The Microbiome Matters
Part 3
2018
Teresa Martin MS, RD, CDE, LD
cdepower@hotmail.com
541-220-1136

Microbiome research is still growing at a rapid rate
Publications (journals, books, articles)
1972=2
1982=8
1992=23
2002=116
2012= 5,512
2015=18,212
2016= 24,224
In the last year...
25,724 peer reviewed articles
53 books and over 34,000 articles published

“death sits in the bowels”…. “
“bad digestions is the root of all evil” – Hippocrates 400BC

“If you don’t like bacteria, you’re on the wrong planet.”
– Stewart Brand

“trust your gut” – Rob Knight

“the 150 year old war against the microbes has got to stop” – Larry Smarr

“the gut is the seat of all feeling”…..

“the junk food diet is one of the most important modifiable risk factors for depression for our adolescent population”
– Prof Felice Jacka

“we need to protect our friends with benefits”
“Food is a language that speaks to our genes”
— Jeff Bland

What will we cover today?
1. Review (quiz)/Deeper Dive
2. Popular Questions
3. Crazy & New Discoveries
4. Teresa’s Top Ten Tips for 2018 (any changes?)

Disclosures
- None
- Senior Educator for the Novo Nordisk Education Program
- The information and ideas presented today are my own and are based on my experience and my review of the current research and literature
- These views do not represent the positions, views or opinions of Novo Nordisk Inc.
What do we still know about the human microbiome?

The human microbiome is huge, diverse, makes us unique, constantly adapting, complex, plays critical role in our health and wellbeing.
Joshua Lederberg coined the term “microbiota” in what year?

A. 1954  
B. 1960  
C. 1986  
D. 2001

How much money are federal agencies pooling to forward the causes of the National Microbiome Initiative?

A. $667 million  
B. $412 million  
C. $121 million  
D. $10 million

How much money did the Bill & Melinda Gates Foundation invest to study human and agricultural microbiomes?

A. $100 million  
B. $10 million  
C. $5 million  
D. $1 million
Microbes play a role in 9 out of the top 10 global causes of death

A. True
B. False

Global Burden of Disease Study
- Huge global, regional, and national comparative risk assessment that is funded by Bill & Melinda Gates Foundation
- 1990-2016
- Run every 2 years
- 1800+ researchers around the world
- 180+ Countries
- Examined 84 different behavioral, environmental, occupational and metabolic risk factors
- Most comprehensive study about health & risk factors for disease
What has this study found?

Poor diet is the second leading cause of early death across the globe.

Number one in men, middle and high income countries.

Over nutrition kills more people than undernutrition.

What is a Poor Diet?

Not enough of what we NEED

- Fruit
- Vegetables
- Whole Grains
- Nuts & Seeds
- Beans
- Fiber
- Omega 3 FAs

Too much of what we DON'T NEED

- Red meat
- Processed meats
- Added sugar
- Sugar sweetened beverages
- Trans fat
- Sodium

~Professor Felice Jacka

Definitions

- Genome
- Microbiota
- Microbiome
- Metabolome
Alessio Fasano MD has a metaphor using a piano that helps us understand how these all relate.

In his metaphor which is:

The piano?
The piano player?
The music sheets?

What is possible
What appears to be happening
What makes it happen
What is happening
(Canaries of the Genome)

How big is the human microbiome?
(~# of microbial cells)

A. 3,000
B. 3,000,000
C. 3,000,000,000
D. 39,000,000,000,000
What % human are we genetically?

A. 50%
B. 30%
C. 10%
D. 1%

What are some of the major sites of microbial colonization identified in the human body?
- Airway
- Oral
- Skin
- Urogenital
- Gastro-Intestinal

What are the two distinct microbiota populations in our gut?

Luminal
Mucosal
How long does it take for new babies to fully develop their gut microbiomes?

A. ~6 months
B. ~1 year
C. ~3 years old
D. ~6 years old

How do we define a healthy microbiome?

A. Diverse
B. Large Mass
C. Resilient
D. All of the above
What helps make a healthy microbiome?
- Vaginal Birth
- Breast Feeding
- Early exposure to dirt, whole foods, animals, pets, people, places
- Limited exposure to antibiotics- especially the 1st 3yrs of life
- Playing outdoors
- Pets- dogs all ages- especially children (asthma)
- Adequate sleep
- Stress management- meditation, yoga

What else helps make a healthy microbiome?
- Exercise- outdoors
- Plant based diets
- High plant diversity
- Limited animal products-processed
- Limit processed foods (added sugars, emulsifiers, sugar substitutes)
- Limited exposure to antibiotics, PPIs, long term use of other medications
- Being young- diversity/mass decline after 65yrs

Which of the following is a function of the gut microbiome?
A. Allow us to adapt to our environment faster than our own genes
B. Immune and protective functions
C. Digestion and metabolic functions
D. Major player in the gut-brain axis with a sig role in production of neurotransmitters
E. All of the above
What are SCFAs?
A. Fatty Acids that are made through hydrogenation to solidity liquid oils
B. A class of FA’s that can lower the levels of cholesterol and LDL in the blood- found in fish, walnuts, flaxseeds
C. A very beneficial microbial waste product that results from microbes fermenting certain fibers in our diet
D. Basic building block of lipids/fats with 14 or more carbons- found in olive oil, soybean oil, nuts, avocado

Deeper dive into SCFA’s (cont)
Most abundant types of SCFAs in humans include (~98%)
- butyrate
- propionate
- acetate
- ENERGY
  - Provide ~10% of our daily energy requirements
- IMMUNE SYSTEM
  - Lowers the colonic pH
  - Provide intestinal barrier function-via activation of mucin
  - Anti-inflammatory effects
Deeper dive into SCFA’s (cont)

Play a role in lipid metabolism

➢ Increase fatty acid oxidation in liver, muscle, and brown adipose tissue
➢ Inhibit storage of fat in white adipose tissue
➢ Decreased FFA
   ◦ Decreases FFA-induced insulin resistance

Deeper dive into SCFA’s (cont)

Impact weight, insulin signaling, glucose tolerance, intestinal transit time

➢ Alter expression and secretion of gut hormones (GLP-1, GLP-2, peptide YY, ghrelin)
SCFAs provide gut-brain crosstalk to influence appetite, type of food intake, mood

Recent studies using SCFA's
- Low levels of SCFAs linked to neurodevelopmental disorders such as Parkinsons, Bipolarism, PTSD, MS
- Oral administration of acetate and propionate decreased glycemia in mice
- SCFAs reduced plasma concentration of cholesterol (rodents and humans)
- SCFAs are currently being used to help treat UC, CD Colon CA and antibiotic-associated diarrhea (promising results yet limited)
What will your patients ask?
○ How much fiber do we need to eat?
○ Which type of fiber do these microbes like... soluble or insoluble fibers?
○ Do over the counter fiber supplements work?

How much fiber?
Ancestors ate 100-130 grams/day
Tanzanians eat 100 gms/day
Current SAD: 5-15 grams/day

Current Daily Recommendations:
AHA, ADA: 25-30 gm
AND: 14g/1000 kcals [25-38 gm]
Microbiome Experts: 35-50 gm

Study- how much is upper limit?
50 gm- people get full
80 gm- max most people could consume in a day

What is better for our microbes... soluble or insoluble?
Switching definitions
OLD: (chemical definition)
Soluble- bind with FAs and help lower LDL
[psyllium, pectin, gums, inulin, oligofructose, beta-glucans, resistant starch]
Insoluble- provide bulk and decrease colon cancer
[cellulose, lignin]
NEW: (FDA- July 26th, 2018) (biological activity)
Intrinsic fiber- intact, found naturally in foods
Synthetic fiber- added fibers with beneficial physiological effects to human health
Current FDA approved intrinsic fibers
- Beta-glucan soluble fiber - bran fiber (heart dz)
- Psyllium husk
- Cellulose
- Guar gum (Regular Girl, SunFiber)
- Pectin
- Locust bean gum
- Hydroxypropyl methylcellulose - gluten free foods

Which fibers are best for SCFA production?
- Resistant starch
- Fructo-oligofructose (FOS)
- Inulin
- Cellulose
- Pectin
- Lactulose

May depend on the person and the microbes present

Food Sources that increase SCFAs
- Jerusalem Artichoke
- Bananas
- Onions
- Chicory root
- Garlic
- Asparagus
- Jicama Root
- Leeks
- Flaxseeds
- Barely
- Sugar beets
- Dandelion Greens
- Carrots
- Wheat Bran
- Oats
- Apples
- Konjac Root / Elephant Yam
- Burdock Root
- Yacon Root
Can’t I just take butyrate supplements?

- Not FDA regulated
- Butyrate has an offensive odor
- Free butyrate has been shown to be largely absorbed in the upper GIT
- The administration of a daily butyrate enema (10,000 mg/kg) benefited healthy individuals yet did not for pts with UC
- Not enough research to know which form and how much has the most benefit

Which of the following has been associated with the highest level of microbial diversity?

A. Organic foods
B. High plant diversity
C. Fermented foods
D. Intermittent fasting

Which of the following has been associated with the highest level of microbial diversity?

A. Organic foods
B. High plant diversity
C. Fermented foods
D. Intermittent fasting
Dietary interventions that increase microbial diversity/mass:
- High consumption of plant fibers (prebiotics)
- High-plant diversity
- Low-heat cooking
- Low-protein –esp animal protein
- Low-refined carbohydrates
- Fermented foods (probiotics)
- Intermittent fasting
- High-polyphenols (green tea, red wine, legumes, flaxseeds, dark chocolate, coffee)
- High Omega 3 Fas
- Organic (dirty dozen)

Organic Matters

Dirty Dozen
- Strawberries
- Spinach
- Nectarines
- Apples
- Grapes
- Peaches
- Cherries
- Pears
- Tomatoes
- Celery
- Potatoes
- Sweet Bell Peppers

Clean Fifteen
- Avocados
- Sweet Corn
- Pineapples
- Cabbages
- Onions
- Sweet Peas
- Paclavas
- Asparagus
- Mangos
- Eggplants
- Honeysdew
- Kiwis
- Cantaloupes
- Cauliflower
- Broccoli

What can hurt a healthy microbiome and cause dysbiosis? (decreased diversity and decreased mass)
Which of the following have been found to contribute to dysbiosis?

A. Emulsifiers
B. GMOs
C. Vaccines
D. Moderate Alcohol

What else?

Studies have shown all the following things can limit/damage our microbial ecosystem:

- C-section
- Formula
- Sleep deprivation
- Smoking
- Inactivity
- Certain medications
- Repeated antibiotics
- Hand sanitizers
- Stress
- Highly processed diet (emulsifiers, nitrates)
- Diet high in added sugar (>25gm/day)
- High salt/nitrates
- Excess alcohol
- Insufficient fiber intake
- Animal protein
- Sugar substitutes
Dysbiosis has been observed in all of the following, except?

A. Diabetes  
B. Autism  
C. Dwarfism  
D. Depression  
E. Anxiety  
F. Jet Lag  
G. CVD

What else has been associated with microbial dysbiosis?

- Malnutrition  
- Food allergies  
- Eczema  
- Anorexia  
- Gout  
- Osteoporosis  
- COPD  
- Jet Lag  
- Insomnia  
- Autism  
- Multiple Sclerosis  
- Parkinson's  
- Alzheimer's  
- Depression  
- Anxiety  
- OCD  
- PTSD  
- ADHD
Asthma

- Significant increased rates over last 50 years
- 25% of children suffer from asthma
- Highest rates are in developed countries (US, Canada, UK, Australia)
- Lowest rate- Africa

20% less like to get asthma if....
- You have a dog
- Live on farm

20% more likely to get asthma if....
- C-section
- Exposed to antibiotics before 3 yrs of age

Asthma (cont)

- 4 predictive species of microbes- if you are missing these at 3 months old your are much more likely to develop asthma
- In mice, gave these 4 microbes (FMT from humans) to asthma prone mice and it protected them from getting asthma
- Same microbes were not predictive of asthma if found in 1 year old

GUT-BRAIN Connection

Dysbiosis observed with
- Autism (70% suffer GI symptoms)
- Parkinson’s Disease
- Bipolarism
- MS
- Depression
- Anxiety
- Alzheimer’s
- Huntington’s Disease
- Stroke
- OCD
- ADHD
GUT-BRAIN Connection

- Gut is responsible for:
  - >90% of circulating serotonin
  - >50% of circulating dopamine
  - Oxytocin production
  - GABA production

Butyrate producing probiotics fed to mice reduced anxiety in rats.

FMT from timid mouse can cause outgoing mouse to become timid.

Butyrate producing probiotics fed to anxious adults led to lower reported psychological stress.

Children fed high fiber diets demonstrated better cognitive control than children on low fiber diet.

Depression

- Mediterranean diet decreased risk of developing post partum depression by 30%.

- Dietary support showed 33% more pts experiencing clinical remission than traditional social support (67 females)
  - $3000 less expensive to treat
  - Patient paid $30 less per week on food

GUT-BRAIN Connection

- Stress increases stress hormones- cortisol and adrenaline-both can impact the microbiome within one day- less Bacteroides more Firmicutes alters SCFA production

- Mindfulness practice/meditation altered microbes in one day.

- Study found MIND Diet may reduce the risk of Alzheimer's by as much as 50% (900 seniors over 5 year period)
MIND Diet

Eat these foods
- Beans
- Berries
- Fish
- Green leafy vegetables
- Nuts
- Poultry
- Olive oil
- Other vegetables
- Whole grains
- Wine- 1 glass

Limit/Avoid these foods
- Butter and stick margarine
- Cheese
- Fast or fried foods
- Pastries and sweets
- Red meats

ADHD

>6 million kids currently have ADHD; 1 in 40 have autistic spectrum
- Higher Bifidobacterium in infancy has been associated with increased risk of developing ADHD and Asperger syndrome
  - This difference led to decreased synthesis of phenylalanine (precursor of dopamine)
- 75 infants randomized to either receive Lactobacillus rhamnosus or not- followed 13 yrs
  - 17% in placebo group got ADHD or autistic spectrum vs zero in probiotic group

What will your patients ask?
What about stevia?
- Very few studies on stevia plant
- Rats fed high doses of stevioside for 22 months, sperm production was severely reduced
- Consumption of saccharin, sucralose, stevia, aspartame all found to cause increased weight gain and adiposity in mice
- Some reports of negative side effects with stevia
  - Dizziness
  - Muscle pains
  - Numbness
  - Nausea
  - Gas
  - Bloating
  - Insomnia

What about my ketogenic diet?

Calorie Distribution on a Ketogenic Diet

- 75% From Fat
- 20% From Protein
- 5% From Carbohydrates

- GI Disturbances
- Inflammation
- Kidney Stones
- Thinning Hair
- Impaired mood
- Muscle cramps
- Weakness
- Hypoglycemia
- Hypercholesterolemia
- Hypertriglyceridemia
- Heart arrhythmias
- MI
- Foggy Brain
- Nutrient deficiencies
- Mineral loss and malabsorption
- Poor growth in children
- Increased bruising
- Dark circles under eyes
- Increase infections
- Acute pancreatitis
- Cardiomyopathy
- Menstrual irregularities
- Death

Not sure how you can eat 35-50gms of fiber on a ketogenic diet and.....
And what about that meat?
L-carnitine (in meat) and choline (in eggs) broken down by microbes and liver and causes increased blood levels of trimethylamine-N-oxide (TMAO)

High levels of TMAO directly linked to atherosclerosis and more recently to prostate cancer

L-carnitine supplements to vegetarians vs meat eaters- vegans did not produce TMAO

Can’t I just fix it with a probiotic?
It is a complex world

How do you pick a 'good' probiotic?

- Gastric acid and bile salt stable
- No adverse side effects reported
- Manufacturers need to show stability during processing and stable shelf life – therefore, look for expiration date
- Test supplement to see if it is live/active (milk test)
- Accurate identification (genus, species, strain)
- Clinically documented and validated health effects for efficacy of the strain
  Actions are STRAIN specific

http://usprobioticguide.com
How do you prescribe a probiotic?

Be specific - like you would with any medication

- Take supplements with meals/food
- Don’t take at the same time as antibiotic
- Try for 4 weeks - stop probiotic if no improvement or any negative side effects (look at your poop)

Which probiotics should I take to prevent antibiotic induced diarrhea?

Level III Evidence

- Florastor Capsule 2 per day
- GoodBelly Capsules 2 per day
- GoodBelly Probiotic Oat Drink Shot-1/day
- GoodBelly Probiotic Juice Drink-1/day
- Ideal Bowel Support 2 per day
- NatureMade Digestive Probiotic Daily Balance-2
- UltraFlora Intensive Care-2/day

http://usprobioticguide.com

What probiotic should I take if I’m constipated?

Eat some plants and drink 4-6 cups water

Exercise

Consider taking fiber supplement - results depend on microbes

- Psyllium: Psyllium husk and Metamucil
- Methyl cellulose: Citrucel
- Glucomannan: Glucomannan capsules or PGX
- Inulin: Benefibre (Canada), Fiber Choice or Fibersure
- Partially hydrolyzed guar gum: Hi-Maize
- Wheat dextrin: Benefiber (US)

Below are level (II) Probiotics - no level III probiotics yet

- Visbiome
- VSL#3

http://usprobioticguide.com
Crazy & New Discoveries

Synthetic Biology-Synlogic has created a bacteria that sucks up **phenylalanine** and breaks it down into fragments and then releases these fragments into the urine

- Just tested in healthy humans with positive results
- Hoping to test in people with PKU and then gain FDA approval

Crazy & New Discoveries

- Engineering cancer fighting bacteria
- Certain microbes regulate chemotherapy and determine whether the treatment will work or not (fluoropyrimidine based drugs)

Engineered Germ Eating Bacteria

Defense Advanced Research Projects Agency (DARPA) funded

Discovered predatory bacteria attacks 150 out of the 165 known human pathogens (plague, bacterial lung infections, antibiotic resistant bacteria)

- *Bdellovibrio*- bores into large bacteria eats from the inside out- attacks 145 out of the 165
- *Myxococcus*- wolf pack
- *Vampirococcus*- vampires

The nasty bugs cant become resistant
Microbiology Society &
British Society for Immunology

Launched on JUNE 27th 2018
http://worldmicrobiomeday.com/

What's in our future?
- Personalized medicine/diets
- Microbiome Rights Activists
- Smart toilets- data dump (R Knight)
- Smart mirrors- analyze the microbial changes in your breath (R Knight)
- Bar codes on food could inform you what foods you need to help reshape/balance your microbiome
- Narrow spectrum antibiotics
- Phagtherapy-Virus that latches on particular microbe (lady bug to take of aphids)
- Psychobiotics instead of antidepressants; social pills for introverts
- FOOD POLICY CHANGES (protect our kids and pregnant women)
The healthcare providers role...
No longer is the role to exterminate the things that are making us sick...
Instead, the HCP is now more like a park rangers trying to protect all the healthy species when an invasive weed gets into the park

Teresa’s Top Ten Tips for 2018
1. Encourage healthy pregnancies, vaginal births and breastfeeding
2. Encourage plant based diets:
   - Work your way up to eating >30 different plant species a day
   - Some cooked and some raw
   - Eat in season if possible
   - 35-50gms fiber/day
3. Learn to cook and help teach your patients how to cook

Teresa’s Top Ten Tips for 2018 (cont)
4. Limit microbial assassins (the list is getting larger)
   - Refined carbs and added sugar (<25g added sugar/day)
   - Sugar substitutes
   - Processed foods- emulsifiers (polysorbate-80 and carboxymethylcellulose are the worst so far)
   - Smoking, Vaping
   - Chronic Stress
   - Antimicrobial soaps, sanitizers, antibiotics, PPIs
   - High fat diets, processed meats
   - Being inside and inactive all day
Teresa's Top Ten Tips for 2018 (cont)

5. Move every day (move at least 30min and don't sit for more than 30-60 min)
6. Open a window; get outside; play in the dirt
7. Relax (yoga/meditation/mindfulness)
8. Sleep 6-8 hrs
9. Be cautious with probiotics- use ones that have some evidence of efficacy and safety; strain specific; don't use with immune compromised or the very ill
10. Look at your poop!

THANK YOU!

Experts in the microbiome field
- Prof Felice Jacka Professor at Deakin University, Director of the International Society for Nutritional Psychiatry Research (ISNPR)
- Anne Bikle and David Montgomery - *The Hidden Half of Nature* (soil health)
- Alessio Fasano MD- pediatric gastroenterologist and researcher; heads the Center for Celiac Research at Mass General Hospital for Children; discovered zonulin; Gluten Freedom
- B Brett Finlay PhD and Marie-Claire Arrieta PhD - *Let them Eat Dirt* (asthma and diarrhea)
Experts in the microbiome field

- Prof David Relman - Microbiologist, Stanford University
- Dr John Cryan - Neuropharmacologist, Ireland, Univ College Cork
- Prof Rob Knight - Prof Univ of CA San Diego, Co-founder of American Gut Project and Earth Microbiome Project; Follow Your Gut; Dirt is Good
- Prof Jo Handelsman - Prof Wisconsin Institute for Discovery, Microbiologist
- Prof Martin Blazer - Prof of Translational Medicine, Director of NYU Human Microbiome Program; Missing Microbes
- John Cryan Phd Ted Dinan MD, Scott Anderson - The Psychobiotic Revolution