Guarding the Microbiome in Women's Health

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- I have no disclosures or conflicts of interest

Overview

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The Microbiome – Characteristics & Functions

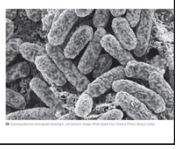
Intestinal Barrier Function

Microbiome and Immune, CNS, Metabolic and Detoxification systems

Early development of the human microbiome- pregnancy, birth, infancy

Diversity and Extinction

KEY CONCEPTS



Early stages of research

-
  - Thousands of species, all interacting with each other and with the host
  - Vast individual variation in MB composition
  - Much research in animal models
  - Human research mostly descriptive
  - Correlation vs causation

Could a deteriorated gut microbiota (MB) be at the root of western diseases

- **microbial cells that work in harmony**
- **Intestinal microbiome as "control center" for human biology, wired into immune system, metabolism, brain**
- **Pregnancy & birth – key impact on health**

All disease begins in the gut

– Hippocrates

Sonnenburg & Sonnenburg 2014

THE INTESTINAL MICROBIOME

Characteristics of the Human Microbiome

- Abundance – trillions
  - 100x more bacterial genes than human genes
- Complexity and Diversity
  - ~ 1000 species per individual human gut
- Variability
  - Distinct by body site, by individual human,
- Stable in adults, unstable in infants/children
- Microbial cross-talk and cross-feeding
- Interface of the self and environment

MAC's – Microbiota Accessible Carbohydrates

1) Plant-derived
   - dietary fiber, complex CHO
2) Animal-derived
   - Cartilage, collagen, gelatin –
   - Glucosaminoglycan and N-linked glycans 1
3) Synthesized by other bacteria
   - (food-born or supplement e.g fermented food or probiotics)

Vast variation of types of MACs

Each species of MB has a specialized collection of enzymes to break down MACs

Typical human MB w 1000 species has 60,000 types of enzymes

1) Koropatkin, Cameron & Martens 2012; 2) Sonnenburg ED & JL Sonnenburg, 2014

Dietary MACs converted to Short Chain Fatty Acids (SCFA)

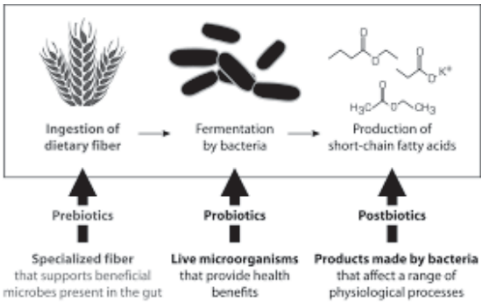
- Fermentation end-products absorbed into circulation
  - Butyrate, Proprionate, Acetate, others
- Diet alters ratios and concentrations of SCFA

Arpaia et al 2013; Furusawa et al 2013; Smith et al 2013; Trompette et al 2014; De Vadder 2014, Neyrinck et al 2012

Short-chain fatty acids (SCF)

- Energy source for colonic cells
- POTENT ANTI-INFLAMMATORY EFFECTS
  - Increase number of T-reg cells, calm inflammation
  - Modulates multiple inflammatory pathways
  - Influence immune cells precursors in bone marrow
- Regulate metabolism
  - Influences gluconeogenesis, improve metabolic profiles and insulin sensitivity, protects against obesity
- Neuroprotective, decrease anxiety/depression, reduce appetite

Lynch SV (2016). Annals Amer Thoracic Soc, 13 Suppl 1, S51-S54. Hamer et al (2008)

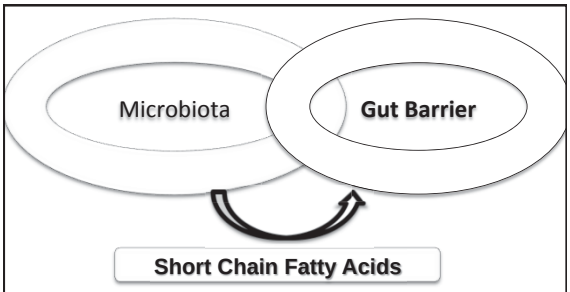


https://www.thinkbiome.com/prebiotics/

Microbiome Functions

1) Preserve barrier function of gut mucosa
   - SCFA butyrate energy source for colonic epihelium
2) Immunomodulation
3) Interact with CNS
4) Regulate metabolic function
5) Detoxification of drugs, hormones, toxins
6) Mineral absorption **(?add this?)**

Alcock 2014



Intestinal Barrier Function

Intestinal Tight Junctions

Single layer of cells

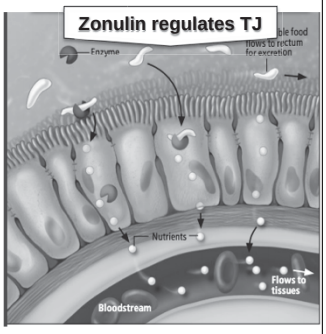
Barrier between gut microbiota and host

Dynamic, tightly controls antigen trafficking

Dictates balance btwn tolerance and immune response

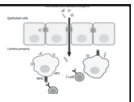
Bacterial pathogens disrupt

Dysfx = inflammation



Fasano 2009, 2011, König et al (2016). Clinical translational gastroenterology 7(10) e196-e196.

Intestinal Permeability and Inflammation



Translocation

Stimulation of TLR on innate immune cells

Systemic inflammation

LPS activates toll-like receptors w

production inflammatory mediators that are considered key in development of insulin resistance and a chronic inflammatory state

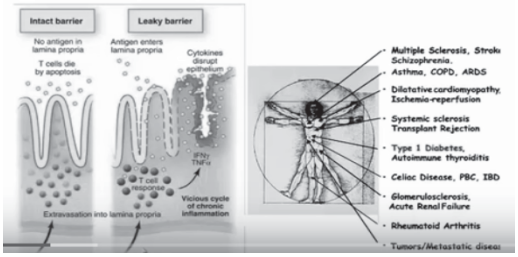
Associated with:

- Autoimmune diseases (type 1 Diabetes, RA, MS, IBD)
- Diseases of chronic inflammation (IBS, asthma, allergy, CFS, depression)

Intestinal Permeability and Disease

- Inflammatory bowel disease
- Celiac disease
- Multiple Sclerosis
- Rheumatoid arthritis
- Type 1 diabetes
- Asthma
- Necrotizing enterocolitis
- Mood disorders, cognition
- Autism Spectrum Disorders

Is impaired intestinal barrier a cause of disease or an epiphenomenon?



Fasano, A. (2012). Zonulin, regulation of tight junctions, and autoimmune diseases. Annals of the New York Academy of Sciences, 1258, 25-33.

Intestinal Barrier Permeability and Autoimmune Disease

- Leaky gut a necessary precursor to development of autoimmune disease
- Need three factors:
  - genetic susceptibility
  - environmental trigger
  - intestinal permeability –
- Must have all three

Sturgeon & Fasano (2016).Tissue barriers 4(4), e1251384-e1251384.

The two factors known to trigger excess Zonulin

- Intestinal dysbiosis
- Gliadin (in Gluten)

Leads to "inappropriate and uncontrolled antigen trafficking"
Production of pro-inflammatory cytokines
Breakdown of immune tolerance
Onset of chronic inflammatory disease, type determined by host genetics

THE MICROBIOME
AND
THE IMMUNE SYSTEM

Microbiome impact on immune system

- GALT
- Maintain tolerance to benign organism 1
- Regulate host defenses to infection 2
  - Modulates both innate and adaptive immunity, Resistance to GI infection, airway infection, systemic and CNS infection
- Mediates cancer development, progression and response to treatment 2
- Mediate inflammation – T-reg and T-effector cell activity

Thaiss et al 2016 535, 65-742) Brown, & Clarke (2017). , 150(1), 1-6. 3) Pope et al. (2017) Translational Research, 179, 139-154.

Stress response
Mood
Cognition
Behavior

THE NERVOUS SYSTEM

The New York Times

Can the Bacteria in Your Gut Explain Your Mood?

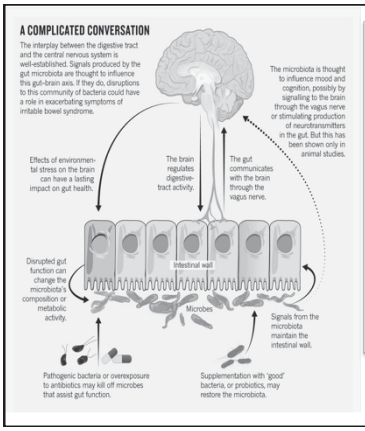
The rich array of microbiota in our intestines can tell us more than you might think.

By PETER ANDREY SMITH JUNE 23, 2015

THE Mind-Gut CONNECTION

How the Hidden Conversation Within Our Bodies Impacts Our Mood, Our Choices, and Our Overall Health

Emeran Mayer, MD



The Gut-Brain Axis

MB produces NTs

Vagus nerve

Dysbiosis

Eisenstein M 2016

Mental health and Cognition

- Alterations in MB composition implicated in a wide range of neurologic and psychiatric conditions,
  - including depression, anxiety, chronic pain,
- Prebiotic (GOS) reduces waking cortisol response and alters emotional bias towards the negative in healthy adults
- Fiber intake improves deep sleep

Matthew R, Hillmire et al Psych Res 2015; St-Onge MP et al J Clinc Sleep Med 2016; Schmidt, Cohen, harmer 2014)

CNS effects of probiotics

- Multiple sclerosis:[1]
  - RCT, favorable effects on disability scale, mental health parameters, inflammatory factors, markers of insulin resistance
- Improved cognitive status in Alzheimer's Ds [2]
- Improved scores on depression/anxiety scales
  - Systematic review, 10 articles 2016
- In healthy women, affect activity of brain regions that control central processing of emotion and sensation , Decreased signs of psychological stress and improved task function, compared w placebo

1) Kouchaki, Tamtaji et al 2016; 2) Akbari, Asemi et al 2016; 3) Pirbagiou et al 2016

Implications for Pregnancy/ Offspring

Gut–brain axis: how the microbiome influences anxiety and depression

Jane A. Foster and Karen-Anne McVey Neufeld

Gut microbiota in early life play a role in programming the HPA axis and stress reactivity over the lifespan

Restoration of microbiome w probiotic *L reuteri* in mice with autism-like behavior and decreased oxytocin levels completely restored oxytocin levels and reversed social deficits

Buffington, S. A., Di Prisco, G. V., Auchtung, T. A., Ajami, N. J., Petrosino, J. F., & Costa Mattioli, M. (2016). Microbial Reconstitution Reverses Maternal Diet-Induced Social and Synaptic Deficits in Offspring. Cell, 165(7), 1762-1775.

Eating Behavior

- Gut Microbes may:
  - Generate cravings for foods that nourish them or suppress their competitors
  - Induce dysphoria until we eat foods that enhance their fitness
- Mechanisms:
  - Produce hormones that alter hunger and satiety
    - Structurally similar to ghrelin and leptin
  - Alter taste receptors

Alcock, J., Maley, C., Aktipis, C. A. (2014). Is eating behavior manipulated by the gastrointestinal microbiota? Evolutionary pressures and potential mechanisms. BioEssays, 36(10), 940-949.

Obesity
Diabetes

METABOLIC FUNCTION

Dysbiosis mechanism of impact on Metabolism

- Increase energy harvest from food
- Increased gut permeability/translocation
- Inflammation
- Altered production of satiety hormones
- Disturbed immune and metabolic signaling

Causality of small and large intestinal microbiota in weight regulation and insulin resistance

Torsten P.M. Scheithauer[1, 2, 3], Geesje M. Dallinga-Thie[1], Willem M. de Vos[4], Max Nieuwdor 2016,

Obesity – Microbiome Associations

- MB of obese humans are less diverse than that of their lean twins
- Obese humans w lower MB diversity gain more weight over time
- Lean mice inoculated with MB from obese mice or obese humans become obese
- Some probiotics reduce fat mass, improve insulin sensitivity, decrease food intake (VSL#3 in mice)
- Yogurt was the food most associated with reduced weight gain over 20 years in Nurses Health Study

Alcock, J., Maley, C., Aktipis, C. A. (2014); Le Chatelier et al 2013;

Obesity – Probiotics & Prebiotics

- 9 of 10 cohort studies show inverse association between yogurt consumption and risk of overweight/obesity
- Scarce evidence for probiotics:
  - Meta-analysis 13 RCTs
  - L gasseri and L plantarum consistent anti-obesity effects, but minimal (1 kg wt loss over 3 mo)

Sayon et al. (2017). : Int Rev Jo, 8(1), 146S-154S; de Clercq et al. 2016. Adv Nutr 15;7(6):1080-1089; Million et al (2012) 53(2), 100-108. Nova et al. (2016). Nutri in clin pract, 31(3), 387-400

Metabolic Syndrome / Diabetes

- Insulin sensitivity in humans improved by transferring gut MB from lean donors to those w metabolic syndrome

The post-dieting microbiome

- With weight loss, all metabolic and physiologic parameters normalize EXCEPT microbiome
- Can precisely predict wt regain by look at composition of microbiome
- The post-dieting microbiome rapidly degrades two dietary flavonoids key for burning fat and preventing weight re-gain
- Supplementing w these flavonoids prevented weight re-gain
- Apigenin and narengenin
  - Chamomile, parsley, citrus, celery, fennel, cilantro
  - Other effects: regulate tight junctions, decrease inflammation, neuro-modulation

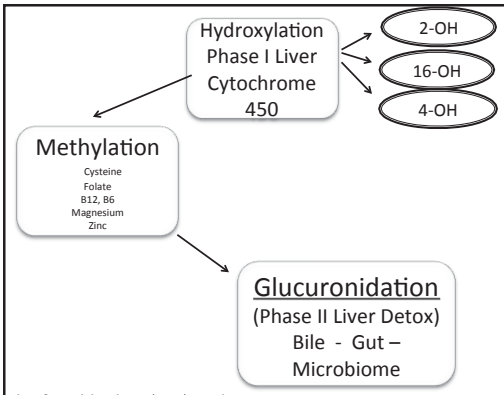
Thaiss, Itav et al 2016

ESTROGEN METABOLISM

Estrogen and the Microbiome

- Dietary phytoestrogens metabolized by MB
- Production of estrogen-metabolizing enzymes which increase intestinal reabsorption of estrogens, increasing estrogenic load
- Ratio of estrogen metabolites in women's urine directly correlated w MB composition and diversity
  - Diverse MB assoc w favorable ratio estrogen metabolites
- Connections of dysbiosis and antibiotic use with increased Breast Cancer risk via higher levels of circulating estrogens

Chen & Madak Erdogan (2016).Trends endocrin metabol, 27(11), 752-755; Yang et al (2016). Breast Cancer, Oct 5 2016 epub; Fuhrman et al. 2014. Jo Clin Endocrin & Metab.



Chen & Madak Erdogan (2016).Trends endocrin metabol, 27(11), 752-755;

ENVIRONMENTAL INFLUENCES ON THE MICROBIOTA

DIVERSITY AND EXTINCTION

Low microbiome ***diversity*** associated with disease in humans

- People w more MB diversity are leaner and have better metabolic function
- Low diversity: Increased adiposity, insulin resistance, LDL and markers of inflammation
- Associated with several autoimmune disorders

1) Cotillard et al 2013, Le Chatelier 2013; Yan Yang, Long Gang, 2014

The extinction inside our guts

MONDAY MAY 23, 2016

By Erica Sonnenburg and Justin Sonnenburg

- Our guts resemble a "landscape in decline"
- Gut ecosystem is malleable but also fragile.
- Lost species may never be recovered

Low-Fiber Diets Cause Waves of Extinction in the Gut

Sonnenburg & Sonnenburg (2014). , 20(5), 779-786.

Eating for Two: Diet shapes the MB

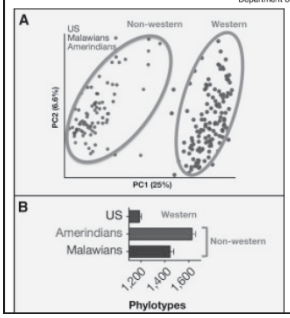
- Diet rapidly and reproducibly alters human MB
  - Eating a completely animal vs plant based diet sort term dramatically alters composition of MB [1]
  - Volunteers fed successively w different control diets over 10 weeks-blooms of specific bacterial groups occurred rapidly after each diet change [2]
  - Controlled feeding of human subjects high vs low fiber/fat changes in MB within 24 h [3]

1) David, Maurice Carmody et al 2014 Nature; 2) Walker, Ince et al 2011; Wu, Chen et al 2011

Starving our Microbial Self: The Deleterious Consequences of a Diet Deficient in Microbiota-Accessible Carbohydrates

Cell Metabolism 2014

Erica D. Sonnenburg[1] and Justin L. Sonnenburg[1,*]
[1]Department of Microbiology and Immunology, Stanford University School of Medicine,

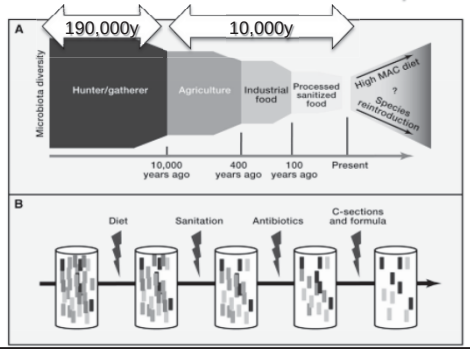


Non-modern societies – MB with greater diversity and different composition

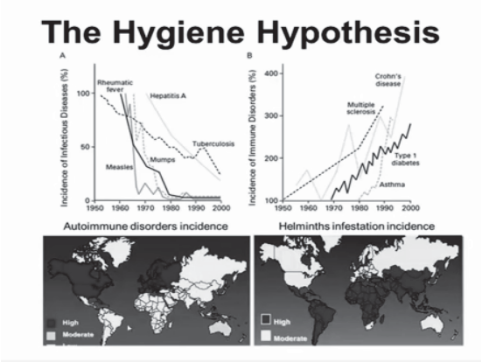
MACs

- Average daily fiber intake USA: 15 grams
- Recommended intake: 35 grams
- Intake of hunter-gatherers: 150 grams

The Multiple-Hit Hypotheses for how the MB of Industrialized Societies has Lost Diversity over Time



Sonnenburg, E. D., Sonnenburg, J. L. (2014). Starving our microbial self:. Cell metabolism, 20(5), 779-786.



Diet-induced extinctions in the gut microbiota compound over generations

Erica D. Sonnenburg[1]*, Samuel A. Smits[1]*, Mikhail Tikhonov[2,3], Steven K. Higginbottom[1], Ned S. Wingreen[4,5] & Justin L. Sonnenburg[1]

- Low fiber diet over several generations results in progressive loss of diversity
- Bacterial species may be irreversibly lost in the individual AND IN THEIR OFFSPRING
- Recovery requires BOTH replacement of the missing species AND dietary MAC

Sonnenburg et al (2016). , 529(7585), 212-215.

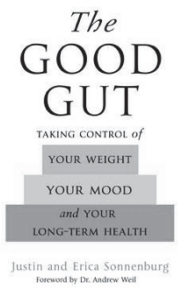
Severe Consequences of low MB diversity

- Starving microbes begin to digest the mucus lining of the gut and eventually the epithelial lining of the gut itself, triggering immune reactions and chronic inflammation
- Lower diversity-less ability to resist opportunistic pathogens like *difficile* or *Salmonella*
- Connected with obesity, metabolic disorder, IBD

Impaired gut barrier integrity

The solution: commit to a dietary fiber intake that "borders on the comical"

NY Mag Profile of the Sonnenburg family



Fiber:

- Abundance
- Variety
  - Many types of MACs
  - Doing a lot of just one type can drive diversity <u>down</u> instead of up

Effects of Dietary Fiber

- Restores microbiome diversity
- Improve quality of sleep
  - Higher fiber diet = better sleep quality
  - Higher simple carb intake – more nighttime awakening
- Decreases estrogen levels
- Decrease visceral fat
  - For every additional 10 g/d soluble fiber there was 3.7% les visceral fat over five years.

St-onge MP, Roberts et al 2016; Deehan & Walter 2016; Hairston et al (2012). 20(2), 421-427.

<u>Replace</u>

Probiotics
Fermented Foods

<u>Replenish</u>

Fiber
Prebiotics

<u>Remove</u>

Toxins Triggers

IMPROVING THE MICROBIOME

Fermentation

- CLA fatty acids are increased
- Flavonoids become biologically active
- Undesirable food constituents are decreased (phytate)
- Synthesis of new nutritive/bioactive compounds
- Increased bioavailability of nutrients
- Anti-inflammatory, gut-protective compounds
- B-vitamins: folate, riboflain, B12
- Compounds with neuro-transmitter-like and neuro-modulatory functions
- Strong assoc w weight mainenance
- Yogurt: reduced risk CVD, DM, overall mortality

Karczewsk, Troost et al *Physiol Liver Physiol* 2010; 298:G851-859;
Marco et al (2016). *Current opinion biotech*, 44, 94-102.

KimChi

- Anti-obesity, anti-constipation, colorectal health promotion, cholersterol reduction, fibrolytic effects, anti-oxidant, anti-aging properties, brain health, immune function promotion, skin health, inhibits H pylori,
- Obese women who added KimChi to diet had more weight loss than w placebo
- In pre-diabetic women dietary Kimchi increases insulin sensitivity and improved BP, vs placebo

Patra JK et al 2016; An SY et al 2013; Kimchi review; Ahn SJ 20007

A Review of Fermented Foods with Beneficial Effects on Brain and Cognitive Function

- Fermented dairy, soy, rice, roots and tubers, vegetables, fruits
- Modulation of neuro function an of HPA axis
- Contains compounds with neurotransmitter-like functions
- Fermented dairy product for 4 weeks decreases brain activity r/t social anxiety compared w a placebo group
- Fermented food intake in 700 college students correlated w decreased social anxiety in those with neuroticism, independent of exercise and fruit/veg intake.

Kim et al (2016). , 21(4), 297-309; Tillische 2013; (Hilimire DeVylder & Forestell 2015)

Prebiotics

Non-digestible compound,

- Selectively fermented by gut microbes
- Modulate composition and/ or activity of the gut MB
- Confers a health benefit on the host.
  - Fructooligosaccharides (FOS)
  - Galactooligosaccharides (GOS)
  - Inulin, Resistant starch
  - Beta-glucan, Pectin
  - Others

Probiotics

- Live microorganisms, when delivered in adequate amounts, confer a health benefit on the host
- Transient, don't attach or colonize, no impact on composition of MB

Steinert et al. (2016). *Clin Nutr* 70(12), 1348-1353;
Sánchez et al (2017). *Molecular nutrition & food research*, 61(1)

PREBIOTICS

Prebiotic Mechanism of action

- Increase production of beneficial SCFAs such as butyrate
- Create more acidic environment
  - Enhanced generation of enterocytes
  - Improved colonic surface area
  - Greater capacity to absorb minerals
- Modulate multiple neurotransmitters
- Modulate stress hormones

Dietary Sources of Prebiotics
(Microbiota Accessible Carbohydrates)

- Inulin
  - Dandelion root
  - Chicory root
  - Burdock root
  - Jerusalem artichokes
  - Garlic
  - Leeks, onions
  - Asparagus
- Arabinogalactin:
  - Carrots, radish, pears, tomatos, coconut
- Resistant Starch
  - Tubers, roots, legumes,beans, nuts
  - Cold rice, cold potato
- Oligosaccharides FOS GOS XOS
  - Onion leek endive oats, grains
- Pectin – avocado, fruit

Prebiotic effects – mood, glucose metabolism, bone

- Reduces waking cortisol and alters emotional bias toward the negative
  - Anxiolytic effects similar to that seen with SSRI
  - GOS galactooligosaccharide 5 g qd
- Prebiotic inulin improves markers of metabolic fx in women with Type 2 Diabetes
- Prebiotic inulin improves bone turnover markers and BMD in adolescent girls

Schmidt, K., Cowen, P. J., Harmer,. (2015); Aliasgharzadeh et al 2015; Weaver CM 2015

Inulin (Fructans)

- Bifidogenic. Inexpensive
- Enhance mineral absorption
- Dozens of studies on infants/children for constipation, diarrhea, decrease infection, allergy
- Improve glucose control in T2DM
  - Meta-anlaysis, 20 RCTs w 600 participants
- Reduce inflammatory markers in overweight adults
  - Ten trials, n=500, alone or w GOS
- Present in many vegetables

Fernandes et al (2016). *Clinical nutrition*; Liu et al (2017).. *Europ Jo Clin Nutri*, 71(1), 9-20; Shoaib et al. (2016). CHO polymers, 147, 444-54; Firmansyah et al (2016). *Asia Pac Jo Clin Nutri,* 25(4), 652-675.

PROBIOTICS

Systematic review: probiotics in the management of lower gastrointestinal symptoms in clinical practice -- an evidence-based international guide.

Hungin AP[1], Mulligan C, Pot B, Whorwell P, Agréus L, Fracasso P, Lionis C, Mendive J, Philippart de Foy

Effectiveness of probiotics in irritable bowel syndrome: Updated systematic review with meta-analysis.

Didari T[1], Mozaffari S[1], Nikfar S[1], Abdollahi M[1].

- Benefits evident in IBS, Antibiotic-associated diarrhea, C difficile prevention/treamtent, traveler's diarrhea, children diarrhea

http://darwinian-medicine.com/probiotic-supplements-are-they-doing-you-more-harm-than-good/

Key points on Probiotics

- Effects are strain-specific
- Production methods and delivery matrices impact efficacy
- Effects depend on the host characeristics (existing gut microbiota, clinical condition, diet
- Difficult to accumulate a body of knowledge because varying strains, doses, routes, duration of treatment and selection criteria are used.

Areas of Abundant Research

Triennial Yale/Harvard Workshop on Probiotic Recommendations

- Childhood infectious diarrhea – treatment
- Prevention of antibiotic associated diarrhea
- Prevention and treatment of *difficile* disease
- Prevention and treatment of travelers diarrhea
- Irritable bowel syndrome
- Inflammatory bowel disease
- Eczema treatment/prevention
- Vaginitis/vaginosis

Recommendations for Probiotic Use—2015 Update
Proceedings and Consensus Opinion
Martin H. Floch, MD, W. Allan Walker, MD,†,‡*

C difficile Prevention/Probiotics

- 45,000 adults pts on abx /BioK+ simultaneously
  - *acidophilis CL1285*, *L casei LBC80R and L rhamnosus CLR2*
- 39% reduction in cases of C difficile
  - Incidence of CDI decreased from 18 cases per 10,000 patient-days to 2.3 cases per 10,000 patient-days
- Other study: two cap vs 1 cap/day
  - 24% w placebo; 10% w 1cap/d and 1.2% w 2 cap/d
- Several meta-analyses have found it effective

Maziade PJ et al 2015; Gao XW et al 2010; Goldenberg JZ et al 2013; Johnson Maziade et al 2012; Johnston BC et al 2012

Probiotic Bacterial and Fungal Strains: Claims with Evidence.

Szajewska H[1], Konarska Z, Kołodziej M.

Lactobacillus rhamnosus GG

- Acute gastroenteritis Rx
  - (11 RCTs)
- Prevention of AAD
  - (10 RCTs)
- Prevention of nosocomial diarrhea
- Prevention of URI in children in day care

Saccharomyces boulardii

- Acute gastroenteritis Rx
  - (20 RCTs)
- Prevention of AAD
  - (21 RCTs)
- Prevention of *C dificile*
- Travelers diarrhea
- IBS

Commercial products easily available

Probiotics – infants- *Reuteri DSM 17938*

- Cesarean infants developed a microbiome more similar to that found after VB
- Infant colic in breast-fed infants
- Mgmt of acute gastroenteritis
- Reduces incidence of diarrhea in children in day care centers
- Mice w autism-like behavior: restored normal oxytocin levels and reversed behavioral deficits

Rodenas CL et al 2016, Chau, Lau, Greenberg et al 2015, Urbanska, Szajewska 2014; Buffington et al (2016). *Cell,* 165(7), 1762-1775

Choosing a probiotic

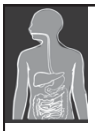
- Clinical evidence for the strain /condition
- **USP logo**
  -
- Strain names, colony count, expir. Dates
  - Labeled w "live content at *expiration* date" not at time of manufacture"
- At least 1 billion CFU (fewer for some strains)
- Ck company website: info about studies

Prebiotics

World Gastroenterology Org Practice Guideline on Prebiotics and Probiotics

Systematic review and meta-analyses for the specific condition

PROBIOTIC GUIDELINES



Clinical Guide to Probiotic Products

Available in the United States: 2016 Edition

Indications, Dosage Forms and Clinical Evidence to Date

International Scientific Association for Probiotics and Prebiotics

- Commercially available products w level of evidence rated
- Covers a range of GI disorders, oral health, glucose metabolism, childhood eczema, functional abdominal pain
- Website and app "USprobioticguide"

http://usprobioticguide.com/

GET IT ON Google Play | Download on the App Store

Probiotic cautions

- Immunosuppression
- Critical illness
- Structural heart disease
- Presence of central venous catheter

Szajewska, H., Konarska, Z., Kołodziej, M. (2016). Probiotic Bacterial and Fungal Strains: Claims with Evidence. Digestive diseases, 34(3), 251-259.

Kresser; Martin Blaser, Dethlefsen

Abx use causes permanent changes to the microbiota
This effect is transgenerational

THE HIGH PRICE OF ANTIBIOTIC USE – CAN OUR GUTS EVER RECOVER?

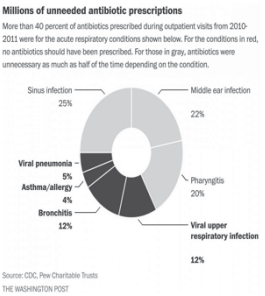
The Collateral Damage of Antibiotics

Prevalence of Inappropriate Antibiotic Prescriptions Among US Ambulatory Care Visits, 2010-20[illegible]

JAMA. 2016;315(17):1864-1873.

Katherine E. Fleming-Dutra, MD; Adam L. Hersh, MD, PhD; Daniel J. Shapiro; Monina Bartoces, PhD;

- A third of antibiotics given in the outpatient setting are unnecessary
- 40% of adults and 70% of children take one or more antibiotic every year
- JAMA 2016



Unwanted impact of antibiotics broader, more complex than previously known

- Abx use not only depletes Microbiota, also destroys intestinal epithelium
  - Impairs mitochondrial fx – epithelial cell death occurs
- Disrupts mucosal immunity
- Impacts a gene critical to communication between host an microbe

Morgun (2015). *Gut,* 64(11), 1732-1743
https://www.sciencedaily.com/releases/2015/02/150210212634.htm

Antibiotic-induced changes in MB linked to disease

- Obesity
- Allergies
- Colitis
- Inflammatory bowel disease
- *C-difficile* and *Salmonella* growth
- Disrupted glucose metabolism
- Depression, anxiety

13

Morgun (2015). *Gut,* 64(11), 1732-1743

Taking Antibiotics Can Change the Gut Microbiome for Up to a Year

- One-week courses of Clindamycin, Ciprofloxacin, Amoxicillin, Minocycline, placebo
- Clinda and cipro; dramatically decreased butyrate-producing bacteria
  - Butyrate lowers inflammation
- Broadest and Longest impact with Cipro
  - Decreases one-third of taxa (Dethlefsen 2008)

Zaura e al(2015).. *mBio*, 6(6), e01693-e01615. ;
http://www.theatlantic.com/health/archive/2015/11/taking-antibiotics-can-change-the-gut-microbiome-for-up-to-a-year/415875/

Profound Alterations of Intestinal Microbiota following a Single Dose of Clindamycin Results in Sustained Susceptibility to *Clostridium difficile*-Induced Colitis

- Single dose of Clindamycin
- Loss of 90% of normal flora lasting for several months
- Emergence of *C difficile*
- Confers long-term susceptibility to *C diff* infection
- Similar findings for single dose of cephalosporins

Buffie (2012). *Infection and immunity*, 80(1), 62-73.

Incomplete recovery and individualized responses of the human distal gut microbiota to repeated antibiotic perturbation

Les Dethlefsen[a] and David A. Relman[a,b,1]

- Two courses of Cipro in healthy adults, MB analysis over ten months
- "Profound and rapid" loss of diversity and shift in composition
- Increased deterioration with the second round of abx, making it less likely to recover to original state
- Return to initial state often incomplete

El-Ansary et al. Gut Pathogens 2013, 5:9
http://www.gutpathogens.com/content/5/1/9

Gut Pathogens

RESEARCH Open Access

The neurotoxic effect of clindamycin - induced gut bacterial imbalance and orally administered propionic acid on DNA damage assessed by the comet assay: protective potency of carnosine and carnitine

Afaf El-Ansary[1,2,4*], Ghada H Shaker[3], Amina R El-Gezeery[1] and Laila Al-Ayadhi[2,3,4]

Clindamycin causes overgrowth of species that produce propionic acid, a SCFA known to be neurotoxic.

Decreasing the harm of abx use

- Probiotic
  - Decrease risk of *C difficile* disease
    - S boulardii, LGG
  - Decrease abx-associated diarrhea
- Fermented foods
  - Lifeway kefir
- Dietary fiber
- Family pet

Recommendations

- Carefully consider evidence base and clinical need for each antibiotic prescription
- Use the narrowest spectrum abx
- Educate client about benefits of probiotic use any time you prescribe an antibiotic
  - To decrease risk of C difficile, AAD
    - Saccharomyces boulardii
    - Bio-K+
    - Florastar
    - BioGaia ProTectis
    - Culturelle

THE MICROBIOME IN PREGNANCY AND BIRTH

The Development of the Human Microbiome

Maternal diet shapes infant microbiome

- In non-human primate model, maternal diet during pregnancy has a persistent effect on the offspring up to at least one year of age
- Human cohorts – composition of infant infant gut MB asociated w mternal diet in last trimester, independent of mode of delivery and maternal obeisty

Chu DM et al. 2016. *Genome Med* 8, 77
Hu J et al. 2013 *PLoS One* 8, e78257

Not sterile at birth

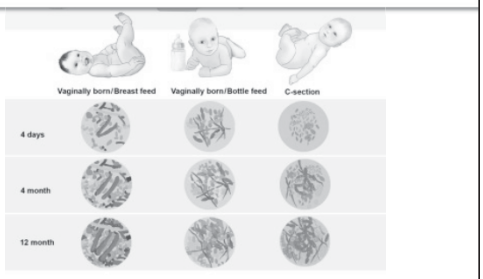
- Maternal transmission of bacteria to fetal gut during pregnancy
- Placental MB reflects maternal oral cavity
- Meconium reflects MB of placenta and amniotic fluid.
- Meconium MB varies by maternal glycemic control

Chu DM, Ma, Prince et al. 2017. *Nature Medicine* accessed online: http://www.nature.com/nm/journal/vaop/ncurrent/full/nm.4272.html

- Increasing diversity over first 3 years of life
- "Primary succession" a well established series of ecologic events that occurs during the initial colonization which defines the ecosystem conditions and influences subsequent patterns of colonization.
- Early life aberrant colonization may be rich in pathogenic species and lack commensal species necessary for development of a healthy immune system.

Gut Microbiota and Allergic Disease
New Insights
Susan V. Lynch
March 2016

Early-Life Gut Microbiome Development



Development of the Human Gastrointestinal Microbiota

Backhed et al 2015 Cell Host & Microbe 17(5):690-703
http://dx.doi.org/10.1016/j.chom.2015.04.004

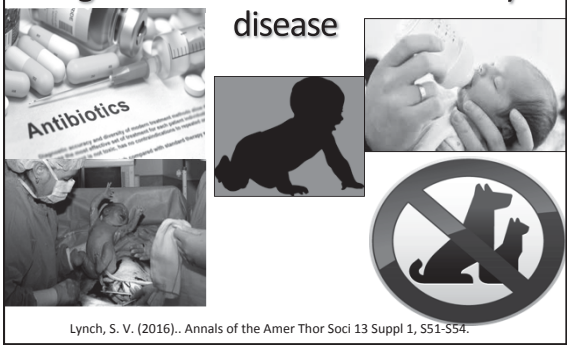
Dominguez-Bellow, Blaser et al 2011

Childbirth and consequent atopic disease: emerging evidence on epigenetic effects based on the hygiene and EPIIC hypotheses

H. G. Dahlen[1*], S. Downe[2], M. L. Wright[3], H. P. Kennedy[3] and J. Y. Taylor[3]

- **Likely the tip of the iceberg** – autoimmune ds
- Abx likely cause epigenetic changes – alter gene expression, influences immune function, **permanent or long-term changes in physiology**

Factors that disrupt MB: higher rate chronic inflammatory disease



Lynch, S. V. (2016).. Annals of the Amer Thor Soci 13 Suppl 1, S51-S54.

Antibiotic Use
Cesarean Birth
Formula Feeding

PERINATAL DISRUPTION OF THE NEONATAL MICROBIOME

ANTIBIOTIC USE DURING PREGNANCY

Cox et al (2014). *Cell,* 158(4), 705

BMC Med. 2016 Jun 17;14(1):91. doi: 10.1186/s12916-016-0636-0.

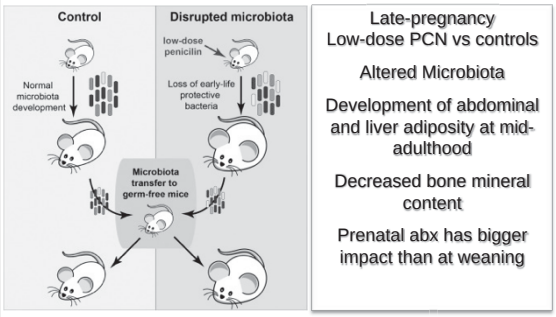
Antibiotic use during pregnancy: how bad is it?

Kuperman AA[1,2], Koren O[3].

- Abx use in pregnant women leads to
  - alterations in the vaginal microbiome prior to birth
  - Long-term effects on the colonization of the newborn
  - Strong Association with childhood obesity , childhood asthma & allergic ds
- Maternal MB during pregnancy drives early postnatal innate immune development

Cox et al (2014). *Cell,* 158(4), 705
Mueller et al 2015; Metsala et al 2014; Mueller 2016, Kaatsch 2010, Marild K 2014;

Altering Intestinal MB during a Critical Development Window has Lasting Metabolic Consequences



Laura M. Cox, Shingo Yamanishi, Jiho Sohn, Alexander V. Alekseyenko, Jacqueline M. Leung, Iseung Cho, Sungheon G. Kim, Huilin Li, Zhan Gao, Douglas Mahana, Jorge G. Zárate Rodriguez, Arlin B. Rogers, Nicolas Robine, P'ng Loke, Martin J. Blaser **Altering the Intestinal Microbiota during a Critical Developmental Window Has Lasting Metabolic Consequences;** null, Volume 158, Issue 4, 2014, 705–721. http://dx.doi.org/10.1016/j.cell.2014.05.052

Early Gut Microbiota Perturbations Following Intrapartum Antibiotic Prophylaxis to Prevent Group B Streptococcal Disease

- Fecal microbiota of breastfed infants receiving Ampicillin intrapartum was significantly reduced in diversity and richness at day 7
- Partial recovery at day 30
- Early research showed increased ampicillin-resistant Enterobacteria in infants receiving IAP
- Differences persist to 12 months

Mazzola et al (2016). *PLoS One*, 11(6), e0157527-e0157527 Aloisio et al (2016). *Applied Microbiology and Biotechnology*, 100(12), 5537-5546. Azad et al (2016).. BJOG 123(6), 983-993.

MODE OF DELIVERY

Mode of delivery association w allergic and autoimmune diseases

- Multiple studies show:
  - Association of CS with allergic and AI disease
  - Distinctly different infant MB by mode of delivery
- Numerous confounders:
  - Antibiotics, NSAIDs, co-morbidities, exposure to labor, infant feeding method, maternal obesity
  - Differences seen in MB of infants born by emergenc vs non-emergent CS (Azad M et al 2013)

Chu DM, Ma, Prince et al. 2017. *Nature Medicine* accessed online: http://www.nature.com/nm/journal/vaop/ncurrent/full/nm.4272.html

Journal of Midwifery & Women's Health

Updates from the Literature

Nancy A. Niemczyk, CNM, PhD

Prenatal exposure to antibiotics, cesarean section and risk of childhood obesity

NT Mueller[1,2], R Whyatt[3], L Hoepner[3], S Oberfield[4], MG Dominguez-Bello[5], EM Widen[1,2],

- Prospective cohort study, 436 women
- Preg abx use 2nd/3rd trimester: 84% higher risk of obesity at age 7
- Accounted for confounding variables: sex, ethnicity, birth weight, prepregnancy BMI, feeding method
- Cesarean: 46% higher risk of childhood obesity

Antibiotic use and laboring more important than mode of delivery?

- CS-born infants – less diversity at time of birth
- At 4-6 weeks of age, no detectable difference in MB composition by mode of delivery (p=0.057)
- *Strongest factors* impacting infant colonization patterns:
  - *Intrapartum antibiotics*
  - *Cesarean-with-labor* vs Cesarean-without labor.
    - CD with labor: populated by vaginal microbes
    - CD without labor: populated by maternal skin

Chu DM, Ma, Prince et al. 2017. *Nature Medicine* accessed online: http://www.nature.com/nm/journal/vaop/ncurrent/full/nm.4272.html

Maternal Outcomes
- Gestational Diabetes
- Preeclampsia
- Reduced risk mastitis
- Reduced postpartum central adiposity

Outcomes in the offspring
- Reduced risk of eczema
- Restoration of MB in Cesarean-born infants

PROBIOTICS IN PREGNANCY REVIEW OF EVIDENCE

Probiotics in pregnancy and maternal outcomes: a systematic review

- Six RCT's, one prospective cohort study
- Significant reductions in:
  - Maternal fasting glucose
  - Incidence of GDM
  - Incidence of preeclampsia
    - Severe preeclampsia OR 0.61, 95% CI 0.43-0.89
  - Levels of C-reactive protein
  - Central adiposity at six months postaprtum (OR 0.30)

Lindsay KL, Walsh CA,Brennan L and FM McAuliffe 2013; VanderVusse L et al 2014

GDM and probiotics:

Decreased GDM incidence three-fold (Luoto)
- 13% w probiotic 36% with no intervention p=0.003
- Also reduced fetal macrosomia
- *L rhamnosus GG* and *B lactis* Bb12
- Single products available, Nestle just filed for a patent for this combo

In women with GDM:
- Improved FPG, serum insulin, insulin sensitivity in women with GDM, all statistically significant (Karamali; Dolatkhan)
- Six weeks of L acidophylus, L casei, B Bifidum vs placebo
- Modulate inflammatory markers in GDM (VSL3)
- Decrease wt gain and FBG

Karamali et al (2016). *Diabetes & metabolism*, 42(4), 234-241. Jafarnejad et al(2016). *Jo Nutri Metabolism*, 2016, 5190846-5190846; Luoto et al (2010). British Jo Nutrition, 103(12), 1792-1799; Dolatkhah et al (2015). Jo Health, Pop Nutr, 33, 25-25

Probiotics: Reduced postpartum central adiposity and blood glucose

- Dietary counseling plus probiotic or placebo, first trimester
  - Central adiposity: risk lower at 6 mo postpartum
    - OR 0.03; 95% CI 0.11-0.85
  - Glucose regulation better during pregnancy and until 12 months postpartum
    - P=0.013
  - L *rhamnosus GG* ATCC53103 and *B lactis*

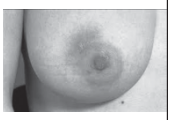
Ilmonen et al(2011). Clinical nutri, 30(2), 156-164; Laitinen e al (2009). British Jo Nutr, 101(11), 1679-1687.

Preeclampsia

- Altered gut microbiota seen in pts with preeclampsia (Liu J et al 2016)
- Intake of probiotic foods associated with reduced risk of preeclampsia (Brantsaeter et al 2011)
- Intake of probiotic yogurt in pregnancy assoc w decreased inflammatory markers (Asemi et al 2011)
- Increased gestational BP assoc w altered microbiome composition in early pregnancy (Gomez-Arango et al 2016)

Prevention/treatment of mastitis

- Prevention: Probiotic 30 weeks GA until birth
  - Mastitis in first 3 months postpartum decreased:
    - 25% probiotic, 47% placebo P=0.001
  - Infections less severe w probiotic
    - lower colony counts and pain scores
    - *L salivarius* PS2, available commercially



- Treatment:
  - Cure higher in probiotic than antibiotic group
    - by colony counts (p<0.01)
    - By pain symptoms
  - Recurrence rate higher in abx group (p< 0.001)
  - *L fermentum* CECT5716 or *L salivaris* CECT5713

Fernández et al (2016). Clinical infect dis, 62(5), 568-573; Arroyo et al(2010). Clin infect ds, 50(12), 1551-1558.

Normalizing MB of infants born by CS

- Cesarean-born infants: strong modulation effect of probiotic: shift toward composition of vaginally-born infants at 2 wks and 4 mo
- Organism isolated from breast milk; used in multiple infant disorders, commercially available in drops.
- 62 infants: vaginal and CS, probiotic or placebo
- Probiotic partially restored MB of CS infants towards that of those born vaginally
- No impact on MB of vaginally born babies

Garcia Rodenas et al (2016). Jo of ped gastroenterology nutri, 63(6), 681-687.

L reuteri 17938: infants and children

- Prevention of AAD in children Infant colic
- Colic, regurgitation and constipation
- Infant constipation Functional abdominal pain in children
- Reduce bronchial inflammation in children w asthma
- Necrotising enterocolitis in VLBW infants, nosocomial infection in PT infants
- Diarrhea and URI in children

Kolodziej et al BMJ 2017; Chau et al 2015 J Pediatr 166:74-78; (Szajewska et al J Pediat 2013; 162:257-262; Indrio et al 2014 JAMA Pediatr 168;228-233; Coccorullo et al 2010; J Pediatr 157;598-602; Jadresin et al 2016 J Ped Gastroent ; Nutr' Miraglia del Giudice et al 2012 J Biol Reg 26;35-40; Agustina et al 2012

Eczema risk in offspring

- Several Meta-analysis: prenatal probiotic use decreased incidence of eczema
- World Allergy Association: probiotics in preg/lactation approved for prevention of eczema if there is a family history of eczema
- Less evidence for asthma, food allergy, allergic rhinitis
- Effective species:
  - L rhamnosus GG 53103
  - Bifidobacteria lactis Bb-12
    - These strains also effective in alleviation of eczema and food allergy symptoms in infants in children

West, Jenmalm et al 2016; Kuitunen et al 2009, Pelucchi et al 2012,, Panduru et al 2015; Kalliomäki et al (2003) The Lancet, 361(9372), 1869-1871

REDUCING PERINATAL ANTIBIOTIC USE

Minimize antibiotic exposure
Prevent GBS colonization
Ensure shared decision-making about abx use
Vaginal seeding
GBS alternative treatments

DECREASING HARM OF PRENATAL/INTRAPARTUM ANTIBIOTIC USE

MINIMIZING PERINATAL ANTIBIOTIC EXPOSURE

Routine abx prophylaxis for CS

- Risk of post-op infection varies widely
  - ROM status, labor status
- 1000 receive abx to prevent 10 cases of infection
- Adapt current risk-scoring strategies for pregnancy
- Give abx after cord clamping
  - Partial solution

Ledger & Blaser (2013). BJOG: an international journal of obstetrics and gynaecology, 120(12), 1450-1452.

Reducing abx exposure: prophylactic abx after manual removal of placenta

- A common practice that has *not* been shown to reduce the occurrence of endometriosis or puerperal fever after manual delivery of the placenta
- WHO: recommendation is based on low quality evidence

Chibueze (2015).. *BMC Pregnancy and Childbirth*, 15(313). World Health Organization (2012). *WHO recommendations for the prevention and treatment of postpartum haemorrhage*. Retrieved from http://apps.who.int/rhl/guidelines/9789241548502/en/

Minimize antibiotic exposure: use the evidence to achieve the minimum effective dosing for GBS prophylaxis

Clinical Triggers to Initiate Intrapartum Antibiotics

- The Dilemma:
  - Recommendations (CDC, ACOG) are for at least 4 hours of abx prior to delivery
  - Our understanding of the time course of delivery is imperfect
  - Initiation of abx early in labor achieves adequate duration of treatment, but excessive exposure to antibiotics occurs
  - How to balance this?

Hamar, Illuzi & Funia, 2006

Findings of the study:

- In nullips, delaying antibiotics until either
  - In active labor
    - (either by subjective evaluation of the clinician or cervix 4 cm)
    - Receives narcotics or epidural
  - results in shorter antibiotic duration, with equivalent rates of adequate duration of antibiotic therapy, compared to those who received antibiotics at admission
- The clinical triggers do not perform well for multiparous women

NULLIPS

Clinical Trigger for Initiation of Abx	% rec'd ≥ 4h abx	Mean duration abx (hr)
At admission	90.8	10.1
When oxytocin started	83	9.8
4 cm dilation	76.7	6.6
ACTIVE Labor: clinician eval of labor pattern or pain score ≥6 out of 10 (subjective criteria)	79.7	7.4
PAIN (epid. or narcotic)	75	7.0
LABOR (Active or 4 cm)	82.6	7.5
PAIN + LABOR	86.2	8.1

Scope of the problem
Shared Decision-making, decision aid tools
Alternative treatments

GBS PROPHYLAXIS

Intrapartum Antibiotic Prophylaxis (IAP)– Evidence Based?

Cochrane review (Ohlsson & Shah 2010)

- There are only 4 RCTs conducted 20 years ago involving 852 GBS+ women, and they were not well designed
- "IAP is not supported by conclusive evidence"
- Management driven by advocacy groups, media attention and medicolegal concerns

Effect of Intrapartum Antibiotic Prophylaxis on the neonate

- Decreased levels & diversity of gut bacteria at 1 week of life
- Different composition of MB at one year of life
- Increased risk atopic dermatitis w IAP use for > 24 hours

PLoS One. 2016 Jun 22;11(6):e0157527. doi: 10.1371/journal.pone.0157527. eCollection 2016.

Early Gut Microbiota Perturbations Following Intrapartum Antibiotic Prophylaxis to Prevent Group B Streptococcal Disease.

Mazzola G[1], Murphy K[2,3,4], Ross RP[4], Di Gioia D[1], Biavati B[1], Corvaglia LT[5], Faldella G[5], Stanton C[2,4].

Aloisio et al 2014; Corvaglia et al 2016; Azad et al 2016; Wohl et al 2015;

Decrease GBS colonization

- Prevent gut dysbiosis
  - Dietary fiber, fermented foods
  - Source of GBS is the gut
- Support maternal immune function
  - The persistence of GBS colonization is dependent on the host immune response
  - Host immune response is crucial in clearing vaginal colonization

Characterization of host immunity during persistent vaginal colonization by Group B *Streptococcus*

Patras et al. (2015). *Mucosal immunology*, 8(6), 1339-1348.

Oral *Lactobacillus rhamnosus* GR-1 and *Lactobacillus reuteri* RC-14 to reduce Group B *Streptococcus* colonization in pregnant women: A randomized controlled trial

- Healthy pregnant women, 35-37 wks GA with GBS cultures positive
- Oral capsules, two caps qhs, 20 days of Rx
- GBS culture changed to negative in:
  - 43% in the probiotic group
  - 18% in the placebo group
  - P=0.0007
- No adverse effects
- Longer duration of treatment might be beneficial
- Products available commercially

Ho et al (2016). Taiwanese Jo ObGyn, 55(4), 515-518.

L rhamnosus GR-1 and *L reuteri* RC-14– *in vitro*

- Adheres to vaginal epithelium, interferes w urogenital pathogens (Petrova 2016)
- Inhibit Candida glabrata biofilms *in vitro,* shuts down metabolism of all *C. glabrata* strains (Chew 2015)
- Potentiates immune activity in E-coli infected bladder cells in vitro (Karlsson)
- Disrupts biofilms: BV, E. coli (McMillan)
- Inhibits ability of C albicans to infect cells and induce inflammation (Martinez)

L rhamnosus GR-1 and L reuteri RC-14– human

- Increases abundance of L crispatus or L iners (Macklaim 2015)
- Improves Nugent score and has immunomodulatory effect in postmenopausal women (Bisanz)
- Augments metronidazole in curing BV (Anukam 2006)
  - 88% cure w abx/probiotic vs 40% in abx/placebo p=<0.001, oral route
- Restores normal flora in women w BV:
  - Probiotic restored normal vag flora in 61.% vs 26.9%, P<-0.001, n=544, (Vujic 2013)
- Improves cure rate of fluconazole in Candidiasis (Martinez 2009)

L rhamnosus GR-1 and L reuteri RC-14– Clinical trials

- Augments metronidazole in curing BV (Anukam 2006) (oral)
  - 88% cure w abx/probiotic vs 40% in abx/placebo
  - p=<0.001
- Oral probiotic vs placebo in 544 women w BV over 6 weeks:
  - Probiotic restored normal vag flora in 61.% vs 26.9%, P<-0.001
  - Vujic 2013
- Improves cure rate of fluconazole in Candidiasis (Martinez 2009)

Decreasing risk of GBS colonization at end of pregnancy

- Start probiotic at around 30 weeks
- Especially if at high risk of GBS colonization
  - Health care workers
  - High BMI
  - GBS colonized in prior pregnancy
  - Black women

Vaginal chlorhexidine during labor for GBS prevention

- Four studies, 1125 infants, term and preterm
- No difference in early-onset GBS disease
- May be a reduction in neonatal colonization with GBS
- Low quality evidence
- Wipes out normal flora

Ohlsson, Shah & Stade 2014 Cochrane Review

Intrapartum Abx Prophylaxis: A Decision Aid

With thanks to Juliet Huntington, CNM

Assisting women to make informed choices about screening for Group B Streptococcus in pregnancy: A critical review of the evidence

-
- GBSin term infants rare
- A variety of valid strategies are used in various countries
- Need to screen ~3000 women at term to prevent one instance of EOGBSD
- Several reports of zero mortality w term EOGBSD
- It should be a SDM process with woman's decision respected
- GBS colonization or refusal of screening should not limit women's childbirth options
- IV abx can be provided at home births

Sheehy, A., Davis, D., Homer, C. S. (2013

A Decision Aid for IAP

- Increased SDM, improve the IC process
- Improve quality of care,
- Reframe the question from consent to choice
- AND not increase duration of the encounter

Standards exist to guide development/evaluation

- Present absolute risk, use a consistent denominator, use visual aids such as icon array

Options Grid Collaborative

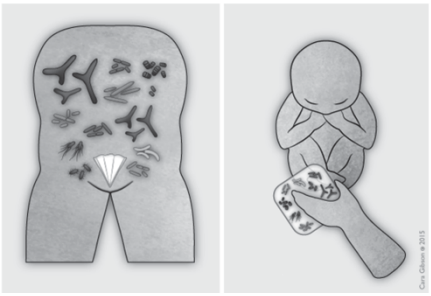
- Dartmouth Institute for Health Policy
- Provides guidance and support for development

Summary

- Intrapartum management:
  - Use clinical triggersof active labor to initiate abx prophylaxis in nullips – minimize duration of abx use
  - Minimize FSE use in GBS colonized women
- Prenatal
  - Support immune function
    - Low sugar, adequate vitamin D status, fermented foods
  - Diet rich in fiber and fermented foods
- Consider probiotics at ~30 weeks, esp if at high risk for GBS

VAGINAL SEEDING

Vaginal Seeding of Newborn Microbiome

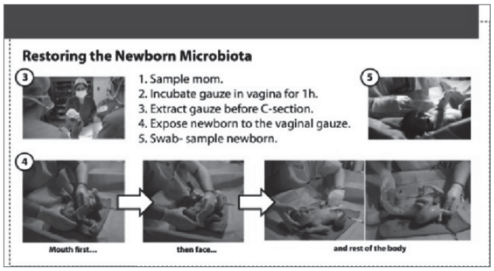


https://www.scienceandsensibility.org/p/bl/et/blogid=2&blogaid=825

Partial restoration of the microbiota of cesarean-born infants via vaginal microbial transfer

Maria G Dominguez-Bello[1,2], Kassandra M De Jesus-Laboy[2],

- 18 mom-infant pairs (11 CS, 7 VB); swab in hour preceding scheduled CS, swab infant within 2 min after birth (mouth, face, body)
- 1500 samples analyzed in 1st month of life
- Exposing neonates born by CS to maternal vaginal fluids partially normalizes the microbiota to resemble that of vaginally delivered infants
  - Successful even in cases w abx exposure
- Health outcomes have not yet been assessed
- Inclusion criteria:
  - GBS negative, no viral or bacterial infections, no signs BV, acidic vaginal pH <4.5



From a poster at the recent Boston meeting of the American Society for Microbiology. (Courtesy Dr. Dominguez-Bello)

"VAGINAL SEEDING" AFTER CAESAREAN SECTION

Safety of vaginal microbial transfer in infants delivered by caesarean, and expected health outcomes

- Concerns: transfer of pathogens
  - GBS infection or unknown GBS status
  - STI's, CT, GC, Herpes
- Increasingly common DIY by parents
- Inadequate knowledge about what IS a healthy vaginal MB. Varies by race. Need deeper understanding
- Clinical trial in process w 78 mom/infant pairs through first year of life

Clemente, J. C., Dominguez Bello, M. G. (2016). Safety of vaginal microbial transfer in infants delivered by caesarean, and expected health outcomes. BMJ. British medical journal, 352, i1707-i1707.

ACOG Practice Advisory: Vaginal Seeding

November 8, 2016

- Theory is biologically plausible but data is scant
- No assessment of clinical outcomes
- Transfer of maternal pathogens could result in severe adverse consequences for the infant:
  - GBS
  - Herpes
  - Chlamydia
  - Gonorrhea
- Recommend AGAINST this practice until better data available

Working Group to create a shared decision-making tool for GBS prophylaxis

Guide to evidence on prenatal use of probiotics for providers

WHAT NEXT??

References available upon request

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Key researchers to follow Web pages and Pubmed

- Gregor Reid, vaginal MB
- Martin Blaser, director NYU Human Microbiome Program
- Justin and Erica Sonnenberg, directors Stanford Microbiome Project
- Rob Knight, UCSD
- Susan V Lynch, UCSF
- Emeran Mayer
- Maria Domenguez-Bello
- Int'l Scientific Assoc for Probiotics and Prebiotics

Blogs of Academic Centers/ Researchers

- American Gut
- The Good Gut
- The Gut Institute
- Human Microbiome Project
- Center for Microbiome Informatics and Therapeutics at MIT
- Emeran Mayer, UCLA on gut-brain
- UCLA Ctr for Neurobiology of stress and resiliance microbiome section

Other blogs

- Gut Microbiota for Health Experts Exchange
- Terry Wahls TED talk (MD controls her MS w diet)
- Ubiome
- My New Gut Project
- Chris Kresser
- Institute for Functional Medicine/Functional Forum
- Human Food Project
- Ancestral Health Society
- Living Antibiotics
- Tight Junctions blog

Fermenting

- Body Ecology
- Cultures for Health
- FermentWorks