BEYOND YOGURT

PROBIOTICS 101

"All disease begins in the gut." – *Hippocrates*

"Should I take a probiotic? Which one?" - *Most of our patients*

21 May 2024

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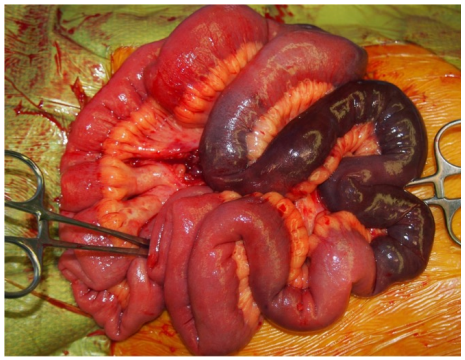
  - **Morrison Health, NY**
- **No disclosures.**
- **No financial interests/relationships to any products mentioned**

@JerrythePA

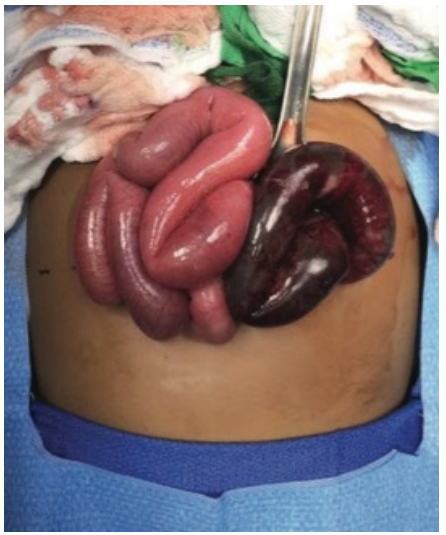
MY INTEREST

- I have a 25 year interest in the GI tract.

- It began simply as a surgical/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



26 YEAR OLD FEMALE



- 12 year history of inflammatory bowel disease
- Hypothyroidism –on T4 levothyroid
- Mild depression –long term SSRI "good results" but still with regular symptoms.
- Developed ACUTE ONSET abdominal pain and obstipation, found to have perforated viscus (small bowel) from an inflammatory twist of bowel.
- Needed significant resection of ileum
- Weeks after bowle resection, she developed increasing depression and new issues with panic.
  - Constant "Butterflies in my stomach"
  - Low B12 (intrinsic factor)
  - Worsening hypothyroid

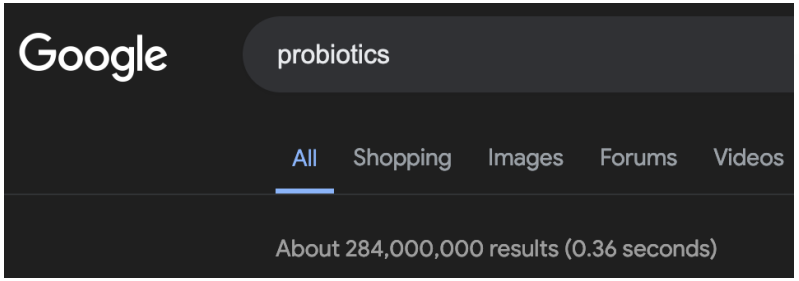
OBJECTIVES

- Define prebiotic, probiotic, psychobiotic, and synbiotics
- Compare and contrast the major strains of probiotics
- Describe the appropriate use and dose of probiotics during antibiotic administration
- List food sources rich in pre- and probiotics
- Describe the potential complications of these products

&
come to appreciate the vital role of our microbiome

EVERYONE IS TALKING ABOUT THE MICROBIOME

...AND YOU SHOULD BE TOO!



Fermented foods sustain both microbiomes and cultural heritage

Published: April 17, 2024 8:19am EDT

FEATURED

In the Search for Wellness, *Hack Your Health* Goes Straight to the Gut

In the new doc, four people undergo an experiment that may be … hard to digest.

BY ROXANNE FEQUIERE APRIL 29, 2024

NETFLIX

HOW OFTEN DO YOU GET THESE QUESTION?

- Should a take a probiotic?
- Why do I need a probiotic?
- What is it good for?
- What do you recommend?

WHAT TO THINK ABOUT…

- When should we target the gut microbiome?
- What evidence is there that it works?
- What probiotic should be used?
- What specific intervention?
  - Prebiotic, probiotic,, and/or postbiotic
  - Food based probiotics (yogurt, kimchee, sauerkraut, etc.) & Prebiotic foods (bananas, beans, flax chia)
- When are probiotics not indicated?

We must be prepared to discuss the role of probiotics, describe appropriate use and explain when probiotics may not be beneficial. This is a marketable skill!

OUR MICROBIOME

- Human microbiota
  - Our indigenous bacteria, viruses, fungi, and other single-celled animals that live in the body.
  - Our collective organism!
  - These are 100 trillions nonhuman cells- 10x more than human cells!
- Microbiome
  - All of the genes/genomes inside these microbial cells
- Major microbiome phylum:
  - Firmicutes
  - Bacteroidetes
  - Proteobacteria
  - Actinobacteria
  - Akkermansia- "keystone"

Fun fact:

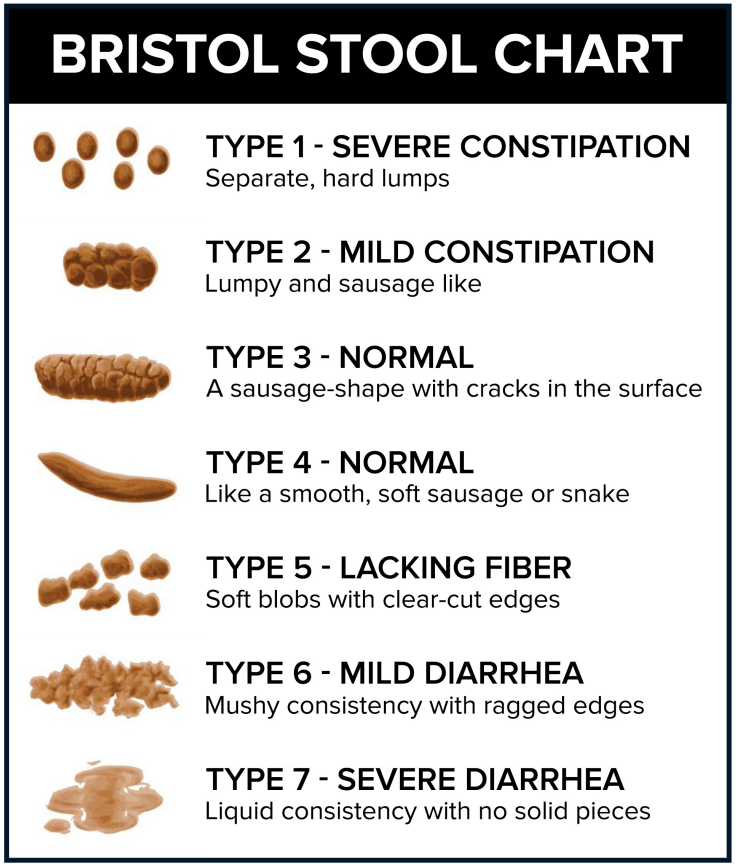
BM= loss of 1/3 of microbiome Sender, et.al 2016

- Loose stool and diarrhea
  - Loosing the microbiome!

- Constipation
  - Inadequate microbiome

Type 1 & 2
Type 6 & 7

Both need probiotics!



Fun fact:

BM= loss of 1/3 of microbiome Sender, et.al 2016

WHAT ABOUT THE "GUT MICROBIOME"

- We need our gut microbiome!
  - Encourage patients to take care of their bugs with whole foods & time restricted eating
- Gut microbes have an impact our physiology, both in health & disease.
  - contribute metabolic functions
  - protect against pathogens
  - educate the immune system
  - produce vitamins.
  - Enhance nutrient absorption
  - Stimulate enzyme production
  - Enhance the uptake of vit D (early data shows a + for osteoporosis) & more!
- Each person has their own unique microbiome
- An individual's microbiome but there is variability at the extremes of age and among different individuals based on their environment.
  - The very young and very old have less gut diversity, more need for probiotics

Shreiner, 2015

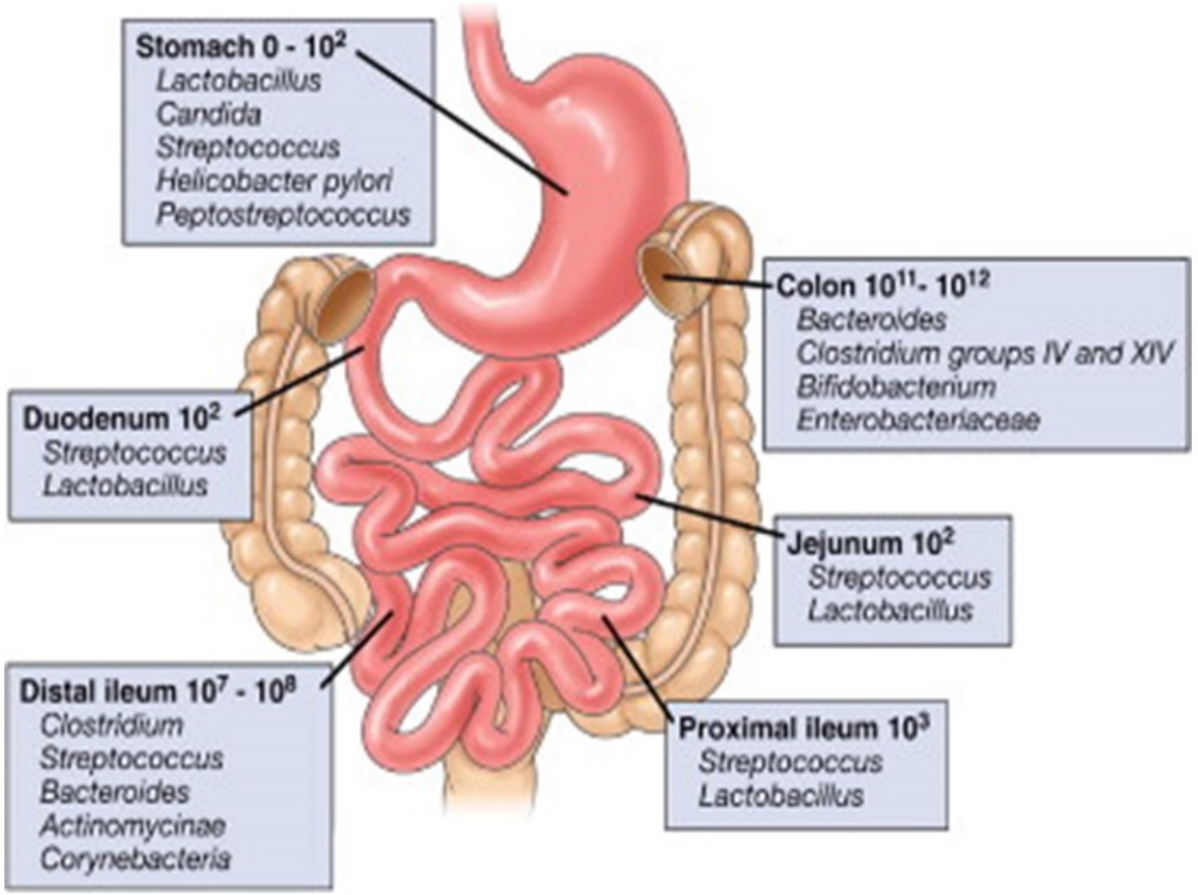
COMPOSITION AND LUMINAL CONCENTRATIONS OF DOMINANT MICROBIAL SPECIES CHANGES AS YOU MOVE THROUGH THE GI TRACT

Key point:

Our microbiome is diverse

Food intake should be!

Probiotics should be also!



Gastroenterology 2008 134(2)

- **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
- **SIBO**: Small Intestinal Bacterial Overgrowth
  - Excessive aerobic and anaerobic microbes that are normally present in the colon.
  - Bloating, flatulence, abdominal discomfort, or diarrhea.

UpToDate 2 April 2024

HOW TO ASSESS THE MICROBIOME: GET A DIET HISTORY

- The more plant types eaten, the higher the gut diversity.
- People eating 30+ different plant types a week, had microbiomes that were more diverse than those of people who ate 10 plant types/wk.
- Antibiotics significantly lowered the microbial diversity of the gut.
  - The diversity of the molecules found in people who had taken antibiotics, was much higher than in people who haven´t taken antibiotics for > a year.
- Detection of agricultural antibiotics in people who claimed that they haven't taken antibiotics in the year prior to their sample collection.
  - Especially meat eaters
- Strong link between the composition of the microbiome and depression.
- Ask about fiber intake! Fiber – not broken down by digestive enzymes, so they make it to our colon and can be fermented by gut bacteria into something GOOD

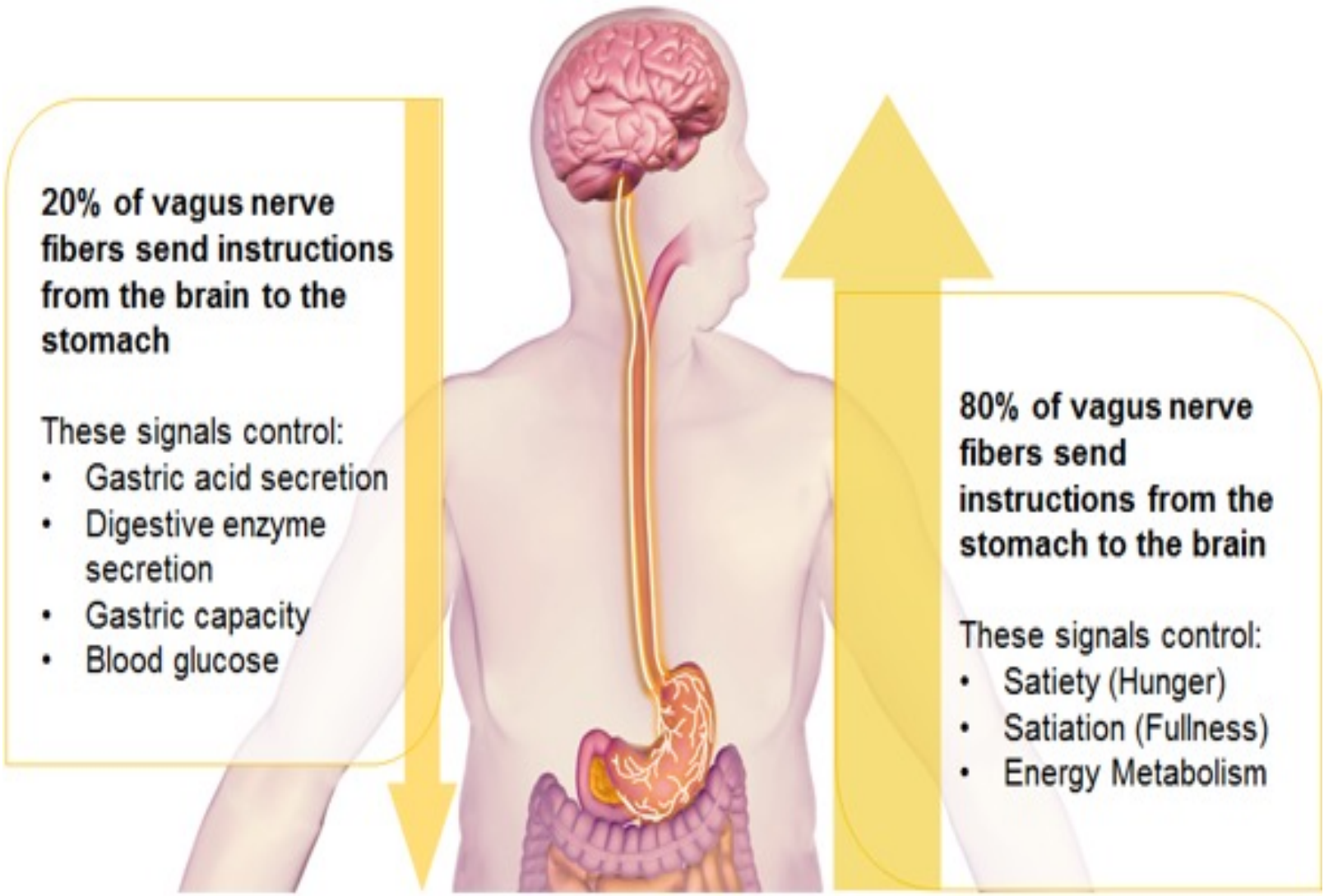
American Gut Project, UC San Diego 2018

ASSESS THE MICROBIOME:
FACTORS DEPLETING THE INTESTINAL MICRO ECOSYSTEM

- Medications:
  - Antibiotics exposures, especially under the age of 2
  - Proton pump inhibitors (PPI + Antibiotics = strong risk of C.diff)
- Microbial infections
  - H Pylori
  - Parasites etc.
- Diet (highly processed, low fiber foods)
  - Lack of colorful food diversity
  - There is an epidemic of fiber deficiency in America & this is the ultimate prebiotic!
- Chronic diarrhea
- Stress
- Chlorinated water
- Radiation and chemotherapy
- Birth by c-section
  - Consider a "wipe down" with vaginal secretions

Join my battle to fight fiber deficiency in America!

The history:
Get a neuro & psych history
--
Think of the neuro-transmitters produced in the gut!



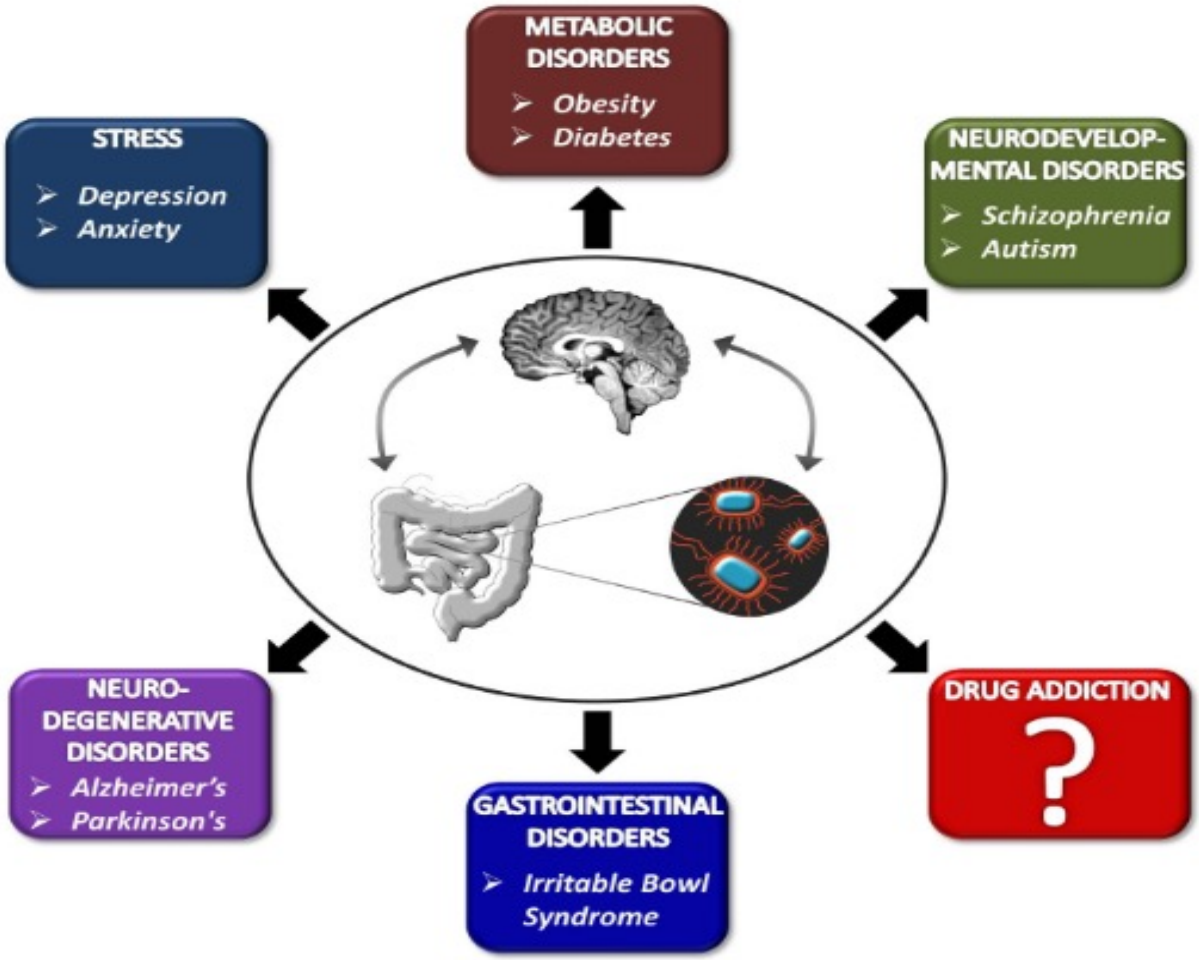


Fig. 1. Known disorders of the gut–brain axis. Microbiota in the gut play important roles in maintaining homeostasis, and their dysfunction has been linked to various psychiatric and nonpsychiatric disorders. Note that, to date, no studies have examined the gut–brain axis in drug addition. Figure adapted from Burokas et al. [13].

During the history, consider the micro-biome's role in these issues!

NIH Human microbiome project

HOW TO ASSESS THE MICROBIOME

- PHYSICAL EXAM
  - Oral/tongue exam
  - Abdomen
  - Skin turgor
  - Muscle tone
  - Neuro exam
- LAB TESTING
  - Breath testing
    - H Pylori, SIBO
  - Blood
    - IgA, C-reactive protein, H Pylori, celiac, LFTs (fatty liver), lipids
  - Stool
    - A favorite! We need to do more stool testing in GI patients!

The New York Times

How the Right Foods May Lead to a Healthier Gut, and Better Health

A diet full of highly processed foods with added sugars and salt promoted gut microbes linked to obesity, heart disease and diabetes.

Jan 11 2021
A. O'Conner

BASIC STOOL TESTS
COVERED BY INSURANCE: USE THE RIGHT CODES!

-INFECTION

Bacteriology; Aerobic; stool CPT: 87045
Bacteriology, stool CPT: 87045
H.pylori, stool, eia CPT: 87338
Stool Culture CPT: 87045 001 87427 001 87046 001
White Blood Cells (WBC), Stool CPT: 89055 001
Yeast culture, stool CPT: 87102

-INFLAMMATION

Fecal Zonulin CPT: 83520
Lactoferrin, stool CPT: 83631
CALPROTECTIN, FECAL CPT: 83993

-ABSORPTION

Assay of fecal fat CPT: 82715
ph, stool CPT: 83986

R10.0: Abdominal pain unspecified (ICD10), R10.9: Gas pain (ICD10), R19.5: Other fecal abnormalities (ICD10), R19.8: Oth symptoms and signs involving the dgstv sys and abdomen (ICD10), D72.9: Disorder of white blood cells, unspecified (ICD10)

Date Collected: **12/21/2023**

Celiac Disease Panel

Test	Current Result and Flag	Previous Result and Date		Units	Reference Interval
Endomysial Antibody IgA [C, 01]	Negative				Negative
t-Transglutaminase (tTG) IgA [C, 01]	<2			U/mL	0-3
Immunoglobulin A, Qn, Serum [C, 01]	127	76*	06/27/2022	mg/dL	87-352

```
Negative        0 -  3
Weak Positive   4 - 10
Positive          >10
Tissue Transglutaminase (tTG) has been identified
as the endomysial antigen.  Studies have demonstr-
ated that endomysial IgA antibodies have over 99%
specificity for gluten sensitive enteropathy.
```

IgA

HLA-DQB1*(3)	0201	01/16/24
HLA-DQB1*(3)	0202	01/16/24
HLA-DQ2(3)	Positive	01/16/24
HLA-DQ8(3)	Negative	01/16/24

COMMENTS: SPLIT 10/05/2023 FROM 0004314

Test Name	In Range	Out Of Range	Reference Range
PH, FECES		5.7 L	7.0-7.5 pH units

CAMPYLOBACTER SPP. AG,EIA

Micro Number:	19188232
Test Status:	Final
Specimen Source:	Stool
Specimen Quality:	Adequate
Campy Ag Result:	Not Detected
Reference Range:	Not Detected

FECAL LEUKOCYTE STAIN

Micro Number:	19190633
Test Status:	Final
Specimen Source:	Stool
Specimen Quality:	Adequate
Fecal Leukocyte:	Not Detected
Reference Range:	Not Detected

HELICOBACTER PYLORI AG, EIA, STOOL

Micro Number:	19190190
Test Status:	Final
Specimen Source:	Stool
Specimen Quality:	Adequate
H.pylori Ag:	Not Detected

ADVANCED STOOL TESTING
MICROBIAL IMBALANCE
STOOL TESTING FOR PROBIOTICS/MICROBIOME

Gut Microbiome and Metabolic Health

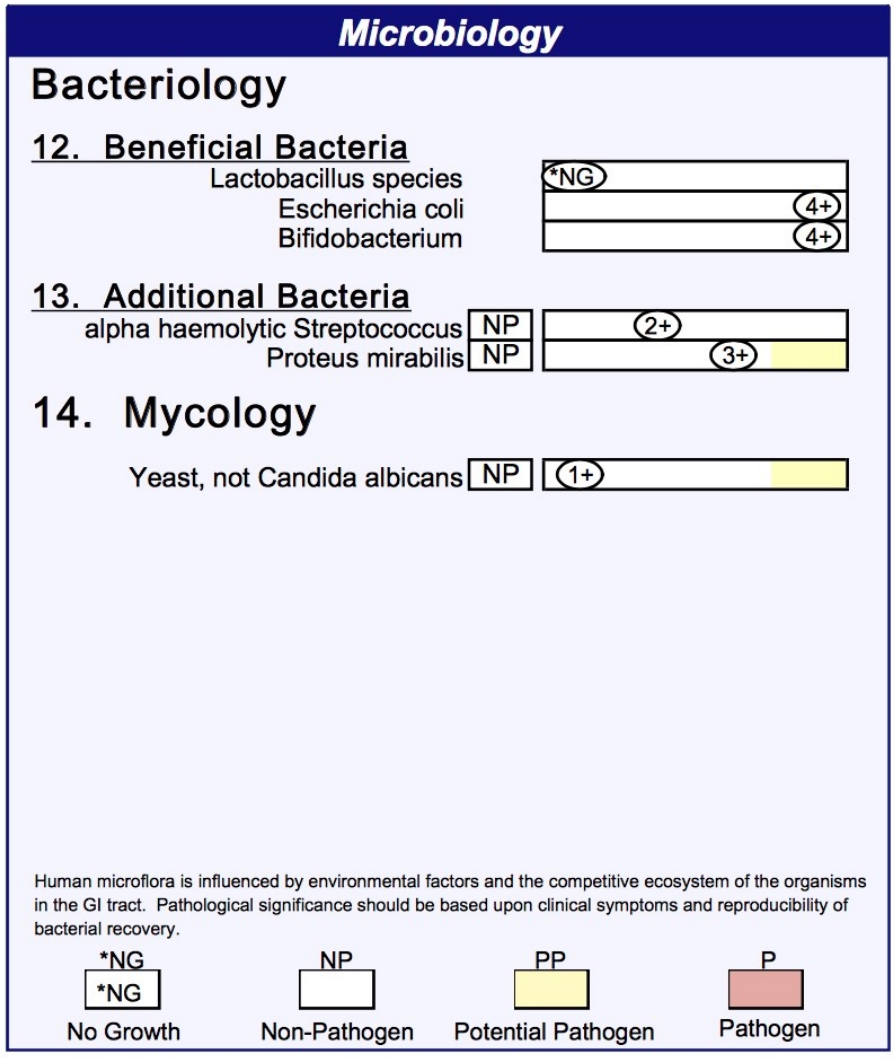
Genus/Species	Abundance	Previous	Rating	Potential Associated Risk*
Lactobacillus reuteri	LOW↓		★★★★	Obesity
Lactobacillus casei	OPTIMAL↔		★★★	
Lactobacillus paracasei	OPTIMAL↔		★★★★★	
Methanobacteriales	OPTIMAL↔		★	
Bifidobacterium Animalis	OPTIMAL↔		★★★★	
Methanobrevibacter smithii	OPTIMAL↔		★★★★	
Staphylococcus	OPTIMAL↔		★★★	
Blautia	OPTIMAL↔		★★	
Oscillospira	OPTIMAL↔		★★★★★	
Alistipes	OPTIMAL↔		★★★	
Roseburia	LOW↓		★★★★★	Type II Diabetes
Eubacterium	LOW↓		★★★★★	
Eggerthella	OPTIMAL↔		★★★★★	

Potential Risk Mitigation Choices

Probiotics

Consider taking probiotics containing Lactobacillus reuteri, Lactobacillus paracasei, Lactobacillus rhamnosus, and Bifidobacterium animalis.

Gut Microbiome and Nutrition I	Genus/Species	Abundance	Previous	Rating	Potential Associated Risk*
	Bifidobacterium bifidum	OPTIMAL↔		★★★★	K Vitamins and B Vitamins Production affected
	Bifidobacterium longum	OPTIMAL↔		★★★★	
	Lactobacillus plantarum	OPTIMAL↔		★★★	
	Bifidobacterium breve	OPTIMAL↔		★★★★	
	Bifidobacterium adolescentis	OPTIMAL↔		★★★★	
	Bacillus subtilis	OPTIMAL↔		★★	Vitamin K2 production affected
	Lactobacillus reuteri	LOW↓		★★	Vitamin B12 production affected
	Propionibacterium freudenreichii subsp. shermanii	OPTIMAL↔		★★	
	Lactobacillus fermentum	OPTIMAL↔		★★	


Microbiology
Bacteriology
12. Beneficial Bacteria
Lactobacillus species
*NG
Escherichia coli
4+
Bifidobacterium
4+
13. Additional Bacteria
alpha haemolytic Streptococcus
NP
2+
Proteus mirabilis
NP
3+
14. Mycology
Yeast, not Candida albicans
NP
1+
Human microflora is influenced by environmental factors and the competitive ecosystem of the organisms in the GI tract. Pathological significance should be based upon clinical symptoms and reproducibility of bacterial recovery.
*NG
*NG
No Growth
NP
Non-Pathogen
PP
Potential Pathogen
P
Pathogen

Genova CDSA

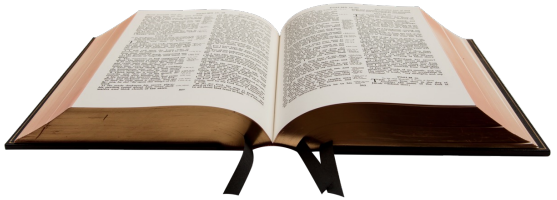
OUR WAY OF THINKING ….

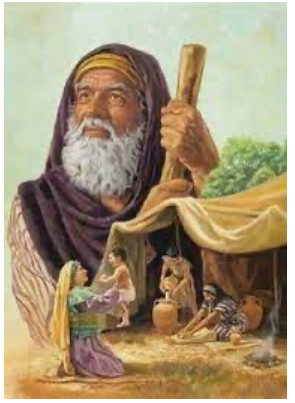
- MICROBES are BAD & cause DISEASE
  - They colonize & infect
  - They need to be killed with
    - Disinfectants
    - Antimicrobial soaps
    - Antiviral
    - Antibiotic
    - Antiparasitic
    - Antifungal

We need to change our thinking:

We are not just one organism
We need to nurture our beneficial microbes!

ARE PROBIOTICS A NEW IDEA??





4000 BC Old Testament (Genesis 18:8)

Abraham owed his longevity to the consumption of sour milk.

175 years old!

76 BC Plinius recommended fermented milk for gastritis/gastroenteritis

2024 –We get fermented milk as Kefir

-look for organic low fat milk with no added sugar

-plain less calories than fruit flavor

GUT-BRAIN CONNECTIONS
DR. GEORGE PORTER PHILLIPS

- Early 1900's 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 gave them fermented milk (keifer) which contains lactobacillus
- N=18 patients
  - 11 were cured completely
  - 2 others showing significant improvement.
  - Birth of PSYCHOBIOTICS!

PSYCHOBIOTICS

Many mental health providers now do a detailed GI history!

Contents lists available at ScienceDirect

Brain, Behavior, and Immunity

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

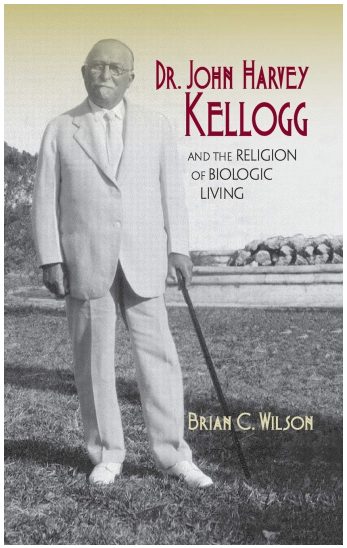
A randomized controlled trial to test the effect of multispecies probiotics on cognitive reactivity to sad mood ☆

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

JOHN HARVEY KELLOGG MD

- Founder and director of Battle Creek Sanatorium
- "Abnormal colonic bacteria built up from a heavy meat diet and caused **autointoxication"**
- Special diets, laxatives and fiber improved the intestinal flora
  - Pioneer in the field of fiber
  - Innovator in the field of community mental health
- Prescribed enemas for sanatorium patients
- Enema included yogurt
- After enema, oral yogurt



- 2020's RCT-DB show probiotics are excellent for mood and constipation

WHAT CAN YOU RECOMMEND?

- PREBIOTICS-*fuel probiotic production*
  - *In disease state, you always need more than a prebiotic*
  - Supplement (Inulin & Fiber)
  - Fiber rich foods
- PROBIOTICS-*gut guardians and worker bees!*
  - Food (sauerkraut, kimchi, kombucha)
  - Supplement
- SYNBIOTICS
  - Prebiotic+Probiotics
- POSTBIOTICS-*Enhance beneficial microbiota*
  - "Microorganisms and/or their components that confers a health benefit on the host." *ISAPP 2021*
  - Fecal transplant

Image: GLAC biotech

PREBIOTICS

- An undigestable carbohydrate.
  - Dietary fiber
  - Inulin: garlic, onions, chicory root, asparagus, whole wheat, rye, barley, apples
- Fermentation of prebiotics produces short chain fatty acids (i.e. butyrate) =
  - Increase the height of villi and depth of the crypts =absorptive mucosa
  - Strengthen tight junctions and thus prevent intestinal leakage =improved barrier function
  - SCFAs enter bloodstream and help regulate inflammation
  - Increase secretion of mucous and the thickness of the mucosal barrier (Raises IgA!)
- Stimulates the growth of BENEFICIAL **colonic** bacteria.
  - *Bifidobacterium* and *Lactobacillus*.

- Associated with
  - reduced colon CA
  - enhancing calcium absorption
  - Improvement in constipation
  - Improvement in malabsorption syndromes

Fiber is the great stool "equalizer"

CLINICAL TRIAL: PREBIOTICS ON MOOD

- Prebiotic strategy
  - Schmidt, et al., 2014, Journal of psychopharmacology:
    - Modify the GI tract microbiome by starving "bad" bacteria and nourishing "good" bacteria
    - Those taking the prebiotic had a reduced tendency to pay attention to negative information and lower levels of cortisol
  - Peter PJ. Jackson, et.al, EFFICAD Trial, RC Nov 2023 trial
    - "Inulin-type fructans alter both microbial composition and appear to alleviate stress-induced mood… compared to placebo (maltodextrin)"
      - *The American Journal of Clinical Nutrition, Vol 118, Issue 5*
  - Reminder, we are dependent on the amino acid **tryptophan** from our diet!

For patients with neurological or psychiatric conditions, ask about gut symptoms, their diet, do a PHQ and Adverse Childhood experience assessment, and give pre-biotics!

PROBIOTIC SOURCES

- Try food first!
- Sauerkraut
- Kimchee
- Kombucha
- Yogurt
- Cereals
- Frozen Yogurt
  - LaLoo's Goat's Milk Frozen Yogurt

Yogurt Juice

- *Goodbelly, organic fruit juice-based probiotic*
  - *<u>L.Plantarum</u> 299v, has effects on IBS*
- *Aged cheeses*
  - *Gouda, cottage cheese, some cheddar*

YOGURT!

- Yogurt starts as fresh milk or cream. It is often first pasteurized, then fermented with **live bacteria cultures**, and incubated at a specific temperature to encourage bacteria growth.
  - This produces lactic acid, which gives yogurt its distinctive flavor.

- Not all yogurts are healthy!
  - Yogurt products that go through heat treatment have no active bacteria
  - Yogurt-covered raisins are an example.
  - Not all yogurts actually have probiotics!

Most common cultures

Most Common Probiotics

Commercially Used

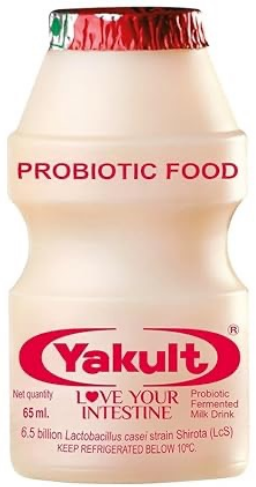
Lactobacillus acidophilus/johnsonii/gasseri
Lactobacillus casei
Lactobacillus paracasei
Lactobacillus rhamnosus
Lactobacillus plantarum
Lactobacillus reuteri
Bifidobacterium animalis/lactis
Bifidobacterium bifidum
Bifidobacterium breve
Bifidobacterium longum
Bifidobacterium adolescentis

- Kefir
  - plain- is best- no additives!
- Cashew based yogurt

- Yakult Dairy Drink
  - Probiotic, cultured dairy beverage
  - Sold in single-shot containers that contain around

    8 billion live and active *Lactobacillus casei*

    Good for preventing diarrhea!

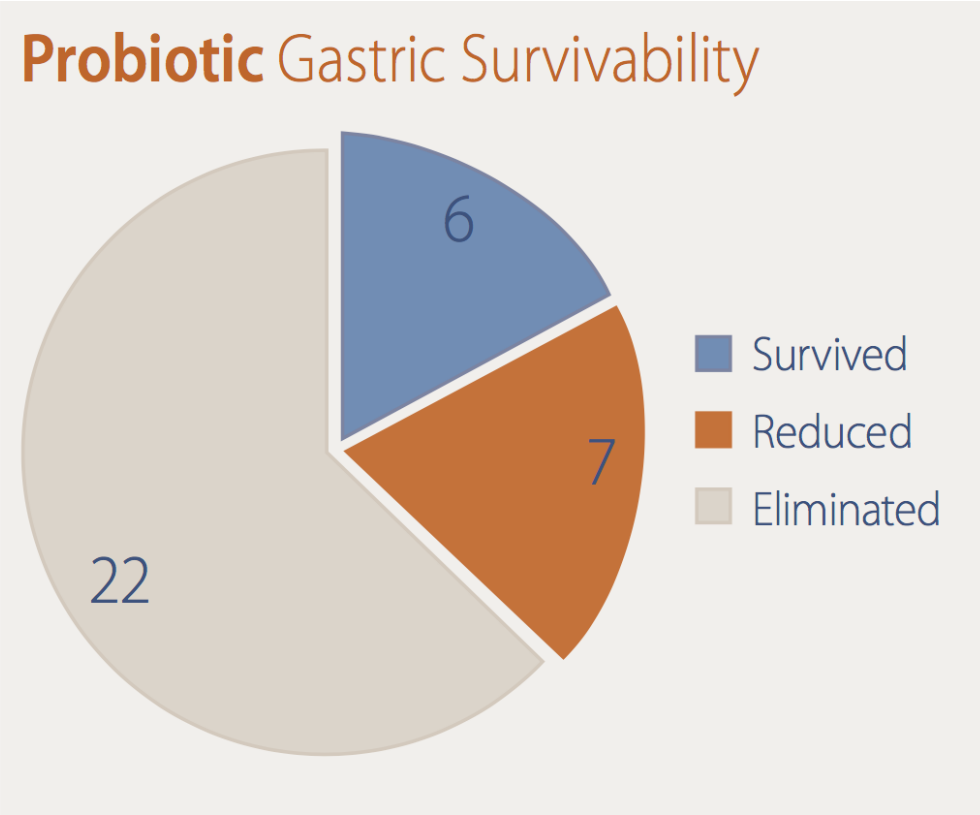


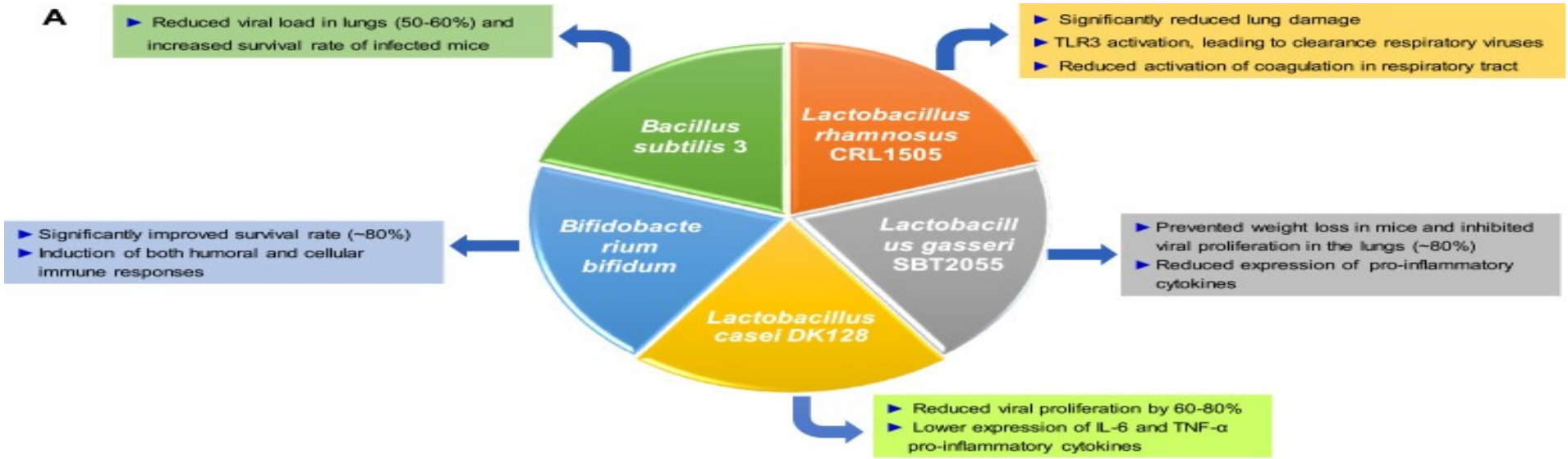
BRUH! Added sugar, corn starch, etc.

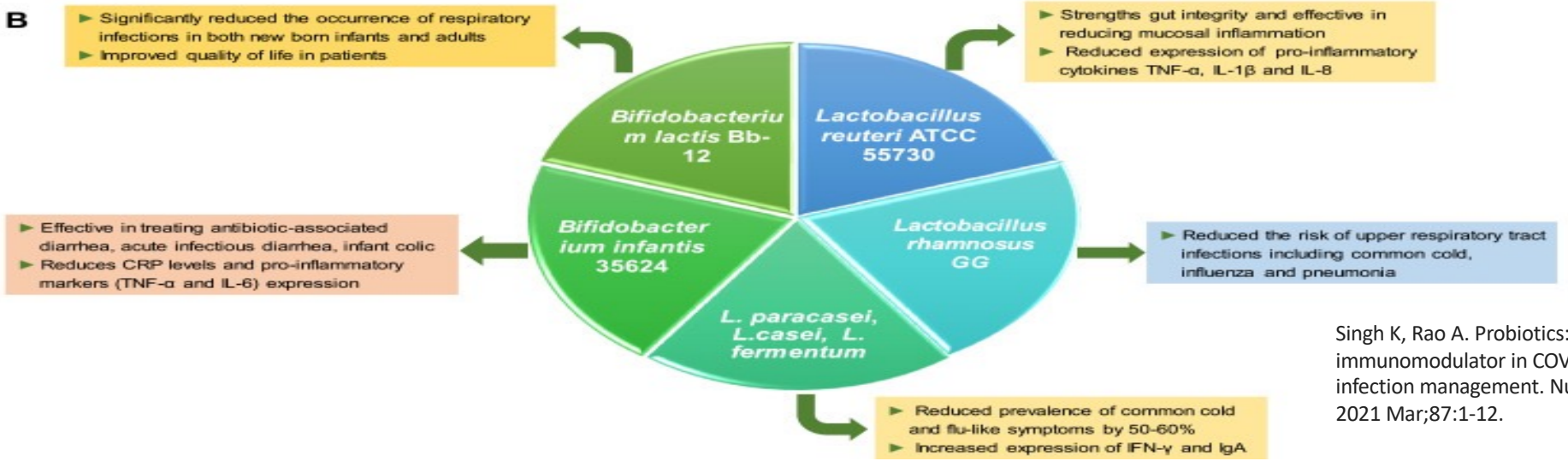
PROBIOTIC SUPPLEMENTS

- Multispecies better than single!
  - Pick a probiotic with multiple specie
- Enteric coating
  - Need to get to the gut/colon
  - *Redding University and the Food Standards Agency*

Look for doses in the BILLIONS!







Singh K, Rao A. Probiotics: A potential immunomodulator in COVID-19 infection management. Nutr Res. 2021 Mar;87:1-12.

PROBIOTIC 'PRESCRIPTION'

- **Look for multiple strain names on the label!**

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

Masters Formula

Proprietary Blend
Lactobacillus acidophilus La-14®
Bifidobacterium longum BI-05™
Lactobacillus plantarum Lp-115®

409 mg (50 Billion CFU†)

Xymogen

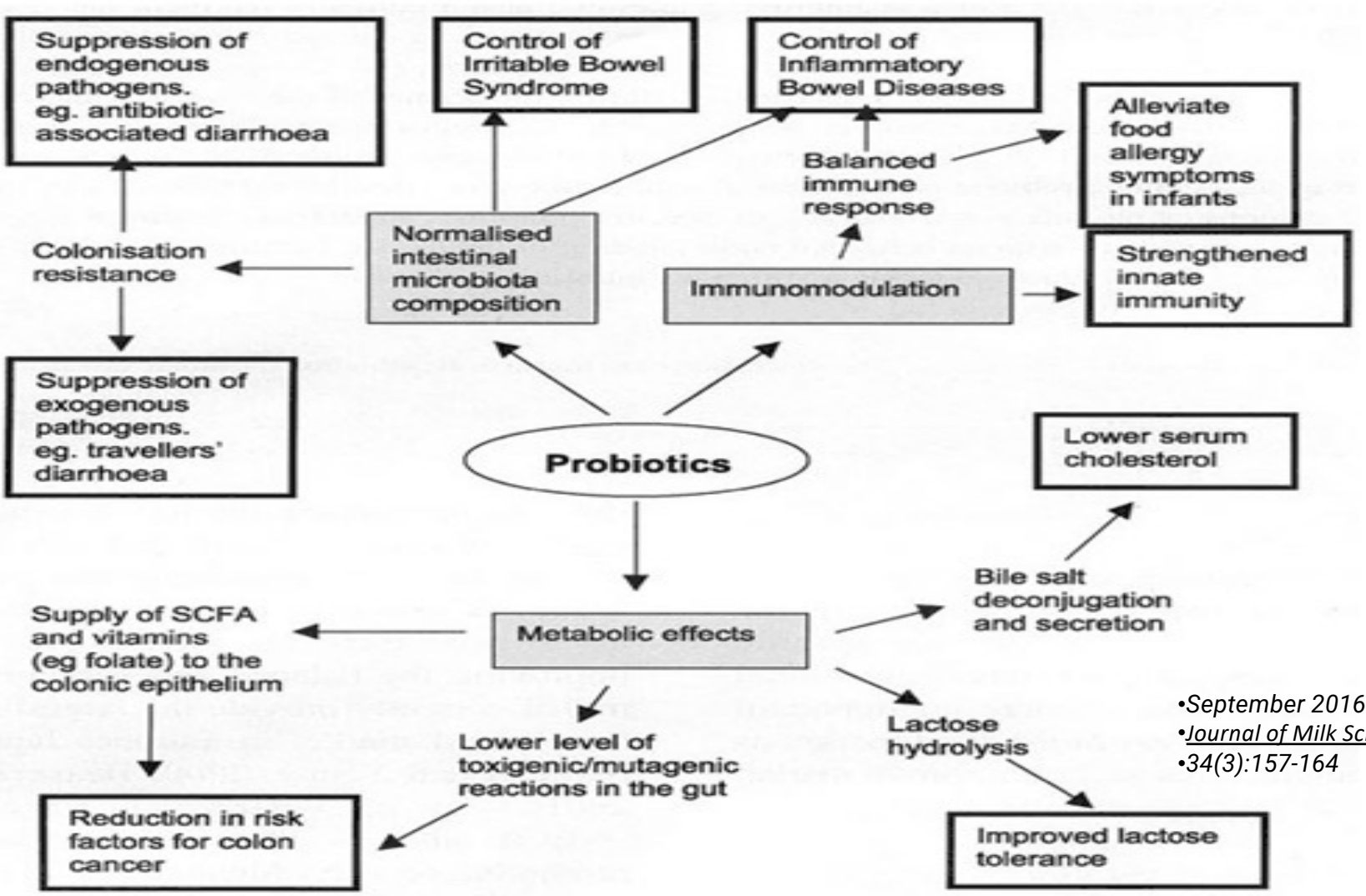
IMPORTANT –
Dose your probiotics in the BILLIONS! Why?

WHAT CONDITIONS WILL USE OF A PROBIOTIC PROVIDE BENEFIT?

A healthy gut microbiota imparts specific function in host nutrient metabolism, xenobiotic and drug metabolism, maintenance of structural integrity of the gut mucosal barrier, immunomodulation, and protection against pathogens.

You need to select the appropriate probiotic based on your patients needs.

More than 30 different diseases have been studied and have shown benefit w minimal or no harm!



Proposed health benefits stemming from probiotic consumption.

•*September 2016*
•*Journal of Milk Science and Biotechnology*
•*34(3):157-164*

1. PROBIOTICS PREVENT ANTIBIOTIC ASSOCIATED DIARRHEA

- Produce lactic acid which lowers the pH of intestines
  - This inhibits *Clostridium, Salmonella, Shigella*, *E. coli,* etc.
- **82 RCT's** on probiotics and reducing ABX associated diarrhea (N= >11,000)
- Probiotics= overall benefit, NNT = 13 (Hempei, JAMA 2021 May 9 Vol 307)
- <u>Prevention of antibiotic-associated diarrhea</u>:
  - *Saccharomyces boulardii* I-745, *Lactobacillus acidophilus, Lactobacillus casei*
  - Drinking *Lactob. Casei (*N= > 3800) = 21% risk reduction in C.diff, no adverse reactions, NNT= 5, "moderate strong evidence" (Johnson etal, 2012 Ann Int. Med)
- **Especially important in patients on a PPI**

- AGA 2020 clinical practice guideline:

- "In adults and children on antibiotic treatment, we suggest the use of one of the following:

  S boulardii

  2-strain combo of *L acidophilus* CL1285 and *L casei* or

  3-strain combo of *L acidophilus*, *L delbrueckii* subsp *bulgaricus*, and *B bifidum*;

  4-strain combo of *L acidophilus*, *L delbrueckii* subsp *bulgaricus*, *B bifidum*, and *S salivarius* subsp *thermophilus*

  over no or other probiotics for prevention of *C difficile* infection."

Reminder- Lactobacillus produces lactic acid that inhibits bad bacteria!

2. HELP MITIGATE LACTOSE INTOLERANCE

- Over 60 percent of the human population has a reduced ability to digest lactose due to low levels of lactase enzyme activity.
- Probiotics enhance production of β- D- galactosidase enzymes that break down lactose.
  - Lactobacillus produces lactase, the enzymes that breaks down milk sugar (Lactose!)
- 15 DB RCT trials show benefit!

- *Sophia J. Oak & Rajesh Jha (2019) The effects of probiotics in lactose intolerance: A systematic review, Critical Reviews in Food Science and Nutrition, 59:11*

3. LOWERING CHOLESTEROL

Probiotics inhibit bile's reabsorption in the gut, which would enter blood as cholesterol.

-Patients with high cholesterol, taking *L. reuteri* for 9 wks lowered total cholesterol by 9%, LDL by 12%

Jones ML, Martoni CJ, Prakash S. Cholesterol lowering and inhibition of sterol absorption by Lactobacillus reuteri NCIMB 30242: (RCT) Eur J Clin Nutr. 2012

-''In atherosclerosis patients, the gut microbiome could be contributing to inflammation by producing more pro-inflammatory mediators. A growing body of evidence has demonstrated that probiotic bacteria can effectively regulate hypercholesterolemia by improving lipid profile'' Mohamed J. Saadh, et.al. Therapeutic potential of lipid-lowering probiotics on the atherosclerosis development, European Jour Pharm, Vol 9712024

-Compared to controls total cholesterol was significantly reduced in probiotics group.

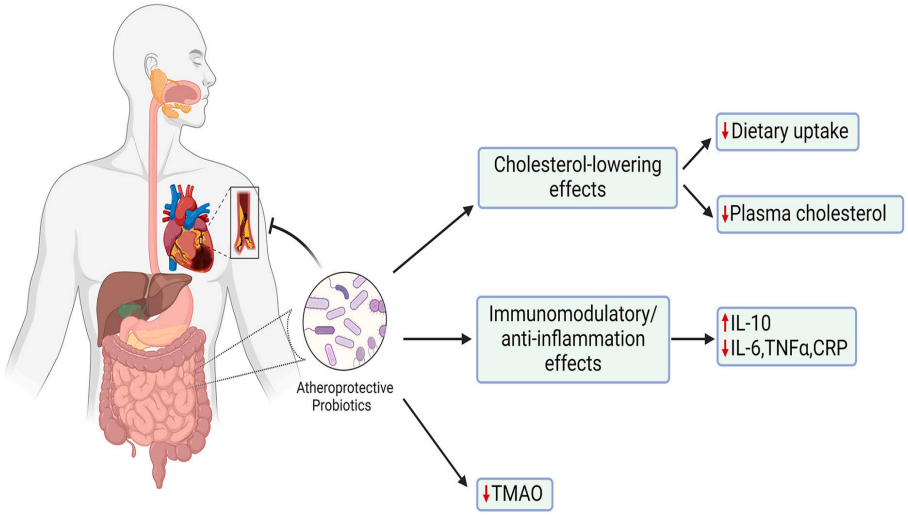
L. acidophilus and *Bifidobacterium Lactis*

VSL#3

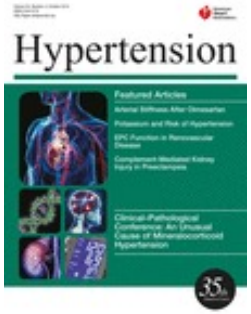
L. plantarum

Wang L, et.al The effects of probiotics on total cholesterol:

A meta-analysis of randomized controlled trials. Medicine 2018 Feb;97(5)



4. PROBIOTICS AND HTN



- Consumption of milk fermented with *Lactobac* results in modest **reductions in blood pressure**, due to the ACE inhibition-like peptides produced during fermentation.
- ”Meta-analysis suggests that probiotics may improve BP, with a potentially greater effect when baseline BP is elevated, multiple species of probiotics are consumed, the duration of intervention is ≥8 weeks, or daily consumption dose is $\geq 10^{11}$ CFUs”
  - *S. Khalesi, Hypertension, Oct 2014*
- “We’re some way from being able to tell you exactly which yogurt to eat to try to promote lower BP, but I think that being able to provide that sort of information is the long-term hope—gather all of the puzzle pieces, and put them together”
  - *J. L. Pluznick. Ph.D, Johns Hopkins 2020*
  - *Cardoso, A. M. (2024). Microbial influence on blood pressure: unraveling the complex relationship for health insights.*

5. MITIGATION OF VIRAL INFECTIONS

Reduction in the common cold

More than 15 studies on probiotics and reduction and treatment of common cold and influenza.

2015 Cochran review: probiotics reduce cold frequency & duration N=37270 (DB/RCT)

*Better than Vit C

(my opinion: Probiotics +

50,000u Vitamin D hammer!)

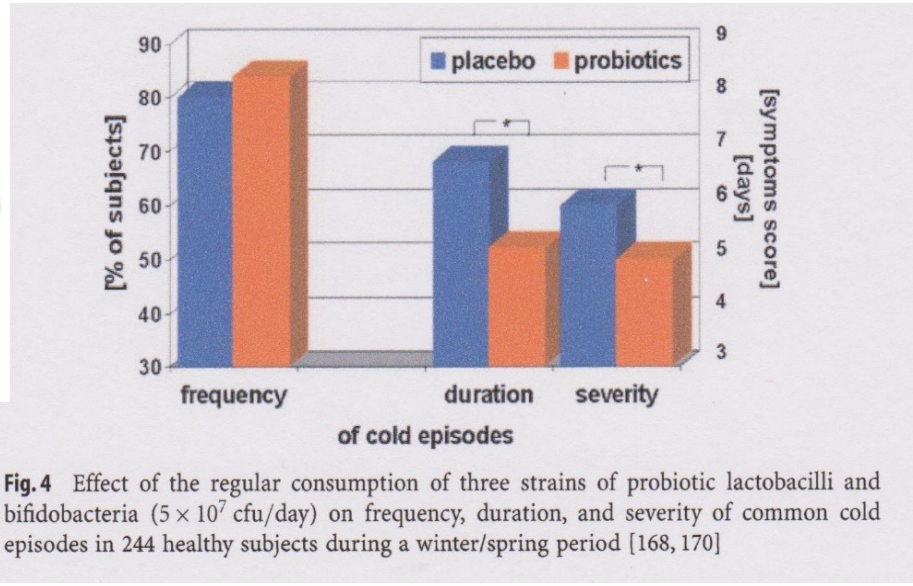


Fig. 4 Effect of the regular consumption of three strains of probiotic lactobacilli and bifidobacteria (5×10^7 cfu/day) on frequency, duration, and severity of common cold episodes in 244 healthy subjects during a winter/spring period [168, 170]

PROBIOTICS AND VIRAL INFECTION REDUCTION

- "Probiotic bacteria can hinder the adsorption process via directly binding to the virus and inhibiting entry into epithelial cells.
- Probiotic bacteria releases antimicrobial substances (such as bacteriocins, biosurfactants, lactic acid, hydrogen peroxide, nitric oxide, organic acids) and intestinal mucins from mucosal cells, which can effectively inhibit virus proliferation.
- Binding of probiotic bacteria to the epithelial surface can cause steric hindrance and block the virus's attachment to the host cell receptor.
- Virus neutralized by secretory antibodies like IgA."
  - *Kuljit Singh,Alka Rao, Probiotics: A potential immunomodulator in COVID-19 infection management, Nutrition Research, Elsevier, March 2021*

Prevention of COVID-19

Treatment adjunct of COVID-19

NUTRITION RESEARCH 87 (2021) 1–12

Available online at www.sciencedirect.com

ScienceDirect

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

Review Article

Probiotics: A potential immunomodulator in COVID-19 infection management

Kuljit Singh[a,#], *Alka Rao*[a,b,*]

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[b] Academy of Scientific and Innovation Research (AcSIR), Ghaziabad, Uttar Pradesh 201002 India

Singh K, Rao A. Probiotics: A potential immunomodulator in COVID-19 infection management. Nutr Res. 2021 Mar;87:1-12. doi: 10.1016/j.nutres.2020.12.014. Epub 2021

6. WEIGHT MANAGEMENT

- Multiple studies show probiotic = decreases in both body fat mass and waist circumference
  - Especially if combined with intermittent fasting (my opinion)
- Eating yogurt with *Lactobac. fermentum* or *Lactobac. amylovorus* reduced body fat by 3–4% over 6 wks
- A study of 125 overweight investigated the effects of *Lactobacillus rhamnosus* on weight loss & weight maintenance.
  - Women taking the probiotics lost 50% more weight over 3 mo, compared with placebo. They also continued to lose weight during the weight maintenance phase.

Lim S, et.al Effect of Lactobacillus sakei, a Probiotic Derived from Kimchi, on Body Fat in Koreans with Obesity: A Randomized Controlled Study. Endocrinol Metab (Seoul). 2020 Jun;35(2):425-434.

Sanchez M, et.al A. Effect of Lactobacillus rhamnosus CGMCC1.3724 supplementation on weight loss and maintenance in obese men and women. Br J Nutr. 2014 Apr 28;111(8)

Kadooka, et.al. 2010Euro J Clin Nutr, 64, 636

7. MOOD, ANXIETY, OCD

- *Lactobacillus plantarum*
  - When given to patients with IBS
  - Significantly reduced their anxiety and improved their quality of life
- *Bifidobacterium longum*
  - Show to help depression, reduces cortisol, address obsessions, compulsions, paranoia, anxiety.
- GABA: main inhibitory and relaxing neurotransmitter
  - Studies suggest that *lactobacillus rhamnosus* may reduce anxiety by changing the expression of GABA receptors

"I've got Butterfly's in my stomach"

References at the end

Trends in Food Science & Technology 103 (2020) 386–387

Contents lists available at ScienceDirect

Trends in Food Science & Technology

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

Check for updates

Psychobiotics: An emerging alternative to ensure mental health amid the COVID-19 outbreak?

To the editor:

COVID-19 is a highly infectious disease caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), which is responsible for the development of serious and even fatal respiratory complications, resulting from the failure of the response adaptive immunology in the early stage of the disease (incubation period) (Shi et al., 2020; Zhang et al., 2020). In addition to respiratory complications and the potential threat of death, COVID-19 outbreak can also threaten the mental health of the general public and health professionals, causing problems such as stress, panic, depression, anxiety, sleep disorders, lower mental well-being, and even suicide (Rajkumar, 2020; Roy et al., 2020).

Social isolation associated with the occurrence of infections and deaths of family and friends and the lack of a possible vaccine for COVID-19 can be considered stressful factors, which lead to the development of feelings such as loneliness and anger, and cause short-term post-traumatic stress (Ahmed et al., 2020). In addition, the advance of

Screenshot

Bacillus coagulans, *Clostridium butyricum*, and others (Cheng et al., 2019; Gualtieri et al., 2020; Vaghef-Mehrabany et al., 2020).

Ingestion of adequate amounts of these bacteria can assist in the production of neuroactive substances, such as gamma-aminobutyric acid (GABA), norepinephrine, dopamine, acetylcholine, cholecystokinin, serotonin, substance P, glutamate, glucagon-like peptide-1, glucagon-like peptide-2, peptide YY (PYY), neuropeptide Y (NPY), and may regulate proteins such as brain-derived neurotrophic factor (BDNF), which are important in the regulation of functions and behaviors related to the central nervous system (CNS) and also in gut-brain communication, through immunological, humoral, neural and metabolic pathways (Cheng et al., 2019; Dinan et al., 2015, 2013; Lyte, 2013). Several studies have suggested that the administration of psychobiotics can be effective in treating depression (Hao et al., 2019; Tian et al., 2020; Wei et al., 2019), stress (Allen et al., 2016; Savignac et al., 2014), and anxiety (Liang et al., 2015; Messaoudi et al., 2011).

A clinical study conducted on 22 healthy volunteers showed that ingesting strains of *Bifidobacterium longum* 1714 (1×10^9 colony-form-

- *Lactobacillus gasseri CP2305* during 12 weeks it was effective in recovering from fatigue and in relieving anxiety and depressed mood in 49 male university students and improved mental status and sleep quality in young students exposed to chronic stress

8.

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.

Many
Neuro PAs
now
do a detailed
GI history!

nature

ALZHEIMER'S

- Data from 3 RCTs involving 161 individuals with Alzheimer's disease receiving *Lactobacillus* and *Bifidobacterium* strains showed no beneficial effect of probiotic supplementation on cognitive function with very low certainty of evidence.
- However, probiotic supplementation improved plasma triglycerides, vLDL, insulin resistance, and plasma malondialdehyde. No RCTs included synbiotic supplementation or assessed microbiota composition.
- Current evidence regarding the use of probiotics and synbiotics for individuals with dementia is insufficient to support their clinical application
- No documented harm in their use
  - *Jenifer F Krüger, et.al. Probiotics for dementia: a systematic review and meta-analysis of randomized controlled trials, Nutrition Reviews, Volume 79, Issue 2, February 2021, Pages 160–170*

BEST PSYCHOBIOTICS

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

9. NEC PREVENTION IN PRETERM INFANTS

- AGA 2020 Practice guideline
- Moderate/High evidence
- In preterm (less than 37 weeks gestational age), low-birth-weight infants, we suggest using a combination of
- *Lactobacillus* spp and *Bifidobacterium* spp
- Showed a significant reduction in NEC in preterm infants

POSTBIOTICS

REBYOTA™
(fecal microbiota, live-jslm) suspension, for rectal use

1. Classic fecal transplant
   via colonoscopy
   C.diff patients
2. Rebyota
   - Current FDA approval for prevention of C.Diff recurrence after a documented infection
3. Thenabiotic OTC
   - "Post-biotic"
   - "Stool derived whole-biome multi-biotic supplement that contains prebiotics, thousands of heat-killed probiotics, and hundreds of distinct postbiotics." *Thaena.com*

PROBIOTICS- CAUTIONS

- Can be an unnecessary expense in those who do not require them.
- Diet enriched with soluble, but not insoluble, fiber induced HCC in dysbiotic mice (Inulin) *Singh et al., 2018, Cell 175,*
- Some probiotics supplements have been associated with infections in patients who are immunocompromised.
  - skin rash, fever, bloody stools etc.
- Rare cases cause bloating, diarrhea, abdominal pain.
- Severe pancreatitis (Lancet 2008)
- Lactobacillus bacteremia- rare!
- Sometimes interact with immunosuppressive drugs leading to life threating conditions.

PROBIOTICS ARE GRAS

- More than 60 human studies since 2008
- Many RCTs/DB
- 60 strains evaluated
- No morbidity

SUMMARY: SUPPORTING THE MICROBIOME

- Intermittent fasting
- Consume prebiotic fibers:
  - Pectin, inulin, fructo-oligosaccharides, asparagus, garlic, onions, leeks, bananas
- Eat fermented foods:
  - Kombucha, fresh sauerkraut, kimchi
- Take probiotics in the billions
  - Lactobacilli (multiple species)
  - Bifidobacteria (multiple species)

IN SUMMARY,

- More than 30 diseases benefits from probiotics, many have RCT-DB studies
- Probiotics are beneficial when used correctly
- Not all patients need probiotics
- Encourage patients to eat their probiotics in food/drink
- Remind patients:
  - They need 30 gm of fiber a day
  - "You are what you eat" – eating healthy helps address the three leading causes of deaths—cardiovascular disease, cancer and type 2 diabetes — can be largely preventable, and including probiotics can help!
- LOOK FOR
  - Lactobacillus (firmicutes)
  - Bifidobacterium (actinobacteria) Doses should be in the BILLIONS!
- Not all probiotics are the same
- For antibiotic associated diarrhea, any strain will work, just pick the correct dose
- We need more double blind & RCTs
- Combine with prebiotics!

THANK YOU!

- Remember you are not alone & you are what you eat!
- I hope you come to share my excitement for safe, affordable and logical use of probiotics
- Any questions or comments?
- Jerry Simons
- @JerrythePA
- **Gerald.simons@stonybrook.edu**

AASPA
American Association of Surgical Physician Assistants

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