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**Inflammation**
The Oral Systemic Connection

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**WHAT IS AN EXPERT?**

- A person who lives more than 50 miles away
- A person that carries a Briefcase
- A person that has a PP presentation (slides)
- A person who knows everything about something and nothing about anything else.
- An expert is a person who has made all the mistakes that can be made, in a very narrow field.
- A person who makes three correct guesses, consecutively
- A person who knows more and more about less and less, until eventually knowing everything about nothing.

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**FOCAL INFECTION HYPOTHESIS**

- Principles of infectious disease by Koch and Pasteur-Mid 19th Century
- Invasion of bloodstream by bacteria from a localized infection could spread to distant organs and tissues
- Tonsillectomies, Appendectomies, full mouth EXT's
- 20th Century, Fell out of Favor
- Unable to correlate with confidence a particular systemic disease with a preceding oral infection or dental procedure
- Early 1990s, re-ignited with increasing evidence and greater emphasis on Inflammation as the root cause of certain diseases.
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**HISTORICAL ORAL-SYSTEMIC ASSOCIATION**

The dental profession considered systemic diseases in the context of their influence on the predisposition, severity, and progress of Periodontal Disease.

The recognition of Inflammation as the underlying source of many systemic diseases has led to considering a two-way relationship between systemic disease and periodontal disease.

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**WHAT IS INFLAMMATION?**

- Latin, Inflamma, “I ignite, set alight”
- A non-specific protective cellular and biochemical response designed to rid the body of the initial cause of cell injury and the consequences of that injury.
- Without this process, we would not survive.

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[Image of teeth and gums]
TYPES OF CELL INJURY THAT TRIGGER INFLAMMATION

- Trauma
- Genetic defects
- Physical and Chemical Agents
- Radiation
- Tissue Necrosis
- Foreign Bodies
- Immune Reactions
- Microorganisms*
- Allergy
- Malignancy

CARDINAL SIGNS OF INFLAMMATION

- Rubor (Redness) ↑ Vascularity
- Calor (heat) ↑ Blood Flow
- Tumor (swelling) △ Fluid Exudation
- Dolor (pain) △ Chemical Mediators & Stretching of nerves
- Functio Laesa (loss of function)

* Microorganisms include microorganisms and viral infections.
INITIAL INFLAMMATORY PROCESS (ACUTE)

- Bacterial Biofilm (Plaque)
  - Production of organic acids, chemotactic peptides, Endotoxins, Protein Toxins
  - Penetrate superficial layers of sulcular epithelium
  - Production of biologically active mediators (Cytokines, Prostaglandins, TNF-α, matrix metalloproteinases, interleukins)
  - Recruitment of PMNs, ↑ Perm of gingival vessels, extravasation of plasma proteins
  - Tissues respond with antimicrobial peptides (Immunoglobulins)
  - Salivary defense systems flush area, bacterial aggregation factors, antimicrobial proteins

AS THE DENTAL BIOFILM MATURATES (CHRONIC)

- Stimulation of epithelium to produce bioactive mediators
- Recruitment of variety of cell types, including PMNs, T cells, Monocytes
- Signaling of underlying cells to produce pro-inflammatory cytokines
- Host responds → Antibodies
- Gingival inflammation and production of C-Reactive Protein (CRP), Fibrinogen, Complement (opsonization) by both local cells and the Liver
- In some people, continues to breakdown of PDL collagen and bone resorption (Periodontitis)
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DESIRED END RESULT OF INFLAMMATION

- **Regeneration**
  - When tissue damage is minor
  - Restores original tissue form and function

- **Repair**
  - Wound healing without original form and function
  - Occurs when there is extensive damage
  - Scar Formation

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SYSTEMIC EFFECTS OF INFLAMMATION

- **Fever**
- **Leukocytosis**
- **Arthritis** - Joints
- **Glomerulonephritis** - Kidneys
- **Vasculitis** - Heart and Blood Vessels
- **Atherosclerosis** - Blood Vessels
- **Diabetes** - Pancreas
- **Periodontitis**

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**POPULATION STATISTICS**

- Gingivitis 50-63%
- Mild PD 21%
- Moderate to Advanced PD 12%

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**GINGIVITIS AND INFLAMMATORY INFILTRATE**

- "Pristine Gingiva"
  - Virtually no inflammatory infiltrate, small subset of population comprises 1%
- Normal Healthy Gingiva
  - Minimal inflammatory infiltrate
  - (We doubt these conditions are clinically separable)
- Gingivitis
  - Multiplication biology, clinical S & S, significant inflammatory infiltrate
- Periodontitis
  - Extensive biofilm, anaerobes, gram-negative bacteria and Spirochetes
  - Significant inflammatory infiltrate

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**POSSIBLE PATHWAYS FOR SYSTEMIC MANIFESTATIONS**

- Bacteremia through Bacterial Translocation
- Systemic Dissemination of locally produced inflammatory mediators
- Provocation of Immune Response (autoimmune)
- Aspiration or Ingestion of Oral Contents into the GI or Respiratory Systems
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**DIRECT SYSTEMIC EFFECTS**

BACTERIAL TRANSLOCATION (BACTEREMIA)

- Inflammation → ulceration of gingival sulcular epithelium → bacterial translocation
- Minor disruptions to gingival integrity occurs during daily activity of chewing, speaking, and rubbing, not just during dental procedures
- PDL area is estimated to be 72 cm² = Post - it note
- 50% attachment loss = 15-40 cm² (1/3), 4-5 mm pockets = 10-20 cm² (1/4)
- Increased risk of bacterial translocation
- Promotes continual, low grade, chronic bacteremia

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**PERIODONTAL / PERI-IMPLANT DISEASE**

- Multifactorial process triggered by infection by Gram-Negative bacteria
- (P. Gingivalis, T. Forsythensis, A. Actinomycetemcomitans)
- Formation of Pellicle-adherent sub-gingival bacterial biofilm
- Biofilm: Organisms form a primitive, yet complex system of communication, intercellular transport, and commensalism. Bacteria here are inaccessible to host defense mechanisms and therapeutic measures.
- 300+ different organisms in biofilm
- Co-factors
- Host tolerance, smoking, DM, poor oral hygiene, socioeconomics, race, etc
HOST RESPONSE ↔ INFLAMMATION

- Host with adequate OH and normal biochemical defenses
  - Chronic Inflammatory Response
  - PMNs patrol the gingival crevicular space and phagocytise bacteria
  - IgG, non-secretory IgA, Complement, are present in the GCF

- Host with insufficient qualitative and quantitative response + poor OH
  - Biofilm persists
  - Elaborates noxious substances that directly and indirectly recruit monocytes and lymphocytes
  - Host attempts to wall off infection by destroying tissue adjacent to infection site
  - Fibrotic response is induced
  - This response has local and systemic inflammatory manifestations
POSSIBLE MECHANISMS FOR THE DEVELOPMENT OF CARDIOVASCULAR DISEASE (ATHEROSCLEROSIS) FROM ORAL INFECTIONS

- Circulating PMNs, Monocytes, and Lymphocytes
- Affect vascular endothelial lining
- Oxidation of LDL
- Monocytes → Macrophages → become “Foam Cells”
- Local Inflammation releases Mediators
- Extracellular Matrix is degraded by proteolytic enzymes → rupture
- Atherosclerotic lesion begins to bulge within the lumen of the vessel
- Extracellular Matrix is degraded by proteolytic enzymes → rupture
- Local bacterial translocation occurs directly affect atherosclerotic lesion

Most recognized and consistent markers of systemic inflammation and poor cardiovascular prognosis is the acute-phase protein called CRP.

AUTOIMMUNE RESPONSE AS A POSSIBLE MECHANISM FOR INFLAMMATION INDUCED CVD

- Most humans have immune reaction against microbial Heat Shock Protein 60 (HSP60)
- Antibodies against the bacterial HSP cross reacts with human HSP
- Causing autoimmune response
- Stimulating vascular injury and Atherosclerosis

PERIODONTAL DISEASE AND DIABETES MELLITUS

- Diabetes ↑ PD ↔ Periodontitis ↑ poor glycemic control
- Inflammation (referenced in Chapter 1)
- Research has shown chronic levels of inflammatory mediators in the GCF of poorly controlled diabetes patients can increase risk of cardiovascular disease
- Mortality in uncontrolled PD patients with an equivalent mortality challenge
- TDG has been shown to be higher in individuals with poor glycemic control
PERIODONTAL DISEASE AND ADVERSE PREGNANCY OUTCOMES

- Premature births
- Low birth weight
- Uterine contractions stimulated by Oxytocin (hypothalamus) and Prostaglandins produced by the placenta
- Chronic Infections → Inflammation → ↑ amniotic PGs → premature rupture of membranes and preterm labor
- Periodontal pathogens may also travel from the gingival sulcus to the placenta and stimulate preterm birth

TRANSLATING SCIENCE TO PRACTICE

- Understanding the association between oral and systemic health
- Reframe protocols
- Practice Periodontal Medicine
  - Comprehensive periodontal examination
  - Review of systems and Vital signs
  - Head and neck exam, X-rays, Probing,
  - Biological and Genetic Testing
- Identify risk factors
- Age, HBP, dyslipidemia, smoking, obesity, CVD, DM, pregnant women with poor OH
- Educating the patient on the Oral-Systemic Connection
Chair side periodontal kits provide immediate reports of the microflora associated with the disease compared to cumbersome and time-consuming traditional laboratory procedures.

Chair side periodontal test kits can be categorized as:

- **Microbiological test kits**
  - Omnimyco DNA, Evalusite (ELISA), Perioscan (BANA)
- **Biochemical test kits**
  - Perio 2000, Progno-Stik, Perio-Check, PerioWatch
- **Genetic kits**
  - PST (Periodontal Susceptibility Testing) Interleukin based

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**REFRAMING OUR APPROACH**

**Practice of Dental Hygiene**

**Past**

- Dental Plaque
- Bacterial Biofilm
- Emphasis on physical removal of plaque
- Emphasis on local gingival health
- Emphasis on oral hygiene
- Educating patient based on patient health

**Future**

- Dental Plaque
- Bacterial Biofilm
- Emphasis on biology of biofilm & host
- Emphasis on control of inflammation, local and systemic
- Emphasis on identification of systemic risk factors
- Educating patient on local and systemic consequences of poor oral health
- Biochemical methods of monitoring
  - Biological testing, GCF assays, saliva tests, blood tests, etc.

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**Practice of Periodontal Medicine**

**Past**

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**Future**

- Dental Plaque
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The dental profession does not get paid for Preventive Solutions

- Dental care traditionally based on procedures (2 fillings and a crown)
- Insurance companies pay for doing, not thinking!

- Psychologists paid for counseling, Attorneys paid for time, Physicians paid for thinking and diagnosing

- Current systems revolve around money

- Research Limitations in Oral Biology
  - Not life threatening/low priority research/progress slow
  - Research emphasis in areas having profit potential
  - Most research supported and conducted by for-profit companies
  - There is no money in prevention

- Emphasis on selling products with questionable efficacy
  - Which toothpaste should I use?
  - Which mouthwash should I buy?
  - Which mechanical toothbrush is best?

- Increasing awareness by our medical colleagues as to the oral-systemic connection
- Insurance companies have continued to push to think that there is no such connection in the mouth and it is just simply bacteria

- The dental profession’s self-image: “I’m not a doctor, I’m a dentist”