroblast inhibitory factor
- bone resorption inducing factor
- degradation of immunoglobulins
- cytolethal distending toxin - immunsuppresive effect
- exotoxin - can destroy lymphocytes

Actinobacillus actinomycetemcomitans

- it is suspected that AA. initially colonizes the oral cavity by attachment to the surfaces of the oral epithelium

- is able to invade epithelial cells, vascular endothelial cells - it has been cultured from atheromatous plaques, cause or contribute to endocarditis

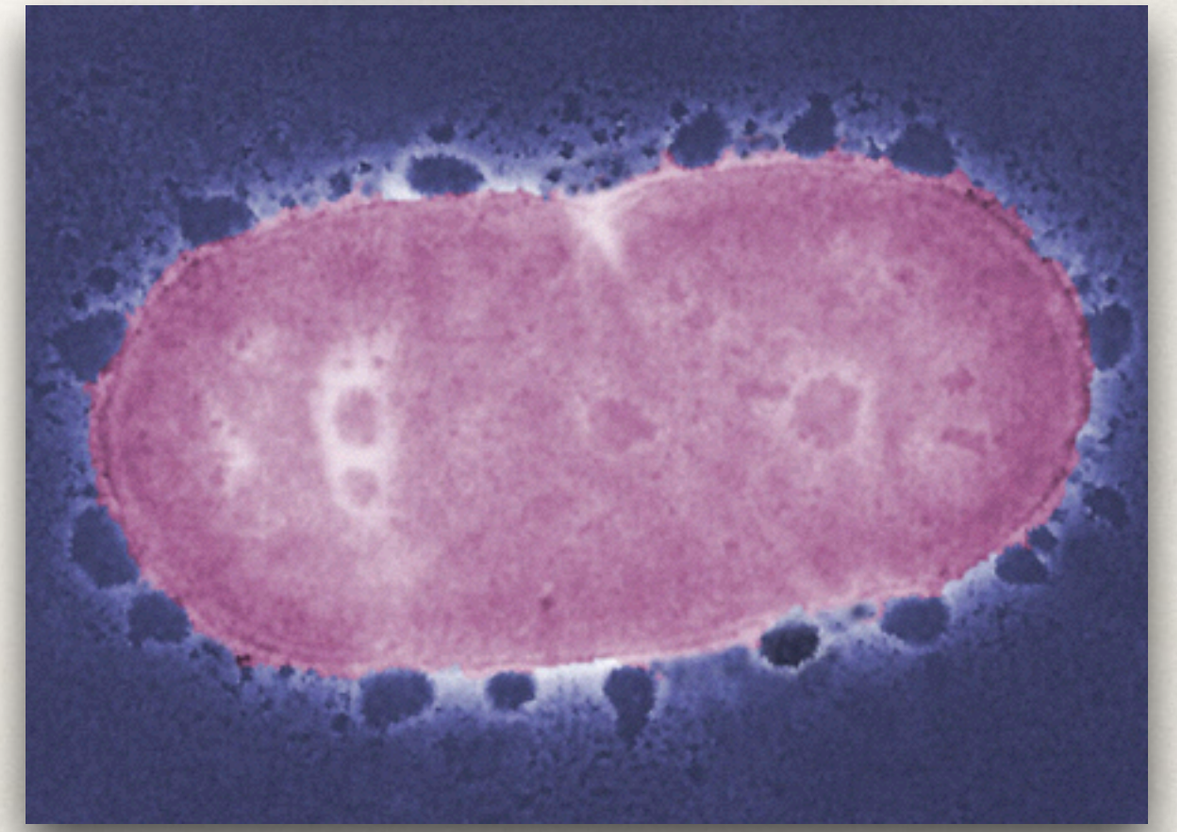
- penetrate the underlying connective tissues (periodontal pockets)

Porphyromonas gingivalis

- Gram-negative, obligatory anaerobic, non-motile, asaccharolitic, short rod

- originally all black pigmented bacteria were named: Bacterioides melaninogenicus

- today: asaccharolytic species - P.gingivalis, mild saccharolytic activity - Prevotella intermedia, strong sacch.activity - Prevotella melaninogenica



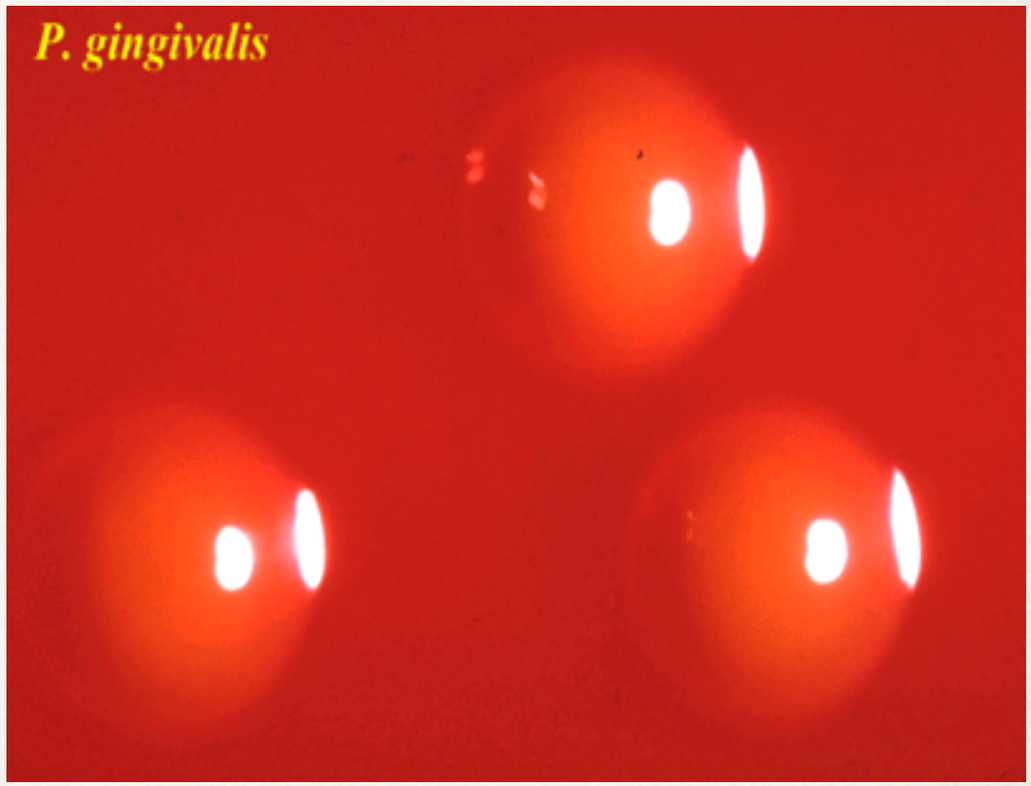
Porphyromonas gingivalis

- P.gingivalis fimbriae mediate the binding of the bacteria to epithelial cells

- by binding to integrines could damage the normal turnover of the connective tissue

- can bind to different bacterial surface proteins

- can occur in very limited number in healthy sulcus and gingivitis, significantly increased in periodontitis

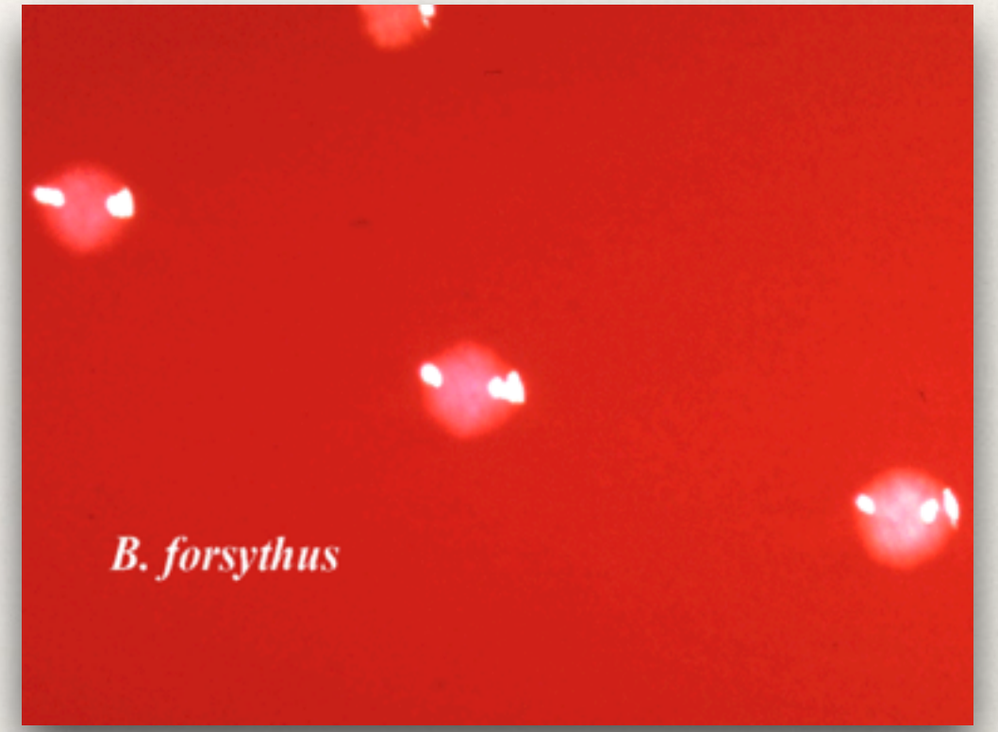


Porphyromonas gingivalis

- invasion is important component of virulence
- P.gingivalis can be detected within mucosal epithelial cells, and can rapidly invade epithelial cells, causing local bacterial invasion
- patients with periodontitis in the past history, always have elevated serum level of anti P.gingivalis antibody
- produce abundant quantity of collagenase and proteinase, and different factors that adversly affect PMNs

Tannerella forsythia

- earlier - Bacterioides forsythus
- Gram-negative, anaerobic, non-motile rod
- very difficult to culture and to grow on plates
- significantly higher numbers in deep pockets than in gingivitis
- patients with periodontitis in the past history, always have elevated serum level of anti T.forsythia antibody, especially in the refractory cases

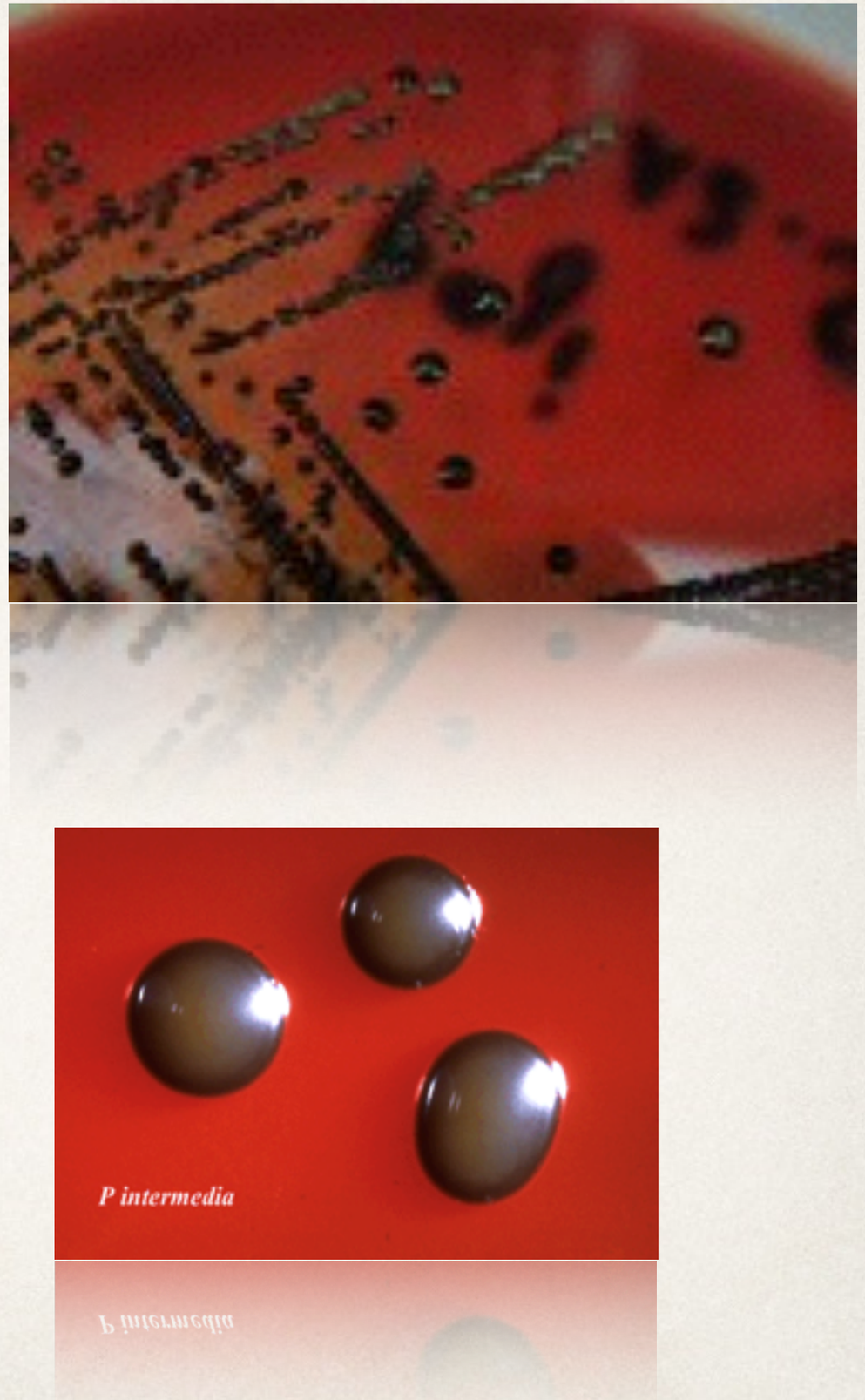


Prevotella intermedia/ nigrescens

- Gram-negative, anaerobic short rod

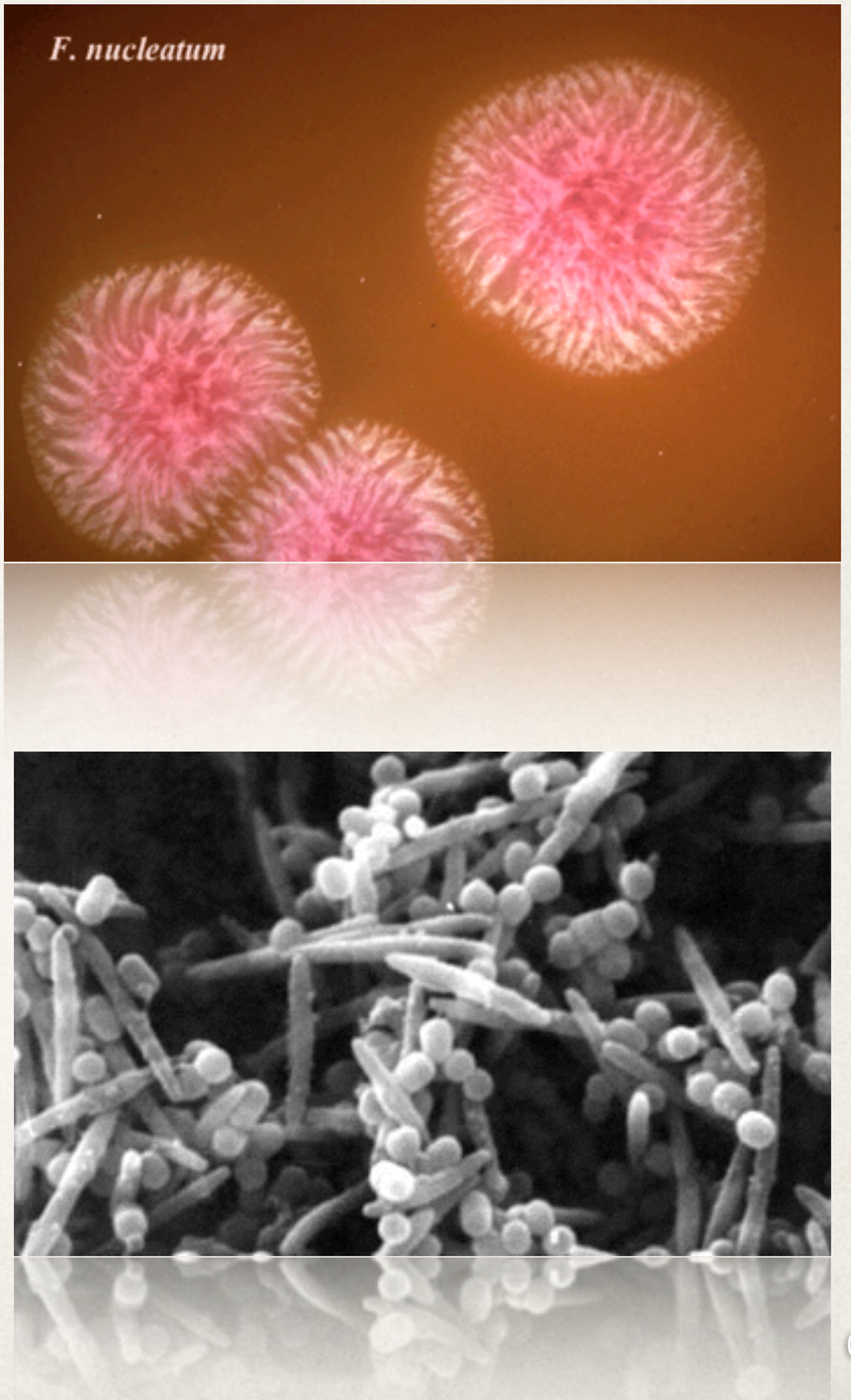
- very high number in acute ulcerative gingivitis, pregnancy gingivitis and chronic periodontitis

- for elimination mechanical therapy and antibiotics are needed



Fusobacterium nucleatum

- Gram-negative, anaerobic spindle shape rod
- the most common isolate found in deep pockets
- the most important role in the subgingival ecosystem is its function as “bridging” species, facilitating coaggregation



Campylobacter rectus

- Gram-negative, anaerobic
- motile vibrio
- it utilizes hydrogen for its energy sources
- it produces leukotoxin similar to AA

Eikenella corrodens

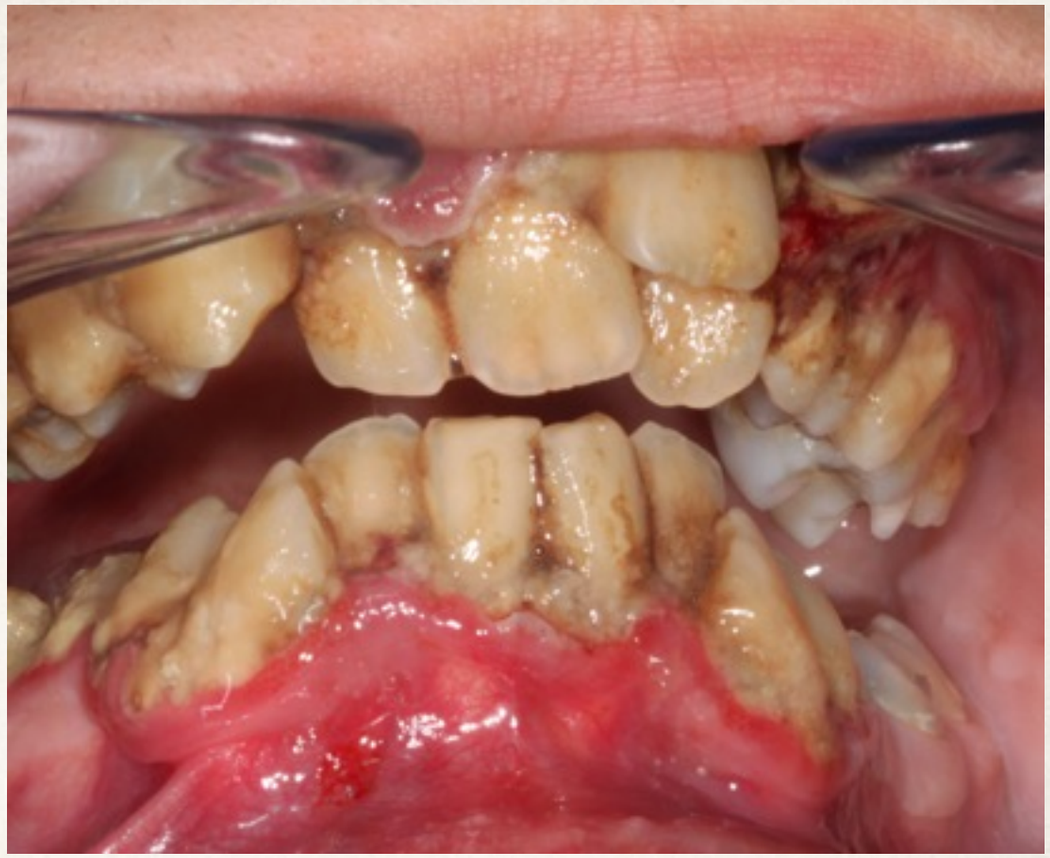
- Gram-negative, capnophylic, asaccharolytic
- short rod with blunt ends
- common in osteomyelitis and necrotic pulp
- commonly occurs in association with AA in LAP

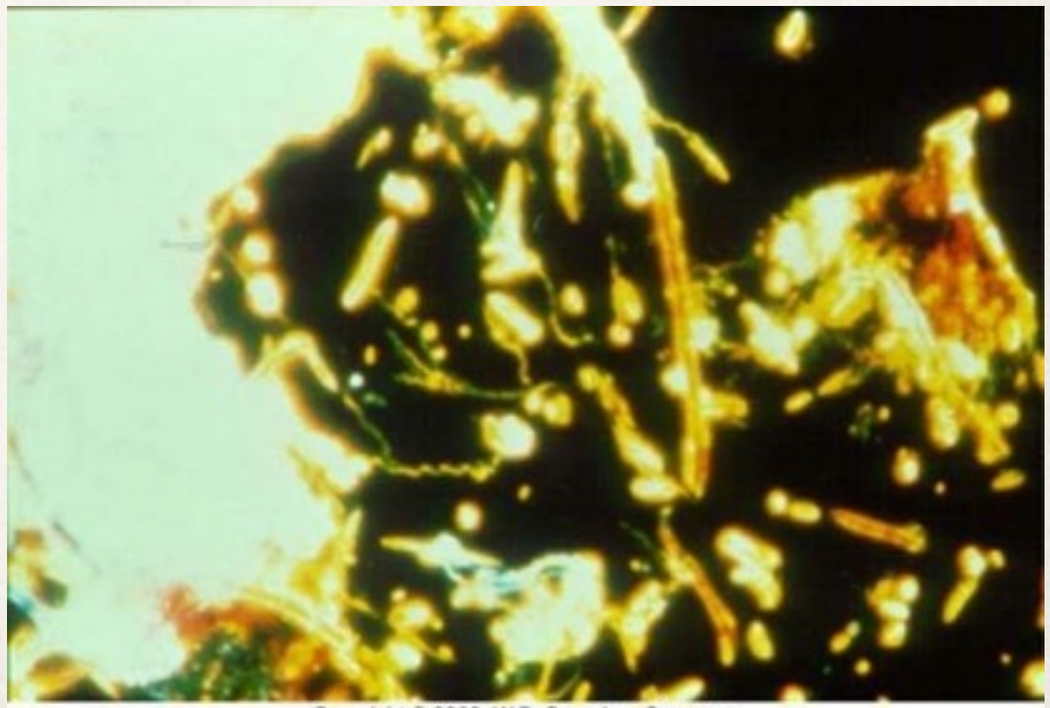
Other species

- Peptostreptococcus micros
- Selenomonas species
- Eubacterium species
- Streptococcus intermedius

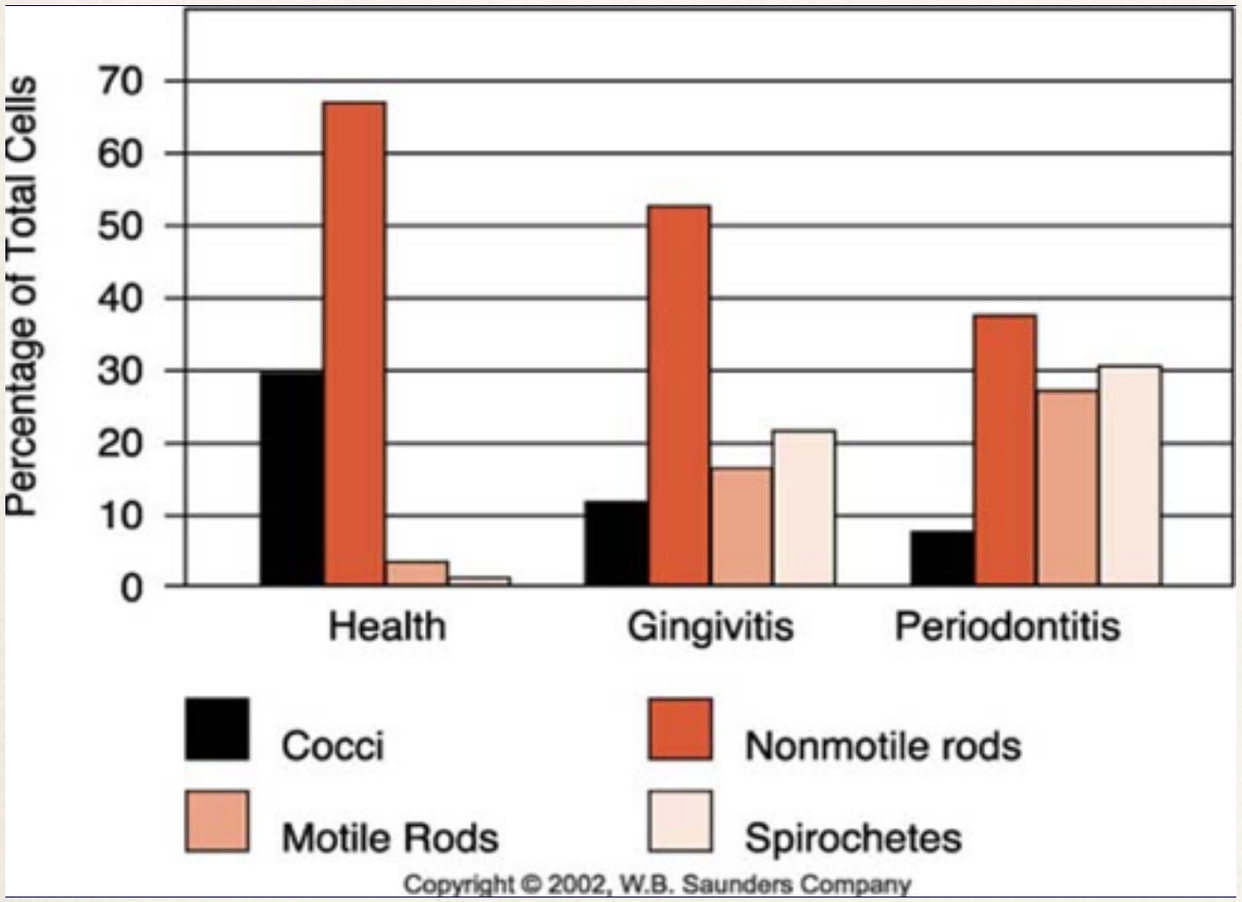
Spirochetes

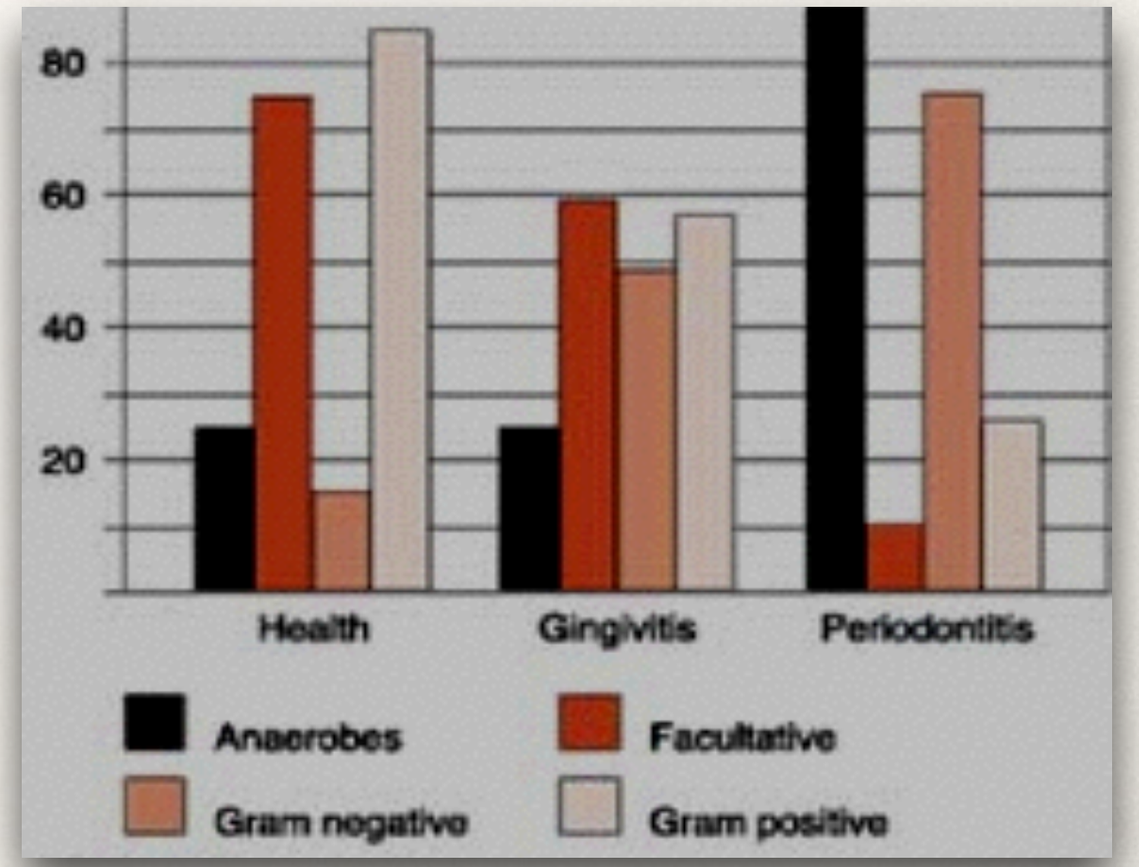
- Gram-negative, anaerobic, very motile
- direct etiologic factor in ANUG
- difficult or impossible to cultivate
- Treponema denticola
- it can penetrate sulcus epithelia and invade connective tissue





Mixed infections





Mixed periodontal infection

- periodontal infection is always a mixed infection caused by a complex bacterial flora

- the inflammation is the consequence of special bacterial interactions

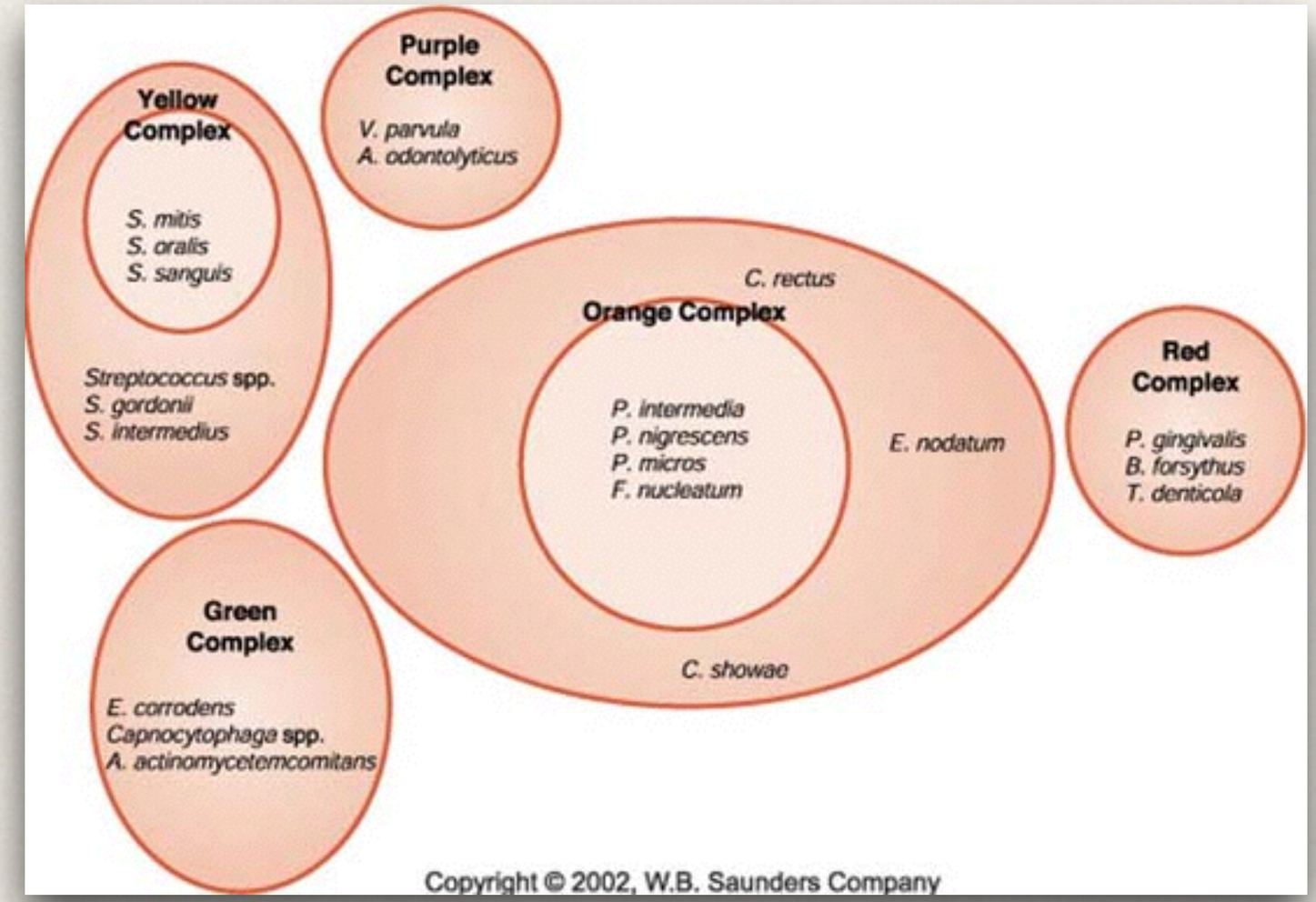
- the most common combinations:

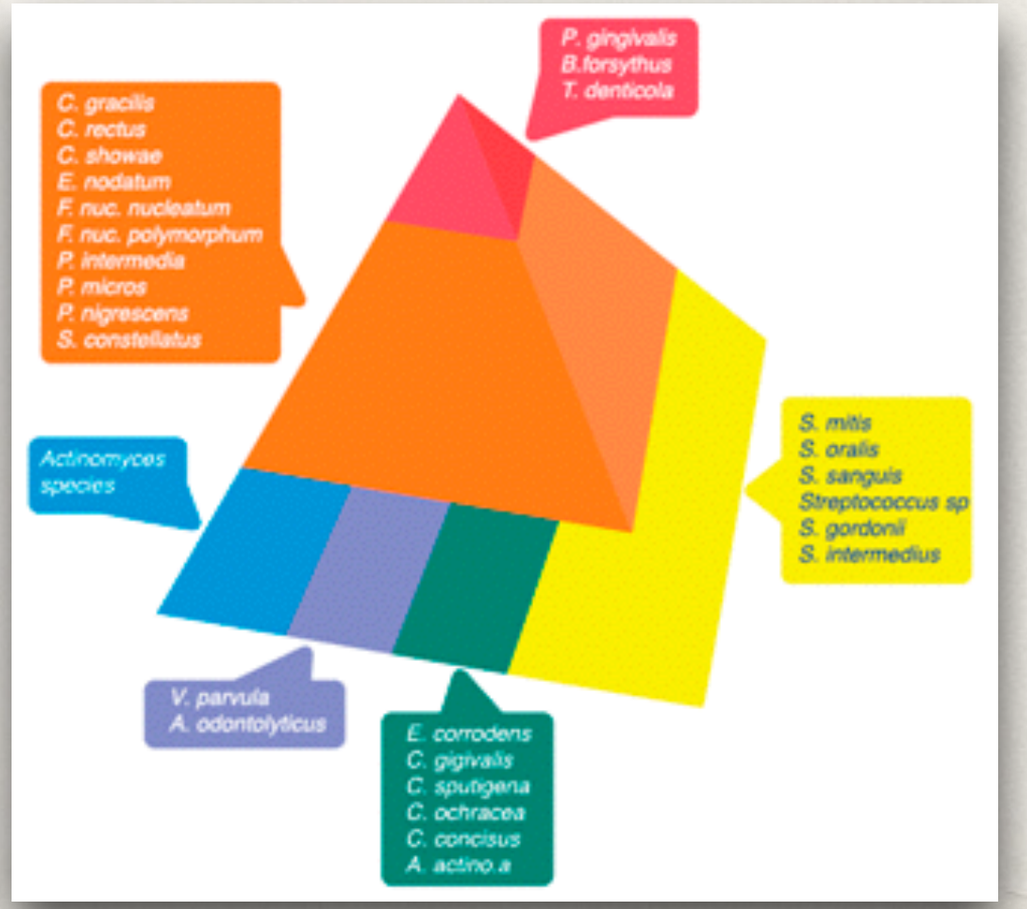
  - F.nucleatum, T.forsythia,C.rectus
  - S.intermedius,P.gingivalis, P.micros
  - F.nucleatum, P.gingivalis
  - AA, P.gingivalis

Microbial complexes

- Socransky et al. (1998) - 6 microbial complexes were recognized
- 1. Actinomyces
- 2. yellow complex: Streptococcus
- 3. green complex: A.actinomycetemcomitans, Eikenella corrodens, Campylobacter
- 4. purple complex: Veillonella pervula, Actinomyces odontolyticus - early plaque-forming bacteria
- 5. orange complex: Campylobacter rectus, Fusobacterium nucleatum, Prevotella intermedia, Prevotella nigrescens
- 6. red complex: Porphyromonas gingivalis, Tannerella forsythia, Treponema denticola

Microbial complexes





Mechanisms of pathogenicity

- the pathogenic bacteria causes disease if they can:
  - attach to available surfaces
  - multiply
  - compete succesfully for nutrients
  - can evade host defense mechanisms

Mechanisms of pathogenicity

- adhesion - with adhesion molecules -adhesins, most bacteria can find certain specific surface receptors on host cells/surfaces to which to adhere

- coaggregation - most bacteria do not directly attach to host cells, but rather attach to other bacteria which had already attached - AA early colonizer!!

Mechanisms of pathogenicity

- multiplication - determined by:

- microenviroment temperature (pocket depth)
- ph, oxidation-reduction potencial
- nutrient availability
- growth factors
- interbacterial relationships - A.viscosus and S.sanguis can inhibit recultivation of AA in pockets of LAP patients

Mechanisms of pathogenicity

- overcoming host defensive mechanisms:

- the mechanical flushing effect of the saliva and crevicular fluid
- salivary bactericide factors (S-IgA)
- crevicular fluid antibodies (IgG,IgM,IgA)
- PMN leukocytes and monocytes
- epithelial desquamation

Overcoming host defensive mechanisms

- AA produces leukotoxin to kill PMN cells
- P.gingivalis, P.intermedia can escape antibody reactions by changing their surface antigens
- P.gingivalis, P.intermedia, Capnocytophaga produses proteinases to destroy antibodies and complements
- susceptible host - immune deficiencies, PMN leukocyte disorders, metabolic diseases, smoking, diabetes, genetics

Bacterial transmission

- the most periopathogenic microorganisms do not occur in the environment, soils, water or in the oral flora of animals

- those are acquired during our life from other human beings by direct infections

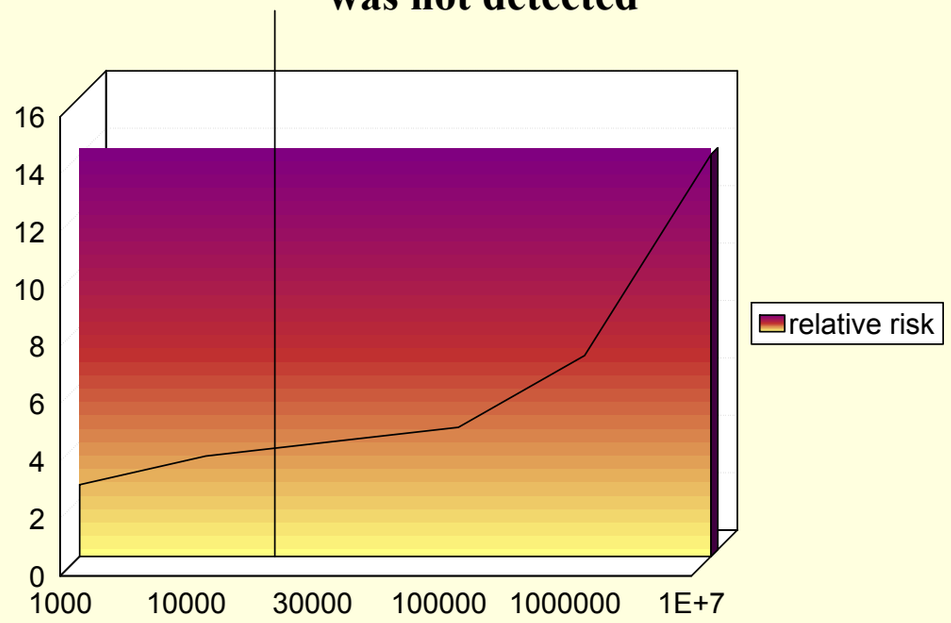
- vertical transmission

- horizontal transmisson

Bacterial risk analysis

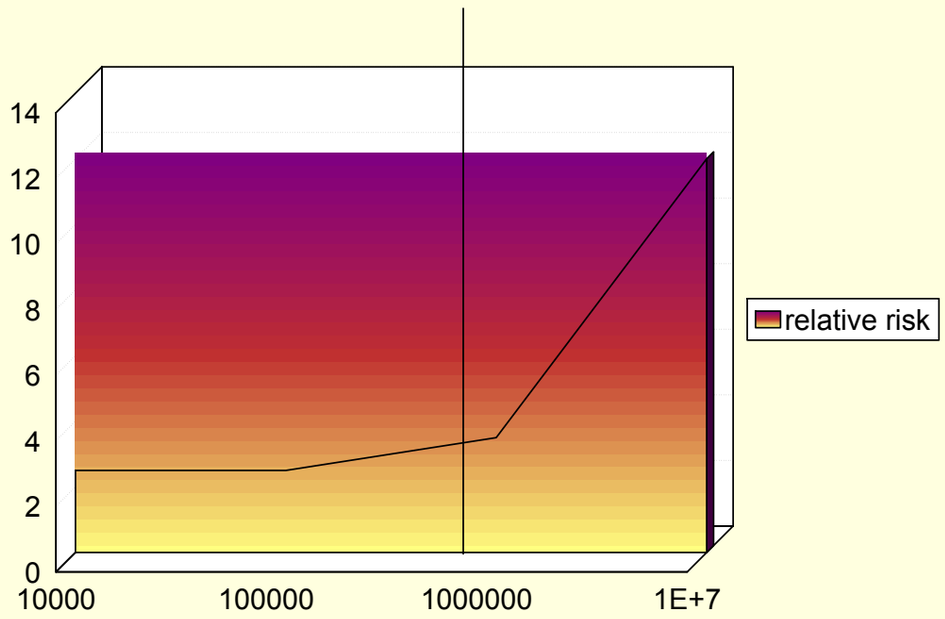
RELATIVE RISK FOR NEW ATTACHMENT LOSS WITH DIFFERENT THRESHOLD LEVELS OF A. actinomycetemcomitans

computed against the risk at sites at which the species was not detected



RELATIVE RISK FOR NEW ATTACHMENT LOSS WITH DIFFERENT THRESHOLD LEVELS OF P. gingivalis

computed against the risk at sites at which the species was not detected



Therapy

- mechanical plaque control - non surgical/surgical therapy

- chemical plaque control - chemoprofilaxis, chemotherapy

Chemical supragingival plaque control

- does not replace mechanical toothbrushing
- main target: to maintain a stable “peaceful” equilibrium
- there is no agent which would be appropiate for a long-term everyday use

Chemical supragingival plaque control

- first generation agents: phenols, essential oils - Listerine, triclosan (no effect on subgingival microflora)

- second generation agents: bisbiguanide antiseptics - chlorhexidine

- third generation agents - inhibits the adherence of the biofilm (antiplaque agents)

Chlorhexidine

- the most effective antiseptic agent to date, “gold standard”
- optimal concentration: 0,2%, twice per day
- not effective against mature plaque bacteria
- local side effects: brown discoloration, tasting problems, loss of appetite, glossitis, parotid swelling
- indication: preop., postop. for 2 weeks, pregnancy (2.-3.trimester), systemic disease (AIDS, leukaemia, diabetes), mentally and physically handicapped persons, root canal treatment, cavity, periodontal pocket irrigation

Periodontal chemotherapy

- it can be used topical and systemic (per os, parenteral)
- the diagnose indicates the therapy
- active process
- if possible after antibiotics-sensitivity test
- only additional therapy
- 1-2 days before periodontal surgery, postop. 1-2 weeks

Systemic antibacterial therapy

- Metronidazol (Klion) - effective against the most anaerobes

- 2-3 x 250 mg

- refractory periodontitis/aggressive periodontitis: metronidazol +amoxicillin

- Penicilline - amoxicillin - broad-spectrum

- profilaxis: 2g one hour before the treatment

- therapy: 3x375 mg or 3x625 mg per day for one week

Systemic antibacterial therapy

- Clindamycin (Dalacin C) - is able to concentrate in bone

- in case of penicilline allergy the first choice

- 3x300 mg

- Tetracyclin - bacteriostatic

- Ciprofloxamin (Cibrobay) - nowadays all AA species are still sensitive, dose: 2x250-500 mg

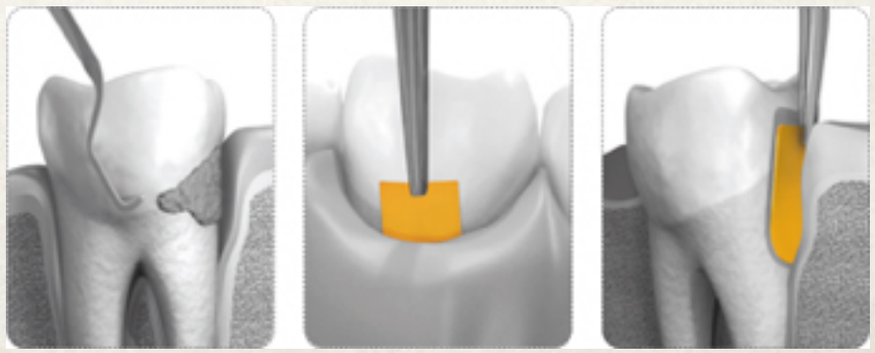
Local antibacterial therapy

- main target: to eliminate local side effects, to keep permanent therapeutic concentration in the sulcus gingivae

1. Actisite - tetracyclin containing fibers

2. Antibacterial gels - Elyzol (metronidazol), Minocyclin, Ebrimycin

3. Antiseptic gels - 1 % chlorhexidine gel, Periochips (2,5 mg chlorhexidine)



Full mouth disinfection

- "full mouth disinfection" - Quirynen (1995)

1. full mouth scaling and root debridement within 24-hours
2. tongue brushing
3. to rinse with 0,2 % CHX more times per day
4. subgingival irrigation with 1% CHX, repeated three times within 10 minutes
5. 0,2% CHX for two weeks
6. very good oral hygiene (tongue!)

- "full mouth debridement"

Full mouth disinfection

- significant clinical and microbiologic improvements
- chlorhexidine does not have further potentiating effects
- longer recall period
- in serious aggressive periodontitis the treatment of the close environment (bacterial transmission)