This talk will

• Review research on the role of the oral microflora in the pathogenesis of pneumonia
• Review research on the role of the oral microflora in the pathogenesis of COPD
• Review research on the role of the oral microflora in the pathogenesis of asthma
Bacterial Pneumonia:

- is the sixth most common cause of death in the U.S.
- is the most common cause of infection-related mortality.

Types of Pneumonia

- Community acquired pneumonia - occurs in non-institutionalized patients.
- Nosocomial pneumonia - occurs in patients following admission to an institution (hospital, nursing home).

Respiratory infection depends on aspiration of pathogens from proximal sites (e.g. oro-pharynx into the respiratory tree).
Ventilator associated pneumonia (VAP)

- Leading cause of death from nosocomial infections
- Second most common nosocomial infection in the United States
- Occurs in up to 25% of ventilated patients
- Mechanically ventilated patients have a 6-21-fold increased risk of pneumonia
- Risk increases 1% with each day of ventilation
- VAP associated with increase of >$40,000 in mean hospital charges

Aspiration Pneumonia

- "An inflammatory condition of the lung parenchyma initiated by the introduction of unaccustomed matter into the alveolar sacs"
- Dysphagia is an important risk factor

Aspiration pneumonia

- Typically caused by anaerobic organisms in patients with swallowing disorders and/or depressed consciousness (e.g. those with greater incidence of aspiration). The bacteria involved are usually part the oral flora, often anaerobic, associated with periodontal disease.
- Cultures generally show mixed bacterial growth.
- May be both community-acquired or nosocomial.
- More common in elderly, nursing home and other institutionalized patients.
Aspiration pneumonia
Nursing home acquired

- Second most common nursing home infection (21% of all NH infections)
- Affects 18-48% of nursing home residents/yr
  - 0.27-2.5 [1.0] / 1,000 pt-days
- Most common cause for hospitalization
- Leading cause of death in nursing home residents (mortality rate up to 44%)
- Length of stay 21-40d
- $9,460-$33,430/episode of care
### TABLE 1. Results of Single Culture Surveys.

<table>
<thead>
<tr>
<th>Study Group</th>
<th>No. of Subjects</th>
<th>Cultures Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal subjects</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonhospital associated</td>
<td>82</td>
<td>2</td>
</tr>
<tr>
<td>Hospital associated</td>
<td>47</td>
<td>2</td>
</tr>
<tr>
<td>Patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psychiatry service</td>
<td>20</td>
<td>0</td>
</tr>
<tr>
<td>Moderately ill</td>
<td>81</td>
<td>16</td>
</tr>
<tr>
<td>Mortally ill</td>
<td>23</td>
<td>57</td>
</tr>
</tbody>
</table>

**Species**

- **Staphylococcus aureus**
  - MICU: 2 (55; 10-100)
  - PDC: 5 (53; 17-100)
  - Mucosa: 0
  - Dental plaque: 1 (6)

- **Pseudomonas aeruginosa**
  - MICU: 8 (32; 1-100)
  - PDC: 7 (40; 1-100)
  - Mucosa: 0
  - Dental plaque: 0

- **Klebsiella pneumoniae**
  - MICU: 2 (50.5; 1-100)
  - PDC: 5 (60.8; 1.6-100)
  - Mucosa: 0
  - Dental plaque: 0

- **Serratia marcescens**
  - MICU: 3 (51; 1-90)
  - PDC: 4 (36; 1-90)
  - Mucosa: 0
  - Dental plaque: 0

- **Enterobacter aerogenes**
  - MICU: 0
  - PDC: 0
  - Mucosa: 0
  - Dental plaque: 1 (<0.1)

- **Enterobacter cloacae**
  - MICU: 1 (<0.1)
  - PDC: 1 (<0.1)
  - Mucosa: 0
  - Dental plaque: 0

- **Enterobacter asburiae**
  - MICU: 0
  - PDC: 0
  - Mucosa: 0
  - Dental plaque: 1 (<0.1)

- **Proteus mirabilis**
  - MICU: 1 (100)
  - PDC: 0
  - Mucosa: 0
  - Dental plaque: 0

- **Escherichia coli**
  - MICU: 0
  - PDC: 0
  - Mucosa: 0
  - Dental plaque: 0

- **Citrobacter diversus**
  - MICU: 1 (<0.1)
  - PDC: 1 (<0.1)
  - Mucosa: 0
  - Dental plaque: 0

- **Acinetobacter calcoaceticus**
  - MICU: 0
  - PDC: 0
  - Mucosa: 0
  - Dental plaque: 0

- **Pasteurella sps.**
  - MICU: 0
  - PDC: 0
  - Mucosa: 1 (15)
  - Dental plaque: 0

**Total Strains Cultured**

- MICU: 18
- PDC: 24
- Mucosa: 1
- Dental plaque: 3

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Colonization of dental plaque by respiratory pathogens in medical intensive care patients

Frank A. Scannapieco, DMD, PhD; Ellen M. Stewart, MS; Joseph M. Skolpyn, MD

• Pathogens colonize the teeth and are released from plaque biofilm
• They attach to and form biofilms on tubing
• Aspirated into lower airway
-> INFECTION

Biological Plausibility

Genetic relationships between respiratory pathogens isolated from dental plaque and bronchoalveolar lavage fluid from mechanically ventilated-intensive care patients

Methods

Oral, tracheal and BAL strains were assessed for genetic relatedness by

- Pulse-field gel electrophoresis (PFGE)
- Multilocus sequence typing (MLST) – Internal fragments of seven house keeping genes (400-500bp) were sequenced for each species, and each sequence (allele) was compared to sequences of known alleles in the MLST website (http://www.mlst.net or http://pubmlst.org/paeruginosa).
Conclusions

1. Isolates recovered from dental plaque and tracheal secretions from a single patient were genetically identical from isolates of the same species from BAL samples from that patient.

2. The present results support the idea that dental plaque is a reservoir for respiratory pathogen colonization in intensive care unit patients at risk of bacterial pneumonia.

Hypothesis: Improved oral hygiene may prevent oral colonization by respiratory pathogens and VAP
What is the simplest oral intervention to prevent VAP?

Objective: To determine the minimum frequency (once or twice a day) of 0.12% chlorhexidine gluconate (CHX) needed to improve oral hygiene and reduce oral colonization by potential respiratory pathogens in intubated patients admitted to a trauma ICU.
**Study Design**

Patients admitted to ICU (175 consented)

- Group 1 – placebo (vehicle control) 2x day (59 enrolled)
- Group 2 – chlorhexidine 1x day; placebo 1x day (58 enrolled)
- Group 3 – chlorhexidine 2x day (58 enrolled)

**Major microbiological outcomes of the pilot clinical trial:**

- Neither application of CHX once a day or twice a day resulted in a significant reduction in plaque scores when compared to the placebo control group.
- The total number of cfu recovered, or the percentage of the cultivable flora as enterics, or Pseudomonas and Acinetobacter, respectively, were not reduced by CHX.
- A statistically significant reduction was noted in the numbers of S. aureus in the CHX groups when compared to the placebo group.

**Major clinical outcomes of the clinical trial:**

- Dental plaque scores were not different between the groups.
- A non-significant reduction in VAP rate was noted in groups treated with CHX compared to the placebo group (Relative Risk = 0.59, p = 0.1459).
- Comparison of time to VAP between placebo and CHX treated groups indicated slower VAP development for the CHX treated group (Hazard ratio = 0.555), but this did not reach statistical significance (p = 0.1268).
Improved Oral Hygiene to Prevent Pneumonia
Systematic Reviews and Meta-Analyses

Oral hygiene care for critically ill patients to prevent ventilator-associated pneumonia (Review)

Chlorhexidine (mouthrinse or gel) versus placebo/usual care for critically ill patients to prevent ventilator-associated pneumonia (VAP)

**Summary**

- There is moderate quality evidence from 17 RCTs (2402 participants, two at high, 11 at unclear and four at low risk of bias) that chlorhexidine, as part of OHC, compared to placebo or usual care, is associated with a reduction in VAP (NNT of 15).

- There is no evidence of a difference between CHX and placebo/usual care in the outcomes of mortality, duration of mechanical ventilation, or duration of ICU stay. (MD 0.21, 95% CI: -1.48 to 1.89 days).

- Few adverse effects, and these were mild with similar frequency in CHX and control groups.
Limitations/barriers for implementation of improved oral hygiene to prevent pneumonia:

- Most studies underpowered.
- Variable study design and interventions considered.
- Pre-existing oral biofilm (dental plaque) likely limits effectiveness of topical antimicrobials – need to remove biofilm mechanically!!!!
- Adherence to rigorous oral hygiene protocols is likely limited (by both patients and care givers) in hospitals and nursing homes.
- Some cases of pneumonia are viral and may not be preventable by oral hygiene.

**“Unofficial” Guidelines for Managing Intensive Care and Ventilated Patients**

- Remove all dental appliances upon admission to the unit.
- Conduct oral examination initially, then daily by a registered nurse.
- Brush teeth 2 to 3 times per day; floss if possible.
- Rinse all oral surfaces with antimicrobial rinses.
- Frequent deep suction of oral and pharyngeal secretions as needed, as well as prior to repositioning the tube or deflation of the cuff.
- If possible, remove hard deposits (eg, tartar/calculus) from the teeth.
- For elective procedures, have teeth professionally cleaned before admission to the hospital.

The Association of Oral Health and Pneumonia in Nursing Home and Elderly Patients
**Colonization of Respiratory Pathogens in Chronic Care vs. Ambulatory Dental Patients**

<table>
<thead>
<tr>
<th>Chronic care subjects</th>
<th>Dental outpatients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence of respiratory pathogen colonization &gt; 1.0% of flora</td>
<td>14% (4/28) *</td>
</tr>
<tr>
<td>% of cultivable plaque flora</td>
<td>42.9 ± 53.4</td>
</tr>
</tbody>
</table>

* p ≤ 0.05, Fisher’s Exact Test

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Can frequent, oral care reduce pneumonia in nursing home residents?

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**Table 3. Effect Estimates in Parallel Group Randomized Controlled Trials: n = 4.**

<table>
<thead>
<tr>
<th>Reference (Intervention)</th>
<th>Experimental Group</th>
<th>Control Group</th>
<th>Absolute Risk Difference (95% CI)</th>
<th>Number Needed to Treat (95% CI)</th>
<th>Outcome Measure</th>
<th>Follow-up Period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prophylactic and antibiotic prophylaxis</td>
<td>90</td>
<td>105</td>
<td>66-72% (0.6-11.2)</td>
<td>12.5 (1.7-51.5)</td>
<td>Respiratory Unit readmission</td>
<td>2 years</td>
</tr>
<tr>
<td>24-hour oral care every 6 hours</td>
<td>114</td>
<td>116</td>
<td>86-92% (0.7-10.5)</td>
<td>11.6 (0.5-50.3)</td>
<td>Pneumonia</td>
<td>2 years</td>
</tr>
<tr>
<td>30-second oral care every 4 hours</td>
<td>75</td>
<td>104</td>
<td>83-93% (0.3-10.7)</td>
<td>11.3 (0.5-44.9)</td>
<td>Death from pneumonia</td>
<td>2 years</td>
</tr>
<tr>
<td>40-second oral care every 2 hours</td>
<td>50</td>
<td>40</td>
<td>11.1 (0.3-24.9)</td>
<td>11.4</td>
<td>Death from pneumonia</td>
<td>2 years</td>
</tr>
</tbody>
</table>

*Prophylactic and antibiotic prophylaxis*.

*Bracketed values are 95% confidence intervals.

Conclusions

• The RCTs revealed positive preventive effects of oral hygiene on pneumonia and respiratory tract infection in hospitalized elderly people and elderly nursing home residents, with NNTs from 8.6 to 15.3 individuals.
• Approximately one in 10 cases of death from pneumonia in elderly nursing home residents may be prevented by improving oral hygiene.
• Dentures should be removed during sleep to prevent pneumonia events.
• Obstacles to dental care in the nursing home setting are needed.
Obstacles to dental care delivery in nursing homes

- Demographic and health characteristics of the residents.
  - Dementia
  - Physical limitations
- Dental "IQ" of residents, family and care givers - lack of appreciation by patients and caregivers of how oral health may influence medical conditions, well-being, etc.
- Medical conditions take priority over oral health care/hygiene – nursing staff have little-time, little knowledge of how to provide oral care, little appreciation for oral – care needs.
- Use of chlorhexidine may not be sufficient by itself to improve oral hygiene – it is likely that more stringent interventions to remove biofilm are required.

Chronic Obstructive Pulmonary Disease

**Definition** - progressive development of airflow limitation that is not fully reversible.

**COPD** = Chronic obstructive bronchitis and Emphysema

- Obstruction of small airways,
- Productive cough for more than 3 months
- Enlargement of air spaces,
- Destruction of parenchyma,
- Reduced lung elasticity,
- Closure of small airways

for more than two successive years
Chronic Obstructive Pulmonary Disease

- condition in which there is chronic obstruction to airflow with excess production of sputum resulting from chronic bronchitis and or emphysema.

- Epidemiology - 14 million people in the U.S.

- Risk factors for COPD:
  - prolonged tobacco smoking.
  - environmental particulates (& working in confined spaces).
  - air pollution.
  - passive smoking.

- Genetics (variant alpha 1-antitrypsin, alpha 1-antichymotrypsin, alpha 2-macroglobulin, vitamin D-binding protein and blood group antigens).

COPD and tobacco use - not all cigarette smokers experience accelerated decline in lung function

- occurs in only a minority of smokers.
- could be due to genetics.
- familial clustering of COPD (early onset).
- other factors (periodontal disease)?

Inflammation in COPD

Chronic airway inflammation has a critical role in producing symptoms > clinicians Rx anti-inflammatory agents, especially inhaled corticosteroids for Tx of COPD.

Acute Exacerbation

- Experience varies between patients
- Increased symptoms (fever, cough, sputum) & decreased lung function.
- Likely triggered by bacterial or viral infection.
- Elevated neutrophils, IL-6, IL-8 in broncho-alveolar lavage fluid.
- Contributes to disease progression.

Evidence for an association of periodontal disease with COPD
<table>
<thead>
<tr>
<th>Reference</th>
<th>Number of Subjects</th>
<th>Odds Ratio (95% CI)</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scannapieco et al., 1998</td>
<td>Cross sectional study of NHANES II – 386 with COPD</td>
<td>4.50 (1.06-18.99)</td>
<td>Oral hygiene measured – effect for worst quartile</td>
</tr>
<tr>
<td>Scannapieco and Ho, 2001</td>
<td>Cross sectional study of NHANES I – 386 with COPD/12,982 without COPD</td>
<td>1.45 (1.02-2.05)</td>
<td>Perio evaluated by mean attachment level</td>
</tr>
<tr>
<td>Leuckfeld et al., 2008</td>
<td>Case-control – 1096 with COPD/30 patients without COPD</td>
<td>3.0 (1.29-6.77)</td>
<td>Perio evaluated by radiographic bone levels</td>
</tr>
<tr>
<td>Kallfelte et al., 2012</td>
<td>Prospective cohort - 1163 subjects from Study of Health in Pomerania (SHIP)</td>
<td>10.0 (1.03–97.47)</td>
<td>Perio evaluated by probing depth and CAL</td>
</tr>
<tr>
<td>Yen et al., 2010</td>
<td>Case-control - 133 with COPD/538 without COPD</td>
<td>Hazard ratio - Edentulism - 2.37 (1.03–5.45)</td>
<td>Perio not associated after adjustment for center, race, gender, age, smoking, education and BMI to evaluation for more severe COPD</td>
</tr>
<tr>
<td>Barros et al., 2013</td>
<td>Prospective cohort - 440 edentulous subjects and 1195 dentate subjects from Atherosclerosis Risk in Communities (ARIC)</td>
<td>Hazard ratio - Edentulism - 2.37 (1.03–5.45)</td>
<td>Perio not associated after adjustment for center, race, gender, age, smoking, education and BMI to evaluation for more severe COPD</td>
</tr>
</tbody>
</table>

Levels of Lung Function by Dental Health Status

<table>
<thead>
<tr>
<th>Gingival Bleeding</th>
<th>(FEV1)/(FVC) x 100 (Mean ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 20% site</td>
<td>79.31 ± 8.19</td>
</tr>
<tr>
<td>≥ 20% site</td>
<td>79.25 ± 9.80</td>
</tr>
<tr>
<td>Mean Attachment Loss</td>
<td></td>
</tr>
<tr>
<td>&lt; 1.5 mm*</td>
<td>81.26 ± 7.63</td>
</tr>
<tr>
<td>≥ 1.5 mm</td>
<td>79.28 ± 10.20</td>
</tr>
<tr>
<td>&lt; 2.0 mm*</td>
<td>80.04 ± 9.58</td>
</tr>
<tr>
<td>≥ 2.0 mm</td>
<td>73.88 ± 10.98</td>
</tr>
<tr>
<td>&lt; 3.0 mm*</td>
<td>79.64 ± 8.82</td>
</tr>
<tr>
<td>≥ 3.0 mm</td>
<td>72.26 ± 10.66</td>
</tr>
</tbody>
</table>

* significantly greater lung function when compared to those with more mean attachment loss (p<0.0001, weighted t-test)
Oral Health and Asthma

• There is evidence that children and adults with asthma have more gingivitis and periodontal disease than healthy controls.
**Findings**

- In total, 34.23% of the individuals were classified as having periodontitis, 29 participants in the control group and 60 in the case group.
- The visible plaque (PI) and bleeding upon probing indexes (BOP) showed the worst conditions in the group of individuals with severe asthma.

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Crude and adjusted odds ratio (OR) and 95% confidence interval (CI) for the association between periodontitis and controlled severe asthma (N = 260)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model</td>
<td>OR</td>
</tr>
<tr>
<td>Crude</td>
<td>2.96</td>
</tr>
<tr>
<td>Adjusted1</td>
<td>3.20</td>
</tr>
<tr>
<td>Adjusted2</td>
<td>3.09</td>
</tr>
<tr>
<td>Adjusted3</td>
<td>3.21</td>
</tr>
<tr>
<td>Adjusted4</td>
<td>3.04</td>
</tr>
<tr>
<td>Adjusted5</td>
<td>3.07</td>
</tr>
<tr>
<td>Adjusted6</td>
<td>3.22</td>
</tr>
<tr>
<td>Adjusted7</td>
<td>3.09</td>
</tr>
<tr>
<td>Adjusted8</td>
<td>3.05</td>
</tr>
</tbody>
</table>

The crude association analysis found that, in individuals with periodontitis, the chance of having severe asthma was, approximately, three times greater than in participants without periodontal disease [ORcrude = 2.98 (95% CI: 1.74–5.11)].
An electronic search without date or language restriction was carried out in PubMed/MEDLINE, Cochrane Central Register of Controlled Trials, Web of Science, and LILACS until May 2017.

A specific electronic search was performed on the following journals’ websites: Journal of Periodontology, Journal of Clinical Periodontology, International Journal of Periodontics & Restorative Dentistry, and Journal of Periodontal Research.

A search of the Grey Literature Report and OpenGrey databases revealed unpublished studies (grey literature).

The findings suggest an association between exposure to periodontitis and severe asthma that was observed even after performing regression models adjusted for nine different sets of potential confounding variables.
Oral health is essential for good health

For institutionalized patients (hospital, nursing home, etc.) good oral care
• Fosters better quality of life, comfort and well being.
• May prevent pneumonia and other infections.
• May reduce progression of COPD and asthma?

Challenges and quandaries
• It is difficult to accurately diagnose pneumonia and assign etiology (bacterial, viral, pneumonitis).
• It is difficult to quantitate oral health status – plaque score? clinical findings? inflammatory burden? microbiome?
• Many medical personnel lack working knowledge of dental medicine. Knowledge of oral hygiene techniques, correct frequency of application, are not widely known/appreciated.
• Ethical dilemma – why provide oral care to extend the life of frail and failing elders?

Take home messages....
• Periodontal intervention/improved oral care may influence respiratory infections such as pneumonia.
• Periodontal intervention/improved oral care may reduce progression COPD.
• Epidemiologic studies link asthma and periodontal disease.
• Improved oral hygiene and oral care likely to reduce risk for these conditions.
• Additional high quality RCTs are necessary.
• Mechanisms are need to fund oral care interventions for vulnerable populations.
Thank you for your attention!