**PERIO GUIDE**

**Lecture 7**

***Microbial Etiology of Plaque. Plaque-Related Periodontal Diseases***

Pathogenic subgingival submicrobiota (bad stuff) + a susceptible host = inflammation & biological changes 🡪 leading to attachment loss and bone resorption 🡪 leading to periodontitis ( a virus may also be involved)

3 basic bacterial structures: Rods, cocci, spirochetes

Gram positive bacteria stains blue and gram negative bacteria stains red.

Aerobic bacteria need oxygen for growth and survival. Anaerobic bacteria will die in presence of oxygen. Facultative bacteria can live with or without oxygen.

Dental plaque

Soft biofilm adheres to teeth and hard oral surfaces

- spatially organized communities of microbes attached to a surface and enclosed in a matrix of extracellular material

-from both the component species and the environment.

1. Organisms have novel phenotypes compared to growth in liquid culture.

2. Properties of microbe community are more than sum of individual species.

3. Enhanced resistance to antimicrobial agents (MIC values 1,000x higher for cells attached to a surface)

Plaque

-Supragingival plaque - at or above gingival margin, important in dental caries, forms rapidly (hours), sugar-dependent, microorganisms present

-Marginal plaque - in direct contact with tissues of gingival margin, important in gingivitis

-Subgingival plaque - located below gingival margin between tooth surface and gingival sulcular tissue, important in periodontitis, matures slowly (weeks, months), asaccharolytic (protein dependent), microorganisms prominent

-lots and lots of microorganisms - one gram of wet plaque contains 2 x 1011 bacteria

-microorganisms embedded in intercellular matrix (makes up 20 20-30% of plaque mass)

-intercellular matrix forms hydrated biofilm gel (protective barrier against host defenses, made

up of organic materials and inorganic materials

-can see after 1-2 days of no oral hygiene

- white white, gray or yellow in color

- most common on ***gingival 1/3*** of tooth surface

-prefers to grow in tooth cracks, pits & fissures, under overhanging dental restorations, and on misaligned teeth

- rate of formation affected by diet, saliva flow, oral hygiene and *pre pre-existing tissue inflammation*

3 phases of formation

1. Pellicle formation-provides substrate for bacterial colonization to non shedding surfaces in oral cavity.
2. Initial microbial colonization of teeth, dentures and dental implants. Adhesions on gram + streptococci & *Actinomyces* species bind to proline-rich proteins in dental pellicle (protein adhesion on link to pellicle)

* Initial microbial layer is monomer and then proliferates to form plaque biofilm
* Plaque growth by bacteria cell division
* Proliferating bacteria grow away from tooth surface in columnar microbial colonies
* Protein adhesions and electrostatic interactions keep plaque on teeth

1. Secondary microbial colonization & plaque maturation - co aggregation by gram negative anaerobic species onto surfaces of initial gram positive colonizers

* Coaggregation bridges can be formed (via ***Prevotella loescheii***)

MICROBIOLOGY IN PERIODONTAL HEALTH

-In periodontal health thin, loosely aggregated subgingival plaque mass has mostly non-motile gram positive coccoid cells & filamentous rods (75% is this). *Examples of these are streptococcus (strep) sanguis, strep mitis, strep oralis, veillonella parvula, actinomyces species, and rothia dentocariosa*.

* + Microbial Homeostasis – stability of resident microflora on an environmentally exposed surface of the body, resulting from a dynamic balance between intermicrobial interactions and host-microbial interactions
    - Resident microflora acts as barrier to exogenous microorganisms – colonization resistance
    - Can break down from changes in local environment affecting relative competition among microbial species and altering balance in microflora composition
      * Get a specific selection of pathogenic organisms
      * Increases risk of disease
      * Low pH in plaque following high sugar intake and metabolism
        + Get selection of cariogenic mutans strep (can grow in acidic environment)
        + Other bacteria killed because pH too low
      * Decreased saliva from meds, neutrophils dysfunction from diabetes, smoking, poor oral hygiene
* Effects of Poor Oral Hygiene
  + Bacterial plaque mass increases, inducing elevated neutrophils infiltration into gingival tissues
  + Neutrophil-derived neuraminidase increases in gingival crevicular fluid
  + Neuraminidase destroys sialic acid residues on epithelial cells reducing attachment by health-associated strep
  + Neuraminidase exposes galactosyl residues – increasing attachment by the perio pathogens, including *Prevotella intermedia* and *Fusobacterium nucleatum*
  + Note – enzyme activities associated with poor oral hygiene and gingivitis modulate adhesion and colonization of bacteria in gingival crevice
    - Good plaque removal favors streptococcal colonization
      * Produce hydrogen peroxide which inhibits growth of many perio pathogenic bacteria
      * Patients lacking this bacteria may be treated by replacement therapy

Poor plaque removal favors perio pathogen colonization

* Bacterial Replacement Therapy
  + EvoraPlus probiotic mints – contain freeze-dried mixture of 100million CFU each of three health-associated oral bacteria known to be antagonistic to perio pathogens and cariogenic organisms
    - *Strep oralis* and *Strep uberis* – inhibit anerobic periodontal pathogens by secreting hydrogen peroxide
    - *Strep rattus* – lactic acid-deficient strain that blocks colonization of cariogenic mutans strep

Leeuwenhoek first to discover that there was lots of organisms under the microscope when looking at the gunk from between his teeth.

Then a guy named Miller said periodontal disease was the result of infectious process caused by backteria.

From 1920-1960 these were thought to cause periodontitis (non-plaque etiology of periodontitis):

Traumatic occlusion, systemic diseases, genetic status, atrophy or degeneration, mechanical irritation by local factors, or bacterial plaque (rarely considered)

A guy named Hartzell formed first perio dept at U of Minnesota School of Dentistry.

-“Plaque formation, periodontal disease, and dental caries in Syrian hamsters.”- first big study that linked plaque w/periodontitis and used reliable animal model. By Paul Keyes

-First documentation of microbial specificity in the pathogenesis of periodontitis, and infectious spread of periodontopathic bacteria

- *Actinomyces viscosus* associated with experimental periodontitis and root caries in hamsters

More important people:

-Keyes & Likins , 1946 experimental hamster periodontitis

-Waerhaug, , 1952 examination of extracted human teeth

-Löe et al. 1965, experimental human gingivitis

-Schroeder & Lindhe 1975 ligature-induced periodontitis in beagle dogs

Non Specific Plaque Hypothesis

All dental plaque microorganisms thought to be equally capable of causing periodontal pathology if present in high enough numbers.

Microbial Specificity In Periodontitis

Only a limited number of plaque microorganisms appear to act as periodontal pathogens out of the approximately 500 different bacterial species that can colonize subgingival sites.

Specific Plaque Hypothesis

Certain dental plaque microorganisms are specifically capable of causing periodontal pathology – disease related more to quality of plaque composition rather than merely plaque quantity.

Ecological Plaqye Hypothesis

Certain dental plaque microorganisms are preferentially selected & increase as a result of changes in local oral environment which adversely alters normal protective microbial homeostatic mechanisms.

More important people

Listgarten (1976) plaque ultrastructure in health & disease - more gram negative rods and spirochetes in periodontitis

Slots (1976-1980) *Aggregatibacter actinomycetemcomitans* in aggressive periodontitis (LJP) *Porphyromonas gingivalis* in chronic (adult) periodontitis

Tanner (1979) and Socransky/Haffajee (1980s) specific microbial species associated with progressive attachment loss (disease activity)

Just remember…

Mostly gram + microflora & facultative anaerobes = perio health

Mostly gram – microflora & obligate anaerobes = periodontitis

**Lecture 8**

***Pathogenesis of Plaque Related Periodontal Disease I***

-when the pathogenic microbial challenge is greater than (or outweighs) the host response, the outcome is **disease progression**.

-the bacterial factors can be described as bacterial load and bacterial composition (viruses also play a role)

- host response factors consist of inflammatory response and immunological response. These factors can change based on smoking, diabetes, drugs, etc.

These factors can be modulated by:

Site-based risk factors- such as plaque, retentive overhanging margins.

Subject-based risk factors- such as neutrophil function

Host defense responses to pathogenic microbial challenge:

1. limit infection to gingival crevice and/or surrounding tissues,

2. regulate remodeling of connective tissues with cycles of destruction & reconstruction

The host immune response:

-Distinguishes “self” from “nonself”

-Normally protects host from infection, but *can be detrimental* to host as in allergies (hypersensitivity) and tissue damage due to autoimmunity

Innate immunity

-Has no memory, no increase in response with repeated exposure -

- Examples: skin/mucosa barrier, lysozyme, phagocytosis (macrophage or PMN), complement-mediated lysis (alternative pathway), NK (natural killer) cells

The immune system and innate immunity protecting against perio pathogens

• gingival mucosa/ sulcular & junctional

epithelium barrier

• phagocytosis

 engulf and destroy bacteria

• complement

 facilitates phagocytosis & lysis of bacteria through opsonization

• lysozyme in saliva

 causes nonspecific bacterial lysis

• NK cells

 causes nonspecific killing of tumor or viral viral-infected cells

“immune clearance” of biofilm 🡪 perio health

“immune frustration” (can’t clear biofilm) 🡪 chronic inflammation 🡪 soft tissue and alveolar bone destruction 🡪 tooth loss (how body resolves infection)

* + Non-Specific Host Defense Mechanisms – The First Line of Defense
    - Saliva mechanically cleanses, buffers bacterial acids, and contains inhibitors of microbes
      * Lysozyme – hydrolytic enzyme against bacterial cell walls
      * Lactoperoxidase-thiocynate system – reduces lysine and glutamic acid which are bacterial growth factors
      * Myeloperoxidase from leukocytes – kills bacteria and inhibits microbial attachment to hydroxyapatite
      * Secretory IgA antibodies – high levels are normally in saliva
      * Antiproteases
      * Defensins – small cationic antimicrobial peptides in saliva that kill a wide range of bacteria and some viruses
        + Alpha – found in neutrophils
        + Beta – produced by epithelial cells
      * Gingival Crevicular Fluid (GCF) – inflammatory exudates from serum/blood
        + Little or none present in healthy mouth
        + Permeates through junctional and sulcular epithelium
        + Carries protective neutrophils, antibodies, enzymes, and cytokines
        + Flow increases with daytime, ovulation, pregnancy, oral contraceptives, mechanical stimulation (chewing, tooth brushing), smoking and after trauma
        + Collected commonly on paper strips

Small amounts - .43-1.5μL for a gingival index less than 1

Volume measured with transducer or Periotron instrument which detects change in flow of an electronic current with wetness of paper strip

* + - * Leukocyte Migration into Gingival Sulcus – found even in healthy mouth
        + Major protective mechanism against microbial plaque
        + Increases with inflammation
        + Neutrophils are initial leukocyte in acute inflammation
      * Neutrophil response to microbial biofilm infection
        + Low numbers in healthy mouth
        + Increased in acute inflammation with potential destructive effects on Periodontium if unable to resolve infection (frustrated immunity)
        + Grow to full maturity in bone marrow
        + Circulate in blood and migrate into tissues
        + Comprise 40-70% of circulating WBC
        + Lifespan of 7-20 hours
        + Function in phagocytosis and bacterial killing by hydrolytic enzymes and oxygen-dependent mechanisms
        + Migration:

Chemotatic attraction

Margination – neutrophils adhere to vascular endothelium

Diapedesis – neutrophils migrate across endothelium

Neutrophil Adhesion molecues – expression upregulated during inflammation

CD18 is one type – absent in persons with leukocyte adhesion deficiency (LAD-1) – get severe early onset periodontitis

* *Porphyromonas gingivalis* may inhibit neutrophil recruitment by downregulating neutrophil transepithelial migration from gingival tissues into periodontal pockets.

Primed neutrophils have greater phagocytic activity and larger respiratory burst response upon interaction with bacteria

Respiratory burst – used to generate reactive oxygen species (ROS) which are cidal to bacteria but can also damage host tissues

* + - * + Binding to target microorganism:

Opsonization – coating of target particle with recognizable molecules to enhance phagocytic ingestion by neutrophils

Opsonin types – C3b (complement metabolite) and IgG antibody Fc surface receptors

* Complement system  comprised of 11 serum proteins in blood which aid in phagocyte recruitment, ingestion of pathogens by phagocytes, & mediating vascular responses.
  + - * + Neutrophil Morphology

Azurophilic granules – primary lysosomes

Myeloperoxidase

Proteases, including collagenase and elastase

Other hydrolytic enzymes, lysozyme

Specific granules – NADPH oxidase (in membrane of granule and cell)

Collagenase, lysozyme, lactoferrin

Neutrophil antimicrobial systems

* + - * + Oxidative – toxic oxygen metabolites are formed from oxygen reduction (NADPH oxidase, myeloperoxidase, hydrogen peroxide
        + Nonoxidative – membrane-disruptive peptides (lysozyme, lactoferrin, elastase, calprotectin)
        + Inflammation – redness, swelling, heat, loss of function, pain

Acute inflammation – sudden onset, short duration, exudative reaction with fluid, serum proteins, and leukocyte migration to area of injury, neutrophils first to appear, pain usually marked

Chronic inflammation – long standing, proliferative response with proliferation of fibroblasts and vascular endothelium and influx of chronic inflammatory cells (lymphocytes, plasma cells, macrophages), minimal pain, may occur without acute phase

Stages:

Sublethal injury – initiates reaction

Hyperemia – get dilation of capillaries and venules

Increased vascular permeability – leads to inflammatory exudates containing neutrophils, macrophages, and lymphocytes

Neutralization of initiating factor or irritant

Containment of inflammation – area is circumscribed by new fibrous connective tissue

Initiation of repair

Chemical mediaters of vascular response

Histamine – important in early phases of acute

Released from mast cells, contracts endothelial cells to increase vascular permeability

Caused by mechanical trauma, radiant energy, ultraviolet radiation, bacterial toxins

Kinin system – vasoactive agents inducing arteriolar dilation and increasing venule permeability by increasing gaps in between endothelial cells

10 minute duration

Acts in delayed phase of vascular permeability

Fibrinolytic system – active in later stages of acute response, leads to plasmin production

Prostaglandins and leukotrienes – produced by neutrophils and macrophages

Responsible for prolonged phases of vascular permeability

Complement system – comprised of 11 serum proteins in blood which aid in phagocyte recruitment, injestion of pathogens by phagocytes, and mediating vascular responses

* + Specific Host Defense Mechanisms – The Second Line of Defense
  + Acquired Specific Immunity- has memory, more rapid w/repeated exposure
    - Humeral – B cell mediated 🡪 plasma cell 🡪 antibodies made
    - Cellular – T cell mediated 🡪 kills tumor and viral cells
    - T-helper cells can help both B and T cells 🡪 lymphokines 🡪 macrophage activation
    - Antibodies – proteins that bind tightly to targets
      * Made of two identical light chains and two identical heavy chains-Highly specific
      * Can opsonize bacteria and facilitate phagocytosis
      * Can activate complement system
      * Can inhibit bacteria from sticking to host tissues

**Lecture 9**

Plaque-related Perio II

Periodontal disease and the immune system response is still not well understood.

It is likely that some bacteria in plaque cause direct damage to periodontal tissues via their virulence factors (i.e., proteases from *Porphyromonas gingivalis gingivalis*).

In addition, the immune system response may be involved in contributing to some periodontal destruction ( immunopathology).

Immune responses can be either:

- Specific (for pathogen) or

– Non specific- may be deleterious mostly protective, especially if the response is exaggerated or hyperactive

Mechanisms for immunopathology in perio disease

Theory #1- hyper and hypoactivity of PMNs (neutrophils)

-PMNs mainly found in junctional epithelium & subgingivally

-Have hydrolytic enzymes that kill bacteria after phagocytosis (i.e., acid hydrolases

hydrolases, collagenase) – overstimulated. collagenase can leak out of cell and damage periodontal tissues, especially if PMNs are overstimulated.

-can be oxidative (toxic oxygen metabolites formed from oxygen reduction) or nonoxidative (membrane disruptive peptides)

-PMN chemotaxis defect found in 60-70% of patients with localized and generalized forms of aggressive periodontitis.

-PMN adhesion defects also associated with aggressive periodontitis.

-certain periodontal pathogens produce toxins that can decrease PMN function *( actinomycetemcomitans* JP2 strains secrete leukotoxin).

***Bottom Line***

hyperactivity of PMNs can cause damage to periodontal tissues, and hypoactivity of PMNs can lead to reduced protection of the periodontium from periodontal pathogens capable of causing periodontal tissue damage.

Theory #2

-Stimulation of monocytes/ macrophages by gram negative bacterial LPS ( endotoxin).

* Monocytes and macrophages are stimulated by LPS from gram-negative bacteria and can secrete cytokines:

IL-1, PGE2 , TNF - can increase bone loss

IL-1 can increase secretion of PGE & fibroblast collagenase, affect PDL

IL-6 - increases B cell differentiation into plasma cells

IL-8 - i ncreases PMN chemotaxis

* Macrophages from patients with periodontitis secrete much higher levels of IL-1and PGE2 when stimulated with LPS in vitro (indicating a possible genetic susceptibility trait).

Theory #3

- Polyclonal activation of B cells by gram negative bacterial LPS ( endotoxin)- leading to large numbers of locally produced, non specific antibodies that may react with host tissues, leading to periodontal destruction.

-*Polyclonal Activation of B cells* Refers to non specific activation of many B cells having specificity for many different antigens. This may be induced by many factors as LPS ( lipopolysaccharide from gram negative bacterial cell walls) many gram negative bacteria are potent polyclonal B cell activators**.**

-Antibodies may be locally produced with irrelevant specificity -do not bind to the molecule that elicited the response.

-most antibodies in periodontal tissues are **not** specific for periodontal pathogens.

-The result could be opsonization of host tissues via autoantibody reactive with the periodontal tissues, such as collagen in PDL. This would allow for destruction of host tissues by phagocytosis. Hyperactive B cells may also be a source of IL-1and contribute to bone loss.

*Bottom Line* – non-lymphocyte hyperactivity is non-specific, non protective, and probably causes damage to the periodontium.

Theory #4

-Excessive activation by T – helper cells of macrophages, B cells and T cells leading to periodontal bone loss and tissue destruction.

-T-helper cells secrete lymphokines which can activate macrophages. If excessive macrophages, then cytokines are at high levels and may include prostaglandins, E2 (PGE2), IL-1; all of these can cause bone loss

Theory #5

-elevated T suppressor cells (CD8). Suppress protective effects of CD4 cells and may contribute to non-specific B-lymphocyte stimulation.

-pts will have a decrease CD4/CD8 ratio

-*Bottom Line* – Some type of T cell/B cell deregulation is occurring in periodontitis

Theory #6

-NK (natural killer) cell recognition of tissue- bound autoantibodies leading to periodontal tissue destruction.

-If autoantibody is present that binds to PDL fibroblasts, then the PDL fibroblasts could be killed by NK cells (antibody dependent cell cytotoxicity -ADCC).

NONE OF THESE POSSIBLE MECHANISMS HAVE BEEN PROVEN. ETIOLOGY OF PERIODONTITIS IS LIKELY MULTI-FACTORAL.

Destructive Periodontal Disease

-loss of crest alveolar bone height, loss of periodontal attachment, apical migration of junctional epithelium

Direct effects of specific bacterial plaque species acting as periodontal pathogens:

proteolytic enzymes, collagenase collagenase, toxic metabolic by products (hydrogen sulfide), and lipopolysaccharide (LPS; endotoxin the cell walls of gram negative bacteria) have direct adverse impact on periodontal tissues, leading to inflammation, connective tissue degradation, and bone resorption

Indirect effects: inflammatory reactions 🡪 tissue damage 🡪release of neutrophil enzymes that can destroy periodontal tissues

Activation of host monocytes, lymphocytes, and fibroblasts by plaque bacteria LPS promotes release of pro inflammatory cytokines and mediators (such as interleukin 1, tumor necrosis factor alpha, prostaglandin E2) they in turn promote release of bone and extracellular matrix destroying matrix metalloproteinases (including collagenase) from host cells.

Bacteria 🡪 direct tissue damage

Trigger of host cells releasing pro-inflammatory cytokines 🡪 indirect tissue damage

It seems as though host response is responsible for most of the tissue damage.

Occurrence of Periodontitis

Ginigivititis ALWAYS precedes periodontitis

NOT ALL gingivitis becomes periodontitis

Exact pathologic mechanisms of periodontitis are not fully understood

1. Continuous model of disease progression shows that there is a linear breakdown of periodontal attachment that occurs over time (classic model)
2. Episodic model of disease progression- sporadic periods of disease progression followed by extended periods of inactivity.

Both of the previous models can occur in different pts, at different sites within the same pt, or at different times within the same pt.

Loe studied Sri Lanka tea laborers w/ no dental hygiene and no dental care. Found 3 rates of destructive disease progression:

-8%- rapid progression- yearly AL of 0.1 to 1.0 mm

-81%- moderately aggressive periodonititis- yearly AL 0.05 to 5.0 mm

-11%- minimal or no progression – yearly AL 0.05-0.09mm

Period of exacerbation- increased inflammation due to plaque 🡪 progressive tissue and bone loss (episodic)

Period of quiescence- reduced inflammation and no tissue or bone damage

Site specificity of periodontitis

Destruction doesn’t occur in all areas of the mouth at the same time- happens on a few teeth at a time or on some surfaces of a given tooth at a time.

Destruction often found next to tooth surfaces with little or no periodontal breakdown.

**Lecture 10**

***Plaque-Associated Gingivitis***

* Clinically, normal human gingiva contains only low numbers of inflammatory cells, consisting predominantly of T cells with very few B cells or plasma cells
  + In gingivitis, there is coronal swelling of inflamed tissue with no periodontal attachment loss
  + Increased size of subgingival compartment – changes local environment favoring anaerobic bacterial plaque growth
  + Clinically, there is bleeding on probing
* Course and Duration
  + *Acute Gingivitis* – has sudden onset, short duration, possible pain
    - Clinically – diffuse tissue puffiness, sloughing, vesicle formation
    - Histologically – diffuse edema of acute inflammation, necrosis with pseudomembrane function, inter- and intracellular edema with cell wall rupture
  + *Recurrent Gingivitis* – reappears after being eliminated by treatment or on its own
  + *Chronic Gingivitis* – slow in onset, has long duration, usually painless, most common type of gingivitis, usually a fluctuating disease (inflammation persisting and resolving at different time points)
    - Clinically – marginal and interdental gingival are smooth, edematous and discolored; soggy tissue puffiness that pits on pressure or firm, leathery consistency
    - Histologically – inflammatory fluid and cell infiltration or fibrosis and epithelial proliferation
* *Gingival bleeding* – on probing is one of the earliest clinical signs of gingivitis
  + Appears earlier than redness or other visual changes
  + More objective
  + Intensity of inflammation regulates BOP severity and ease of provocation
  + BOP sites have inflammatory cell rich and collagen-poor tissue
  + Chronic gingival bleeding – caused by chronic inflammation from microbial plaque or mechanical trauma
    - engorged capillaries and thin epithelium permit rupture upon slight stimuli
  + acute gingival bleeding – may be spontaneous
    - caused by injury, ANUG, some systemic medical disorders (Vit C deficiency, platelet disorders, Vit K deficiency in liver disease, hemophilia, leukemia, multiple myeloma) and excessive doses of some medications (aspirin, anticoagulants)
    - severity of the bleeding and the ease of its provocation depend on the intensity of the inflammation
* Gingival Color – color change is important clinical sign of gingival disease
  + Red color caused by **increase vascularization and reduced epithelial keratinization in** disease (most intense with acute inflammation)
  + Blue hue related venous stasis in chronic inflammation
  + Color changes start at interdental papillae and gingival margin, then spread to attached gingiva
  + Black line following contour of gingival caused by heavy metal exposure to bismuth, arsenic and mercury
  + Bluish red or deep blue linear pigmentation of margin cause by lead (burtonian line)
  + Violet linear pigmentation of margin caused by silver (also get diffuse blue-gray color on oral mucosa)
* Suspension of Oral Hygiene – Experimental Gingivitis Model
  + 12 people abstained from any oral hygiene; developed gingivitis in 10-21 days with the mean GI score going from .27 to 1.05
  + Inflammation completely resolved within 1 week of resuming oral hygiene
  + First study demonstrating cause and effect relationship between plaque and gingivitis
  + Local inflammation will persist as long as the biofilm is present adjacent to gingival tissues
  + Increased numbers of plaque microorganisms (particularly spirochetes and motile rods) as a result of impaired oral hygiene associated with onset and duration of gingivitis
  + Cocci always present but amount of motile rods followed by spirochetes increased as oral hygiene decreased
  + More gram- anaerobic bacteria in gingivitis than in perio health-Increase from 15% to nearly 50%
  + Total number of subgingival bacteria reached a maximum at 3 days
  + Get a 20% decrease in *Actinomyces* species in dental plaque and rapid growth of *Fusobacterium periodonticum, Eubacterium nodatum, Eikenella corrodens, Preotella intermedia*, motile rods and *Treponema* species (spirochetes)
* Gingivitis changes relative to age
  + Older people get gingivitis more rapidly and severely than younger people in presence of poor plaque control
  + However, both old and young people heal equally well when oral hygiene is resumed
* Development is in 3 stages (based on histopathologic evidence)
  + 1 – initial lesion
    - Subclinical (not visually seen)
    - Occurs 2-4 days after plaque growth as an acute inflammatory response
    - Get vasculitis and dilation of microvasculature subjacent to junctional epithelium
    - Increased PMN migration and GCF (Gingival Crevicular Fluid) flow into junctional epithelium (JE), CT and sulcus
    - PMNs are predominant immune cells
    - Increased crevicular leukocyte (PMN) migration correlates w/increased gingival crevicular fluid into gingival sulcus
    - 5-10% inflammatory infiltrate in connective tissue
    - Extravascular serum protein (fibrin)
  + 2 – early lesion
    - Erythema and BOP (Blood on Probing) clinically seen
    - Occurs after 4-7 days after plaque left undisturbed
    - Get vascular proliferation
    - **Lymphocytes (75% mainly T cells)** dominate inflammatory infiltrate subjacent to JE
      * here inflammatory response starts to change
      * **T-cells not as bad as B-cells**
    - JE remains densely infiltrated with PMNs
    - Fibroblasts decrease collagen production and show cytopathic alterations, rete pegs in JE, JE basal cells start to proliferate
    - 15% inflammatory infiltrate in connective tissues
    - 60-70% collagen loss in infiltrated area
    - primarily circular and dentogingival ribers
    - **\*\* primary lymphocyte response in early gingivitis lesions mainly involve T-cells-particularly Th1 cell subset (T helper 1). Th1 cells promote cell-mediated immune responses and suppress B cells and plasma cells. (contrast-Th@ cells induce B cell immune responses which is bad). If you get Th1 cells, you don’t get periodontitis.**
  + 3 – established lesion
    - Moderate-severe inflammation, no bone loss, more CT loss
    - Occurs after 14-21 days and can be long lasting without progression
    - Get vascular proliferation and blood stasis
    - Plasma cells and B lymphocytes dominate inflammatory infiltrate in JE and CT
    - Antibodies in JE and extravascular CT
    - Proliferation, lateral extension of JE, pocket epithelium forms
    - Rete ridges from JE, widened JE intercellular spaces, increased collagenase enzyme levels in GCF
    - 2 types:
      * Some remain stable and do not progress for months or years
      * Others become more active and convert to progressively destructive lesions with loss of perio CT attachment
    - Inverse relationship between number of inflammatory cells infiltrating gingival CT and number of intact supracrestal collagen bundles in gingival tissues
    - The more inflammation, the lesser number of intact collagen bundles
    - Established lesion and advanced lesion (periodontitis) have same histological characteristics except in advanced lesion, the extension of the lesion causes bone loss and attachment loss. (into bone and PDL)
    - **\*\*it’s proposed that strong innate immune responses lead to high levels of IL-12 produced by PMNs and macrophages, which in turn leads to a Th1 response, cell-mediated immunity, protective antibody formation, and a stable gingivitis lesion**.
    - **\*\*contrast- poor innate immune responses by PMNs and macrophages result in polyclonal B cell activation is assoc w/ a Th2 response, production of non-protective antibody formation, and therefore, progressive periodontal disease.**

***How is gingivitis treated?***

Clinical Dx of plaque-induced gingivitis:

-inflammation of the gingival in the absence of clinical periodontal AL, with redness & edema of gingival tissues, BOP, presence of plaque and/or calculus, no radiographic evidence of bone loss

Therapeutic goals:

* Establish gingival health by eliminating plaque, calculus, and plaque-retentive factors.

Treatment considerations: contributing systemic risk factors:

- Diabetes, smoking, certain perio bacteria, aging, gender, genetic predisposition, certain systemic disease causing immunosuppression, stress, nutrition, pregnancy substance abuse, HIV, certain meds

Treatment Plan for Active Therapy

* + - \*\*Patient education\*\* and customized oral hygiene instructions
    - Debridement of teeth to remove plaque and calculus
    - Adjunctive antimicrobial therapy useful only for patients not able to adequately perform traditional mechanical oral hygiene procedures (only occasionally used)
    - Removal of plaque-retentive factors (overhangs or open margins, over or under contours crowns, open contacts, caries, etc)
    - Surgical correction of gingival deformities that hinder plaque control (very rarely needed)
    - Lastly, re-evaluation
      * Outcomes Assessment – get satisfactory results with…
        + Reduction of clinical signs of gingival inflammation
        + Stability of clinical perio attachment levels
        + Reduction of clinically-detectable plaque to level compatible with gingival health
      * Outcomes Assessment – Non-response may be due to…
        + Patient non-compliance with home plaque control
        + Systemic disease
        + Residual supra or subg calculus
        + Plaque retentive restorations
        + Lack of compliance with coming to the dentist
      * Outcomes Assessment
        + Consider additional oral hygiene instructions, alternative methods of plaque removal, medical consultation, additional mechanical tooth debridement, increased frequency of prophylaxis, microbial assessment, continuous monitoring & evaluation.

\*Keep bringing them back until the gingivitis is gone, otherwise you may miss a medical problem that’s causing the gingivitis and not plaque.