Methylation Implications with Periodontal Disease

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Maine Dental Hygienists’ Association
10 April 2015
Methylation Implications

Gingival Characteristics

Dental Hygiene Diagnosis
DH DX
Slight Periodontal Disease
Methylation Implications
Dental Hygiene Diagnosis
What is methylation
What is methylation?

The addition of a single carbon group with three hydrogens onto a compound
Methylation Functions

• Turn on and off genes
• Process xenobiotics or chemicals, endogenous
  • Biotransformation-histamine, mercury, arsenic, fluoride
• Build neurotransmitters
  • Norepinephrine → epinephrine, serotonin → melatonin
  • Sleep and sound mental health
• Metabolize neurotransmitters
  • Dopamine and epinephrine
  • Behavioral health and the processing of local anesthesia
Methylation Functions

- Process hormones (estrogen)
- Build immune cells (T cells, NK cells - natural killer cells)
- DNA synthesis
- Produce Energy (CoQ10, carnitine, creatine, ATP)
- Produce protective coating on nerves, myelination
- Build and maintain cell membranes (phosphatidylcholine)
MTHFR Gene Variant or SNP
DNA is a Nucleic Acid made up of nucleotides which contain

1. Nucleobase
2. Deoxyribose-a pentose sugar
3. Phosphate Group
Genetics: What is DNA made of?

Nucleobases:

Adenine and Guanine = Purines
Cytosine and Thymine = Pyrimidines
A pairs with T
C pairs with G

Uracil = RNA base

Uracil when methylated becomes Methyl-Uracil
Thymine
Lack of methylation

Uracil base incorporation into DNA = Bad
BAD = Under-methylation creates gene splicing without repair
Incorporating RNA into DNA creates expression of Gene
DNA + RNA combination = splice and repair, splice and repair
Genetics: What is a SNP?

SNP=Single Nucleotide Polymorphism

Wild Type is when a single nucleotide differs from the majority.

SNPs occur between genes or intergenic

SNPs vary in terms of severity and benefit due to location and redundancy

SNPs may cause gene instability due to decreased micronutrients

SNPs may be bypassed by increasing micronutrients and providing end products

Most SNPs do NOT govern genetic function and expression
**Genetics: SNPs**

<table>
<thead>
<tr>
<th>Nuclear DNA (nDNA)</th>
<th>Mitochondrial DNA (mDNA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comes from both parents</td>
<td>Comes from Mother</td>
</tr>
<tr>
<td>Protection with Histones</td>
<td>Majority of ATP produced in mitochondria</td>
</tr>
<tr>
<td>Repair mechanisms</td>
<td>SNPs can be pathologic</td>
</tr>
</tbody>
</table>

- Cancer
- Diabetes
- CVD
- Neurodegenerative disease
- Aging
- Degenerative
- Lack of Histones or protection

1.4 million locations
Nuclear DNA SNPs

- Folate
- B12
- Methyltransferases
- Detoxification

- MTHFR
- TCN2
- COMT
- PON1

- MTHFD
- MMAB
- PEMT
- Cyt P450’s

- DHFR
- BHMT
- SULT

- SHMT
- GAMT

- FOUR
# Nuclear DNA SNPs

<table>
<thead>
<tr>
<th>Glutathione</th>
<th>Methionine Cycle</th>
</tr>
</thead>
<tbody>
<tr>
<td>GSTM1</td>
<td>MTR/MTRR</td>
</tr>
<tr>
<td>GCS</td>
<td>MAT1</td>
</tr>
<tr>
<td>GPX1</td>
<td>CBS</td>
</tr>
<tr>
<td>GR</td>
<td></td>
</tr>
</tbody>
</table>
MTHFR Variant or Gene SNP

- MTHFR is a gene code for the enzyme Methylenetetrahydrofolate reductase
- MTHFR enzyme helps the body manufacture proteins
- Mutations in the MTHFR gene are associated with Thromboembolic events (stroke, blood clots, pulmonary embolism, heart attack)

Cardio Vascular Disease
MTHFR Variant or Gene SNP

- Two clinically significant mutations to MTHFR
- Found on Chromosome 1p36.6
- Both are single-nucleotide polymorphism or SNP
- The most common affecting 40% of certain populations
  C677T
- Another SNP affecting 20% of certain populations
  A1298C
MTHFR

• The MTHFR enzyme is functional with SNPs
  Heterozygous=1 copy of the gene from either parent
  Homozygous=1 copy of the gene from each parent

MTHFR C677T Heterozygous=40% loss of function
MTHFR C677T Homozygous =75% loss of function

MTHFR A1298C Heterozygous=20% loss of function
MTHFR A1298C Homozygous =40% loss of function

MTHFR C677T and MTHFR A1298C Compound Heterozygous

40% loss of function for the enzyme

Riboflavin (Vitamin B2) more rapidly disassociates from the altered MTHFR enzyme rendering it unstable.

Riboflavin is imperative for optimal thyroid function. Hypothyroid patients should supplement with riboflavin-5-phosphate 400mg daily.

You may have not have the MTHFR variant, have hypothyroidism and have compromised methylation capacity.
MTHFR Variants

- **MTHFR C667T**
  - Significant reduction in enzyme stability
  - Increased FAD (riboflavin) stabilizes function of B2
  - Bypass with L-5-MTHF or 6S-5-MTHF

- **MTHFR A1298T**
  - SAM binds to and slows MTHFR down
  - Enzymatic reduction when combined with C667T
MTHFR Variant Genetic Implications

• The presence of either SNP C677T or A1298C carries an increased risk for miscarriages and of neural tube defects in newborns of women carrying the altered gene.
• Individuals with either of both mutations often have significant alterations in the metabolism of B vitamins.
• This results in an elevated homocysteine level
• Placing an increased risk in thromboembolic and CVD
Disorders or conditions of poor methylation

- Anxiety
- Chronic Pain
- Chronic Fatigue
- Nerve Pain
- Migraines
- Elevated homocysteine levels
- Fibromyalgia
- Irritable Bowel Syndrome
- Alzheimer’s
- Bipolar disorder
- Schizophrenia
- Parkinson’s
- Stroke
- Heart Disease
- Recurrent Miscarriages
- Still births
Disorders or conditions of poor methylation

- Birth Defects
- Autism
- Downs Syndrome
- Depression
- Periodontal Disease
Contributors to the Dysfunction of Methylation

Inflammation
Oxidative stress
Hypothyroidism
Cardiovascular dysfunction
Dysglycemia, diabetes, hypoglycemia
Poor or decreased behavioral health
Who are at risk for MTHFR Mutations?

Approximately 45% of the population has 1 copy of MTHFR C677T

Genetic Testing for MTHFR

**Blood Test**
SpectraCell Labs
Quest
LabCorp
Baylor Research Institute

**Saliva Test**
Access Genetics
Oral DNA Labs
Molecular Testing Labs
Buccal Swab test
23 and Me

TEST EVERYONE
<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>C677T Mutation</td>
<td>Homozygous</td>
</tr>
<tr>
<td>A1298C Mutation</td>
<td>Negative</td>
</tr>
</tbody>
</table>

This sample has two copies of the C677T mutation and is negative for the A1298C mutation. This genotype is associated with:

- decreased enzyme activity (apx. 30% for normal activity)
- increased homocysteine levels
- increased risk of CVD
- potential methotrexate intolerance
Environmental Factors affecting Methylation
Transsulfuration pathway
Arsenic and mercury affect this path
Epigenetics affect Methylation
Main Pathway (Low Protein)

Backup (High Protein)

SAMe Excess (High Protein)
Primary Methyl Donor
SAM  \textit{s-adenosylmethionine}

- SAM is a widely used enzymatic substrate in the body.
- Requires ATP (adenosine triphosphate), magnesium, methionine for formation
- Easily inhibited by its end product SAH
  - S-adenosylhomocysteine
- SAH converts to homocysteine
- SAH can be elevated even if homocysteine is not.
Primary Methyl Donor – SAM
s-adenosylmethionine

• If SAM production is disrupted, pathologies may occur.
• If SAM cannot be utilized, pathologies may occur.
• SAM production and recycle back up system

• Dependent on Methylfolate and its recycling
Methylation is Disrupted by

1. Micronutrients supporting methylation (Zn, B2, Mg, Choline, B6, B12)
2. Missing substrate driving methylation forward (Methionine, Homocysteine)
3. Antacids, methotrexate, metformin, *nitrous oxide*
4. High dose niacin depletes methyl groups
5. Environmental toxicity, heavy metals, chemicals (acetylaldehyde, mercury)
6. Feedback inhibition from DMG, SAM, SAH, Homocysteine
Methylation is Disrupted by

7. Genetic mutations (MTHFR, others GSTM1(Kidney) PEMT, MAT, GAMT, SOD
8. Mental Health or lack of due to stress, anxiety, lack of sleep
9. Receptor site blocking by folic acid or antibodies
10. Polyphenols Green Tea (EGCG) and Coffee
11. Carrier protein deficiency (transcobalamin, folate binding proteins)
12. Hormones such as elevated estrogen, cortisol
13. Inflammation

Benjamin Lynch ND 2014
Disruption of Methylation with Nitrous Oxide in the Dental Office
What do these have in common?
Cobalamin or B12

Active form of B12
- Methylcobalamin
- Adenosylcobalamin
- Hydroxocobalamin

Synthetic form of B12
- Cyanocobalamin
- Not to be used at any time.
Active forms of B12

Methylcobalamin is utilized most commonly.

Combinations of both methylcobalamin and adenosylcobalamin can be very effective in supporting MTHFR variant and hypothyroid patients.

Adenosylcobalamin is best for hypothyroid patients initially.

Hydroxocobalamin is used to reduce nitric oxide. Always use first while resolving inflammation-periodontal disease
Initial Methylation begins within the Methionine Cycle

• Dependent on the symbiotic relationship between B12 and Folate
• B12 sets the stage for methylation to occur in tandem with Folate
• Without one or the other methylation is inhibited
Nitrous Oxide

- Known Oxidizer of cobalamin
- Destroys B12 in the body, unless adequate nutrients are available to restore B12
- Breathing Nitrous Oxide dismantles methylation
- Those with the C667T variant or C677T + A1298C
- Single A1298C does not predispose much risk, A1298C Homozygous does
Symptoms of intolerance to Nitrous Oxide

- Slow the rest of the day after receiving N2O
- Mood changes for some time afterwards
- Bilateral numbness and tingling in extremities
- Memory loss
- Systemic symptoms: fatty liver, insomnia, irritability, sadness
Antidote for exposure to N2O

- Utilize both methylcobalamin and L-5-MTHF in a lozenge
- Place in your mouth daily when exposed in office setting
- Patient to place in mouth prior to using nitrous oxide
  - Use one lozenge postoperatively also
- Liposomal glutathione protects B12 levels intra-cellularly
  
  Utilize ¼ teaspoon daily away from food one week prior to dental appointment

Day of appointment increase to 1 teaspoon a day, continue for one month. Gradual increase of glutathione is important.
Could it Be B12?
An Epidemic of Misdiagnosis
Periodontal Disease and Methylation
Periodontal Disease and Methylation

Inflammation

Current understanding of the relationship between periodontal and systemic diseases.
Mawardi HH¹, Elbadawi LS, Sonis ST.

Periodontal disease (PD) is among the most common infectious diseases affecting humans. While the burden of periodontal disease on oral health has been extensively investigated, a possible specific relationship between the disease and systemic health is a relatively new area of interest. More recently it has been suggested that PD has an etiological role in the development of atherosclerotic cardiovascular disease, diabetes mellitus, and preterm low-birth weight, among others. In this review, we critically evaluate the current knowledge on the relation between PD and systemic diseases overall, and specifically with cardiovascular diseases. The best available evidence today suggests that the infection and inflammatory reaction associated with PD may contribute toward systemic disease. It is critical that dentists and physicians are well informed of the potential general health impact of periodontal disease so that they are in a position to knowledgeably counsel patients.
Oxidative Stress

Vitamin E Deficiency


**Saliva and oxidative stress in oral cavity and in some systemic disorders.**

**Buczko P**¹, **Zalewska A**, **Szarmach I**.

Particularly, the evaluation of oxidative stress status was proposed as an important factor in diagnosing the development and progress of such general diseases as periodontal disease, oral cancer, diabetes, rheumatoid arthritis, chronic renal failure, obstructive sleep apnea syndrome, and HIV.
Oxidative Stress


**Association of metabolic syndrome and periodontal disease in an Indian population.**

Patel SP, Kalra N, Pradeep AR, Martande SS,

Metabolic syndrome, the whole of interconnected factors, presents with local manifestation, such as periodontitis, related by a common factor known as oxidative stress. The aim of the present study was to assess the association between metabolic syndrome and periodontal disease in an Indian population.

**Conclusion** The association between metabolic syndrome and periodontal disease was significant, and abdominal obesity appeared to be the most important contributing metabolic factor to periodontal disease.
Expression of Leptin and Visfatin in Gingival Tissues of Chronic Periodontitis With and Without Type 2 Diabetes Mellitus: A Study Utilizing Enzyme Linked Immunosorbent Assay and Real-time Polymerase Chain Reaction.

Ghallab NA\(^1\), Amr EM, Shaker OG.

**BACKGROUND**

The aim of this study was to investigate the protein and gene expression of leptin and visfatin in gingival tissue from patients with chronic periodontitis (CP), patients with CP and type 2 diabetes mellitus (CP+DM) and healthy individuals.

**Conclusion**: Expression of leptin and visfatin in the gingival tissues might suggest a possible role for these adipokines in the pathogenesis of chronic periodontitis and type 2 diabetes mellitus.
Periodontal Disease and Methylation

Behavioral Health


Role of chronic stress and depression in periodontal diseases.
Warren KR, Postolache TT, Groer ME, Pinjari O, Kelly DL, Reynolds MA.

Abstract
An extensive body of experimental and clinical evidence documents the negative impact of chronic psychological stress and depression on the immune system and health. Chronic stress and depression can result in general dysregulation of the immune system, of both cellular and humoral pathways, which may contribute to pathogenic infection and concomitant periodontal tissue destruction.
Modifications of interdental papilla microcirculation: a possible cause of periodontal disease in Hashimoto’s thyroiditis?

Scardina GA¹, Messina P.

RESULTS:
An interdental papilla vascular modification results in HT. In patients suffering from HT, it was possible to observe a reduced caliber of capillaries, as well as a greater number and tortuosity of capillary loops.

CONCLUSIONS:
This study shows that capillary alterations in patients suffering from Hashimoto’s Thyroiditis occur in gingival microcirculation.
Abstract
Efficiency of some drugs in the treatment of periodontitis in combination with corrective treatment of thyroid function was evaluated in 70 patients with hypo- and hyperthyrosis with different initial level of nonspecific resistance. The therapeutic complex including drugs commonly used in the treatment of periodontitis and irrigation of the periodontium with lithium chloride and chlorohexidine solutions was highly effective in patients with thyroid dysfunction and relatively favorable status of nonspecific resistance of the organism. In patients with hypo- and hyperthyrosis with poor nonspecific resistance the best effect in the treatment of periodontitis was attained with potassium orotate as an immunomodulator and lithium chloride.
Periodontal Disease and Methylation

Cardiovascular and Autoimmune Disease


Relationship between vascular endothelium and periodontal disease in atherosclerotic lesions: Review article.

Saffi MA¹, Furtado MV¹, Polanczyk CA¹, Montenegro MM¹, Ribeiro IW¹, Kampits C¹, Haas AN¹, Rösing CK¹, Rabelo-Silva ER¹.

Abstract

Inflammation and endothelial dysfunction are linked to the pathogenesis of atherosclerotic disease. Recent studies suggest that periodontal infection and the ensuing increase in the levels of inflammatory markers may be associated with myocardial infarction, peripheral vascular disease and cerebrovascular disease. The present article aimed at reviewing contemporary data on the pathophysiology of vascular endothelium and its association with periodontitis in the scenario of cardiovascular disease.
In the case of periodontitis, gingival epithelial cells form the first line of defense against pathogens. Innate immune dysregulation in these cells relates to severe disease pathology. We recently identified a blunted Toll Like Receptors2 TLR2 expression in certain gingival epithelial cells expressing diminished cytokine signaling upon P. gingivalis stimulation. ... tissues obtained from periodontitis patients also exhibited differential TLR2 promoter methylation, as revealed by bisulfite DNA sequencing. Taken together, DNA methylation of TLR2 can modulate host innate defense mechanisms that may confer increased disease susceptibility.

TLR2 promoter hypermethylation creates innate immune dysbiosis. Benakanakere M$^1$, Abdolhosseini M$^1$, Hosur K$^2$, Finoti LS$^1$, Kinane DF$^3$
Interleukin-1 receptor antagonist levels in gingival crevicular fluid and serum in nonsmoking women with preterm low birth weight and intrauterine growth retardation.

Kayar NA¹, Alptekin NO², Haliloglu S³.

OBJECTIVE:
The aim of this study was to evaluate interleukin (IL)-1 β and IL-1 receptor antagonist (IL-1ra) levels in gingival crevicular fluid (GCF) and serum (S) in nonsmoking women with normal birth (NB), preterm low birth weight (PLBW), and intra-uterine growth retardation (IUGR).

RESULTS:
Greater pocket depth and clinical attachment loss were observed in PLBW and IUGR women than in NB women (P < 0.05). The total amounts of IL-1ra and IL-β of GCF were higher levels in NB women than PLBW and IUGR women (P < 0.05). The lowest total amount of IL-1ra of GCF was found in IUGR women (P < 0.05). The concentrations of IL-1ra in serum samples were not statistically significant for any of the study groups (P > 0.05).

CONCLUSION:
It can be suggested that worse periodontal conditions and the low levels of IL-1ra in GCF may be an important factor in adverse pregnancy outcomes.
Periodontal Disease and Methylation

IL-6

- Interleukin-6 gene promoter methylation in rheumatoid arthritis and chronic periodontitis.

Methylation status of the cytokine genes may play a role in the pathogenesis of inflammatory diseases, such as rheumatoid arthritis (RA) and chronic periodontitis (CP).

Conclusion: These results suggest that hypomethylated status of a single CpG in the IL-6 promoter region may lead to increased levels of serum IL-6, implicating a role in the pathogenesis of RA and CP.
Epigenetics and Nutrigenomics

“As an organism grows and develops, carefully orchestrated chemical reactions activate and deactivate parts of the genome at strategic times and in specific locations.

Epigenetics is the study of these chemical reactions and the factors that influence them.”

“Epigenetic changes are environmentally responsive mechanisms that can modify gene expression independently of the genetic code.”

http://Learn.genetic.Utah.edu/content/epigenetics/ and Epigenetics and the development origins of inflammatory bowel diseases
Epigenetics and Periodontal Disease

Epigenetics and Its Role in Periodontal Diseases: A State-of-the-Art Review. 
Larsson L¹, Castilho RM, Giannobile WV.

Abstract
The immune response to oral bacteria and the subsequent activation of inflammatory signaling is not only dependent on genetic factors. The importance of so-called epigenetic mechanisms presents additional regulatory pathways of genes involved in maintaining chronic inflammation, including gingivitis and periodontitis. The term epigenetics relates to changes in gene expression that are not encoded in the DNA sequence itself and include chemical alterations of DNA and its associated proteins. These changes lead to remodeling of the chromatin and subsequent activation or inactivation of a gene. Epigenetic mechanisms have been found to contribute to disease, including cancer and autoimmune or inflammatory diseases. In this state-of-the-art review, the authors provide the latest findings on the involvement of epigenetic modifications in the development of periodontal disease and present emerging therapeutic strategies aimed at epigenetic targets (epidrugs) associated with the disruption of tissue homeostasis and the development of periodontitis.
Environmental Factors affecting the Epigenome
Epigenetics and Methylation
Folate
Importance of Folate

“The function of folate in human physiology are relatively simple, but the implications of their activity (and dysfunction) can be profound and far reaching.”

Functions:
- Synthesis of nucleic acids for DNA production and repair of tRNA
- Methylation or single carbon metabolism
- Assists in the conversion of amino acids for neurotransmitter production and detoxification
- Formation and maturation of RBC
- Production of platelet and WBC

Source: Herb, Nutrient and Drug Interactions by Stargrove et al
Difference between Folate and Folic Acid

• Several types of Folate
  • Folinic Acid (5-FormylTHF)
  • Methylfolate (5-MTHF)
  • Folic Acid (unmetabolized folic acid)

• Folic Acid does not each Folate
• Folic Acid is not found in nature
• Folic Acid requires numerous biochemical transformations prior to utilization.
Comparing Folic Acid to 5-Methyltetrahydrofolate

Folic Acid

Methylfolate

5-Methyltetrahydrofolate
Converting Folic Acid to Folinic acid and MTHF

Requires:
1) Uncooked Leafy Greens
2) Functioning Enzymes
3) Available Receptors
4) Transport

5) Vitamins, Minerals and pH:
   • B2
   • B6
   • B12
   • Acidic environment (for absorption)
Salivary Diagnostics
MTHFR C677T (XT)
MyPerioPath
OraRisk Candida
MyPerioID
OraRisk HPV
CYP2C19 Genotyping (Plavix)
CYP2C9/VKORC1 Genotyping (Warfarin Sensitivity)
CYP2D6 IVD Genotyping (Beta-blocker)
CYP3A4/5 Genotyping
Celsius One
DNA DRUGMAP: INHERITED THROMBOPHILIA
Salivary Diagnostics

Find out what your DNA says about you and your family.
• Learn what percent of your DNA is from populations around the world
• Contact your DNA relatives across continents or across the street
• Build your family tree and enhance your experience with relatives
$99
Personalized Oral Medicine
Personalized Oral Medicine

• **Oral health** Salivary Diagnostics
  • Periodontal disease and Caries
  • HPV and Oral cancer
  • MTHFR

• **Systemic Health** Salivary Diagnostics
  • HIV GI health
  • Breast cancer DHEA
  • Insulin Adrenal
  • Endocrine health IgA-gluten intolerance
MyPerioPath® Result Report

Gloss, John A.
Office of Dr. GLOSS
Gloss, Max

Results: P. intermedia | Periodontal Bacteria Reported Above Threshold

Electrical Risk: 2022 - Very strong evidence of increased risk for attrition

Legend:
- Red: High Risk
- Green: Low Risk
- Orange: Moderate Risk

Pathogens:
- P. aeruginosa
- F. nucleatum
- P. gingivalis
- T. forsythia
- E. corrodens
- G. vaginalis

Clinical Data Review:
- High Risk Pathogens
- Moderate Risk Pathogens
- Low Risk Pathogens

Treatment Considerations:
- Office Periodontal Therapy: Protocols to disrupt biofilms and restore patency.
- Systemic Antibiotic Option to Augment Therapy at Clinician’s Discretion:
  - Clinicians to determine if oral antibiotics (e.g., metronidazole) are necessary based on clinical findings.
- Home Care: Office recommends procedures to disrupt biofilms.

Rationale:
- Compare clinical signs and bacterial levels prior and post-treatment.

- A third sample should be collected 3-4 weeks post-therapy.

Additional Risk Factors:

- Additional information is available from MyOralDNA.com.cn.

Disclaimer:
- Contact MyOralDNA for any questions regarding clinical treatment protocols and developments. The information on this report is intended to provide general information about periodontal health and should not be construed as medical advice. The information is not intended to replace professional medical advice, diagnosis, or treatment. For further information, please contact OralDNA or seek advice from a qualified oral healthcare professional.
Periodontal Inflammation Risk
LOW  INTERMEDIATE  HIGH

Interpretation: IL-6

Individual's interleukin 6 genotype (IL6) is G/C.

Risk: Individuals carrying an IL6 G allele are associated with increased odds of the coincident detection of A. actinomycetemcomitans, P. gingivalis and T. forsythensis.

Consider: IL-6 is a potent stimulator of osteoclast differentiation and bone resorption, is an inhibitor of bone formation, and overproduction has been implicated in systemic diseases such as juvenile chronic arthritis, rheumatoid arthritis, osteoporosis, Paget's disease and Sjogren's
Diagnostic Data

Shelby Kahl BS RDH
Dirty Dozen

A. actinomyctencomitans
P. gingivalis
T. forsythia
T. denticola
E. nodatum
F. nucleatum
P. intermedia
C. rectus
P. micros
E. corroden
C. species group (gingivalis, ochreacea, sputigena)
Pathogen Grouping

Result: POSITIVE - 3 PATHOGENIC BACTERIA REPORTED ABOVE THRESHOLD

Bacterial Risk: HIGH - Very strong evidence of increased risk for attachment loss

Legend:
- Pathogen Load Threshold
- DL = Detection Limit

Result Interpretation: Periodontal disease is caused by specific, or groups of specific bacteria. Threshold levels represent the concentration above which patients are generally at increased risk for attachment loss. Bacterial levels should be considered collectively and in context with clinical signs and other risk factors.

High Risk Pathogens

Moderate Risk Pathogens

Low Risk Pathogens

High Risk | Moderate Risk | Low
Non Responsive to SRP
Aa, Pg, Pm, Td, Tf

Increase cardiovascular risks

P. Gingivalis + T. denticola

A. a + T. denticola
Associated with Type I Diabetes
Tannerella forsythia
Treponema denticola
Capnocytophaga species group
Increase following active therapy

F. nucleatum and C. species

Affects pregnancy term and birth weight

Han et al Obs & Gyn 2010 Feb
Transmissible from parent to child
& a lesser degree between partners
Porphyromonas gingivalis
Patient Protocols
Product Choice

Product recommendation
- Zinc Citrate
  - Strep mutans
  - F. nucleatum
- Stabilized ClO2-CloSYS®
  - A. a
  - P. intermedius
  - P. gingivalis
  - S. mutans
- Pro-Biotics Evora Pro®
- Providone iodine
- Botanical Compounds
- Ozone

Saliva Testing

Oral Pathogen
- A. a
- P. Gingivalis
- T. forsythus
- T. denticola
- P. intermedia
- P. micros
- F. nucleatum
- C. rectus
- E. nudaum
- E. nodatum
- E. corroden
- C. spec (gingivalis, ochreacea, sputigena)
Oral Probiotic use for pathogens

• **T. forsythia**
  Associated with refractory periodontitis
  ⏩ Pocket Depths
  Resistant to Doxycycline ≠ Atridox

Both are SRP Resistant

• **T. Denticola**
  Invasive in cooperation with other bacteria associated with periodontal disease

• **Capnocytophaga species group**
  Associated with PD, DM and Pregnancy
  🔄 After active therapy
Systemic Conflict with Periodontitis
Systemic Conflict and Oral Health

Endocrine System
Digestion
Nervous System
Systemic “Conflict”

Interleukin markers
- IL-1α, IL-β, IL-6, IL-17A, Beta-defensin 1, CD 14, TNFα,
- TLRF4 (Toll like receptor factor), Matrix metalloprotein 3

Gene variant of methylation, MTHFR

Systemic support options pre/pro/post periodontal therapy
- Pre Perio therapy antibiotic recommendation per lab results
- IL-1 modulate with Boswellia
- IL-6 modulate with Ashwaganda
4 week reTest
Non responsive perio therapy

• Viral Opportunist post active periodontal therapy
  • HPV test
  • Herpetic influence

• Residual Fungal invasion-now you can test with Access Genetics
• Methylation Variant – consider testing initially as a diagnostic
**Tongue Diagnosis (Jihva)**

**CONDITIONS:** A discoloration and/or sensitivity of a particular area of the tongue indicates a disorder in the organ corresponding to that area (see diagram). A whitish tongue indicates *Kapha* derangement and mucus accumulation; a red or yellow-green tongue indicates *Pitta* derangement; and a black-to-brown coloration indicates *Vata* derangement. A dehydrated tongue is symptomatic of a decrease in the *dhatu Rasa* (plasma), while a pale tongue indicates a decrease in the *dhatu Rakta* (red blood cells).

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**Diagram 6**

[Descriptions and images related to tongue conditions and their corresponding organ system are shown in the diagram.]

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Note: This diagram is used to look at one's own tongue in a mirror. It is a mirror image.
Methylation gene variant

MTHFR SNP
C677T
A1298C

Strong influence nonresponsive PD Therapy
Identifies predispositions and risks
More to it than taking folate
Reduce nitric oxide with pathogen elimination (B12)
6-8 week post therapy
Re-Test

- Clinical Evaluation
- ReTest pathogen load
- Establish Supportive periodontal maintenance
  90 day interval
- Systemic Nutritional Support
- Integrative co-management
Periodontal Methylation Case
Implicated in CVD
Aggressive tissue invasion
SRP resistant

P. Gingivalis + A.a. + T. denticola
Methylation and Inflammatory Marker Support
Ozone or ClO2 twice a day
Probiotic lozenge post brushing 1/day
With Antibiotic use /gut probiotic 72 hrs prior
4-6 weeks Anti-viral protocol
4-6 weeks Anti-Candida protocol
Methylation Implications

Dental Hygiene Diagnosis
Slight Periodontal Disease

MTHFR Compound
Homozygous

Hematomachrosis
Homozygous
Case Diagnostics

- P. micros above threshold
- C. species present
- IL-6 C/G Low Risk for periodontitis
- MTHFR C677T heterozygous
Case Diagnostics

- Peptostreptococcus micros
  - SRP resistant
  - Implicated in CVD
  - In small numbers it is normal
  - Sensitive to Clindamycin
  - Stabilized Chlorine Dioxide effective agent for home
Case Diagnostics

Capnocytophaga species group

- Produces tissue degenerative enzymes
- Increases following active therapy
- Implicated in Diabetes
- Sensitive to Oral Probiotic

Ciantar et al J. Perio 2005 76: 194-203
Case Patient Protocol

MTHFR 677 heterozygous
• Reduce nitric oxide load with reduction in oral pathogens
• Hydroxocobalamin

IL-6 support with Ashwaganda
Case Patient Protocol

Patient At Home OTC protocol

- ClōSYS® tooth paste and mouth rinse/ twice a day
- Evora Pro Oral Probiotic 1/day post brushing
- Hydroxocobalamin 2000mcg/day
- Ashwaganda 5ml 1-2/day or 300mg bid
Personalized Oral Medicine

Consider the Systemic Process

- Infectious Disease
- Identify what you are treating
- Utilize Diagnostics
- Maximize your results
- Individualized therapy

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