Update for Nutrition Educators: The Interactive Role of the Human Microbiome, Nutrition, and Health

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August 1, 2016
Food

Microbiome

Health

Protection

Commensal Bacteria
- Layers
- Antimicrobial compounds
- Immune stimulation

Normal Microbiota

Gut
Premature Death

Intestinal Microbiota and Disease

Diet & Environment

Intestinal Microbiota

Proliferation of Pathogens

Production of Toxins

Metabolites

Blood

Damage?

Decreased immunity
Autoimmune disease
Allergy
Metabolic Syndrome
Heart disease
Cancer
Neurological disease
The Gastrointestinal Tract

- Largest interface to the outside world
- Digestion and absorption of nutrients and water
- Largest immune and endocrine organ in the body
- Regulates food intake and glucose homeostasis
Human Microbiome

- Human cells = 10 trillion
- Microbial cells ~ Human cells
- Estimated weight of 1.5 kg
- 1,800 genera and between 15,000 and 36,000 species of bacteria
- Microbes in our gut collectively contain 100 times as many genes as the human genome
Communities

Human-ecosystem linked model of sustainability, the basis of the sustainability indicators framework for South West Victoria

From: http://www.gswreportcard.org/RCFramework.htm
Bacterial Community Example

- Some gut inhabitants:
  - *Bacillus subtilis* (inhabits human gut and found in soil); used as a probiotic in Japan (fermented soybeans)
  - *Bacteroides* (primary fermenter in the distal gut – digests complex plant materials that human enzymes can’t)
  - *Methanobrevibacter smithii* (Archaea bacteria)
Bacteria in the GI Tract

• All bacteria belong to the kingdom: Bacteria

• Out of 28 Bacterial phyla, > 99% of gut bacteria come from 4 phyla:
  – Firmicutes ~ 64%
  – Bacteroidetes ~ 23%
  – Proteobacteria ~ 8%
  – Actinobacteria ~ 5%
Microbial Abundance vs Dietary Substrate Availability

Dynamic and Elastic Changes in Microbial Community Structure with Diet

Chemical Exposures and the Microbiome


Microbes Respond to Exposures

The Microbiome is Shaped by Diet and Environmental Exposures

• What you eat impacts the microbiome
• What you are exposed to impacts the microbiome
• Some changes are transitory
• Others will last a lifetime
• Changes can be good, bad, or neutral

How do we know that the microbiome plays a role in a particular disease?
Associating Diet-induced Obesity with the Microbiome

Lean mouse → High Fat/Sugar Diet → Obese mouse

Germ-free mouse → High Fat/Sugar Diet

Conventionalization:
Lean microbiome → Ger-free mouse
Obese microbiome → Obese mouse
Microbiota and Metabolism

Microbial Fermentation

Directly affects intestinal mucosa

SCFA acting on cell surface receptors including GPR43, GPR41 and Olfr78 regulate blood pressure.

Alter fat metabolism and lipogenesis

Impact liver metabolism through changes in lipogenesis, gluconeogenesis, β-oxidation, cholesterol synthesis, etc.
Development of Kwashiorkor is Related to the Child’s Microbiome

- 13 twin pairs discordant for Kwashiorkor

Gnotobiotic (germ free) mice

Inoculate with fecal material from discordant twins

Microbiome, Diet, Phenotype

Dynamics of the Microbiome

Is there a path back?

## Infant Nutrition

- **Statistics in the US:**

<table>
<thead>
<tr>
<th></th>
<th>Ever breastfed</th>
<th>Breastfeeding at 6 months</th>
<th>Breast-feeding at 12 months</th>
<th>Exclusive breastfeeding at 3 months</th>
<th>Exclusive breastfeeding at 6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Percentage</strong></td>
<td>76.5%</td>
<td>49%</td>
<td>27%</td>
<td>37.7%</td>
<td>16.4%</td>
</tr>
</tbody>
</table>

*Ref: Breastfeeding Report Card, CDC, 2013*
World Wide Breast-feeding Statistics

Evolution of Human Milk Substitutes

1784 -- M. Underwood (England), a physician, recommended cow’s milk as alternative to breast-feeding

1800 -- Glass feeding bottles

1845 – E. Pratt (US) patents rubber nipple

Late 1800s – early 1900: Pasteurization of milk; increase milk safety and quality

1838 -- F. Simon (Germany) determines cow’s milk has more protein than human milk

1920-1950: evaporated or fresh cow’s milk water and added CHO by corn syrup to reduce relative protein kcals (prepared at home)

1915-1920 – synthetic milk adapted formula (aka infant formula); need only add water

1930-1960: concentrated liquid formulas, hydrolysed formulas, elemental formulas and ready-to-feed formulas introduced

1960 – Commercially prepared infant formula becoming increasingly popular
U.S. Birth Rate
Evolution of Human Milk Substitutes

1959: Iron fortification

1962: Whey: casein ratio was made similar to human milk

1984: Taurine fortification

Late 1990: Nucleotide fortification; acts as growth factor and enhance infant immune system

Early 2000: Polyunsaturated fatty acid (DHA, ARA) fortification; improve brain development

We still don't understand human milk!!
Development of the Gut Microbiome

Effect of Diet on the Serum and Urine Metabolomes

Serum Metabolome and Infant Diet

High in FF
High in BF
Not significant
Not measured

Long term Effects of Breastfeeding

• BF is protective against type-2 diabetes
  – *Systematic review: Horta and Victora, WHO, 2013*

• BF is protective against obesity and low HDL

• BF leads to higher IQ at 30
  – *Victora et al., Lancet Glob Health 3, e199 (2015)*
Summary

• Microbes interact with each other and their host

• The microbiome is not static and can change with diet, but can revert back to its original state

• The microbiome becomes dysfunctional in disease states

• Early childhood (and breastfeeding) is important for development of the microbiome

• Food is complex, and its interactions with the microbiome and the host are still not understood
Acknowledgment

Slupsky lab:
Xuan He
Darya Mishchuk
Shin-Yu Chen
Emily Padhi
Jennie Sotelo
Elizabeth Chin
Shannon McClorry
Caitlin French
Alice Martinic
Hanna Lee
Aidong Wang
Yu Hasegawa
Laurynne Chetelat
Christopher McNeil

Slupsky lab Alumni:
Aifric O’Sullivan
Ann Spevacek
Elizabeth McNiven

Collaborators:
Bo Lönnerdal
Olle Hernell
Christina West

Collaborators:
Maria Marco
Helen Raybould
Funding

Dairy for life

NATIONAL INSTITUTES OF HEALTH

USDA

Arla

Mead Johnson Nutrition

Hero Institute for Infant Nutrition