

Risk Factors for the Periodontal Diseases
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General references

- **Volume 32- Periodontal Risk Factors and Indicators, 2003**
- **Volume 43- Host Responses in Periodontal Diseases, 2007**
- **Volume 44- Human Disease and Periodontology, 2007**
- **Volume 50- Concepts, Controversies, Consensus and Conclusions, 2009**
- **Volume 53- Comparison of Chronic and Aggressive Periodontitis, 2010**
- **Volume 62- Learned and Unlearned Concepts in Periodontology, 2013**
- **Volume 64- Modifiable Risk Factors in Periodontal Disease, 2014.**
<http://onlinelibrary.wiley.com/doi/10.1111/prd.2013.64.issue-1/issuetoc>

RISK: The likelihood that a person will get a disease in a specified time period.

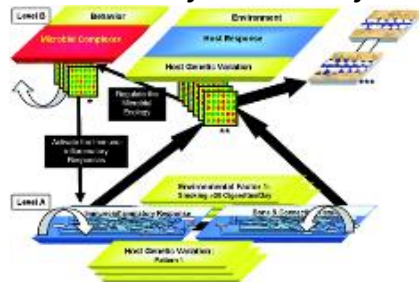
RISK FACTOR: The characteristics of individuals that place them at increased risk for getting a disease.

Risk factor is defined as “any characteristic, behavior, or an exposure with an association to a particular disease. The relationship is not necessarily causal in nature...” Garcia, Nunn, Dietrich, 2009

RISK INDICATORS: Probable or putative risk factors that have been identified in cross-sectional studies but not confirmed through longitudinal studies.

Need a susceptible host- risk factors contribute to, but do not directly cause, the initiation or progression of disease.

Current View of Risk Factors for the Periodontal Diseases



Local and Systemic Risk Factors for the Periodontal Diseases

Local Risk Factors

- **Plaque**
- **Calculus**
- **Anatomic factors**
- **Occlusal factors**
- **Restorative factors**
- **Other factors**

Biofilm (plaque) is necessary but not sufficient to produce periodontal inflammation.

'Socransky Criteria'

- **Association with disease;**
- **Elimination or suppression of the organism results in disease remission;**
- **Host response- detection of adaptive immune responses to the organism;**
- **Demonstration that the organism is pathogenic in an experimental animal;**
- **The organism should possess an array of virulence factors that can be linked to the pathogenesis of periodontal inflammation.**

Common Periodontal Pathogens

- **Aggregatibacter actinomycetemcomitans**
- **Campylobacter rectus**
- **Eubacterium nodatum**
- **Fusobacterium nucleatum**
- **Herpesvirus**
- **Peptostreptococcus micros**
- **Prevotella intermedia/nigrescens**
- **Porphyromonas gingivalis***
- **Streptococcus intermedius**
- **Tannerella forsythia (B. forsythus)***
- **Treponema denticola***
- **Current list of suspected periodontopathogens includes 20-30 bacterial species.**
- ***- late colonizers- "Red Complex"**

Concepts of Periodontopathogens

- *Lists of specific bugs.*
- *Sometimes use the eradication of a specific bacteria as a primary study outcome- is this valid based on the polymicrobial nature of the infections?*
- *Problematic because the bacteria do not act in isolation.*
- *Still do not know EXACTLY which bacteria(s) and their relationships initiate and cause progression of disease.*
- *Periodontal diseases are polymicrobial infections.*
- *This may be the reason that routine microbial testing appears to have limited clinical utility.*
- *Pathogens may be found in low levels in clinically healthy people. Concept of healthy biofilm and pathogenic biofilm.*
- *Human microbiome is being characterized as a dynamic organ system.*
- *How do viruses affect the pathogenesis of specific bacteria? May alter immune response and disrupt homeostasis. Not necessarily cause and effect.*

Calculus Composition

- *Calcium*
- *Phosphorus*
- *Carbonate*
- *Na, Mg, K*
- *Hydroxyapatite ($Ca_5(PO_4)_3 \times OH$) is major crystal form in mature calculus. Whitlockite is the most common form in subgingival calculus.*
- *Also has octacalcium phosphate ($Ca_8H(PO_4)_3 \times 2H_2O$), whitlockite ($B-Ca_3(PO_4)_2$), and brushite ($CaH(PO_4) \times 2H_2O$).*

Calculus Mechanisms of Attachment

- *Secondary cuticle (organic pellicle that also calcifies).*
- *Mechanical locking into irregularities in cemental surface.*
- *Close adaptation of calculus undersurface depressions to unaltered cementum surfaces.*
- *Bacterial penetration of cementum (not universally accepted).*
- *Mandel- JCP, 1986- Excellent review on calculus. "Subgingival calculus contributes significantly in the chronicity and progression of the disease, even if it can no longer be considered as responsible for initiation."*
- *Greenstein- JP, 1992, JADA, 2000- Comprehensive reviews of scaling and root planing and other aspects of non-surgical therapy.*

Furcation Anatomy Bower RC, J Periodontol 1979;50:23-25 and 1979;50:366-374.

- ***81% of maxillary and mandibular first molars have furcation entrances \leq 1 mm.***
- ***58% of furcation entrances < 0.75 mm.***
- ***Curette widths range from 0.7-1.0 mm.***

Cervical Enamel Projections Masters DH, Hoskins SW. J Periodontol 1964;35:49-53.

- ***Cervical enamel projections were found in > 90% of mandibular isolated furcation involvements.***

Restorative Factors

- ***Subgingival margins***
- ***Overhangs***
 - ***Lang- JCP 1983- debt-ridden dental students- 1 mm overhangs harbored black-pigmented Bacteroides even with good plaque control.***
 - ***Jeffcoat and Howell- JP 1980- the more severe the periodontal disease, the greater the role of the overhang appeared.***
 - ***Brunsvold- JCP 1990- at least 25% of restorations and 33% of patients had overhangs....and he was optimistic!!!***
 - ***Pack- JCP 1990- 56% of restorations had overhangs, 32% of pockets associated with overhangs bled.***
 - ***Jansson- JCP 1994- "The influence of a marginal overhang on pocket depth and attachment loss decreases with increasing pocket depth."***
- ***Inadequate embrasures***
- ***Open margins***
- ***Marginal ridge relationships***
- ***Root surface caries***

Review Article: Detection of localized tooth-related factors that predispose to periodontal infections. Matthews DC, Tabesh M. Periodontol 2000, 2004;34:136-150.

Local Tooth-related Factors

- ***Molars***
 - ***Furcations***
 - ***Root trunk length***
 - ***Size of furcation entrance***
 - ***Bifurcation ridges***
 - ***Root concavities***

- *Cervical enamel projections*
- *Premolar concavities*
- *Overhanging restorations*
- *Subgingival margins and biologic width*
- *Restorative materials*
- *Prostheses- TKPs. Increased mobility, inflammation, and pocketing around abutments.*
- *Crowding*
- *Vertical root fractures*
- *Mucogingival deformities*
- *Adjacent hopeless teeth.*

Systemic Disease Overview- Risk Assessment in Clinical Practice. Ronderos M, Ryder MI. Periodontol 2000 2004;34:120-135.

- *Behavioral risk factors*
 - *Smoking*
 - *Compliance*
- *Systemic risk factors*
 - *Diabetes and glycemic control*
 - *HIV infection*
- *Systemic risk factors*
 - *Osteoporosis*
 - *Familial and genetic risk factors*
 - *Psychological factors*
 - *Aging*
 - *Microbiological risk factors*

Diabetes and Periodontal Disease

Potential Pathogenic Mechanisms in Periodontally Related Destruction- "Expression of RAGE is enhanced in diabetics. AGE-EC RAGE interaction results in a shift to favor clot formation, increased monolayer permeability, and enhanced expression of VCAM-1 and IL-6. Also see increases in IL-1, IL-8, and TNF-a." E. Lalla

6 Complications of Diabetes

- *Cardiovascular disease*
- *Kidney disease*
- *Eye complications*
- *Neuropathy*
- *Foot and skin complications*
- *Periodontal disease- Loe- 1993*

Periodontal Disease with Poor Diabetic Control

- ***Genco Group- Pima Indians which have the highest incidence of Type 2 diabetes, >50% of adults. Found that poorly-controlled diabetics had significantly more attachment loss and bone loss than well-controlled diabetics or non-diabetic controls. Smoking also contributed. Also found that treatment of perio disease may affect metabolic control.***

“Diabesity®” What is it, who has it, what can be done about it?

Metabolic Properties of Fat

- **Increases levels of C-reactive protein (CRP), a key inflammatory marker.**
- **Produces cytokines such as TNF- α , Il-6, and others.**
- **Has resident macrophages that proliferate as fat increases.**

Obesity and Inflammation

- **TNF- α**
- **Il-6**
- **Plasminogen activator inhibitor-1**
- **Angiotensinogen**
- **Vascular endothelial growth factor**
- **C-reactive peptide**

An Update on HIV and Periodontal Disease. Ryder MI. J Periodontol 2002;73:1071-1078.

- **HAART therapy- highly active antiretroviral therapies- reverse transcriptase inhibitors and protease inhibitors- viral loads may decrease to undetectable levels.**
- **With HAART, atypical HIV-associated oral lesions have decreased by 30%.**
- **Necrotizing disease suggests low CD4 counts.**
- **HIV patients have more AL than healthy patients.**
- **Periodontal treatment has not changed in 15 years.**

■ **HIV-infected individuals may exhibit the following:**

- **Linear gingival erythema**
- **Necrotizing ulcerative gingivitis/ periodontitis**
- **Severe localized periodontitis**
- **Severe destructive necrotizing stomatitis affecting gingiva and bone**

San Giacomo, et al. OOOO, 1990; Williams, et al. OOOO, 1990; Winkler, et al. 1996; Winkler, et al. JADA, 1989.

Hormonal Influences. Mealey BL, Moritz AJ. Periodontol 2000 2003;32:59-81.

- **Primarily estrogens and progestins affect gingival tissues.**
- **See selective overgrowth of *P. intermedia* by substituting estradiol and progesterone for menadione.**
- **Pregnancy gingivitis in 30-100% of pregnant females and 10% develop pyogenic granulomas.**

■ **Sooriyamoorthy and Gower. JCP 1989;16:201-208. A good review. High counts of *B. intermedius* (*P. intermedia*) have been observed in users of oral contraceptives and in the 2nd trimester. This is due to the competitive binding of progesterone and naphthaquinone, an essential nutrient for bacterial growth. See increased *P. intermedia* counts and pseudopockets, rather than attachment loss.**

Stress and Psychosocial Factors

Warren, KR, et al. Role of chronic stress and depression in periodontal diseases. Periodontol 2000 2014;64:127-138.

Stress and Depression

- **Psychoneuroimmunology- psychological stress as a co-factor in disease. Genco- financial strain and inadequate coping style.**
- **Chronic stress- a state of inflammation.**
- **Depression also elevates serum markers of inflammation.**

Boyapati L, Wang H-L. The role of stress in periodontal disease and wound healing. Periodontol 2000, 2007;44:195-210.

Review Article. Dongari-Bagtzoglou A. Drug associated gingival enlargement. An AAP Information Paper. JP 2004;75:1424-1431.

- **A MUST READ!**
- **Over 20 drugs cause enlargement.**
- **Prevalence info difficult to get- current thinking- phenytoin 50%, nifedipine 6-15%, CsA 25-30%.**
- **Enlargement of CT, collagen and ground substance. More fibroblasts controversial.**
- **Mechanism poorly understood.**
- **Fibroblasts react to IL-1B.**
- **Recurrence rate of overgrowth about 40%.**

Medications

- **Phenytoin**
- **Nifedipine, other calcium channel blockers**
- **Cyclosporin A**
- **Tacrolimus- (Prograf®)- 14% of subjects may have gingival overgrowth. (Sekiguchi, et al. 2007)**

Periodontitis Modified by Systemic Factors Medications- Anti-seizure drugs. Kinane D. Ann Periodontol 1999;4:54-63.

- **Some degree of gingival enlargement in 36-67% of patients- Klar, JPHD, 1973. May be higher in institutionalized patients- Hassel, et al. JCP, 1984.**
- **Labial gingiva more severely affected. Thorstensson, Swed Dent J, 1995.**
- **Valproic acid and vigabatrin may also cause gingival overgrowth. Katz, et al. JCP, 1997.**

Medications- Cyclosporin A

- **Acts solely on cell-mediated immunity**
- **Resembles phenytoin overgrowth clinically and histopathologically, is seen in 30% of recipients, related to serum concentration of drug- Seymour, et al. JCP, 1987.**
- **Combination of nifedipine and cyclosporin shows greater overgrowth than cyclosporin alone- Ellis, et al. JCP, 1999.**

Calcium Channel Blockers and Gingival Overgrowth

- **Dihydropyridines**
 - **Nifedipine (Adalat®, Procardia®)- 10-15%- often reversible with d/c of drug. Almost 80% of all CCB overgrowth reported cases.**
 - **Others (amlodipine- Norvasc®)- yes**
- **Others- rare overgrowth**
 - **Diltiazem (Cardizem®)**
 - **Verapamil (Calan®)**

- **Bepidil (Vascor®)**
- **Calcium-channel blockers- influence fibroblasts to overproduce collagen matrix and ground substance when stimulated by gingival inflammation- Ellis, JP, 1999.**
- **No link with periodontitis**
- **Similar to phenytoin overgrowth- Bullon, et al. OOOO, 1995.**

Alani A, Seymour R. Systemic medications and the inflammatory cascade. Periodontol 2000, 2014;64:198-210.

Medications and the Inflammatory Cascade

- **Steroids- good and bad- as medication, beneficial. As a result of stress (cortisol)- destructive.**
- **Cox-1 and Cox-2 inhibitors- have anti-inflammatory and perhaps anti-PD properties but may interfere with resolution molecules (Van Dyke).**
- **Low dose ASA and omega- 3 FA may have salutary effect on PD. (El-Sharkawy, et al. J Periodontol, 2010;81:1635-1643)**

Genetic Approaches- Michalowicz- JP, 2000- Looked at MZ and DZ twins. Calculated that adult periodontitis had a 50% heritability (half of the variance in disease in the population is attributed to genetic variance)

Kinane DF, Shiba H, Hart TC. The genetic basis of periodontitis. P2000 2005;39:91-117. Among other things, debunks the utility of IL-1 testing. Useful in only 30% of Europeans, 2.3% of Chinese, and low in African-American populations. Very good review.

Smoking and Periodontal Disease

- **Bergstrom, Preber Group- Several studies in JCP from 1987-2005. With other factors controlled for, found smokers had more bone loss than nonsmokers. One study was done in a group of dental hygienists with a high degree of oral hygiene. Also found that smoking affected therapy, causing less probe depth decrease. This was more evident after scaling the maxillary anterior segment. Rate of bone loss slows once a patient stops smoking. More calculus found in smokers- dose dependent.**

Smoking and inflammation: evidence for a synergistic role in chronic disease. Johansen, et al. Periodontol 2000, 2014;64:111-126.

Smoking and Inflammation

- **Significant increases in periodontopathogens in smokers.**
- **Negative impacts on leukocytes.**
- **Significant decrease in humoral immunity, esp. decreases in IgG.**
- **Impaired fibroblast function.**
- **Possible gene-smoking interactions- may be related to Il-1B and leukocyte function.**

Evidence for Smoking as an Etiologic Factor in Periodontitis. Criteria for Causation. Johnson GK, Hill M. J Periodontol 2004;75:196-209.

- **Strength of association- cross-sectional and case-controlled studies demonstrate a moderate to strong association between smoking and periodontitis**
- **Consistency- multiple studies of various designs have demonstrated this association**

- *Specificity- disease progression slows in patients who stop smoking compared to those who continue to smoke*
- *Temporality- Longitudinal studies show that smokers do not respond as well to periodontal therapy as non-smokers*
- *Biologic gradient- there is a dose-response effect in that heavy smokers have increased disease severity compared to light smokers*
- *Biologic plausibility- supported by tobacco's negative effects on microbial and host response parameters*
- *Coherence- the effects of smoking on periodontitis are consistent with our knowledge of the natural history of periodontal disease*
- *Analogy- periodontal effects of smoking are analogous to other adverse smoking-related general health effects*
- *Experiment- evidence not currently available*

Genco Group- 5 Major Risk Factors

- *Age*
- *Smoking**
- *Uncontrolled diabetes**
- *Bacteroides forsythus (Tannerella forsythia)*
- *Porphyromonas gingivalis*

****The double whammy!!!**

Medical Conditions Related to Periodontal Disease

- *Cardiovascular disease*
- *Pre-term low birth weight infants*
- *Rheumatoid arthritis*
- *Diabetes*
- *Pneumonia*

Is it causality, contributory, or coincidence???

Hill's Criteria to Accept a Causal Relationship

- *Biological plausibility*
- *Consistency of associations*
- *Strength of the association*
- *Temporal consistency*
- *Specificity of the association*
- *Consistency of the findings*
- *Dose-response effect*
- *Support from experimental evidence*

Calculating Odds Ratios

For example: If the incidence of oral cancer in a smoking population is 0.002 and in a nonsmoking population is 0.0004, the odds ratio is $0.002/0.0004 = 5$

Must have odds ratio over 3 to be meaningful.