


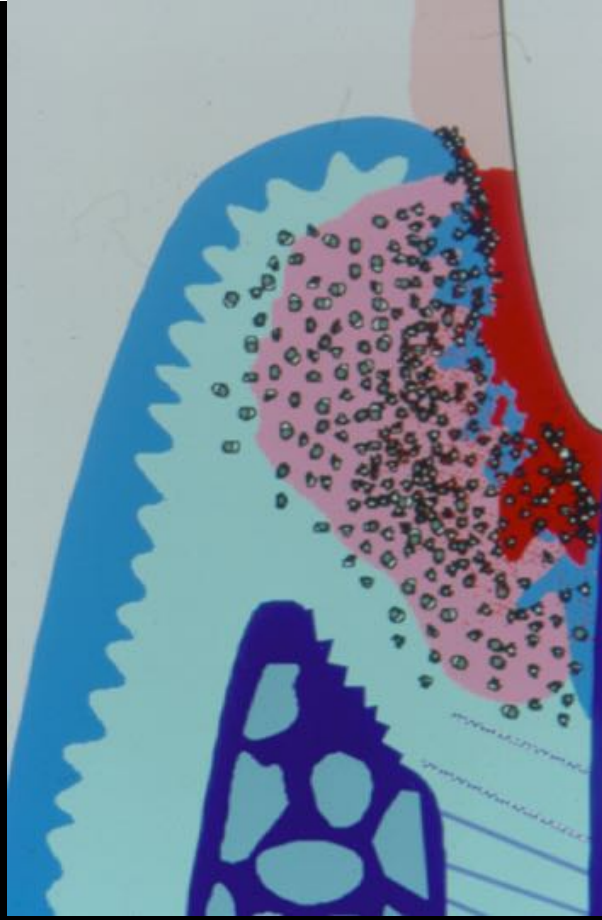
Risk Factors and Indicators Periodontal Diseases

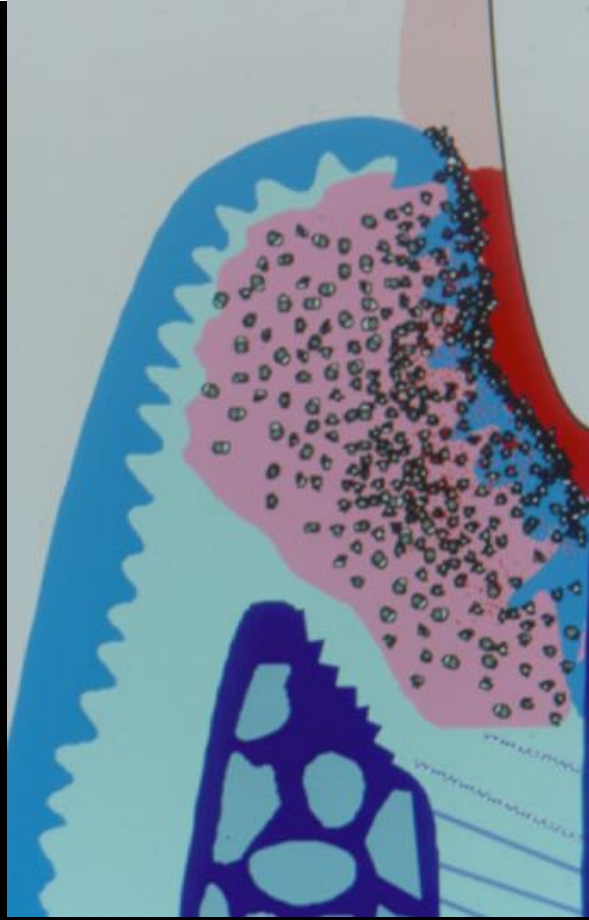
Principles of Periodontology II
PER 712

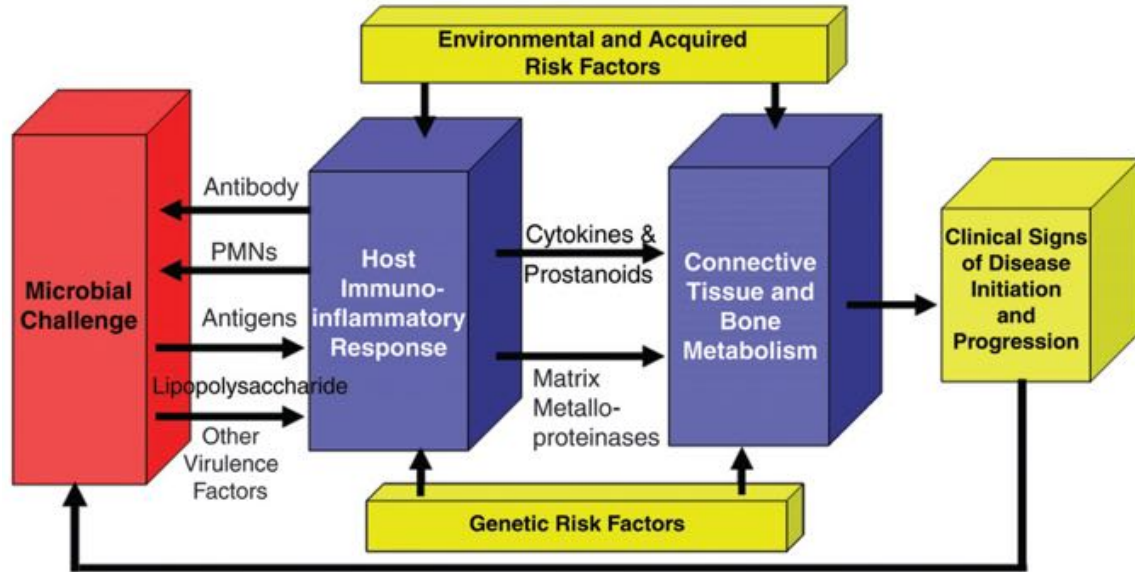
Dr. Phillip Marucha, DMD, PhD
Department of Periodontology

Lecture Objectives

- ▶ Describe the pathogenesis of periodontitis
 - ▶ Define terms related to risk assessment
 - ▶ Examples of risk factors, determinants, indicators, predictors
 - ▶ Genetics and periodontal disease
 - ▶ How to develop a clinical risk assessment protocol
- 









Page RC, Kornman KS. The pathogenesis of human periodontitis: An introduction. *Periodontology* 2000 1997;14:9-11.


Definitions

- ▶ **Risk:** probability that an individual will develop a specific disease in a given period - varies from individual to individual.
 - ▶ **Risk factors:** environmental, behavioral or biologic factors that, when present, increase the likelihood that an individual will get the disease.
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Risk Factors

- ▶ Identified through *longitudinal* studies of patients with the disease of interest.
 - ▶ Exposure may occur at a single point in time or over multiple times (separate or continuous).
 - ▶ The exposure must occur before disease onset.
 - ▶ Interventions can help mitigate risk factors.
- 

Common Disease Risk Factors

- ▶ Quantity and pathogenesis of microbial tooth deposits, including calculus
 - ▶ Tobacco consumption
 - ▶ Poorly controlled diabetes
 - ▶ Anatomic factors: furcations, root concavities, developmental grooves, cervical enamel projections, enamel pearls, etc.
 - ▶ Restorative factors: overhangs and subgingival margins
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Quantity and pathogenesis of microbial tooth deposits



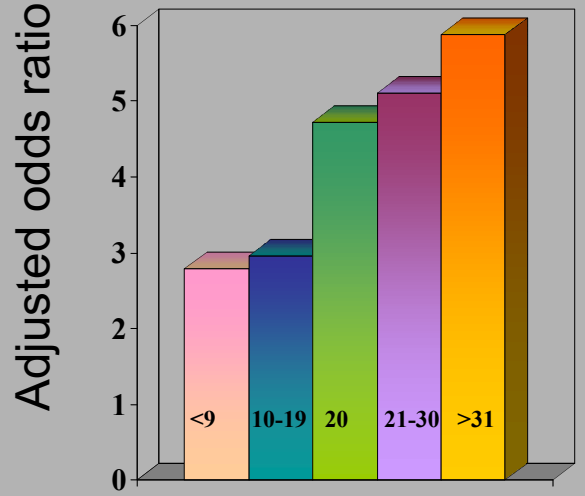


Tobacco

Odds Ratios of smokers developing periodontitis

| Location | O.R. | References |
|----------|---------|---|
| USA | 6.2 | Beck et al. 1990 |
| USA | 6.1 | Haber and Kent 1992 |
| USA | 4.75 | Grossi et al.1994 |
| Sweden | 2.6/8.4 | Bergstrom and Preber 1994/ Stoltenberg et al. 1993 |
| USA | 5.3 | Beck and Slade 1996 |

The risk of Periodontitis increases with increasing cigarette smoking



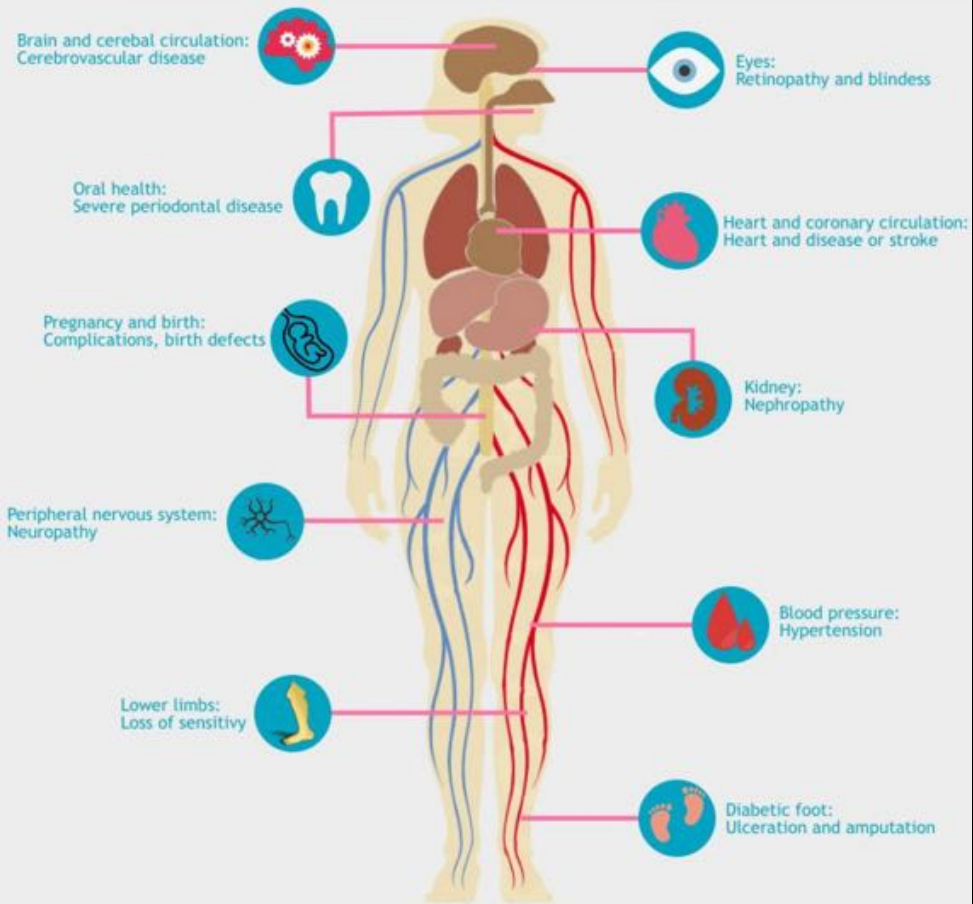
Number of cigarettes smoked/day



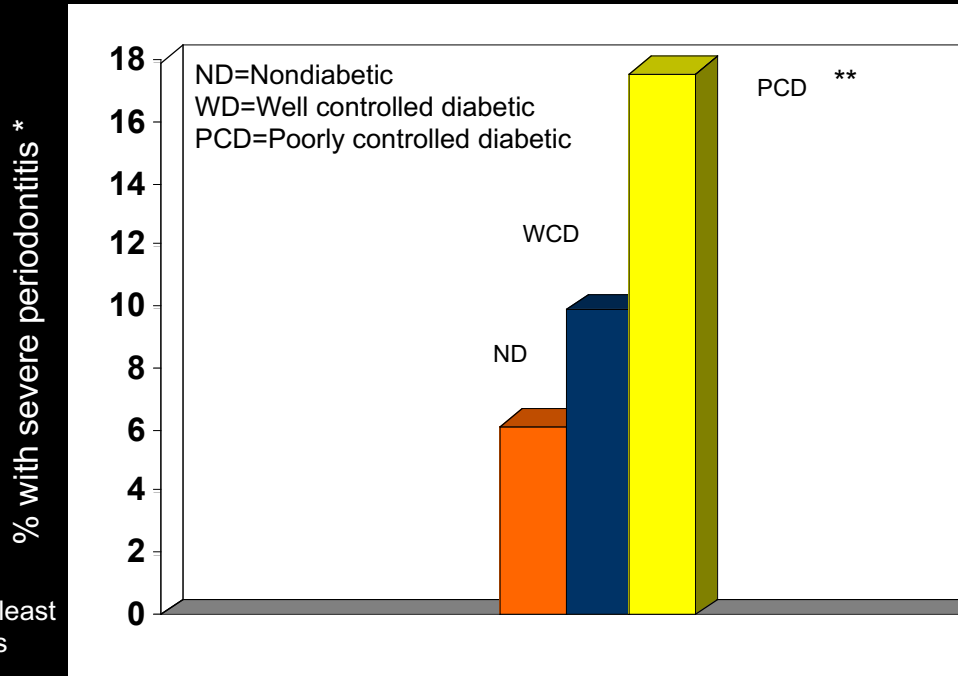
Smoking and Etiology/Pathogenesis of Periodontal Diseases

| Etiologic Factor | Impact of Smoking |
|------------------------------|---|
| Microbiology | No effect on rate of plaque accumulation |
| | ↑ Colonization of shallow periodontal pockets by periodontal pathogens |
| | ↑ Levels of periodontal pathogens in deep periodontal pockets |
| Immune-inflammatory response | Altered neutrophil chemotaxis, phagocytosis, and oxidative burst |
| | ↑ Tumor necrosis factor- α and prostaglandin E ₂ in gingival crevicular fluid |
| | ↑ Neutrophil collagenase and elastase in gingival crevicular fluid |
| | ↑ Production of prostaglandin E ₂ by monocytes in response to lipopolysaccharide |
| Physiology | ↓ Gingival blood vessels with ↑ inflammation |
| | ↓ Gingival crevicular fluid flow and bleeding on probing with ↑ inflammation |
| | ↓ Subgingival temperature |
| | ↑ Time needed to recover from local anesthesia |
| ↓, Decreased; ↑, increased. | |

Diabetes



Severe Periodontitis in NHANES III



* At least 2 sites with at least 6 mm of attachment loss

** Significantly different from ND and WCD

Tsai et al. Commun. Dent. Oral. Epidemiol. 2002. Data from NHANES III (n= 4866)

Proposed mechanisms of linkage between periodontal disease and diabetes

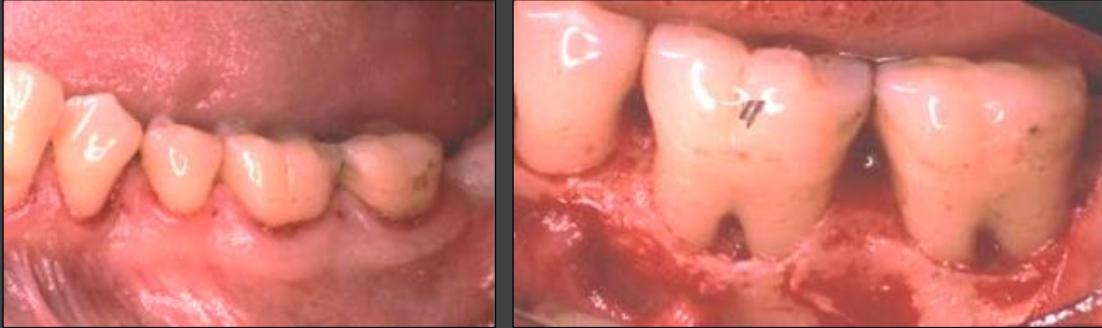
- Reduced PMN function
- Abnormalities in collagen metabolism
- Increased secretion of proinflammatory cytokines (adipocytes are potent source of proinflammatory mediators, e.g., TNF)
- Formation of advanced glycation end products (AGE)
 - AGE adversely affect collagen integrity, vascular integrity
 - AGE increase IL-1 and TNF secretion by macrophages

Anatomical Factors

Examples Anatomic Factors



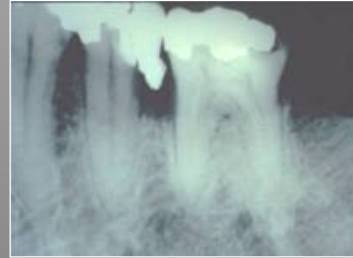
Examples Anatomic Factors



- Cervical enamel projections (CEP)
- Short root trunk
- Intermediate bifurcation ridge

Restorative Factors

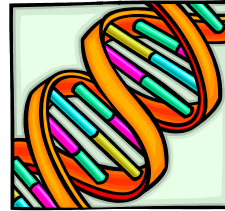
Examples of Restorative Factors



Risk Determinants/*background characteristics*

Risk factors that cannot be modified

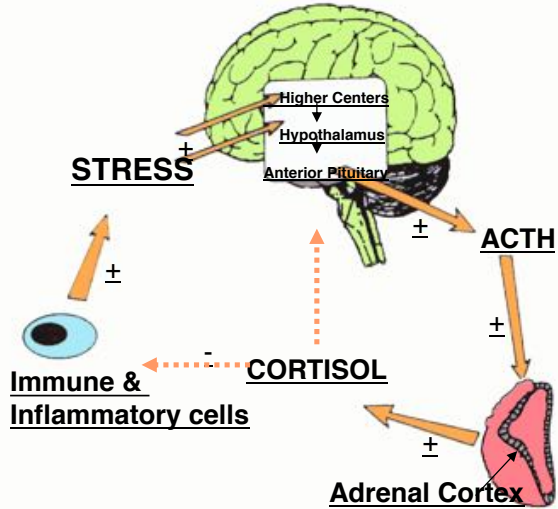
- Age
- Gender
- Socioeconomic Status
- Stress
- Genetic Factors



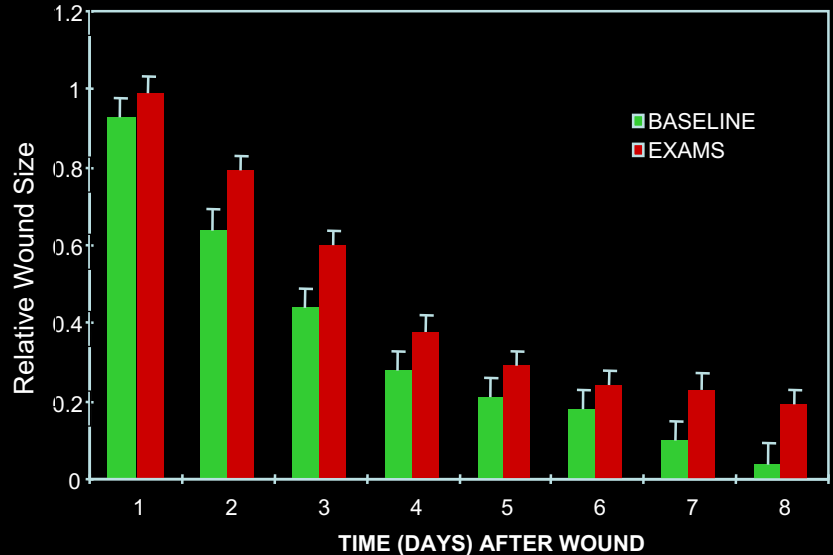
United States, National Health and Nutrition Examination Survey, 2009-2012

| Characteristic | % with periodontal disease | % with severe periodontal disease |
|--|----------------------------|-----------------------------------|
| Age | | |
| 30-34 years | 22.7 | 2.2 |
| 35-49 years | 29.7 | 7.5 |
| 50-64 years | 40.8 | 11.9 |
| Sex | | |
| Male | 41.6 | 13.3 |
| Female | 32.7 | 4.7 |
| Race and Ethnicity | | |
| White, non-Hispanic | 34.0 | 6.8 |
| Black, non-Hispanic | 43.5 | 15.6 |
| Hispanic | 47.7 | 15.8 |
| Poverty Status (compared to federal poverty level) | | |
| Less than 100% | 47.4 | 14.9 |
| 100 to 199% | 43.3 | 13.7 |
| Greater than 400% | 28.0 | 4.9 |
| Education | | |
| Less than High School | 49.9 | 17.1 |
| High School | 43.8 | 11.9 |
| More than High School | 31.4 | 5.7 |

Stress-Induced Activation of the Hypothalamic-Pituitary-Adrenal (HPA) Axis



ACADEMIC STRESS IMPAIRS WOUND CLOSURE



Genetics and Periodontal Diseases

- ▶ Genotype: the genetic composition of an individual
- ▶ Phenotype: the collection of traits or characteristics of an individual
 - Phenotype is determined by the interaction of genes and the environment
 - Multifactorial: diseases with etiologies that include both genetic and environmental factors – *most common diseases are multifactorial*


Genetic Basis of Human Disease

- ❶ The etiologic basis of disease can be defined in terms of gene-gene or gene-environment interactions.
- ❷ Periodontitis is a classic Gene - Environment Disease



Genetics and Periodontal Diseases

Primary focus on genetic differences related to host defense or host response to explain susceptibility

- ▶ Genetic defects of structural genes in host defense
 - ▶ Twin studies
 - ▶ Familial aggregation in more aggressive forms of periodontitis
 - ▶ Single nucleotide polymorphisms
- 

Hereditary Diseases with Neutrophil Dysfunction

- Chediak-Higashi Syndrome
- Chronic Granulomatous Disease
- Familial Benign Chronic Neutropenia
- Cyclic Neutropenia
- Leukocyte Adhesion Deficiency diseases
- Papillon Lefevre Syndrome
- Glycogen Storage Disease Type Ib
- Acatlasia
- Congenital Neutropenia
- Myeloperoxidase Deficiency

Cyclic Neutropenia

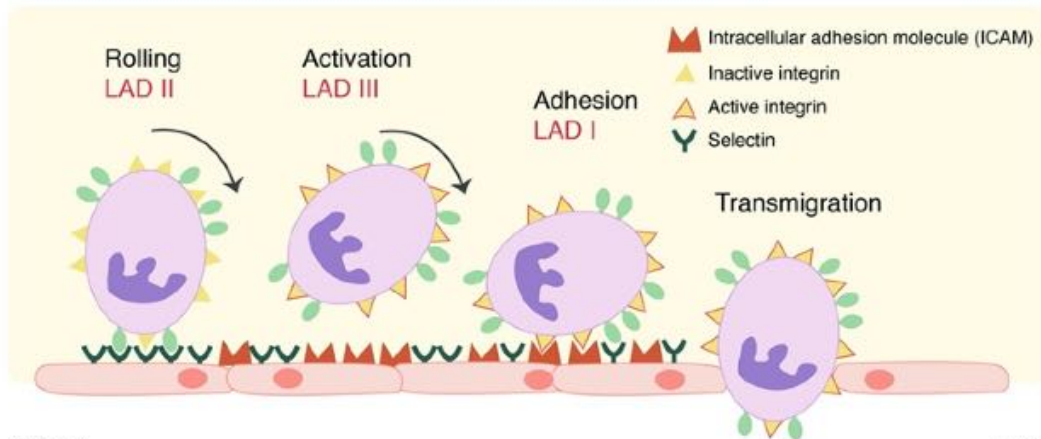


autosomal dominant disease caused by ELANE

Neutrophil elastase gene

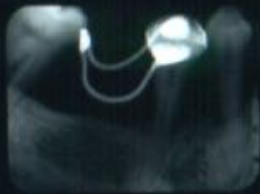
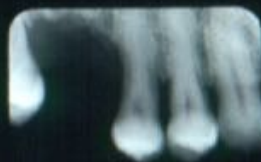
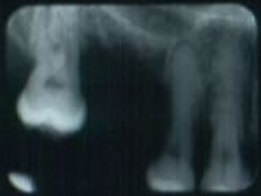
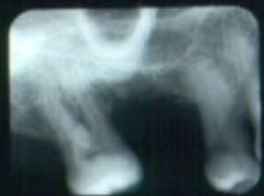


Leukocyte Adhesion Deficiency Types I-III



Leukocyte Adhesion Deficiency





Twin Studies

- Corey *et al*, 1993, surveyed 4,908 twin pairs, 420 self-reported to have chronic periodontitis
 - Concordance rate: 0.38 MZ twins, 0.16 DZ twins
 - Conclusion: genetic factors make an important contribution for risk of chronic periodontitis

From: Corey, *et al*, J Periodontol 64(12) 1205-1208 1993

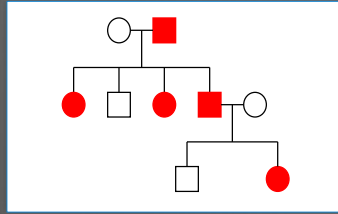
- Michalowicz, *et al*, 2000, 117 twin pairs (64MZ, 53DZ)
 - Complete periodontal exam, results: MZ were more similar than DZ twins with estimated 50% heritability which was adjusted for smoking.
 - Suggested a heritable component to probing depth, attachment loss.

● From: Michalowicz, *et al*, J Periodontol 71(11) 1699-1707 2000

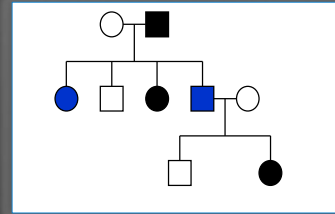
Formal Genetic Studies of Aggressive Periodontitis

⚙ Segregation Analysis

- ⚙ Evaluate the pattern of disease segregating in families and determine if it is consistent with a genetic model



Dominant



Recessive

Autosomal, X-linked, Dominant/Recessive, Polygenic, Sporadic (not genetic)

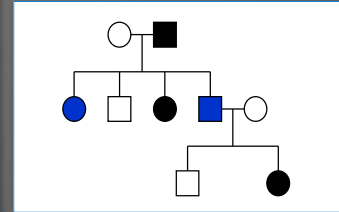
Formal Genetic Studies of Aggressive Periodontitis

- ❁ Segregation analysis for aggressive periodontitis

- ❁ Saxen 1980 (Finland)

- ❁ Autosomal recessive transmission

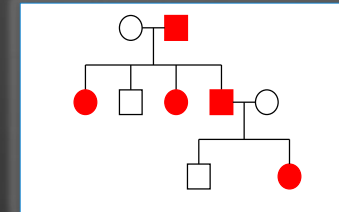
From: Saxen, J Clin Periodontol, 7 (4) 276-288 1980



- ❁ Marazita, et al 1994. 100 Aggressive Periodontitis families (Virginia, USA)

- ❁ Autosomal dominant transmission, 70% penetrance
 - ❁ Disease allele frequency estimated as
 - ❁ 0.016 African American
 - ❁ 0.001 Caucasian

From: Marazita, J Periodontol, 65(6) 623-630 1994



- ❁ Findings support a gene of major effect for aggressive periodontitis

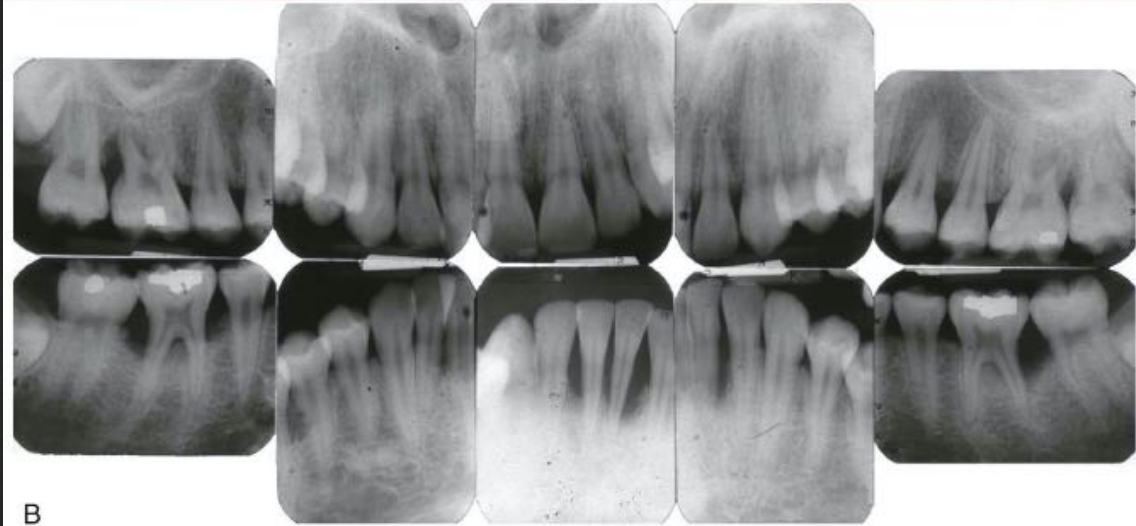
****similar clinical Phenotype, likely different genotype (genetic risk factors) in different populations



A



C



B

Formerly known as
Localized juvenile
periodontitis
in 15 year old
black female
(twin with similar
presentation)

Single Nucleotide Polymorphisms


- ⊗ Generally single base changes that are regulatory regions of genes that increase or decrease gene expression. Can change expression by 2 times or more. Does not impact the structure of the protein.
- ⊗ Single Nucleotide Polymorphisms (SNPs)- association studies in small subject groups- SNPs for cytokines and molecules involved in immunity have been described: TNF- α , IL-1 β , Fc- γ , IL-10, CD-14, none are etiologic for AP
- ⊗ Evidence supports genetic heterogeneity (multiple genes of can predispose to AP type conditions in different populations/families)

Genetics and Periodontal Diseases

What can I do as a clinician today?

- Medical and dental history
- Family history
- Discuss with the patient what evidence is available today
 - Advanced periodontitis found in young adults (FKA aggressive periodontitis)
 - Periodontitis in general (~ 50%)
- Is there value in a commercially available genetic test? Is it going to help my patient and/or how I am going to treat him/her?

Risk Indicators and Predictors

- ▶ **Risk indicators**: *Probable* or *putative* risk factors that have been identified in cross-sectional studies but not confirmed through longitudinal studies
 - ▶ **Risk predictors/markers**: do not cause the disease but are associated with increased risk for disease
- 

Other Etiologic Risk Indicators

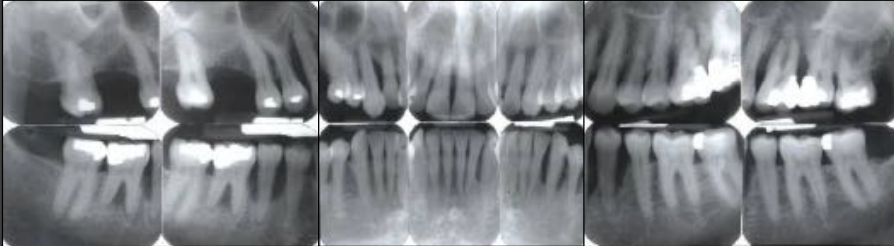
- ▶ Oral Hygiene (strong association)
- ▶ Nutrition (weak data, needs further evidence)
 - Vitamins B12, B complex, C, D, E, lycopene
- ▶ Obesity
- ▶ Other Systemic Diseases (increasing evidence)



Risk Predictors/Markers

Do not cause the disease but are associated with increased risk for disease

- ▶ Previous History of Periodontal Disease
- ▶ Bleeding on Probing



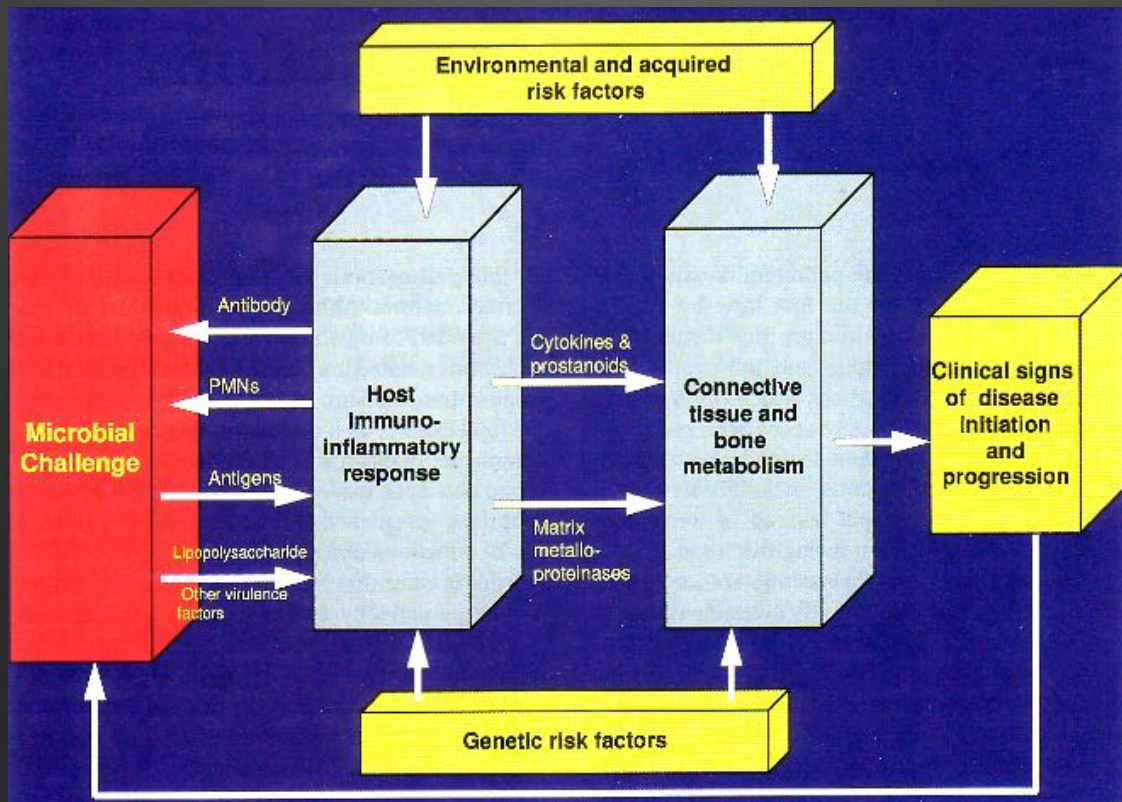
RISK ASSESSMENT

The process of predicting an individual's probability of getting a disease.

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

The Pathogenesis Paradigm

From Page RC, Kornman KS, Periodontol 2000, 1997;14:9-11.



Clinical Risk Assessment for Periodontal Disease

▶ Demographic Data

- Age
- Gender
- Socioeconomic Status
- Stress

▶ Medical History

- Diabetes
- HIV/AIDS
- Tobacco Smoking
- Osteoporosis
- Stress

▶ Dental History

- Family history of early tooth loss
- Genetic predisposition to Aggressive Periodontitis
- Previous history of periodontal disease and treatment
- Frequency of dental care

▶ Clinical examination

