Diabetes & the Gut Microbiome

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In 400 B.C. -Hippocrates stated that, “...death sits in the bowels...” and “...bad digestion is the root of all evil....”

“Always trust your gut”

“I’ve got a gut feeling”

“Gut instinct”
Friend or Foe?

“The shift in our perception of bacteria from pathogen and enemy to our most important health ally represents the greatest turnaround in science and medicine in 150 years.”

~Raphael Kellman, MD
The human microbiome is being called.....

"the forgotten organ"

"the software of the human body"
“We are at the beginning of a cultural shift in the way we practice medicine, to the way we raise our children and how we clean our house…”

~Kris Campbell
Science Writer for Microbiome for Health

“We are not individuals, we are colonies of creatures”

~Dr Bruce Birren – Genome Sequencing and Analysis Program at MIT
5 W’s we will cover today:

- What is it?
- Where is it?
- What do we know about it?
- What do we know about the gut microbiome and diabetes?
- What will we do differently with this information?
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 is the microbiome?
What is the microbiome?

**Microbes:** Tiny organisms—too tiny to see without a microscope, yet they are abundant on Earth. They live everywhere—in air, soil, rock, and water. Examples include bacteria, fungi, protozoans, unicellular eukaryotes, viruses.

**Bacteria:** Single-cell organisms that lack a nucleus. These cells are complete, self-contained beings. They breathe, move, eat, eliminate wastes, defend against enemies, and reproduce.

**Microbiota:** All the microorganisms that live in a particular environment, for example, the air, the soil, the ocean, the human body, the gut.

**Microbiome:** The entire collection of genes found in all of the microbes associated with a particular host or within a particular site. An ecosystem of microbes that live on and in the human body (human microbiome).
How are we learning about the human microbiome?

- The Earth Microbiome Project
- The Human Microbiome Project - NIH $173 Million (2007-2012) (300 subjects)
- The Human Microbiome Project 2 (2014- present)
- The American Gut Project — (>10,000 subjects and growing)
How are we learning about the human microbiome? (cont)

- The American Microbiome Institute
  - Your Private Microbiome
- International Society of Microbiota
- MetaHIT: Metagenomics of the Human Intestinal Tract ($28 million project)
- Genome Sequencing and Analysis Programs at many universities and microbiome companies from around the world
- And more...
Types of gut microbiome studies

- Infectious/Antibiotic Studies
- Observational Studies
- Germ Free Mice
- Dietary Manipulation
- Prebiotics/Probiotics
- Fecal Transplants
So what have we learned?
The human microbiome is GINORMOUS!!

- ~10-37 trillion human cells (depending on who you ask)
- ~10 trillion fungal cells
- ~100 trillion bacterial cells
- ~500 trillion viral cells
- ~20,000 human genes (Human Genome Project)
- ~8 million microbial genes and counting
- Estimated to make up ~3-6 lbs of our body weight… or about the size of the brain
The human gut contains ~1 trillion microbes ~1000 times the number of stars in a galaxy
5 Major Sites of Microbial Colonization in the Human Body:

- Nasal
- Oral
- Skin
- Urogenital
- Gastro-Intestinal
Bacterial Distribution by Body Site
(www.genome.org)

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<thead>
<tr>
<th>Site</th>
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<tr>
<td>Eye</td>
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<td>Blood</td>
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<td>Oral</td>
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<tr>
<td>GI Tract</td>
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What makes us unique is more likely our microbiome vs our genes

- You only have one genome and it is 99.9% similar to other humans
- Each of us has a unique set of microbial genes, that changes dramatically during the first 2 years of life and is only 10% similar to other humans
- We leave a microbial footprint everywhere we go (forensics)
"So tell me, Daniel... when will we get to meet your microbes?"
Functions of our gut microbiome

- Allow us to adapt to our environment faster than our own genes will allow us to adapt

- Essential for maintaining health
  - Digestion and Metabolic Functions
  - Immune and Protective Functions
Digestive & Metabolic Functions

- Microbes break down our food to extract nutrients
- Determine how much energy we get and store
- Play a role in appetite control
- Influence lipid and cholesterol metabolism
- Influence our ability to metabolize polyphenols which allows them to have antioxidant benefits
- Influence our ability to synthesize essential amino acids and certain vitamins (biotin, folate, vit K)
- May help metabolize dietary carcinogens
- Involved in our bodies ability to make SCFA
Immune & Protective Functions

- Intestinal mucosal layer protects the intestine against exogenous pathogens and other harmful indigenous microorganisms
- Compete for space and nutrients
- Restrict overt immune stimulation
- Inhibit growth of their competitors by producing antimicrobial peptides (proteins)
- Teach our immune systems how to recognize dangerous invaders
- Produce helpful anti-inflammatory compounds that fight off other disease-causing microbes
Additional Functions are being discovered every day

- Play a significant role in the absorption and bioavailability of drugs and their metabolites

- Major player in the gut-brain axis... microbes can influence the brain
  - Microbes create other metabolites that produce neurotransmitters that influence behaviors (dopamine, serotonin)
  - Play a role in our circadian rhythms
The gut microbiome is influenced by:

- Birthing process (C-section vs vaginal)
- Infant feeding method (breast vs formula)
- Hygiene – Pets, # in household
- Lifecycle stages
- Geography
- Environment (outdoors/indoors)
- Diet (fat, fiber, processed)
- Stress-exercise, metabolic, psychological
- Medications (antibx)/Radiation
- Illness/Food Poisoning
- Sleep deprivation
- Age
- Smoking
Dysbiosis

- A microbial imbalance on or inside the body that diminishes a person’s essential population of good bacteria and allows pathogenic bacteria that are normally present in low amounts to flourish.
- Dysbiosis is most commonly reported as a condition in the digestive tract but can occur anywhere.
Microbial dysbiosis has been associated with the following:

- Diabetes
- Obesity
- Heart Disease
- Malnutrition
- Crohn’s Disease
- Celiac Disease
- Ulcerative Colitis
- Food allergies
- Eczema
- Asthma
- Anorexia
- Gout
- Rheumatoid arthritis
- Osteoporosis
- Cancers-colon, colorectal
- COPD
- Jet Lag
- Autism
- Multiple Sclerosis
- Necrotizing Enterocolitis
- Liver Disease- non-alcoholic liver disease
- Mental Health-depression, anxiety, OCD

Lux Research, Eating for 100 Trillion:Symbiotic Metabolism and the Microbiome Revolution, March 2014.
Obesity Studies-observational

- Maternal antibiotic prescriptions in the 2nd/3rd trimester or within 30 days before delivery was associated with an increased risk of obesity in the offspring by school age (USA, Denmark 2015)
- Danish registry found increased risk of obesity in boys whose mother’s used antibiotics during pregnancy (2013)
- Six recent observational studies found increased prevalence of obesity in children after antibiotic treatment
- One case-controlled study found exposure to antibiotics before 12months increased the risk of being overweight and of central obesity in children 9-12yrs by more than twofold (Canada 2014)
Comparisons between the geography of obesity and antibiotic use, 2010

Antibiotic prescriptions per 1000 persons, 2010

L Segal & MJ Blaser, PATS 2013; in press
Obesity - Observational (cont)

- Obesity and antibiotic use has been positively correlated (humans and animals)
- Can predict obesity more accurately based on microbiome vs the 32 validated obesity risks identified through genome
- **Obese people have significantly lower bacterial gene counts** (less diversity, less abundance)
- Examples of altered levels of microbes observed in obese humans:
  - Low levels of Firmicutes
  - Low levels of Bifidobacterium (breast fed link?)
  - High levels of Bacteroidetes
  - High levels of Lactobacillus casei/paracasei and Lactobacillus plantarum
Obesity – Interventional Studies

- Colonization of the gut of germ free mice through fecal transplant can cause weight gain. The degree the mice gained weight was dependent on the weight of the donor.
- Microbiota can increase energy extraction from indigestible polysaccharides:
  - FMT mice to mice and human to mice studies
- Hijack our genes and change how energy is expended and stored
- Capable of changing our appetite controls
- Lean humans given broad-spectrum antibiotic cocktail lead to suppression of gut bacteria abundance and average of 1.3 kg weight gain 180 days post exposure.
T1DM Studies-Observational

- Incidence of T1DM is increasing worldwide at a rate that is much higher than genetic predisposition can explain and these rates differ in different regions (environment)
- Identical twin studies show that if one twin gets T1 there is only a 13-33% chance that the other twin will get T1DM (environment)
- Correlational studies show higher rates of DM & Obesity in children that were delivered via C-section, formula fed, and/or had antibiotics before age 3
T1DM Studies-Observational (cont)

- The increased use of antibiotics in humans correlates with the increased incidence of T1DM
- Mice studies show an increased incidence in the development of T1DM if given antibiotics early in life
- Observe accelerated insulitis in mice that are raised under germ-free conditions (hygiene hypothesis)
- High levels of Bacteroides species are observed in people who later develop T1DM
- Certain species of Bacteroides increase the risk of autoimmunity by up to 20 times
T2DM Studies-observational

- Pathogenesis of T2DM is less well understood than T1DM
- Like T1DM, genetics alone can not account for significant increased prevalence of T2DM
- Bariatric surgery causes significant changes in the microbiome that play a role in the significant improvements in T2DM and decreased CV risk even before weight loss - Roseburia intestinalis increases after surgery
- Roseburia intestinalis is deficient in PWD
T2DM Studies: Observational

T2DM is associated with altered bacterial gene counts (less diversity, less abundance)

- The ratio of Bacteroidetes to Firmicutes and Bacteroides-Prevotella to Clostridium coccoides-Eubacteria rectale correlate positively and significantly with plasma glucose concentrations (human)
- Betaproteobacteria was high in T2DM and positively correlated with plasma glucose
- Tight junctions break down in the absence of Bifidobacterium which leads to inflammation and insulin resistance
- Bifidobacterium and Faecalibacterium prausnitzii are lower in PWD (T2DM)
- High fat diets lower the amount of Bifidobacterium
T2DM Studies: Observational

- High levels of Ralstonia (gram (-) bacteria) in visceral fat and in feces are strong predictors of developing T2DM (humans and mice)
- Observed an increased risk of developing diabetes with c-section, formula fed, and/or with increasing exposure to antibiotic use
- Antibiotics given to healthy adults altered the gut-microbiome and decrease diversity for up to 4 months (amoxicillin/minocycline) and up to 12 months (clindamycin/ciprofloxacin)
Diabetes Studies: Interventional

- If Ralstonia is transplanted into lean, germ free mice, they develop more visceral fat and are more likely to get diabetes
  - Vaccinating mice with inactivated Ralstonia prevented them from getting DM (Vrieze et al, 2013)

- Mice with DM that were fed whole grain oats for 8 wks had increased levels of Prevotellaceae, Lactobacillaceae, and Alcaligenaceae families of bacteria and improved insulin sensitivity and glucose levels

- Mice fed polyphenol-rich cranberry extracts resulted in improved insulin tolerance and decreased glucose-induced hyperinsulinemia during an OGTT
Diabetes Studies: Interventional (Human)

- Infusing intestinal microbiota from lean donors to male recipients with metabolic syndrome lead to significant increase in butyrate producing microbes and temporarily improved insulin sensitivity in individual with metabolic syndrome up to six weeks after infusion (Vrieze et al 2012)
- 20 obese people with metabolic syndrome given vancomycin or amoxicillin for 7 days- found no change in glucose yet found reduction in peripheral insulin sensitivity with vancomycin only (study has not been replicated)
- But….3 controlled interventional short-term studies on adults found no impact of antibiotics on FBG, PPG or hepatic insulin sensitivity
Diabetes and LPS studies

- Microbiota-derived lipopolysaccharide (LPS) is a key molecule involved in the early development of inflammation and metabolic diseases
- LPS is a powerful proinflammatory molecule
- High LPS in plasma led to increased FBG, insulinemia and ileal inflammation (mice)
- High plasma LPS correlated to obesity & T2DM in humans
- High fat diets have been shown to increase plasma LPS levels (humans and mice)
Diabetes/Obesity and SCFAs

Gut microbes in colon ferment complex plant polysaccharides into Short Chain Fatty Acids (SCFAs)

Functions of SCFAs:
- Provide ~10% of our daily energy requirements
- Help ensure healthy intestinal barrier function
- Alter expression and secretion of gut hormones (GLP-1, GLP-2, PYY) which has an effect on metabolic and energy balances
- Influence appetite and food intake
- Play a role with weight gain, insulin signaling, glucose tolerance, intestinal barrier function and intestinal transit time
Mar. Drugs 2016, 14, 27
SCFA Studies

Many researchers suggest that a lack of SCFAs, particularly Butyrate, is a possible link to diabetes

- Butyrate-producing bacteria protect against development of insulin resistance
- Butyrate is the preferred fuel of the colonic epithelial cells and also plays a major role in the regulation of cell proliferation and differentiation
- Clostridiales, Faecalibacterium, Roseburia, Eubacterium are associated with butyrate production
More studies on SCFAs

- Animal studies have shown that giving SCFA protected against diet-induced obesity and insulin resistance (Remely et al, 2014)
- Some evidence to support that SCFA may directly prevent low-grade inflammatory response
- Antibiotics have been shown to alter the production of SCFAs and change the gut hormone levels in animal studies and human studies (broad spectrum)
Diet and SCFAs

- Higher carbohydrate and fiber intake (indigestible polysaccharides) produces more SCFAs.
- Higher levels of SCFAs are associated with decreasing luminal pH.
- E Coli and Enterobacteriaceae do not thrive in lower pH ranges (5.5-6.5) and they prefer proteins as their energy source.
Role of Bile Acids

Roles of bile acids:
- Lipid digestion and absorption
- Play a role in the regulation of gut hormone secretion
- Regulate TG, glucose and energy homeostasis
- Gut bacteria modulate the bile acid pool and bile acids also signal back to the gut microbiota

- Bile acid pool size and composition are altered in both animal models and in humans with T1/T2DM
- Antibiotics have been shown to alter fecal and serum levels of bile acids
- Diet influences bile acid production
Summary of Gut Microbiota & Diabetes/Obesity

- Positive association between altered gut microbiome and obesity, diabetes and metabolic syndrome
- Altering the microbiome impacts risk of developing obesity and diabetes in animal studies (causality)
- Fecal transplants and some pre/probiotic studies are showing it is possible to alter the gut microbiome and have short-term effects on glucose metabolism & wt
- Antibiotics have been associated with increased risk of obesity and diabetes in both animals and humans yet not all short term human studies support this observation
- Three potential pathways where gut microbes can influence body weight and glucose metabolism include:
  1. LPS
  2. SCFAs
  3. Bile Acids
Three potential pathways where gut microbiota can influence body weight and glucose metabolism

Source: Mikkelsen et al. Diabetes, Obesity, and Metabolism 2016;1-10
Next up.....

- Sugar Substitutes
- Processed Food
- Probiotics/Prebiotics
- Metformin and other news
Sugar Substitutes

- Mice fed saccharine, sucralose, or aspartame for 4 weeks all had dysregulation of their glycemic control - saccharine had the most pronounced effect
- An antibiotic was able to correct the dysbiosis and reverse the saccharine induced glycemic intolerance in these mice
- Healthy humans that consumed artificial sweeteners resulted in increase in A1c, decreased glucose tolerance, impaired FBG, increased hip/waist ratio and increased weight and this was a dose related response
Sugar Substitutes (cont)

- Saccharine lead to profound dysbiosis in some people, which also led to abnormal glucose tolerance. When the saccharine was removed their glucose tolerance returned to normal (Korem et al 2014)

- Saccharine induced a microbial response that lead to increased appetite, increased absorption of glucose and increased insulin resistance

- Aspartame, Sucralose, Saccharine caused significant alterations in microbial diversity within 1 week in humans
Impact of Processed Foods

- Switching rats from low-fat, plant polysaccharide-rich diet to a high-fat/high-sugar diet changed the representation of metabolic pathways in the microbiome and altered microbiome gene expression within one day.
- High protein and sulfate diets (derived primarily from food additives) have been shown to damage the gut mucosa in humans.
- McDonald’s 10 day diet (1400 species lost-40%)
More on processed foods…

- Emulsifiers in food have been shown to damage the mucosa allowing it to be more penetrable—allowing unwanted materials from the gut to get into the bloodstream—Resulting in increased inflammation (human/mice)

- Examples of emulsifiers in our food:
  - polysorbate 80
  - Lecithin
  - carrageenan
  - Polyglycerols
  - carboxymethylcellulose
  - xanthan and other “gums”

~Dr Andrew Gewirtz 2015
Probiotics

- WHO - Live microorganisms with potential health benefits for the host if consumed in adequate amounts
- An oral supplement or a food product
- Used in infant formulas and tube feedings
- Evidence beginning to support probiotic use for many GI conditions (diarrhea, constipation, Crohn’s disease, UC) and allergic disorders
Example of Probiotics - Food

Fermented Foods (raw, lacto-fermented, or unpasteurized)

- Sauerkraut
- Kimchee (spicy pickled cabbage)
- Yogurt and Kefir - "live active cultures" = 100 million cultures per gram (or 10 million cultures per gram for frozen yogurt)
- Kombucha Tea
- Miso Soup
- Pickles
- Tempeh
Probiotics - Pills, Powders, Capsules, Liquid Shots

- Most contain Lactobacillus and Bifidobacterium
- "CFU" = colony forming units
- 4-40 billion live organisms per dose (CFU)
- Everyone is making them
- $$$$$
Prebiotics

- Non-digestible food ingredients that stimulate the growth or activity of bacteria (oligosaccharides)
- Provide the nutrients for multiplication of a desirable gut bacteria and for other species of microorganisms in the gut that may be favorable to health
- Available as dietary supplements and in foods
Popular Prebiotic- Supplements

- Inulin
- Oligosaccharides
  - Fructo-oligosaccharides (FOSs)
  - Galacto-oligosaccharides (GOSs)
  - Soybean oligosaccharides
Natural Prebiotics

- Chicory Root
- Jicama
- Jerusalem Artichoke
- Dandelion Roots/Greens
- Garlic
- Leek
- Onion
- Asparagus

- Wheat bran
- Whole Wheat Flour
- Banana
- Radishes
- Tomatoes
- Carrots
- Burdock Root

All unprocessed whole plant foods 😊
Studies with pre/probiotics and DM

- Inulin increases bifidobacter levels and resulted in reductions in fat mass, glucose intolerance and inflammation in mice.
- Germ free mice fed high fat diets without probiotics showed impaired glucose tolerance compared to mice fed high fat diets with probiotics (SG2 culture).
- Prebiotics given to humans (that ferment into SCFAs) have been shown to increase plasma levels of GLP-1, GLP-2, and PYY; inhibit the release of ghrelin; and increase satiety feeling.
Studies with pre/probiotics and DM

- Systematic meta-analysis showed that probiotics can lower LDL, BP, inflammatory mediators, blood glucose and BMI; increase HDL (human and animal)

- Zhang et al concluded from their meta-analysis that probiotics appear to improve glucose metabolism to a modest degree and a greater effect is seen when given >8wks and if multiple species are consumed (Dec 2015)
Keep in mind….

- A few studies have shown that pre/probiotics fail to maintain significant effects on lipid profiles and/or BG levels with T2DM; lacking studies on T1DM
- We are lacking solid clinical trials (esp w T1DM) to support the use of pre/probiotics as a treatment for DM and/or Obesity
- No standard safety guidelines
- No one regulating the production of pre/probiotics
Antibiotics and Pre/Probiotics

Increasing evidence that pre/probiotics may help prevent or treat antibiotic-induced diarrhea and help w/IBS. A few researchers recommend the following guidelines (GI ONLY)

- **Saccharomyces boulardii**, Lactobacillus rhamnosus 5-10 billion CFU/day
- Multi-strain formula with Bifidobacterium, L. casei, and/or Lactobacillus acidophilus
- Lactobacillus GG, Lactobacillus sporogenes, Saccharomyces boulardii at 5-40 billion CFU/d

- Take 1 hr before or 2hrs after antibiotic dose
- Increase intake of prebiotics (inulin 6-24g/day)
- Take for 30 days

*caution with immunocompromised and very ill*
A few tips for those that want to try probiotics

- Lactobacillus and Bifidobacterium
- At least 20 billion live organisms per dose (CFU)
- Switch brands often
- One study showed it is best to take probiotics with food
- Test to see if it contains live/active cultures by putting 1 dose into ¼ cup milk, leave out on counter- it should start to curdle within 24-48 hrs
Other headlines....

- Metformin & the Gut Microbiome
- Lack of vitamin D receptors causes dysbiosis
- Bariatric Surgery Alters Gut Microbiota
- ADA & JDRF Research Symposium: DM and the Microbiome (Oct 2014)
- Stool consistency associated with gut microbiota richness and diversity
- Psychobiotics
I see the problem. Your gut microbiome is out of balance. One moment.

I think you mean microbiome. ...right?

No. Here, swallow this. That's a wolf. Do you need a glass of water?
Be careful not to oversell the microbiome

Gaps in our understanding of the gut microbiome:

- We do not have a sophisticated understanding of causation
- We do not know the dynamics of change
- We do not know how the inventory of the microbiota relate to functional status
- We do not know the inputs and outputs of each community
- What receptors do each species trigger
Gaps in our understanding of the gut microbiome (cont)

- What are all the metabolic products?
- How long do the effects last when we change the microbiome? (probiotics/FMT)
- Are the changes we observe cause or consequence?
- What is good for one person may not be good for another
- Lateral gene transfer and shear #s of species complicates everything
high exposure to antibiotics
How do we define a healthy microbiome?

- Diversity and mass
- Capable of supporting the health of the host
- An ecosystem that is resilient
  - recovers quickly from perturbation (toxins, foods, drugs, other microbes)
  - remains stable during insults involving inflammation

Winning football team
WHAT DO THE EXPERTS RECOMMEND?

AACE 2016

- Eat a **plant based** diet high in PUFA & MUFA
- **Sleep** 6-9 hours
- Avoid trans fats, limit saturated fat
- Limit sucrose containing foods and high glycemic-index foods
- >150min moderate exertion **physical activity** plus strength training
Dietary Guidelines 2015-2020

- A variety of vegetables from all of the subgroups—dark green, red and orange, legumes (beans and peas), starchy, and other
- Fruits, especially whole fruits
- Grains, at least half of which are whole grains
- Eat a variety of nutrient dense foods
- Limit added sugars to <10% of calories
- Limit SF to <10%
- <2,300 milligrams (mg) per day of sodium
- Alcohol in moderation
ACADEMY OF NUTRITION & DIETETICS (AND)

Mediterranean Diet:
- An abundance of food from plant sources, including fruits and vegetables, potatoes, breads and grains, beans, nuts and seeds.
- Olive oil as the principal fat, with total fat ranging from less than 25% to over 35% of energy, with saturated fat no more than 7% to 8% of energy.
- Daily consumption of low-to-moderate amounts of cheese and yogurt.
- Twice-weekly consumption of low-to-moderate amounts of fish and poultry and up to 7 eggs per week (including those used in cooking and baking).
- Fresh fruit as the typical daily dessert.
- Moderate consumption of wine, normally with meals; about one to two glasses per day for men and one glass per day for women. From a contemporary public health perspective, wine should be considered optional and avoided when consumption would put the individual or others at risk.
- Red meat a few times per month.
- Regular physical activity at a level that promotes a healthy weight, fitness and well-being.
The mean intake of dietary fiber in the United States is 17 g/day with only 5 percent of the population meeting the Adequate Intake. Higher intakes of dietary fiber reduce the risk of developing several chronic diseases, including cardiovascular disease, type 2 diabetes, and some cancers. 14 g total fiber per 1,000 kcal, or 25 g for adult women and 38 g for adult men. Properties of dietary fiber, such as fermentability and viscosity, are thought to be important parameters influencing the risk of disease. Rec increase consumption of whole grains, legumes, vegetables, fruits, and nuts.
Teresa’s Top Ten Tips for a healthy microbiome

1. Encourage women to have vaginal births and breast feed (whenever possible)

2. Limit your exposure to antibiotics
   - Use antibiotics responsibly and only when absolutely necessary
   - Pay attention to where your meat and dairy come from (antibiotic-free)

3. When you are taking antibiotics—eat a ton of fruits/veg and consider using probiotics (look up the current research)
Teresa’s Top Ten Tips (cont)

4. At home, stop using so many sanitizers. Instead, use soap and water (save the sanitizers for the doctor’s office and hospitals) ~Martin Blaser MD

5. Sleep 6-8 hours on a regular cycle

6. Limit/Avoid the healthy bacteria assassins: processed foods, diet soda, emulsifiers, smoking, added sugars
   - <25 gms females, <37 gms for males/day
Teresa’s Top Ten Tips (cont)

7. Eat a variety of plant species every day (>30)
   ➢ Shoot for >30 gms fiber/day

8. Don’t be a hostage to the food industry and **Learn to Cook**

9. Meditate and Exercise Daily

10. Participate in the research
    ➢ NIH Human Microbiome Project
    ➢ American Gut Project
    ➢ My Private Biome
The 3 M’s of diabetes management may need to change to the 4 M’s

**Move**

**Meds**

**Meals**

**Microbiome**
Where can you go for more on the microbiome?

https://commonfund.nih.gov/hmp/overview NIH research projects, can participate, no charge yet very extensive screening and consent forms
http://www.microbiomeinstitute.org – blogs, podcasts
http://humanfoodproject.com/americangut/ - information and link to the American gut project
https://fundrazr.com/campaigns/4Tqx5 send in your own samples for research and get your own microbiome mapped for $99, agree to be part of research
http://www.yourprivatebiome.org/ - vaginal microbiome project, several ways to participate, $70-$2000 donation required