THE AMERICAN ACADEMY FOR ORAL SYSTEMIC HEALTH

"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

Plaqu

Distribution of *Porphyromonas gingivalis fimA* genotypes in cardiovascular specimens from Japanese patients

K. Nakano[1], H. Inaba[2], R. Nomura[1], H. Nemoto[1], H. Takeuchi[2], H. Yoshioka[3], K. Toda[4], K. Taniguchi[4], A. Amano[2], T. Ooshima[1]

Departments of [1]Pediatric Dentistry and [2]Oral Frontier Biology, Osaka University Graduate School of

Evid Based Dent. 2008;9(1):8.

Possible link between periodontal disease and coronary heart disease.

Matthews D.

Link between PD

Arterioscler Thromb Vasc Biol. 2005 Jul;25(7):1446-51. Epub 2005 Apr 21.

Porphyromonas ... ary and aortic atherosclerosis in normocholesterolemic and hypercholestero...

Brodala N, Merricks EP ... K J, Madianos P, Sotres D

119 *PORPHYROM... EROSCLEROSIS IN ... ASTY*

Location: Room 15 ... ter)

A. LUCAS, R. VERN... ANUJAM, J. KIM, S. P... Gainesville, FL

Pg accelera...

And atherosclerosis

<>Background: Pe... e both chronic inflam... o demonstrated peri... *Porphyromonas gi*... ve: With this study we asse... n on atherosclerotic ... ApoE^{null} mouse models wit... njury. Methods: Apo... and without balloon angioplasty surgery. Mice were infected with *P. gingivalis* FDC ... ks. Oral bacterial samples were collected and colonization/infection assessed by PCR. ... on. Serum IgG antibody ... enomic DNA responses to *P. gingivalis* ... ely. Results: *P. gingivalis* was detected by PCR in nearly all mice throughout the ex... ad elevated IgG antibody compared to controls. *P. gingivalis* increased maxillary ... ABR when compared to control mice. Similarly, *P. gingivalis* increased aortic plaque after BA in mice on normal diet on comparison to uninfected contro... in the intimal and adventitial layer... This is the first study examinin... atherosclerosis in ApoE^{null} mice. We found accelerated periodontal disease (ABR) and plaque in non-injured mice but not in mice with angioplasty injury. Supported by University of Florida Opportunity Research Fund, R01DE015720-01, and U24 DE016509 from the NIH, NIDCR.

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MEDICINE

Electric Current to the Brain Boosts Memory

Stimulating a particular region in the brain via non-invasive delivery of electrical current improves memory and may help treat disorders from stroke, Alzheimer's disease and brain injury, according to Northwestern Medicine.

Streptococci- Plaque Kingdoms

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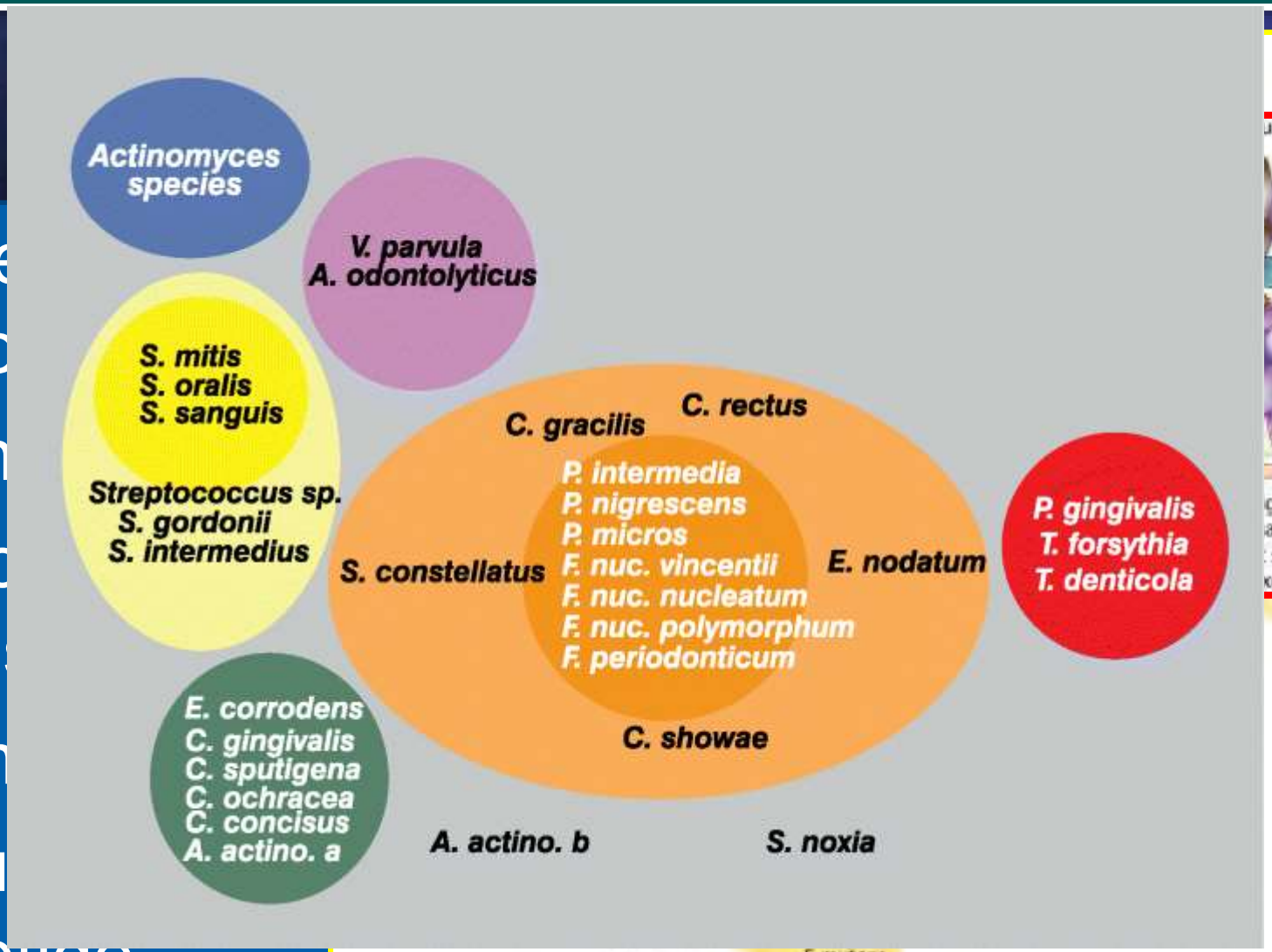
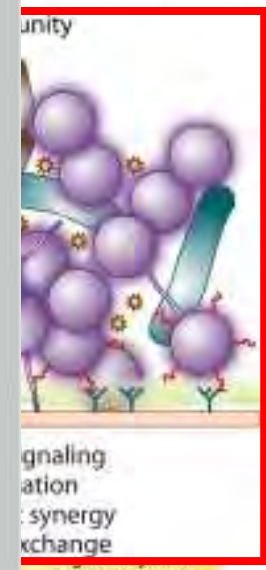
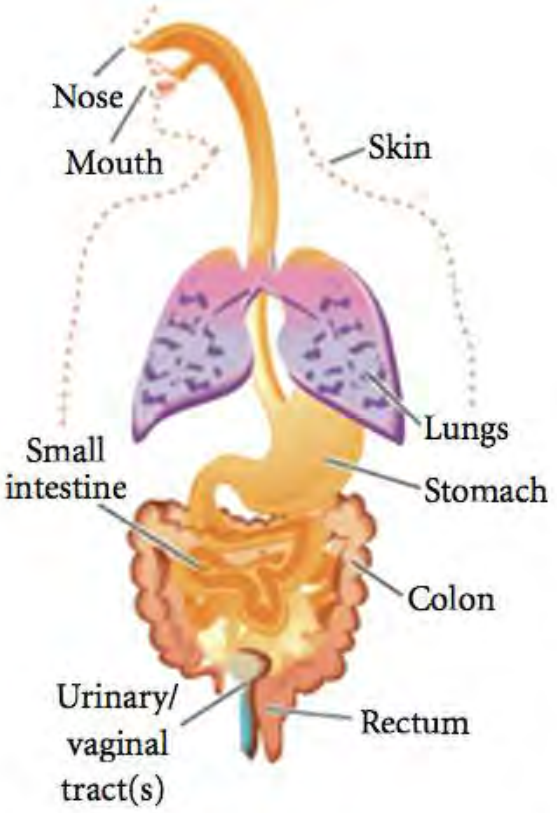




It's contagious too....



Human body 10^{13} cells 23,000 genes

Normal flora 10^{14} microbial cells on the human body. 3.3 million genes

Amount of bacteria per gram of cellular component

- Stomach – 10^1 to 10^2 cells
- Duodenum – 10^3 cells
- Jejunum – 10^4 cells
- Ileum 10^4 to 10^7 cells
- Proximal colon 10^{10} to 10^{11} cells
- Transverse colon 10^{11} to 10^{12} cells
- Distal colon $>10^{12}$ cells

The Transmission of Anaerobic Periodontopathic Organisms
Y Lee et al, J Dent Res 85(2):182-186 2006

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 Me
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- Born May 1
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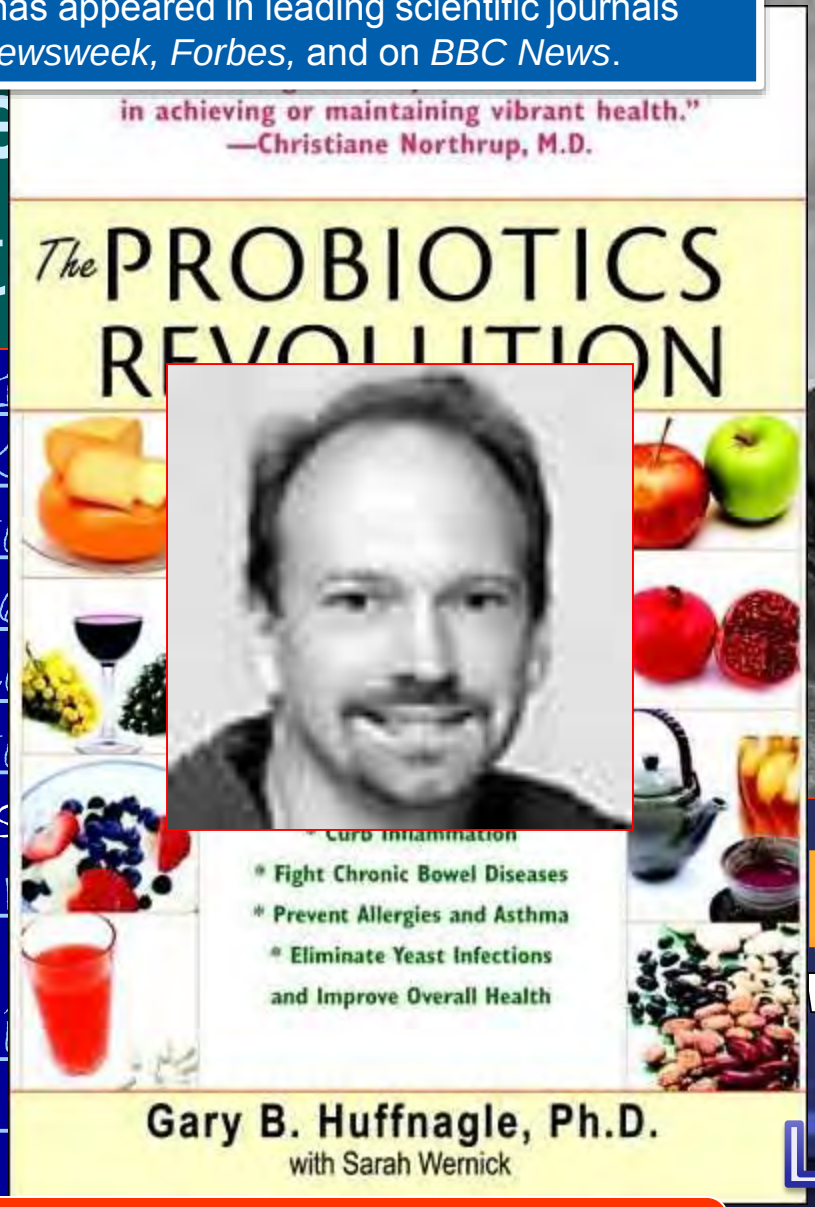
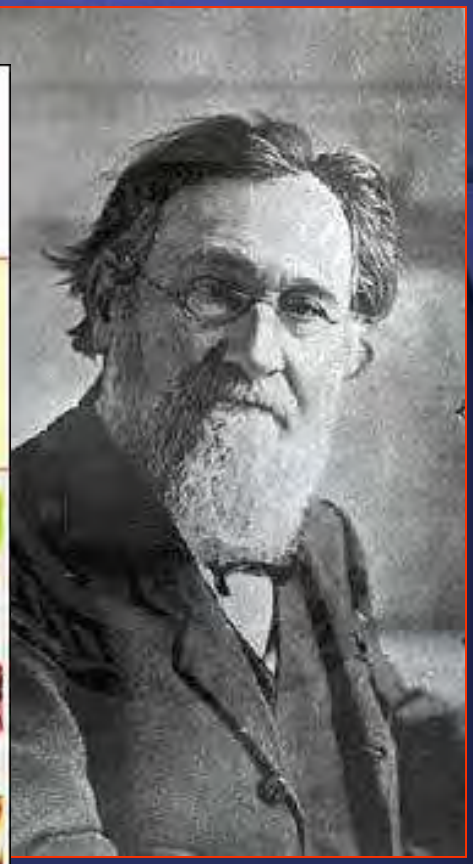
- Nobel Prize

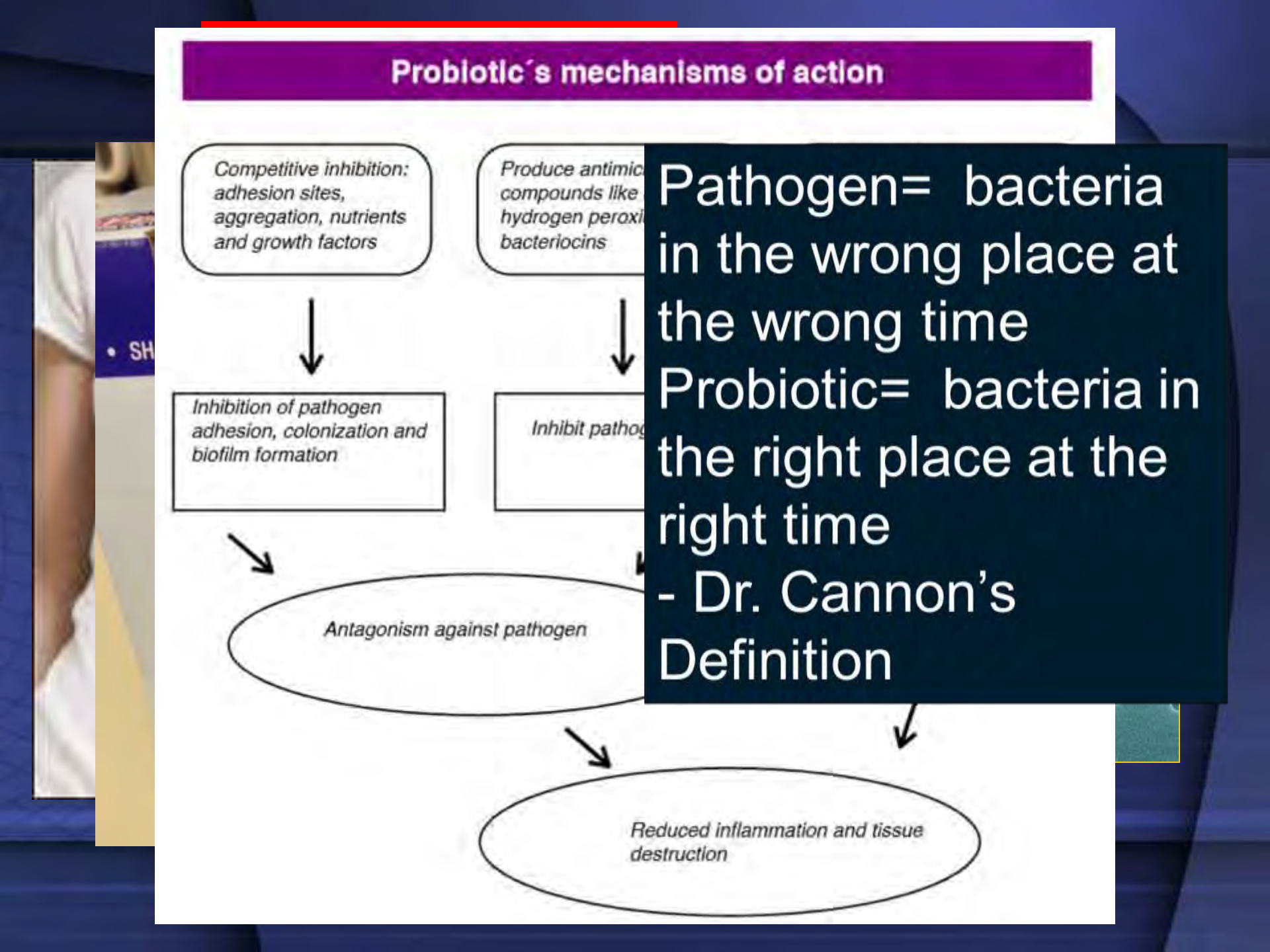




robiotics
"pioneer"

Lactobacillus bulgaricus

"A general belief is that microbes are harmful. This belief is erroneous. There are many useful microbes....."


Probiotic´s mechanisms of action
Competitive inhibition: adhesion sites, aggregation, nutrients and growth factors
Produce antimic
compounds like
hydrogen peroxi
bacteriocins
Inhibition of pathogen adhesion, colonization and biofilm formation
Inhibit pathog
Antagonism against pathogen
Reduced inflammation and tissue destruction
Pathogen= bacteria in the wrong place at the wrong time
Probiotic= bacteria in the right place at the right time
- Dr. Cannon's Definition

“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

- PubMed data base

Global report on s

the effective
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viruses and fungi. A
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Century. This WHO
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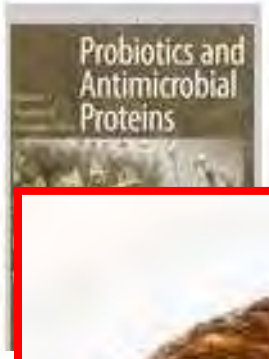
curate a picture as is
MR and the current

- **Preservation of Antibiotics for Medical Treatment**
  H.R. 1549/S. 619

PROBIOTICS AND ANTIMICROBIAL PROTEINS
Volume 4, Number 1, 47-58, DOI: 10.1007/s12602-012-9090-2

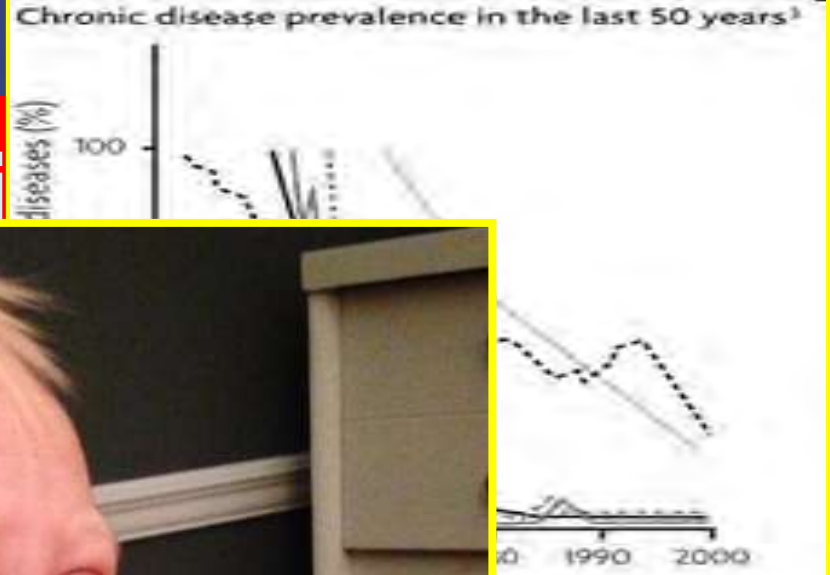


Characterization ... l Probiotics

Tejinder Pal Singh, Gur ... as and Suman Kapila

...olated from ...ins isolated from ...d LR34) showed ...eir high tolerance ...rong hydrophobic ...d not exceed 40%, ...c isolates was ...afety of the nine ...rted by the absence of transferable antibiotic resistance ... activity and hemolysis. The results obtained so far suggest that ...bile salts and duodenum juice, so they could survive when passing ...stinal tract and fulfill their potential probiotic action in the host ... *L. reuteri* strains isolated from human infant feces possess interesting probiotic properties that make them potentially good candidates for probiotics.

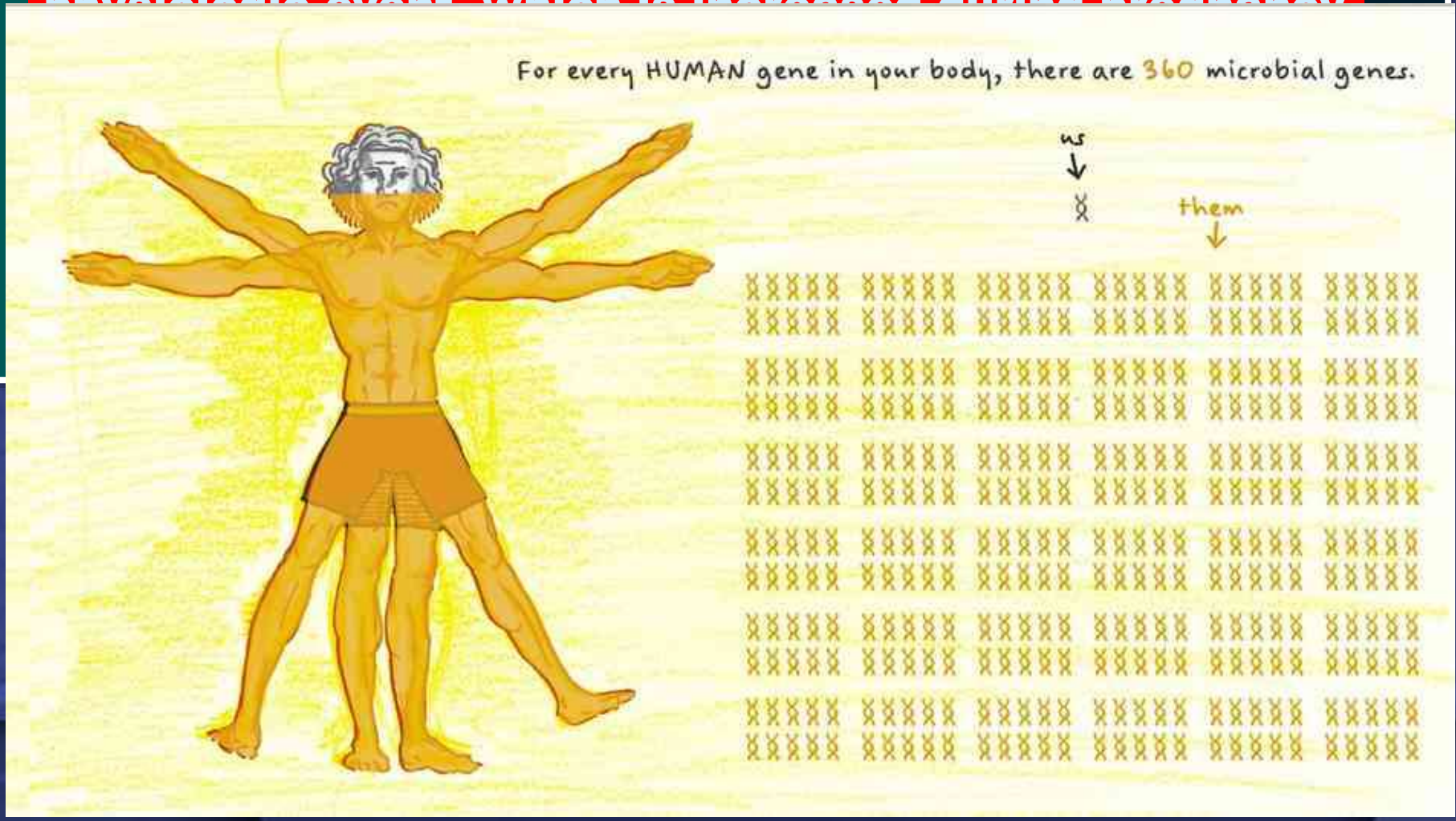
How do probioti



Gastrointestinal Diseases in Children: Hard and Not-
Evidence of Efficacy. *J Pediatr Gastroenterol Nutr* 2
75.

MATERNAL IMPRINTING

- **CONCLUSIONS. Bacterial translocation is a unique physiologic event, which is increased during pregnancy**



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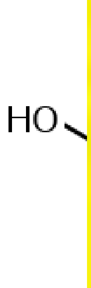
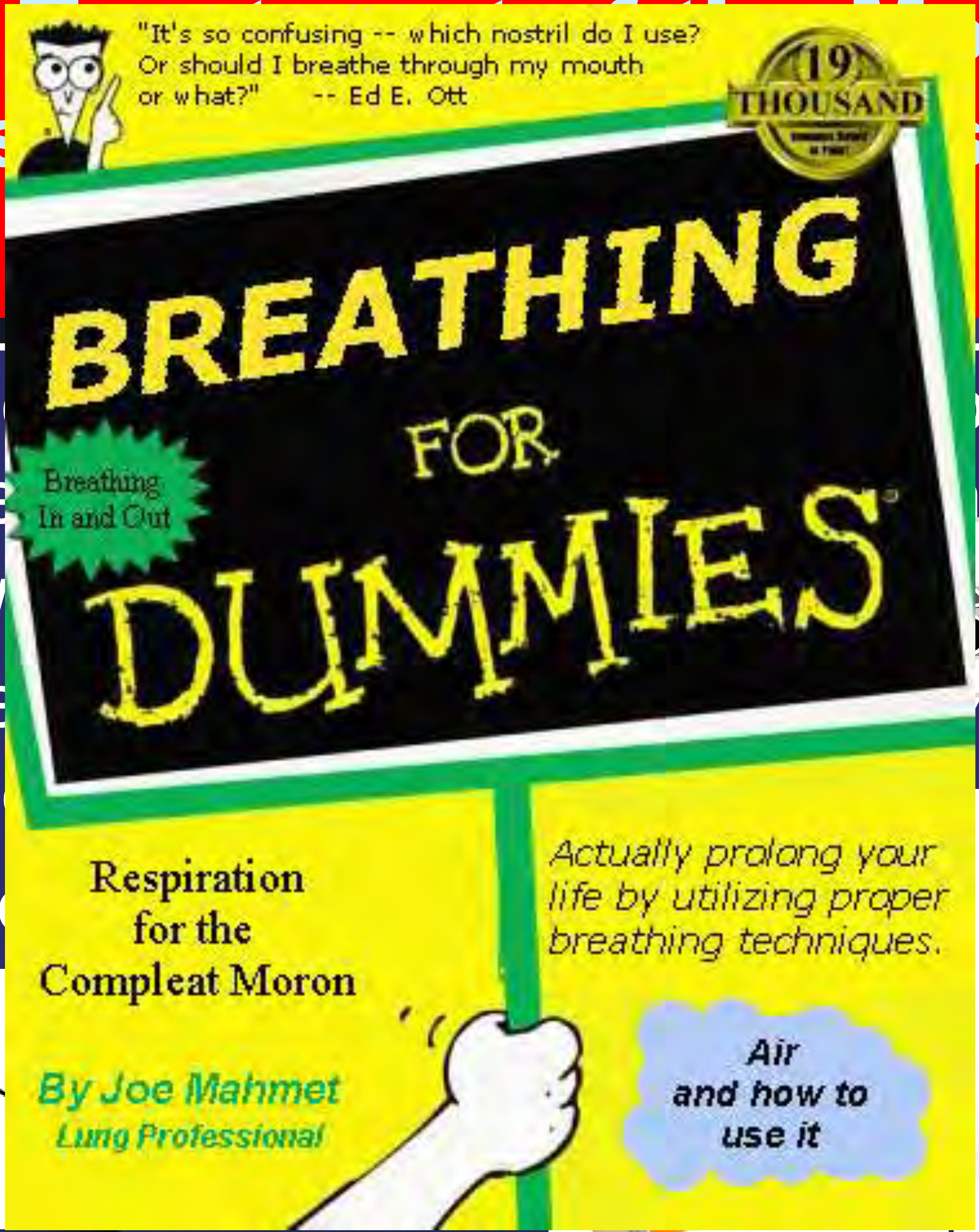
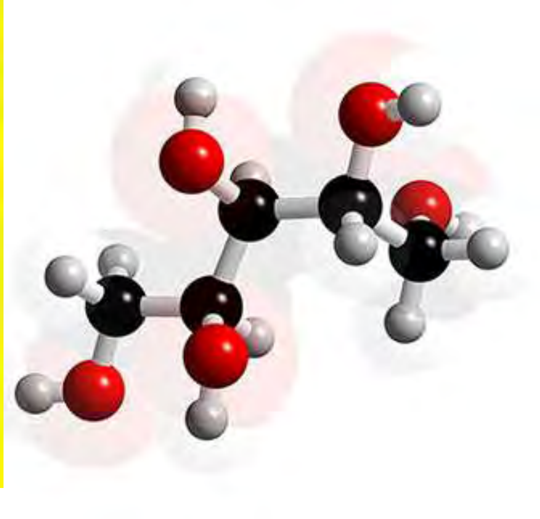






L. reuteri effect on infections in infants attending child care

- *Results of a study by Weizman, Z. et al. (2005), Pediatrics: Effect of a probiotic infant formula on infections in child care centers: comparison of two probiotic agents.*
  - 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

Control

L. reuteri

L. reuteri inhibits intestinal pathogenic microorganisms

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

El-Ziney (2000), Ejehorn (2000)

NU study: Dirt's good for kids

Playing in, and even eating, dirt helps develop immune system, report says

Thom McDade sorts plasma samples at Northwestern University in Evanston. McDade participated in research that shows that kids who are exposed to dirt and germs have healthier hearts. (Andrew A. Nelles, Chicago Tribune / March 7, 2010)

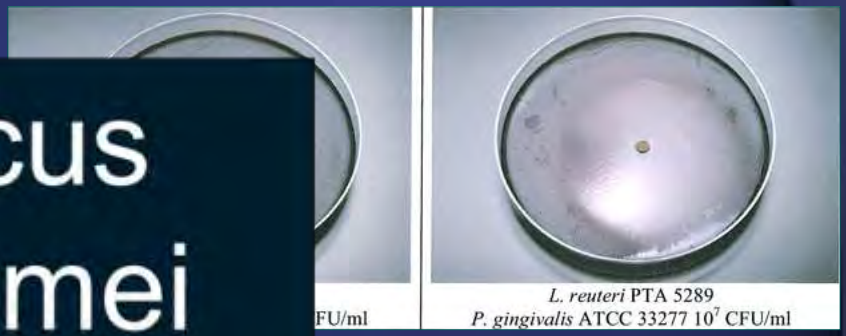
Symb ble

in *Lactic Acid Bacteria in Health and Disease*, Ed 1, p. 76. Elsevier Applied Science.

L. reuteri inhibits oral pathogenic bacteria

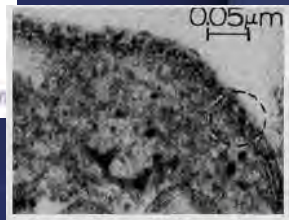
- *A. actinomycet*
- *Fusobacterium*
- *Porphyromona*
- *Prevotella inter*
- *Streptococcus*

"inimicus inimici mei amicus meus est"



nhibits growth of *P. gingivalis*

The Global Bioresource Center



Magnified view of T. ferrooxidans showing multi-layered cell-wall (molecular) structure observed in the transmission-electron microscope (TEM) after phosphotungstic acid staining.

Hedberg (2006), Nikawa (2004), Caglar (2006, 2007)

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

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BioGaia Probiotic loz

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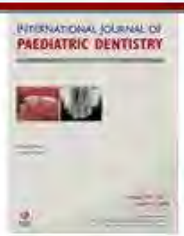
International Journal of Paediatric Dentistry

Volume 18 Issue 1 Page 35-39, January 2008

To cite this article: ESBER ÇAGLAR, OZGUR ONDER KUSCU, SULE KAVALOGLU CILDIR, SENEM SELUI KUVVETLI, NUKET SANDALLI (2008) A probiotic lozenge administered medical device and its effect on salivary mutans streptococci and lactobacilli International Journal of Paediatric Dentistry 18 (1) , 35–39 doi:10.1111/j.1365-263X.2007.00866.x



10 days lozenge

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 SELUI KUVVETLI & 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

Abstract

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 (1.1×10^8 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

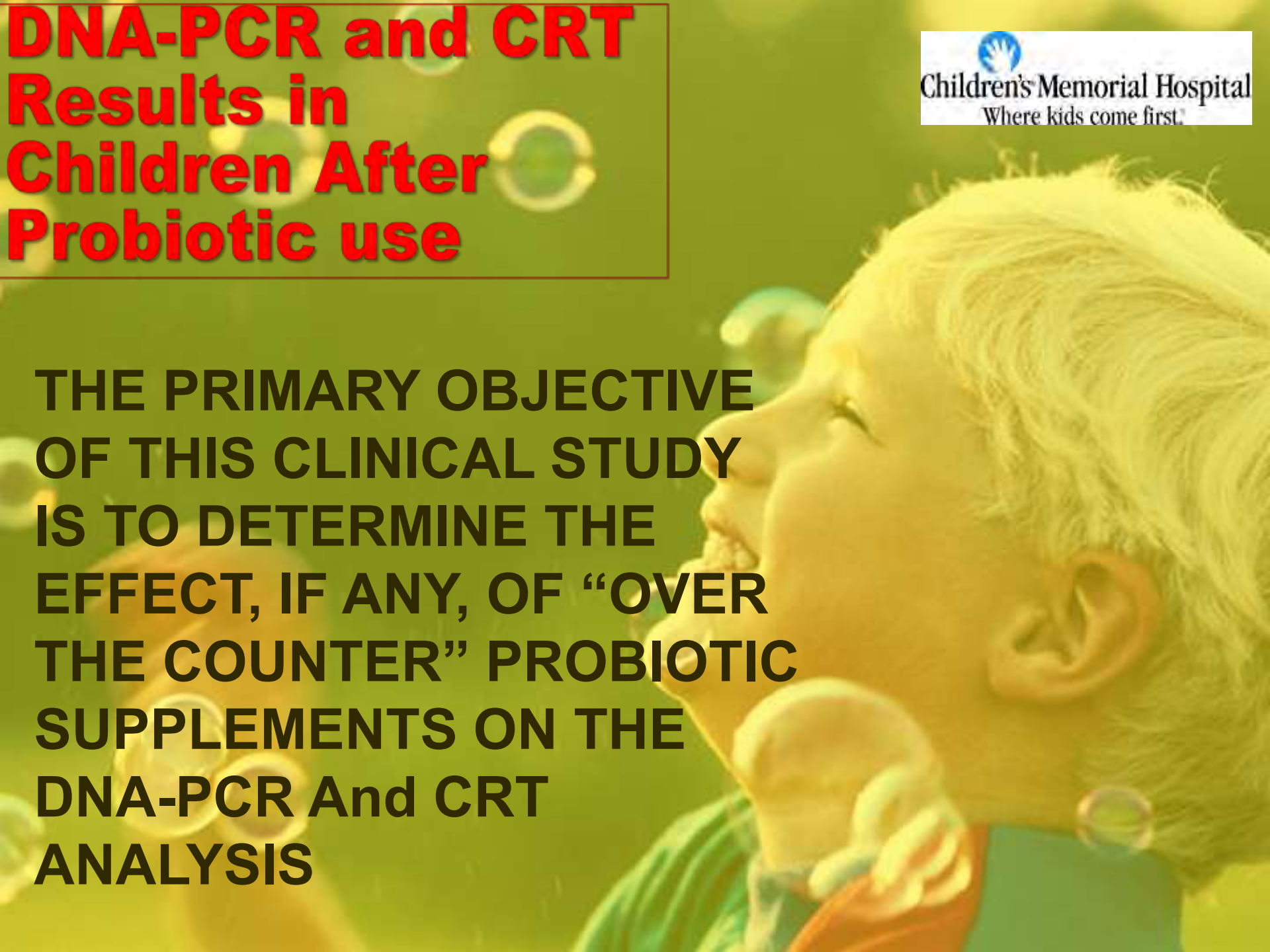
Children's Memorial Hospital
Where kids come first.

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

DNA-PCR and CRT Results in Children After Probiotic use

Children's Memorial Hospital
Where kids come first.



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

DNA-PCR and CRT Results in Children After Probiotic use

Children's Memorial Hospital
Where kids come first.

Methods

-Frozen samples in CRT tubes
Kept at minus 80 degrees Celsius
Glycerol stabs of colonies for further analysis.

Current Research

Children's Memorial Hospital
Where kids come first.

- Statistically

Results

ANOVA Table

Analysis of Variance

Source	Sum of Squares	Df	Mean Square	F-Ratio	P-Value
Between groups	84.3711	7	12.053	10.36	0.0000
Within groups	242.087	208	1.16388		
Total (Corr.)	326.458	215			

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

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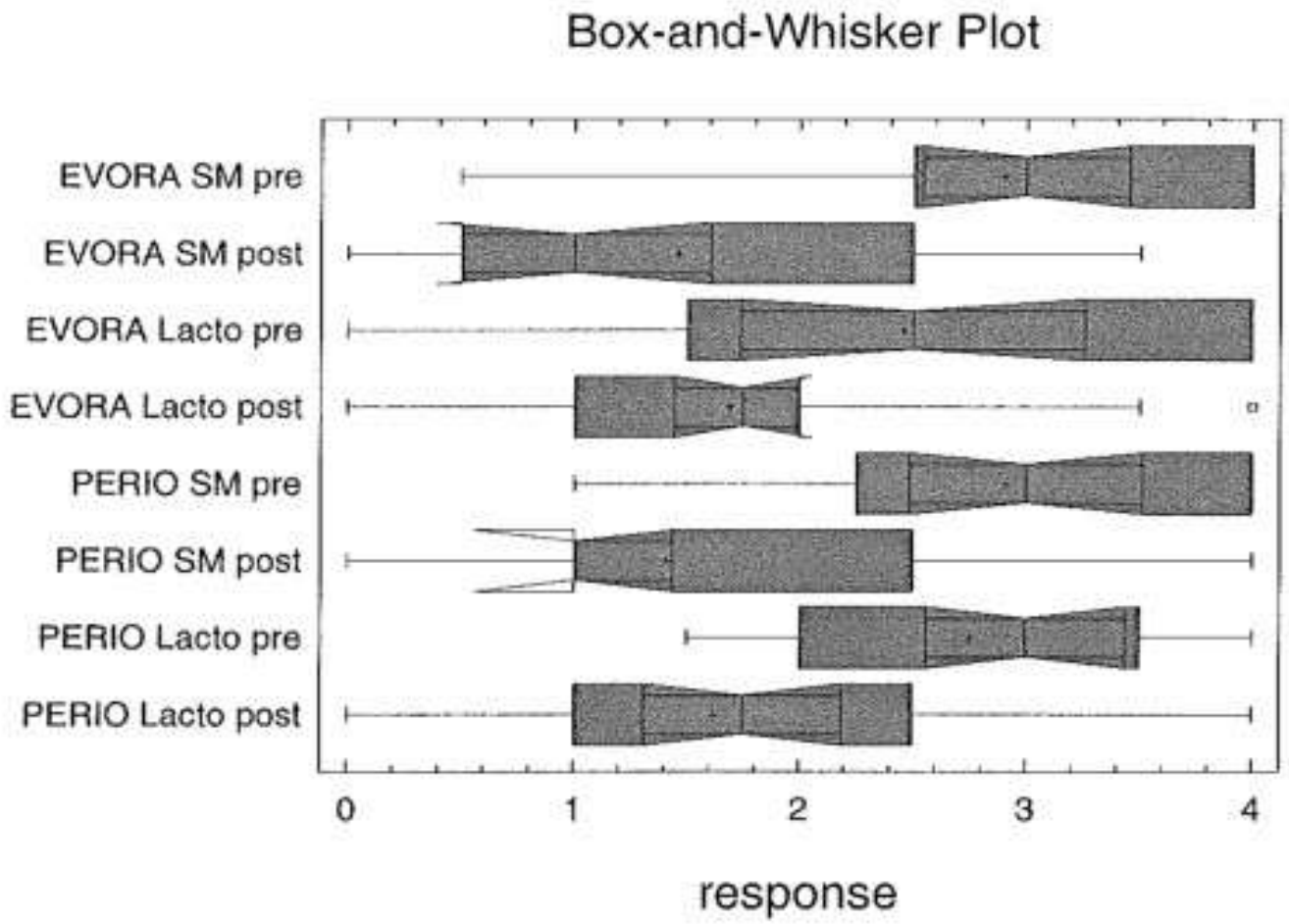
Where kids come first.

Statistics



DNA-PCR and CRT Results in Children After Probiotic use

Children's Memorial Hospital
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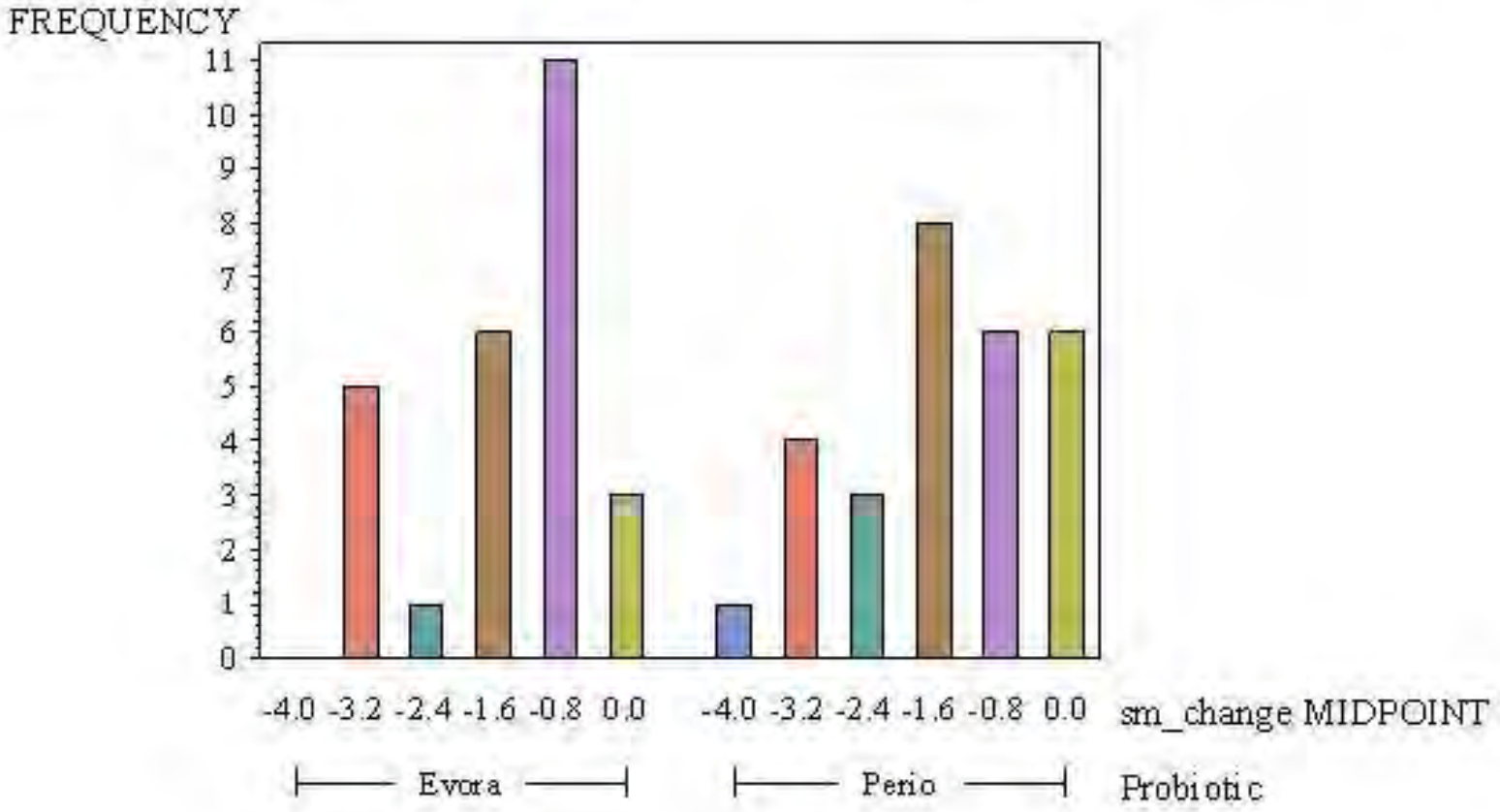
Statistics

Changes in SM before/after probiotic treatment



DNA-PCR and CRT Results in Children After Probiotic use

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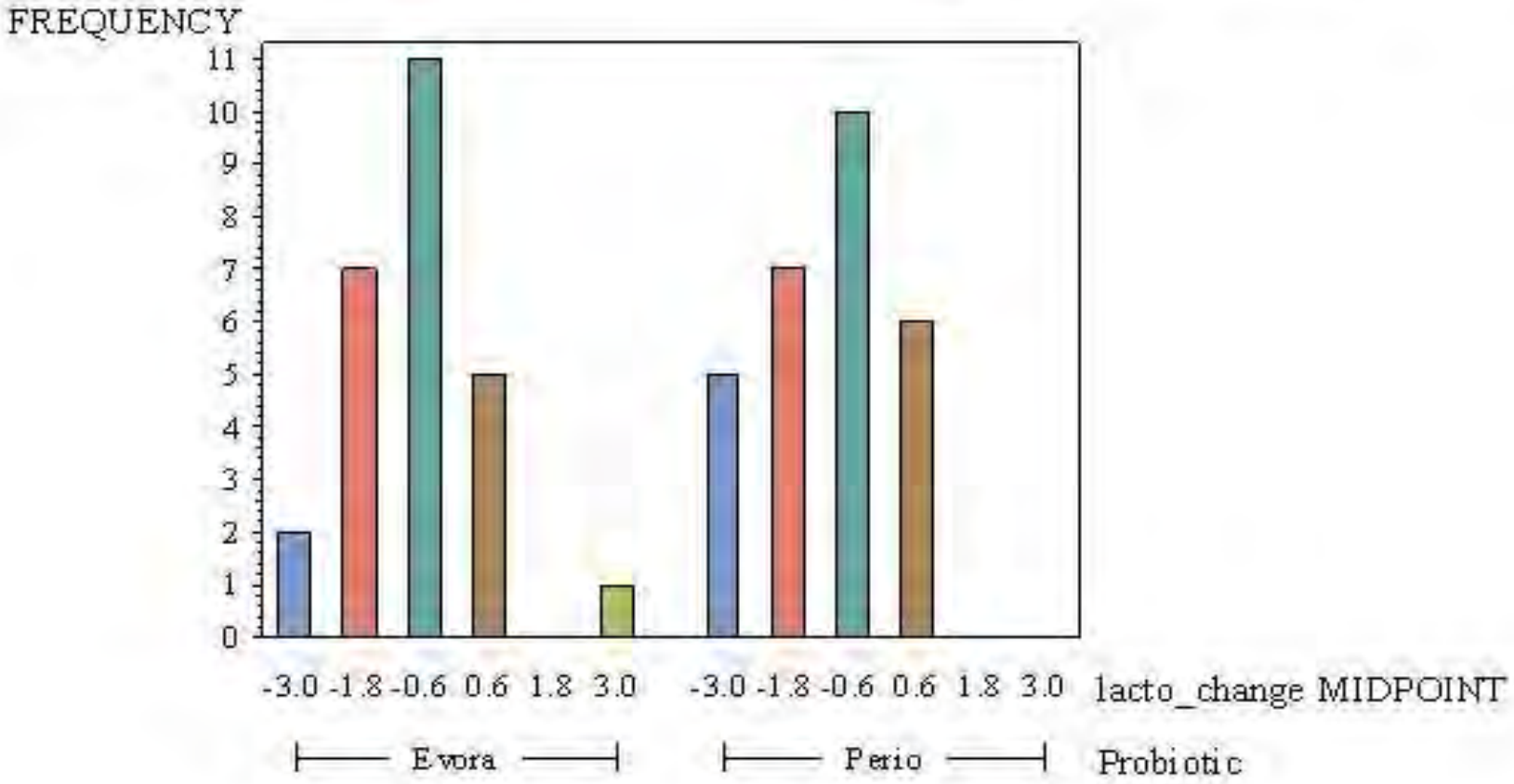
Statistics

Changes in Lacto before/after probiotic treatment



DNA-PCR and Results in Children After Probiotic use

Difference between the two probiotics?

Wilcoxon Two-Sample Test	
Statistic	762.5000
Normal Approximation	
Z	0.8244
One-Sided Pr > Z	0.2048
Two-Sided Pr > |Z|	0.4097
t Approximation	
One-Sided Pr > Z	0.2067
Two-Sided Pr > |Z|	0.4134
Z includes a continuity correction of 0.5.	

Kruskal-Wallis Test	
Chi-Square	0.6942
DF	1
Pr > Chi-Square	0.4047

NOT enough evidence to indicate that EvoraPlus and PerioBalance changes the ‘SM’ or ”Lacto” measurements differently

DNA-PCR and CRT Results in Children After Probiotic use

Children's Memorial Hospital
Where kids come first.

Reasons?

1. Selective agar complicated DNA extraction contaminating some samples.
2. *Streptococcus rattus* (included in EvoraPlus) was mis-identified as SM but is a mutans streptococci.
3. Other technical difficulties

The glucosyltransferase-I 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 reference sequences for *Streptococcus mutans* in the NCBI database.

Conclusions:

Children's Memorial Hospital
Where kids come first.

Both EvoraKids

A clini
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prone
PerioB
Evora

Effectiveness of CRT at Measuring the Salivary Level of Bacteria in Caries Prone Children with Probiotic Therapy

Cannon M* / Trent B** / Vorachek A*** / Kramer S**** / Esterly R*****

Aim: *This IRB approved clinical trial was to determine the effect of "over the counter" probiotic supplements on the Caries Risk Test- CRT- (Ivoclar) results of the oral microflora in high caries risk children.* ***Study design:*** *Sixty subjects 6 to 12 years old with a caries risk assessment (CAMBRA) of moderate to high (caries prone) were evaluated by an analysis of the difference in the salivary levels of pathogenic bacteria (mutans streptococci and Lactobacilli). The subjects were randomly selected by randomizing software and assigned to two different Groups. Group A used PerioBalance (Lactobacilli reuteri-CFU of 200 million) lozenges for 28 days. Group B used the EvoraKids (Streptococcus uberis KJ2, Streptococcus oralis KJ3, Streptococcus rattus JH145, ≥ 100 million) probiotics chewable tablets for 30 days. Salivary samples were collected then incubated for 48 hours for colony counting and ranking. Follow up testing with the CRT was performed after 60 days at a follow up visit.* ***Results:*** *There was a statistically significant difference in the CRT results between the pre and post use of the probiotics. PerioBalance; SM results t= -6.78 p< .0001 Lactobacilli results t= -5.762, p< .0001, EvoraKids SM results t= -7.33, p< .0001, Lactobacilli results t= -2.952, p= .0068.* ***Conclusions:*** *The CRT values obtained with caries prone children may be significantly affected by probiotic use. Based on this study's results the following conclusions can be made: Both EvoraKids and PerioBalance affected the CRT results by significantly decreasing the number of S. mutans and lactobacilli present in the salivary samples.*

Further Research

Children's Memorial Hospital
Where kids come first.

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?

Further Research

Children's Memorial Hospital
Where kids come first.

Retrospective Review of Probiotic Therapy.

ML Cannon DDS MS

A Vorachek DDS

K White DMD

C Le DMD

An IRB Approved Study

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.

Ma

en ap th m ca Ev cu m Te (C he st

respect to published national norms.

Further Research

Children's Memorial Hospital
Where kids come first.

Retrospective Review of

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 3. Caries History Compared to Nationally Reported Values.

Caries Experience	Pre Probiotic	National Average	Post Probiotic
Per patient- 3 years	5.51	1.84	0.75

	Caries Active	Caries Resistant	Caries Static
PerioBalance	2	12	15
EvoraKids	2	11	11
Caries Count	17	0	36

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

Current Research

Eur J Oral Sci. 2007 Aug;115(4):308-14.

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

Simark Mattsson C, Emilson CG, Håkan

Arch Oral Biol. 2009 Jun;54(6):602-7. Epub 2

Final pH affects the interfere

1420 SELECTION OF MUTA

Location: Exhibit Hall D (Walte

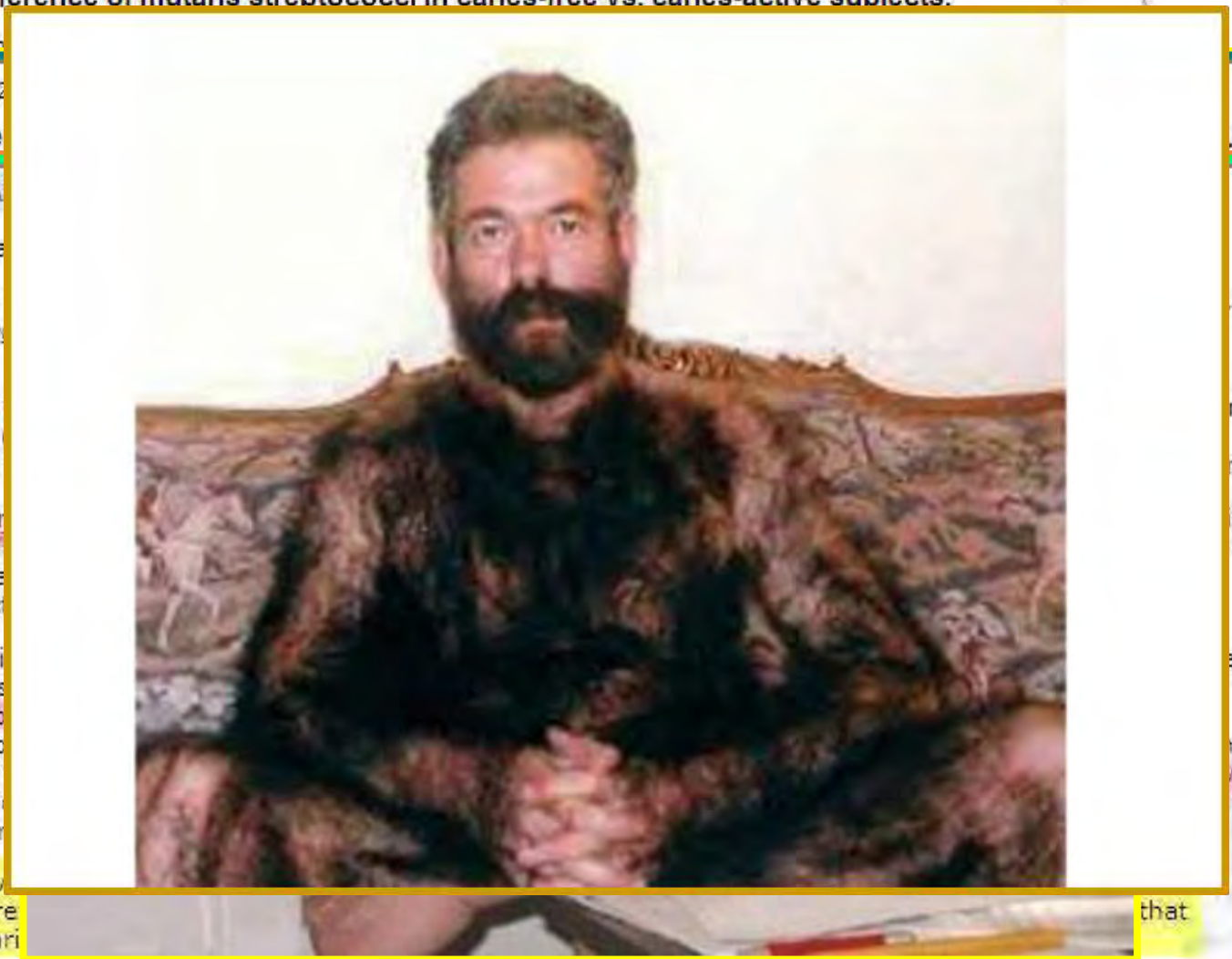
E. PALMER, T. FINLAYSON, T. MAIER, and C. MACHIDA, Ore

Objectives: Dental caries are children. Mutans streptococci genetically define and assess

Methods: Using arbitrarily-prir undergoing caries preventive post-treatment (2-4 weeks), a genotypic groups, and charact

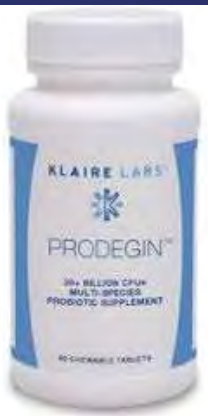
Results: Inter-patient variabili and post-treatment collections increased from 14% to 78% c SE=0.017) after 3 days of gro pH values of 4.67-4.89 (n=4; treatment, and was highly aci bacterial numbers surviving tr

Conclusions: Caries preventiv implications are that caries pre well-accepted practices for cari



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?????

Probiotics- Antagonism and Inhibition

What is the dough doing while it is “resting”

Alimentary Pharmacology & Therapeutics

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 Pharmacol Ther. 2013;38(3):226-245.

Gluten sensitivity epidemic

Clin Nutr. 2013 Dec;32(6):1043-9. doi: 10.1016/j.clnu.2013.02.003. Epub 2013 Feb 14.

Evaluation of the safety of ancient strains of wheat in coeliac disease reveals heterogeneous small intestinal T cell responses suggestive of coeliac toxicity.

Šuligoj T[1], Gregorini A, Colomba M, Ellis HJ, Ciclitira PJ.

⊕ Author information

Ancient grains NO better!!

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

Gluten sensitivity epidemic

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. TIAN[1], G. WEI[1], D. SCHUPPAN[2], F.G. OPPENHEIM[1], and E.J. HELMERHORST[1], [1]Dept. of Periodontology & Oral Biol, Boston University, Boston, MA, [2]Beth Israel Deaconess Medical Center, Boston, MA

Gluten sensitivity epidemic

1745 Comprehensive Screening of Saliva and Dental Plaque for Gluten-Degrading Microorganisms

Friday, March 22, 2013: 10:45 a.m. - 12:15 p.m.
Location: Room 614 (Washington State Convention Center)
Presentation Type: Oral Session
M. FERNANDEZ-FEO[1], G. WEI[1], F.E. DEWHIRST[2], D. SCHUPPAN[3], F.G. OPPENHEIM[1], and **E.J. HELMERHORST**[1], [1]Dept. of Periodontology & Oral Biol, Boston University, Boston, MA, [2]Forsyth Institute, Cambridge, MA, [3]Harvard University, Boston, MA

3. Microflora changes

What causes oral microflora changes?

Gluten sensitivity epidemic

- 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.

Gluten sensitivity epidemic

- Inhibition of Rothia Species by OTC Products and Bacterial Antagonists

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

Ann & Robert H. Lurie Children's Hospital of Chicago

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.

Probiotics- Antagonism and Inhibition

Rothia inhibition and antagonism

Rothia Aeria is inhibited by:
1. Chlorhexidine
2. Listerine Smartrinse™.

TABLE 1a. Susceptibility Experiment: The Effect of Over the counter Oral Hygiene Products on Oral Bacteria

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

Note: All dimensions shown in millimeters

Probiotics- Antagonism and Inhibition

Rothia inhibition and antagonism

Rothia Aeria is inhibited by:
1. Chlorhexidine

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

	S. aureus	*S. salivarius*	*E. coli*	*P. aeruginosa*	VRE
Spry™ Mouthwash	0	0	0	0	0
Embrace™ varnish	0	0	0	0	0
Spry™ Xylitol gel diluted in PBS	0	0	0	0*	0
PBS control	0	0	0	0	0

Note: All dimensions shown in millimeters

*but for a short period showed inhibition

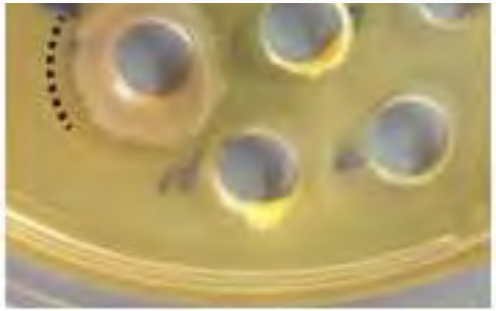
Probiotics- Antagonism and Inhibition

Rothia inhibition and antagonism

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

	R. dentocariosa	*R. mucilaginosa*	*S. salivarius*	*E. coli*	*P. aeruginosa*
R. mucilaginosa	0, 0	0, 0	0, 0	0, 0	0, 0
VRE	0, 0	0, 0	0, 0	0, 0	0, 0
E. coli	0, 0	0, 0	0, 0	0, 0	0, 0
P. aeruginosa	inhibits	0, 0	0, 0	0, 0	0, 0
S. salivarius	0, 0	0, 0	0, 0	0, 0	0, 0
R. dentocariosa	0, 0	0, 0	0, 0	0, 0	0, 0
S. aureus	0, 0	inhibits	0, 0	0, 0	0, 0

Note: All dimensions shown in millimeters



Probiotics- Antagonism and Inhibition

Inhibition of Rothia Species by OTC Products and Bacterial Antagonists

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

Ann & Robert H. Lurie Children's Hospital of Chicago

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. 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. 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. dentocariosa, R. mucilaginosa, S. mutans*, or Lactobacillus were obtained from isolation plates and grown in Mueller-Hinton media to a McFarland Standard of 0.5. Either Brucella agar plates, Rogosa agar, or Mueller-Hinton agar plates with 5% sheep blood were wholly spread with one cotton swab inoculation of chosen bacteria. Five cotton discs were evenly distributed on the plate 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

Trypticase Soy Agar (TSA) was autoclaved and cooled to 56 degrees and aliquots of 25mL were cooled and inoculated with 2mL of 0.5 McFarland Standard suspensions of *R. dentocariosa, R. mucilaginosa, Streptococcus salivarius, Escherichia coli*, or *Pseudomonas aeruginosa* prior to pouring agar plates. Impregnated plates were then inoculated in punched zones using a disposable 10 microliter loop with 0.5 McFarland Standards of bacteria species: *Streptococcus salivarius, Staphylococcus aureus*, Vancomycin-resistant *Enterococcus, Pseudomonas aeruginosa, Escherichia coli*, and *R. dentocariosa* or *R. mucilaginosa*. The plates were evaluated after 24 hours of growth at 36 degrees. Calipers were used to measure zones of inhibition.

Results:

Bacterial growths of all tested bacteria were inhibited by Crest ProHealth™, ACT™, Listerine SmartRinse™, and Chlorhexidine. *R. aeria* and *R. mucilaginosa* were also inhibited by Embrace™ varnish, and Spry™ Xylitol Toothpaste Gel inhibited *R. mucilaginosa*. Growth of *R. dentocariosa* was inhibited by *P. aeruginosa* and growth of *R. mucilaginosa* was inhibited by *S. aureus*.

TABLE 1a. Susceptibility Experiment: The Effect of Over the counter Oral Hygiene Products on Oral Bacteria

Reagent	*Rothia Aeria* on blood agar	*R. dentocariosa*		*R. mucilaginosa*		PERIO probiotic (*Lactobacillus*)		*S. Mutans* on blood agar
		on blood agar	on Brucella	on blood agar	on Brucella	on blood agar	on Rogosa	
Spry Xylitol Mouthwash™	0, 0	0, 0	0, 0	0, 0	0, 0	0, 0	0, 0	0, 0
Crest ProHealth™	9, 9	12, 12	11, 11	14,16	14, 10	15, 13	16, 13	12, 12
ACT fluoride rinse™	10, 10	11, 12	14	12, 14	16, 14	17, 15	16, 15	13
Listerine SmartRinse™	9, 9	10, 11	9, 9	14, 14	9, 8	14, 12	13, 12	11, 11
Chlorhexidine (11.6% alcohol)	13, 12	18, 18	13, 12	14, 14	11, 11	16, 16	15, 15	15, 14
Listerine™ (27% Alcohol)	0, 0	0, 0	0, 0	0, 0	0, 0	9, 8	0, 0	0, 0
Phosphate Buffered Saline (PBS)	0	0, 0	0	0, 0	0	0	0	0
27% Alcohol	0, 0	0, 0	10	0, 0	0	10	0	0
Embrace Varnish™ (has xylitol	8, 9	0, 0	0, 0	12, 12	0, 0	0, 0	0, 0	0, 0
Spry™ Xylitol toothpaste gel	0, 0	0, 0	0, 0	10, 12	0, 0	0, 0	0, 0	0, 0
50% Spry™ Xylitol toothpaste gel in PBS		0, 0		0, 0				
Levofloxacin (5 micrograms)	30	30	30	30	20	0	0	20

Note: All dimensions shown in millimeters

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

	S. aureus	*S. salivarius*	*E. coli*	*P. aeruginosa*	VRE
Spry™ Mouthwash	0	0	0	0	0
Embrace™ varnish	0	0	0	0	0
Spry™ xylitol gel diluted in PBS	0	0	0	0*	0
PBS control	0	0	0	0	0

Note: All dimensions shown in millimeters

*but not a strict partial diameter inhibition

TABLE 2. Diffusion Experiment: Bacterial Species Inhibition of Each Other

	R. dentocariosa	*R. mucilaginosa*	*S. salivarius*	*E. coli*	*P. aeruginosa*
R. mucilaginosa	0, 0	0, 0	0, 0	0, 0	0, 0
VRE	0, 0	0, 0	0, 0	0, 0	0, 0
E. coli	0, 0	0, 0	0, 0	0, 0	0, 0
P. aeruginosa	completely	0, 0	0, 0	0, 0	0, 0
S. salivarius	0, 0	0, 0	0, 0	0, 0	0, 0
R. dentocariosa	0, 0	0, 0	0, 0	0, 0	0, 0
S. aureus	0, 0	completely	0, 0	0, 0	0, 0

Note: All dimensions shown in millimeters

Discussion:

In vitro results 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 mere fact that OTC products, that may be used ad libitum 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 13mm.

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 equilibrium is changed by using OTC oral hygiene products, a domino effect can effect the entire oral microbiome, which is the gateway to the digestive tract.

Conclusion:

Rothia species, *S. mutans* and Lactobacillus species, are decreased in quantity by the over 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, Irritable Bowel Syndrome, and exacerbating ulcerative colitis increasing Celiac disease clinical prevalence. The Forsyth Institute noted at the poster session of the AADR 2012 meeting that *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, Zamkhcharli, M, Dewhirst, F, Schuppan, D, Oppenheim, F, Helmerhorst, E. Rothia Bacteria as Gluten-Degrading Natural Colonizers of the Oral Cavity, 2012).

Rothia Aeria is inhibited by:
1. Chlorhexidine
2. Listerine Smartrinse™

Rothia mucilaginosa is inhibited by:
3. ACT fluoride rinse™
4. Crest Prohealth™

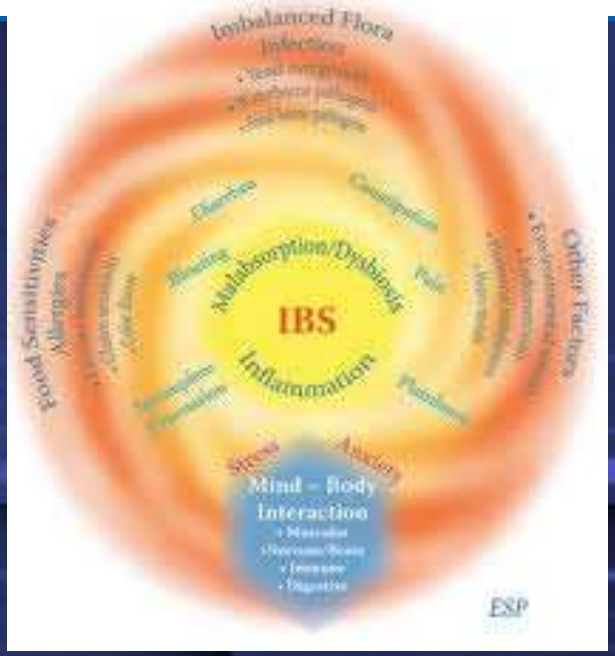
Rothia dentocariosa is inhibited by:
5. Levofloxacin
6. 27% alcohol.

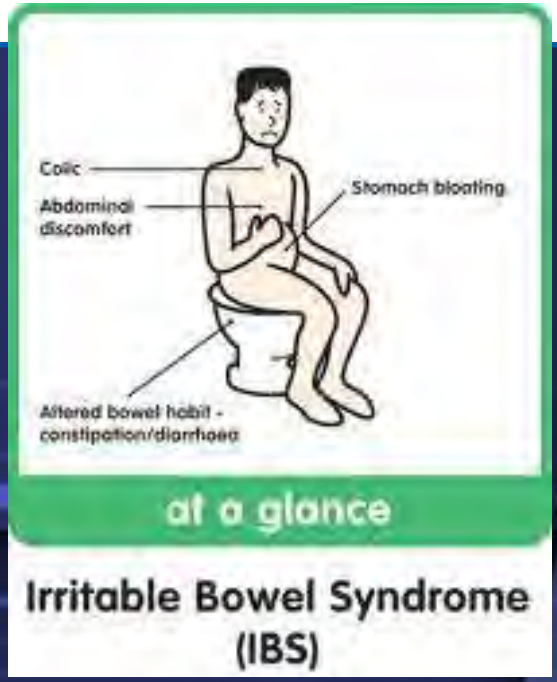
R. dentocariosa inhibits *P aeruginosa*.

Gluten sensitivity epidemic

Conclusion:

Rothia species*, S. mutans* and Lactobacillus species, are decreased in quantity by the over 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, Irritable Bowels Syndrome, and exacerbating ulcerative colitis increasing Celiac disease clinical prevalence.





Probiotics- Antagonism and Inhibition

Fluoride Inhibits Good and Bad Bacteria- Benefit/Risk Ratio

Oral Microbiol Immunol. 2005 Dec;20(6):323-32.

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

NOT PC

230 ppm

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

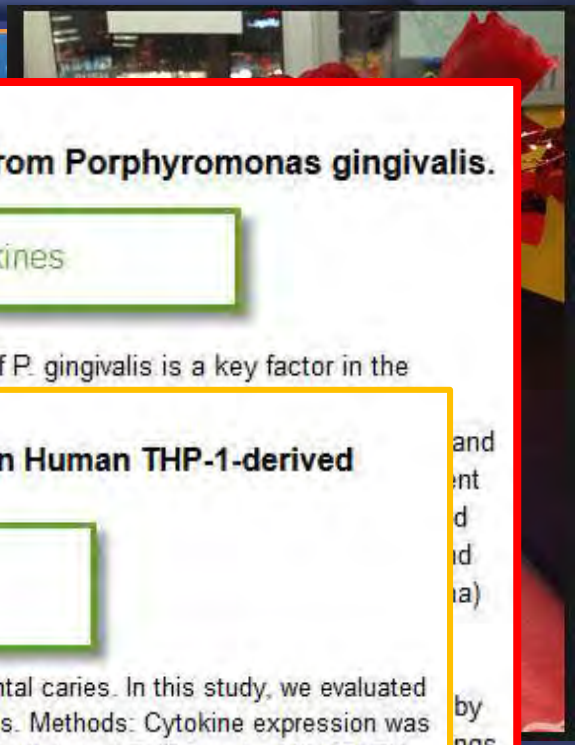
Mouth rinses intended for home use can be purchased over-the-counter. Higher strength mouth rinses for those at high risk of tooth decay must be prescribed by a dentist or physician.

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



Clin Diagn Lab Immunol. 2005 Nov;12(11):1285-91.

Xylitol inhibits inflammatory cytokine expression induced by lipopolysaccharide from Porphyromonas gingivalis.

Han SJ[1], Jeong SY, Nam YJ, Yang KH, Lim HS, Chung J.

⊕ **Author information**

Xylitol inhibits inflammatory cytokines

Abstract

Porphyromonas gingivalis is one of the suspected periodontopathic bacteria. The lipopolysaccharide (LPS) of P. gingivalis is a key factor in the

J Periodontol. 2014 Mar 4. [Epub ahead of print]

Xylitol, an Anti-caries Agent, Exhibits Potent Inhibition of Inflammatory Responses in Human THP-1-derived Macrophages Infected With Porphyromonas Gingivalis.

Park E[1], Na HS, Kim SM, Wallet S, Cha S, Chung J.

⊕ **Author information**

Xylitol an anti-inflammatory agent

Abstract

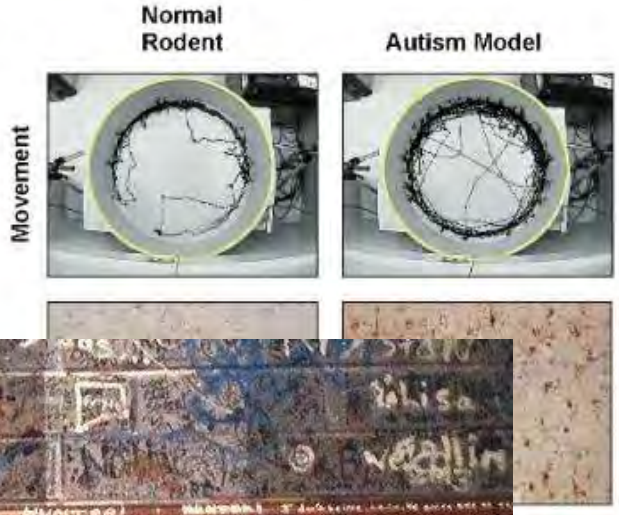
Background: Xylitol is a well-known anti-caries agent and has been used for the prevention and treatment of dental caries. In this study, we evaluated the anti-inflammatory effects of xylitol for possible usage in the prevention and treatment of periodontal infections. Methods: Cytokine expression was stimulated in THP-1 (human monocyte cell line)-derived macrophages by live Porphyromonas gingivalis (P. gingivalis), and ELISA and a MILLIPLEX MAP kit were used to determine the effects of xylitol on live P. gingivalis-induced production of cytokine. The effects of xylitol on phagocytosis and the production of nitric oxide were determined using phagocytosis assay, viable cell count, and Griess reagent. The effects of xylitol on P. gingivalis adhesion were determined by immunostaining and co-stimulatory molecule expression was examined by flow cytometry. Results: Live P. gingivalis infection increased the production of representative proinflammatory cytokine, TNFα (Tumor necrosis factor) and IL-1β (Interleukin-1) in a MOI- and time-dependent manner. Live P. gingivalis also enhanced the release of cytokines and chemokines such as IL-12-p40 (Interleukin 12), Eotaxin, IP-10 (Interferon gamma-induced protein 10), MCP-1 (Monocyte chemotactic protein-1), and MIP-1α (Macrophage inflammatory protein-1). The pretreatment of xylitol significantly inhibited the P. gingivalis-induced cytokines production and nitric oxide production. In addition, xylitol inhibited the attachment of live P. gingivalis on THP-1-derived macrophages. Furthermore, xylitol exerted anti-phagocytic activity against both Escherichia coli and P. gingivalis. Conclusions: These findings suggest that xylitol acts as an anti-inflammatory agent in THP-1-derived macrophages infected with live P. gingivalis, [illegible] periodontitis.

Xylitol

Probiotics- Neurologic Implications

- Autism
- "Autism Spectrum Disorder"
- Evidence mounts,

Short-chain fatty aci
products of the gut
implications in autis
disorders



Transl Psychiatry. 2013 Jan 22;3:e220. doi: 1

Unique acyl-carnitine profile
disorder.

Frye RE[1], Melnyk S, Macfabe DF.

⊕ Author information

Abstract

Autism spectrum disorder (ASD) has
a specific genetic mutation to explain
Acquired MD has been demonstrated
ASD-associated gut bacteria, is infus
neuropathologic and neurophysiologic
short-chain and long-chain acyl-carnit
abnormal fatty-acid metabolism are p
underwent screening for metabolic dis
reviewed. Acyl-carnitine panels were
these abnormalities were verified by repeated testing. Overall, 17% of individuals with ASD demonstrated consistently abnormal acyl-carnitine panels.

Glyphosate- microbiome implications

- Dr. Seneff- MIT scientist reports:

Glyphosate and Autism*

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

Open

Review

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

Anthony Samsel [1] and Stephanie Seneff [2,*]

+ Authors' affiliations

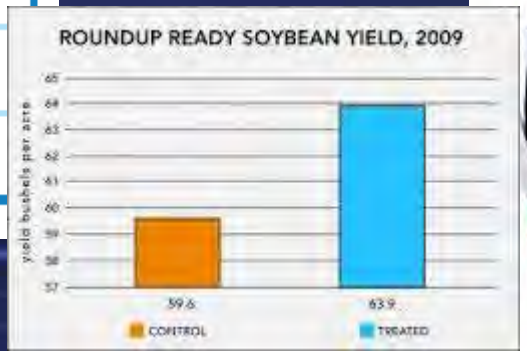
Received: 15 January 2013; in revised form: 10 April 2013 / Accepted: 10 April 2013 / Published: 18 April 2013

	diseases such as inflammatory bowel disease, chronic diarrhea, colitis and Crohn's disease	
Allergies	Cardiovascular disease	Depression
Cancer	Infertility	Alzheimer's disease
Parkinson's disease	Multiple sclerosis	ALS, and more

1990 1992 1994 1996 1998 2000 2002 2004 2006 2008 2010

Year

* http://www.examiner.com/article/data-show-correlations-between-increase-neurological-diseases-and-gmos



Probiotics- Neurologic Implications

- Obesity and the

EPMA J. 2014 Jan 13;5(1):2. doi: 10.1186/1878-5085-5-2.

The efficacy of probiotics for monosodium glutamate-induced obesity: dietology concerns and opportunities for prevention.

Savcheniuk OA, Virchenko OV, Falalyeyeva TM, Beregova TV, Babenko LP, Lazarenko LM, Demchenko OM, Bubnov RV[1], Spivak MY.

Author information

Probiotics prevented Weight gain!

Abstract

INTRODUCTION: Obesity becomes endemic today. Monosodium glutamate was proved as obesogenic food additive. Probiotics are discussed to impact on obesity development.

AIMS AND OBJECTIVES: The aim was to study the effects of probiotics on the development of monosodium glutamate (MSG)-induced obesity in rats.

MATERIAL AND METHODS: We included 45 Wistar male rats and divided into three groups (n = 15). Newborn rats of group 1 (control) received subcutaneously 8 μl/g saline. Group 2 received 3 to 4 mg/g MSG subcutaneously on the second, fourth, sixth, eighth and tenth day of life. Within 4 months after birth, rats were on a standard diet. Group 3 received an aqueous solution of probiotics mixture (2:1:1 Lactobacillus casei IMVB-7280, Bifidobacterium animalis VKL, B. animalis VKB) at the dose of 5 × 109 CFU/kg (50 mg/kg) intragastrically. Administration of probiotics was started at the age of 4 weeks just after weaning and continued for 3 months during 2-week courses. Group 2 received intragastrically 2.5 ml/kg water. Organometric and biochemical parameters in all groups of rats were analyzed over 4 months. The concentration of adiponectin was determined in serum, and leptin - in adipose tissue.

RESULTS: Administration of MSG led to the development of obesity in rats; body weight had increased by 7.9% vs controls ($p < 0.05$); body length had increased by 5.4% ($p < 0.05$). Body mass index and Lee index and visceral fat mass had increased ($p < 0.001$). Under the neonatal injection of MSG, the concentration of total cholesterol, triglycerides, VLDL cholesterol and LDL cholesterol significantly increased ($p < 0.001$), in comparison with controls. Adipose-derived hormones changed in MSG obesity rats: adiponectin decreased by 58.8% ($p < 0.01$), and leptin concentration in adipose tissue had increased by 74.7% ($p < 0.01$). The probiotic therapy of rats from group 3 prevented obesity development. Parameters of rats treated with probiotic mixture did not differ from that in the control.

CONCLUSIONS: The introduction of MSG to newborn rats caused the obesity in adulthood. Periodic administration of probiotic mixture to rat injected with MSG neonatally resulted in recovery of lipid metabolism and prevention of the obesity development.

microbiota is hypothesized to influence weight gain.

Probiotics- Neurologic Implications

- Bacteria- obesity, depression

Gut Microbes. 2013 Jan-Feb;4(1):17-27. doi: 10.4161/gmic.22973. Epub 2012 Nov 30.

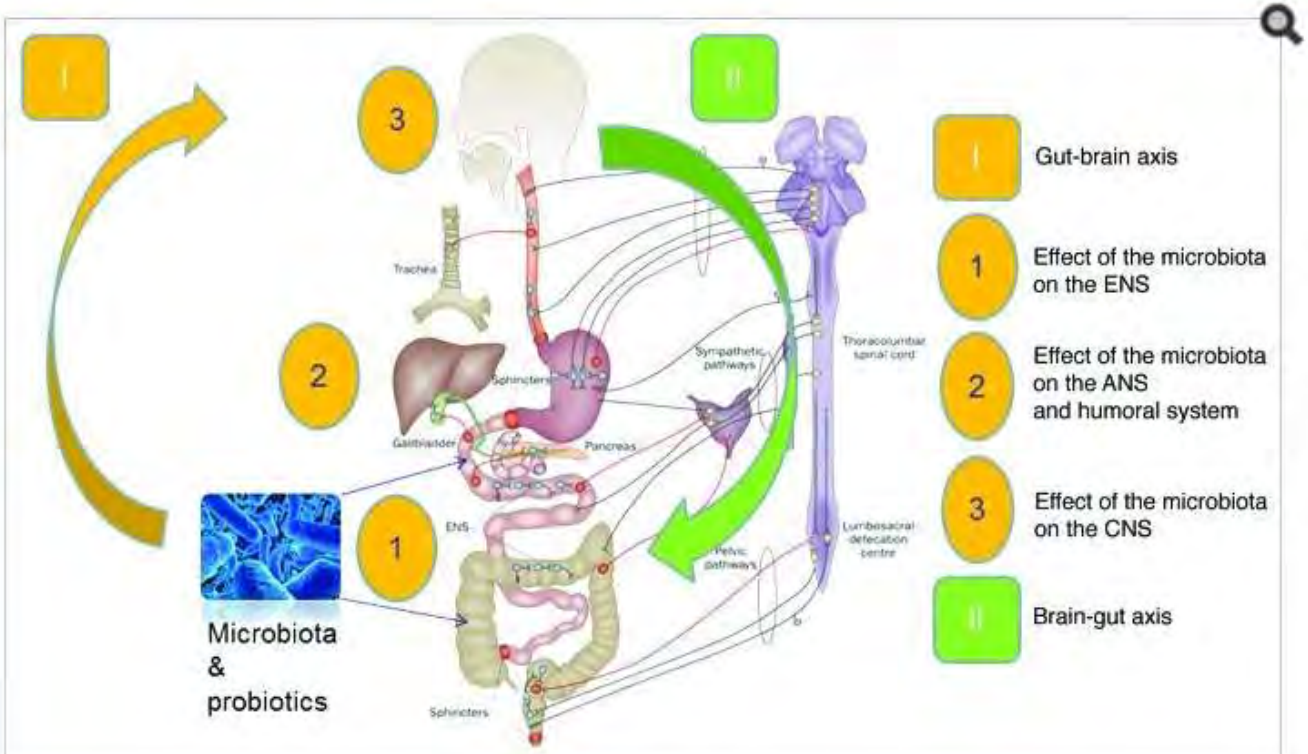


Figure 1. Interaction of the gut microbiome, probiotics and prebiotics on the brain gut axis. Modified from reference [85].

Probiotics- Neurologic Implications

- Prevention and Probiotics- kefir and BLIS?

013.02.043. Epub 2013

otic modulates brain activity.

Legrain-Raspaud S, Trotin B, Naliboff B, Mayer EA.

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.

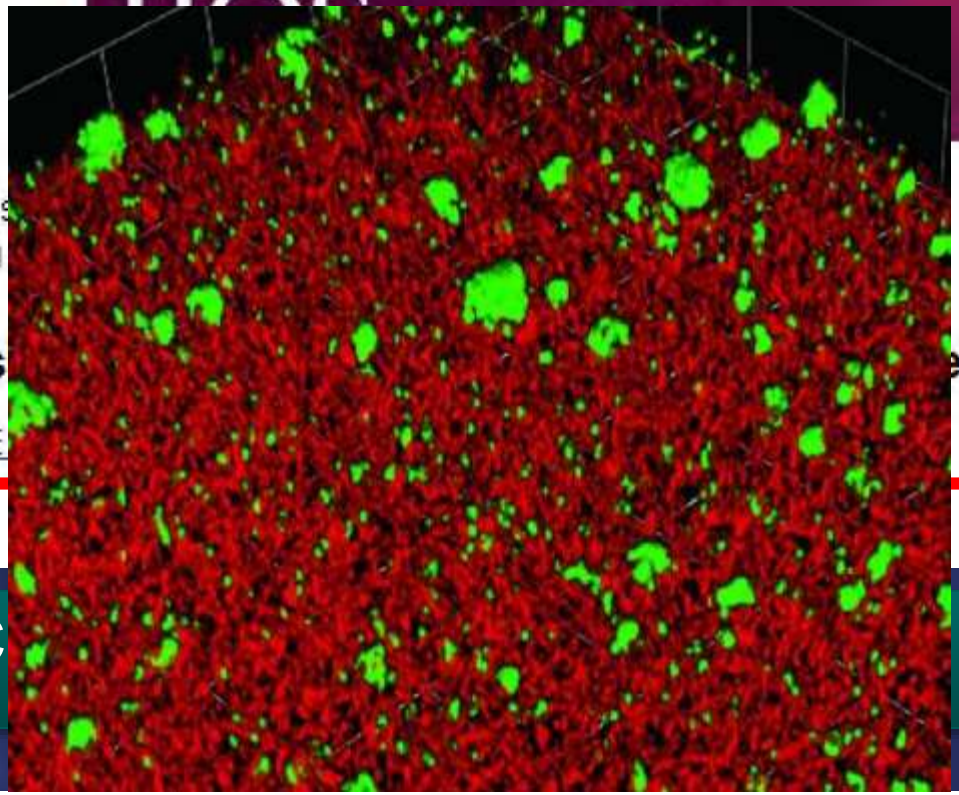
METHODS: Healthy women with no gastrointestinal or psychiatric symptoms were randomly assigned to groups given FMPP (n = 12), a nonfermented milk product (n = 11, controls), or no intervention (n = 13) twice daily for 4 weeks. The FMPP contained Bifidobacterium animalis subsp Lactis, Streptococcus thermophiles,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

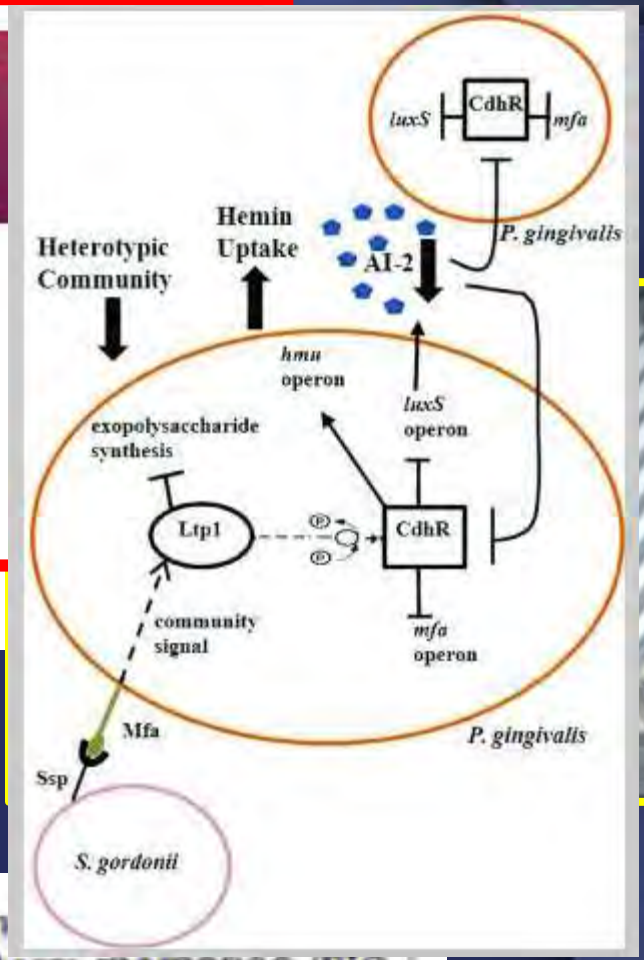
RESULTS: FMPP intake was associated with reduced task-related response of a distributed functional network (49% cross-block covariance; P = .004) containing affective, viscerosensory, and somatosensory cortices. Alterations in intrinsic activity of resting brain indicated that ingestion of FMPP was associated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

MRI and emotional brain tasking

Probiotics- Neurologic Implications





Int J Oral S
Published

Tyros

Sarah E

- TC

High levels of STEP proteins keep synapses in the brain from stren
strengthening is 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].

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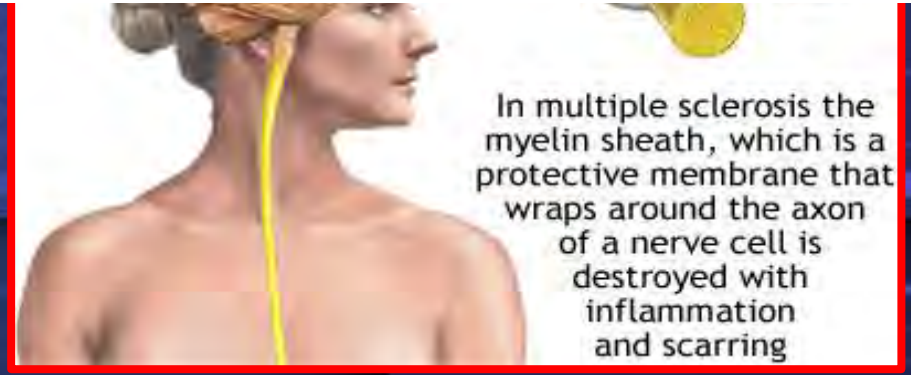
Intestinal Barrier Dysfunction Develops at the Onset of Experimental Autoimmune Encephalomyelitis, and Can Be Induced by Adoptive Transfer of Auto-Reactive T Cells

Mehrnaz Nouri, Anders Bredberg, Björn Weström, Shahram Lavasani

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

PLOS | ONE



DIABETES- insulin is not a cure!!

Gut Microbiota Is a Key Modulator of Insulin Resistance in TLR 2 Knockout Mice

Andréa M. Caricilli, Paty K. Picardi, Lélia L. de Abreu, Mirian Ueno, Patrícia O. Prada, Eduardo R. Ropelle, Sandro Massao Hirabara, Ângela Castoldi, Pedro Vieira, Niels O. S. Camara, Rui Curi, José B. Carvalheira, Mário J. A. Saad

Published: December 06, 2011 • DOI: 10.1371/journal.pbio.1001212

PLOS | BIOLOGY

Proc Natl Acad Sci U S A. 2011 Jul 12;108(28):11548-53. doi: 10.1073/pnas.1108924108. Epub 2011 Jun 27.

Naturally transmitted segmented filamentous bacteria segregate with diabetes protection in nonobese diabetic

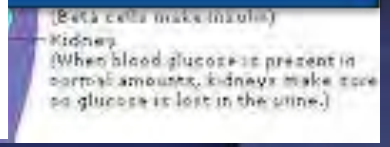
- Vertebrates typically harbor a rich gastrointestinal microbiota, which has coevolved with the host over millennia and is essential for several host physiological functions, in particular maturation of the immune system. Recent studies have highlighted the importance of a single bacterial species, segmented 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,

PLoS Pathog. Dec 2013; 9(12): e1003794. PMCID: PMC3873456
Published online Dec 26, 2013. doi: 10.1371/journal.ppat.1003794

Host Susceptibility Factors to Bacterial Infections in Type 2 Diabetes

Yunn-Hwen Gan*

halomyelitis.



Oral and gut bacteria are repeatedly reported in the research literature to be involved in:

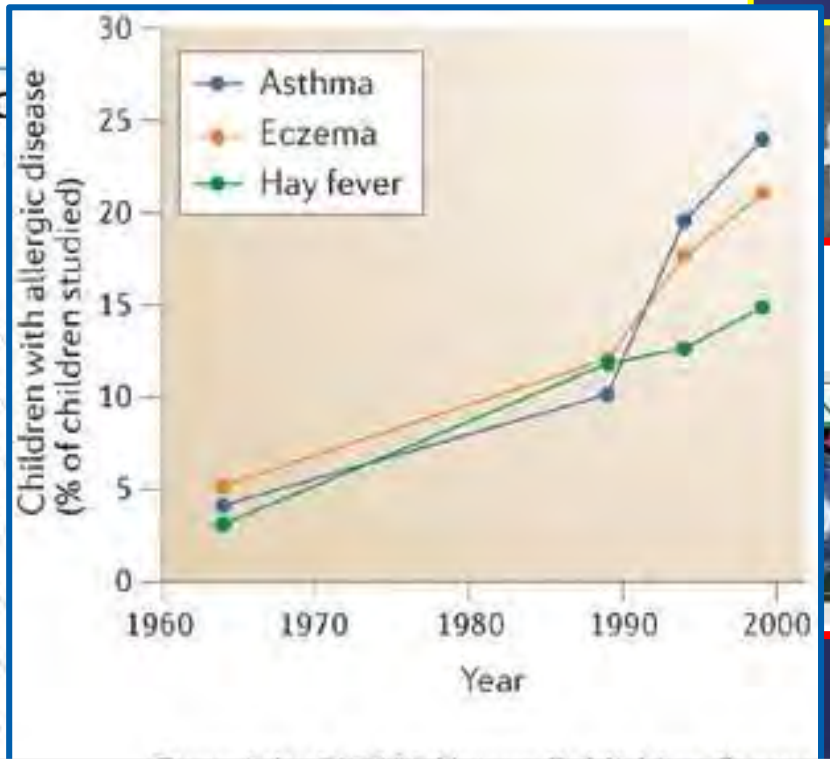
- Aut
- Dia
- RA
- Com
- sens
- Andrew
- Sarkis K
- Dionysio
- Rea
- All
- Agi
- Glu
- Cel

More U.S. Children Have Fo

Prevalence of food allergies has been

% U.S. Children with

6.0%
5.0%
4.0%
3.0%
2.0%
1.0%
0.0%



Bostock J. Case of a periodical affection of the eyes and chest. Med Chir Trans. 1819;10:161.

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

New Sealant Technology

- Bis Phenol A- IS BACK IN THE M

BPA's possible role in miscarriages

.Int Dent J. 2012 Apr;62(2):65-9. doi: 10.1111/j.1875-595X.2011.00089.x.

Dental composite fillings and bisphenol A among

.J Dent Hyg. 2010 Summer;84(3):145-50. Epub 2010 Jul 5.

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

National Health and Nutrition Examination Survey

nhanes

National Center for Health Statistics

nchs CDC

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

Environ Health Perspect. 2012 Sep;120(9):1297-300. doi: 10.1289/ehp.1104114. Epub 2012 May 29.

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

Acta Diabetol. 2013 Aug;50(4):625-31. doi: 10.1007/s00592-013-0472-z. Epub 2013 May 1.

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

J Clin Endocrinol Metab. 2011 Dec;96(12):3822-6. doi: 10.1210/jc.2011-1682. Epub 2011 Sep 28.

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. ashankar@hsc.wvu.edu

THE SECRETS!!! SHHHHHH!!!

Urinary bisphenol A and obesity: NHANES 2003–2006 ☆

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

Environ Health Perspect. 2011 January; 119(1): 63–70. PMCID: PMC3018502
Published online 2010 September 8. doi: 10.1289/ehp.1002347

Research

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

THE SECRETS!!! SHHHHHH!!!

Diabetes Care. 2012 Mar;35(3):520-5. doi: 10.2337/dc11-1043. Epub 2012 Jan 25.

Helicobacter pylori infection is associated with an increased rate of diabetes.

Jeon CY, Haan MN, Cheng C, Clayton ER, Mayeda ER, Miller JW, Aiello AE.

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 disease, there is interest in how infections affect risk of diabetes.

RESEARCH DESIGN AND METHODS: We examined the association between serological evidence of chronic viral and bacterial infections and incident diabetes in a prospective cohort of Latino elderly. We analyzed data on 732 individuals aged 60 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 other covariates.

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.

2.7X increase of diabetes

When seropositive for H. pylori

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 pr

Zoonotic Disease: When Humans and Animals Intersect

"CROWD" DISEASE-symptom of the times…..

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 peopl world, including remote Pacific islands and the Arctic, and killed 50 to 100 million of them- percent of t natural disasters in hum

Most influer r already weakened pati contrast the y young adults. Modern using virus t that the virus kills throu storm (over nune reactions of young the body, w ddle-aged adults resulte deaths amo

Historical ar pandemic's geographic c implicated i

To maintain ness and mortality in Ge France, and epidemic's effects in neu (such as the grave illness of King Alfonso XIII), creating a false impression of Spain as especi thus the pandemic's nickname Spanish flu.

Influenza (Flu)

Types
Avian (A/H5N1 subtype)
Canine · Equine
Swine (A/H1N1 subtype)

Vaccines
2009 pandemic (Pandemrix)
Fluzone · Influvac
Live attenuated · Optaflu

Treatment
Amantadine · Arbidol
Laninamivir · Oseltamivir
Peramivir · Rimantadine
Vitamin D · Zanamivir

Pandemics
2009 swine
1968–1969 Hong Kong
1957 Asian flu
1918

Outbreaks
2008 West Bengal
2007 Bernard Matthews H5N1
2007 Australian equine
2006 H5N1 India
1976 swine flu

People and animals are not meant to be stacked on top of each other!

Zoonotic Disease: When Humans and Animals Intersect

Interesting facts about zoonotic diseases

- About 75% of recently emerging infectious diseases affecting humans are diseases of animal origin, and approximately 60% of all human pathogens are zoonotic.
- Tick-borne diseases, including Lyme disease and Rocky Mountain spotted fever, are serious public health problems, infecting tens of thousands in the United States each year. CDC is working closely with local communities, developing innovative control approaches and researching improved diagnostics.
- Almost all persons infected by rabid animals will die if not treated appropriately. Dogs are responsible for most human rabies deaths worldwide, but the public health threat of canine rabies has been virtually eliminated in the United States.
- There have been 1.5 million West Nile virus infections since 1999. 2.5 billion people are at risk for dengue in more than 100 endemic countries with 50 million cases of dengue fever each year.

For more information on zoonotic diseases, visit www.cdc.gov/ncezid or call 1-800-CDC-INFO.

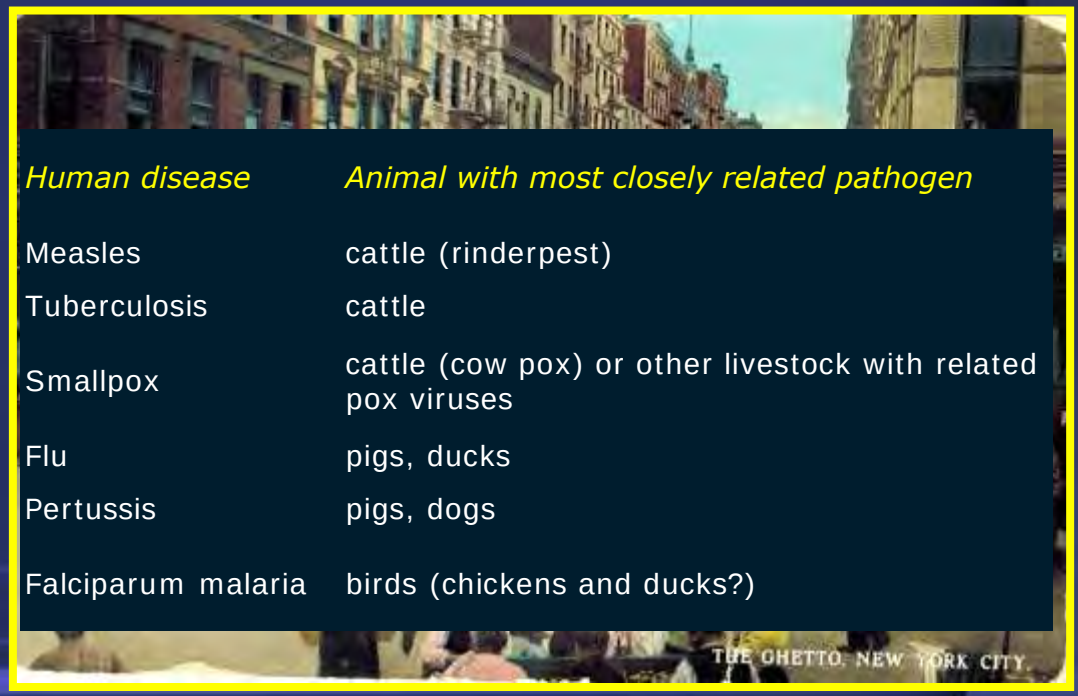
Zoonotic diseases are contagious diseases spread between animals and humans. These diseases are caused by bacteria, viruses, parasites, and fungi that are carried by animals and insects. Examples are anthrax, dengue, Ebola hemorrhagic fever, Escherichia coli infection, Lyme disease, malaria, Plague,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

- 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.

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.



Human disease	*Animal with most closely related pathogen*
Measles	cattle (rinderpest)
Tuberculosis	cattle
Smallpox	cattle (cow pox) or other livestock with related pox viruses
Flu	pigs, ducks
Pertussis	pigs, dogs
Falciparum malaria	birds (chickens and ducks?)

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?

Clin Exp Pharmacol Physiol. 2011 Nov;38(11):734-8. doi: 10.1111/j.1440-1681.2011.05583.x.

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

Arhant-Sudhir K[1], Arhant-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 cardiovascula 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.

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.

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

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

zoonotic

J Appl Microbiol. 2014 May;116(5):1308-1314. doi: 10.1111/jam.12477. Epub 2014 Mar 14.

Pathogen exclusion properties of canine probiotics are influenced by the growth media and physical treatments simulating industrial processes.

Grześkowiak L[1], Collado MC, Beasley S, Salminen S.

Author information

Probiotics for dogs- from human sources or shared???

Abstract

AIMS: Manufacturing process used in preparation of probiotic products may alter beneficial properties of probiotics. The effect of different growth media and inactivation methods on the protective properties of canine-originated probiotic bacteria against adhesion of canine enteropathogens was investigated.

METHODS AND RESULTS: Three established dog probiotics, Lactobacillus fermentumVET9A, Lactobacillus plantarumVET14A and Lactobacillus rhamnosusVET16A, and their mixture were assessed using the dog mucus pathogen exclusion model. The pathogens used were Enterococcus canis, Salmonella enterica serovar Typhimurium and Clostridium perfringens. The effect of growth media, one reflecting laboratory and the other manufacture conditions, and viability (viable and heat inactivated, 80°C per 30 min) on the pathogen exclusion properties of probiotics were characterized. Greater pathogen exclusion percentages were noted for probiotics growing in conditions reflecting manufacture when compared to laboratory ($P < 0{\cdot}05$). Inactivation of probiotics by heat (80°C per 30 min) increased pathogen exclusion compared with their viable forms ($P < 0{\cdot}05$).

CONCLUSIONS: Manufacturing process conditions such as growth media, incubation temperature and pretreatment methods may significantly affect the protective properties of the tested strains.

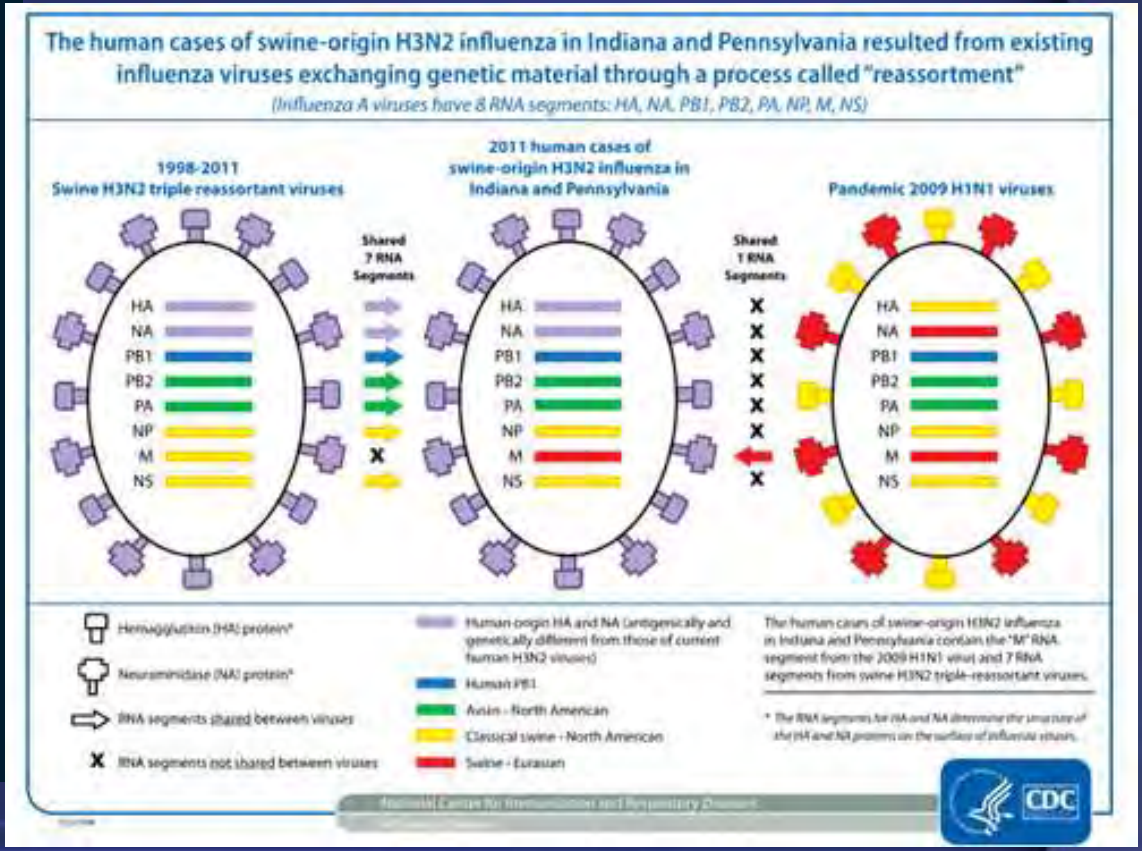
SIGNIFICANCE AND IMPACT OF THE STUDY: Growing conditions and pretreatment methods should be carefully considered when designing new probiotics to reduce the risk of common infections in dogs. The studied probiotics are promising potential feed additives for dogs.

between ownership of furry pets during the first 2 years of life and reduced likelihood of becoming sensitized to aero-allergens.

CONCLUSIONS: Pet ownership in early life did not appear to either increase or reduce the risk of asthma or allergic rhinitis symptoms in children aged 6-10. Advice from health care practitioners to avoid or to specifically acquire pets for primary prevention of asthma or allergic rhinitis in children should not be given.

? 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

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bacterial

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nhibition.

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

A1, A2, A3, A4, A5, A6, A7, A8, A9, B1, B2, B3, B5, B6, B7

Analysis of Variance Results

Source	DF	SS	MS	F	P
Total	44	5060.9778	115.02222		
A	14	3348.9778	239.2127	4.1918113	0.00048
Error	30	1712	57.066667		

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.

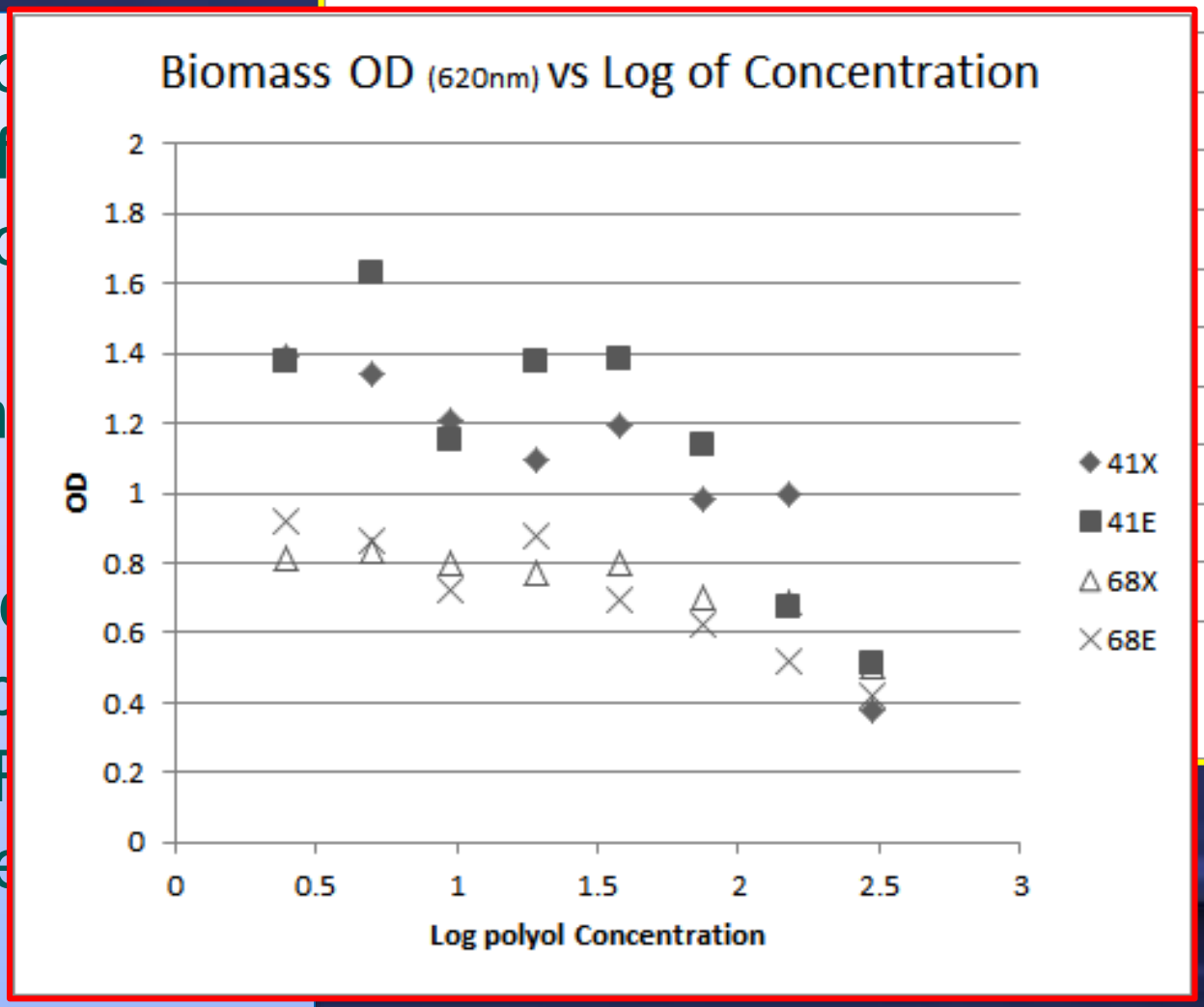
Investigation into Gluten Metabolizing Bacterial Species and their Inhibition

How will xylitol and erythritol help?

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

- Concentratio
  Gradients of
  and Erythrito
  different
  combination
  research
- Special Infe
  Disease Lab
  of Ann and R
  Lurie Childre
  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!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