What Guts Have To Do With It…

The Microbiome, Health & Chronic Disease

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Objectives

• Provide a brief introduction to the gut microbiome
• Describe association of the microbiome with several chronic diseases
• Review dietary components that influence the microbiome and health
History

• 17th century: Antonie van Leeuwenhoek, single lens microscope saw “animalcules” (bacteria)

• 2001: Josh Lederburg, “gut microbiome” or gut flora (bacteria, viruses, fungi)
NIH Human Genome Project

- Collaborative effort, NIH sponsored
- Identify, observe genetic potential & metabolic activities of the body’s various microbes related to health and disease

www.hmpdacc.org
www.human-microbiome.org
“All disease starts in the gut.”
Hippocrates

• Gut basic functions: digestion, absorption, immunity

• Gut health influenced by: microbiome, lifestyle, medications, aging, environment

https://www.azquotes.com/author/22138-Hippocrates
Definitions

• Gut Microbiota
  – Ecosystem of microorganisms that have adapted to live on intestinal mucosal surface or within the gut lumen (bacteria, archaea, fungi, viruses)

• Gut Microbiome
  – Collection of all the microbiota, their genes and metabolic products

WGO Handbook on Gut Microbes (2014)
Gut Microbiome: Complex Ecosystem
Microbiota Starts Early in Life

Alou et al. (2016)
Microbiome Maturation

Alou et al. (2016)

Maturation due to the influence of genetics, environment, diet and gut physiology

1 year old
Akkermansia muciniphila
Bacteroides
Veillonella
Clostridium cocoides group
Clostridium botulinum group

Adult gut microbiota
Firmicutes (Lachnospiraceae, Ruminococcaceae)
Bacteroidetes (Bacteroidaceae, Prevotellaceae, Rikenellaceae)
Actinobacteria (Streptomycetaceae, Coriobacteriaceae)
Proteobacteria
Fusobacteria
Verrucomicrobia (Akkermansia muciniphila)
Cyanobacteria
Euryarchaeota (Methanobreibacter smithii)
Gut Microbiome

- Large intestine most densely populated
- Gut microbiota: trillions, bacteria-most studied, more than 1000 species known, more than 3 million genes

Rajoka et al.
Macronutrients and Gut Microbiota

Alou et al. (2016)

High carbohydrate diet

Increased species (high fermenting power)
- Clostridium cluster XVIII
- Lachnospiraceae (Clostridium clostridioforme)
- Ruminococcaceae (Faecalibacterium prausnitzii)
- Prevotella

Decreased species
- Bacteroides
- Bifidobacterium
- Enterobacteriaceae

High fat diet

Increased species
- Bile tolerant species
- Alisites
- Bacteroides
- Bilophila

Increased species
- Butyrate producing species
- Clostridium cluster XIV
- Roseburia
- Eubacterium rectale
- Faecalibacterium prausnitzii
- Bifidobacteria
- Lactobacilli
- Proteobacterial species
- Bacteroides

High protein diet
Gut Microbiota
Metabolic and Immune Functions
Backhed et al. (2012)
Metabolism

• Various gut bacteria digest dietary fibers: Short Chain Fatty Acids (SCFAs)-energy source for host intestinal epithelium

• SCFAs (butyrate, propionate, acetate)
  – Regulate gut motility, inflammation, glucose homeostasis, energy harvesting
  – Deliver various vitamins to the host

Wang et al. (2017)
Microbiota and Homeostasis of Immune System

Rajoka et al. (2017)
Balance & Diversity for Healthy Gut Microbiome

- What we eat matters for microbiome composition and actions
  - Saturated fats & processed, refined sugars can cause dysbiosis and trigger inflammation
  - Nutritional quality and quantity, important
Interaction Between Diet, Gut Microbiota and Host
Rajoka et al. (2017)
Dysbiosis Associated with Disease
Backhed et al. (2012)

- Diversity and balance disrupted
- Overgrowth of pathogenic microbes
- Inflammation, translocation

- Obesity
- Metabolic syndrome
- Diabetes
- Atherosclerosis
- NAFLD
- Inflammatory bowel diseases
- Irritable bowel syndrome
- Autism
- Allergy
- Asthma
- Celiac disease
Chronic Inflammation
Hand et al. (2016)
Obesity & Metabolic Syndrome

• Studies show link with dysbiosis:
  – Microbiota harvests increased calories, enhanced fat storage
  – Reduced insulin sensitivity, inflammation

• Adipose tissue accumulation
  – Promotes cell damage, chronic inflammation

Rajoka et al. (2017)
Type 2 Diabetes

- Associated with deficiency of SCFAs from microbial fermentation of dietary fiber
  Zhao et al. (2018)
- Insulin sensitivity affected by composition and functions of gut microbiota
- Mechanism not well understood
  Rajoka et al. (2017)
- Inflammatory condition
- Lifestyle changes: weight management, regular exercise & whole, plant foods
  Bodai et al. (2018)
Cardiovascular Diseases (CVD)

• Bacterial DNA found in atherosclerotic plaques associated with CVD development

• In atherosclerosis patients—decreased beta carotene gene production (anti-inflammatory) and increased peptidoglycan synthesis gene (pro-inflammatory)

• Lifestyle intervention (diet, physical activity)

Rajoka et al. (2017)
Nonalcoholic Fatty Liver Disease (NAFLD)

- Associated with high gut permeability, insulin resistance, obesity, dyslipidemia
- Studies show probiotics may play a role in treatment
- Synbiotic supplement (Lactobacillus reuteri with guar gum and inulin)-useful treatment to reduce steatosis but did not improve intestinal permeability (Ferolla et al. 2016)
- More study needed
Inflammatory Bowel Disease
Ulcerative colitis (UC), Crohn’s disease (CD)

• Reduced gut microbial diversity, affects immune system
• Synbiotic treatment shows potential for CD (B. longum & Synergy 1)
• VSL#3 probiotic-useful for UC

S. Haque & M. Haque (2017)
Clostridium difficile Infection (CDI)

- Risk factor: disrupted gut microbiome
- Leading cause of antibiotic–associated diarrhea
  - Mortality, high treatment costs

- Fecal Microbiota Transplantation (FMT)
  - Treatment of recurring, persistent C-difficile infection (CDI)
  - After antibiotics failed, at least 2 reoccurrences or 3 CDI episodes

Gupta et al. (2018)
Gut Microbiota-Brain

• Dysfunctions in microbiota-gut-brain axis (neuro-hormonal factors, gut microbiota influence)
  – Changes in microbiota associated with various types of pain
  – Complex communication pathways (gut microbiota stimulates production of SCFAs & neurotransmitters)

Rajoka et al (2017)
Artificial Sweeteners (AS)

• Prevalent in thousands of products (foodfacts.com)

• May have an effect on gut motility
  – further research is needed Spencer et al. (2016)

• Some research has shown gut bacteria can process AS into SCFAs, may increase calorie absorption and activate TLR4 inflammatory pathway

  Myles (2014)
Prebiotic

• A substrate that is selectively utilized by host microorganisms conferring a health benefit
  Gibson et al. (2017)

• Non-living, food for friendly gut bacteria
  – Inulin, fructo-oligosaccharides, galacto-oligosaccharides, polyphenols & PUFA

• Artichokes, asparagus, banana, oats, apples
Benefits of Prebiotics for GI Tract

- Inhibit pathogens
- Stimulate immune system
- Reduce blood lipid levels
- Improve insulin resistance
- Influence brain function, energy and cognition
- Assists mineral bioavailability

Gibson et al. (2017)
Prebiotics and Obesity Research

Children

• a prebiotic improved appetite control, reduced caloric intake (11-12 yo)
  Hume et al. (2017)

• a prebiotic reduced body fat & changed gut microbiota
  Nicolucci et al. (2017)
Probiotics

- Live microorganisms that, when administered in adequate amounts, confer a health benefit on the host (must resist digestion in upper gut)

  Gibson et al. (2017)

- Pill/capsule form—many choices
  - May/may not be useful—need more data
  - Discuss with your PCP
Future: More Research

• Explore manipulating specific microbes in the microbiome to prevent, treat and manage various diseases
• Personalized medicine-customized clinical interventions
What to do?

• Breast feed baby if possible-helps develop beneficial Bifidobacteria
• Take antibiotics only when medically necessary
• Achieve, maintain healthy weight
• Do regular physical activity
• Get adequate sleep
• Manage stress
• Adopt a gut microbiome-friendly eating plan
“Let food be thy medicine and medicine be thy food.”
Microbiome Friendly?
Gut Microbiome-Friendly Foods

- Apples, avocado, berries, black currants, cherries, pomegranate
- Asparagus, beans/legumes, beets, carrots, cruciferous veggies, Jerusalem artichokes, jicama, kimchi, okra, sauerkraut, spinach, potatoes
- Nuts, ground flaxseed, chia seeds
- Rice: brown, black, red; oats, quinoa
- Kefir, yogurt
- Cinnamon, turmeric
- Cacao (70% or higher)
- Green tea, red wine, EVOO

Source: AADE18 Gut Glucose Connection Microbial Support for Blood Glucose Control, presentation by Angelique Crandall, MS, RDN, CDE
How many servings of vegetables did you eat yesterday?

9 of 10 Americans
Do not eat the recommended amount

https://www.cdc.gov/media/releases/2017/p1116-fruit-vegetable-consumption.html
Plant based foods
Plant Foods
Dietary Fiber

• Feeds healthy gut microbes
• Promotes bowel regularity
• Promotes blood sugar control
• Helps reduce cholesterol
• Delays stomach emptying
• Provides fullness, satiety
Key Nutrition Recommendations

• Choose a variety of colorful, high fiber plant foods: vegetables, fruits, beans, peas, lentils, whole grains
• Choose lean proteins, plant proteins and low fat dairy products
• Eat less red meats, processed meats
• Choose healthy fats: fish, EVOO, avocado, nuts, seeds
• Limit added sugars, saturated fat, trans fats, sodium
• Use herbs and spices
• Drink water
Healthy Eating Plans

• Mediterranean
  www.oldwayspt.org

• DASH
  www.nhlbi.nih.gov/health-topics/dash-eating-plan

• ChooseMyPlate
  www.choosemyplate.gov
Questions?