

# Connecting the Dots Between Cancer, Chronic Illnesses & Periodontal Diseases

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Karen Davis, RDH, BSDH

*The preservation of health is easier than the cure of the disease*

## WHAT DO YOU WANT FOR YOUR PATIENTS?

*"We are drowning in a Tsunami of chronic diseases."* Dr. Jeffrey Bland

Overweight & Obesity Increase the Risk for These Cancers:

Esophageal	Breast (Post-Menopausal)
Liver	Gall Bladder
Kidney	Pancreatic
Stomach	Ovarian
Colorectal	Endometrial
Prostate (Advanced)	

American Cancer Society, Surveillance Research 2016:

Lifetime risk of developing cancer for Men \_\_\_\_\_

Lifetime risk of developing cancer for Women \_\_\_\_\_

## Disturbing Trends:

- Steady Rise in Overweight & Obesity: 2/3 of population
- Rise in Colorectal Cancer in Young Adults
- Snapshot of Diabetes: ~30 million Diabetes / 86 million Pre-Diabetes
- Cardiovascular Disease: Leading Cause of Death – 1 in 3 will have CVD
- Pathogens influence Bi-Directional Links of Periodontal Disease & Rheumatoid Arthritis
- Chronic inflammation breaks down immune tolerances / > 100 autoimmune diseases
- Periodontal Pathogens Increase Risk of Pancreatic Cancer
- Rise in HPV-Related Oral Cancers in Men
- Alzheimer's Disease: 3-Fold Increase in next 30 years
- Periodontal Disease: 50% of population – 70% by age 65

**Cancer, Epidemiology, Biomarkers & Prevention 2017:** Periodontal disease increases risk of total cancer among older women (54-86) irrespective of smoking and certain anatomic sites appear to be vulnerable. (Breast, lung, esophageal, gallbladder and melanoma skin cancers.

*Oral complications of chronic illnesses & autoimmune diseases: chronic periodontitis, dental caries, xerostomia/burning mouth syndrome, ulcerations/mucosal diseases, candidiasis, swallowing difficulty.*

American Institute for Cancer Research - [www.AICR.org](http://www.AICR.org) - Not-for-profit national cancer charity. Continuous Update Project Reports (CUP) provides ongoing evidence-based science for cancer prevention.

Bale Doneen Method of Heart Attack, Stroke & Type II Diabetes Prevention – [www.baledoneen.com](http://www.baledoneen.com) The Heart Attack Gene by Brad Bale and Amy Doneen

### **Epigenetics Modifications to Gene Expression:**

Aging, stress, diet, exercise, drugs, microbiome

***“From our understanding of the biology of the relationship between periodontitis and systemic disease, it remains clear that the relationship is not linear, but complex.”***

Van Dyke TE, van Winkelhoff AJ, Infection and inflammatory mechanisms. European Federation of Periodontology and American Academy of Periodontology 2013. 1-7.

## **Connecting the Dots: Lifestyle / Inflammation / Pathogens**

### **Drivers of Inflammation:**

#### Pathogens

Keystone Pathogens

Dysbiosis

Inflammatory Mediators

Susceptible Host

#### Lifestyle

Physical Activity

Diet

Airway

Alcohol/Tobacco

Weight

Innate Immunity – First Responders

Adaptive Immunity – Second Responders

High Risk Periodontal Pathogens:

*Aggregatibacter actinomycetemcomitans*

*Porphyromonas gingivalis*

*Fusobacterium nucleatum*

*Treponema denticola*

*Tannerella Forsythia*

### **Periodontal Disease is a Polymicrobial Inflammatory Disorder**

- Pathogens, biofilm required but not sufficient to promote disease alone
- Synergy of pathogens and commensal microbiota
- Keystone pathogens subvert immune responses to eliminate inflammation
- Dysbiosis fosters inflammation
- Host inflammatory response to pathogens initiates abundance of pro-inflammatory cytokines
- Susceptible hosts influence the onset, severity and duration of the inflammatory disorder
- Homeostasis = health

**Oral DNA Laboratories** – identification of pathogens & genetic susceptibility through salivary diagnostics [www.oraldnalabs.com](http://www.oraldnalabs.com)

**Circulation 2005:** Direct relationship between atherosclerosis and pathogenic burden.

**Journal of the American Heart Association 2013:** CIMT progressed in a direct and dose-responsive manner to bacterial burden.

According to a 2001 study in **Atherosclerosis** of 10,000 asymptomatic adults happens if you have evidence of atherosclerosis and you do nothing?

### **Post-Graduate Medical Journal 2016:**

1. ASVD is a complex multifactorial disease process.
2. PD due to high-risk pathogens is a contributory cause of ASVD.
3. PD is neither required nor sufficient for pathogenesis of ASVD.
4. Causal classification requires therapy to mitigate the risk of its effect.

High-Risk Periodontal Pathogens Influence on the Atherogenic Triad:

**Step 1:** Increased lipoprotein concentration in the artery – High-risk pathogens can increase concentrations of lipoprotein ApoB (small, dense LDL cholesterol), which will promote the pathogenesis of ASVD.

**Step 2:** Endothelial Permeability – High-risk pathogens (*Fusobacterium nucleatum*) can generate endothelial dysfunction and increase the permeability of the endothelium enabling bacterial to enter or exit the artery.

**Step 3:** Lipoprotein binding in the Intima – High-risk pathogens stimulates an increase in synthetic smooth muscle cells, which generate my proteoglycan (Velcro) for adhesion in the artery.

### **Think Differently About CVD**

- Primary prevention – no evidence
- Secondary prevention – evidence; no event
- Tertiary prevention – evidence, event, prevention of next event

**Journal of Oral Microbiology 2017: “Comorbidity of periodontal disease: two sides of the same coin? An introduction for the clinician” (SYNOPSIS OF DATA)**

1. Swedish ‘PAROKRANK’ study as reported in Circulation 2016 – largest and most well conducted case-control study to date. 805 patients <75 years of age with Acute Myocardial Infarction (AMI) compared to 805 controls without AMI revealed an increased risk (+49%) of AMI among patients with periodontitis. After adjusted for confounding factors (smoking, diabetes, socioeconomic status) the risk remained increased (+28%) among patients with periodontitis.
2. Recent systematic review with meta-analysis as reported in the Journal of Clinical Periodontology 2014 revealed that periodontal treatment improves a number measures for atherosclerosis including endothelial dysfunction and lipid parameters, HbA1c, high-sensitive C-reactive protein and inflammatory marker IL-6 especially among those that suffer from CVD and diabetes.
3. Periodontal treatment reduced periodontal pathogens with a dose-responsive manner correlating to a reduction of Carotid Intima-media Thickness (CIMT) in 420 patients with subgingival samples followed for 3 years as reported in the Journal of the American Heart Association in 2013.
4. In the Swedish ‘PAROKRANK’ study 9.3% of patients with AMI and 5.2% of the control group had undiagnosed diabetes. Another study reported in the Journal of Periodontology 2016 revealed that 3.1% of 291 patients seeking dental treatment had HbA1c above the threshold for type 2 diabetes and 27.1% had HbA1c above the threshold for pre-diabetes.
5. P gingivalis antibodies are higher in rheumatoid arthritis (RA) patients than healthy controls. Pg is the only pathogen with a capacity to produce an enzyme that initiates conversion of harmless amino acid arginine into a version that becomes a target for pathogenic T cells that drive RA. Small studies have shown that non-surgical periodontal treatment reduces symptoms, and biomarkers of RA.
6. Late Alzheimer’s Disease (AD >65 years of age) includes inflammatory changes in the brain, which may be initiated by local or systemic infection. Microorganisms most frequently associated with AD are bacteria, viruses and yeasts that are frequently found in periodontal pockets. Lipopolysaccharides (LPS) derived from Pg have been detected human brains with AD but not in control brains. In a study of 2,355 people >60 years of age as reported in Alzheimer’s Dementia 2012 a positive correlation between periodontitis and cognitive impairment was found. T. denticola may contribute to AD using a range of inflammatory mechanisms by which neurons would be attacked.

Chronic Apical Periodontitis can increase risk for CVD – Identify asymptomatic lesions.

**Oral Biology & Dentistry 2017:** 1.7% Hydrogen peroxide gel and a custom formed tray delivery system modify the biofilm to *reduce virulence and numbers of pathogens*.

[www.perioprotect.com](http://www.perioprotect.com)

**Frontiers of Medicine 2017:** After controlling for confounding factors, the mean Periodontal Inflamed Surface Area (PISA) was a significant risk factor for HBA<sub>1c</sub> and a significant risk factor for diabetic Retinopathy and neuropathy.

**Journal of Clinical Periodontology 2016:** Obese patients with PD harbored higher levels and/or higher proportions of several periodontal pathogens than those with normal weight and PD.

**World Journal of Gastroenterology 2016:** complex pathogenic interaction between PD and IBD. One disease might alter the composition of the microbiota and increase the inflammatory response related to the other disease.

**Gut 2016:** F. nucleatum influences colorectal cancer and its presence in the gut influences chemotherapy and survival outcomes

**C-Reactive Proteins:**

<1mg/L – low risk for CVD

1 – 3 mg/L – moderate risk for CVD

>3mg/L – high risk for CVD

Periodontal therapy can dampen or reduce CRP which when elevated, is a higher risk factor for CVD than elevated cholesterol.

Plaque HD® Toothpaste has been shown to reduce CRP due to improved biofilm removal. [www.plaquehdpro.com](http://www.plaquehdpro.com)

**Journal of Periodontal Research 2016:** CRP increased with greater numbers of lost teeth

**Periodontology 2000, 2005:** A systemic increase in cytokines essentially becomes “metastatic inflammation”. Intervention in disease-promoting biofilm is required to drive down inflammation.

Biofilm management through AirFlow technology utilizing low-abrasive powders is safe for teeth, restorative materials, and implants, is more efficient than curettes or ultrasonics, and perceived more comfortable compared to ultrasonics, curettes or lasers by patients.

[www.Hu-Friedy.com/biofilm](http://www.Hu-Friedy.com/biofilm)

[www.Hu-Friedy.com/powerrequest](http://www.Hu-Friedy.com/powerrequest)

[www.Acteongroup.com](http://www.Acteongroup.com)

### **Host-Modulation Therapy**

Sub-antimicrobial dose doxycycline (SDD)  
Chemically-modified tetracyclines (CMT)

**RDH Magazine 2016:** Sub-antimicrobial dose doxycycline helps prevent collagen breakdown by targeting collagenase and MMPs in periodontitis, and has been shown to reduce inflammatory cytokines in patients with periodontitis and diabetes or cardiovascular diseases.

**Pharmacological Research 2011:** SRP + SDD: 12% improvement in HbA1C.  
No change in HbA1C other groups

**Pharmacological Research 2011:** 6 mo. regimen SDD on CVD patients  
58% reduction in CRP  
34% reduction in IL-6

**Journal of Enzyme Inhibition & Medicinal Chemistry 2016:** Promising anti-cancer research with SDD and CMT

### **Inverse relationship between CRP and Omega 3 intake**

Ideal ratio: 3 Omega-6 fatty acid for every 1 Omega-3 fatty acid consumed in diet

### **International Journal of Molecular Sciences 2016:**

#### **Lifestyle Alterations to Reduce Pathogen-Influenced Risk for CVD:**

- Increase Omega-3 fatty acids to down-regulate pro-inflammatory gene expression
- Increase Omega-3 fatty acids for anti-bacterial effect & inhibition of High-Risk Pathogens
- Reduce pro-inflammatory Omega-6 fatty acids and pro-inflammatory “calorie-rich” saturated fats
- Reduce “calorie-rich” saturated fats, to reduce production of low-density LDL

**Journal of Periodontology 2010:** Omega-3 + low-dose aspirin may provide a sustainable, low-cost intervention to augment periodontal therapy

**Journal of Investigative and Clinical Dentistry 2016:** Periodontal disease severity is correlated to an increase in the presence of P gingivalis, which has been shown to alter the host through the decrease of HDL cholesterol, influencing the risk of CVD.

## Lifestyle Influences on Inflammation & Health

AICR Recommendation – consume no more than 18 oz. of red meat per week. Avoid processed meats, saving them for special occasion.

**Cancer Science 2017:** >13,000 Japanese men and >16,000 Japanese women, aged 35+ observed for 16 years. Positive correlation with processed red meat intake and colorectal cancer in men.

American Heart Association recommendation for daily limit of saturated fats: 7% or less.

American Heart Association guideline for daily intake of added sugar: 24g for women and 36g for men.

**American Journal of Clinical Nutrition 2017:** Moderate alcohol intake daily (0.5 – 1 for women and 1-2 for men) was shown to have a beneficial impact on HDL cholesterol.

**Nature 2018:** Alcohol creates acetaldehyde, which can damage DNA, and mutations can contribute to cancer. If individuals are missing or have genetically damaged enzymes (ALDH) that convert acetaldehyde to acetate, they are at higher risk of alcohol-influenced cancer.

Alcoholic drinks have been associated with an increased risk for oral, pharynx, larynx, Oropharyngeal, breast cancer and colorectal cancer in men according to AICR.org

### **Nutrition Journal 2010:**

1. Plant-based diets protects against chronic  
Oxidative-stress related diseases
2. Antioxidants improve cell maintenance & DNA repair
3. Bio-availability determines effectiveness
4. Antioxidants work synergistically – wide variety desirable
5. Antioxidant values vary

### **World Journal of Gastroenterology 2015:**

- Curcumin  
Anti-inflammatory, Apoptosis of colon cancer cells
- Polysaccharides (Apples and Mushrooms)  
Apoptosis of colon cancer cells
- Resveratrol (Berries, Grapes, Peanuts, Wine)  
Inhibits tumor initiation and progression
- Quercetin (Fruits, Tea, Wine)  
Antioxidant, Anti-inflammatory, Anti-proliferative

Periosciences topical antioxidants: antibacterial and anti-inflammatory:  
[www.periosciences.com](http://www.periosciences.com)

Biophotonic Scanner for Antioxidant Levels: [www.pharmanex.com](http://www.pharmanex.com)

Nutrition Action Newsletter: [www.nutritionaction.org](http://www.nutritionaction.org)

Evidence-based nutritional decision-making? [www.Nutritionfacts.org](http://www.Nutritionfacts.org)

**According to AIDR, regular exercise can decrease risk of:**

Post-menopausal breast cancer  
Endometrial cancer  
Colorectal cancer

**British Medical Journal Open Diabetes Research & Care 2016:** Exercise trumps diet in prevention of Pre-Diabetes in later years.

**Journal of the American College of Cardiology 2015:** 92% lowered risk of heart attack with healthy lifestyle behaviors:

- No Smoking
- BMI 18.5 – 24.9
- Physical Activity  $\geq$ 2.5 hrs/week
- Television Viewing <7 hrs/week
- Alcohol 1 serving per day
- Healthy Diet

**Journal of Periodontology 2016:** Higher level of periodontitis, inflammatory mediators, and CRP in patients with Obstructive Sleep Apnea.

Airway Centric – Michael Gelb, DDS [www.Airwayhealth.org](http://www.Airwayhealth.org)  
GASP available on [www.Amazon.com](http://www.Amazon.com)

**Family Practice News 2008:**

- 276 Adults / 21-64 / followed 6 yrs.
- Obesity 27% greater ave. 5-6 hrs.
- Obesity 21% greater ave. 9-10 hrs.
- 7-8 hours nightly for weight management

**Annals of Internal Medicine 2012:** Even fat cells need sleep!

4.5 hours sleep / 4 nights: insulin sensitivity of fat cells decreased by ave. of 30%

### Connecting Your Dots:

- Periodontal pathogens can adversely impact more than the oral cavity
- Early diagnosis and risk assessment – know your enemy (Salivary diagnostics)
- Intentional and therapeutic treatment of pathogenic biofilms (AirFlow )
- Identification & elimination of Peri-apical disease
- Incorporate anti-inflammatory adjuncts (SSD, Perio Protect, Periosciences)
- Prioritize healthy weight management/BMI/Waist circumference (BMI <30)
- Adopt an antioxidant/plant-predominant diet (raw and organic when possible)
- Commit to daily/weekly exercise (30 min a day in any way)
- Achieve sleep quality & quantity (7-8 hours nightly)

### Definitions Helpful to Understand:

**Apoptosis** – Programed or routine cell death (opposed to necrosis which is a form of traumatic cell death). Analogy: leaves falling from a tree. Excess apoptosis results in atrophy, whereas insufficient amount or inhibition can result in autoimmune diseases, inflammatory diseases, and cell proliferations leading to cancers.

**Carotid Intima-Media Thickness (CIMT) Test** – Ultrasound of the carotid to “see inside the artery” and examine for atherosclerotic calcified or soft plaques within the artery. It also measures the thickness of the intimal and medial layers of the artery wall.

**Commensal** – microorganisms that live in close contact with a host and benefits from this association, whereas the host is not adversely affected

**Cytokines** – Low molecular weight proteins that initiate and perpetuate inflammation as well as regulate the amplitude and duration of the response. .Examples are tumor necrosis factor, chemokines and interleukins.

**C-Reactive Proteins** – Proteins produced by the liver and measured in the blood that rise in response to inflammation in the body.

**Dysbiosis** – An imbalance in the abundance of microbial species within an ecosystem that is associated with disease. Dysbiosis can either be the cause or the consequence of disease.

**Epigenetics** – Heritable factors other than DNA that influences gene function.

**Homeostasis** – Equilibrium or balance between the host tissue and microbiota that prevents destructive inflammation of disease.

**Keystone species** – Species that has a disproportionately large effect on its environment relative to its abundance.

**Keystone pathogen** – A keystone microbial species that remodels a microbial community or biofilm that promotes disease pathogenesis.

**Lipoprotein(a)** – Genetic variant lipoproteins that attach to LDL cholesterol particles or triglycerides that “drive” cholesterol into the artery, increasing the risk for CVD.

**Lipopolysaccharides (LPS)** – Also referred to as an endotoxin. A component of gram-negative bacteria that induces inflammatory responses (Cytokines)

**Matrix Metalloproteinase (MMP's)** - enzymes involved in tissue remodeling and collagen degradation. MMPs are thought to have a roll in cell proliferation, adhesion, migration, angiogenesis, apoptosis, and host defenses.

**Pathobiont** – A normally harmless organism that can become pathogenic under certain environmental conditions (Immunocompromised hosts or during loss of homeostasis).

**Prostaglandins** – Messengers similar to hormones that work within the cells. Excessive PG2 amplifies inflammation.

**Resolvins** – Chemical mediators that are synthesized from Omega-3 fatty acids that have anti-inflammatory effects.

**Symbiosis** – Cooperative existence of microorganisms that may be of differing species.