COPE WEBINAR SERIES FOR HEALTH PROFESSIONALS

September 26, 2018

The Gut Microbiome-Diabetes Connection

Moderator: Lisa Diewald MS, RD, LDN
Program Manager: MacDonald Center for Obesity Prevention and Education

OBJECTIVES

1. Describe the microbiome development and maturation
2. Recognize the microbiome relationship to human body metabolism, obesity, metabolic syndrome and Type 2 diabetes and the dietary factors that contribute to disruption
3. Identify 2 clinical applications of the gut microbiome-diabetes relationship in patient care.

CE DETAILS

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- Villanova University College of Nursing Continuing Education/COPE is a Continuing Professional Education (CPE) Accredited Provider with the Commission on Dietetic Registration
- The American College of Sports Medicine’s Professional Education Committee certifies that Villanova University College of Nursing Continuing Education, Center for Obesity Prevention and Education (COPE) meets the criteria for official ACSM Approved Provider status (10/2018-9/2021). Providership #698849

CE CREDITS

- This webinar awards 1 contact hour for nurses and 1 CPEU for dietitians
- Suggested CDR Learning Need Codes: 2000, 5000, 5190, 5370
- Level 2
- CDR Performance Indicators: 8.1.2, 8.1.5, 6.3.11

THE GUT MICROBIOME-DIABETES CONNECTION

Patricia Davidson, DCN, RDN, LDN, CDE, FAND
Associate Professor, Nutrition Department
College of Health Sciences
West Chester University-Pennsylvania
Neither the planners or presenter have any conflicts of interest to disclose.

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THE GUT-DIABETES CONNECTION
DR. PATRICIA DAVIDSON RDN, CDE, LDN, FAND
WEST CHESTER UNIVERSITY
PDANIELSON@WCUPA.EDU

OBJECTIVES
• DESCRIBE THE MICROBIOME DEVELOPMENT AND MATURATION
• RECOGNIZE THE MICROBIOME RELATIONSHIP TO HUMAN BODY METABOLOIS, OBESITY, METABOLIC SYNDROME AND TYPE 2 DIABETES AND THE DIETARY FACTORS THAT CONTRIBUTE TO DISRUPTION
• IDENTIFY 2 CLINICAL APPLICATIONS OF THE GUT MICROBIOME-DIABETES RELATIONSHIP IN PATIENT CARE.

MICROBIOTA IMPORTANCE
Pathogenesis – linked to inappropriate activation of GI immune system toward the gut microbiota in genetically susceptible hosts &under the influence of environmental factors

CONSIDERING ROLE OF MICROBIOTA AND DISEASE
“ALL DISEASE BEGINS IN THE GUT”
“HEALTH IS DETERMINED BY THE MICROBIOTA IN OUR GUT”
HIPPOCRATES 460 BC – 370BC

DEFINITIONS
• Microbiota: the microorganisms (bacteria, viruses, fungi, etc) associated with the human body
• Microbiome: the total number of different genes that the microbiota as a whole possesses
• Gut microbiota: microorganisms in the digestive tract, most of which are present in the large intestine
• Dysbiosis: deviations from a healthy pattern of gut microbiota
THE ADULT GUT MICROBIOTA

- > 100 trillion organisms (10 x’s human cells)
- Most present large intestine
- Mostly bacteria
- 100-200 x’s genes (>3 million) than human genome
- 1000 bacterial species
- Phyla firmicutes and bacteriodetes predominate

MICROBIOTA IN THE GASTROINTESTINAL TRACT

BACTERIA PREDOMINATING IN HUMAN MICROBIOTA

<table>
<thead>
<tr>
<th>Phyla</th>
<th>Genus</th>
<th>Percentage</th>
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</thead>
<tbody>
<tr>
<td>Firmicutes</td>
<td>Ruminococcus</td>
<td>60%-80%</td>
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<tr>
<td></td>
<td>Clostridium</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lactobacillus</td>
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</tr>
<tr>
<td>Bacteriodetes</td>
<td>Bacteriodes</td>
<td>20%-30%</td>
</tr>
<tr>
<td></td>
<td>Prevotella</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Xylanibacter</td>
<td></td>
</tr>
<tr>
<td>Actinobacteria</td>
<td>Bifidobacterium</td>
<td>&lt;10%</td>
</tr>
<tr>
<td>Proteobacteria</td>
<td>Escherichia</td>
<td>&lt;1%</td>
</tr>
<tr>
<td></td>
<td>Enterobacteriaceae</td>
<td></td>
</tr>
</tbody>
</table>

FUNCTIONS OF HEALTHY MICROBIOTA

- Strengthens the immune system
- Protective metabolites from digestion dietary fiber and resistant starch (short-chain fatty acids acetate, propionate, butyrate)
- Influences serotonin levels
- Maintains intestinal epithelial barrier
- Anti-inflammatory activity
- Competes with pathogens
- Detoxifies drugs and other substances
- Synthesizes biotin, vitamin K, folate

DEVELOPMENT OF THE MICROBIOTA

- In utero first develops
- Vaginal delivery vs caesarean
- Antibiotic use
- Breast vs bottle feeding
- Solid food
- 2-5 years of age adult-like microbiota

INFLUENCING FACTORS

- Genetics/epigenetics
- Antibiotic use
- Food and water sanitation
- Drugs (metformin)
- Bariatric surgery
- Weight loss
- Diet
HEALTHY MICROBIOTA

- Higher proportion of bacteriodetes, actinobacteria
- Lower proportion of firmicutes
- Greater SCFA production
- Less methane production
- Greater diversity of species
- Less nitrogenous fermentation products (hydrogen sulfide)
- Anti-inflammatory cytokines

GUT MICROBIOME GLUCOSE HOMEOSTASIS SUMMARIZED

MICROBIOTA DIABETES CONNECTION TYPE AND TYPE 2?

CONNECTION TYPE1 DIABETES AND MICROBIOTA

GUT MICROBIOME AND TYPE 2 DIABETES DIABETES RELATED MICROBIOME DYSBIOSIS

DYSBIOSIS AND ENERGY AND MACRONUTRIENT IMBALANCES

- Enhanced absorption of nutrients
- Enhanced SCFA production and lipogenesis
- Reduced activity of fasting-induced adipose factor
- Reduced activity of amp-activated protein kinase
- Inflammation and intestinal permeability
- Hyperactivity of the endocannabinoid system
DYSBIOSIS CONTINUED

- Altered bile acid metabolism
- Methanogens
- Nitrogenous metabolic products
- Fat-rich, high animal protein, low fiber diet

APPETITE REGULATION

- Enteroendocrine peptides - regulation of energy balance, appetite, glucose regulation
- Gut peptide - GLP-1
  - SCFAs directly influence endogenous secretion
  - Acetate plays a role in this important regulation, modulation of plasma SCFAs
- Gut peptide - PYY
  - Link between microbial activity and gut peptide secretion and appetite

HORMONE REGULATION

- Leptin, Ghrelin
  - Appetite Regulation
- GLP-2 Regulation of Energy Storage
- Gut Barrier Integrity
- Insulin
  - Inflammation, Insulin Resistance, Glucose excursions
- Hormone Regulation

NUTRITION AND MICROBIOME DISRUPTION

MACRONUTRIENT

- Food ingredients absorbed and utilized by gut microbiota
- High fat diet
  - Inc exposure to pro-inflammatory FFAs
  - Leads to metabolic endotoxaemia and dysbiosis
  - T2DM and obesity
  - Alterations in GLP-2 production and mucosa integrity

NUTRITION AND MICROBIOME DISRUPTION

DIETARY PATTERNS

- Western diet
- Vegetarian/ Vegan
- Dietary composition effects enterotypes or gut flora
- Acute changes in diet
  - Calorie intake relative to need
    - > Kcal to wt maintenance needs = Inc firmicutes and dec bacteriodetes = Inc nutrient absorption of 150 kcal
    - > Kcal to needs = > kcal absorbed to needs and less excreted
    - < Kcal to need = Inc bacteriodetes and more excreted

NUTRITION AND MICROBIOME DISRUPTION

CARBOHYDRATES

- Resistant starch (RS) and non starch polysaccharides (NSP)
- RS and NSP improve microbial fermentation
  - Release of insulin (RS) and phytochemicals (NSP)
  - RS more residue = fermentation
**NUTRITION AND MICROBIOME DISRUPTION**

**PRE-BIOTICS**

- Non-digestable food ingredients stimulate the growth of microbes in the gut
  - Examples:
    - Common: Inulin, Jerusalem artichokes, Chicory
    - Novel: Polyphenols, Calcium, B-vitamins
  - Fermentation of prebiotics by gut
    - Long term intake > then short/acute intake – mixed
    - Specialized infant formulas – oligosaccharides

**PRE-BIOTICS BENEFITS**

- Modulation of gut peptides
  - Hunger and increased satiety
  - ↓ E intake 10%
  - ↓ ghrelin and ↑ peptide-Y
- Increase in GLP-2
- Improved glucose tolerance and leptin sensitivity
- Controlling development of white adipose tissue
- Regulation of inflammation
  - ↓ endotoxemia
  - ↓ cytokines and oxidative stress markers

**NUTRITION AND MICROBIOME DISRUPTION**

**PROBIOTICS**

- Probiotics are “live microorganisms, which, when administered in adequate amounts, confer a health benefit on the host”.
- Two main groups: lactobacillus and bifidobacterium
- Food examples: fermented milk, miso, tempeh, soy beverages and some juices
- Supplements: come in different forms such as capsules, tablets, and powders

**NUTRITION AND MICROBIOME DISRUPTION**

**PROBIOTICS**

- Benefits
  - Mucosal integrity
  - Reduce gut permeability
  - Increase secretions
  - Weight management
  - Strain specificity: Lactobacillus and bifidobacterium

**INTERACTION OF DIET AND GUT MICROBIOTA SUMMARIZED**

- Diet Manipulation
  - Host Metabolism
  - Beneficial Bacteria
  - Microbiota
  - SCFA

**CLINICAL APPLICATION**

- The GI tract is colonized by a large number of complimentary bacteria
- Composition is heavily influenced by environment (diet)
- Microbiota provides essential signals to ensure health host-microbial homeostasis
- Microbial dysbiosis is found in many different diseases
- A causal link and mechanistic insight will pave the way to new therapies to treat and prevent disease
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Complete the evaluation soon after receiving it. It will expire after 3 weeks.

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QUESTIONS & ANSWERS

Moderator: Lisa K. Diewald MS, RD, LDN
Email: cope@villanova.edu
Website: www.villanova.edu/COPE