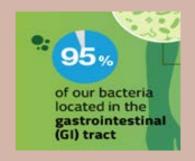


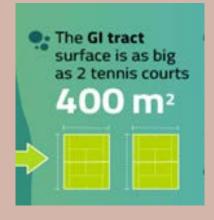
Objectives

- Probiotics and Prebiotics
- Human milk oligosaccharides (HMO)
- Factors derailing HMO
- Symbiosis vs Dysbiosis
- ▶ Researches focusing on effects of missing Gut microbiome

Some facts revised



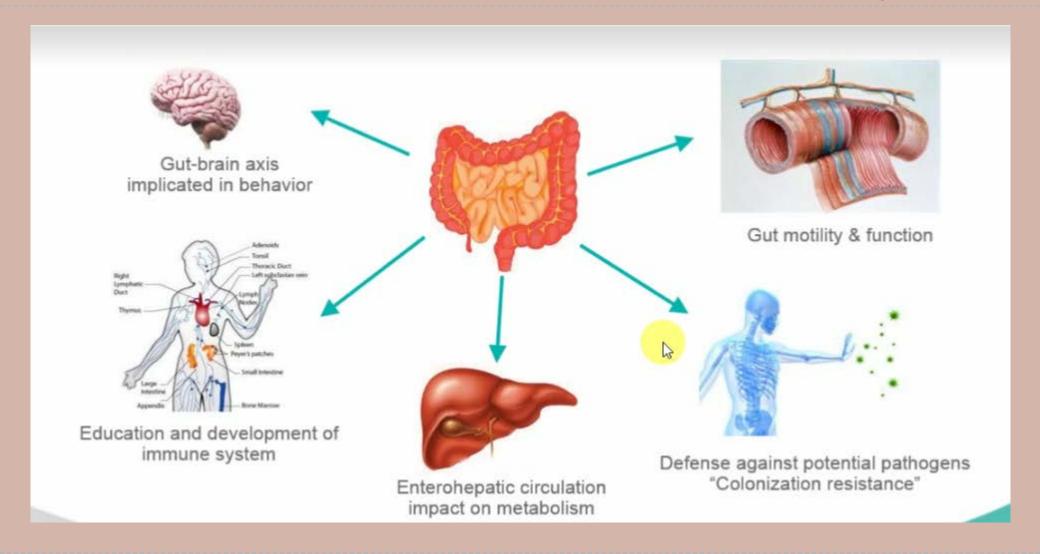








Gut microbiome impacts whole body



Difference between Probiotics and Prebiotics

Probiotic: The term was defined by Parker (1974) as

"organisms and substances which contribute to intestinal microbial balance."

Prebiotics

are nondigestible substances that feed the probiotics, helping them to thrive in the GI tract.

HUMAN MILK OLIGOSACCHARIDES

- •A family of structurally diverse unconjugated glycans
- Recent studies show that HMO—a prebiotic found naturally in human milk—can serve as food for beneficial bacteria in the infant gut.

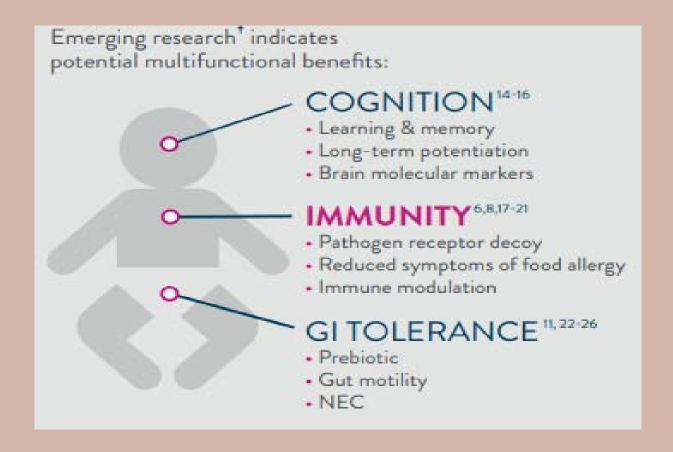


Early immune development



Of immune system is in gut, prebiotics supports colonization of gut which helps in immune system development

Prebiotics and more functions

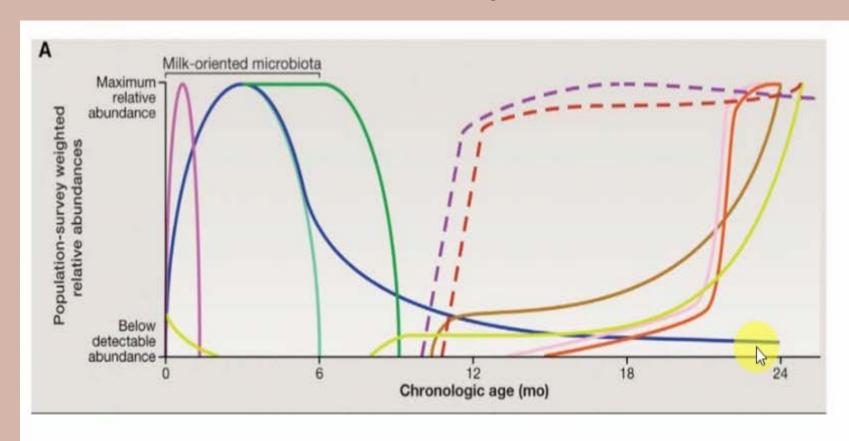


Bienenstock J, Buck R, Linke H, Forsythe P, Stanisz AM, Kunze WA. Fucosylated but not sialylated milk oligosaccharides diminish colon motor contractions. PLoS One. 2013;8(10):e76236.

https://anhi.org/conferences/50-espghan-hmo-pediatric-nutrition/hmo-mechanisms



The Early Gut Microbiome



- Staphylococcus sp.
- Streptococcus sp.
- Bifidobacterium sp. (putative breve)
- Bifidobacterium longum
- Lactobacillus ruminis
- Dorea longicatena
- Dorea formicigenerans
- Bifidobacterium sp. (putative catelunatum)
- Faecalibacterium prausnitzii
- Ruminococcus species

Cultivating Healthy Growth and Nutrition through the Gut Microbiota

Sathish Subramanian, 1.2 Laura V. Blanton, 1.2 Steven A. Frese, Mark Charbonneau, 1.2 David A. Mills, and Jeffrey I. Gordon 1.2.1

But...humans have changed almost everything



Gut microbiome described 100 years ago

"In four of the others, the results were nearly identical. The films showed the punctate form of B. bifidus in nearly pure culture...in the flora of breastfed infants (the ideal), the acid-tolerant group is immeasurably predominant and is of the strictly anaerobic type called B. bifidus."

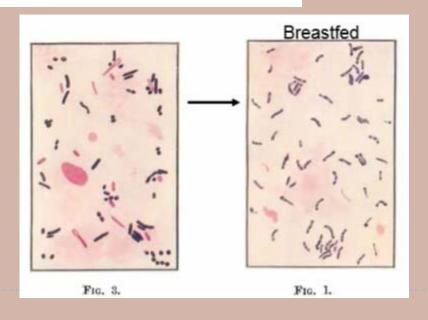
—Logan, in 1913, echoing the findings of his contemporaries, Tissier and Moro

Journal of Pathology and Bacteriology, Vol. XVIII.

THE INTESTINAL FLORA OF INFANTS AND YOUNG
CHILDREN.¹

By W. R. Logan, M. D.

From the Research Laboratory of the Royal College of Physicians, Edinburgh.



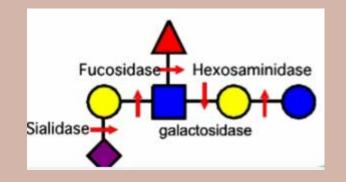
Bifidobacterium longum infantis and HMO.



Dr. David Mills

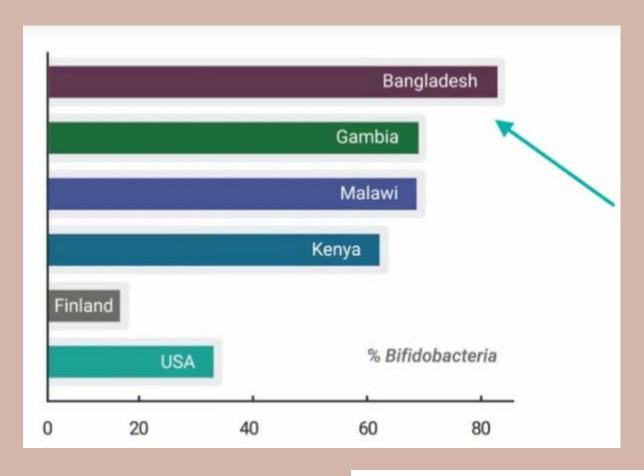
Professor in Food Science and Technology
and Endowed Chair in Dairy Food Science
at UC Davis

UCDAVIS
FOODS FOR HEALTH INSTITUTE



4 enzymes needed to break HMO

Its still diverse for some parts of world



Some countries like Bangladesh still have high levels of bifido among breast feeding infants.

While developed countries have much lower abundance

Huda et al 2014; Davis et al 2017; Vatanen et al 2016;

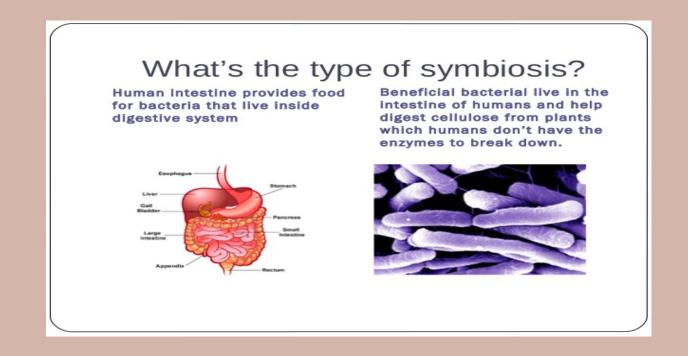
Yatsunenko et al 2012; Frese et al 2017; Subramanian et al 2014; Lewis et al 2014

Factors that derail the healthy Gut microbiome

- Formula feeding
- Mode of delivery
- Antibiotics
- In absence of Bifidobacterium dysbiosis sets in

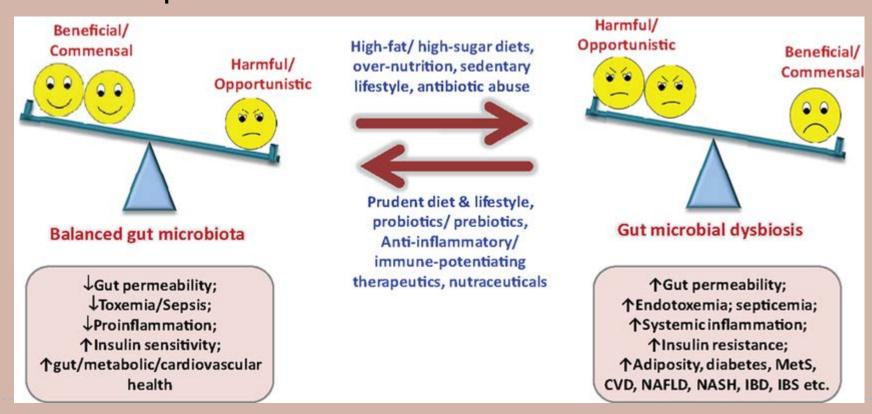
Dysbiosis is opposite of Symbiosis

Symbiosis: to live together with our microbes in a relationship where we are useful to each other



Dysbiosis

Is a term for a microbial imbalance or maladaptation inside the body, such as an impaired microbiota.



What happens in dysbiosis in infancy

- Colic
- Infections
- Contipation
- Excessive weight gain

Gut bacteria dysbiosis and necrotising enterocolitis in very low birthweight infants: a prospective case-control study

Barbara EWarner, Elena Deych, Yanjiao Zhou, Cafa Hall-Moore, George M Weinstack, Erica Sodergren, Nurmohammod Shalith, julie A Haffmann, Laure A Linnerson, Aaron Harrison, Gertilia Khanna, Lucina C Rouggly-Nickless, EMalick Ndoq, Berkley A Shands, Marilyn Escobeda, Janice E. Sollivan, Paula G Radmacher, William D Shannon, Phillip I Tar

Neonatal gut microbiota associates with childhood multisensitized atopy and T cell differentiation

Kei E Fujimura¹, Alexandra R Sitarik², Suzanne Havstad³, Din L Lin¹, Sophia Levan¹, Douglas Fadrosh¹, Ariane R Panzer¹, Brandon LaMere¹, Elze Rackaityte¹, Nicholas W Lukaca³, Ganesa Wegienka², Homer A Boushey⁴, Dennis R Ownby⁵, Edward M Zoratti⁶, Albert M Levin², Christine C Johnson^{2,7} & Susan V Lynch^{1,7}

> Antibiotic Exposure in Infancy and Risk of Being Overweight in the First 24 Months of Life

Anti: Sauri, MD^{III}, Lauri J. Virta MD, 790°; UNa Sankdampi MD, 790°; Lee Gunkel MD, 790°; Harri Saven MD, 790°

Stool Microbiota and Vaccine Responses of Infants

AUTHORS: M. Nazmul Huda, MS, ab Zachery Lewis, BS, c Karen M. Kalanetra, PhD, c Mamunur Rashid, MS, b Shaikh M. Ahmad, PhD, c Rubhana Ragib, PhD, c Firdausi Qadri,

What happens in dysbiosis in adulthood

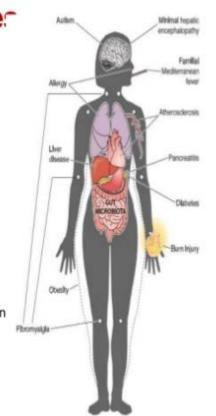
Dysbiosis and disease:

Diseases of the GUT

- Malabsorption syndrome
- Malignancies: Colorectal cancer
- Inflammatory Bowl disease (IBD)
- Irritable Bowl syndrome
- Diarrheal diseases
- Clostridium Difficile Infection (CDI)

Non-mucosal diseases

- Obesity and metabolic syndrome
- Malignancies: liver cancer, breast cancer
- Complications of liver cirrhosis
- Allergic conditions
- Autoimmune disorders (T1DM, arthritis etc)
- Abnormalities of the gut-brain axis- Autism an other neurological disorders
- Obesity and other metabolic disorders
- Chronic fatigue syndrome
- Periodontal diseases



Some microorganisms go missing resulting in chaos in gut, leading to diseases

Gut microbiome in hospitalized infants

- 12 subspecies found in rooms and infants
- Most common were Klebsiella pneumoniae, Escherichia coli, Pseudomonas aeruginosa
- Authors concluded that room habitats contained bacterial groups that often colonize infants housed in the NICU

ARTICLE OPEN

Strain-resolved analysis of hospital rooms and infants reveals overlap between the human and room microbiome

Brandon Brooks 1, Matthew R. Olm¹, Brian A. Firek², Robyn Baker³, Brian C. Thomas⁴, Michael J. Morowitz² Jillian F. Banfield⁴

Discussion

Newborn preterm infants are commonly colonized by nosocomial antibiotic-resistant pathogens, and are at increased risk for serious infection and death. The detailed genomic evidence presented here demonstrates that rooms can be reservoirs for early-stage colonizers of the microbiome of hospitalized premature infants. This finding provides a mechanism to explain how infants in the same NICU could be colonized by the same strains, despite hospitalization periods separated by years. We conclude that the room environment should be regarded along with diet, mode of delivery, and antibiotics as a determinant of the early gut microbiome.





Reintroduction of a symbiont

Symbiont :an organism living in symbiosis with another.







Dr. Mark Underwood

Kathisen Anglupton" and Mark A. Underwood"

RESEARCH ARTICLE



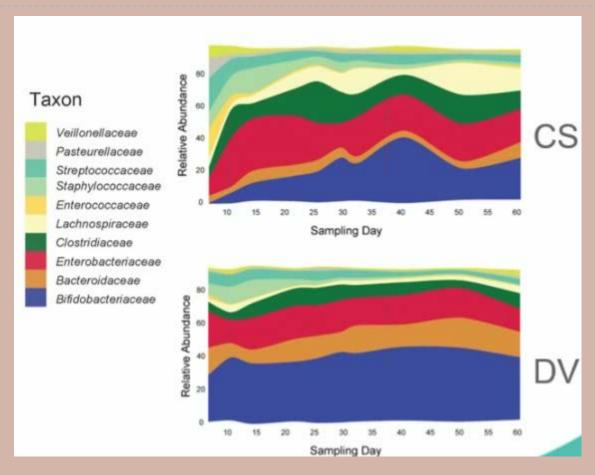
•66 mothers were recruited ,all were term infants exclusively breast fed, born vaginally or C- section

•One group received B infantis 18 billion CFU/day for 21 days, starting 7 days after birth

Safety and tolerability of Bifidobacterium longum subspecies infantis EVC001 supplementation in healthy term breastfed infants: a phase I clinical trial Servider T. Smilpuitz¹⁰⁷, Jackelon Moya¹, Mellosa A. Breck¹, Chelses Cook¹, Arrests Fineberg¹.

•Both group received lactation support for first 60 days .Fecal samples were collected throughout 60 days .

Key finding of the research



Blue area shows the bifidobacteria

The supplementation increased the bifido population and sustained over time

40%

Higher bifido bacteria in vaginal delivered infants

25%

Lesser bifido in C- section delivery







Breast feeding had a significant impact on microbiome

Probiotics for infants and children

- Probiotics are promoted for
- Diarrhea.
- ▶ Infant colic
- Allergy
- Eczema symptoms

However, the evidence is mixed on whether probiotics are actually effective for a range of infant conditions.



Safety of Probiotics

- Safe and well tolerated in normal, healthy infants and children.
- Good tolerance has also been observed in premature infants.
- Very low birth weight babies
- HIV-infected children and adults.
- Late pregnancy.
- Some cases of probiotic septicaemia in immunocompromised adults and children,



Vázquez E, Santos-Fandila A, Buck R, Rueda R, Ramírez M. Major human milk oligosaccharides are absorbed into the systemic circulation after oral administration in rats. Br J Nutr. 2017;117(2):237-247.

Probiotics with antibiotics

Probiotics must be prescribed with start of antibiotics and continue for at least one week after the end of the course.

•

Commercially available probiotics in Pakistan

- Biflor-(saccharomyces boulardii)
- Enflor





Ecotec

- Lactobacillus acidophillus LA-5,
- Bifidobacterium BB-12,
- Lactobacillus delbrueckii ssp.bulgaricus LBY-27,
- Streptococcus thermophilus STY-31.



Gutcare

Ingredients: Bifidobacterium 420mg, Clostridium Butyricum 500mg



Ezegut and Imutec



Drops for infants Ingredients: Lactobacillus



Ingredients: Bifidobacterium

Foods containing natural probiotics

- Yogurt
- Cottage cheese
- Buttermilk
- Kefir
- Soy sauce
- Miso (fermented soyabean)
- ▶ Tempeh (fermented soyabean)
- ▶ Fresh sauerkraut

Prebiotics

Foods containing Prebiotics

- Wheat
- Barley
- Rye
- ▶ Flax
- Oatmeal
- Onion
- ▶ Garlic

- Leeks
- Legumes
- Asparagus
- Leafy greens
- Berries
- Bananas
- Honey



Gut Microbiome - May Hold Key to Immunotherapy Outcomes

The microbial environment in the intestines, not only may affect an individual's risk of developing and surviving colorectal cancer but may also have a dramatic impact on the efficacy of anticancer immunotherapies

Significance of Gut Bacteria in Multiple Sclerosis

People with multiple sclerosis (MS) show differences in gut bacteria composition compared with those without the disease.

Researchers evaluated 42 stool samples from patients who had relapsing-remitting MS or secondary progressive MS with relapses and compared them with samples from 28 healthy donors.

Gut Microbiome can control Anti tumor immune function in Liver

Scientists found that if mice were treated with antibiotics certain bacteria in gut were depleted which resulted in change in composition of immune cells, leading to tumor growth in liver.

National Cancer Institute, USA recently published a paper on may 24th, 2018

Probiotics effective in prevention of C- diff

What is Clostridium Difficile infection

is a bacterium that can cause symptoms ranging from diarrhea to life-threatening inflammation of the colon.

Organism can spread from contaminated objects & surfaces especially in hospitals.

Mild infection can lead to diarrhea while severe one can lead to sepsis.

evidence suggests that probiotic prophylaxis is a useful and safe Clostridium difficile infection prevention strategy.

'Too Clean' Could Be a Trigger for Childhood Acute Leukemia

Institute of Cancer Research (ICR) in London, United Kingdom, presents strong evidence that the disease is caused through a "two-step process" of genetic mutation and exposure to infection.

Acute leukemia is the most common childhood cancer in developed countries and accounts for about one third of all pediatric malignancies.

a lack of microbial exposure in early life could increase the risk of developing leukemia.

The paper was published on May 21, 2018 in Nature Reviews Cancer.

FDA issues final rule on safety and effectiveness of antibacterial soaps and sanitizers

September 2, 2016

The U.S. Food and Drug Administration issued a final rule establishing that over-the-counter (OTC) consumer antiseptic wash products containing certain active ingredients can no longer be marketed.

Companies will no longer be able to market antibacterial washes with these ingredients because manufacturers did not demonstrate that the ingredients are both safe for long-term daily use and more effective than plain soap and water in preventing illness and the spread of certain infections.



https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm517478.htm



Promote breast feeding

Make sure to avoid unnecessary antibiotics

Probiotics must be taken as soon as you start the antibiotics and continue for at least one week after the end of the course.

Normal soaps are good enough to clean

Promote weaning with natural foods