

Oral Health and General Health; What's the Connection?

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It's a Two-Way Street

- “The mouth mirrors the body” – Many systemic diseases have oral manifestations.
 - E.g. HIV, diabetes mellitus, anemias
- Oral disease can affect treatment for systemic disease.
 - E.g. Solid organ transplants; Cancer Chemotherapy; Osteoradionecrosis; Glycemic control in diabetes mellitus
- Treatment for systemic disease can affect oral health.
 - Oral mucositis from chemotherapy; Xerostomia from medications

“It’s a Two Way Street”

- Oral health affects quality of life.
 - Xerostomia, Missing Teeth, Tooth Pain and Quality of Life
- Oral disease can increase risk for systemic disease.
 - Periodontal Disease and COPD, Cardiovascular disease, Adverse pregnancy outcomes

Oral Manifestations of Systemic Disease

- **Early detection** of systemic disease through oral examination and recognition of oral manifestations – an opportunity for oral health professionals
 - Oral manifestations of HIV/AIDS; Accelerated periodontal bone loss and diabetes
- **Control/lack of control** of systemic disease can be detected in the mouth through oral examination
 - E.g. glycemic control of diabetes

Gingival Infiltration in Acute Myelogenous Leukemia

Oral Manifestations of AIDS

- 36 year old dentist
- 4 months pregnant with 4th child
- Sudden onset
- Dry mouth & eyes
- Enlarged salivary glands

Sjogren's Syndrome

- Dry mouth & eyes
- Enlarged salivary glands
- May also involve thyroid, lung, kidney, liver, bladder
- Family predisposition sometimes
- **Relative risk of lymphoma 40X**

Primary Sjogren's (Sicca):

no second autoimmune disease
4:1 female predominance, middle age

Secondary Sjogren's:

second autoimmune disease is also present

usually rheumatoid arthritis
(75%)

F:M 10:1

GI Disorders and the Teeth

“Silent” GERD

Dental Erosion

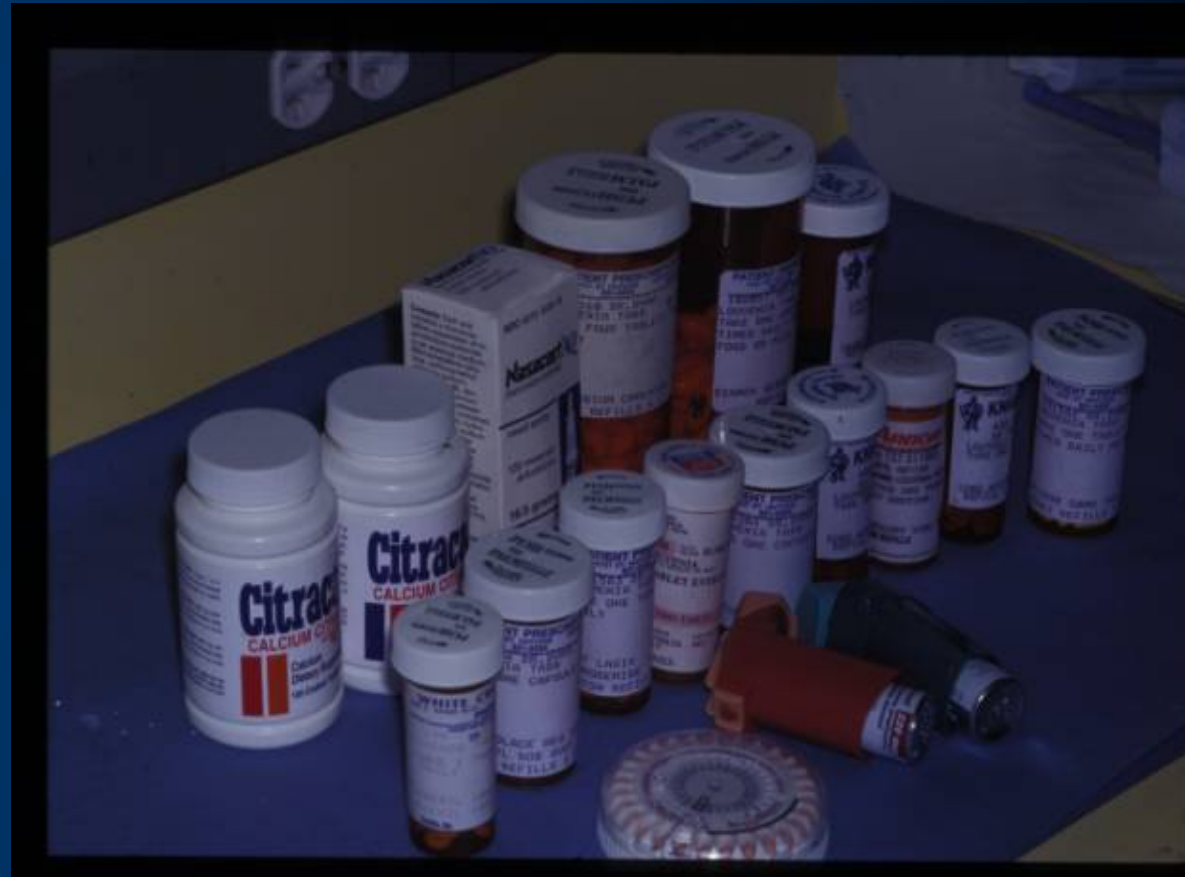
- Diet
 - Lemons and citrus, vinegar
 - Carbonated beverages
 - Wine!
- Gastric contents
 - GERD, other G.I. disease
 - Vomiting – Bulimia
- Environmental
 - Metal processing plants – industrial acids
 - Chlorinated swimming pools

Oral Manifestations of Bulimia

- Sensitive teeth
- Dehydration and xerostomia
- Caries
- Palatal petechiae from vomiting
- Parotid Gland Swelling

Drug Reactions

- Xerostomia
- Gingival hyperplasia
- Chemotherapy/Radiation
- Osteonecrosis
- Secondary Infections
 - Candidiasis
- Other Reactions
 - Lichenoid Mucositis
 - Erythema Multiforme
 - Oral Ulceration



Toxic Mucositis

Lichenoid Drug Reaction

- Increasing prevalence
- Antibiotics, antihypertensives, antimalarials, diuretics, gold compounds, NSAIDS
- Resembles erosive lichen planus
- Posterior buccal mucosa
- Painful, central erythematous area of erosion, radiating striae

Erythema Multiforme

Cocaine Abuse and the Mouth

Bisphosphonate-Related Osteonecrosis

**Osteonecrosis of the jaws associated with the use of
bisphosphonates: A review of 63 cases**

Journal of Oral and Maxillofacial Surgery

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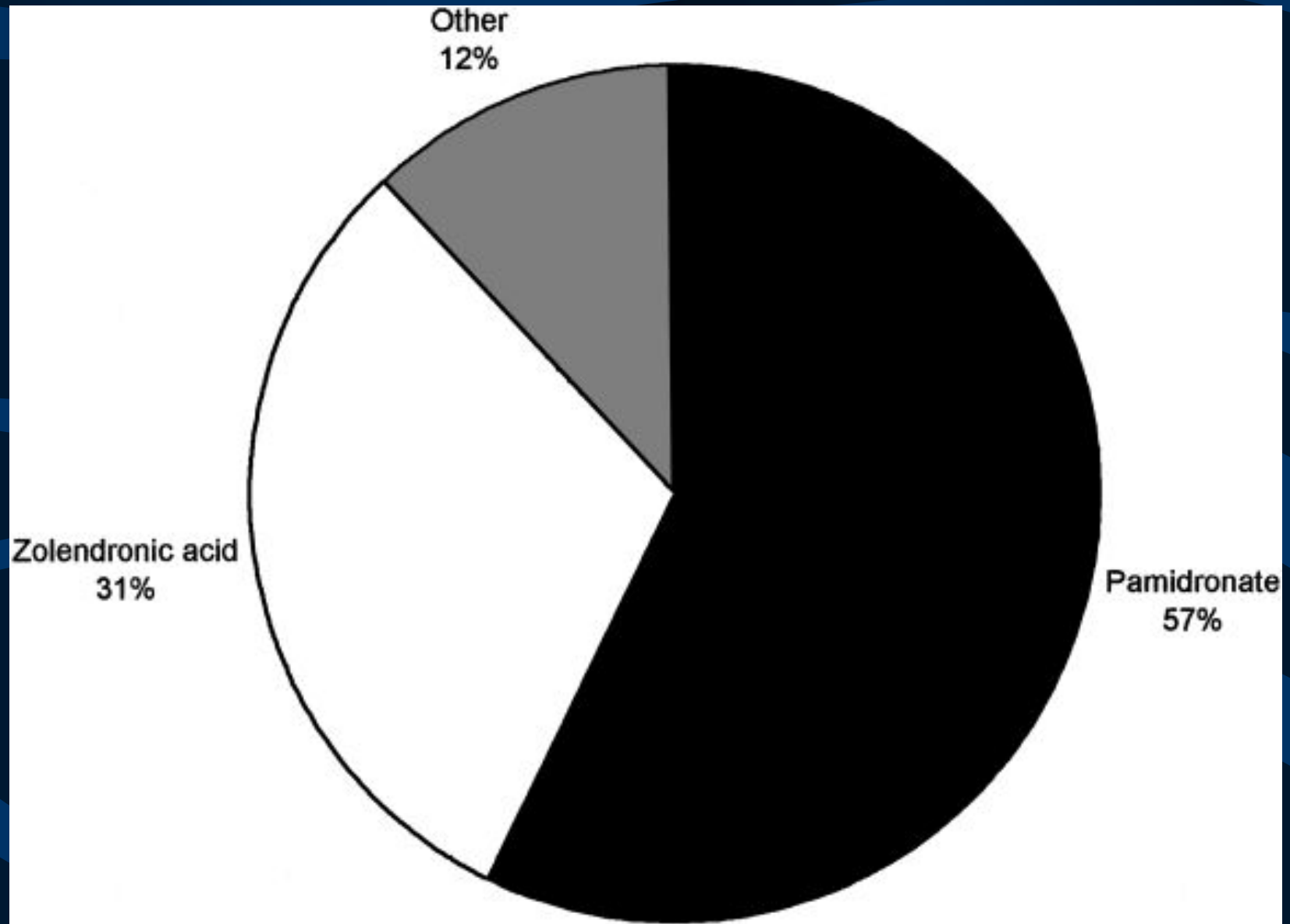
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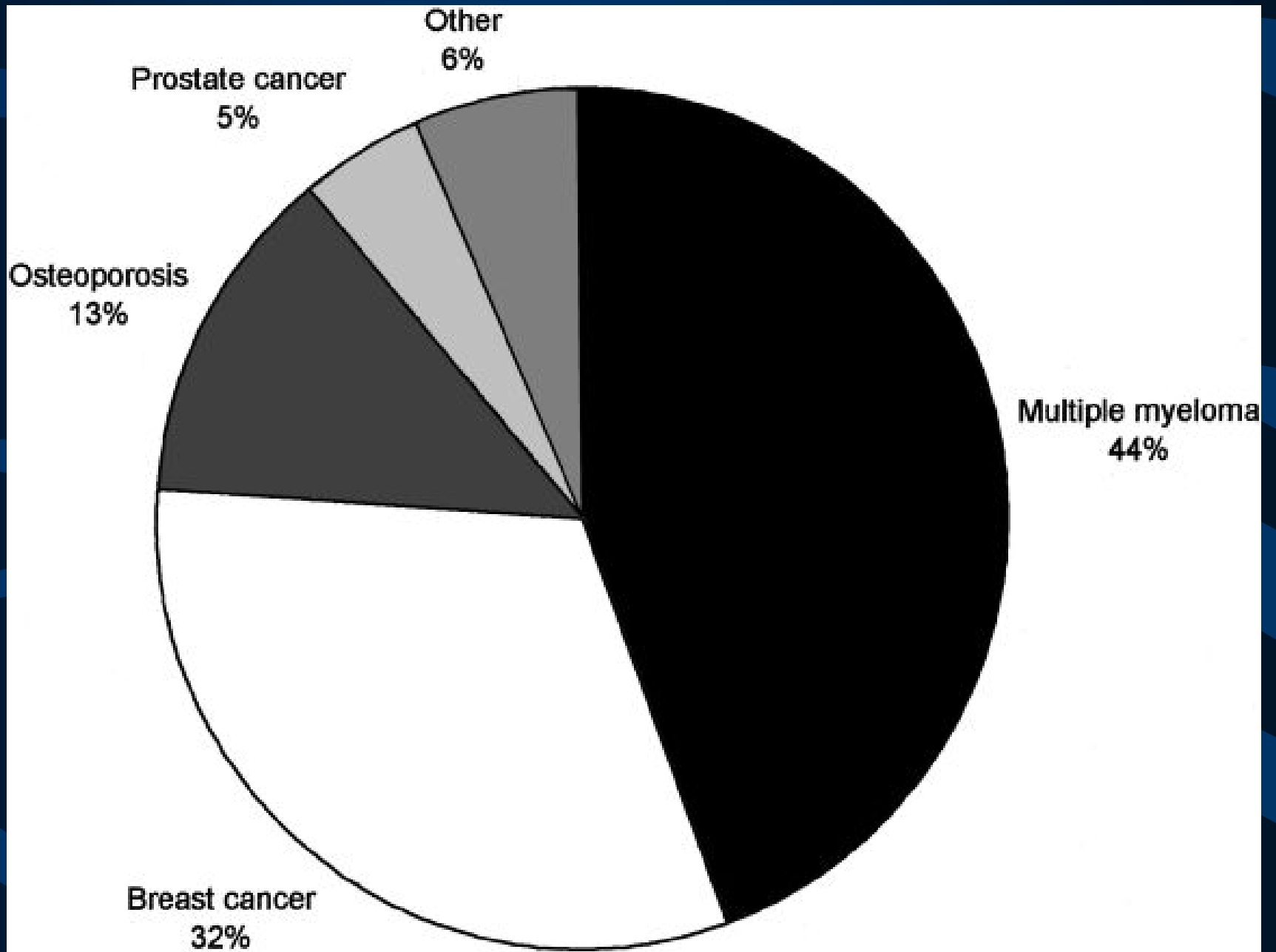
Bisphosphonates

- Drugs used to control bone resorption by osteoclasts to help control or prevent further metastasis in bone
 - Multiple myeloma, metastatic breast, prostate cancer
- Same or similar drugs used in lower doses to treat osteoporosis
 - **MANY MORE** patients use these drugs for this indication

63 Cases-Long Island Jewish Medical Center

- Twenty-four patients (38%) with maxillary bone
 - 19 unilateral and 5 bilateral)
- 40 (63%) had mandibular bone involvement
 - 37 unilateral and 3 bilateral
- The typical presenting symptoms were pain and exposed bone at the site of a previous tooth extraction.
- 9 of the 63 patients (14%) had had no history of a recent dento-alveolar procedure and nevertheless presented with spontaneous exposure and necrosis of the alveolar bone.





Mechanism?

- Hypothesis: Bisphosphonates inhibit new vessel formation, thereby impairing healing
- Documented risk factors: diagnosis of cancer, concomitant therapies (steroids, chemo, radiation), comorbidities (anemia, coagulopathies, infection, pre-existing dental disease)
- Most cases were associated with iv. therapy but some associated with oral meds
- Withdrawing drug has no effect, no proven tx
 - Medical Journal of Australia –Purcell and Boyd, 2005

Treatment

- Conservative debridement
- Long term suppressive antibiotics
- Preventive dental treatment

What to do when patients with a history of bisphosphonate use require extractions or periodontal surgery?

Oral Disease Can Affect Treatment for Systemic Disease –Medically Necessary Dental Treatment

- Diabetes Mellitus
- Cancer Treatment
- Cardiac Patients
- Renal Disease – Hemodialysis
- Organ Transplants
- Nutrition –surgical cases

Radiation Therapy and Oral Health

- Patients receiving radiation therapy (RT) for head and neck cancer require dental evaluation and elimination of potential sources of infection, prior to RT
- Current dental guidelines for patients pre-RT are aggressive because dental infection or oral surgery can cause significant morbidity and even mortality as a consequence of osteoradionecrosis (Little JW, Falace DA, et al, 2002)

Dental Disease Before RT

Dental Disease After RT

Radiation Caries

Oral Disease Can Increase Risk of Systemic Disease (?)

- Oral Bacteria and Bacterial Endocarditis
- Periodontal Disease and Glycemic Control in Diabetes Mellitus
- Periodontal Disease and Pre-Term Low Birthweight
- Oral Disease and Cardiovascular Disease
- Oral Microbes and Pneumonia
- Periodontal Disease and Renal Insufficiency

Focal Infection Theory

- The mouth is a reservoir of bacteria that can
 - Spread through the blood to cause infections at distant site
 - Bacterial endocarditis
 - Bacterial pneumonia, nursing home patients
 - Stimulate an immune response; circulating inflammatory mediators cause damage throughout the body
 - C-reactive protein and atherosclerosis

Periodontal Disease

- Chronic oral infection characteristically associated with Gram-negative bacteria and production of inflammatory mediators which leads to loss of periodontal attachment
 - *P. gingivalis*, *F. Nucleatum*, *E. corrodens*, *A. actinomycetumcomitans*

Periodontal Abscess

Chronic periodontitis

Acute necrotizing ulcerative gingivitis

Periodontal Disease and Glycemic Control in Diabetes Mellitus

Bidirectional Adverse Interrelationship between Diabetes Mellitus and Periodontal Disease

- Observational studies support an association of worse periodontal health in pts with diabetes
- Tsai et al, 2002 – pts with poorly controlled DM had a significantly higher prevalence of severe periodontitis than those without diabetes (OR=2.90) NHANES data
- Cross-sectional studies support an association between poorer glycemic control and more frequent or severe periodontal disease – 13/18 papers published since 1990 (Systematic review by Taylor GW et al, 2002)

- Overall the evidence supports the view that the relationship between diabetes and periodontal disease is bidirectional
- Further rigorous study is needed to firmly establish that treating periodontal infections can contribute to glycemic management and possibly a reduction in the complications of diabetes mellitus
 - This study is ongoing at University of Michigan – GW Taylor is the primary investigator

Adverse Pregnancy Outcomes

- Every year in USA, 1/10 births arrive too early and too small
- Preterm birth represents the major cause of neonatal mortality and among survivors, a major contributor to long term disability
- African-American women have 2-3 times greater risk of having baby pre-term compared to Whites or Hispanics

- Incidence of preterm birth has not decreased over last 40 years!
 - Those preemie females born after 1960 are now having their own babies.
- We have not yet identified all causes of pre-term birth
- Smoking and alcohol are the two major modifiable risk factors

Other Risk Factors for Preterm Birth

Number of previous births (most common in first births)

Maternal age – young and old

Short cervix

Short maternal stature

Low maternal weight

High physical and psychological stress

Low SES

Poor maternal nutrition

Infections of the reproductive tract -Chorioamnionitis

Family History and Genetics

“If a woman herself was born preterm, she is also at increased risk of spontaneous preterm labor and preterm birth, with the risks being highest for those women who were themselves born very preterm (before 32 weeks)” .

Varner and Esplin. BJOG. 2005;112 Suppl 1:28-31. Current understanding of genetics factors in preterm birth.

Recent genetic study found association with single gene polymorphisms in TNF-alpha-308; IL-1 beta, and IL-6 - 174, all inflammatory cytokines

PTLBW infant

- Infant with a birthweight less than 2500 grams
 - Very low birthweight (VLBW) is defined as less than 1500 grams
- Pre-term labor is defined as that occurring before 37 weeks gestation

Pre-Term Labor and Low Birthweight

- 40 % of PTLBW infants do not survive
- Neonatal complications: hyaline membrane disease and RDS, anemia, apnea, retinopathy of prematurity, infection, feeding difficulties, growth
- Long- term complications include cerebral palsy (20% of VLBW); neuromotor deficiencies, learning disabilities, respiratory disease, vision problems ...
- Costs?

Periodontal Disease and PTLBW

- Evidence from animal studies, and human case-control and RCT studies support an increased risk for having a pre-term low birthweight infant, in women with periodontal disease
- A few recent studies have shown that treating periodontal disease, during pregnancy, decreased this risk

Pyogenic granuloma:
“Pregnancy tumor”

Conflicting Evidence for a Link

- Jeffcoat, Hauth et al. 2001. 1313 pregnant women, Alabama
 - Antenatal maternal periodontitis an independent risk factor of preterm birth and low birthweight
 - Severe PD is associated with OR= 5.28 for preterm birth at GA<37 weeks and OR=7.07 for very preterm deliveries adjusting for age, smoking, race and parity
- Davenport et al. East London Bangaldeshi population predominant.
 - Case-control study, found no association between PD and PT or LBW deliveries

Oral Conditions and Pregnancy Study (OCAP) – Offenbacher et al, 2001

- 5 year prospective study of pregnant women: 814 deliveries
- Full mouth perio exams at enrollment before 26 weeks; and again within 48 hours of delivery
- Maternal PD classification (Health, Mild Moderate-Severe), incident PD, and PD progression over pregnancy were measures of exposures
- Other variables: race, age, food stamp eligibility, marital status, previous preterm births, first birth, chorioamnionitis, bacterial vaginosis, and smoking

Oral Conditions and Pregnancy Study (OCAP) – Offenbacher et al, 2001

- Maternal PD at antepartum and incidence/progression of PD are sig. associated with higher prevalence rate of preterm births, BW < 2500 g, and smaller BW for GA.
- Women were also at higher risk of pre-eclampsia if they had mod/severe PD at delivery (OR=2.1)

Madianos et al, 2001

- Followed-up with sampling of cord blood samples obtained at birth of the women with PD
- Measured fetal IgM levels as marker for infectious exposure to oral pathogens
 - Prevalence of fetal IgM to *C. rectus* was sig higher for pre-term compared to full term neonates, as well as *P. intermedia*.
 - A lack of maternal IgG to oral peridontopathogens was associated with an increased risk of prematurity
- Maternal periodontal infection in the absence of protective maternal Ab response is associated with disseminated oral organisms that translocate to the fetus resulting in prematurity

Evidence-based Dentistry

- Periodontal disease as a risk factor for adverse pregnancy outcomes. A systematic review.

Scannapieco FA, Busch RB, Paju S. Ann Periodontal. 2003 Dec;8(1):70-8

- **Question:** Does prevention/control of periodontal disease as compared with controls have an impact on initiation/progression of adverse pregnancy outcomes?
- **Inclusion criteria:** RCT's , case-control, and cohort studies. Mothers w or w/o perio, gave birth to PT or mature infants

Main Results

- Of the over 660 studies identified, 12 met the inclusion and exclusion criteria and were analyzed
- While several studies implicated periodontal disease as a risk factor for PT/LBW, few assessed the impact of the prevention and treatment of periodontal disease on outcomes
- Several epidemiologic studies did not support periodontal disease as a risk factor for PT/LBW

Reviewer's Conclusions

- Periodontal disease may be a risk factor for PT/LBW
- Additional longitudinal, epidemiological, and interventional studies are needed to validate this association and to determine whether it's causal
- It is not yet clear whether periodontal diseases play a causal role in adverse pregnancy outcomes
- Preliminary evidence to date suggest that periodontal intervention may reduce adverse pregnancy outcomes

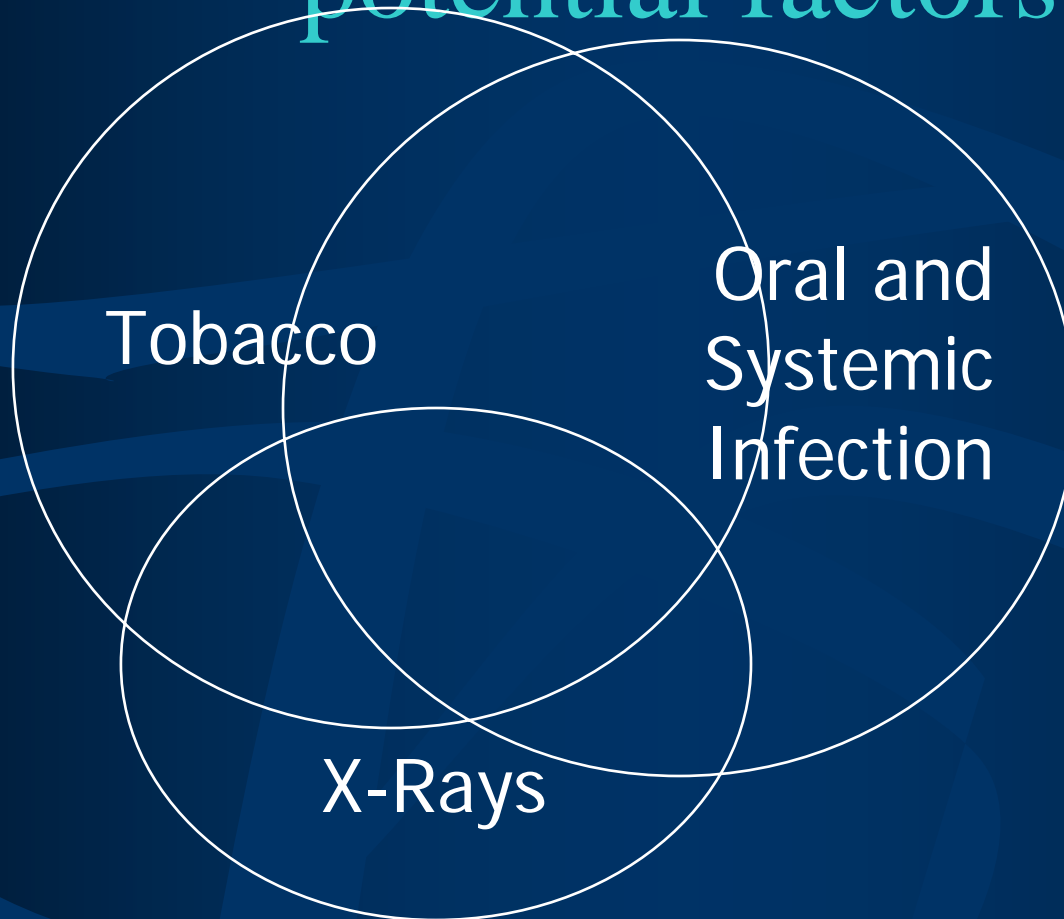
JAMA - Hujuel et al, April 2004

- Risk of low birth weight baby doubles in women who have had 4 BWX
- BUT,....
 - May have needed x-rays because of dental infection
 - Infections increase risk of low birth weight babies
 - Periodontitis - 7x more likely to deliver early/small baby

Problems with the Hujuel Study

- RL. Brent. Health Physics.88(4):379-381, 2005
- No clinical evaluations were done on the 31 subjects in the groups for which the statistical association was calculated.
 - Presence of periodontal disease? Systemic disease? Smoking? Maternal weight?
 - Family history of infants –genetic abnormalities etc?
- Not consistent with the evidence from hundred of controlled animal studies
- Background radiation is comparable to the doses received from dental radiographs
- The biological hypothesis that radiation to the mother's pituitary and thyroid could produce fetal growth retardation is incorrect. Growth hormone does not affect growth until several months after birth.

Preterm birth - potential factors



Radiographs in Pregnancy

- Fetus is shielded by lead apron
- With proper equipment, fetal exposure does not occur
 - X-rays from 2 PAs is 7000x less than natural background radiation
 - Risk of first-generation fetal defect from dental x-rays estimated at 9 in 1 billion
- Necessary x-rays can be taken

Oral Infection and Bacterial Pneumonia

- Terpenning, 2005- “ Probably the most common infectious sequelae of poor oral health in seniors, esp in nursing homes, is aspiration pneumonia”
- Aspiration is frequent in the elderly and increases in frequency with nasogastric tubes, or percutaneous entero-gastric tubes
- In severe aspiration pneumonia, 20% of organisms implicated are anaerobic and 80% aerobic
- Poor oral hygiene increases risk of pneumonia

- Recent studies suggest that mouth may play a role in infections acquired in hospitals and nursing homes, especially infections of respiratory tract
- Aspiration pneumonia has been linked to dental decay, perio, poor hygiene, the need for help feeding, and trouble swallowing- study of 358 older veterans in the USA- Terpenning et al, 2001
- Teeth of patients in ICU become colonized with respiratory pathogens such as *Pseudomonas aeruginosa*, *enterics*, and *Staphylococcus aureus*
- One ICU study demonstrated that only pts with oral colonization by a respiratory pathogen went on to experience pneumonia

- Several studies have shown that daily mechanical oral hygiene with or without an oral antiseptic such as 0.12% Chlorhexidine gluconate or 1% povidone-iodine, reduce prevalence of colonization by oral pathogens
- Reduces the rate of pneumonia by 50%

COPD

- The most important etiologic factor is cigarette smoking
 - risk is dose-related and increases with both number of cigarettes smoked and the duration of smoking

Periodontal Disease and COPD

- Scannapieco et al – 2001:
 - Association between periodontal disease and COPD based on analysis of large database – VA Normative Aging Study and the NHANES III.
 - This association persisted after adjusting for smoking, sex, age, and SES
 - Further studies are required to verify the importance of oral conditions in the pathogenesis of COPD

Periodontal Disease and Atherosclerosis

- The role of C-reactive protein and other markers of inflammation?
 - *C. Pneumoniae*
 - *P. gingivalis*
- Three pathways linking oral infections to systemic effects proposed:
 - Metastatic spread of infection during transient bacteremia
 - Metastatic injury from the effects of circulating oral microbial toxins, LPS
 - Metastatic inflammation caused by an injury induced by oral microbes

- *P. gingivalis* has been isolated from atherosclerotic plaques post-mortem
- *P. gingivalis* can multiply within and activate endothelial cells

Total cholesterol, LDL and TG's are sig higher in subjects with perio than controls

Periodontal Disease and Acute Myocardial Infarction

- Prevalence of PD and mean serum CRP levels were significantly higher in pts with acute MI than controls
- Patients with acute MI who had PD had sig. higher CRP level than AMI pts without PD
- The association of PD with CRP levels were independent of other contributing factors such as smoking, diabetes, infarct size

Deliargyris et al, Am Heart J, 2004.

Interventional studies have shown that tx of periodontal disease was associated with a decrease in markers of inflammation: CRP, IL-6. (D-Aiuto et al, 2003, 2004)

Periodontal Disease and Renal Insufficiency

- Kshirsagar et al, Am J Kidney Disease, 2005
- Cross-sectional study, 5537 middle-aged Black and White Americans, the ARIC study
- After adjustment for important risk factors for CVD and CKD, initial and severe periodontal disease were associated with elevated serum creatinine level and initial and severe periodontitis were associated with $GFR < 60$ ml/min
- This is first study to show association between periodontal disease and renal insufficiency.
- A prospective study is need to determine the exact relationship

Conclusions

- Periodontal disease may affect the host's susceptibility to systemic disease through subgingival biofilms acting as reservoirs of Gram negative bacteria, transient bacteremia, release of microbial toxins, and as a reservoir of inflammatory mediators
- More research is needed to determine the nature of the relationship of periodontal disease to these systemic diseases, and then develop appropriate interventions
- **More research is needed before recommendations can be made to treat periodontal disease as a strategy to prevent or treat CVD, diabetes mellitus, pre-term birth and other adverse pregnancy outcomes**

Oral Health and Quality of Life

Pain

Esthetics

Self-image

Eating and Nutrition

Swallowing

Speech

- Number of missing teeth, presence of loose teeth, pain have all been found to be associated with oral-health-related QOL
- Enough reason to promote preservation of teeth and oral health as an important component of overall health!

Conclusions

- Oral health is important for good outcomes for medical treatment – “Medically necessary dental care”
 - Head and Neck Cancer
 - Solid Organ Transplants
 - HSCT
 - Myelosuppressive chemotherapy for cancer
- In the future we may have the evidence to support the treatment of oral disease to prevent/control systemic disease
 - Evidence is emerging for pre-term labor/ LBW, Glycemic control in diabetes, Oral/dental infection and aspiration pneumonia in the elderly
 - More research , prospective multi-center observational and interventional studies for CVD, COPD, Renal disease