3 MAIN DISEASES DENTISTS TREAT:

1. CARIES
2. PERIODONTAL DISEASES
3. ORAL CANCERS
3 MAIN DISEASES DENTISTS TREAT:

1. CARIES

2. PERIODONTAL DISEASES

3. ORAL CANCERS
3 MAIN DISEASES DENTISTS TREAT:

1. CARIES

2. PERIODONTAL DISEASES

3. ORAL CANCERS

Caused by Plaque Biofilm
3 MAIN DISEASES DENTISTS TREAT:

1. CARIES

2. PERIODONTAL DISEASES

3. ORAL CANCERS

Caused by Genetics and “Epigenetic Factors” (?)
EPIGENETICS

The emerging field of how the environment and your choices impact on the genetic code....and your children
EPIGENETICS IN DENTISTRY
(ESPECIALLY ORAL CANCERS)

- Smoking
- Alcohol
EPIGENETICS IN DENTISTRY

- Oral Hygiene
- Smoking
- Alcohol
- Nutrition
- Others
INTRODUCTION TO MICROBIOME
“Microbes of the Microbiome outnumber cells of the human body by 10:1, and consist of over 1,000 species and millions of genes...."
Microbiome interacts with human cells and contributes to chronic diseases including Diabetes, IBS, Asthma, Allergies, Metabolic Disease, Autoimmune Diseases, Multiple Sclerosis, Rheumatoid Arthritis, Obesity, among others.”

“The Forgotten Organ”
Does Oral Microbiome have an impact on GI tract or Respiratory Flora?

Yes
Does Oral Microbiome have an impact on GI tract or Respiratory Flora?

Yes
Functions of G.I Tract Microbiome

1. Development, training, and maintenance of Immune Response

Functions of G.I Tract Microbiome

2. Enhance integrity of G.I. barriers

Functions of G.I Tract Microbiome

3. Promote G.I. Epithelial Repair

Roca-Saavedra. 2018; J.Phys.Biochem.74:69
Functions of G.I Tract Microbiome

4. Nutrient Extraction from foods

"good" = microbial enzymes help digest carbohydrates, proteins, for absorption.

"bad" = excess extraction and absorption of carbohydrates

Roca-Saavedra. 2018; J.Phys.Biochem.74:69
Iebba. 2016. New Microbiol. 39: 1
Functions of G.I Tract Microbiome

5. Synthesize Vitamins K and B

Functions of G.I Tract Microbiome

6. Modify appetite and food intake

Wu.2015; Trends Endocrin. Metabol. 26:758
Functions of G.I Tract Microbiome

7. Regulate Glucose and Lipid Biochemistry

Functions of G.I Tract Microbiome

8. Metabolize drugs.


Functions of G.I Tract Microbiome

9. Host-Gene Expression

Kodukula. 2017; Biores. Open Access 6:123

Lima-Ojeda. 2017; Front. Psych. 8: 154
Functions of G.I Tract Microbiome

10. Development, Health, Functions of the Brain

Schirmer. Cristiano. 2018; Frontiers Phys. 9:184
Cemit. 2017. World J. Gastro. 23:5486
Cani. 2016. Molecular Metab. 5: 5:743
Test
What Shapes the Microbiome?

Pregnancy, in utero

Lima-Ojeda. 2017

Birth, Vaginal vs C-section

Friedman. 2018
Mohareri. 2018
What Shapes the Microbiome?

Adult:

Diet *Lerner. 2017*


Circadian Rhythm *Deaver. 2018; Kaxz Marek 2017*

Aging *Mohajari. 2018*

Oral Microbiome (Periodontal Diseases, Caries) *Sudhakara. 2018; Marsh. 2015; Gao. 2018; Kilian. 2016*
What Shapes the Microbiome?

Oral Microbiome (Periodontal Diseases, Caries)

*Sudhakara. 2018; Marsh. 2015; Gao. 2018; Kilian. 2016*
What Shapes the Microbiome?

“We swallow approximately 10,000,000,000,000 bacteria per day into our GI tract”


Influences Immune Response


Influences Brain

What Shapes the Microbiome?

“We swallow approximately 10,000,000,000,000 bacteria per day into our GI tract”


Influences Alzheimer’s Disease

Influences Other Systemic Diseases
DENTAL PLAQUBE BIOFILM  
+  
INFLAMMATION  

↓  
BONE LOSS
HOW WE FIGHT INFECTIONS
1. Aggressive Periodontitis Patients (RP, JP, PP)
2. Genetics of Immune Dysfunctions
3. Antineoplastic Cancer Meds
4. Anti Organ Transplant Rejection Meds
5. Diabetics and relatives of Diabetics
6. Steroid Therapies
7. Stress
8. Anyone over age 65 years
Mechanisms of Host-Parasite Interaction

WBC

Bacterial Kill

Bacterial Survival

Health

Disease

Bacteria
Classification of Periodontal and Peri-Implant Diseases and Conditions

Proceedings of the World Workshop Jointly Held by the American Academy of Periodontology and European Federation of Periodontology

Co-edited by Kenneth S. Kornman and Maurizio S. Tonetti
Periodontitis

Necrotizing Periodontal Diseases

Periodontitis

Periodontitis as a Manifestation of Systemic Disease
Other Conditions Affecting the Periodontium

- Systemic diseases or conditions affecting the periodontal supporting tissues
- Periodontal Abscesses and Endodontic-Periodontal Lesions
- Mucogingival Deformities and Conditions
- Traumatic Occlusal Forces
- Tooth and Prosthesis Related Factors
### Classification of Periodontal and Peri-Implant Diseases and Conditions 2017

#### Periodontal Diseases and Conditions

- **Periodontal Health, Gingival Diseases and Conditions**
  - Chapple, Mealey, et al. 2018 Consensus Rept [link](#)
  - Trombelli et al. 2018 Case Definitions [link](#)

- **Periodontitis**
  - Papapanou, Sanz et al. 2018 Consensus Rept [link](#)
  - Jepsen, Caton et al. 2018 Consensus Rept [link](#)

- **Other Conditions Affecting the Periodontium**
  - Jepsen, Caton et al. 2018 Consensus Rept [link](#)
  - Papapanou, Sanz et al. 2018 Consensus Rept [link](#)

#### Peri-Implant Diseases and Conditions

- **Peri-Implant Health**
- **Peri-Implant Mucositis**
- **Peri-Implantitis**
- **Peri-Implant Soft and Hard Tissue Deficiencies**

- **Necrotizing Periodontal Diseases**

- **Periodontitis**

- **Periodontitis as a Manifestation of Systemic Disease**

- **Systemic diseases or conditions affecting the periodontal supporting tissues**

- **Periodontal Abscesses and Endodontic-Periodontal Lesions**

- **Mucogingival Deformities and Conditions**

- **Traumatic Oclusal Forces**

- **Tooth and Prosthesis Related Factors**
How may we use this new Classification System in Periodontal and Implant Treatment Planning?
“...Implant survival rates do not exceed those of compromised but adequately treated and maintained teeth.”
“Biologic Principles should guide the treatment planning process and supersede a mechanically based restorative driven rationale ...”

“Periodontitis staging and grading used in dental implant therapy as a means to ensure maximum conservation of teeth and maximum preservation of alveolar bone?”

*Greenwell, H. et al. J.Periodontol. 2019;90:441*
PLAQUE BIOFILM, INFLAMMATION, AND SYSTEMIC DISEASES
MICROBIOME
AND
SYSTEMIC DISEASES (?)
Gram Negative Periodontal Pathogens

Lipopolysaccharides

G.I. Inflammation

Systemic Inflammation


Gram Negative Periodontal Pathogens

Lipopolysaccharides

Inflammation

Remote Organs

*Lerner. 2017. Microorg. 5:66*
INFLAMMATION AND SYSTEMIC DISEASES (?)
Periodontitis, as an oral infection, may contribute to risk factors for Systemic Diseases

Periodontal therapy should reduce the risk for selected systemic diseases
PERIODONTAL DISEASES AND SYSTEMIC DISEASES (2019)
PERIODONTAL DISEASES AND SYSTEMIC DISEASES

1. CVD (MI)
2. CVA (Stroke)
3. Respiratory Diseases
4. Preterm lowbirth wt babies
5. Osteoporosis
6. Rheumatoid Arthritis
7. Gastric Ulcers
8. Diabetes Mellitus
9. Obesity
10. Pancreatic Cancer, Other Cancers
11. Oral Cancers
12. Alzheimer’s Disease, Dementia (?)
PERIODONTAL DISEASES AND SYSTEMIC DISEASES

1. CVD (MI)
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11. Oral Cancers
12. Alzheimer’s Disease, Dementia (?)
CARDIOVASCULAR DISEASE: MI (HEART ATTACK)
http://medlib.med.utah.edu/WebPath/webpath.html

Permission by Edward C. Klatt MD University of Utah
“INFLAMMATION”

A Core factor for multiple systemic diseases and periodontitis?
"Periodontitis could be a significant risk for CVD especially in those with high CRP, long standing chronic infection and elevated serum antibodies to periodontal pathogens"
Coronary heart disease patients with no teeth have nearly double risk of death

Researchers connect levels of tooth loss (due primarily to poor dental hygiene that leads to periodontal disease) with increasing rates of death and stroke

Coronary heart disease patients with no teeth have nearly double the risk of death as those with all of their teeth, according to a study recently published in the European Journal of Preventive Cardiology. The study, with more than 15,000 patients from 39 countries, found that levels of tooth loss were linearly associated with increasing death rates.

"The relationship between dental health, particularly periodontal disease, and cardiovascular disease has received increasing attention over the past 20 years," said lead author Dr. Ola Vedin, cardiologist at Uppsala University Hospital and Uppsala Clinical Research Center in Uppsala, Sweden. "However, it has been insufficiently investigated among factors and socioeconomic status, every increase in category of tooth loss was associated with a 6 percent increased risk of major cardiovascular events, 17 percent increased risk of cardiovascular death, 16 percent increased risk of all-cause death and 14 percent increased risk of stroke.

746 patients had a myocardial infarction during the study.

Compared with those with all of their teeth, after adjusting for risk factors and socioeconomic status, the group with no teeth had a 27 percent increased risk of major cardiovascular events, 85 percent increased risk of cardiovascular death, 81 percent increased risk of all-cause death and 67 percent increased risk of stroke.

"Levels of tooth loss are linearly related to increasing death rates"

Chronic periodontitis correlated to heart attack prognosis and severity

Researchers have demonstrated for the first time that chronic periodontitis is closely related to the severity of acute myocardial infarction.

In research published in the Journal of Dental Research, titled “Acute myocardial infarct size is related to periodontitis extent and severity,” a team from the University of Granada demonstrated that the extent and severity of chronic periodontitis is related to the size of acute myo-

1. “Chronic periodontitis is a death risk factor and plays an important role in the prognosis of acute myocardial infarction”
2. Acute myocardial infarct size is related to periodontitis extent and severity”.

CARDIOVASCULAR DISEASE: CVA (STROKE)
PERIODONTITIS ➔ STROKE (CVA)

“2 x Risk of CVA with Periodontitis”

Plaque:
  a. Cytokines↑, Inflamm↑, Clotting↑ ➔ Thromboembolism
  b. Platelet aggregation ➔ Thromboembolism
  c. Lipids↑, Fibrinogen↑, C-reactive protein↑ ➔ CVA/CVD

PERIODONTAL DISEASES AND SYSTEMIC DISEASES

1. CVD (MI)
2. CVA (Stroke)
3. Respiratory Diseases
4. Preterm lowbirth wt babies
5. Osteoporosis
6. Rheumatoid Arthritis
7. Gastric Ulcers
8. Diabetes Mellitus
9. Obesity
10. Pancreatic Cancer, Other Cancers
11. Oral Cancers
12. Alzheimer’s Disease, Dementia (?)
Association between Periodontal Disease and lung cancer was stronger in former smokers.

"Smoking + Periodontal Disease increases lung cancer risk."

Mai X, ... Genco RJ. Cancer Causes Control 2014; 25: 1045
PERIODONTAL DISEASES AND PULMONARY ACTINOMYCOSIS

PERIODONTAL DISEASES AND SYSTEMIC DISEASES

1. CVD (MI)
2. CVA (Stroke)
3. Respiratory Diseases
4. Preterm lowbirth wt babies
5. Osteoporosis
6. Rheumatoid Arthritis
7. Gastric Ulcers
8. Diabetes Mellitus
9. Obesity
10. Pancreatic Cancer, Other Cancers
11. Oral Cancers
12. Alzheimer’s Disease, Dementia (?)
PANCREATIC CANCER AND PERIODONTITIS

- 51,000 male physicians
- Periodontitis increases risk for Pancreatic Cancer by 64%
- “Periodontitis infections may trigger generalized inflammation”

51,000 male physicians

Periodontitis increases risk for Pancreatic Cancer by 64%

“Periodontitis infections may trigger generalized inflammation”

Study Urges Men to Brush Up on Their Oral Health

New research finds that men with gum disease have a higher risk of certain cancers.

CHICAGO—June 4, 2008—Most people already know that maintaining oral health is a vital component of achieving overall health, but a recent study reveals why it is especially crucial that men pay close attention to their teeth and gums. Research published in the June issue of The Lancet Oncology found that men with a history of gum disease are 14 percent more likely to develop cancer than men with healthy gums. In fact, researchers uncovered that men with periodontal disease may be:

- 49 percent more likely to develop kidney cancer
- 54 percent more likely to develop pancreatic cancer
- 30 percent more likely to develop blood cancers
Periodontal disease is a significant risk factor for Alzheimer’s disease... potential association between oral disease and neurodegeneration
Alzheimer’s Disease Potential Immune Pathogenesis

Periodontitis Pathogens

Local and Generalized Inflamedation

Brain
Participants (nuns) with the fewest teeth had the highest risk of prevalence and incidence of dementia.
“Tooth loss may be associated with cognitive function; this association is mediated by age and SES”
Alzheimer’s Disease Potential Microbial Pathogenesis

G.I. Microbiome

Helicobacter, Chlamydia, Herpes Simplex, Others

Brain

Dementia Potential Microbial Pathogenesis

Brain

G.I. Microbiome

Practical Implications. The results of this systematic review show that implant survival rates do not exceed those of compromised but adequately treated and maintained teeth, supporting the notion that the decision to extract a tooth and place a dental implant should be made cautiously. Even when a tooth seems to be compromised and requires treatment to be maintained, implant treatment may not be the best choice.
11

Wound Dehiscence: Incision Line Opening

Jon B. Suzuki, Randolph R. Resnik
<table>
<thead>
<tr>
<th>Group</th>
<th>Management</th>
<th>Clinical Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Success (optimum Group health)</td>
<td>Normal maintenance</td>
<td>No pain No mobility No exudate &lt;2mm bone loss &lt;5mm PD</td>
</tr>
<tr>
<td>II. Survival (satisfactory health)</td>
<td>Reduction of stress More maintenance Sx PD reduction Yearly radiographs OH reinforcement</td>
<td>No Pain No mobility No exudate 2-4mm bone loss 5-7mm PD (stable)</td>
</tr>
<tr>
<td>III. Survival (compromised health)</td>
<td>Reduction of stress Drug therapy Surgical reentry Change in prosthesis/implants</td>
<td>No pain No mobility Possible exudate &gt;4mm bone loss &gt;7mm PD</td>
</tr>
<tr>
<td>IV. Failure (clinical or absolute failure)</td>
<td>Removal</td>
<td>Pain Mobility Uncontrolled exudate &gt;50% bone loss</td>
</tr>
</tbody>
</table>
### TABLE 18.9 New Proposed Classification of Peri-Implant Diseases

<table>
<thead>
<tr>
<th>Implant Quality Scales</th>
<th>Clinical Conditions</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Success (optimal health)</td>
<td>No pain or tenderness upon function</td>
<td>Normal maintenance</td>
</tr>
<tr>
<td>Osseointegration/Stage 0 osseoseparation</td>
<td>0 mobility</td>
<td></td>
</tr>
<tr>
<td>Peri-mucositis</td>
<td>&lt;2 mm radiographic bone loss from initial surgery</td>
<td></td>
</tr>
<tr>
<td>Peri-mucosal inflammation</td>
<td>PD ≤ 4 mm (bleeding and/or suppuration on probing)</td>
<td></td>
</tr>
<tr>
<td>Survival (satisfactory health)</td>
<td>No pain</td>
<td>Frequent SPT</td>
</tr>
<tr>
<td>Stage I osseoseparation Peri-mucositis</td>
<td>0 mobility</td>
<td>Nonsurgical debridement (hand, machine, air powder, lasers, etc.)</td>
</tr>
<tr>
<td>Peri-mucosal inflammation</td>
<td>&lt;2 mm radiographic bone loss from initial surgery</td>
<td>Patient self-administered care</td>
</tr>
<tr>
<td>Survival (potentially compromised)</td>
<td>No pain, 0 mobility</td>
<td>Adjunct local and systemic antimicrobials</td>
</tr>
<tr>
<td>Stage II osseoseparation Early peri-implantitis</td>
<td>0 mobility</td>
<td>Soft tissue and/or prosthetic corrections if required</td>
</tr>
<tr>
<td>Peri-mucosal inflammation</td>
<td>2-4 mm radiographic bone loss</td>
<td></td>
</tr>
<tr>
<td>Survival (compromised health)</td>
<td>No pain, 0 mobility</td>
<td>Treatment as above plus surgical reentry and revision</td>
</tr>
<tr>
<td>Stage III osseoseparation Moderate peri-implantitis</td>
<td>PD ± 4 mm (bleeding and/or suppuration on probing)</td>
<td>Laser</td>
</tr>
<tr>
<td>Peri-mucosal inflammation</td>
<td>Peri-mucosal inflammation</td>
<td>Implant surface decontamination</td>
</tr>
<tr>
<td>Survival (compromised health)</td>
<td>Bone loss ≤25% of the implant length</td>
<td>Regeneration</td>
</tr>
<tr>
<td>Moderate peri-implantitis</td>
<td>Treatment as above plus surgical reentry and revision</td>
<td></td>
</tr>
<tr>
<td>Failure (clinical failure)</td>
<td>Laser</td>
<td></td>
</tr>
<tr>
<td>Stage IV osseoseparation Advanced peri-implantitis</td>
<td>PD &gt;6 mm (bleeding and/or suppuration on probing)</td>
<td>Surgical reentry and revision</td>
</tr>
<tr>
<td>Peri-mucosal inflammation</td>
<td>Bone loss &gt;50% of the implant length</td>
<td>Lasers</td>
</tr>
<tr>
<td>Pain upon function</td>
<td>Mobility</td>
<td>Removal of implant</td>
</tr>
<tr>
<td>Failure (clinical failure)</td>
<td>Uncontrolled exudate</td>
<td></td>
</tr>
<tr>
<td>Stage IV osseoseparation Advanced peri-implantitis</td>
<td>Maybe no longer in mouth</td>
<td></td>
</tr>
<tr>
<td>Others (such as retrograde peri-implantitis)</td>
<td>Surgical reentry and revision</td>
<td></td>
</tr>
</tbody>
</table>

Data from Suzuki JB, Hsiao YJ, and Misch CE; Personal communication, 2017.
Why do implants fail?

“Medical Influences”
9.4% of implants were lost in 10 yrs

Patients with osteoporosis and osteopenia presented with more frequent failures

Lamonte MJ... Genco R.J. J Periodontol 2013; 84; 572
A “correlation” between marginal bone loss and the proportion of cortical bone was demonstrated around Brånemark® implants

> 60% cancellous bone, consistent with D1, D2 bone

at 1 year = 0.74 mm bone loss
at 3-4 years = 0.91 mm bone loss

A “correlation” between marginal bone loss and the proportion of cortical bone was demonstrated around Brånemark® implants.

< 30% cancellous bone, consistent with Osteoporosis

at 1 year = 1.49 mm bone loss
at 3-4 years = 1.83 mm bone loss

MEDICATION RISK FACTORS IMPACTING ON BONE DENSITY
MEDICATIONS CONTRIBUTING TO OSTEOPOROSIS

- Glucocorticoids
  (tx allergies, inflammation, autoimmune)
- Anti-cancer drugs
- Thyroid hormones
- Immune-suppressive drugs (Cyclosporine A)
- Antacids
MEDICATIONS CONTRIBUTING TO OSTEOPOROSIS

- Glucocorticoids (tx allergies, inflammation, autoimmune)
- Anti-cancer drugs
- Thyroid hormones
- Immune-suppressive drugs (Cyclosporine A)
- Antacids
HEARTBURN MEDS INCREASE RISK FOR OSTEOPOROSIS

- 1 year on meds
- 44% Increased Risk for Hip Fractures
- 1 year + on meds
  (Biol. Gradient longer on meds increases risk)
- 2 ½ X risk of Hip Fractures

- Gastric pH → Calcium absorption

*Yang, X. J.Am.Med Assoc 2006*
RECOMMENDATIONS FOR PATIENTS ON HEARTBURN MEDICATIONS

- Monitor meds closely
- DXA of bone annually
- Calcium-rich Diet
- Periodontal Exam

MEDS CONTRIBUTING TO OSTEOPOROSIS

- Glucocorticoids (tx allergies, inflammation, autoimmune)
- Anti-cancer drugs
- Thyroid hormones
- Immune-suppressive drugs (Cyclosporine A)
- Antacids
- Antidepressants
ANTIDEPRESSANTS INCREASE OSTEOPOROSIS RISK

(5,008 patients)

Antidepressants → Osteoporosis → Fractures (2X risk)

Goltzman, D. Arch Int Med 2007
SEROTONIN/NOREPINEPHRINE REUPTAKE INHIBITORS ("SSRI")

PRISTIQ
EFFEXOR
CELEXA
LEXAPRO
PROZAC
SYMBYAX
PAXIL
ZOLOFT
MEDICATIONS INFLUENCE ORAL CAVITY (INCLUDING DENTAL IMPLANTS)

- Saliva
- Soft Tissue
- Bone
- Occlusion
MEDICATIONS INFLUENCE SOFT TISSUE

- Peri-implant gingival hyperplasia
- Effect on microbial flora
  - Dilantin
  - Calcium Channel Blockers
  - Ace Inhibitors
  - Cyclosporine
  - Amphetamines
MEDICATIONS INFLUENCE SALIVA

Xerostomia ➔ effect on oral microbiome

- Anti-hypertensives
- Diuretics
- Antidepressants
- Antihistamines
Association between oral bisphosphonate use and dental implant failure among middle-aged women

Conclusion: Findings from this study suggest that dental practitioners should be aware of the increased risk of implant failure associated with oral bisphosphonate use in the population.

“... Dental practitioners should be aware of the increased risk of implant failure associated with oral bisphosphonate use.”
IMPLANT SURGERY IN OSTEOPOROSIS PATIENTS ON ORAL BISPHOSPHONATES (?)

“Maybe”
Dental management of patients receiving antiresorptive therapy

Jon Suzuki, Eddie Scher, Cemal Ucer, and Cameron Lee present the updated ADI guidance on bisphosphonates in full.

Introduction

Bisphosphonates belong to a class of drugs referred to as antiresorptive medications.

Although they are the standard treatment of choice for skeletal problems such as osteoporosis, other bone disorders and certain forms of malignancy, the use of antiresorptive therapy has been implicated in the pathoetiology of osteonecrosis of the jaw.

Figure 4: Illustration of antiresorptive therapy on
"... combined history of oral antiresorptive therapy and now taking IV Zoledronic acid (Reclast). All 4 cases developed Medication related Osteonecrosis of the Jaw after Implant Surgeries."

Lee, C and J.B. Suzuki. Implant Dentistry 2015; 24: 227-231
EUROPEAN WORKSHOP ON PERI-IMPLANTITIS

PERI-IMPLANTITIS IS CAUSED BY EXCESS CEMENT

J.CLIN.PERIO. 2008; 35 (SUPPLEMENT): 282
Local production of IgA- and IgM-rheumatoid factors in adult periodontal disease.

Hirsch HZ, Tarkowski A, Koopman WJ, Mestecky J.
Department of Pathology, University of Alabama, Birmingham 35294.

Rheumatoid factor (RF) distribution in periodontal disease.

Thé J, Ebersole JL.
Department of Immunology, Forsyth Dental Center, Boston, Massachusetts.

Rheumatoid factor from periodontitis patients cross-reacts with epitopes on oral bacteria

J Thé¹, JL Ebersole²
Department of Immunology, Forsyth Dental Center and Harvard School of Dental Medicine, Boston, MA, USA.

Serum rheumatoid factor induced by intraperitoneal administration of periodontopathic bacterial lipopolysaccharide in mice

Antibody responses to *Porphyromonas gingivalis* (*P. gingivalis*)
in subjects with rheumatoid arthritis and periodontitis

Ted R. Mikuls, MD, MSPH†, Jeffrey B. Payne, DDS, MDSc, Richard A. Reinhardt, DDS, MS, PhD†, Geoffrey M. Thiele, PhD†, Eileen Maziarz, MD†, Amy C. Cannella, MD†, V. Michael Holers, MD†, Kristine A. Kuhn, MD†, and James R. O'Dell, MD

†Department of Medicine, Nebraska Arthritis Outcomes Research Center (NAORC), University of Nebraska Medical Center and Omaha Veterans Affairs Medical Center (Omaha, NE, USA)

‡College of Dentistry, University of Nebraska Medical Center (Lincoln, NE, USA)

Department of Medicine, University of Colorado Denver School of Medicine (Denver, CO, USA)

Serum Cytokine and Periodontal Profiles in Relation to Disease Activity of Rheumatoid Arthritis in Japanese Adults

Tetsuo Kobayashi,*‡ Akira Murasawa,*‡ Yasutaka Komatsu,*† Tomoko Yokoyama,*‡ Kohei Ishida,*‡ Asami Abe,*‡ Kouji Yamamoto,*‡ and Hiromasa Yoshie*‡
Effect of Non-Nutritive Sweeteners

G.I. Microbiome Alterations

Weight Gain (?)
Insulin Resistance (?)