Patient #1: “Periodontal Therapies and Osteoporosis”

- What are dental management preventive strategies for osteoporosis patients?
- What is the biological basis for bisphosphonates and adverse dental outcomes?
- What is proposed management?
**Patient #2: “Periodontal Therapies and Cancer Patients”**

- What are dental management strategies for Cancer patients?
- What is the biological basis for “timing” of dental therapies?

**Patient #3**

- Patient: 37 y.o. w. f
- Med. Hx: ASA I, mild allergies
- Rx: Claritin prn
- Dental Dx: “Cracked roots, #8, #9
- T.P. Extractions + Ridge Preservation Sx + Implants + Prosthetics

**Patient #3: “Extractions and Regeneration Therapies”**

- What is the emerging standard of care for dental extractions?
- What modalities of regeneration may be applied in a restorative practice?
- What bone graft products and membranes are considered?
Patient #4

Patient: 45 y.o. w male
Med Hx: ASA II
Rx Hx: none
CC: “Bleeding around lower right implant area”

Patient #4: “Peri Implantitis”

What is Peri mucositis? Peri Implantitis?
What modalities of implant rescue therapies are being developed?

Current Terminologies of “Osteonecrosis of the Jaw”

- BI ONJ
- BRONJ
- BONJ
- ONJ = Osteonecrosis of the Jaw*
- ART = Anti-resorptive Therapies**
- MRONJ = Medication-Related Osteonecrosis of the Jaw***

**Council Scientific Affairs, ADA, J.Am.Dent.Assoc 2011; 142:
***AAOMS. Chicago, June 2014 Newsletter
Risk factors for Osteoporosis

- Age (Older, higher the risk)
- Race (Caucasians and Asians have higher risk)
- Weight (small boned and thin women increase risk)
- Family (heredity)
- Lifestyle (Smoking, lack of exercise, alcohol increase risk)

Ref: National Osteoporosis Foundation, 2014

“T-Score” (Diagnosis of Bone Conditions)

Indicates level of bone health (Using DXA)

- Normal scores (+/- 1.0 s.d of mean)
- Osteopenia (bet. minus 1.0 - 2.5 s.d of mean)
- Osteoporosis (below minus 2.5 s.d of mean)

Ref: National Osteoporosis Foundation, 2012

Osteoporosis should be considered in the treatment plan for dental implants

1. Selected Meds for Osteoporosis increase the risk for ONJ
2. Selected medications may increase risk for Osteoporosis
3. Osteoporosis may impact on bone density for osteotomy implant preparation
4. Both medications and dx osteoporosis may alter site preparation surgeries
Tissue Engineering Triad

<table>
<thead>
<tr>
<th>Scaffold</th>
<th>Cells</th>
<th>Signaling Molecules</th>
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<tbody>
<tr>
<td>- collagen sponge</td>
<td>- cancellous bone</td>
<td>- BMP's</td>
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<tr>
<td>- mineralized bone allograft</td>
<td>- Bone marrow aspirate</td>
<td>- PDGF</td>
</tr>
<tr>
<td>- anorganic bovine bone</td>
<td>- mesenchymal stem cells</td>
<td>- VEGF</td>
</tr>
<tr>
<td>- hydroxylpatite</td>
<td>- periosteum</td>
<td>- TGFβ</td>
</tr>
<tr>
<td>- ceramics</td>
<td>- adipose tissue</td>
<td>rhPDGF-BB</td>
</tr>
<tr>
<td>- polymers</td>
<td>- platelets</td>
<td>rhBMP-2</td>
</tr>
<tr>
<td>- composite</td>
<td>- allogeneic stem cells</td>
<td></td>
</tr>
<tr>
<td>- Titanium mesh</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Primary Indications for Bisphosphonates

- Osteoporosis
- Osteopenia
- Multiple Myeloma
- Paget’s Disease
- Breast CA Therapies
- Prostate CA ADT

Significance of Hip Fractures

- “1 out of 4 patients will die from a hip fracture within a year”
- “50% will die within 5 years after a hip fracture”

NIH 2000 Conference on Osteoporosis
Cooper. Am.J.Epidemiol. 1993
Osteoporosis Drugs- Oral
(USA FDA approved, 2015)

- Fosamax
- Fosamax with Vit D (approved 5-05)
- Actonel
- Actonel with Calcium (approved 9-05)
- Boniva (approved 5-05)
- Atelvia* (approved 2014)

* "OK" after meals

Osteoporosis Drugs- IV
(USA FDA approved, 2015)

- Aredia (30 mg iv/ mo)*
- Zometa (30 mg iv/ mo)*
- Reclast (5 mg iv/ yr)**, 2013

* Rx for Multiple Myeloma, Ca
** Rx for Osteoporosis

American Dental Association
November 2011 Guidelines

- A. “Routine” Dental Tx is OK
- B. Dental Exams before or early in Rx Bisphosphonates
- C. OHI reduces risk
- D. CTX blood test is inconclusive
- E. “Drug Holiday” may not reduce risk

J. Am. Dent. Assoc. 2011 (Nov)
ADA Council on Scientific Affairs.
“CTX is not a reliable predictor of ONJ risk”

LEE, C.Y.S and SUZUKI, J.B.
CTX Biochemical Marker of Bone Metabolism. Is it a Reliable Predictor of Bisphosphonate-Associated Osteonecrosis of the Jaws After Surgery Part I: Biological Concepts with a Review of the Literature

LEE, C.Y.S and SUZUKI, J.B
CTX Biochemical Marker of Bone Metabolism. Is it a Reliable Predictor of Bisphosphonate-Associated Osteonecrosis of the Jaws After Surgery Part II: A Prospective Clinical Study.

Fosamax has extended benefit for 5 years

- 1,100 female pts, 55-81 years
- 10 years on Rx Fosamax
- Osteoporosis protection for 5 years after stopping drug
- Conclusion: “Protective benefit for at least 5 years”

Black, D. J. Am. Med. Assoc 2006 (Dec)

A Decade of Bisphosphonate Bone Complications: What It Has Taught Us About Bone Physiology
Robert E. Marx, DDS

1. Bisphosphonates ½ life in bone = 11 years

2. IV Bisphosphonates accrue in bone 142.8 X Oral Bisphosphonates

How long for Rx to reach maximum efficacy? (Bone Biopsy)

- **Alendronate** (Fosamax) = 2-3 years normal mineralization
- **Risendronate** (Actonel, Atelvia) = 3-5 years normal mineralization

Erickson. Bone 2002; 15: 613
Roschger. Bone 2001; 29: 185

JBS recommendations (not FDA)

1. Proceed with caution on any dental tx for patients using bisphosphonates.
2. Package inserts for Aredia, Zometa, Fosamax, Actonel, Atelvia, Reclast include “dental advisories”; ask patients to read them
3. If on oral bisphosphonates for 3 years of less, dental tx is “probably” ok.
   If on oral bisphosphonates for over 3 years, caution; use Rx Antibiotics*.

JBS recommendations (not FDA)

4. **Adult Prophy** (code 1110) or **Periodontal Maintenance** (code 4910) completed 7-10 days before surgery/ extractions.
5. Antimicrobial Rinses bid 7 days before invasive procedure.
6. Rx Systemic Antibiotics 24 hours before invasive procedure.
Case Report: Fosamax Rx

Pt: 57 y.o. male
CC: Pain upper front tooth
Med Hx: Fosamax q 7d X 6 yrs
Dental Hx: Missing teeth, Periodontitis
Oral Image: “Get me out of pain”

Suzuki, Jon. Temple University Grad Perio Clinic, 2014

Treatment Plan

- Treat CC
- Extract #8
- Comprehensive Periodontal tx w/ dental implants + Restorative
- Maintenance q 3 mos

Post op visit @ 7 weeks

- Febrile (101 F)
- Gingival swelling and purulence
- Bone spicules protruding from #8 extraction socket
- Maxillary gingiva sensitive during chewing
Treatment Plan

- Treat CC
- Extract #8 + PA Film (Bone spicules)
- Comprehensive Periodontal tx w/ dental implants + Restorative
- Maintenance q 3 mos

Issues with Osteonecrotic Bone

1. Angiogenesis impaired
2. Wound healing impaired
3. Antibiotic delivery slower
4. Bone turnover altered
5. Infection risk increased

Dental management of patients receiving antiresorptive therapy

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

Surgical management

In cases of advanced ONJ or cases that have proven to be refractory to conservative treatment, a more surgically aggressive approach is indicated, which includes surgical resection of all infected and necrotic bone to permit wound healing in the form of primary closure of soft tissues (Abd-El et al., 2009; Falsetti et al., 2009; Carlton & Baselie, 2009; Stockmann et al., 2010; Cari et al., 2011; Wilde et al., 2011).

The mainstay of surgical management involves debridement, sequestrectomy and in some instances, resection (Stage 3) for...
Patient #2: “Periodontal Therapies and Cancer Patients”

- What are dental management strategies for Cancer patients?
- What is the biological basis for “timing” of dental therapies?
- Clinical research on cancer patients may be applied to other patients with selected immune deficiencies

Chemotherapy for Cancer

- Local or Systemic Therapies
- Destroys, suppresses, or prevents spread of malignant cells
- Prolongs life
- Extend periods of tumor remission

Chemotherapy of Cancer: Clinical Manifestations (general)

- 1. Acute Periodontal Exacerbations
- 2. Ulceration and Mucositis
- 3. Xerostomia
- 4. Oral Pain
- 5. Hemorrhage

Treatment Plan

1. Review Med/Dental Hx
2. Dx: Periodontitis / Insurance Codes
3. Initial Tx:
   - OHI
   - Occlusal Control
   - Rx CHX, phenol, Cetylpyridinium rinses
   - Ultrasonics Scaling/ RP/ Polish
   - Evaluation (4-6 weeks)
4. Periodontal Surgery
5. Maintenance (q 3 mos)

Recommend 3 OH devices

- Brush (power preferred)
- Floss ("furry")
- One additional oral hyg

WBC Counts and Dental Therapy

- Therapy should be avoided when the WBC is less than 2,000 cells/mm
- Therapy should be avoided when Absolute Granulocyte count is less than 1,500/mm
- If emergency dental therapy is required, use prophylactic antibiotics

Oral Hygiene and CA Chemotherapy

- **No Oral Hygiene** when WBC is less than 2,000/ mm³
- **No Oral Hygiene** when Platelets are less than 20,000/ mm³


---

**OHI During Chemo tx**

- If Granulocytes 2,000 – 5,000 mm³
- Or
- If Platelets 20,000 – 50,000 mm³

Replace brush/floss with oral lavage, super-soft toothbrush

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**Cancer Patient References**

- Deapaola, Peterson,...Suzuki. J.A.D.A. 1986; 112: 198
Organ Transplant Meds

- FK 506 (Tacrolimus), Japan
- Prevent organ rejection
- "Rescue" treatment for organ rejection unresponsive to Cyclosporine
- Decrease T-lymphs, CMI, Humoral

*Med. Let. 1994; 36: 82
*Drugs 1993; 46: 746

Prevent "Rejection" of Organ Transplants

WBCs → Foreign Objects (Organ)

"Reject"

Rx FK-506 (Tacrolimus)
Rx Cyclosporin

"Accept"
New Strategies

- Special issues are involved for dental management of Immunocompromised Patients
- Cancer Patients undergoing either Chemotherapy or Radiation Therapy or both require “timing” strategies in Dental treatment

Stress

High levels of coping modified the effects of stress on PD. Possibly by nullifying the adverse effects of financial stress among those with periodontitis.


Patient #3: “Extractions and Regeneration Therapies”

- What is the emerging standard of care for dental extractions?
- What modalities of regeneration may be applied in a restorative practice?
- What bone graft products and membranes are considered?
Regeneration in Dentistry

Alveolar Ridge Width + Height
Maxillary Sinus Bone Grafts
Extractions; Ridge Preservation
Periodontal Osseous Defects
Genetic Errors of Development
(Cleft Palate)
Trauma
Neoplasia

What bone graft should you use? …and in what order of preference?

<table>
<thead>
<tr>
<th>Type</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>Autograft</td>
<td>Transplants from one region to another in the same individual.</td>
</tr>
<tr>
<td>Allograft</td>
<td>Transplants from one individual to a genetically non-identical individual of the same species.</td>
</tr>
<tr>
<td>Xenograft</td>
<td>Transplants from one species to another.</td>
</tr>
<tr>
<td>Alloplast</td>
<td>Transplants of inorganic (synthetic/natural) or polymer derived bone substitutes.</td>
</tr>
</tbody>
</table>

Biologic/ Molecular Approaches

- **Pepgen P-15** (Dentsply)
- **Emdogain** (Straumann)
- **Gem 21** (Osteohealth)
- **Infuse** (BMP, Bone Morphogenetic Protein (Biohorizons))
### Regional Acceleratory Phenomenon (RAP)

- Bone perforated with high speed round burs or curets
- Bone is stimulated with osteogenic cells + osteogenic molecules
- Bone Regeneration

### Regeneration Surgeries

- Bone Grafts
- Guided Tissue Regeneration
- Biologics
- Regional Acceleratory Phenomenon
Dental Plaque Biofilm, Inflammation, and Systemic Diseases
Clinical Implication

- Periodontitis, as an oral infection, may contribute to risk factors for Systemic Diseases
- Periodontal therapy should reduce the risk for selected systemic diseases

Biofilm Infections

- Periodontal Diseases
- Otitis Media
- Prostatitis
- Prosthesis-related Orthopedic Infections

### Periodontal Diseases and Systemic Diseases (2015)

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. Alzheimer’s Disease, Dementia (?)

### “Shared risk factors for CVD and Periodontitis”

- Atherosclerosis
- Diabetes mellitus
- Cancer
- Periodontitis


### Cardiovascular Diseases

“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”

*Mattila K. Dental Infections and Cardiovascular Disease: A Review. J. Perio 2005*
Periodontitis and Coronary Heart Disease

NHANES III for 5,564 pts (> 40 age)

- Independent variable % of periodontal sites per person with attachment loss ≥ 3mm

“Association (not causality) between periodontal diseases and coronary heart disease”

Arbes 1999

---

Periodontitis and higher risk of Cardiovascular Disease

Profile of Periodontitis patients:
- ↑ total and LDL cholesterol, triglycerides and ↓ HDL cholesterol.
- Chronic inflammatory and immune response.
- ↑ CRP and IgA antibodies.

Conclusion: Periodontitis patients with ↑ CRP, serum antibodies and chronic low grade infection (perio pathogens) makes them at a higher risk of developing CVD.


---

Periodontitis → Stroke (CVA)

NHANES I Sample, 9,962 pts*
* Hx MI, CVA, Cancer excluded

“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

Periodontitis and Ischemic Stroke

- 349 ischemic stroke cases
  - Men < 24 teeth higher risk vs men > 25 teeth
  - Modest association between periodontitis and ischemic stroke

“Periodontitis and fewer teeth may be associated with increased risk of ischemic stroke”

Joshipura 2003

Periodontitis and Ischemic Stroke

Case control (303 patients) within 7 days after acute ischemic stroke or transient ischemic attack.

Severe periodontitis = 4.3 x higher risk for cerebral ischemia in men (< 60 yrs)

Grau 2004

“Periodontal disease with elevated bacterial exposure is associated with Coronary Heart Disease events and early atherogenesis...”

Conclusions: Periodontal disease with elevated bacterial exposure is associated with CHD events and early atherogenesis (CIMT), suggesting that the level of systemic bacterial exposure from periodontitis is the biologically pertinent exposure with regard to cardiovascular risk.
Periodontal Therapy and Endothelial Function

periodontal non-sx tx
(S/RP, extractions, Arestin local Rx)

24 hrs

flow mediated dilation
significantly lower than controls
(supragingival scaling + polish)

Tonetti N.Eng.J.Med. 2007

Acute short term systemic inflammation and endothelial dysfunction

Improvement in endothelial function

Outcome of Periodontal Therapy

- Purpose: Does Periodontal Therapy reduce CRP associated CVD risk?
- Results:
  - Severe and widespread periodontitis had higher chance of having high CRP associated CVD risk (OR 5.6)
  - Age and body mass- significant.
  - After SRP, significant decrease in CVD risks.
- Conclusion: Successful periodontal therapy may reduce CRP associated cardiovascular risk.

D'Aiuto 2004

"Periodontal treatment ...may result in a decreased Coronary Heart Disease risk for treated patients."

“Periodontal treatment resulted in significant decreases in ... lowered serum inflammatory markers. This may result in a decreased CHD Risk for treated patients”


“Periodontal therapy resulted in lowered serum metabolic markers in Coronary Heart Disease and healthy patients...

this may result in lowered risk for CHD”


“Stopping Rx Plavix increases risk of MI by 2 X”

- 3,137 Patients, Veterans Affairs
- 127 VA Hospitals
- “Stopping Rx Plavix increased risk of MI by 2 X”
- Recommend either slower decrease of dosage or supplement with ASA

### Periodontal Diseases and Respiratory Infections

**Anaerobic bacteria forming biofilms with aspiration pneumonia in elderly pts.**
Pathogenicity of bacteria in experimental mouse model.
Co-existence of Pg and Td in chronic periodontal lesions.


### Periodontal Diseases and Respiratory Infections

**Professional oral health care of elderly pts for 6 months ↓ the salivary levels of:**
- protease
- trypsin like activity
- neuraminidase
- influenza


### Respiratory diseases in periodontal patients

- Oral colonization by respiratory pathogens is a risk factor for lung infections in high risk subjects
- Improving oral hygiene and reducing inflammation reduces lung infections in susceptible subjects by 40%.

Respiratory diseases in periodontal patients

- Patients with forced expiratory
  volume in 1 sec < than 65% of predicted volume.
- Radiographic alveolar bone loss is associated with increased risk for COPD.


Periodontal Diseaes and Lung Cancer Incidence

“Periodontal disease is associated with lung cancer in postmenopausal women” (n = 77,485 females)

Results: Periodontal Disease was positively associated with lung cancer risk (after adjusting for smoking hx) Synergistic effect between Periodontal Disease and Smoking Intensity

Mai X, ... Genco RJ et al. Cancer Causes Control 2014; 25: 1045

Osteoporosis

NHANES II (women)
13-18% Osteoporosis
47-50% Osteopenia

Systemic osteoporosis was associated with osteoporosis of the mandible

“Osteoporosis is associated with increased tooth loss”
LaMonte MJ, ... Genco RJ, et al. J.Periodontol. 2014
Dietary Calcium (?)

“Several studies show that calcium and vitamin D supplements used to prevent or treat osteoporosis also appear to have beneficial effects on tooth retention.”

LaMonte MJ, ... Genco R.J. J.Periodontol. 2014 (Oct)

Quality of Bone and Peri-Implantitis

“Quality of cortical bone could jeopardize the long-term stability of the marginal bone surrounding implants placed in the posterior region of the mandible”


Periodontal Diseases and Systemic Diseases (2015)

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- 8. Diabetes Mellitus
- 9. Obesity
- 10. Pancreatic Cancer, Other Cancers
- 11. Alzheimer’s Disease, Dementia (?)
Autoantibody against body’s own tissues

IgG (antibody) combines with RF to form immune complexes
Gastric infection and *H. pylori*

*H. Pylori* in the oral cavity affected the outcome of eradicated therapy and associated with recurrent gastric infection.

*H. Pylori* by nested PCR should be considered as a causal factor in recurrent gastric disease.


**“Bidirectional relationship between Diabetes mellitus and Periodontitis”**

Prospective Study:
37% Diabetic patients glycemic control worsened with periodontitis

vs

11% Diabetic patients glycemic control worsened with periodontal health

"Bidirectional relationship between Diabetes mellitus and Periodontitis"

Prospective Study:
Death rate 28/1,000 Diabetic patients with periodontitis
vs
Death rate 10/1,000 Diabetic patients with periodontal health


Diabetes mellitus and Periodontal Disease

“Two way relationship between diabetes and Periodontal Disease

Prediabetes (impaired fasting glucose or glucose intolerance)

Gestational diabetes

Emrlich et al. 1991


Diabetes mellitus and Periodontal Disease

Importance and clinical significance of reduction in glycated hemoglobin levels.

Reduce microvascular complications (retinopathy and nephropathy)

Altered native immune responses

Emrlich et al. 1991

Periodontal Diseases and Systemic Diseases (2015)
- 1. CVD (MI)
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- 3. Respiratory Diseases
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- 5. Osteoporosis
- 6. Rheumatoid Arthritis
- 7. Gastric Ulcers
- 8. Diabetes Mellitus
- 9. Obesity
- 10. Pancreatic Cancer, Other Cancers
- 11. Alzheimer’s Disease (?)

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


Implant Maintenance

<table>
<thead>
<tr>
<th>Group</th>
<th>Management</th>
<th>Clinical Conditions</th>
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<tbody>
<tr>
<td>Success</td>
<td>Optimum Group Healthy</td>
<td>Normal maintenance</td>
</tr>
<tr>
<td>Survival</td>
<td>Favorable health</td>
<td>Reduction of stress</td>
</tr>
<tr>
<td>Failure</td>
<td>Clinically absolute failure</td>
<td>Change in position/implants</td>
</tr>
</tbody>
</table>

Suzuki, Misch et al, 3rd ed. 2008
Probing Dental Implants

- 9 months post implant placement
- Resin-coated or Stainless Steel probes
- Every 6 months

The aim of this study was to investigate surface roughness on the apical collar of implant abutments caused by probing and scaling instruments.

Probing and Scaling Instrumentation on Implant Abutment Surfaces: An In-Vitro Study
Fakhravar, B... J.B. Suzuki, J. Implant Dent. 2012; Vol 21 (Sept)
Periimplantitis: Implications for Maintenance Care

- Do not probe site for 9 months
- Do not scale subgingival for 9 months
- Oral hygiene is critical
- Recommend antimicrobial (FDA, ADA)
- Take follow up x-rays at 9 months
- Ultrasonic debridement with “specialized tips”
- Scale with Implant Scalers
- Antimicrobial Irrigation of Implant
- Rx Arestin therapy (Off-FDA Label)


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Patient #4: “Peri Implantitis”

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- What modalities of implant rescue therapies are being developed?

Risk Factors for Periodontal Disease

**Individual risk factors**

- Gender, smoking, and alcohol
- Diabetes
- Obesity and metabolic syndrome
- Osteoporosis, Calcium, Vitamin D
- Stress
- Genetic factors

Smoking
Positive relation between prevalence of periodontal disease and increasing severity and # pack years smoked


Alcohol
“May be associated in a dose dependent manner, with increased severity of clinical attachment loss”

(OR: 5, 10, 15, 20 drinks/week = 1.22, 1.39, 1.54, 1.67)