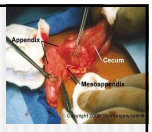
The Gut Microbiome Evaluation and Optimization

Gerald T. Simons, PA-C

"I have a gut feeling"

"I have butterflies in my stomach!"

Stony Brook Southampton Hospital



- **Gerald T. Simons, PA-C**
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- Surgical PA
- AASPA
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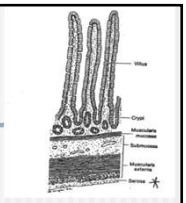
  - BOD
- **No disclosures.**
- **No commercial associations**

Stony Brook School *of* Health Technology and Management

My interest



- I have a 23 year interest in the GI tract.
- It began simply as a technical interest- how to resect the bowel, staple, suture and scope it. As time when on, I became more interested in its physiology, neurologic innervation, absorption etc.
- I've come to realize that the gut
  - is a key part of our immune system & overall ecosystem
  - oral medication can alter its function
  - nutrition can affect and is affected by its role.
  - Probiotics are an important prescription for many
  - FMT will be seem more often

Objectives/Outline

1. Introduction and role of our microbiome & the microbiome in the news.
2. The gut microbiota and inflammation
3. The Gut micro biome and immunity.
4. The micro biome and neurodegenerative diseases (e.g. Parkinson's disease, Alzheimer's disease).
5. You are what you eat: our diet and the gut microbiome

Objectives/Outline

6. Methods to evaluate the microbiome
7. Microbiome through the ages
8. Antibiotics & microbial depletion
9. Greater knowledge vs. greater uncertainty: the future

Question1

Studies by Blaser (2011) & Becattini (2016) suggest that antibiotic use stresses our gut microbiome and triggers an increase incidence of

A. Obesity & type 1 diabetes
B. Long term viral illnesses
C. Melanomas & skin cancers
D. Kidney stones & UTIs

Question 2

- Which of the following is TRUE regarding our gut microbiome?
  A. A gut populated with *Firmicutes* is associated with a **lower BMI.**
  B. Children born by C-section have a **lower** rate of allergies and metabolic diseases.
  C. Long term PPIs **do not** alter the gut microbiome.
  D. Bacteria populating the gut microbiota can secrete **large amounts** of amyloids and lipopolysaccharides.

Question 3

- Which of the following IS **NOT EFFECTIVE** in improving the health of the gut microbiome?
  A. Short Chain Fatty acids- Butyrate
  B. Serum derived bovine immunoglobulin
  C. Diets rich in lean red meats
  D. Prebiotics (oligosaccharides)

Vocabulary-1

- Human **microbiota**
  - The specific bacteria, viruses, fungi, and other single-celled animals that live in the body.
  - Our collective organism!
- **Microbiome**
  - All of the genes/genomes inside these microbial cells
  - "gene content"

Vocabulary-2

UpToDate 2 April 2020

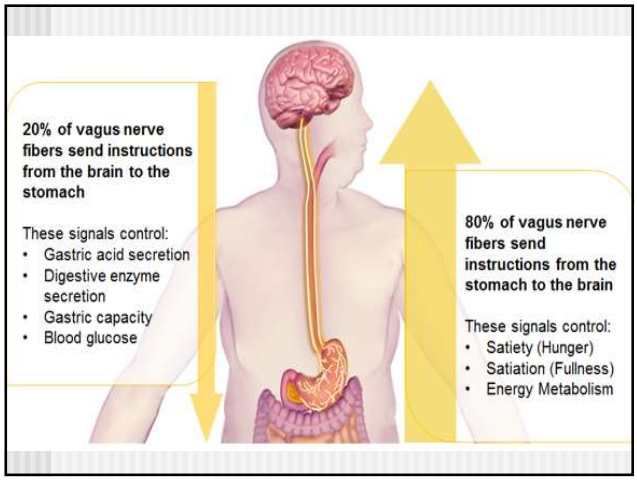
- **Dysbiosis**
  - Imbalance in the gut microbiome
  - High levels of Proteobacteria
    - Gram-negative bacteria. Escherichia, Salmonella, Vibrio, Helicobacter, Yersinia, Legionellales
  - Immunosuppressed patients
    - associated with IBD &CFS
      - Nature.com accessed 2 April 2019
- **SIBO**: Small Intestinal Bacterial Overgrowth
  - Excessive aerobic and anaerobic microbes that are normally present in the colon.
  - Bloating, flatulence, abdominal discomfort, or diarrhea.

Vocabulary-3

- **Prebiotic**
  - Prebiotics are foods (typically high-fiber foods) that feed our microflora. Prebiotics are used to improve the balance of these microorganisms.
- **Probiotic**
  - Live, nonpathogenic microorganism
  - Not FDA regulated
  - Thousands of products
    - Strains
    - Doses

Vocabulary-4
Enteral nervous system

- Unique nervous system of the gut
- Connected to the CNS via the vagus nerve
- As many nerves as the brain of a dog or cat
- Sympathetic and parasympathetic
- Under investigation: GI symptoms in Alzheimer's and Parkinson's



Gut-brain connections George Porter Phillips

- 1910 Bethlem Royal Hospital (London)
- Patients with melancholia had constipation and "general clogging of the metabolic processes"
  - brittle nails, thin hair and pallor.
- It was thought these symptoms were caused by depression
- He removed all meat (except fish) and fed them fermented milk (keifer) which contains lactobacillus
- N=18 patients
  - 11 were cured completely
  - 2 others showing significant improvement.
  - Birth of PSYCHOBIOTICS!

Phillips, J. (1910). The Treatment of Melancholia by the Lactic Acid Bacillus. *Journal of Mental Science, 56*(234), 422-430.

SCIENTIFIC REPORTS

OPEN

Gut microbiome alterations in Alzheimer's disease

Nicholas M. Vogt[1], Robert L. Kerby[2], Kimberly A. Dill-McFarland[2], Sandra J. Harding[1], Andrew P. Merluzzi[1], Sterling C. Johnson[3,1,4], Cynthia M. Carlsson[3,1,4], Sanjay Asthana[3,1], Henrik Zetterberg[5,6,7,8], Kaj Blennow[5,6], Barbara B. Bendlin[1,4] & Federico E. Rey[2]

Received: 21 June 2017
Accepted: 27 September 2017
Published online: 19 October 2017

Alzheimer's disease (AD) is the most common form of dementia. However, the etiopathogenesis of this devastating disease is not fully understood. Recent studies in rodents suggest that alterations in the gut microbiome may contribute to amyloid deposition, yet the microbial communities associated with AD have not been characterized in humans. Towards this end, we characterized the bacterial taxonomic composition of fecal samples from participants with and without a diagnosis of dementia due to AD. Our analyses revealed that the gut microbiome of AD participants has decreased microbial diversity and is compositionally distinct from control age- and sex-matched individuals. We identified phylum- through genus-wide differences in bacterial abundance including decreased Firmicutes, increased Bacteroidetes, and decreased *Bifidobacterium* in the microbiome of AD participants. Furthermore, we observed correlations between levels of differentially abundant genera and cerebrospinal fluid (CSF) biomarkers of AD. These findings add AD to the growing list of diseases associated with gut microbial alterations, as well as suggest that gut bacterial communities may be a target for therapeutic intervention.

nature

Autism & the Gut-brain connection

- Many kids w autism have GI issues
- Microbiota transfer therapy (FMT)
- 45% reduction in language, social interaction and behavior at two years post-treatment
- "We are finding a very strong connection between the microbes that live in our intestines and signals that travel to the brain,"
- "Two years later, the children are doing even better, which is amazing."

Autism symptoms reduced nearly 50 percent two years after fecal transplant

Date: April 9, 2019
Source: Arizona State University
Summary: In a new study, researchers demonstrate long-term beneficial effects for children diagnosed with ASD through a revolutionary fecal transplant technique known as microbiota transfer therapy (MTT).

Psychobiotics

- Amazing w probiotics and L-methyfolate


Contents lists available at ScienceDirect

Brain, Behavior, and Immunity

journal homepage: www.elsevier.com/locate/ybrbi

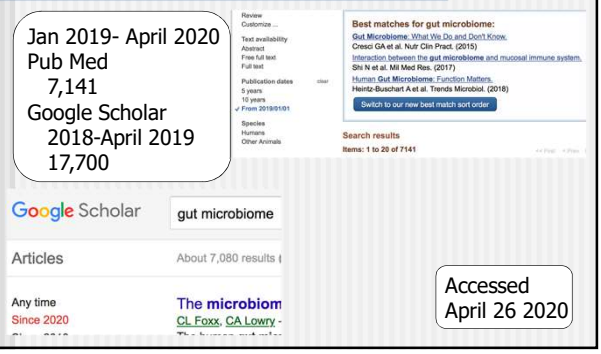
A randomized controlled trial to test the effect of multispecies probiotics on cognitive reactivity to sad mood ☆

Laura Steenbergen [a,b,*], Roberta Sellaro [a,b], Saskia van Hemert [c], Jos A. Bosch [d], Lorenza S. Colzato [a,b]

[a] Leiden University, Institute for Psychological Research, Cognitive Psychology, Wassenaarseweg 52, 2333 AK Leiden, The Netherlands
[b] Leiden Institute for Brain and Cognition, P.O. Box 9600, 2300 RC Leiden, The Netherlands
[c] Winclove Probiotics, Hulstweg 11, 1032 LB Amsterdam, The Netherlands

Scientific interest is increasing

Jan 2019- April 2020
Pub Med
7,141
Google Scholar
2018-April 2019
17,700



Accessed
April 26 2020

"It is reasonable to propose that the composition of the microbiome and its activities are involved in most, if not all, of the biological processes that constitute human health and disease"

Martin J Blaser, MD
J Clin Invest. 2014;124(10):4162-4165

What we know today

- Changes in our basic bacterial balance can cause or exacerbate disease including premature birth, bowel disease, mood and memory changes, and circadian rhythms.
- Diet changes can enhance or inhibit our microbiome
- The enteral nervous system is our second brain
- PAs can enhance or erode a patients microbiota

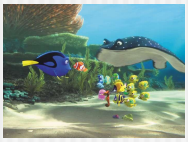
Our way of thinking ….

- MICROBES are BAD & cause DISEASE
  - They colonize & infect
- Detected by microscopy and cultured
- Characterized by growth on specific media, sensitivity to antibiotics
  - They need to be killed with
    - Antiviral
    - Antibiotic
    - Antiparasitic
    - Antifungal

BUT…

NEW WAY OF THINKING

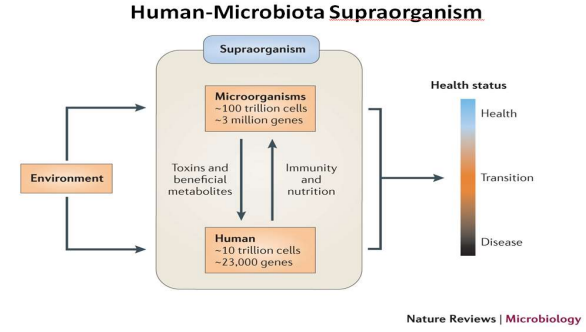
- Your patient is not just one organism!
- Every patient is its OWN unique microbiota
- Most of our organisms are non-pathologic & beneficial
- We are like a warm-blooded coral reefs
  - We contain microbial ecosystems
  - Very diverse
  - Symbiosis is key
  - "Coral Transplant vs FMT"



New way of thinking

- Prescribing probiotics & beneficial bacteria.
- Prescribing fecal transplant
- Prescribing beneficial diets.

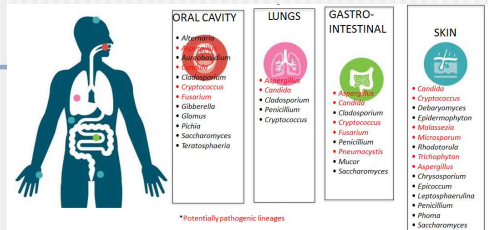
So, how big IS our microbiome?



Nature Reviews Microbiology 11, 639–647 2013

2017 data 37 trillion human cells
Each human has 40 trillion bacteria! *Sender, et.al 2016*

The Human Mycobiome



- Early surveys have revealed several pathogenic species that may increase one's risk of disease when the healthy microbiome is disrupted.
- *Candida* and *Aspergillus* species are among the most common members of the human mycobiome.
- When the balance of a microbial community is disrupted, fungal species can flourish and cause disease

The Scientist. 02.2016. 37

Theory- check for candida/fungal infection in chronic disease?

Our second genome

NIH National Human Genome Research Institute

ANALYSIS CPD

The genome, microbiome and evolutionary medicine

Robert C. Brunham MD

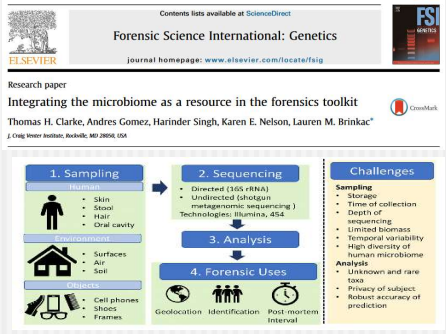
Cite as: *CMAJ* 2018 February 12;190:E162-6. doi: 10.1503/cmaj.170846

KEY POINTS

- The practice of medicine will increasingly be based on an evolutionary understanding of the human genome and microbiome.
- According to the evolutionary medicine framework, disease is conceptualized within six categories that capture genetic, evolutionary and mechanistic causes.
- Evolutionary medicine views patients as individuals whose history has unfolded over the course of an entire life cycle with unique windows of vulnerability during which the environment affects genome expression; the microbiome has co-evolved with animal hosts and protected the host against pathogens, assisted in digestion of food and in the development of the immune system.
- Although evolutionary medicine requires further research to develop its distinctive viewpoint, it offers a secure foundation for future developments in medicine.

Patients are reading this & we need to be prepared!

Microbiome "Fingerprint"



What about the gut flora?

- THREE trillion microorganisms that normally live in the digestive tract
  - 500 different bacterial species in the intestine
  - A probiotic dose should be in the BILLIONS!
- They perform a number of useful functions for their hosts

Why this diversity?

- Gut & Immune function
- The surface of the GI tract is a vast frontier that is a portal of entry into the body.
- The guts lumen is frequently filled with a complex mixture of nutrients that constitute an attractive "culture medium" microbes.
- Intestine is challenged to distinguish between potentially harmful microorganisms, against which it must defend itself, versus the innocuous antigens that occur in food.
- Intestine also has a special need for immune surveillance against malignancy. Thus, the rapid rate of proliferation of intestinal epithelial cells, coupled with exposure of these cells to potential toxins in the intestinal lumen, renders the epithelium uniquely sensitive to cell transformation.

Acquiring our microbiome

- Sterile womb hypothesis
  - Birthing process is the first exposure & seeding of a neonate to microbes, and subsequent interactions shape and seed the neonate's microbial communities
  - Within a MONTH of birth, the microbial genome outnumbers human genes **150:1**
- One of the most complex microbial ecosystems on the planet!
- Under research- transplacental exposure

Acquisition of the Human Microbiome

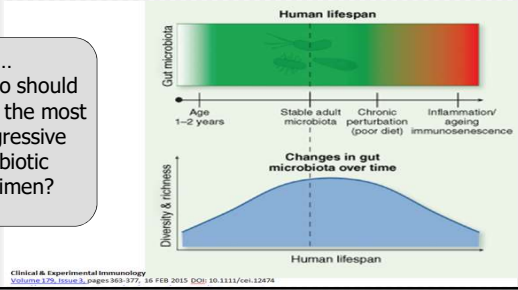
- Vaginal delivery –
  - microbiome develops species similar to mother's vagina
- Cesarean section –
  - microbiome develops predominant species similar to skin flora of mother and hospital attendants
- Breast feeding provides bacteria from mother's GI tract
- The microbes we acquire at birth affect us for the rest of our lives!

PLoS Biol, 2013, Vol 11(8)

The gut microbiota during the human lifespan

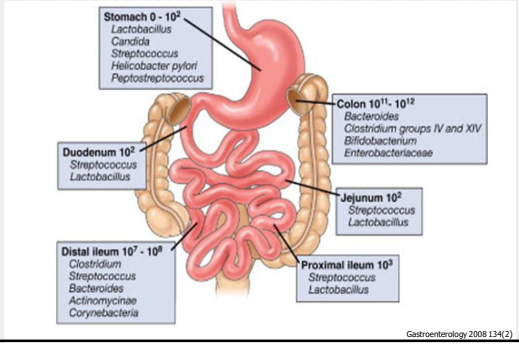
Age & inflammation reduces microbial diversity
Theory: Affects gut- brain axis

SO…
Who should get the most aggressive probiotic regimen?



Clinical & Experimental Immunology
Volume 179, Issue 3, pages 363-377, 16 FEB 2015 DOI: 10.1111/cei.12474

Composition and luminal concentrations of dominant microbial species in various regions of the gastrointestinal tract.



Gut flora have useful functions

- Enhance absorption and storage of lipids.
- Train immune system to respond only to pathogens
- Prevent growth of harmful species
- Increase growth of intestinal epithelial cells and control their proliferation and differentiation. *Important in critical care
- Alter intestinal growth by changing expression of cell surface proteins i.e. sodium/glucose transport.

Gut Microbiome Function

- The small intestine= principle site of nutrient digestion & absorption
- Largest reservoir of immunologically active and hormone-producing cells
  - it's the largest organ of immune and endocrine systems, respectively (SCHWARTZ SURGERY).
- Digestion & metabolism:
  - energy and nutrient extraction
  - Gut breaks down EVERY ORAL MED!
  - Chronic fatigue?
  - Malabsorption

Role of the gut: Immune function

- The GI tract is a vast frontier and is the ultimate portal of entry into the body.
- By the very nature of the physiological function of the gut, its lumen is frequently filled with a complex mixture of nutrients
  - Its an attractive "culture medium" for microbes.
- Intestine is constantly working to distinguish between potentially harmful microorganisms versus benign antigens that occur in food.
- Intestine also has a special need for immune surveillance against malignancy. Thus, the rapid rate of proliferation of intestinal epithelial cells, coupled with exposure of these cells to potential toxins in the intestinal lumen, renders the epithelium uniquely sensitive to cell transformation.

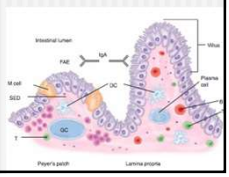
Gut Microbiome role

- Synthesize vitamins & aid in absorption
  - Vit K, biotin, vitamin B_{12}, folic acid, and thiamine.
  - Low levels? Think of the gut!
- Protection against infection
- Maintenance of gut barrier
- Immune modulation
- Gut-brain axis
  - Influences on mood & behavior
  - Limbic system & behavior
  - The gut's enteric nervous system uses and produces over 30 neurotransmitters

HOW?

- It achieves this diversity of action through unique anatomical features that provide it with a massive surface area, a diversity of cell types, and a complex neural network to coordinate these functions.

Gut associated lymphoid tissue



Next…
How we shape our gut microbiome

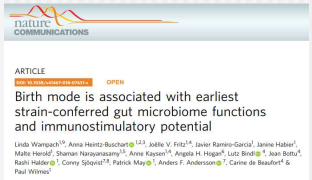
- Implications for your daily practice
- In your history
  - Method of delivery (C section vs vaginal)
  - Use of probiotics/supplements
  - Diet
  - # of antibiotic exposures
    = Increased risk of Asthma, CFS, IBD

Shaping our gut microbiome

- Kissing for 10 seconds transfers an average of 80 million bacteria
  - Couples who reported they kissed more often ended up having more similar microbiota than less-frequent kissers
  - Microbiome, 2014, Vol 2:41
- BM= loss of 1/3 of microbiome
  - Probiotics critical for diarrhea pts
  - Sender, et.al. 2016

Cesarean Sections and the Microbiome

- Babies acquire their founding bacterial populations from their mothers while passing through the vagina at birth
- Some parents will 'rub-down' babies born via C-section with the mother vaginal secretions
  - Blaser; Nature, 2011
  - Vol 476


nature COMMUNICATIONS

ARTICLE

OPEN

Birth mode is associated with earliest strain-conferred gut microbiome functions and immunostimulatory potential

Cesarean Section Delivery Increases Child's Risk of:

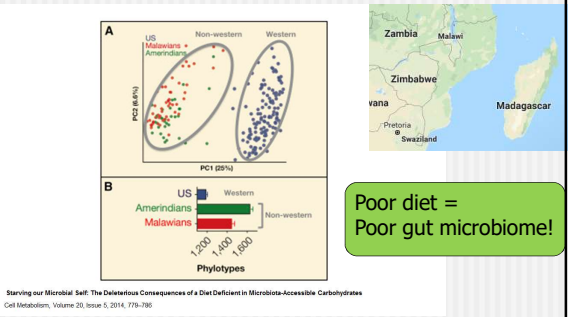
- Allergic Rhinitis
- Asthma
- Celiac Disease
- Type I Diabetes
- Inflammatory Bowel Disease

PLoS Biol, 2013, Vol 11(8): e1001631

Next, Depleting the microbiome

- When you see a patient, think about diet, medications, and supplements.
- **Are you depleting or supporting the microbiome?**
- Remember the new way of thinking!

The Western Microbiota is less diverse than Non-Western Populations



Starving our Microbial Self: The Deleterious Consequences of a Diet Deficient in Microbiota-Accessible Carbohydrates
Cell Metabolism, Volume 20, Issue 5, 2014, 779–786

Poor diet =
Poor gut microbiome!

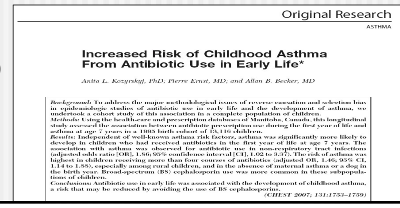
Antibiotic overuse:
Kills of beneficial bacteria

- Our normal, symbiotic microbiome does not recover completely from antibiotics
- Can be replaced in the long term by resistant organisms
- Overuse of antibiotics could be fueling the dramatic increase in conditions such as obesity, type 1 diabetes, inflammatory bowel disease, allergies and asthma, which have more than doubled in many populations

Blaser; Nature, Vol 476: 393-394

Childhood asthma

- Independent of known asthma risk factors, asthma was significantly more likely to develop by age 7 in children who had received abx in the first year of life.
  - Chest, Vol 131 1753-1759

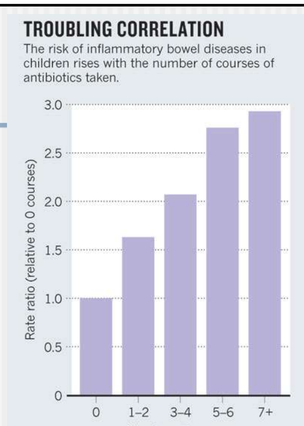


Original Research
ASTHMA

Increased Risk of Childhood Asthma From Antibiotic Use in Early Life*

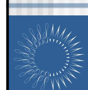
Anita L. Kozyrskyj, PhD; Pierre Ernst, MD; and Allan B. Becker, MD

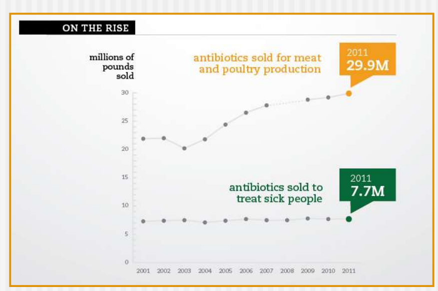
Background: To address the major methodological issues of reverse causation and selection bias in epidemiologic studies of antibiotic use in early life and the development of asthma, we undertook a cohort study of this association in a complete population of children.
Methods: Using the health-care and prescription databases of Manitoba, Canada, this longitudinal study assessed the association between antibiotic prescription use during the first year of life and asthma at age 7 years in a 1995 birth cohort of 13,116 children.
Results: Independent of well-known asthma risk factors, asthma was significantly more likely to develop in children who had received antibiotics in the first year of life at age 7 years. The association with asthma was observed for antibiotic use in non-respiratory tract infections (adjusted odds ratio [OR], 1.86; 95% confidence interval [CI], 1.02 to 3.37). The risk of asthma was highest in children receiving more than four courses of antibiotics (adjusted OR, 1.46; 95% CI, 1.14 to 1.88), especially among rural children, and in the absence of maternal asthma or a dog in the birth year. Broad-spectrum (BS) cephalosporin use was more common in these subpopulations of children.
Conclusions: Antibiotic use in early life was associated with the development of childhood asthma, a risk that may be reduced by avoiding the use of BS cephalosporins.
(CHEST 2007; 131:1753–1759)



Blaser; Nature, 2011, Vol 476: 393-394

Antibiotic use
- 40% of adults
- 70% of all children in the U.S. take antibiotics every year (CDC)





pewtrusts.org/en/multimedia/data-visualizations/2013

PPI Problems

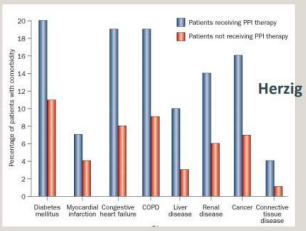
Proton Pump Inhibitor Usage and the Risk of Myocardial Infarction in the General Population

Nigam H. Shah, Paea LePendu, Anna Bauer-Mehren, Yohannes T. Ghebremariam, Srinivasan V. Iyer, Jake Marcus, Kevin T. Nead, John P. Cooke, Nicholas J. Leeper

Published: June 10, 2015 • https://doi.org/10.1371/journal.pone.0124653

PPI-
-40 & 50 y/o M w hip Fx
-MC cause of Acute interstitial nephritis
-Higher risk of death from MI after age 50
-Mineral deficiency
-Diarrhea
-Cdiff
-Memory loss (terrible w a statin!)


Possible Increased Risk of Bone Fractures With Certain Antacid Drugs



Herzig SJ et al. *JAMA* 2009

Leontiadis GI et al. *Curr Treat Opt Gastroenterol* 2014

"Our quantitative RT-PCR results showed that gut dysbiosis was caused by PPI use, corroborating previous results obtained by metagenomic analysis."

Hojo, M., Asahara, T., Nagahara, A. et al. Gut Microbiota Composition Before and After Use of Proton Pump Inhibitors. Dig Dis Sci **63**, 2940–2949 (2018).

Next, Assessing the microbiome

- What can you do on a day to day basis?
- PE:
  - Thick white coated tongue
  - Abdominal distension/tympany
- Lab:
  - IgA
  - CRP
  - Stool culture
  - ? Advanced stool testing

Evaluating the gut microbiome

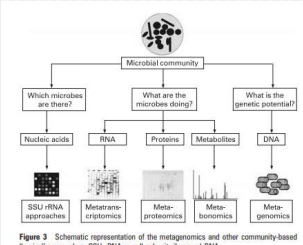


Figure 3 Schematic representation of the metagenomics and other community-based "omics" approaches. SSU rRNA, small subunit ribosomal RNA.

Gut 2008;**57**:1605–1615. doi:10.1136/gut.2007.133603

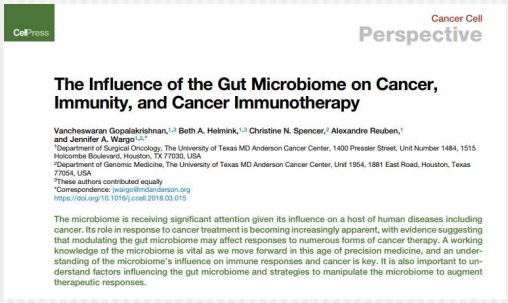
Physical exam

- Oral exam
  - Geographic
  - Thrush
- Abdominal exam
- Rectal exam

Gut & Immune function

- Preserve GALT function
- Recognize, treat, and manage SIBO and dysbiosis
- SIMPLEST TESTS FOR GUT HEALTH:
  - IgA
  - CRP
  - H Pylori testing (breath test or serum IgG/IgM/IgA)
- Advanced testing:
  - SIBO testing

Role in Cancer therapy



CellPress

Cancer Cell

Perspective

The Influence of the Gut Microbiome on Cancer, Immunity, and Cancer Immunotherapy

Vancheswaran Gopalakrishnan,[1,2] Beth A. Helmink,[1,2] Christine N. Spencer,[2] Alexandre Reuben,[1] and Jennifer A. Wargo[1,2,*]
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[2]Department of Genomic Medicine, The University of Texas MD Anderson Cancer Center, Unit 1954, 1881 East Road, Houston, Texas 77054, USA
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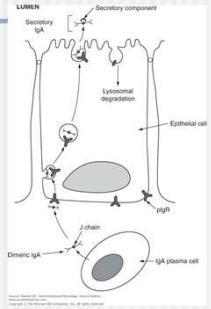
The microbiome is receiving significant attention given its influence on a host of human diseases including cancer. Its role in response to cancer treatment is becoming increasingly apparent, with evidence suggesting that modulating the gut microbiome may affect responses to numerous forms of cancer therapy. A working knowledge of the microbiome is vital as we move forward in this age of precision medicine, and an understanding of the microbiome's influence on immune responses and cancer is key. It is also important to understand factors influencing the gut microbiome and strategies to manipulate the microbiome to augment therapeutic responses.

Enhance IgA

Most abundant antibody in Mucosal secretions!

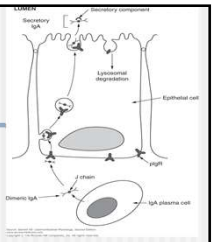
Key to gut luminal health



Gastrointestinal Physiology, 2e, 2014

Gutzeit C, Magri G, Cerutti A. Intestinal IgA production and its role in host-microbe interaction. *Immunol Rev*. 2014;260(1):76–85. doi:10.1111/imr.12189

IgA



- IgA is a marker of gut mucosal/immune health
- IgA is secreted across the intestinal epithelium.

Gastrointestinal Physiology, 2e, 2014

Low Serum IgA levels

- Autoimmune
- Celiac
- Asthma (wow!)
- Allergies
- Malabsorption
- Vitamin/mineral deficiencies

Glutamine improves IgA levels!

Stool testing

- Basic cultures
- Commercial gut microbiome/SIBO testing – many varieties
  - Nutra Hacker (23andMe)
  - Genovia CDSA

www.nature.com/scientificreports

SCIENTIFIC REPORTS

OPEN

Oropharyngeal microbiome evaluation highlights *Neisseria* abundance in active celiac patients

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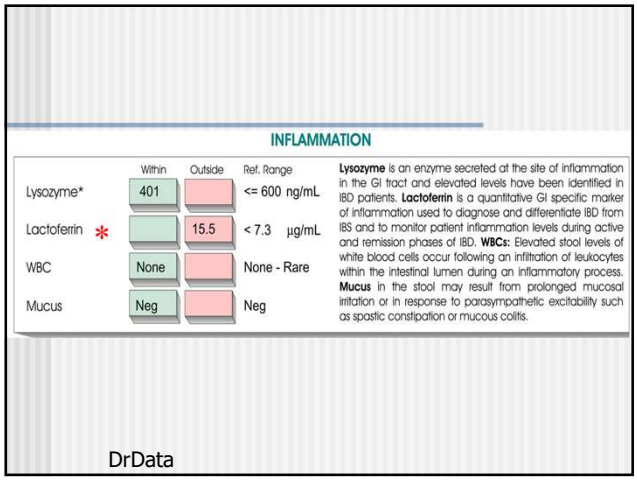
We previously profiled duodenal microbiome in active (a-), gluten-free diet (GFD) celiac disease (CD) patients and controls finding higher levels of the Proteobacterium *Neisseria flavescens* in a-CD patients than in the other two groups. Here, we investigate the oropharyngeal microbiome in CD patients and controls to evaluate whether this niche share microbial composition with the duodenum. We characterized by 16S rRNA gene sequencing the oropharyngeal microbiome in 14 a-CD, 22 GFD patients and 20 controls. Bacteroidetes, Proteobacteria and Firmicutes differed significantly between the three groups. In particular, Proteobacteria abounded in a-CD and *Neisseria* species mostly accounted for this abundance ($p < 0.001$), whereas Bacteroidetes were more present in control and GFD microbiomes. Culture-based oropharyngeal microbiota analysis confirmed the greater abundance of Proteobacteria and of *Neisseria* species in a-CD. Microbial functions prediction indicated a greater metabolic potential for degradation of aminoacids, lipids and ketone bodies in a-CD microbiome than in control and GFD microbiomes, in which polysaccharide metabolism predominated. Our results suggest a continuum of a-CD microbial composition from mouth to duodenum. We may speculate that microbiome characterization in the oropharynx, which is a less invasive sampling than the duodenum, could contribute to investigate the role of dysbiosis in CD pathogenesis.



Next, Supporting the Microbiome

NIH Human Microbiome Project

- Get adequate sleep
- Exercise frequently
- Eat a wide variety of fresh plant foods
- Minimize:
  - Refined carbohydrates
  - NSAIDs
  - Alcohol
  - Antibiotics– especially in kids!
    - Theory – esp. in kids born via C-section!

Supporting The Microbiome

NIH Human Microbiome Project

- Consume prebiotic fibers:
  - Pectin, inulin, fructo-oligosaccharides, asparagus, garlic, onions, leeks, bananas
  - When gut microbiota ferment fiber, they release SCFA which are used for gut microbial fuel. When your gut lining isn't maintained by your gut bacteria, its barrier function is compromised.
- Eat fermented foods:
  - Kombucha, fresh sauerkraut, kimchi
- Take probiotics

Restoring the gut microbiome

- FMT
  - directly change the recipient's gut microbiome to normalize the composition and gain a therapeutic benefit.
  - Hx traced back to the 4th century
  - 2013 FDA approval for recurrent and refractory *C diff* Since then, the range of FMT applications extended rapidly and broadly not only in gastrointestinal disorders, but also in extra-gastrointestinal diseases

Restoring the microbiome

Research

JAMA | Original Investigation

Effect of Oral Capsule– vs Colonoscopy-Delivered Fecal Microbiota Transplantation on Recurrent *Clostridium difficile* Infection
A Randomized Clinical Trial

1986 JAMA November 28, 2017 Volume 318, Number 20

Antibiotic alternative?

Case report

Fecal microbiota transplantation as a potential way to eradicate multiresistant microorganisms

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ABSTRACT

Multiresistant microorganism infection often can produce a life-threatening situation. We report two cases in which fecal microbiota transplantation used for the treatment of recurrent *Clostridium difficile* infection were effective in eradicating colonization by carbapenemase-producing *Enterobacteriaceae*. The presented cases illustrate the potential benefit of fecal microbiota transplantation in resolution of asymptomatic carrier states of multiresistant microorganisms, suggesting the need for further investigations with a view to their applicability in this area.

N=2

Bovine Immunoglobulin

- Binder
- Great for diarrhea
- Upregulates IgA
- Can mix w Xifaxin AND/OR GLUTAMINE- great for brain fog!

L-Glutamine

- Essential for gut microbiome support
- Monitor IgA levels
- Most abundant amino acid in the body and is necessary for the maintenance of many metabolic functions.
  - Under situations of stress, physiological demands increase, triggering a need for glutamine supplementation.
  - Surgical nutrition- glutamine is very popular!

Picking a good probiotic

- What will the patient take/afford
- Prevention of antibiotic-associated D:
  - *Saccharomyces boulardii* I-745
  - *Lactobacillus acidophilus*

Choosing an appropriate probiotic product for your patient: An evidence-based practical guide

Jason C. Sniffen, Lynne V. McFarland, Charlesnika T. Evans, Ellie J. C. Goldstein

Published: December 26, 2018 • https://doi.org/10.1371/journal.pone.0209205

Best psychobiotics?

- Bifidobacterium longum is present in the gut.
  - Show to help depression, reduces cortisol, address obsessions, compulsions, paranoia, anxiety.
- GABA: main inhibitory and relaxing neurotransmitter in the CNS
  - studies suggest that lactobacillus rhamnosus may reduce anxiety by changing the expression of GABA receptors

Best psychobiotics?

- Lactobacillus plantarum given to patients with IBS
  - significantly reduced their anxiety and improved their quality of life

IMPORTANT –
Dose your probiotics in the BILLIONS! Why?

Probiotic 'prescription'

- Look for probiotics in the BILLIONS!

Lactobacillus acidophilus (LA-14)	12 Billion CFU*	**
Lactobacillus acidophilus (LA-1)	10 Billion CFU*	**
Bifidobacterium lactis (BL-04)	15 Billion CFU*	**
Bifidobacterium lactis (Bi-07)	7 Billion CFU*	**
Lactobacillus paracasei (LPC-37)	3 Billion CFU*	**
Lactobacillus rhamnosus (HN001)	3 Billion CFU*	**

** Daily Value (DV) not established

Proprietary Blend — 409 mg (50 Billion CFU†)
Lactobacillus acidophilus La-14®
Bifidobacterium longum BI-05™
Lactobacillus plantarum Lp-115®

Masters Formula & Xymogen
Not an endorsement

GI Healing

- Rifaximin
  - SIBO/IBS-D
- Aloe Leaf extract
  - Heals epithelial tissue
- Licorice root extract
  - Anti-inflammatory

Question1

Studies by Blaser (2011) & Becattini (2016) suggest that antibiotic use stresses our gut microbiome and triggers an increase incidence of

A. Obesity & type 1 diabetes
B. Long term viral illnesses
C. Melanomas & skin cancers
D. Kidney stones & UTIs

Question 2

- Which of the following is TRUE regarding our gut microbiome?
  A. A gut populated with *Firmicutes* is associated with a **lower BMI.**
  B. Children born by C-section have a **lower** rate of allergies and metabolic diseases.
  C. Long term PPIs **do not** alter the gut microbiome.
  D. Bacteria populating the gut microbiota rarely secrete **large amounts** of amyloids and lipopolysaccharides.

Question 3

- Which of the following IS **NOT EFFECTIVE** in improving the health of the gut microbiome?
  A. Short Chain Fatty acids- Butyrate
  B. Serum derived bovine immunoglobulin
  C. Diets rich in lean red meats
  D. Prebiotics (oligosaccharides)

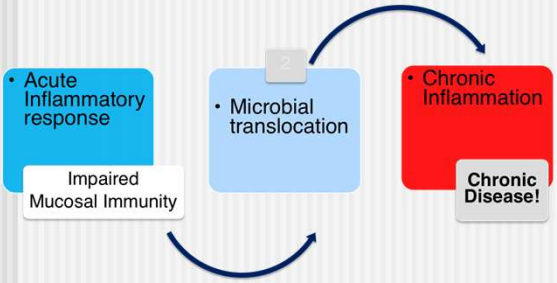
Take home points…

- How can we incorporate the gut microbiome knowledge into everyday practice ?
  - Remember the gut microbiome affects EVERYTHING!
  - Minimize antibiotics
    - Especially in kids!
  - Minimize PPIs
  - Suggest prebiotics/probiotics/psychobiotics
  - Aggressively battle constipation
  - Make a healthy diet a “Rx”. Use your nutritionist

FINAL REMINDER:

Chronic gut inflammation

Inflammation changes the gut Microbiota



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Thank you!

- Remember you are not alone & you are what you eat!
- I hope you come to share my excitement for the gut microbiome!
- Any questions or comments?
- Jerry Simons
- **Gerald.simons@stonybrook.edu**

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