Periodontal Disease and Chronic Diseases: The Evidence

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Disclosure Information
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The Plan

- Focal theory of disease
- Periodontal disease and systemic disease
  - atherosclerosis, diabetes, and others
- Infective endocarditis
- Can we reduce the risk of systemic disease and how

Focal Infection Theory

- 700 B.C. Nineveh, Assyria
- 400 B.C. Hippocrates – “rheumatism”
  - cure of arthritis from tooth extraction
**Focal Infection Theory**

“I have been made happy by discovering that I have only added to the observations of other physicians in pointing out a connection between the extraction of decayed and diseased teeth and the cure of general diseases.”

Benjamin Rush MD, 1801

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**Focal Infection Theory**

Wm. Hunter – 1900 – London

- “Fatal oral sepsis” as a cause of disease*
- 1910 – medical students at McGill University
  - American dentistry: “...veritable mausoleum of gold over a mass of sepsis...”

*Br. Med. J
### Focal Oral Infection and Systemic Disease

- Endocarditis
- Brain abscess
- Obscure fever (FUO)
- Pneumonia
- Diabetes
- Asthma
- Emphysema
- Arthritis
- Neuritis
- Myalgia
- Osteomyelitis
- Skin abscess
- Anemia
- Hodgkin’s disease
- Indigestion
- Gastritis
- Nephritis
- Pancreatitis
- Colitis
- Goiter
- Thyroiditis
- Nervous diseases
- Mental illness

### Antibiotic Prophylaxis: A Historical Perspective

- Focal Infection Theory → tooth extractions
- Scientific data → evidence-based practice
- Penicillin → prevention protocols (AHA)
- Widespread use of antibiotics for prophylaxis
... and then, a rebirth of the focal infection theory


- 1990 – three pathways
  - metastatic spread – bacteremia
  - injury from circulating toxins
  - inflammation from organisms

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Periodontal/Cardiovascular Disease Articles
1989 to 2011

Focal Infection Theory Revisited

- Back then:
  - Arthritis
  - Osteoporosis
  - Mental illness, etc.

- Now:
  - Cardiovascular disease and stroke
  - Low birth weight infants
  - Diabetes, etc. etc.
Periodontal Disease

NHANES data 1999-2004:

- Moderate to severe periodontal disease:
  - 5% 35-49 years
  - 11% 50-64 years
  - 14% 65-74 years
  - 20% >75 years

Combined expenditure for periodontal and preventive dental services in the U.S.

- ~ $14 billion in 1999
Periodontal Disease and Atherosclerosis

Several mechanisms proposed:
- systemic inflammation
- promotion of atherogenesis
- incite cardiovascular catastrophes (MI & stroke)

Many studies with conflicting results:
- some with positive associations
- some that do not find associations after adjustment for confounding variables

Independent, clinically significant association?

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Periodontal Disease and Atherosclerosis

- What we think vs. what we know
- ‘Link’ vs. association vs. causation
  - strength of the association
- How to resolve the controversy?
- What do we tell patients in the meantime?
Why the American Heart Association?

- Tremendous public health burden of ASVD
- Need to identify risk factors
- High volume literature with a spectrum of design, methods, and readership
- Lack of consensus on the evidence among experts
- Confusion among health care providers and public

Why the American Heart Association?

- Inconsistent and sometimes alarming messaging from stakeholders
- Failure of research to date to definitively answer important questions:
  - Does Periodontal disease cause ASVD?
  - Does PD treatment improve ASVD outcomes?
Methods

- 600+ papers identified (2009)
- Multidisciplinary writing committee
- External reviewers (N=8) – Revisions
- AHA – SACC Review (N=13) – No revisions
- Endorsement by AHA and ADA
- Publication in Circulation (2012)

Known Risk Factors for ASVD

Multifactorial contributors to ASVD:
- genetic, environmental, lifestyle factors

Non-modifiable risk factors:
- ethnicity, age, family history

Modifiable risk factors:
- dyslipidemia, hypertension, tobacco use, excess body weight, physical inactivity, diabetes mellitus

PROVEN: Risk factor interventions impede and/or prevent ASVD and have proven cost effectiveness
Overlap of ASVD and PD Risk Factors

ASVD and PD share many prevalent and powerful risk factors:
- Increasing age
- Smoking
- Alcohol abuse
- Race/ethnicity
- Education and socioeconomic status
- Male gender
- Diabetes
- Overweight or obesity

These common, prevalent risk factors could confound a relationship between ASVD and PD

Is there a risk of PD treatment?

Randomized controlled trial- Full-mouth mechanical debridement and application of local antibiotics

The good news:
- Significant improvement in brachial artery diameter at 6 months

The bad news:
- Transient deterioration of diameter and significant increases in multiple plasma inflammatory mediators immediately after debridement
- Procedure-related inflammation may have immediate negative effects on endothelial function


Study based on the U.S. Medicaid claims database:
- Transient increased risk for MI and stroke within four weeks following invasive dental treatment

**Periodontal Intervention and ASVD Risk**

Only 1 multi-center pilot study of periodontal therapy on the secondary prevention of cardiac events

The Periodontitis and Vascular Events (PAVE) investigation

Randomized patients with periodontitis and a history of coronary heart disease to:

- Cases - oral hygiene instruction and non-surgical periodontal therapy
- Controls - community care (supragingival debridement only)

- 25-month follow-up period:
  - Similar frequency of adverse cardiovascular events

**Evidence for Periodontal Disease as a Risk Factor for ASVD**

I. There is an association between PD and ASVD
   Level of Evidence A

II. Periodontal intervention decreases local periodontal inflammation
    Level of Evidence A

III. PD causes ASVD
    Not supported by either level A or level B evidence

IV. Periodontal intervention decreases long term systemic inflammation
    Not supported by either level A or level B evidence
Summary: Assessment of the Literature

What do we do to help the patient?
- Modify known risk factors for both PD and ASVD (e.g., smoking)
- Maintain oral health
- Careful communication regarding the indications for and possible benefits of interventions

“Statements that imply a causative association between PD and specific ASVD events, or claim that therapeutic interventions may be useful based on that assumption, are unwarranted”


Periodontal Disease and Systemic Disease

- Atherosclerosis
- Low birthweight infants
- Diabetes
The Effect of Nonsurgical Periodontal Therapy on Hemoglobin A1c Levels in Persons With Type 2 Diabetes and Chronic Periodontitis
A Randomized Clinical Trial

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Michael R. Folds, DMD, DMSc; Cory E. Lewis, MD, MSPr; Thomas W. Oates, DMD, PhD; Dayhl Tripathy, MD;
Jame A. Kates, DMD, PhD; Philip R. Orbanek, MD; David M. Paganetti, DMD, MPH, DMSc;
Róman Q. Harlow, MD; Michael T. Tsid, PhD

**IMPORTANCE** Chronic periodontitis, a destructive inflammatory disorder of the supporting structures of the teeth, is prevalent in patients with diabetes. Limited evidence suggests that periodontal therapy may improve glycemic control.

**OBJECTIVE** To determine if nonsurgical periodontal therapy reduces levels of glycated hemoglobin (HbA1c) in persons with type 2 diabetes and moderate to advanced chronic periodontitis.

**DESIGN, SETTING, AND PARTICIPANTS** The Diabetes and Periodontal Therapy Trial (DPTT), a 6-month, single-masked, multicenter, randomized clinical trial. Participants had type 2 diabetes, were taking stable doses of medications, had HbA1c levels between 7% and less than 10%, and untreated chronic periodontitis. Five hundred and eight participants were enrolled between November 2009 and March 2012 from diabetes and dental clinics and communities affiliated with 5 academic medical centers.

**RESULTS** Enrollment was stopped early because of futility. At 6 months, mean HbA1c levels in the periodontal therapy group increased 0.17% (SD, 1.0), compared with 0.11% (SD, 1.0) in the control group, with no significant difference between groups based on a linear regression model adjusting for clinical site (mean difference, −0.05% [95% CI, −0.23% to 0.12%]; *P* = .55). Periodontal measures improved in the treatment group compared with the control group at 6 months, with adjusted between-group differences of 0.28 mm (95% CI, 0.18 to 0.37) for probing depth, 0.25 mm (95% CI, 0.14 to 0.36) for clinical attachment loss, 13.1% (95% CI, 8.1% to 18.1%) for bleeding on probing, and 0.27 (95% CI, 0.17 to 0.37) for gingival index (*P* < .001 for all).

**CONCLUSIONS AND RELEVANCE** Nonsurgical periodontal therapy did not improve glycemic control in patients with type 2 diabetes and moderate to advanced chronic periodontitis. These findings do not support the use of nonsurgical periodontal treatment in patients with diabetes for the purpose of lowering levels of HbA1c.
Focal Infection Theory - Lessons

Enthusiasm and hypotheses

Failure of science to prove the theory

- Inability to replicate the experiments of the advocates
- Benefit of removal of foci not proven

Patient Populations Reported to be at Risk for Infection from Invasive Dental Procedures

- Cardiac:
  - Congenital defects (some)
  - Previous infective endocarditis
  - Transplants (some)
  - Prosthetic valves
  - Native valve disease
  - Pacemakers and defibrillators
  - Coronary stents
- Prosthetic joints
- Shunts – CSF, renal dialysis
- Vascular grafts
Transplants - Solid organ, HPSC, BMT
Immunosuppression - Drugs and disease
Type 1 diabetes mellitus
Asplenism
Systemic lupus erythematosus
Implants - non-dental (e.g. deep brain stimulator)
Maxillofacial radiotherapy
Indwelling catheters
Debilitated patients
Autoimmune disease
Implants (breast, penile, etc.)
Hereditary hemorrhagic telangiectasia

>25 patient populations

Systemic infection from dental procedures is rare but one population is at risk from oral bacterial disease...
Patient Populations Reported to be at Risk for Infection from Invasive Dental Procedures

- Cardiac
  - Congenital defects (some)
  - Previous infective endocarditis
  - Heart transplants (some)
  - Prosthetic heart valves
  - Native heart valve disease
- Prosthetic joints

Infected Endocarditis
Support for Antibiotic Prophylaxis: Historical Perspective

- Remnant from Focal Infection Theory
- Morbidity and mortality from IE
  - 40% mortality for elderly

Support for Antibiotic Prophylaxis: Historical Perspective

- Expert opinion, dogma, tradition
- Largely weak science
  - hundreds of case reports
  - epi. studies
"Faith, hope, and charitable interpretations"

The Lancet 1:519, 1976
60 years later: Most recognized of any publication for dentistry

- Top article – JADA readers\(^1\)
- 98% awareness - U.S. Dentists\(^2\)
- 99% awareness (NICE) – U.K.\(^3\)

1. JADA online usage stats., 2008

Pilot Survey: How many times per month are you faced with a clinical situation concerning antibiotic prophylaxis for a patient who may be at risk from a dental procedure (e.g., infective endocarditis, prosthetic joint infection)?

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<th>Frequency</th>
<th>Number of Responses</th>
<th>Response Ratio %</th>
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<tbody>
<tr>
<td>Never</td>
<td>22.1%</td>
<td>1.1%</td>
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<tr>
<td>&lt; 3</td>
<td>29.8%</td>
<td>25.6%</td>
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<td>3-5</td>
<td>25.6%</td>
<td>20.6%</td>
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<td>&gt; 10</td>
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<tr>
<td>No Responses</td>
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N=750
IE Antibiotic Prophylaxis: Why the Debate 60 Years Later?

For prophylaxis:
- Fear of the consequences of IE
- Change can violate long established practice patterns and deeply entrenched beliefs
- Only method for prevention?

Support for Antibiotic Prophylaxis

- Half of about 2,000,000 cases of nosocomial infections involve indwelling devices
- Outcome:
  - prolonged antibiotics
  - surgical removal or replacement
  - disfigurement, disability, death
  - cost to replace device exceeds the cost of initial placement
Total Hip and Knee Replacement Procedures

Antibiotic Prophylaxis: Why the Debate 60 years later?

Against prophylaxis:
- No proof of efficacy – No randomized trial
- Negative epidemiologic evidence
- Even if effective, a huge number of prophylaxis doses required to prevent a small number of cases
- Resistant strains and drug reactions
“Current State of Antimicrobial Resistance”

- “Landmark report”
- “we are rapidly approaching a cliff... if we go over the cliff we will lose our ability to treat infections entirely. We are at risk of returning to the pre-antibiotic era.”

CDC Interview with Director of Antimicrobial Resistance - 9/16/2013. WWW.medscape.com

Bacteremia Incidence

- Dental procedures 0% - 100%

VS.

- Chewing 17% - 38%
- Tooth brushing 3% - 86%

Is there a clinically significant difference?
Should we abandon antibiotic prophylaxis?

- Controversy and diversity of opinion
- Which patients and which procedures to cover?
- Risks to patients and society
- Cost effectiveness
- Data from England

Incidences of Infective Endocarditis Cases (Spells) and Deaths / 10 Million / Month

Dayer, M et al. The Lancet, 2015
Incidence of IE

By March 2013 this amounted to an extra 35 IE cases/month

Dayer, M et al. The Lancet, 2015

Re-focus on Endocarditis Prevention

- Approximately 6,000,000 people at risk for IE in U.S.*
- AP for only 4 groups in U.S. and Europe
  - ~10% of all people at risk for IE*
- What about prevention for the other 90%?

Question ...

Does improved oral hygiene and decreasing gingival disease prevent IE from oral flora?

NIDCR/NIH 5-Year R01 Study

Does poor oral hygiene or periodontal disease result in an increase in infective endocarditis?

Case/Control: 112 hospitalized IE cases
224 at-risk out patient controls

Three enrolling sites
In the meantime: What should we do to prevent IE from oral bacterial species?

- Focus on improving oral hygiene and eliminating gingivitis / periodontitis
- Caries, gingival and periodontal diseases are almost entirely preventable