“Recognizing the Oral Systemic Link in Our Children”

“a tide in the affairs of men which, when taken at the Flood, leads on to fortune”
- Shakespeare
Julius Caesar, Act 4, scene 3

Mark Cannon DDS MS
Professor Feinberg School of Medicine
Northwestern University, Ann and Robert Lurie Children’s Hospital
(Children's Memorial Hospital)
NOT a new concept!!!!

• Slave inspection
• Romans checked teeth
• Egyptians
Patients with poor oral hygiene but no previous dental caries.
BIOFILM

A complex structure adhering to surfaces that are regularly in contact with water, consisting of colonies of bacteria and usually other microorganisms such as yeasts, fungi, and protozoa that secrete a mucilaginous protective coating in which they are encased. Biofilms can form on solid or liquid surfaces as well as on soft tissue in living organisms, and are typically resistant to conventional methods of disinfection. Dental plaque, the slimy coating that fouls pipes and tanks, and algal mats on bodies of water are examples of biofilms. While biofilms are generally pathogenic in the body, causing such diseases as cystic fibrosis and otitis media, they can be used beneficially in treating sewage, industrial waste, and contaminated soil.

We know that life, when you boil it right down, is a flow of electrons: "You eat sugars that have excess electrons and you breathe in oxygen that willingly takes them." Our cells break down the sugars, and the electrons flow through them in a complex set of chemical reactions until they are passed on to electron-hungry oxygen.

In the process, cells make ATP, a molecule that acts as an energy storage unit for almost all living things, making ATP. Moving electrons out of living things, our cells package electrons into molecules that can safely carry the energy. "That's the way we make all our energy and it's the same for every organism on this planet," says Nealson. "Electrons must flow in order for energy to be gained. This is why when someone suffocates another person they are dead within minutes. You have stopped the supply of oxygen, so the electrons can no longer flow."
Streptococci - Plaque Kingdoms

- Disease and colonization
- Adhesins
- Quorum sensing
- Competence
- Stimulating Peptide
If Parent is red complex positive, child is 35–54X more likely to be infected.

• Saliva is the major vector for transmission.
• Periodontal pathogens are communicable.

The Transmission of Anaerobic Periodontopathic Organisms

The Transmission of Periodontopathic Organisms Between Children and Caregivers
Y Lee et al Pre-publication Data
Gary B. Huffnagle, Ph.D., is Professor of Internal Medicine, Microbiology, and Immunology, University of Michigan Medical Center. His research on probiotics has appeared in leading scientific journals and has been featured in Newsweek, Forbes, and on BBC News.

Ilyich Mechnikov (Elie Metchnikoff)

- Born May 16, 1845, Ivanivka, Kharkiv Province, Ukraine
- Died July 16, 1916, Paris, France
- Fields Microbiology
- Institutions Odessa University
- Alma mater Kharkiv University
- Known for phagocytosis
- Nobel Prize

"A general belief is that microbes are harmful. This belief is erroneous. There are many useful microbes......"
Probiotics: live microorganisms which when administered in adequate amounts confer a health benefit on the host.


Pathogen = bacteria in the wrong place at the wrong time

Probiotic = bacteria in the right place at the right time

- Dr. Cannon’s Definition
Probiotics – great interest in research


Key word probiotic

Limits:

Appearance in title or abstract

English

2006: 528 hits

47 human studies

Now over 100 studies published a month

2011: over 1300

Many new journals

According to metabolism, Lactobacillus species can be divided into three groups:

Obligately homofermentative (Group I) L. acidophilus, L. delbrueckii, L. helveticus, L. salivarius

Facultatively heterofermentative (Group II) L. casei, L. curvatus, L. plantarum, L. sakei

Obligately heterofermentative (Group III) L. brevis, L. buchneri, L. fermentum, L. reuteri

Preservation of Antibiotics for Medical Treatment Act

H.R. 1549/S. 619

“A post-antibiotic era — in which common infections and minor injuries can kill — far from being an apocalyptic fantasy, is instead a very real possibility for the 21st century.” (1)

-Dr. Keiji Fukuda, Assistant Director-General for Health Security, World Health Organization

“A post-antibiotic era — in which common infections and minor injuries can kill — far from being an apocalyptic fantasy, is instead a very real possibility for the 21st century.” (1)

-Dr. Keiji Fukuda, Assistant Director-General for Health Security, World Health Organization
L. reuteri is indigenous to the human digestive tract, being present in newborns as well as adults (applies to only 3-4 Lactobacillus species). It should be a lifelong companion to us. Other lactobacilli are only temporary residents of the digestive tract and are supplied through food and drink.


Characterization
Tejinder Pal Singh, Gurpreet S. Kapila.

Isolated from strains isolated from human infant feces (and LR34) showed their high tolerance to strong hydrophobic bile acids. This did not exceed 40%, with one strain isolate possessing these properties and their ability to deconjugate bile salts. The safety of the nine isolates was supported by the absence of transferable antibiotic resistance. The results obtained so far suggest that bile salts and duodenum juice, so they could survive when passing through the intestinal tract and fulfill their potential probiotic action in the host. Some L. reuteri strains isolated from human infant feces possess interesting probiotic properties that make them potentially good candidates for probiotics.
How do probiotics work?

• Preventing the growth of pathogens
• Competitive displacement of pathogens
• Regulating gut microbial ecosystems
• Improving gut function/nutritional uptake
• Modulating immune responses to improve health
CONCLUSIONS. Bacterial translocation is a unique physiologic event, which is increased during pregnancy. Human breast milk cells contain a limited number of viable bacteria but a range of bacterial DNA signatures, as also found in maternal peripheral blood mononuclear cells. Those peripheral blood mononuclear cells showed greater biodiversity than did peripheral blood mononuclear cells from control women. Taken together, our results suggest that intestinally derived bacterial components are transported to the lactating breast within mononuclear cells. We speculate that this programs the neonatal immune system to recognize specific bacterial molecular patterns and to respond appropriately to pathogens and commensal organisms.
Treatment of the Mother Resulted in Less Disease in the Child

- Mothers chewed Xylitol gum for 2 years beginning at 3 months post-partum
- When the children were 5 years old, the need for treatment was 71-75% lower in the Xylitol group

Isokangas et al. JDR 2000
**L. reuteri** effect on infections in infants attending child care

  - Study group: 201 healthy, full-term infants aged four to ten months were studied at 14 child care centers for 21 months, covering two winter and two summer seasons.
L. reuteri effect on infections in infants attending child care
L. reuteri inhibits intestinal pathogenic microorganisms

- Inhibition via reuterin, reutericyclin, organic acids, bacteriocins and other factors
- Bacteria examples:
  - Escherichia coli
  - Salmonella typhimurium
  - Listeria monocytogenes
  - Clostridium perfringens
  - Shigella spp.
  - Pseudomonas aeruginosa
  - Helicobacter pylori
  - Streptococcus mutans
  - Yersinia enterocolitica
  - Bacillus cereus
  - Staphylococcus aureus
  - Campylobacter jejuni


US Patent 7112323 - Intracellular proteinacious antimicrobial agents from lactic acid bacteria derived from fermented food samples

US Patent Issued on September 26, 2006
Estimated Patent Expiration Date: May 7, 2023
<table>
<thead>
<tr>
<th>Species</th>
<th>Human</th>
<th>Pig</th>
<th>Chicken</th>
<th>Cattle</th>
<th>Dog</th>
<th>Mice</th>
<th>Hamster</th>
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<tbody>
<tr>
<td>L. acidophilus</td>
<td>Group</td>
<td>L. acidophilus</td>
<td>(A-1)</td>
<td>b</td>
<td>L. amylovorus</td>
<td>(A-3)</td>
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<tr>
<td>L. crispatus</td>
<td>(A-2)</td>
<td>L. gallinarum</td>
<td>(A-4)</td>
<td></td>
<td>L. gasseri</td>
<td>(B-1)</td>
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<tr>
<td>L. johnsonii</td>
<td>(B-2)</td>
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<tr>
<td>L. murinus</td>
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<td>L. intestinalis</td>
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<td>L. salivarius</td>
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<td>L. aviarius</td>
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<td>L. casei</td>
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<tr>
<td>L. reuteri</td>
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</tbody>
</table>

**Symbols:**
- **M:** Major component of Lactobacillus species;
- **+:** Occasionally recovered;
- **?** Questionable

L. reuteri inhibits oral pathogenic bacteria

- A. actinomycetemcomitans
- Fusobacterium nucleatum
- Porphyromonas gingivalis
- Prevotella intermedia
- Streptococcus mutans


"Computers in the future may weigh no more than 1.5 tons."
- Popular Mechanics, forecasting the relentless march of science, 1949.
Probiotic therapy

BioGaia Probiotic lozenges

As BioGaia Probiotic chewing gum, BioGaia Probiotic lozenges contain *L. reuteri*, which has documented positive effects on oral health. You let the lozenges dissolve slowly on your tongue. Just like BioGaia Probiotic chewing gum, they are sugar free and have a nice fresh mint flavor.

BioGaia Probiotic straw

Another innovative and fun way to get good *Reuteri* bacteria into your system is the probiotic straws. Each straw provides 100 million *L. reuteri* cells contained in an oil droplet which is released when you drink through it. BioGaia Probiotic Straws are for children, for the ill and the elderly, and are sold either separately or attached to drink packages.

International Journal of Paediatric Dentistry


To cite this article: ESBER ÇAGLAR, OZGUR ONDER KUSCU, SULE KAVALOGLU CILDIR, SENEM SELU KUVETLI, NUKET SANDALLI (2008) A probiotic lozenge administered medical device and its effect on salivary mutans streptococci and lactobacilli


Abstract

A probiotic lozenge administered medical device and its effect on salivary mutans streptococci and lactobacilli

ESBER ÇAGLAR, OZGUR ONDER KUSCU, SULE KAVALOGLU CILDIR, SENEM SELU KUVETLI & NUKET SANDALLI

Department of Paediatric Dentistry, Dental School, Yeditepe University, Istanbul, Turkey

Correspondence to: Dr Esber Caglar, Department of Pediatric Dentistry, School of Dentistry, Yeditepe University, Bagdat cad 238, Goztepe 34728 Istanbul, Turkey. Tel. +90 216 3636044/323; Fax: +90 216 3636211; E-mail: caglares@yahoo.com

International Journal of Paediatric Dentistry 2008; 18: 35–39

Background. Previous studies have suggested that lactobacilli-derived probiotics in dairy products may affect oral ecology, but the effects of different delivery methods have received little attention.

Aim. The aim of the present study was to investigate the effect of the probiotic *Lactobacillus reuteri*, delivered by a new medical device, on the levels of salivary mutans streptococci and lactobacilli in young women with high *Streptococcus mutans* counts.

Design. This is a randomized, double-blind, placebo-controlled study involving 20 healthy young women (aged 20 years): 10 as subjects and 10 as controls. The study subjects (Group A) sucked the medical device containing the probiotic lozenge with *L. reuteri* ATCC 55730/L. reuteri ATCC PTA 5289 (1.1 x 10⁸ CFU) once daily for 10 days, while the control subjects (Group B) received placebo medical devices without bacteria. Salivary mutans streptococci and lactobacilli were enumerated with chair-side kits at baseline and 1 day after the final ingestion.

Results. Salivary *S. mutans* levels in the probiotic test group were significantly reduced, with statistical significance of reduction (*P* < 0.05).

Conclusions. A short-term daily ingestion of lactobacilli-derived probiotics delivered via medical device containing probiotic lozenge reduced the levels of salivary mutans.
DNA-PCR and CRT Results in Children After Probiotic use

Methods

- 60 patients 6 to 12 years of age- caries prone with 4 or more restorations and/or lesions
- CRT collected before and after probiotic use
- 8 week (60 day) experimental time period- considered optimal to see effect
THE PRIMARY OBJECTIVE OF THIS CLINICAL STUDY IS TO DETERMINE THE EFFECT, IF ANY, OF “OVER THE COUNTER” PROBIOTIC SUPPLEMENTS ON THE DNA-PCR AND CRT ANALYSIS.
- Frozen samples in CRT tubes
- Kept at minus 80 degrees Celsius
- Glycerol stabs of colonies for further analysis.
Current Research

- Statistically significant differences between and within groups

PerioBalance and EvoraKids both affected the CRT results by reducing levels of S. mutans and Lactobacilli.

ANOVA Table

<table>
<thead>
<tr>
<th>Source</th>
<th>Sum of Squares</th>
<th>Df</th>
<th>Mean Square</th>
<th>F-Ratio</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Between groups</td>
<td>84.3711</td>
<td>7</td>
<td>12.053</td>
<td>10.36</td>
<td>0.0000</td>
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<tr>
<td>Within groups</td>
<td>242.087</td>
<td>208</td>
<td>1.16388</td>
<td></td>
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<tr>
<td>Total (Corr.)</td>
<td>326.458</td>
<td>215</td>
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</tbody>
</table>

The StatAdvisor:

The ANOVA table decomposes the variance of the data into two components: a between-group component and a within-group component. The F-ratio, which in this case equals 10.3559, is a ratio of the between-group estimate to the within-group estimate. Since the P-value of the F-test is less than 0.05, there is a statistically significant difference between the means of the 8 variables at the 95.0% confidence level. To determine which means are significantly different from which others, select Multiple Range Tests from the list of Tabular Options.
DNA-PCR and CRT Results in Children After Probiotic use
DNA-PCR and CRT Results in Children After Probiotic use
DNA-PCR and CRT Results in Children After Probiotic use

Changes in Lacto before/after probiotic treatment

![Bar chart showing changes in Lacto before and after probiotic treatment.

- X-axis: lacto_change MIDPOINT
- Y-axis: FREQUENCY
- Categories: Evora, Perio, Probiotic
- Bars indicate frequency distribution across different lacto_change MIDPOINT ranges.]
NOT enough evidence to indicate that EvoraPlus and PerioBalance changes the 'SM' or "Lacto" measurements differently.

### Difference between the two probiotics

<table>
<thead>
<tr>
<th></th>
<th>Two-Sided Pr &gt; Z</th>
<th>One-Sided Pr &gt; Z</th>
<th>Z</th>
<th>Normal Approximation</th>
<th>Wilcoxon Two-Sample Test Statistic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pr &gt; Chi-Square</td>
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<td>DF</td>
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<tr>
<td>Chi-Square</td>
<td>0.6942</td>
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<tr>
<td>Kruskal-Wallis Test</td>
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<tr>
<td>Z</td>
<td>0.4134</td>
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<tr>
<td>t-Approximation</td>
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<tr>
<td>Z</td>
<td>0.2067</td>
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<tr>
<td>Normal Approximation</td>
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<td>Z</td>
<td>0.4097</td>
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<tr>
<td>Wilcoxon Two-Sample Test Statistic</td>
<td>762.5000</td>
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</tr>
</tbody>
</table>

### DNA-PCR and Results in Children After Probiotic use

No significant differences were found in DNA-PCR results.
1. Selective agar complicated DNA extraction contaminating some samples.

2. Streptococcus rattus (included in EvoraPlus) was mis-identified as SM but is a mutants.

3. Other technical difficulties

The glucosyltransferase-1 gene has previously been identified as a highly specific marker for Streptococcus mutans (Lett Appl Microbiol. 2006 Feb; 42(2):127-31). The primers and probe have 100% homology with all Streptococcus mutans reference sequences for the NCBI database.
Conclusions:

A clinical trial to evaluate the effectiveness of DNA-PCR and CRT at measuring the salivary level of bacteria in caries-prone children with PerioBalance or EvoraKids therapy.

Both EvoraKids and PerioBalance affected the CRT results. The reduction in S. mutans and Lactobacilli was statistically significant.
Further Research

Retrospective Review of Probiotic Therapy.
ML Cannon DDS
MS
A Vorachek DDS
K White DMD
C Le DMD
An IRB Approved Study

Does EvoraKids and PerioBalance affected the caries proneness of the subjects?
Is the reduction in dental caries was statistically significant?
Retrospective Review of Probiotic Therapy.

ML Cannon DDS
MS A Vorachek DDS
K White DMD
C Le DMD

An IRB Approved Study

Materials and Methods:
Dental records of 60 patients that were enrolled in the Institutional Review Board approved study, "A clinical trial to evaluate the effectiveness of DNA-PCR and CRT at measuring the salivary level of bacteria in caries prone children with PerioBalance or EvoraKids Plus therapy" were reviewed as to current caries activity status with measurement of the Decay Missing Filled Teeth index and Caries By Risk Assessment (CAMBRA) determination. The current Oral health status was compared to the prior study enrollment status and then analyzed in respect to published national norms.

Results:
Of the 53 subjects available for follow up, only 4 had remained caries active with a grand total of 17 caries lesions being detected and subsequently restored in this group. Of the original total of 60 patients with 292 initial carious lesions, after probiotic therapy and dental restoration, 36 total restorations were place in the subject group over the following three years. Approximately half of these restorations were required in teeth that had initially presented with smaller lesions and had been placed in a “watch” category. Two of the patients that developed further carious lesions had been randomly assigned to the probiotic PerioBalance, what the other two caries active patients were assigned EvoraKids probiotic.

Of the original group of caries active patients, 23 did not present with any further carious involvement. Another 26 could be categorized as Caries static, as the restorations required were substantially less than before probiotic therapy had been begun.
Retrospective Review of Probiotic Therapy.

ML Cannon DDS
MS A Vorachek DDS
K White DMD
C Le DMD
An IRB Approved Study

Conclusion:
Within the limitations of this retrospective IRB approved study, the tested probiotic supplements had a statistically significant effect on the caries experience of the enrolled subjects.

Table 1. Caries active, Caries resistant and Caries static patients.

<table>
<thead>
<tr>
<th>Caries Experience</th>
<th>Pre Probiotic</th>
<th>National Average</th>
<th>Post Probiotic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Per patient-3 years</td>
<td>5.51</td>
<td>1.84</td>
<td>0.75</td>
</tr>
</tbody>
</table>

Table 3. Caries History Compared to Nationally Reported Values.

<table>
<thead>
<tr>
<th>Caries Experience</th>
<th>PerioBalance</th>
<th>EvoraKids</th>
<th>Caries Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caries Active</td>
<td>2</td>
<td>2</td>
<td>17</td>
</tr>
<tr>
<td>Caries Resistant</td>
<td>12</td>
<td>11</td>
<td>0</td>
</tr>
<tr>
<td>Caries Static</td>
<td>15</td>
<td>11</td>
<td>36</td>
</tr>
</tbody>
</table>

Conclusion:
Within the limitations of this retrospective IRB approved study, the tested probiotic supplements had a statistically significant effect on the caries experience of the enrolled subjects.
Current Research

Lactobacillus-mediated interference of mutans streptococci in caries-free vs. caries-active subjects.


Final pH affects the interference

Selection of mutans streptococci at different pH levels

Location: Exhibit Hall D (Walton Center, Ground Floor)

E. Palmer, T. Finlayson, T. Maier, and C. Machida, Great Smokies Dental Group, Asheville, NC

Objectives: Dental caries are common in children. Mutans streptococci (MS) are genetically defined and assessed for their ability to interfere with the cariogenic potential.

Methods: Using arbitrarily-pITM, we examined the ability of MS to interfere with the post-treatment (2-4 weeks) of patients after receiving caries preventive treatment and post-treatment collections of MS from patients.

Results: Inter-patient variability was observed, with phenotypic analyses showing increased from 14% to 78% of MS, with SE=0.017, after 3 days of growth in pH values of 4.67-4.89 (n=4) cultures treated with post-treatment, and was highly acidic at 24h. The ability of MS to form biofilms was enhanced by these conditions. The findings suggest that the interference of MS may be enhanced by strategies that promote adhesion and biofilm formation.

Conclusions: Caries preventive strategies have implications that caries prevention strategies may enhance biofilm formation. Enhancing well-accepted practices for caries prevention may improve the interference of MS.
Oral Health Probiotics - what to use?

- Periobalance
- Evora Pro
- Evora Plus
- Biogaia
- ProlacSan
- BLIS K12
- Prodegin
- Gluten metabolizers
Probiotics- Antagonism and Inhibition

Ongoing Research

Working in the “probiotic”?

What causes gluten Sensitivity??

Is it an ORAL disease?????
What is the dough doing while it is “resting”
Gluten sensitivity epidemic

The two "celiac disease genes" – HLA-DQ2 and HLA-DQ8 (HLA stands for "human leukocyte antigen") – appear in about 35% to 40% of the U.S. population, most commonly among those with European ancestors. But only about 1% to 4% of those with the "celiac disease genes" will ever be diagnosed with celiac disease, which affects about one in 100 people overall.

Systematic Review: Worldwide Variation in the Frequency of Coeliac Disease and Changes Over Time

J. Y. Kang, A. H. Y. Kang, A. Green, K. A. Gwee, K. Y. Ho | Disclosures

Aliment Pharmaco Ther 2013; 38(3):226-245

Source: Aliment Pharmaco Ther © 2013 Blackwell Publishing
Gluten sensitivity epidemic

Abstract
BACKGROUND & AIMS: Coeliac disease is a chronic small intestinal immune-mediated enteropathy triggered by dietary gluten in genetically predisposed individuals. Since it is unknown if all wheat varieties are equally toxic to coeliac patients seven Triticum accessions showing different origin (ancient/modern) and ploidy (di-, tetra- hexaploid) were studied.

MATERIALS AND METHODS: Selected strains of wheat were ancient Triticum monococcum precoce (AA genome) and Triticum speltoides (BB genome), accessions of Triticum turgidum durum (AABB genome) including two ancient (Graziella Ra and Kamut) and two modern (Senatore Cappelli and Svevo) durum strains of wheat and Triticum aestivum compactum (AABBDD genome). Small intestinal gluten-specific T-cell lines generated from 13 coeliac patients were tested with wheat accessions by proliferation assays.

RESULTS: All strains of wheat independent of ploidy or ancient/modern origin triggered heterogeneous responses covering wide ranges of stimulation indices.

CONCLUSION: Ancient strains of wheat, although previously suggested to be low or devoid of coeliac toxicity, should be tested for immunogenicity using gluten-specific T-cell lines from multiple coeliac patients rather than gluten-specific clones to assess their potential toxicity. Our findings provide further evidence for the need for a strict gluten-free diet in coeliac patients, including avoidance of ancient strains of wheat.

2. Hybridized grains

3. Microflora changes
1746 Isolation of Gluten-degrading Enzyme(s) from Oral Bacteria

Friday, March 22, 2013: 10:45 a.m. - 12:15 p.m.
Location: Room 614 (Washington State Convention Center)
Presentation Type: Oral Session
G. WEI, N. TIAN, F.G. OPPENHEIM, and E.J. HELMERHORST, Dept. of Periodontology & Oral Biol, Boston University, Boston, MA

2266 Human Oral Bacterial Enzymes: Novel Therapeutic Perspectives for Celiac Disease

Friday, March 22, 2013: 3:30 p.m. - 4:45 p.m.
Location: Room 614 (Washington State Convention Center)
Presentation Type: Poster Discussion Session
N. TIAN¹, G. WEI¹, D. SCHUPPAN², F.G. OPPENHEIM¹, and E.J. HELMERHORST¹, ¹Dept. of Periodontology & Oral Biol, Boston University, Boston, MA, ²Beth Israel Deaconess Medical Center, Boston, MA
What causes oral microflora changes?
Objectives: The search for therapies for celiac disease includes investigations into luminal enzymes capable of cleaving gluten into fragments that are unable to elicit inflammatory immune responses. We recently provided evidence that the oral cavity, representing the port of entry to the gastro-intestinal tract, harbors gluten-degrading microorganisms. The goal of this study was to conduct a comprehensive screening of human dental plaque and saliva samples to isolate and identify novel resident gluten/gliadin-degrading bacteria.
Gluten sensitivity epidemic

**Results:** The culturing strategy yielded 87 aerobic and 63 anaerobic strains. Twenty one aerobic strains representing seven oral species showed activity in at least two of the four assays with two species being active in all four assays.

**Conclusions:** New gluten-degrading microorganisms were identified that naturally colonize the upper gastro-intestinal tract. A cocktail of the most active oral bacteria, or their isolated enzymes, may offer promising new treatment modalities for celiac disease.
The purpose of this study was to determine if there is any inhibition of beneficial oral biofilm species such as *Rothia aeria*, *R. mucilaginosa* and *R. dentocariosa*, *Streptococcus mutans* (pathogen-negative control) and also *Lactobacillus reuteri* strains (isolated from PERIO Probiotic) by over the counter (OTC) oral anti-microbials utilizing in vitro laboratory technique. The secondary objective was to determine the antagonism, if any, of the Rothia genus by *Streptococcus* species (mutans and salivarius) and known pathogens. Rothia aeria and mucilaginosa are believed to be important in the processing of gluten.
### TABLE 1a. Susceptibility Experiment: The Effect of Over the counter Oral Hygiene Products on Oral Bacteria

<table>
<thead>
<tr>
<th>Reagent</th>
<th><em>Rothia Aeria</em> on blood agar</th>
<th><em>R. dentocariosa</em> on blood agar</th>
<th><em>R. mucilaginosa</em> on Brucella</th>
<th><em>PERIO probiotic (Lactobacillus)</em> on blood agar</th>
<th><em>S. Mutans</em> on blood agar</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spry Xylitol Mouthwash™</td>
<td>0, 0</td>
<td>0, 0</td>
<td>0, 0</td>
<td>0, 0</td>
<td>0, 0</td>
</tr>
<tr>
<td>Crest Prohealth™</td>
<td>9, 9</td>
<td>12, 12</td>
<td>11, 11</td>
<td>14, 16</td>
<td>15, 13</td>
</tr>
<tr>
<td>ACT fluoride rinse™</td>
<td>10, 10</td>
<td>11, 12</td>
<td>14</td>
<td>12, 14</td>
<td>17, 15</td>
</tr>
<tr>
<td>Listerine Smartrinse™</td>
<td>9, 9</td>
<td>10, 11</td>
<td>9, 9</td>
<td>14, 14</td>
<td>14, 12</td>
</tr>
<tr>
<td>Chlorhexidine (11.6% alcohol)</td>
<td>13, 12</td>
<td>18, 18</td>
<td>13, 12</td>
<td>14, 14</td>
<td>16, 15</td>
</tr>
<tr>
<td>Listerine™ (27% Alcohol)</td>
<td>0, 0</td>
<td>0, 0</td>
<td>0, 0</td>
<td>0, 0</td>
<td>9, 9</td>
</tr>
<tr>
<td>Phosphate Buffered Saline (PBS)</td>
<td>0</td>
<td>0, 0</td>
<td>0, 0</td>
<td>0, 0</td>
<td>0, 0</td>
</tr>
<tr>
<td>27% Alcohol</td>
<td>0, 0</td>
<td>0, 0</td>
<td>10</td>
<td>0, 0</td>
<td>0, 0</td>
</tr>
<tr>
<td>Embrace Varnish™ (has xylitol)</td>
<td>8, 9</td>
<td>0, 0</td>
<td>0, 0</td>
<td>12, 12</td>
<td>0, 0</td>
</tr>
<tr>
<td>Spry™ Xylitol toothpaste gel</td>
<td>0, 0</td>
<td>0, 0</td>
<td>0, 0</td>
<td>10, 12</td>
<td>0, 0</td>
</tr>
<tr>
<td>50% Spry™ Xylitol toothpaste gel in PBS</td>
<td>0, 0</td>
<td>0, 0</td>
<td>0, 0</td>
<td>0, 0</td>
<td>0, 0</td>
</tr>
<tr>
<td>Levoflaxacin (5 micrograms)</td>
<td>30</td>
<td>30</td>
<td>30</td>
<td>36</td>
<td>20</td>
</tr>
</tbody>
</table>

Note: All dimensions shown in millimeters
Probiotics- Antagonism and Inhibition

Rothia inhibition and antagonism

---

Rothia Aeria is inhibited by:
1. Chlorhexidine
2. Haraldia Saliva

---

**TABLE 1b. Susceptibility Experiment: The Effect of OTC Oral Hygiene Products on Other Bacteria of the Human Flora**

<table>
<thead>
<tr>
<th></th>
<th>S. aureus</th>
<th>S. salivarius</th>
<th>E. coli</th>
<th>P. aeruginosa</th>
<th>VRE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spry™ Mouthwash</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Embrace™ varnish</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Spry™ Xylitol gel diluted in PBS</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0*</td>
<td>0</td>
</tr>
<tr>
<td>PBS control</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Note: All dimensions shown in millimeters

*but for a short period showed inhibition
# Probiotics: Antagonism and Inhibition

Rothia inhibition and antagonism

**TABLE 3. Diffusion Experiment: Bacterial Species Inhibition of Each Other**

<table>
<thead>
<tr>
<th></th>
<th>R. dentocariosa</th>
<th>R. mucilaginosa</th>
<th>S. salivarius</th>
<th>E. coli</th>
<th>P. aeruginosa</th>
</tr>
</thead>
<tbody>
<tr>
<td>R. mucilaginosa</td>
<td>0, 0</td>
<td>0, 0</td>
<td>0, 0</td>
<td>0, 0</td>
<td>0, 0</td>
</tr>
<tr>
<td>VRE</td>
<td>0, 0</td>
<td>0, 0</td>
<td>0, 0</td>
<td>0, 0</td>
<td>0, 0</td>
</tr>
<tr>
<td>E. coli</td>
<td>0, 0</td>
<td>0, 0</td>
<td>0, 0</td>
<td>0, 0</td>
<td>0, 0</td>
</tr>
<tr>
<td>P. aeruginosa</td>
<td>inhibits</td>
<td>0, 0</td>
<td>0, 0</td>
<td>0, 0</td>
<td>0, 0</td>
</tr>
<tr>
<td>S. salivarius</td>
<td>0, 0</td>
<td>0, 0</td>
<td>0, 0</td>
<td>0, 0</td>
<td>0, 0</td>
</tr>
<tr>
<td>R. dentocariosa</td>
<td>0, 0</td>
<td>0, 0</td>
<td>0, 0</td>
<td>0, 0</td>
<td>0, 0</td>
</tr>
<tr>
<td>S. aureus</td>
<td>0, 0</td>
<td>inhibits</td>
<td>0, 0</td>
<td>0, 0</td>
<td>0, 0</td>
</tr>
</tbody>
</table>

Note: All dimensions shown in millimeters
Inhibition of Rothia Species by OTC Products and Bacterial Antagonists

Garcia K, Barstad D, Cannon M, Kabat B, Yegev R, Jantra L, Muhammad A, Vorachek A

Introduction:
The purpose of this study was to determine if there is any inhibition of beneficial oral biofilm species such as Rothia aeria, R. mucilaginosa, and R. dentocariosis, Streptococcus mutans, (pathogen-negative control) and also Lactobacillus reuteri strains isolated from FERD (Philadelphia) by over the counter (OTC) oral anti-microbials utilizing in vitro laboratory technique. The secondary objective was to determine the antagonism, if any, of the Rothia genera by Streptococcus species (mutans and intermedius) and known pathogens. Rothia aeria and R. mucilaginosa are believed to be important in the processing of gluten inhibition of these beneficial bacteria by OTC products, either directly or indirectly, would increase gluten sensitivity in patients. Beneficial bacteria may be indirectly inhibited by certain antagonistic bacteria that are relatively less sensitive to OTC products.

Methods:

Susceptibility Experiment:
Three colonies of R. aeria, R. dentocariosis, R. mucilaginosa, S. mutans, and Lactobacillus were obtained from isolation plates and grown in Mueller-Hinton media to a McFarland Standard of 0.5. Either brainheart agar plates, Rogosal agar, or Mueller-Hinton agar plates with 5% sheep blood were wholly spread with one cotton swab inoculation of chosen bacteria. Five cotton swabs were evenly distributed on the plates and 10 microliters of full strength reagent was pipetted directly onto each corresponding disc. The plates were evaluated after 30 hours of growth at 36 degrees. Calipers were used to measure zones of inhibition.

Diffusion Experiment:
Trypsin Soy Agar (TSA) was autoclaved and cooled to 54 degrees and aliquots of 25ml were cooled and inoculated with 3ml of a McFarland Standard suspension of R. dentocariosis, R. mucilaginosa, Streptococcus salivarius, Escherichia coli, or Peptostreptococcus anaerogena prior to pouring agar plates. Inoculated plates were then incubated in punched zones using a disposable 10 microliter loop with 0.5 McFarland Standard of bacteria species: Streptococcus salivarius, Peptostreptococcus anaerogena, Escherichia coli, and P. anaerogena or R. mucilaginosa. The plates were evaluated after 24 hours of growth at 36 degrees. Calipers were used to measure zones of inhibition.

Results:
Beneficial growth of all tested bacteria were inhibited by Crest ProHealth™, ACT™, Listerine SmartRinse™, and Chloraseptic. R. aeria and R. mucilaginosa were also inhibited by Embrace™ varnish, and Spray™ Xylitol Tocopheryl Gel inhibited R. mucilaginosa. Growth of R. dentocariosa was inhibited by P. anaerogena and growth of R. mucilaginosa was inhibited by S. aureus.

Discussion:
It was observed that there should not be interpreted as being always applicable to the clinical situation. Indeed, the complexity of the human oral microbiome would make it difficult to predict a response to any oral intervention with any certainty. The results of the present study are of a pilot nature, a negative finding would mean that there is little need for further investigation. However, limited the significance of in vitro studies for actionable consequences, they are, however, always necessary before progressing into more extensive, time consuming, and financially demanding studies. The inference that OTC products, that may be used an aid by patients, contribute to a reduction in beneficial bacteria should be a concern to all health practitioners. Of greater interest should be the extent of the inhibition, as the zones of inhibition were quite significant in diameter. The average diameter of inhibition with an OTC product was 33mm.

Another very important aspect of this study was the interaction between pathogenic and beneficial bacteria. The interaction, or rather, the inhibition of different bacterial species actually determines the health of the host and, as such, is paramount in importance. The results were significant in that growth of Rothia species was inhibited by other bacteria, suggesting that if the oral flora is in equilibrium is changed by using OTC oral hygiene products, a domino effect can affect the entire oral microflora, which is the gateway to the digestive tract.

Conclusion:
Rothia species, S. mutans and Lactobacillus species, are decreased in quantity by the use of oral anti-microbials. OTC products may alter the oral microbiome creating a situation less conducive for the survival of essential beneficial bacteria. The use of OTC products may decrease the enzymatic degradation of gluten containing foods by Rothia bacteria resulting in gluten sensitivity. Intake Bile Acid Synthase, and exo-acting amylase tablets could increase Carcinoid disease clinical prevalence. The Friesph Institute noted at the poster session of the AAOI 2012 meeting that Rothia aeria and R. mucilaginosa were identified as gluten-degrading strain in the oral cavity. While the human digestive enzyme system lacks the ability to cleave immunogenic gluten, such enzymes are naturally present in the oral microbial enzymes repertoire. (Mit, G. Zanikthakis, M. Dewhurst, F. Schellman, D. Eisinger, F. Holmerez, E. Rothia Bacteria as Gluten-Degrading Natural Colonizers of the Oral Cavity, 2012).
Conclusion:

Rothia species, *S. mutans* and Lactobacillus species, are decreased in quantity by the overuse of oral anti-microbials. OTC products may alter the oral microbiome creating a situation less conducive for the survival of essential beneficial bacteria. The use of OTC products may decrease the enzymatic degradation of gluten containing foods by Rothia bacteria resulting in gluten sensitivity, Irritable Bowels Syndrome, and exacerbating ulcerative colitis increasing Celiac disease clinical prevalence.
Mechanisms of inhibition by fluoride of urease activities of cell suspensions and biofilms of Staphylococcus epidermidis, Streptococcus salivarius, Actinomyces naeslundii and of dental plaque.

Barboza-Silva E, Castro AC, Marquis RE.
Department of Microbiology & Immunology, University of Rochester Medical Center, Rochester, NY 14642-8672, USA.

Abstract

BACKGROUND/AIMS: Fluoride is known to be a potent inhibitor of bacterial ureases and can also act in the form of hydrofluoric acid as a transmembrane proton conductor to acidify the cytoplasm of intact cells with possible indirect, acid inhibition of urease. Our research objectives were to assess the inhibitory potencies of fluoride for three urease-positive bacteria commonly found in the mouth and to determine the relative importance of direct and indirect inhibition of ureases for overall inhibition of intact cells or biofilms.

METHODS: The experimental design involved intact bacteria in suspensions, mono-organism biofilms, cell extracts, and dental plaque. Standard enzymatic assays for ammonia production from urea were used.

RESULTS: We found that ureolysis by cells in suspensions or mono-organism biofilms of Staphylococcus epidermidis, Streptococcus salivarius or Actinomyces naeslundii was inhibited by fluoride at plaque levels of 0.1-0.5 mm in a pH-dependent manner. The results of experiments with the organic weak acids indomethacin and capric acid, which do not directly inhibit urease enzyme, indicated that weak-acid effects leading to cytoplasmic acidification are also involved in fluoride inhibition. However, direct fluoride inhibition of urease appeared to be the major mechanism for reduction in ureolytic activity in acid environments. Results of experiments with freshly harvested supragingival dental plaque indicated responses to fluoride similar to those of S. salivarius with pH-dependent fluoride inhibition and both direct and indirect inhibition of urease.

CONCLUSION: Fluoride can act to diminish alkali production from urea by oral bacteria through direct and indirect mechanisms.
Probiotics- Antagonism and Inhibition

Fluoride Mouth Rinse

Form
Fluoride mouth rinse is a concentrated solution intended for daily or weekly use. The most common fluoride compound used in mouth rinse is sodium fluoride. Over-the-counter solutions of 0.05% sodium fluoride (230 ppm fluoride) for daily rinsing are available for use by persons older than 6 years of age. Solutions of 0.20% sodium fluoride (920 ppm fluoride) are used in supervised, school-based weekly rinsing programs. Other concentrations also are available.

Use
Rinses are used daily or weekly for a prescribed amount of time. The fluoride from mouth rinse is retained in dental plaque and saliva to help prevent tooth decay.

Availability
Mouth rinses intended for home use can be purchased over-the-counter. Higher strength mouth rinses for those at high risk of tooth decay must be prescribed by a dentist or physician.

Recommendations
Children younger than 6 years of age should not use fluoride mouth rinse without consultation with a dentist or other health care provider because dental fluorosis could occur if such mouth rinses are repeatedly swallowed. Because fluoride mouth rinse has resulted in only limited reductions in tooth decay among schoolchildren, especially as their exposure to other sources of fluoride has increased, its use should be targeted to individuals or groups at high risk for decay.
Probiotics - dietary effects - implications

• Autoimmune response
  - causes obesity, sedentary lifestyle, mood shift, behavioral issues, dietary changes as cravings change!

• Comfort food - chocolate, fries, ice cream, etc.

• Other biofilm modifiers
Probiotics - Neurologic Implications

- Autism
- “Autism Spectrum Disorder”
- Evidence mounts,

Short-chain fatty acids: products of the gut microbiome, implications in autism disorders


Unique acyl-carnitine profile disorder.
Frye RE, Melnyk S, Macfabe DF.

Abstract
Autism spectrum disorder (ASD) has been linked to a specific genetic mutation to explain the disease. Acquired MD has been demonstrated to cause ASD-associated gut bacteria, is infusing neuropathologic and neurophysiologic short-chain and long-chain acyl-carnitine metabolism are abnormal. Fatty acid metabolism is a key factor in the development of ASD. Acyl-carnitine was determined to be abnormal if three or more individual acyl-carnitine species were abnormal in the panel and these abnormalities were verified by repeated testing. Overall, 17% of individuals with ASD demonstrated consistently abnormal acyl-carnitine panels.
• Dr. Seneff - MIT scientist reports:

*Entropy 2013, 15(4), 1416-1463; doi:10.3390/e15041416

Review

Glyphosate’s Suppression of Cytochrome P450 Enzymes and Amino Acid Biosynthesis by the Gut Microbiome: Pathways to Modern Diseases†

Anthony Samsel and Stephanie Seneff

Received: 15 January 2013; in revised form: 10 April 2013 / Accepted: 10 April 2013 / Published: 18 April 2013

<table>
<thead>
<tr>
<th>Diseases</th>
<th>Allergies</th>
<th>Cancer</th>
<th>Parkinson’s disease</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>inflammatory bowel disease, chronic diarrhea, colitis and Crohn’s disease</td>
<td>Infertility</td>
<td>Multiple sclerosis</td>
</tr>
<tr>
<td></td>
<td>Cardiovascular disease</td>
<td>Depression</td>
<td>ALS, and more</td>
</tr>
</tbody>
</table>

Probiotics prevented Weight gain!
Probiotics- Neurologic Implications

- Bacteria - obesity, depression.
Probiotics- Neurologic Implications

• Prevention and Probiotics- kefir and BLIS?

Abstract

BACKGROUND & AIMS: Changes in gut microbiota have been reported to alter signaling mechanisms, emotional behavior, and visceral nociceptive reflexes in rodents. However, alteration of the intestinal microbiota with antibiotics or probiotics has not been shown to produce these changes in humans. We investigated whether consumption of a fermented milk product with probiotic (FMPP) for 4 weeks by healthy women altered brain intrinsic connectivity or responses to emotional attention tasks.

METHODS: Healthy women with no gastrointestinal or psychiatric symptoms were randomly assigned to groups given FMPP (n = 12), a nonfermented milk product (n = 11, controls), or no intervention (n = 13) twice daily for 4 weeks. The FMPP contained Bifidobacterium animalis subsp Lactis, Streptococcus thermophiles, Lactobacillus bulgaricus, and lactococcus lactis subsp Lactis. Participants underwent functional magnetic resonance imaging before and after the intervention to test the brain response to an emotional face, attention task, and resting brain activity. Multivariate and region of interest analyses were performed.

RESULTS: FMPP intake was associated with reduced task-related response of a distributed functional network (49% cross-block covariance; P = .004) containing affective, viscerosensory, and somatosensory cortices. Alterations in intrinsic activity of resting brain indicated that ingestion of FMPP was associated with changes in midbrain connectivity, which could explain the observed differences in activity during the task.

CONCLUSIONS: Four-week intake of an FMPP by healthy women affected activity of brain regions that control central processing of emotion and sensation.
Probiotics - Neurologic Implications

- Dementia and Alzheimer's Disease

High levels of STEP proteins keep synapses in the brain from strengthening, a process that is required for people to turn short-term memories into long-term memories. When STEP is elevated in the brain, it depletes receptors from synaptic sites and inactivates other proteins that are necessary for proper cognitive function. This disruption can result in Alzheimer's disease or a number of neuropsychiatric and neurodegenerative disorders, all marked by cognitive deficits.
Probiotics- Neurologic Implications

There is growing evidence for a paradigm shift in our view on the pathogenesis of autoimmune diseases. In addition to genetic susceptibility, making the individual react abnormally to self antigens, the loss of the protective function of epithelial barriers that interact with the environment, not least the gastrointestinal mucosa, seems to be involved in the development of autoimmunity [1]. Recent observations in humans and in a variety of animal models indicate that an increased intestinal permeability (IP), often referred to as a “leaky gut”, is playing a pathogenic role not only in development of gastrointestinal disorders like inflammatory bowel disease (IBD) and celiac disease, but also in systemic autoimmune diseases, like type 1 diabetes (T1D) [1], [2], [3], [4].

Intestinal Barrier Dysfunction Develops at the Onset of Experimental Autoimmune Encephalomyelitis, and Can Be Induced by Adoptive Transfer of Auto-Reactive T Cells

Mehmaz Nouri, Anders Bredberg, Björn Weström, Shahram Lavasani

Published: September 03, 2014 • DOI: 10.1371/journal.pone.0106335

In multiple sclerosis the myelin sheath, which is a protective membrane that wraps around the axon of a nerve cell is destroyed with inflammation and scarring.
Vertebrates typically harbor a rich gastrointestinal microbiota, which has coevolved with the host over millennia and is essential for several host physiological functions, in particular maturation of the immune system. Recent studies have highlighted the importance of a single bacterial species, segmented filamentous bacteria (SFB), in inducing a robust T-helper cell type 17 (Th17) population in the small-intestinal lamina propria (SI-LP) of the mouse gut. Consequently, SFB can promote IL-17-dependent immune and autoimmune responses, gut-associated as well as systemic, including inflammatory arthritis and experimental autoimmune encephalomyelitis.
Oral and gut bacteria are repeatedly reported in the research literature to be involved in:

- Autism
- Diabetes Type II
- RA
- Depression and anxiety
- Obesity
- Dental disease
- Periodontal disease
- Cardiac disease
- Reactive lung disease
- All autoimmune disorders
- Aging
- Gluten sensitivity
- Celiacs

New Sealant Technology

- Bis Phenol A - IS BACK IN THE NEWS!!!

Compendium
September 2013, Volume 34, Issue 8
Published by AEGIS Communications

Bioactive and Therapeutic Preventive Approach to Dental Pit and Fissure Sealants
Mark L. Cannon, DDS, MS; and John C. Comisi, DDS, MAGD

BPA free

GC Fuji TRIAGE
Glass Ionomer Sealant
Surface Protection Material

EMBRACE™ WetBond™
Pit & Fissure Sealant
Fluoride Releasing
Light Cure
New Sealant Technology

- Bis Phenol A - IS BACK IN THE NEWS!!!

BPA's possible role in miscarriages


Dental composite fillings and bisphenol A among


Bisphenol A blood and saliva levels prior to and after dental sealant placement in adults.

Zimmerman-Downs JM, Shuman D, Stull SC, Ratzlaff RE.

College of Health Sciences, Old Dominion University, Norfolk, VA, USA.
New Sealant Technology

- Bis Phenol A - IS BACK IN THE NEWS!!!


Bisphenol A and peripheral arterial disease: results from the NHANES.


Relationship between urinary bisphenol A levels and prediabetes among subjects free of diabetes.


Relationship between urinary bisphenol A levels and diabetes mellitus.

Shankar A, Teppala S.

Department of Community Medicine, West Virginia University School of Medicine, P.O. Box 9190, Morgantown, West Virginia 26506-9190, USA. a.shankar@hsc.wvu.edu

Jenny L. Carwile a, Karin B. Michels a,b,c,*

a Department of Epidemiology, Harvard School of Public Health, 677 Huntington Ave, Boston, MA 02115, USA
b Obstetrics and Gynecology Epidemiology Center, Department of Obstetrics, Gynecology and Reproductive Biology, Brigham and Women’s Hospital, Harvard Medical School, 221 Longwood Avenue, Boston, MA 02116, USA
c Division of Cancer Epidemiology, Comprehensive Cancer Center Freiburg, Freiburg University, Freiburg, Germany

Published online 2010 September 8. doi: 10.1289/ehp.1002347

Does BPA change biofilm?

Estrogenic Activity of Bisphenol A and 2,2-bis(p-Hydroxyphenyl)-1,1,1-trichloroethane (HPTE) Demonstrated in Mouse Uterine Gene Profiles

Sylvia C. Hewitt and Kenneth S. Korach

In vitro Estradiol Hemisuccinate Activity as anti Vaginal Microbiota Biofilm Strategy

M. Marques, A. Farinati, M. Arcos, L. Sibert, A. Orsini
USAL, Buenos Aires, ARGENTINA
Helicobacter pylori infection is associated with an increased rate of diabetes.


Center for Infectious Diseases Epidemiologic Research, Mailman School of Public Health, Columbia University, New York, New York, USA.

Abstract

OBJECTIVE: Chronic infections could be contributing to the socioeconomic gradient in chronic diseases. Although chronic infections have been associated with increased levels of inflammatory cytokines and cardiovascular risk, there is little evidence on how infections affect risk of diabetes.

RESEARCH DESIGN AND METHODS: We examined the association between serologic evidence of chronic viral and bacterial infections and incident diabetes in a prospective cohort of Latino elders. We analyzed data on 7,212 individuals aged 50 years and diabetes free in 1998-1999, whose blood was tested for antibodies to herpes simplex virus 1, varicella virus, cytomegalovirus, Helicobacter pylori, and Toxoplasma gondii and who were followed until June 2008. We used Cox proportional hazards regression to estimate the relative incidence rate of diabetes by serostatus, with adjustment for age, sex, education, cardiovascular disease, smoking, and diabetes levels.

RESULTS: Individuals seropositive for herpes simplex virus 1, varicella virus, cytomegalovirus, and T. gondii did not show an increased rate of diabetes, whereas those who were seropositive for H. pylori at enrollment were 2.7 times more likely at any given time to develop diabetes than seronegative individuals (hazard ratio 2.69 [95% CI 1.10-6.60]). Controlling for insulin resistance, C-reactive protein and interleukin-6 did not attenuate the effect of H. pylori infection.

CONCLUSIONS: We demonstrated for the first time that H. pylori infection leads to an increased rate of incident diabetes in a prospective cohort study. Our findings implicate a potential role for antibiotic and gastrointestinal treatment in preventing diabetes.
THE SECRETS!!! SHHHHHH!!!

- Manufacture Dependent For Levels of Bis Phenol A
- three methods to make Bis GMA
  - Reaction of two moles of glycidyl methacrylate with one mole of bisphenol a.
  - Condensation of sodium salt of bisphenol a with glycidyl methacrylate and anhydrous hydrochloric salt
  - Reaction of glacial methacrylate acid with the diglycidyl ether of bisphenol and a tertiary amine
- no Bis GMA in product
The 1918 flu pandemic (January 1918 – December 1920) was an unusually deadly influenza pandemic, the first of the two pandemics involving H1N1 influenza virus. It infected 500 million people across the world, including remote Pacific islands and the Arctic, and killed 50 to 100 million of them—three to five percent of the world's population—at the height of the deadliest natural disasters in human history.

Most influenza outbreaks disproportionately kill juvenile, elderly, or already weakened patients; in contrast the 1918 pandemic predominantly killed previously healthy young adults. Modern research, using virus taken from the bodies of frozen victims, has concluded that the virus kills through a cytokine storm (overreaction of the body's immune system). The immune reactions of young adults ravaged the body, whereas the weaker immune systems of children and middle-aged adults resulted in fewer deaths among those groups.

Historical and epidemiological data are inadequate to identify the pandemic's geographic origin. It was implicated in the outbreak of encephalitis lethargica in the 1920s.

To maintain morale, wartime censors minimized early reports of illness and mortality in Germany, Britain, France, and the United States; but papers were free to report the epidemic's effects in neutral Spain (such as the grave illness of King Alfonso XIII), creating a false impression of Spain as especially hard hit and thus the pandemic's nickname Spanish flu.
What are zoonotic diseases?

Zoonotic diseases are contagious diseases spread between animals and humans. These diseases are caused by bacteria, viruses, parasites, and fungi that are carried by animals and insects. Examples are anthrax, dengue, Ebola hemorrhagic fever, Escherichia coli infection, Lyme disease, malaria, Plague, Rocky Mountain spotted fever, salmonellosis, and West Nile virus infection.

People and animals are not meant to be stacked on top of each other!
Crowd Disease- a sign of the times!

Crowd diseases could not sustain themselves in small bands of hunter-gatherers and slash-and-burn farmers... [but] could have arisen only with the build-up of large, dense human populations. That build-up began with the rise of agriculture starting about 10,000 years ago and then accelerated with the rise of cities starting several thousand years ago.

- **THE MAJOR KILLERS OF HUMANITY** throughout our recent history—smallpox, flu, tuberculosis, malaria, plague, measles, and cholera—are infectious diseases that evolved from diseases of animals, even though most of the microbes responsible for our own epidemic illnesses are paradoxically now almost confined to humans.

<table>
<thead>
<tr>
<th>Human disease</th>
<th>Animal with most closely related pathogen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measles</td>
<td>cattle (rinderpest)</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>cattle</td>
</tr>
<tr>
<td>Smallpox</td>
<td>cattle (cow pox) or other livestock with related pox viruses</td>
</tr>
<tr>
<td>Flu</td>
<td>pigs, ducks</td>
</tr>
<tr>
<td>Pertussis</td>
<td>pigs, dogs</td>
</tr>
<tr>
<td>Falciparum malaria</td>
<td>birds (chickens and ducks?)</td>
</tr>
</tbody>
</table>
Puppy Periodontal Disease

- Week-end training in Dental care......
- When did this start?
- What pathogens are responsible?


**Puppy Periodontal Disease**

- Human pathogens - zoonotic infection of pets?

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**Pet ownership and cardiovascular risk reduction: supporting evidence, conflicting data and underlying mechanisms.**

Arhart-Sudhir K\(^1\), Arhart-Sudhir R, Sudhir K.

**Author information**

"positive health benefits"

**Abstract**

1. It is widely believed that pet ownership is beneficial to humans and that some of this benefit is through favourable effects on cardiovascular risk. In the present review, we critically examine the evidence in support of this hypothesis and present the available data with respect to major cardiovascular risk factors. 2. There is evidence that dog owners are less sedentary and have lower blood pressure, plasma cholesterol and triglycerides, attenuated responses to laboratory-induced mental stress and improved survival following myocardial infarction compared with non-pet owners. However, conflicting data exist with regard to the association between pet ownership and each of these risk factors. 3. Numerous non-cardiovascular effects of pet ownership have been reported, largely in the psychosocial domain, but the relationship is complex and can vary with demographic and social factors. 4. A unifying hypothesis is presented, linking improved mood and emotional state to decreased central and regional autonomic activity, improved endothelial function and, thus, lower blood pressure and reduced cardiac arrhythmias. 5. Overall, ownership of domestic pets, particularly dogs, is associated with positive health benefits.

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**RESULTS**

A correlation was found between the periodontal destruction index (TMPS-P) and the measured blood parameters. We conclude that chronic periodontal disease does not cause anemia or a reduction in serum albumin. However, active periods of periodontal inflammation may be associated with laboratory values suggestive of a systemic inflammatory response.

**CONCLUSIONS**

Though the distribution of periodontopathic species in both is generally different.

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**METHODS**

Conventional susceptibility tests were performed. There were 35 strains isolated from 22 dogs, and broad-range polymerase chain reaction and sequencing methods revealed that approximately 70% of them were Porphyromonas gulae. In contrast, the frequency of Porphyromonas gingivalis was extremely low. These findings indicate the presence of specific periodontitis-related pathogens in pet dogs, especially Porphyromonas gulae.
Puppy Periodontal Disease

Probiotics for dogs - from human sources or shared???
If share pathogens, do we share probiotics?

- Sharing immunity
- Sharing destiny
- Sharing DNA
- Sharing diseases?
- Sharing health
Investigation into Gluten Metabolizing Bacterial Species and their Inhibition

• Muhammad A., Jantra L., Cannon M., Kabat B., Yogev R.
• Ann and Robert Lurie Children’s Hospital of Chicago
• Northwestern University Feinberg School of Medicine

• It has been previously reported that the gluten metabolizing bacteria in the oral biofilm are involved in the digestion and processing of gluten containing food products and Rothia aeria and R. mucilaginosa were identified as gluten-degrading strains in the oral cavity. While the human digestive enzyme system lacks the capacity to cleave immunogenic gluten, such activities are naturally present in the oral microbial enzyme repertoire (Wei, G, Zamkhcharfi, M, Dewhirst, F, Schuppan, D, Oppenheim, F, Helmerhorst, E. Rothia Bacteria as Gluten-Degrading Natural Colonizers of the Oral Cavity. 2012).
Investigation into Gluten Metabolizing Bacterial Species and their Inhibition

- OTC products may alter the oral microbiome creating a situation less conducive for the survival of essential beneficial bacteria. The use of OTC products may decrease the enzymatic degradation of gluten containing foods by Rothia bacteria resulting in gluten sensitivity, Irritable Bowel Syndrome, and exacerbating ulcerative colitis increasing Celiac disease clinical prevalence. In a previous research study, some of these oral medicaments were determined to greatly inhibit the gluten metabolizers in vitro. Therefore, the importance of the gluten metabolizing bacteria should not be minimized and deserves further investigation. The literature does not report how commonly the gluten metabolizing bacteria are present in the environment and in the oral environment of other mammals.
Investigation into Gluten Metabolizing Bacterial Species and their Inhibition

Purpose: To isolate previously undiscovered gluten metabolizing bacterial species from environmental sources and to determine the factors and antagonistic bacteria responsible for their inhibition.
Investigation into Gluten Metabolizing Bacterial Species and their Inhibition

- Standardized Inhibition study performed on 16 gluten metabolizing strains.
- Bacteriocin inhibition measured with forty standard bacteriocins.

- Results: Oral medicaments, such as, Crest, Listerine, Act Fluoride rinse, Chlorhexidine and Smartrinse inhibited all 16 of the gluten bacterial strains (average 10 mms.). One strain MLC 124 was more resistant to oral medicaments. Xylitol products only inhibited 9 strains, but not MLC 124. Forty standard bacteriocins were applied to agars with Rothia species and the newly isolated bacteria. No zones of inhibition were detected with the strain MLC 124.
Investigation into Gluten Metabolizing Bacterial Species and their Inhibition

- Statistical Analysis:
- Very statistically significant differences between the fifteen strains

### Statistical Analysis:

Factor A: 15 Groups

<table>
<thead>
<tr>
<th>Source</th>
<th>DF</th>
<th>SS</th>
<th>MS</th>
<th>F</th>
<th>P</th>
</tr>
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<tbody>
<tr>
<td>Total</td>
<td>44</td>
<td>5060.9778</td>
<td>115.02222</td>
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<tr>
<td>A</td>
<td>14</td>
<td>3348.9778</td>
<td>239.2127</td>
<td>4.1918113</td>
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<td>30</td>
<td>1712</td>
<td>57.06667</td>
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</tbody>
</table>

The 15 Groups demonstrated significant differences as to Sensitivity to Oral Medicaments (DF) 14, P=0.0005). The following groups presented with significant differences (Bonferroni pair testing): A1 vs B2, B1 vs B2, A1 vs B3, B1 vs B3, B3 vs B5, B3 vs B6, B2 vs B5, and B2 vs B6.
Abstract: This study examined the effects of xylitol on mouse intestinal microbiota and urinary isoflavonoids. Xylitol is classified as a sugar alcohol and used as a food additive. The intestinal microbiota seems to play an important role in isoflavone metabolism. Xylitol feeding appears to affect the gut microbiota. We hypothesized that dietary xylitol changes intestinal microbiota and, therefore, the metabolism of isoflavonoids in mice. Male mice were randomly divided into two groups: those fed a 0.05% daidzein with 5% xylitol diet (XD group) and those fed a 0.05% daidzein-containing control diet (CD group) for 28 days. Plasma total cholesterol concentrations were significantly lower in the XD group than in the CD group ($p < 0.05$). Urinary amounts of equol were significantly higher in the XD group than in the CD group ($p < 0.05$). The fecal lipid contents (% dry weight) were significantly greater in the XD group than in the CD group ($p < 0.01$). The cecal microbiota differed between the two dietary groups. The occupation ratios of *Bacteroides* were significantly greater in the CD than in the XD group ($p < 0.05$). This study suggests that xylitol has the potential to affect the metabolism of daidzein by altering the metabolic activity of the intestinal microbiota and/or gut environment. Given that equol affects bone health, dietary xylitol plus isoflavonoids may exert a favorable effect on bone health.
Xylitol Erythritol Inhibition Studies

- Concentration Gradients of Xylitol and Erythritol in different combinations research
- Special Infectious Disease Laboratory of Ann and Robert Lurie Children's Hospital
The portal to the GI Tract

We know the problem—How do we prevent?

- “You pediatric dentists are the guardians to the portal of the gastro-intestinal tract”
- Pediatric Gastroenterologist

Romantic View—like Knights!