

# Pathogenesis of Periodontal Disease

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# Objectives

1. To understand the histological changes that occur during the development of gingivitis and periodontitis, and how these changes relate to the clinical signs of disease
2. To understand the principles in pathogenesis of periodontitis
3. To understand the importance of the interactions between plaque bacteria and host defence mechanisms in the pathogenesis of periodontitis

# Pathogenesis of periodontal diseases

- Def: Pathogenesis is the sequence of events leading to the occurrence of a disease.
- In periodontology, the pathogenesis of gingivitis and periodontitis are related but tend to be described separately, and
- Although the clinical and histological changes that occur are well known, the details of specific pathogenic mechanisms are less clearly defined.

(Page and Schroeder, 1990)

# Pathogenesis of chronic diseases

- Is complex, cause long time frame allows for many varied individual pt response
- In clinical level, it is possible to describe pathogenic events of most chronic diseases
- Also histologic analyses provided a description of cellular and tissue differences clinical stages
- Then, investigators use this to speculate on the biochemical and cellular mechanism involved in the development and progression of disease

(Page and Schroeder, 1990)

# Gingivitis

# Pathogenesis of plaque associated gingivitis: initial lesion (subclinical gingivitis)

- Bacterial accumulation initiate vascular changes: vascular dilatation and increased vascular permeability
- Vascular leakage of fluid and PMNs or neutrophils into the tissue and gingival sulcus leading to increased GCF flow
- Breakdown of collagen fibers just apical to JE
- This changes within hours (Carranza: 2-4 days)
- Clinically this lesion can't detect yet (subclinical)

(Page and Schroeder, 1990)

# Pathogenesis of plaque associated gingivitis: early lesion (4-7days)

- continued vascular dilatation and increased permeability, with increased fluid exudation, and migration of neutrophils into the tissues
- increased breakdown of collagen subjacent to the junctional epithelium
- accumulation of lymphocytes (particularly T lymphocytes) and macrophages
- cytotoxic changes in fibroblasts, resulting in a reduced capacity for collagen formation
- proliferation of the cells of the junctional epithelium

(Page and Schroeder, 1990 and Heasman, 2003)

## Pathogenesis of plaque associated gingivitis: established lesion (14-21days)

- further engorgement of blood vessels, leading to venous stasis and the superimposition of a dark blue tinge over the erythematous gingiva
- migration of plasma cells into the gingival connective tissues to become the predominant inflammatory cell type
- continued collagen depletion
- continued proliferation of the JE, forming epithelial ridges with widened intercellular spaces.



**TABLE 16-1**

**Stages of Gingivitis**

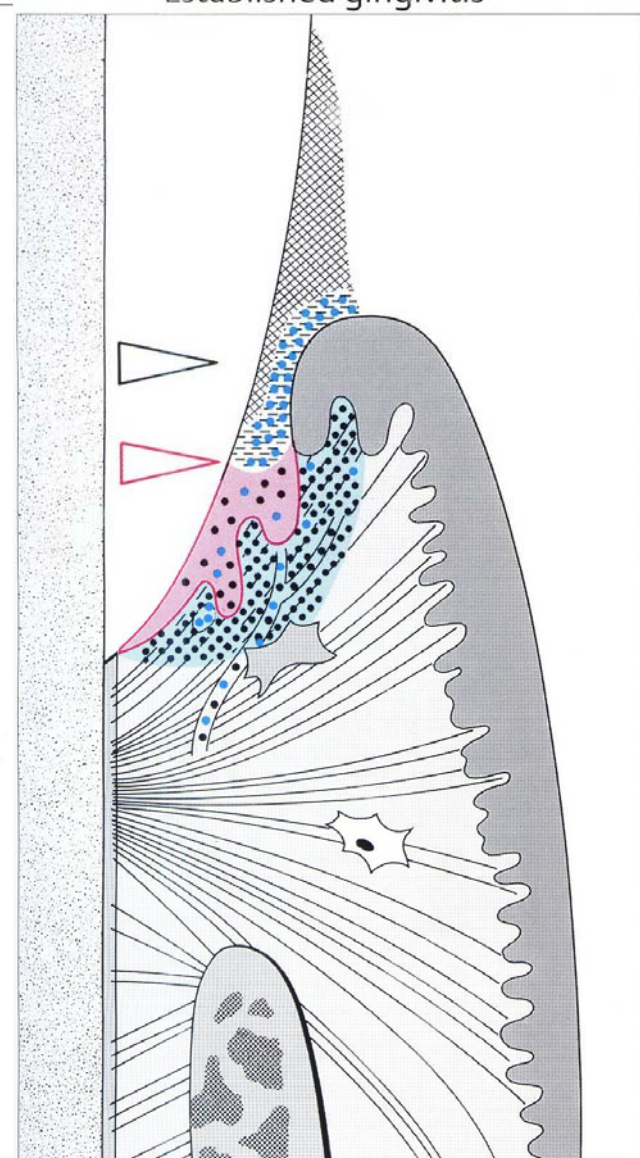
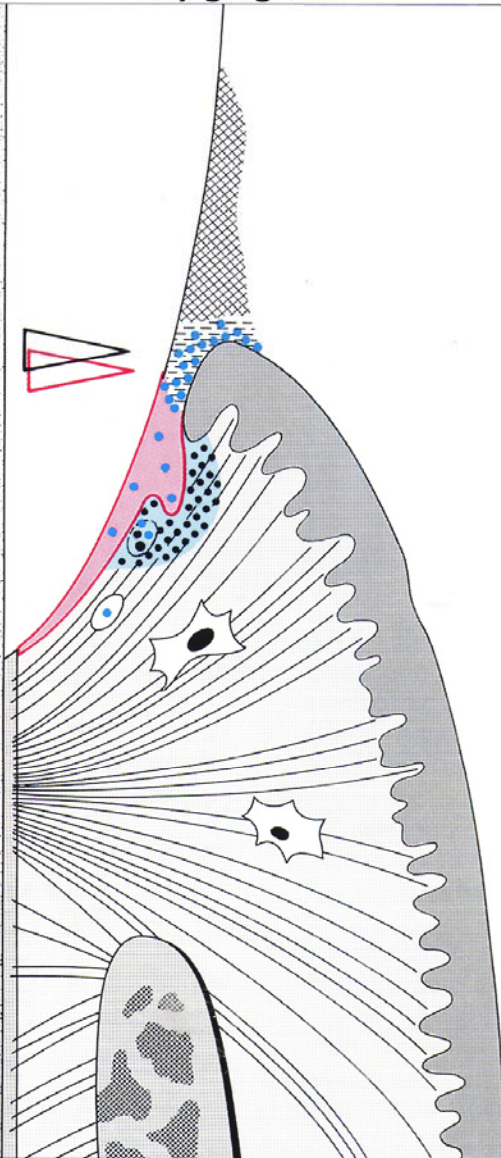
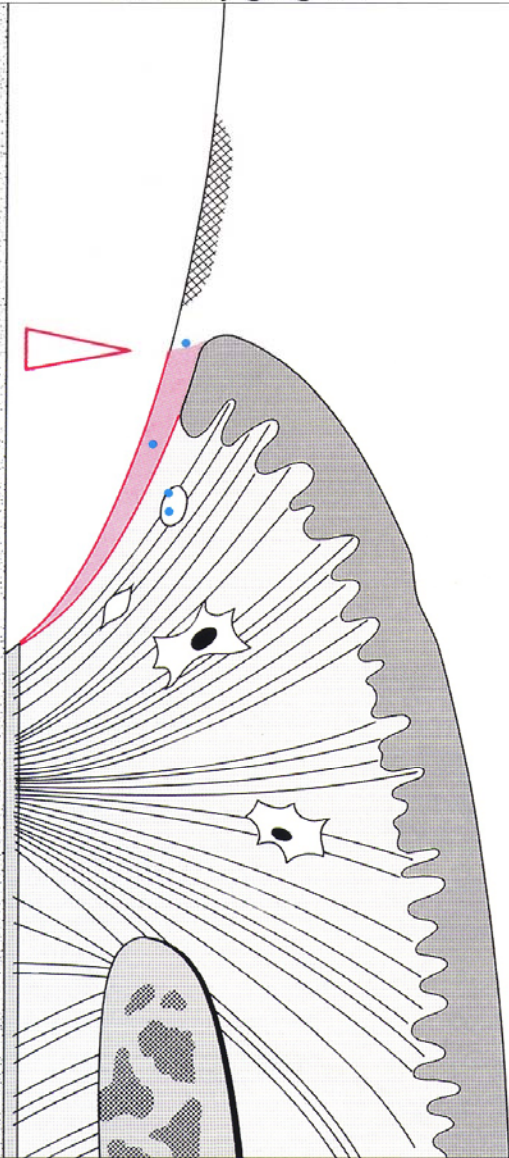
<b>Stage</b>	<b>Time (Days)</b>	<b>Blood Vessels</b>	<b>Junctional and Sulcular Epithelium</b>	<b>Predominant Immune Cells</b>	<b>Collagen</b>	<b>Clinical Findings</b>
I. Initial Lesion	2–4	Vascular dilation Vasculitis	Infiltrated by PMNs	PMNs	Perivascular loss	Gingival fluid flow
II. Early Lesion	4–7	Vascular proliferation	Same as Stage I Rete peg formation Atrophic areas	Lymphocytes	Increased loss around infiltrate	Erythema Bleeding on probing
III. Established Lesion	14–21	Same as Stage II, plus blood stasis	Same as Stage II but more advanced	Plasma cells	Continued loss	Changes in color, size, texture, etc.

PMNs, Polymorphonuclear neutrophils.

Healthy gingiva

Early gingivitis

Established gingivitis





**Healthy Gingiva. Pale pink color, no redness, no swelling, no bleeding on probing of gingival sulcus.**



Score	Criteria
0	<i>Normal gingiva</i>
1	<i>Mild inflammation:</i> slight change in color, slight edema, no bleeding on probing
2	<i>Moderate inflammation:</i> redness, edema and glazing, bleeding on probing
3	<i>Severe inflammation:</i> marked redness and edema, ulcerations; tendency toward spontaneous bleeding

From Löe H, Silness J: Periodontal disease in pregnancy. 1. Prevalance and severity, Acta Odontol Scand 21:533, 1963.



**149 Healthy Gingiva (left)**

The gingiva is pale salmon-pink in color, and stippled. The narrow free gingival margin is distinguishable from the attached gingiva. After gentle probing with a blunt periodontal probe, no bleeding occurs.



**150 Mild Gingivitis (right)**

The localized erythema is scarcely visible, and one observes slight edematous swelling. Some of the former stippling is lost, and there is minimal bleeding upon probing.



**151 Moderate Gingivitis (left)**

Obvious erythema and edematous swelling. No stippling is apparent, and there is hemorrhage following probing of the sulcus.



**152 Severe Gingivitis (right)**

Fiery redness, edematous and hyperplastic swelling; complete absence of any stippling; interdental ulceration, copious bleeding on probing, and spontaneous hemorrhage.



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**TABLE 16-1**

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PMNs, Polymorphonuclear neutrophils.

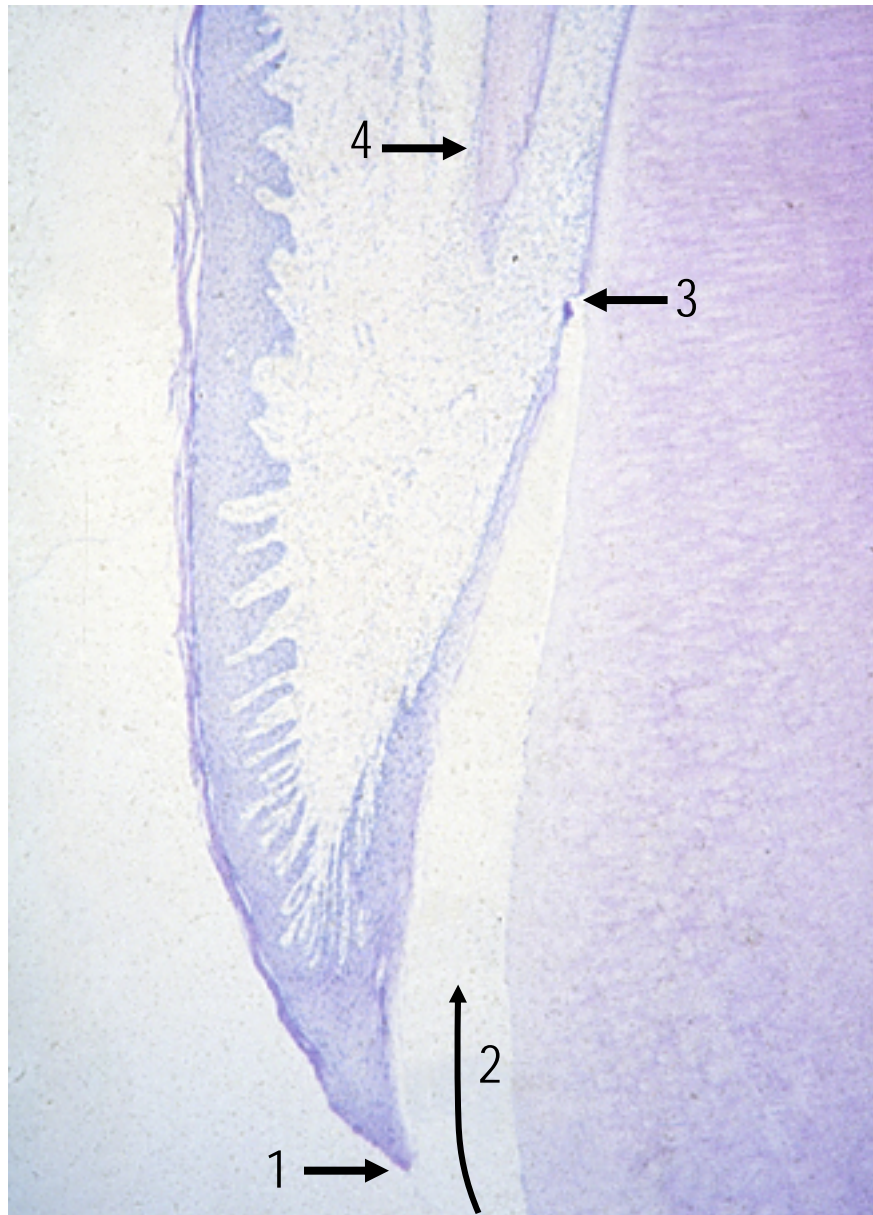
# Histology of normal gingiva



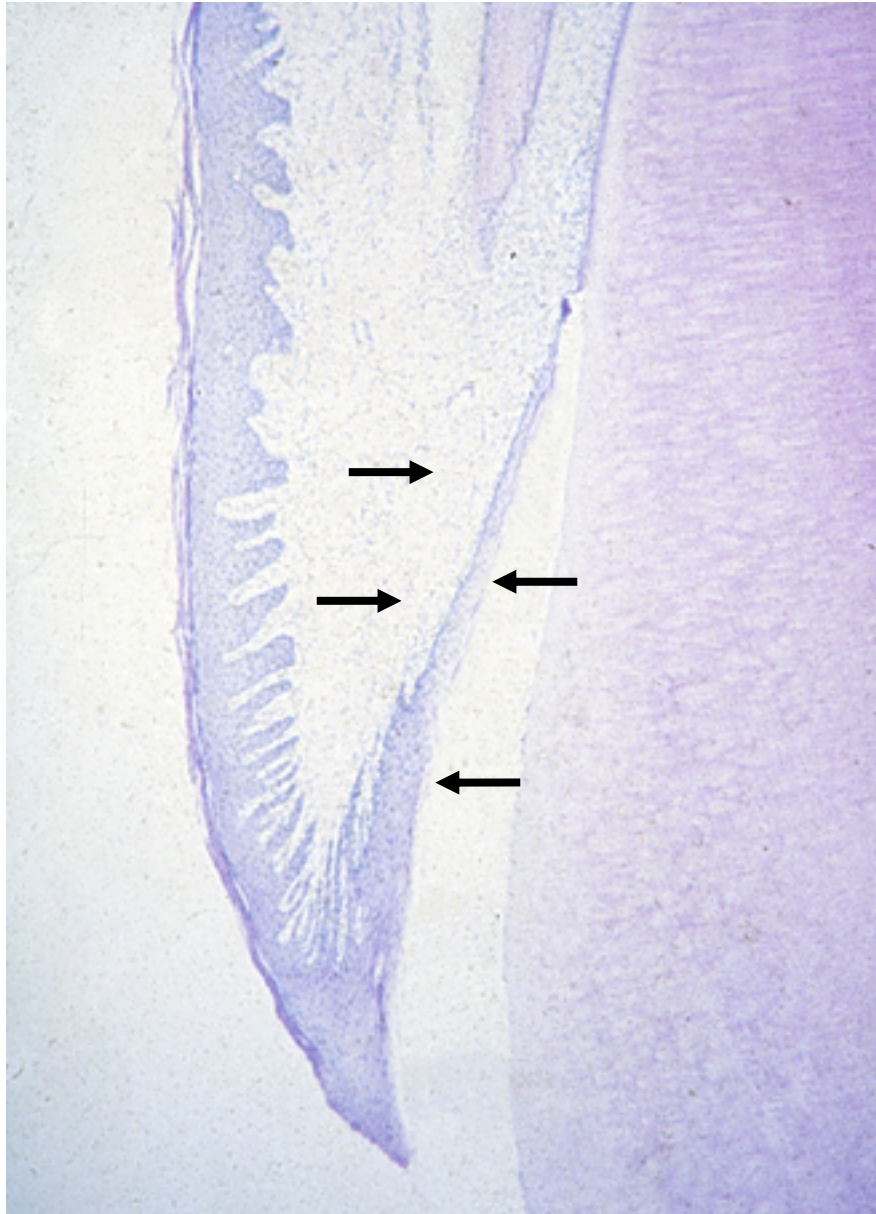
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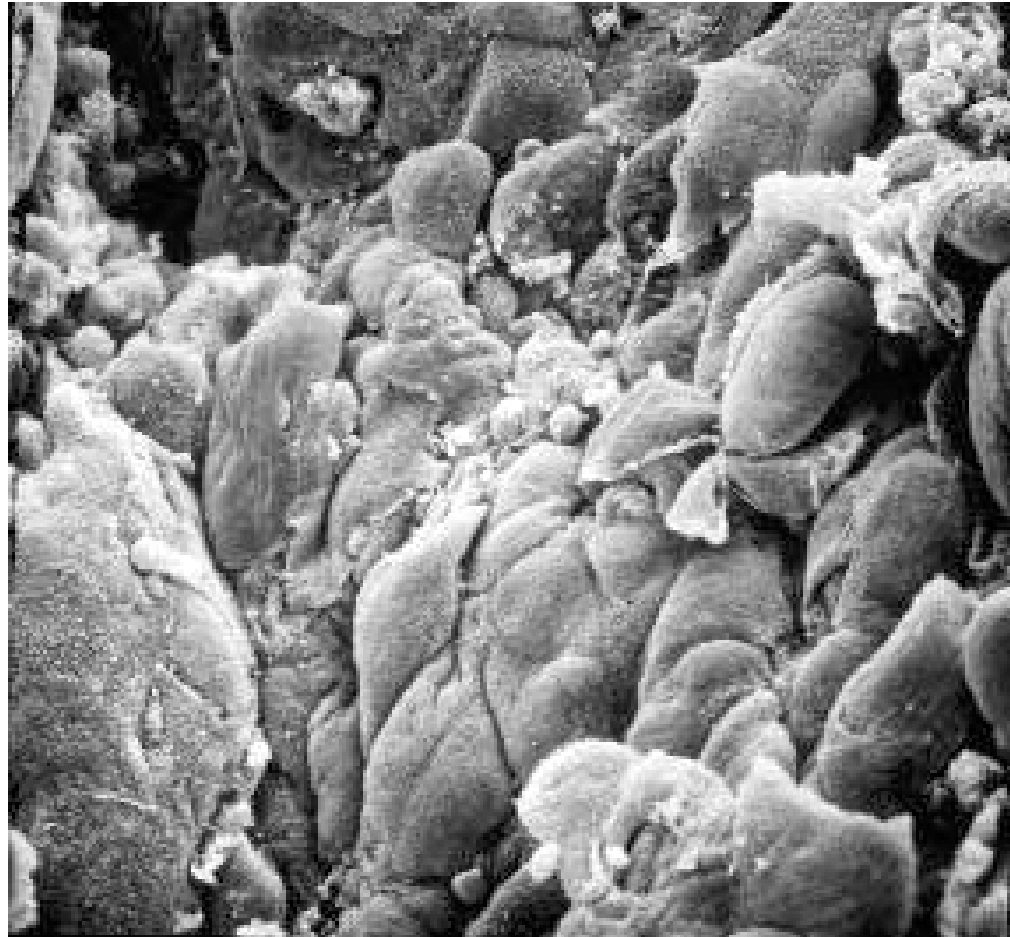


1. Gingival margin
2. Gingival sulcus
3. Cemento enamel junction
4. Crest of bone



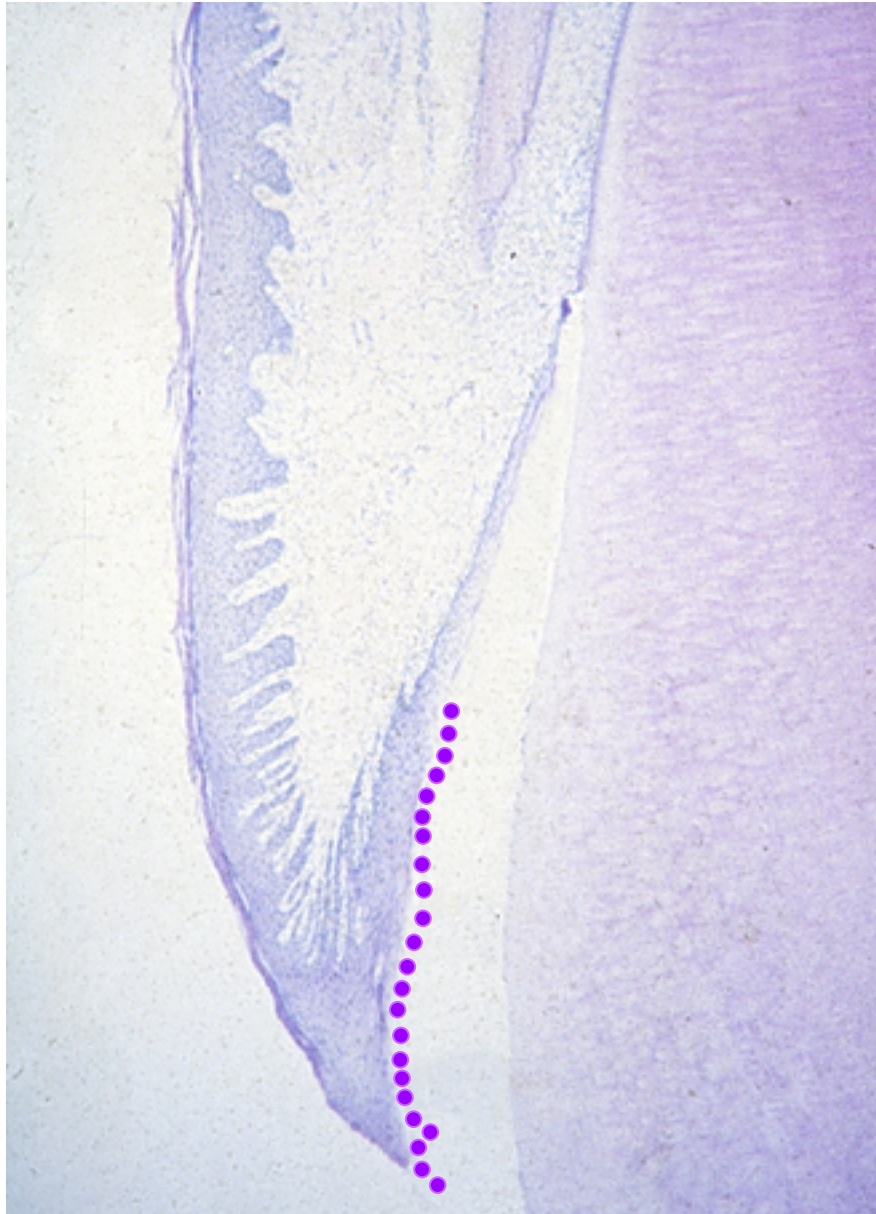
Gingivitis is initiated by interactions of bacterial plaque with epithelium lining gingival sulcus





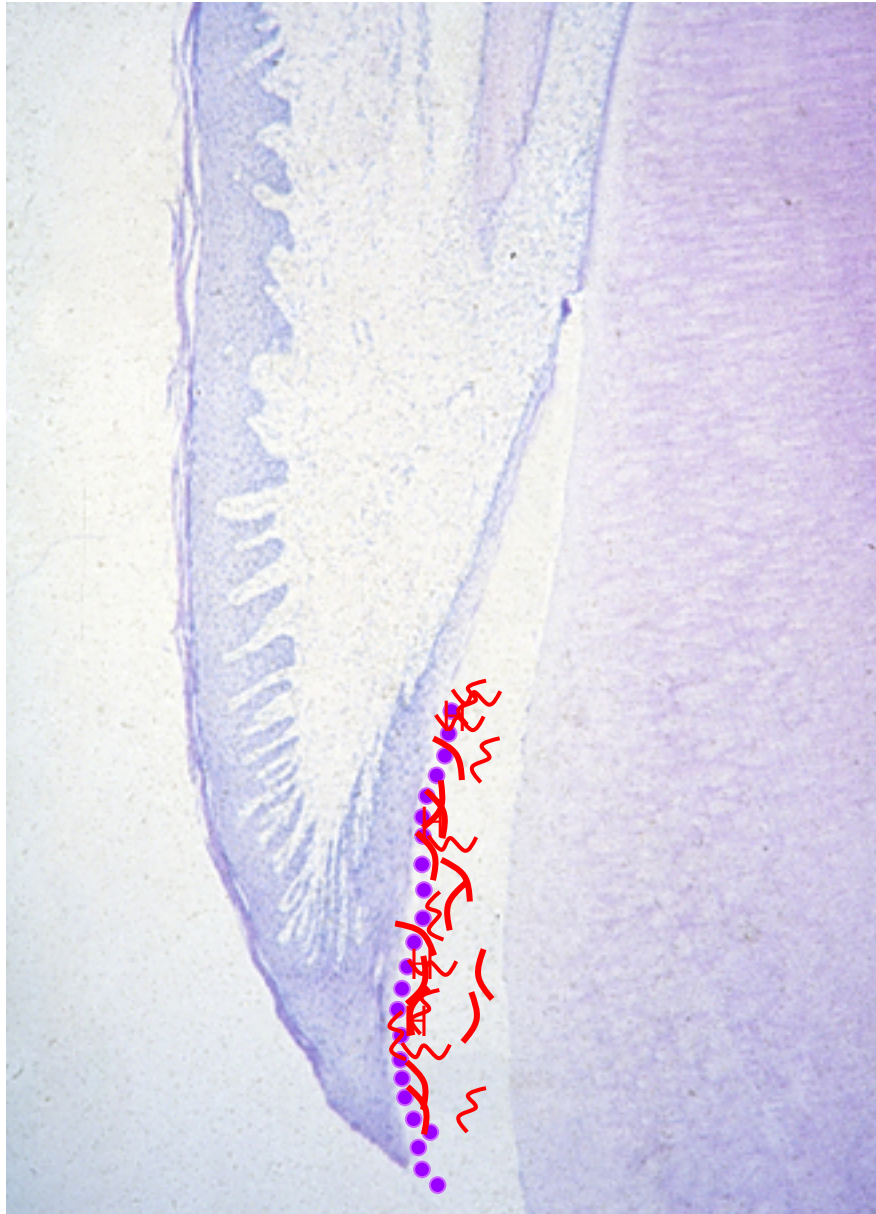
Scanning Electron Micrograph of epithelial surface of healthy gingival sulcus. Cells form an intact surface with no ulceration.

# Initial gingivitis

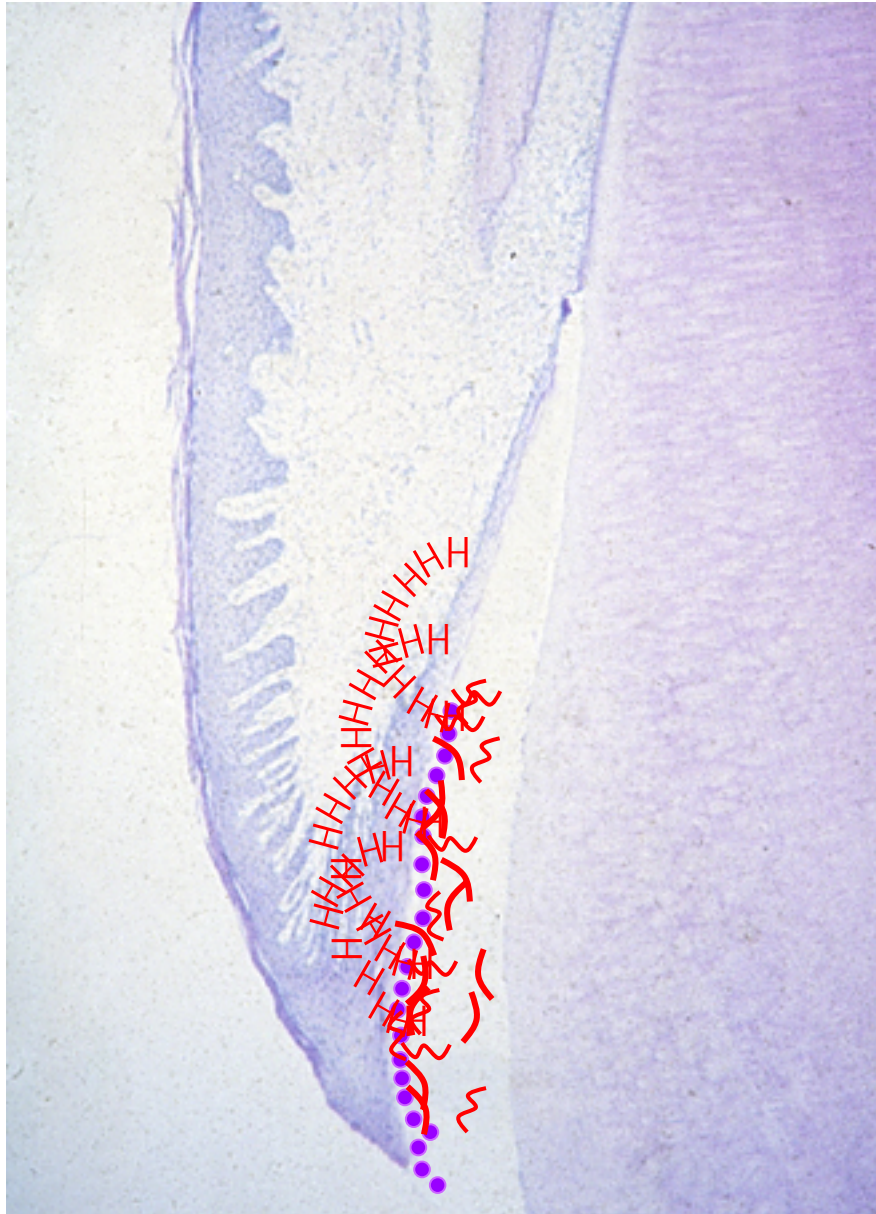


interactions plaque  
with epithelium

Initial subgingival  
plaque (•••) is  
mainly gram  
positive



Gram positive  
bacteria becomes  
mixed with gram  
negative plaque  
(*SKW*) and initiates  
gingivitis



Bacterial toxins  
such as  
Hyaluronidase (H)  
cause openings in  
epithelial lining of  
gingival sulcus

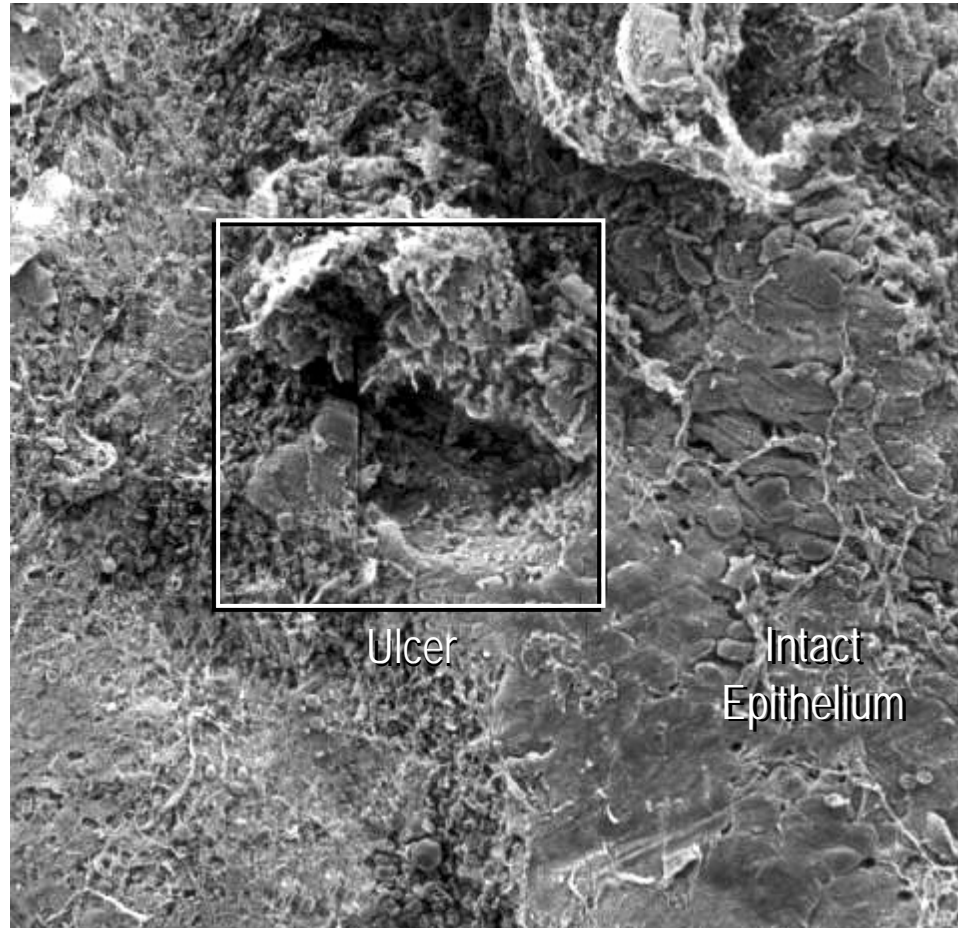




Epithelium  
becomes more  
porous by  
collagenase ( C )  
destroy basement  
membrane and  
connective tissue of  
gingiva

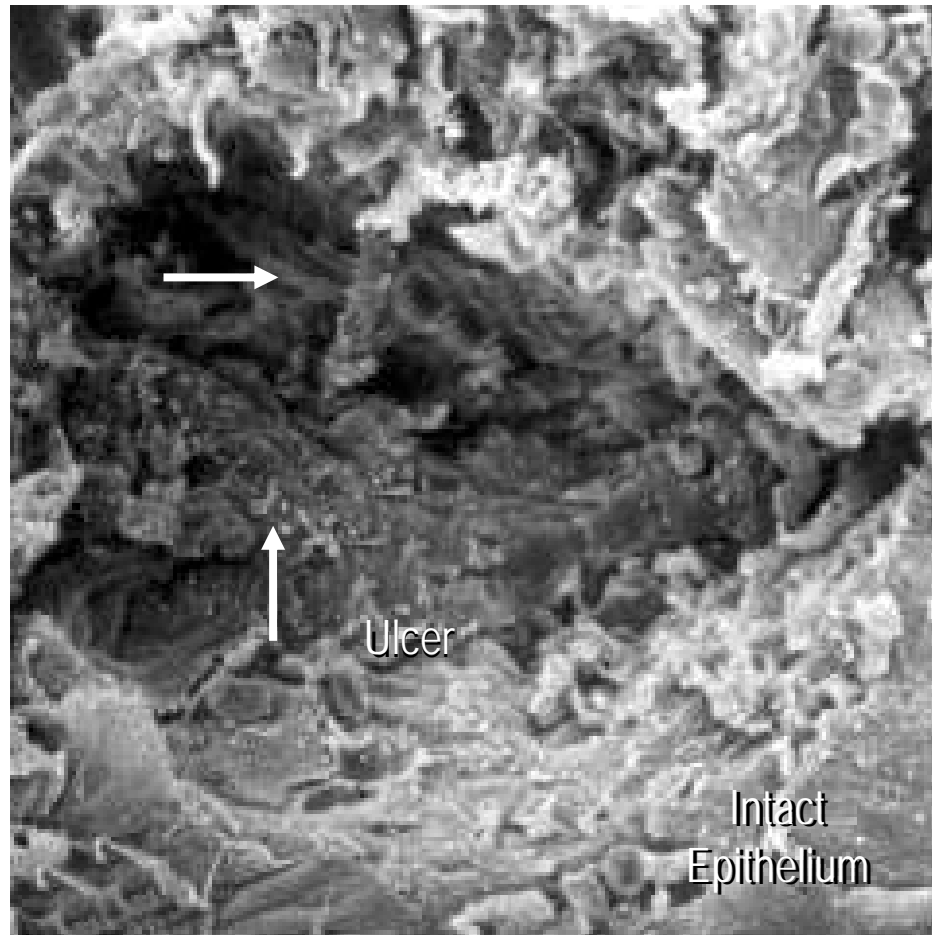


Tissue destruction  
leads to epithelial  
ulceration



Scanning Electron Micrograph of  
ulcerated gingival sulcus epithelium

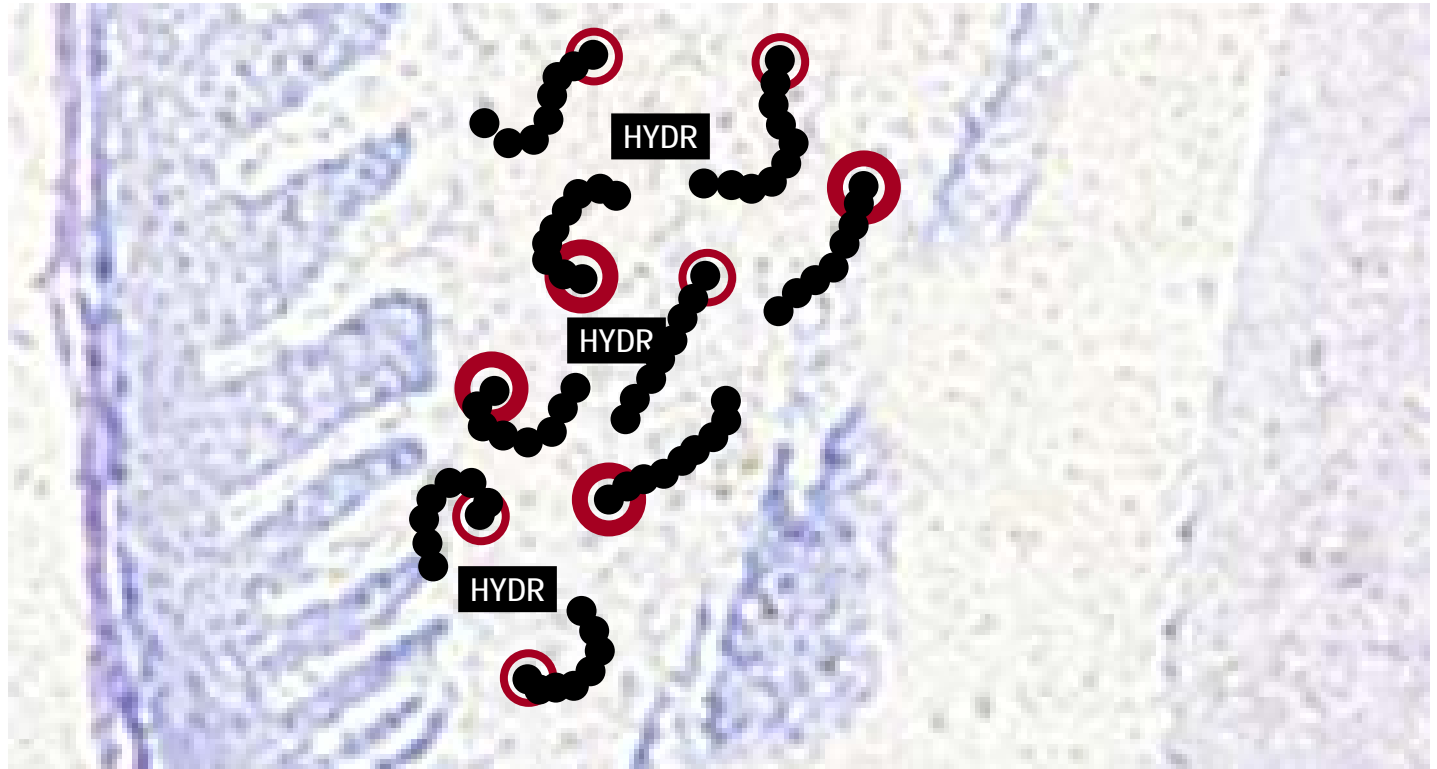




High power view of ulcer. Bacteria have direct access to collagen of gingival connective tissue



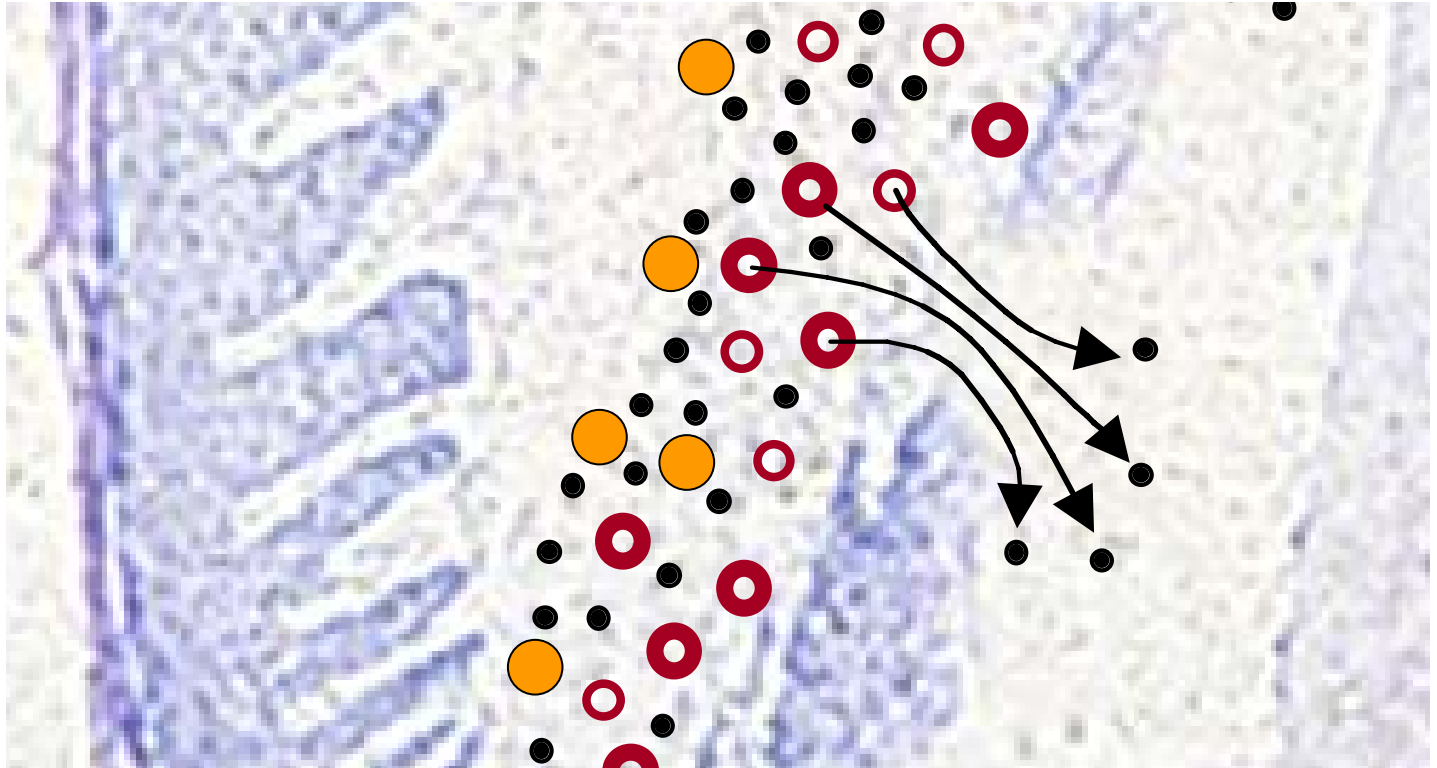
Bacterial products stimulate acute inflammation with vasodilation (○), edema and polymorpho nuclear leukocytes (pmns) (●)



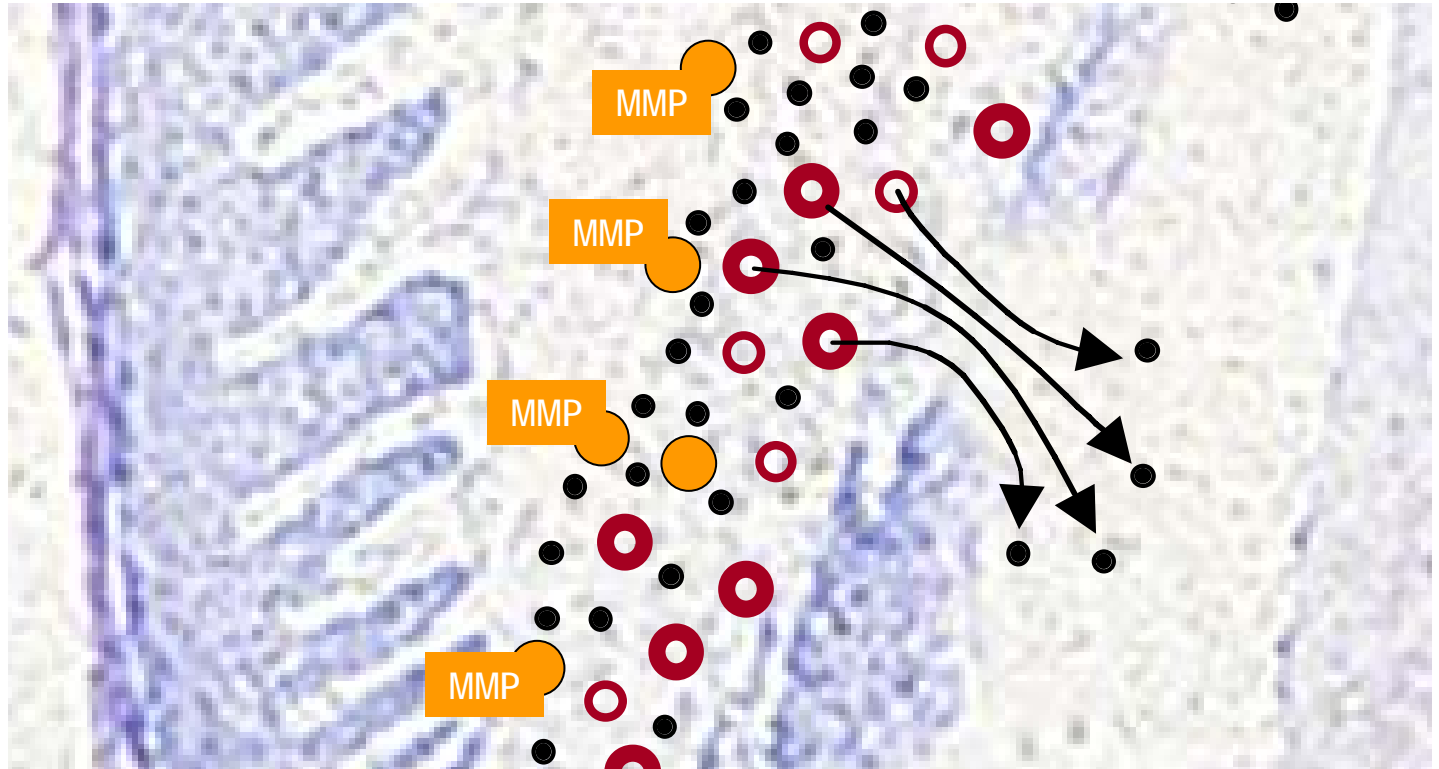
PMNS release lysosomes contain acid hydrolases which destroy both bacteria and gingival tissue



PMNS pass through epithelium into gingival sulcus and are carried into oral cavity by gingival fluid from connective tissue



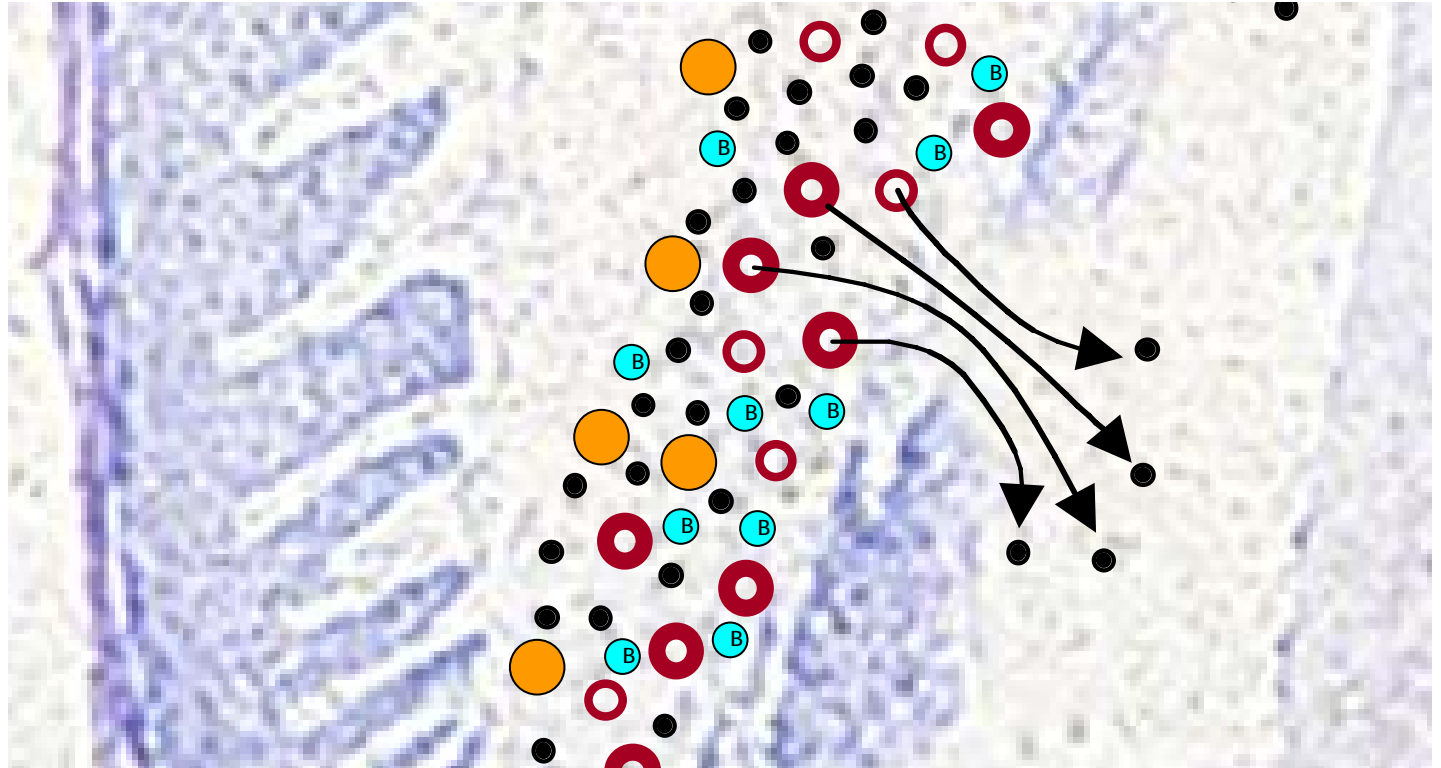
Macrophages originating from  
circulating monocytes appear in gingiva



Macrophages and PMNS produce matrix metalloproteinases (MMP) including collagenase to cause loss of connective tissue

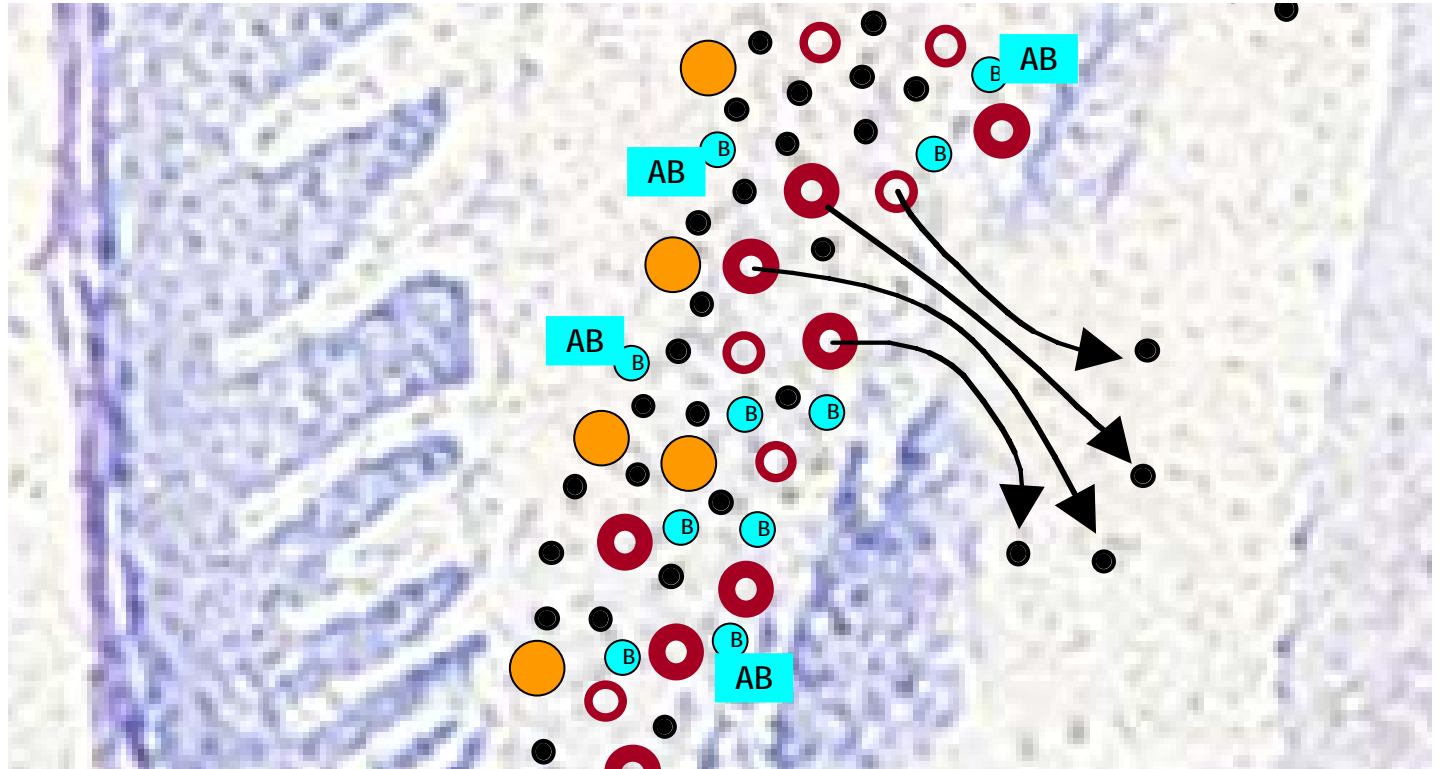
# Early gingivitis



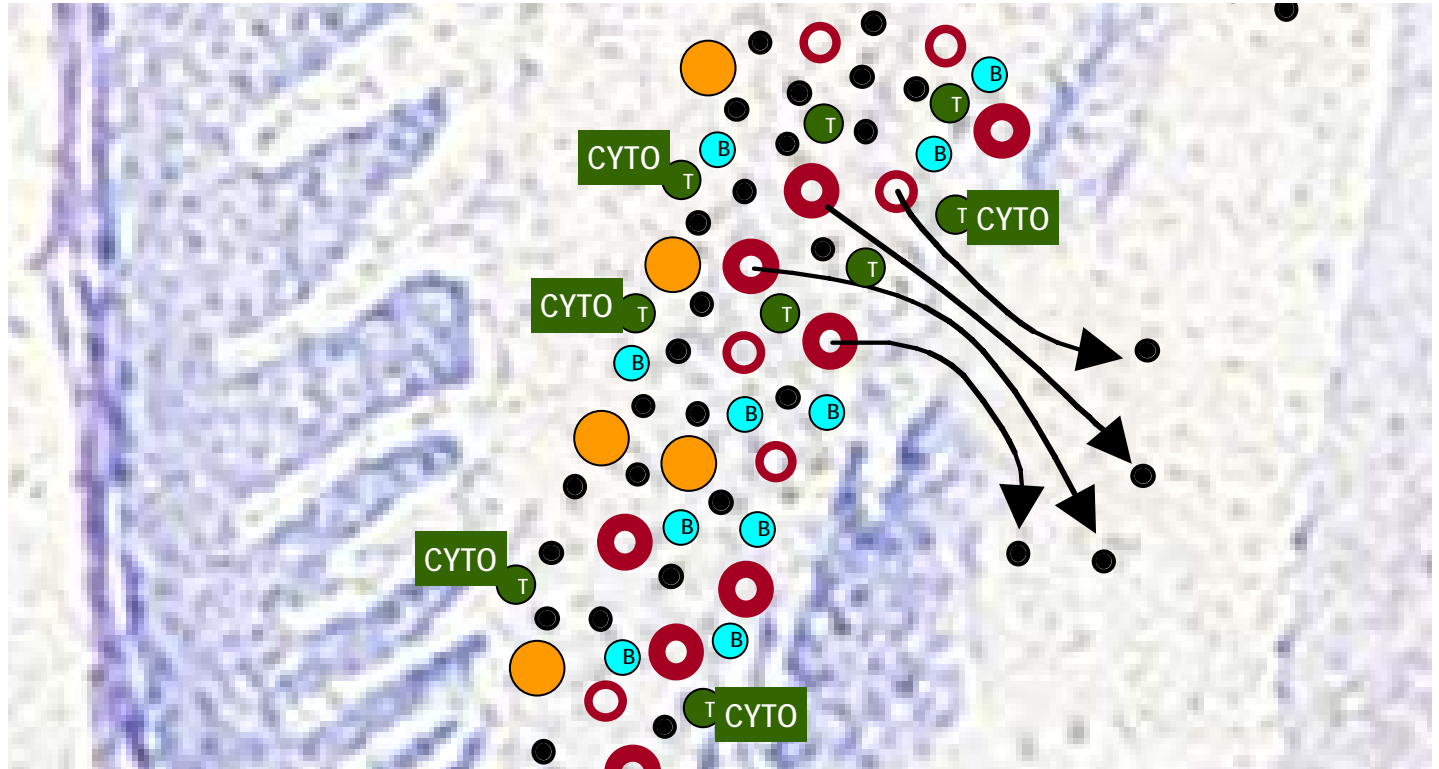


Chronic inflammation is superimposed on the initial acute response with B and T lymphocytes and vascular proliferation





B lymphocytes produce antibody to bacterial antigens



T lymphocytes produce cytokines such as interleukins 1 and 6



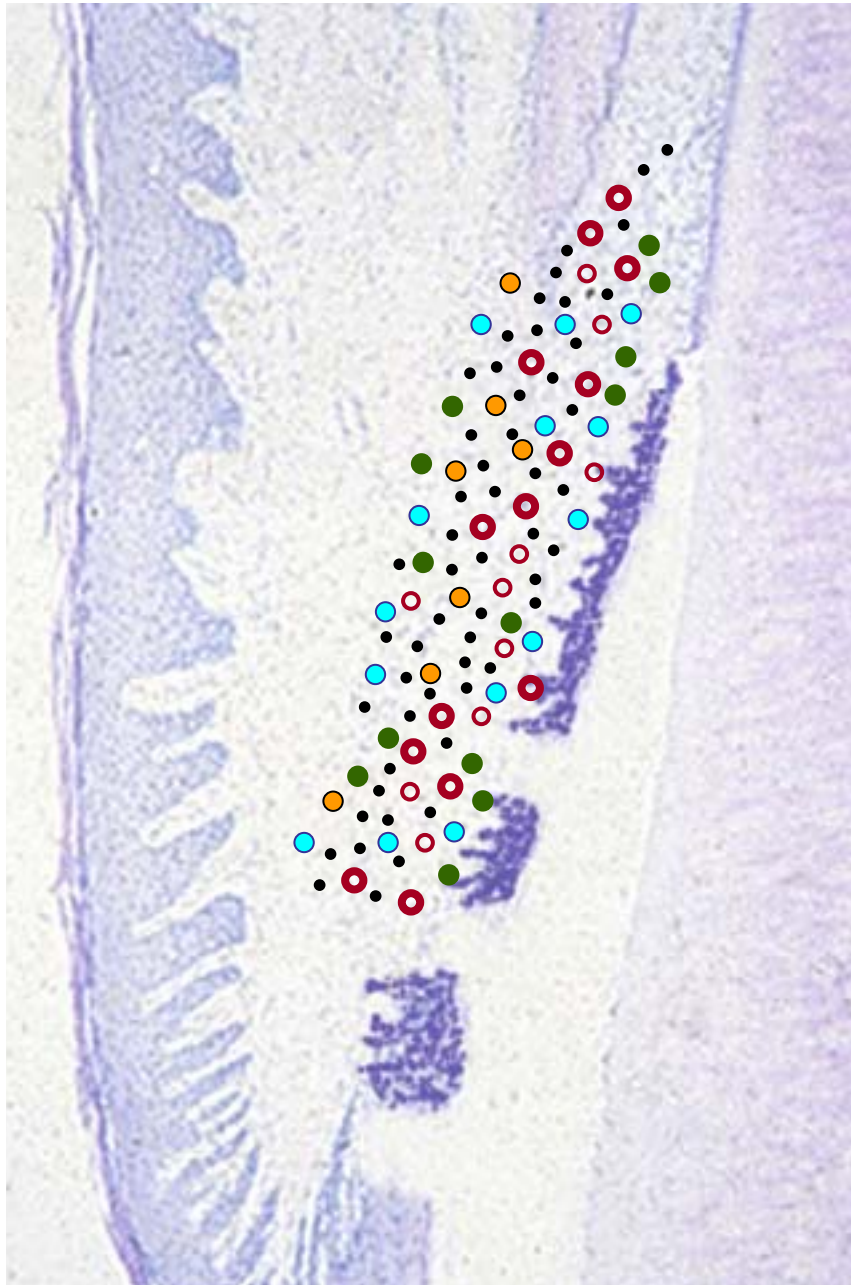
The area of inflammation spreads throughout gingival tissue



Epithelial cells  
proliferate into  
connective tissue

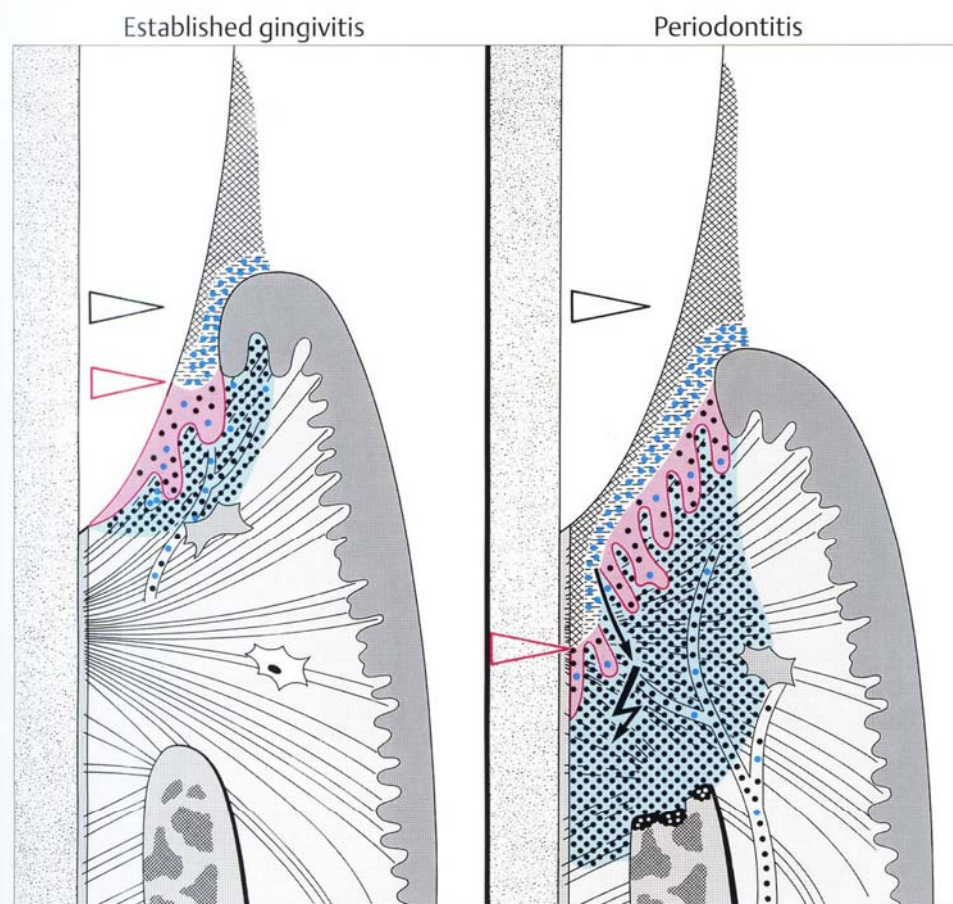
# Established Gingivitis

- Established gingivitis is an extremely frequent condition. Its lesions may be found virtually in every adult's mouth. It is not exactly known how long it takes for typical established lesions to develop if plaque is allowed to accumulate, but speculations range between a few weeks and several months.
- Pathohistologically, established lesions are characterized as follows:
  - Persistent acute components of inflammation
  - Specific populations of inflammatory cells in the infiltrate
  - Immunoglobulins in extravascular connective tissue and junctional epithelium
  - Increasing proportion of plasma cells
  - Further loss of collagen
  - Lateral proliferation of junctional epithelium and gingival pocket formation
- Established gingivitis may remain quite stable for prolonged periods. Usually, there is a delicate balance between the bacterial challenge and the immune response of the host. After an indeterminate period of time, an advanced lesion (periodontitis) may develop



Inflammation spreads  
apically beyond the  
cemento enamel  
junction





Gram-positive and Gram-negative	Sub-epithelial, mainly anaerobic and Gram-negative
Lateral proliferation of JE; apical migration; pseudopocket formation	Apical proliferation of the pocket epithelium, ulceration of the pocket epithelium, true pocket formation
Acute inflammatory alterations; plasma cells; immunoglobulins in connective tissue and sulcus; elevated GCF flow; leukocyte "wall" at plaque front.	Acute inflammatory manifestations as with gingivitis; massive infiltration; plasma cell dominance; copious and partially suppurative exudation; expansion of the inflammation and immunopathology.
Severe fibroblast damage, further collagen loss, stabilization of the exudates.	Further collagen loss in the infiltrated tissues, simultaneous fibrosis in peripheral gingival areas
Normal	Resorption of alveolar bone (attachment loss)
Manifest 3-4 weeks after plaque accumulation, but can persist for many years without further progress	Periods of stagnation and exacerbation, slowly or rapidly depending upon the type of disease

# Summary

## pathogenesis of gingivitis

- Bacterial plaque
- Bacterial toxin
- Epithelial, basement membrane and connective tissue destroy
- Epithelial ulceration
- More bacterial toxin enter
- Bacterial toxin stimulate acute inflammation
- PMNs and Macrophages appear
- Chronic inflammation
- Vascular proliferation
- Inflammation spreads throughout gingival tissue
- Epithelial proliferation



# Periodontitis

# Principles in pathogenesis of periodontitis

(Wilson and Kornman, 1996)

- Bacterial plaque is essential for the initiation of periodontitis
- The principal clinical signs on disease are the result of activated inflammatory and immune mechanisms rather than the direct effects of bacteria
- The quantity of bacterial plaque and the types of bacteria found in the plaque do not by themselves appear to explain the severity of clinical disease

# Principles in pathogenesis of periodontitis

(Wilson and Kornman, 1996)

- The host factors responsible for the clinical signs of disease appear to be influenced by both genetic factors and acquired factors that exert prolonged stress on the host
- Because different host responses may translate the bacterial challenge in different way, the response to therapies focusing on reduction of the bacterial challenge may produce different results in different individual

# New Concepts of Pathogenesis

- Research on the etiology and pathogenesis of periodontitis has provided new knowledge in recent years
- Concerning biofilms (microorganisms), molecular biology, host susceptibility, risk factor and genetics

# Biofilm

- The adherent bacterial flora—dental plaque—is a highly organized biofilm.
- Bacteria within the biofilm are well protected from the host response as well as from antimicrobial agents
- The only effective therapy is purely physical destruction and elimination of the biofilm by scaling

# Molecular Biology

- New knowledge about molecular and cellular mechanism has led to better understanding of the processes by which bacteria in the biofilm elicit immune and inflammatory reactions in the host, leading to connective tissue destruction and resorption of the alveolar bone

# Host Sensitivity and Risk Factors

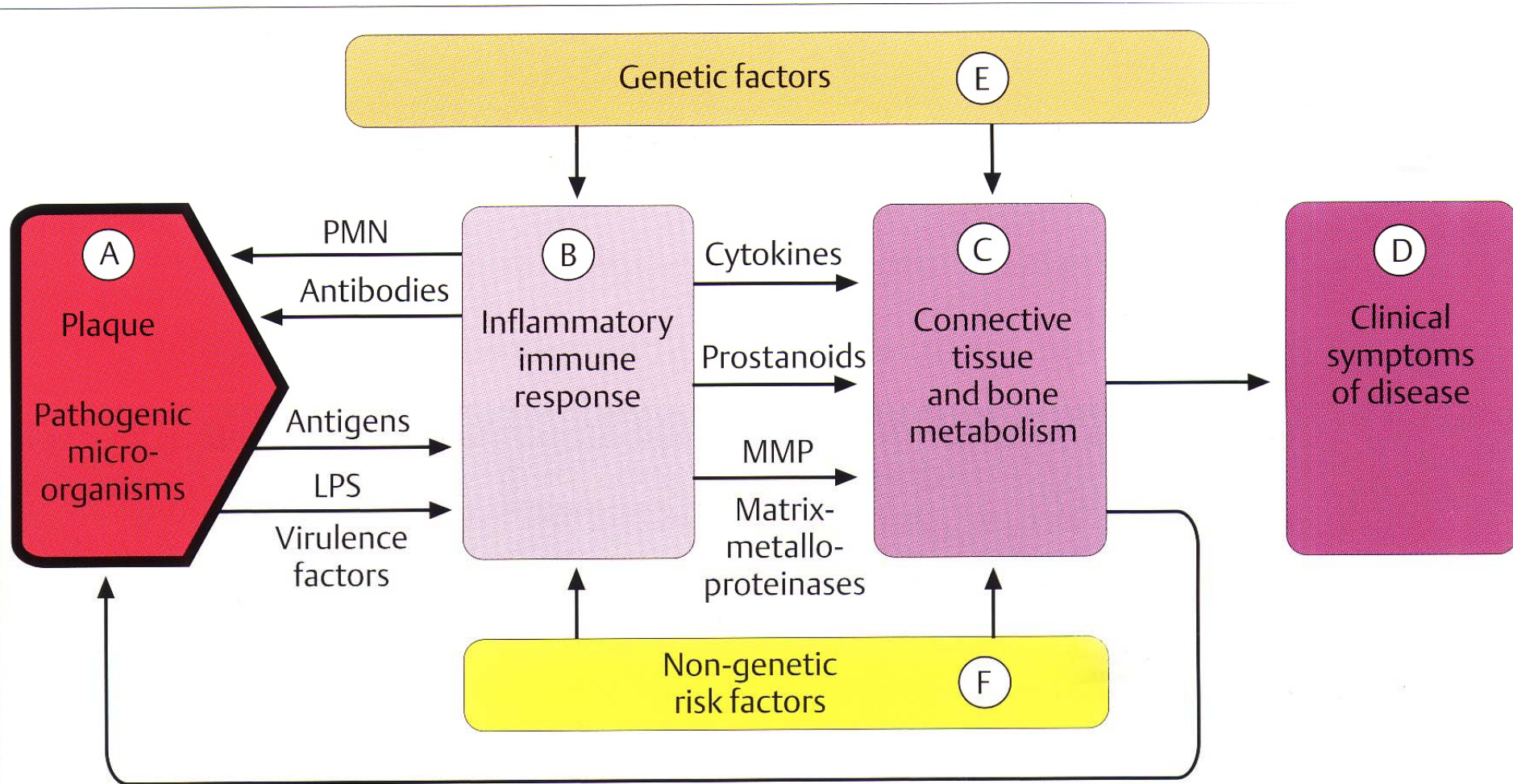
- In order for the aforementioned mechanisms to occur, leading to the initiation and establishment of periodontitis, a susceptible host must be present. The microorganisms, by themselves, *cannot* cause the disease process.
- Environmental factors and risk factors such as smoking or inherited (unfavorable) host defense mechanisms modify the host reaction and are primarily responsible for the destruction progression, severity and clinical picture of periodontitis



# Genetics

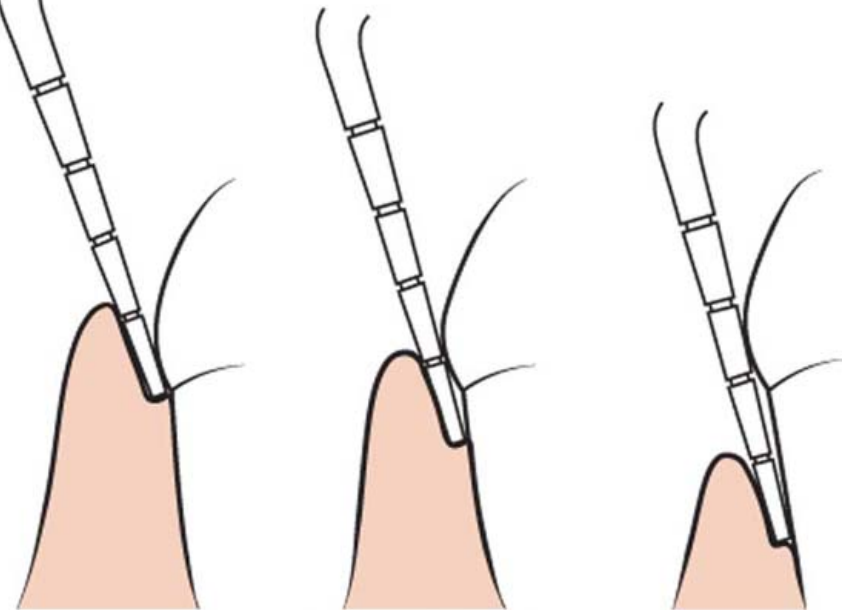
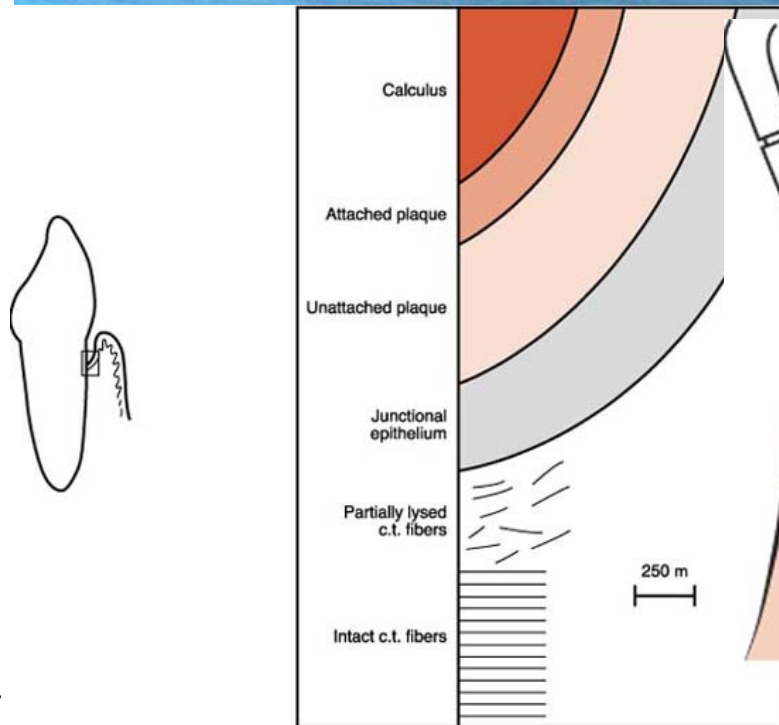
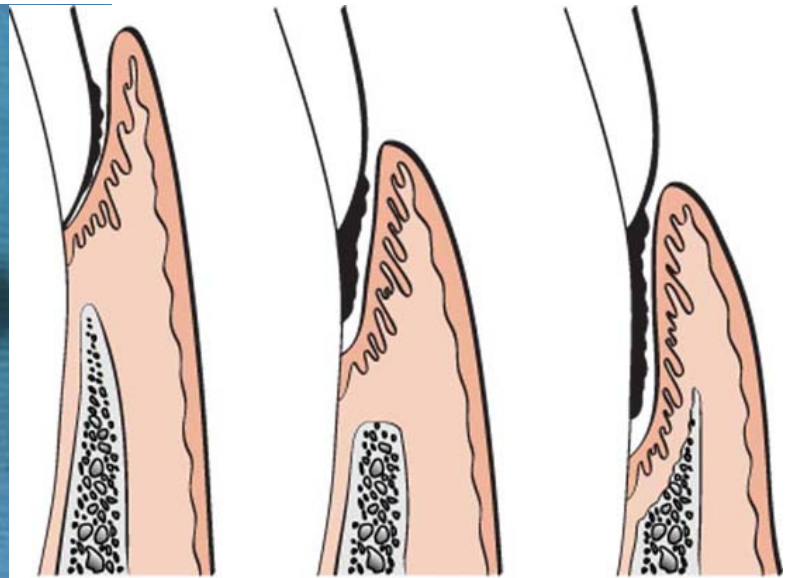
- The various molecular biological mechanisms, the host susceptibility to inflammatory damage, and congenital risk factors are determined for the most part by genetics
- Therefore heredity assumes a much larger significance today than was previously assumed; humans are born with their predisposition towards periodontitis

# Pathogenesis of periodontitis



# Periodontitis

- Clinically differentiated from gingivitis by
  - the loss of the connective tissue attachment
  - loss of the periodontal ligament and disruption of its attachment to cementum
  - resorption of alveolar bone.
  - migration of epithelial attachment
  - alteration of cementum



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# Histopathology of periodontitis

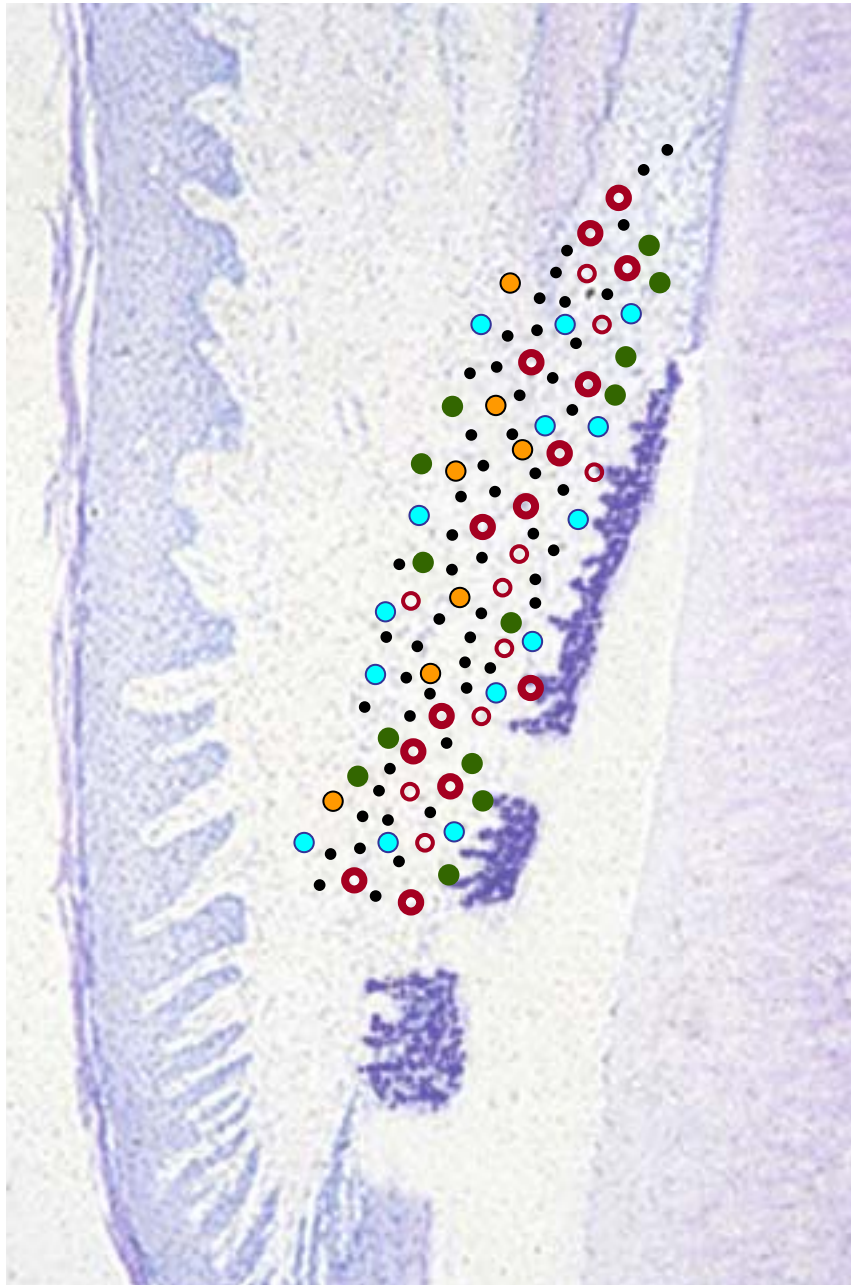
The transition from established gingivitis to periodontitis, which is characterised by:

- vascular proliferation and vasodilatation; vessels becoming engorged with blood
- plasma cells and B lymphocytes in the connective tissues
- the pocket epithelium being very thin, frequently ulcerated and permeable to bacterial products, inflammatory mediators and defence cells
- connective tissues exhibiting signs of degeneration and foci of necrosis

# Histopathology of periodontitis

- fibres of the periodontal ligament apical to the junctional epithelium being destroyed by collagenases
- the junctional epithelium proliferating in an apical direction
- exposed cementum adsorbing bacterial products and becoming soft and necrotic
- osteoclast bone resorption, driven by plaque and host-derived mediators such as endotoxin, prostaglandins, interleukins and tumour necrosis factor (TNF), becoming evident

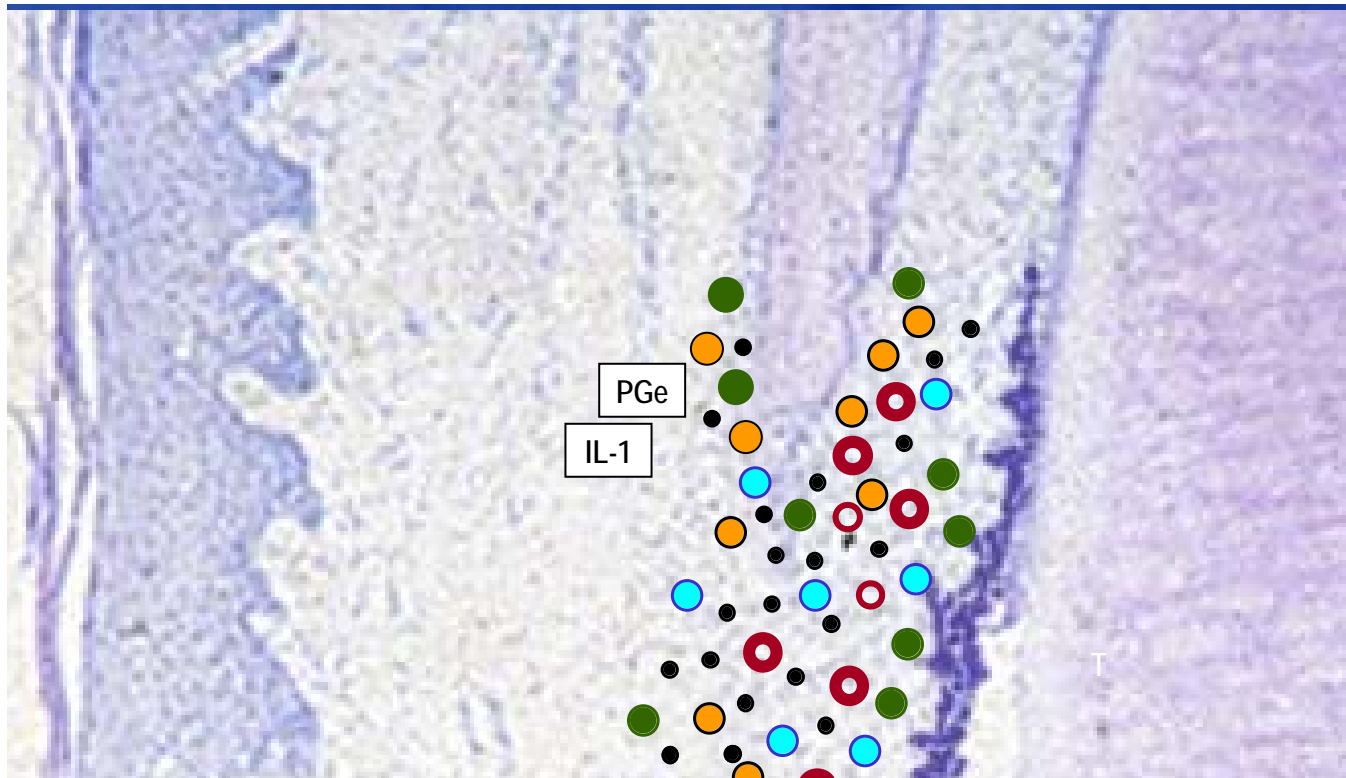




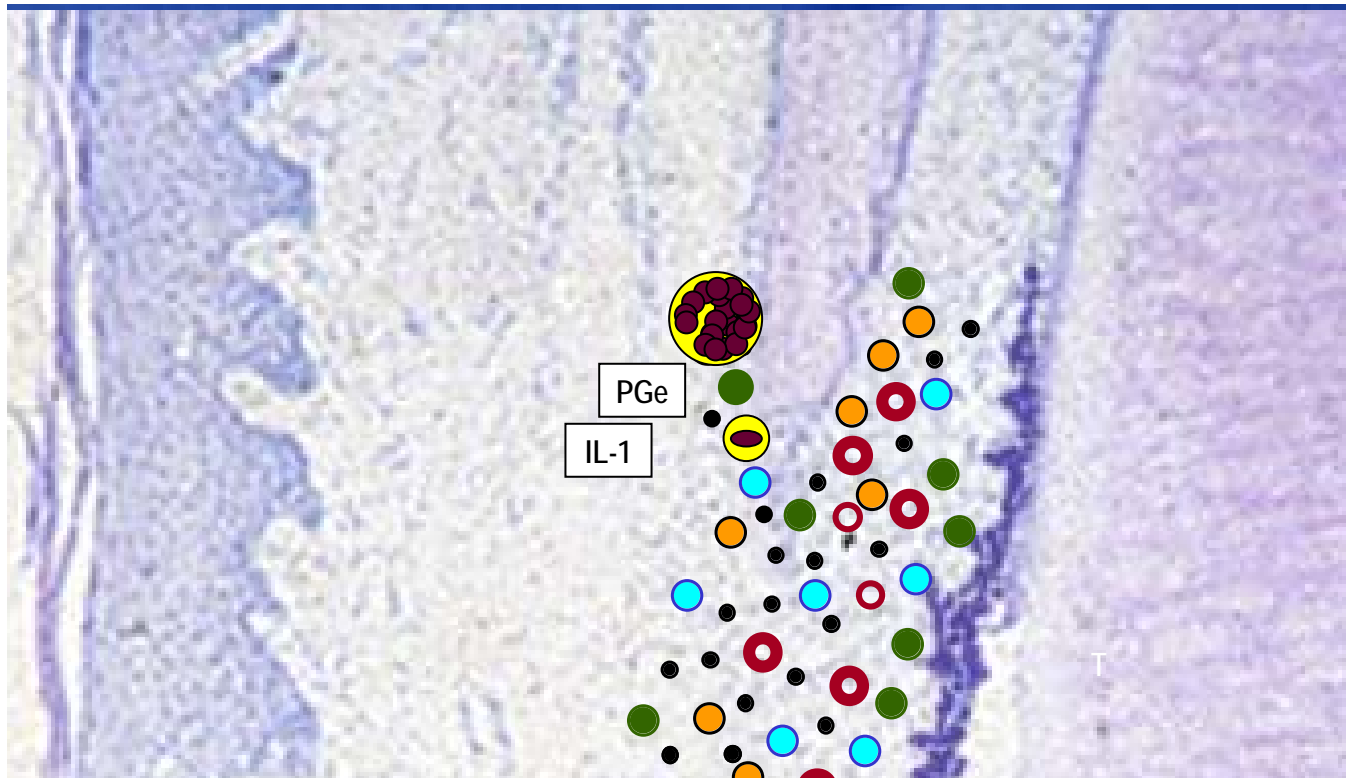
Inflammation spreads  
apically beyond the  
cemento enamel  
junction



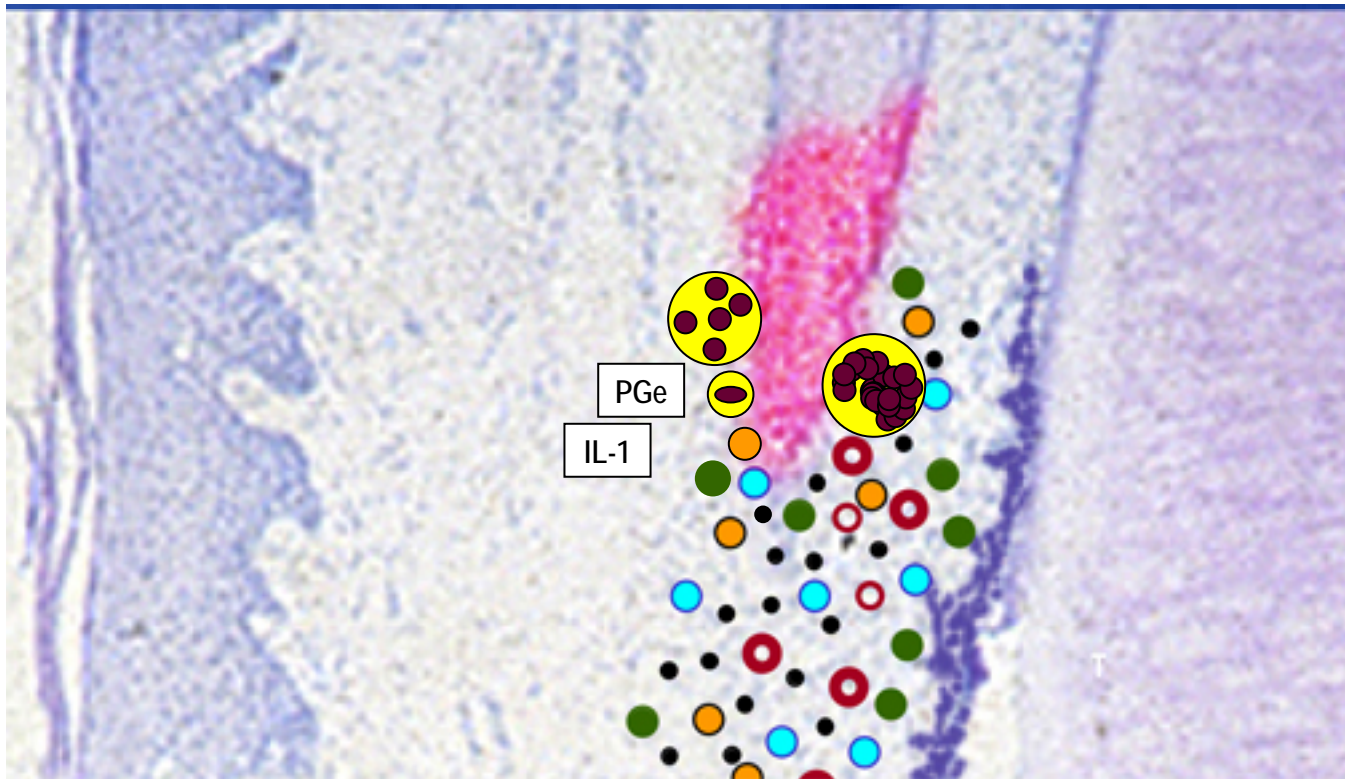
Epithelium  
proliferates apically  
with pocket formation  
and gingivitis  
becomes  
periodontitis



Inflammation surrounds bone crest and inflammatory cells produce interleukins and prostaglandins

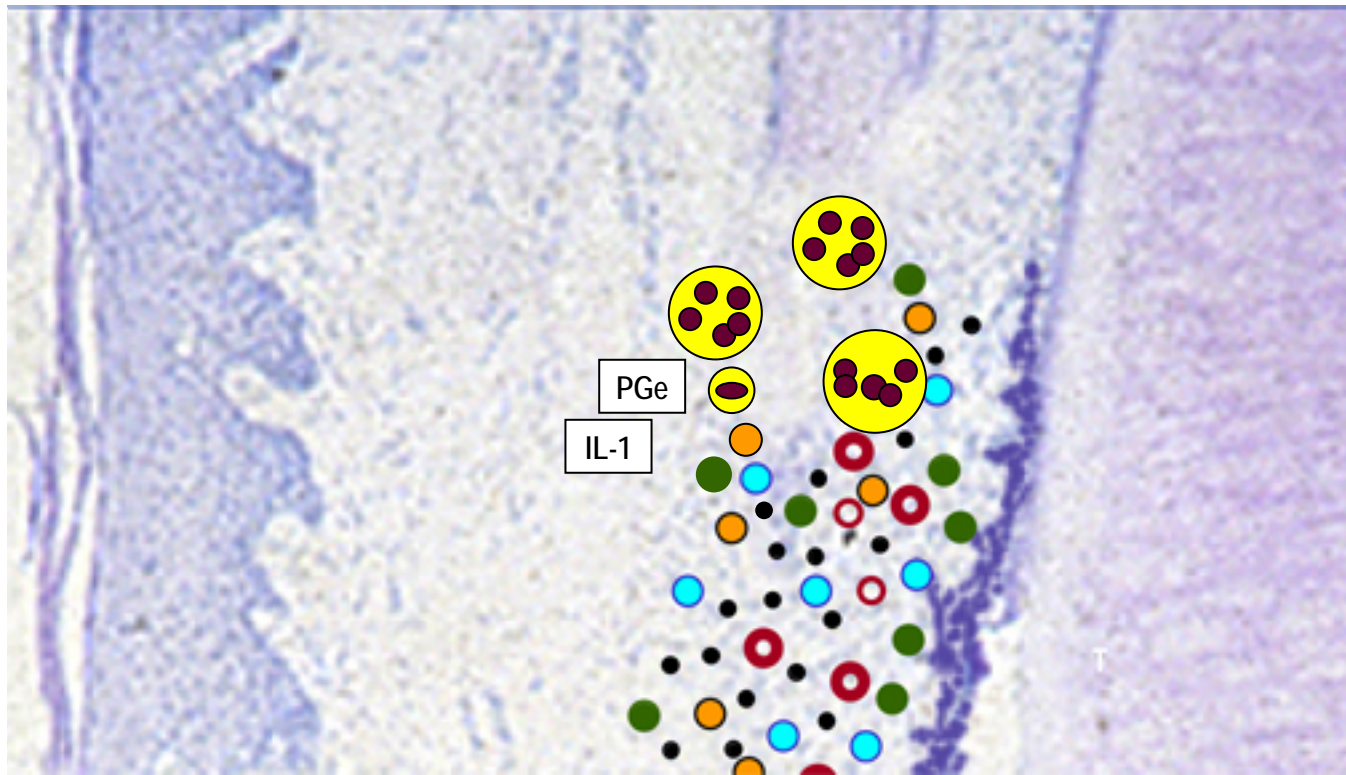


Prostaglandins and interleukin 1 cause osteoblasts to upregulate activity of multi-nuclear osteoclasts



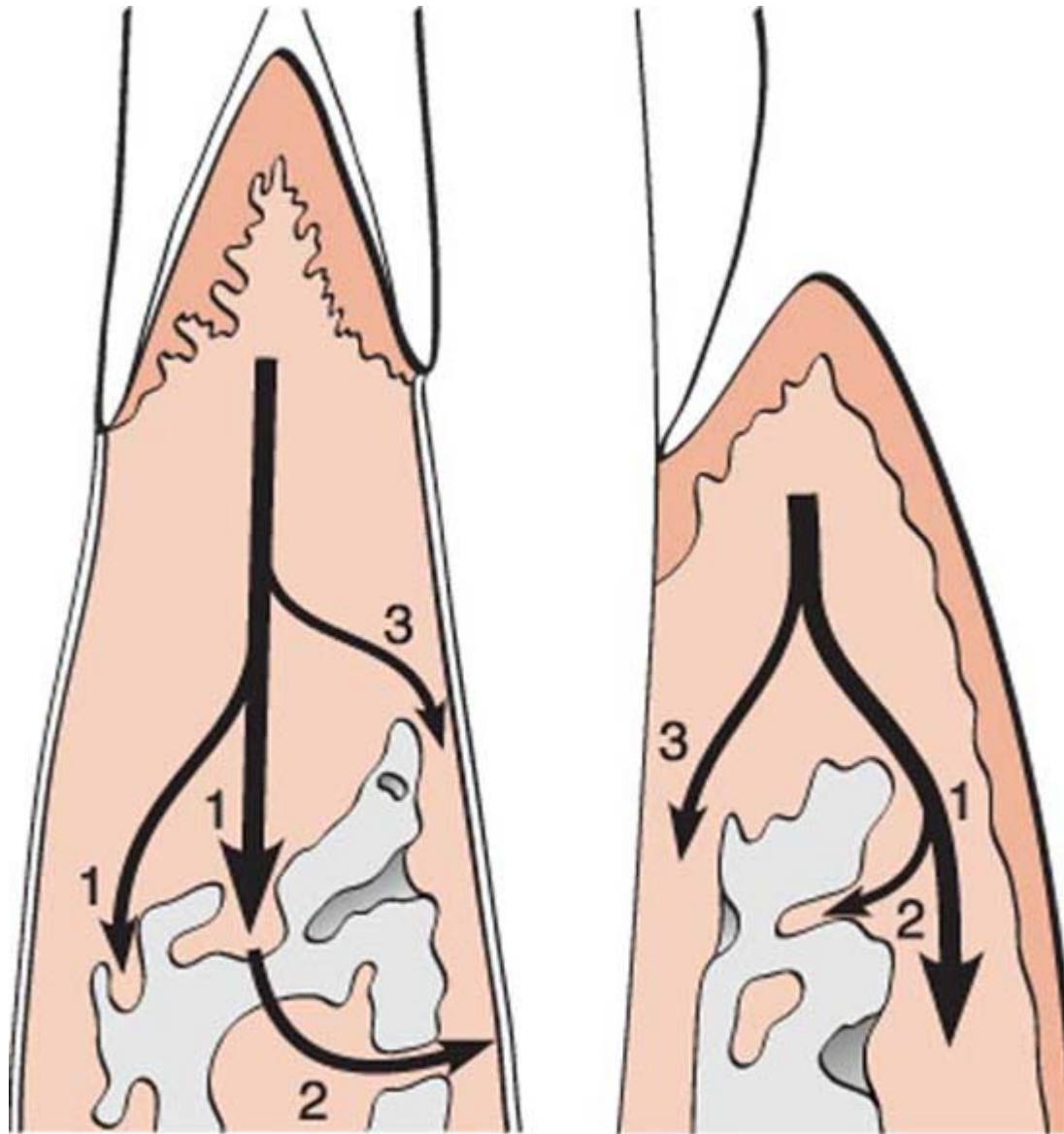
Osteoclasts and osteoblasts together begin bone resorption





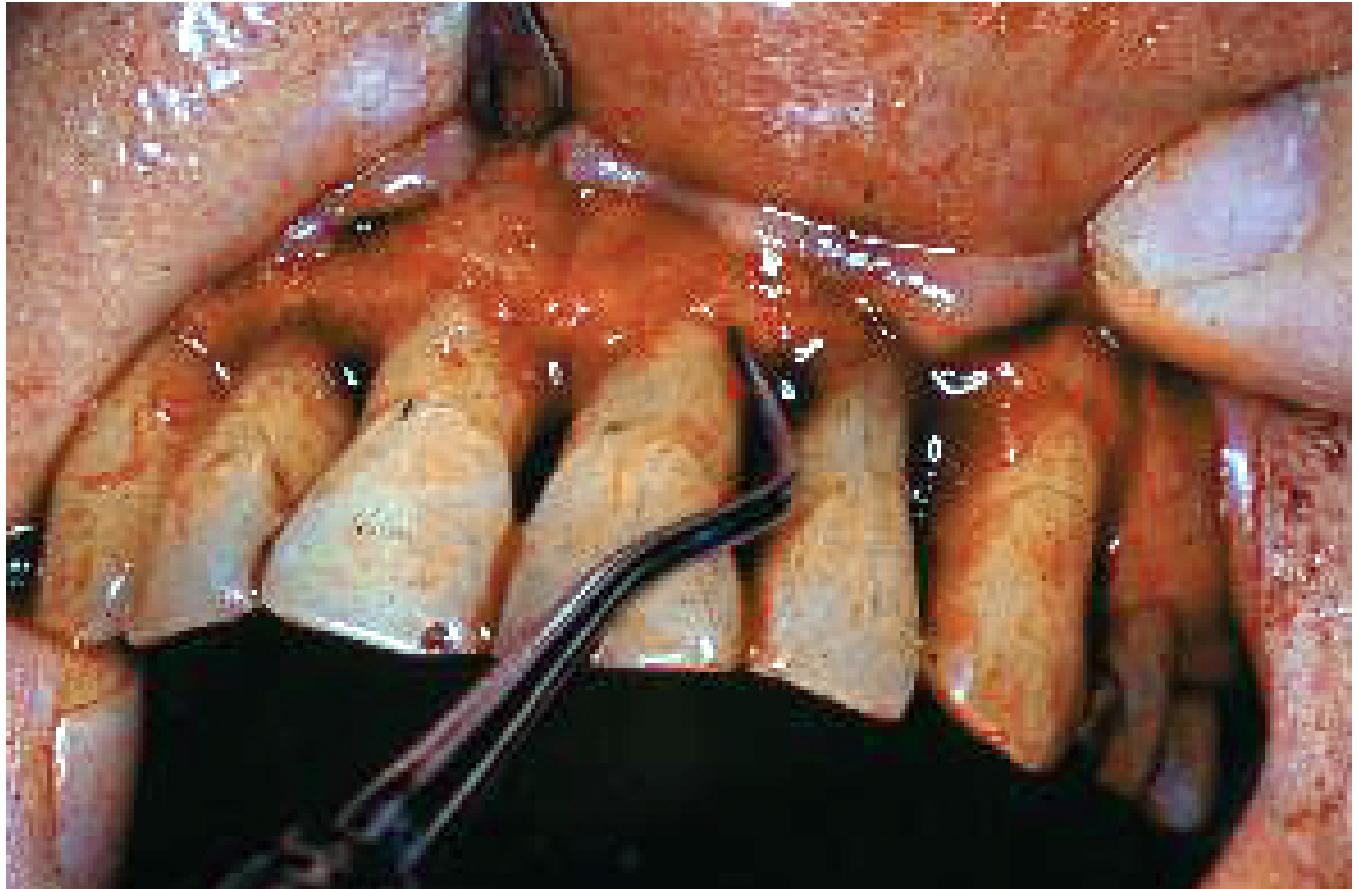
Crestal bone is destroyed and tooth becomes mobile and eventually lost



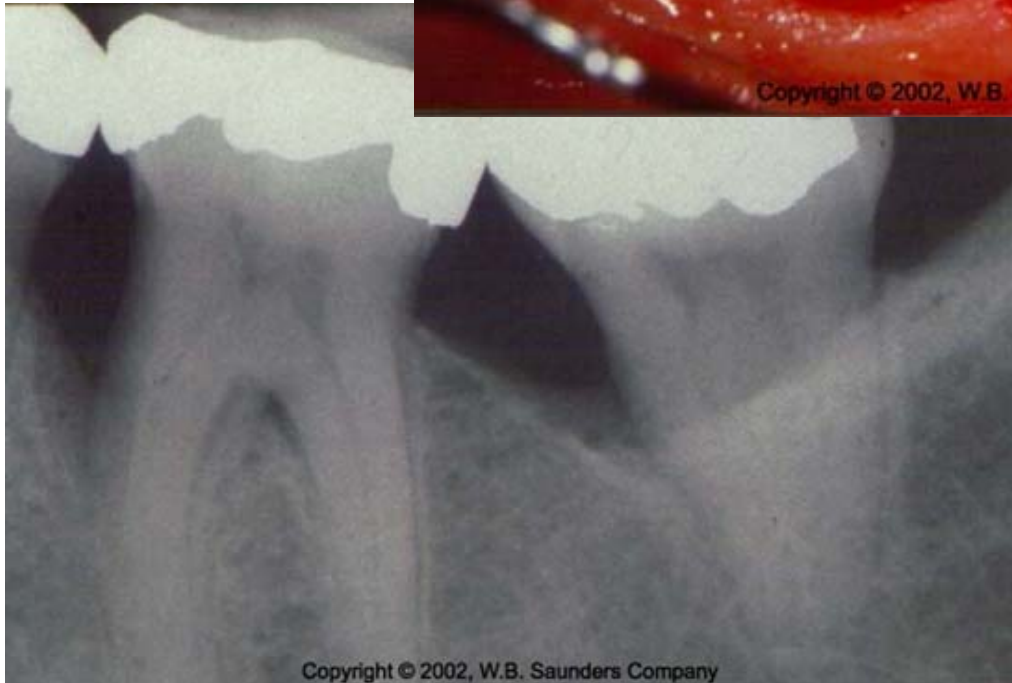


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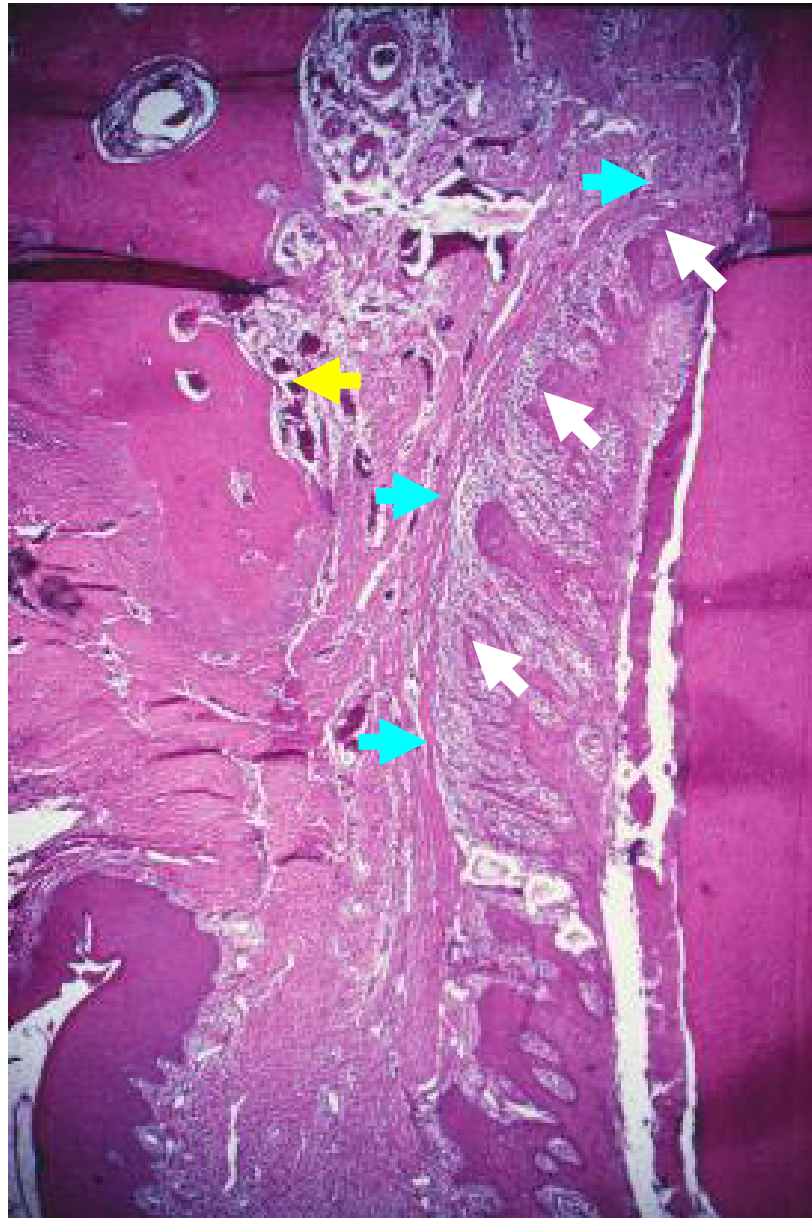
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Periodontal flap surgery to treat periodontitis. Note loss of crestal bone.



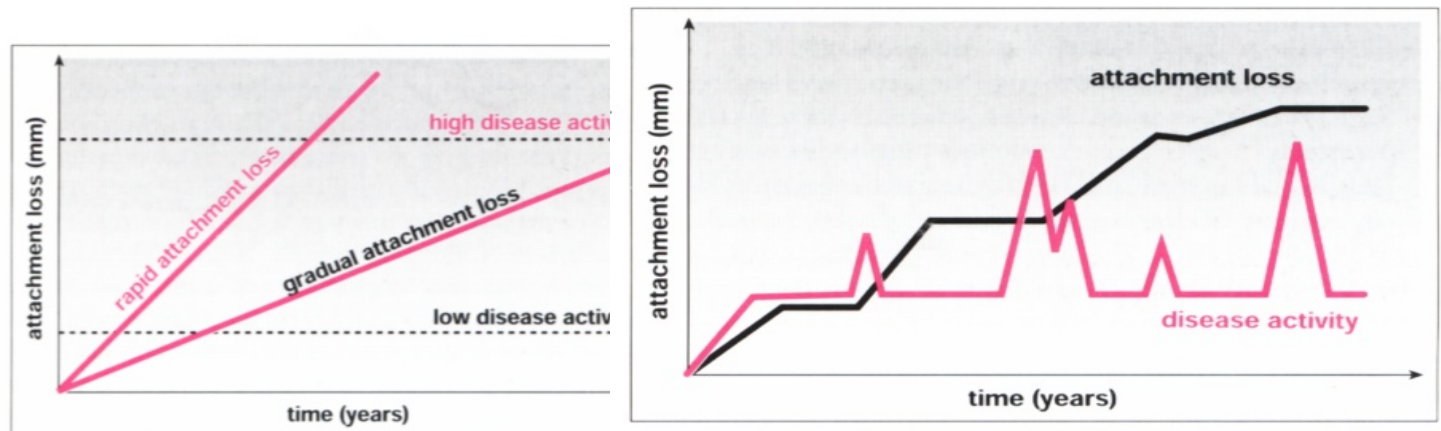
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Periodontitis.  
Histopathology of  
intrabony defect  
showing bone  
resorption (*yellow*),  
inflammation (*green*)  
and epithelial  
proliferation (*white*). 63

# Patterns of progression of periodontitis

- rates of CAL in some individuals can be too slow/fast to fit a linear model
- many sites do not change over long periods (which is inconsistent with the linear progression model)
- destruction at a site may arrest and progress no further



# References

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- Kenney,EB: Periodontal Disease As A Predictor Of Coronary Artery Atherosclerosis, UCLA School of Dentistry, 2000