Microbiome, obesity, and eating disorders

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Microbes maketh man
Human Microbiome Based Drugs and Diagnostics Market 2016: Global Industry Insights, Statistics, Market shares and Forecasts to 2022
Objectives

• Provide an overview of gut microbiome
• Review role of microbiome in childhood and adolescent obesity
• Discuss modulation of microbiome as target for obesity treatment
Microbiota

• Human infant exposed to numerous microbes found on mother and surrounding environment
• Microbes rapidly form assemblages on skin and in gut, intestines, mouth and other areas of the body
• These microbial communities are called microbiota
Microbiome

• Number of body-associated bacterial cells is estimated to be 10 times greater than the number of human cells in the body
• The totality of the microbes, including their microbial genes and environmental interactions, constitute the microbiome
• The microbial genes in the human microbiome are estimated to exceed the number of human genes by 100-fold
• The microbiome evolves over the life span to influence health and disease
Figure 171-1 Common molecular methodologies for identifying the components and the functions of complex microbial communities.
Figure 171-2 Physiologic and pathologic roles of the microbiome relevant to pediatrics. The human microbiome has an impact on health and development from pregnancy through to adulthood, including infection and non–infection-related processes.
Microbiome and obesity

• Obesity associated with changes in intestinal microbiome composition and metabolic function
• Increased ratio of phyla Firmicutes:Bacteroidetes
• Specific increase of Prevotellaceae
• Changes in Firmicutes subgroups that produce butyrate likely more important
• Other complex mechanisms involved
Original Research Article

Developmental Origins of Obesity: Early Feeding Environments, Infant Growth, and the Intestinal Microbiome

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<table>
<thead>
<tr>
<th>Feeding type</th>
<th>Predominant colonies</th>
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<tbody>
<tr>
<td>Breastfeeding (BF)</td>
<td>&gt;Bifidobacteria and Lactobacillus&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>&gt;Staphylococcus and Lactobacillus rhamnosus</td>
</tr>
<tr>
<td>Formula-feeding (FF)</td>
<td>&lt;Bifidobacteria and Lactobacillus&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>&gt;Clostridium, Bacteroides, Enterobacteria, and Enterococcus</td>
</tr>
<tr>
<td>BF + solids</td>
<td>=Enterobacteria and Bifidobacteria&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>FF + solids</td>
<td>&gt;Enterococcus and Bacteroides</td>
</tr>
<tr>
<td>Weaned infants</td>
<td>Fewer changes&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>Adult-like &gt; 400 species</td>
</tr>
</tbody>
</table>

<sup>a</sup>Modified from (Orrhage and Nord, 1999).
<sup>b</sup>Compared to FF.
<sup>c</sup>Compared to BF.
<sup>d</sup>Compared to BF only.
<sup>e</sup>Compared to FF only.
The Infant Gut Microbiome: Evidence for Obesity Risk and Dietary Intervention

Petra T. Koleva 1,2; Sarah L. Stolzman 1,2 and Ania L. Kozierska 1,2,3

Nutrients 2015, 7

Figure 1. Pre and postnatal exposures demonstrated to modify the infant gut microbiota (A) and hypothesized to impact childhood obesity risk through microbial induced mechanisms (B).
A) Altered gut microbiota

- SCFA
- FIAF
- Gut permeability
- AMPK

- Lipogenesis
- Fat storage
- LPL
- Fat storage
- LPS
- Cytokines proinflammatory
- eCB
- Adipogenesis
- Oxidation of fatty acids
- Adipogenesis

B) Restored gut microbiota

- Prebiotics and/or Probiotics

- SCFA
- FIAF
- Gut permeability
- AMPK

- PYY
- GLP-1
- Ghrelin

- Satiety
- Energy intake
- Body weight
Early Factors Leading to Later Obesity: Interactions of the Microbiome, Epigenome, and Nutrition

Lilly Chang, MD, and Josef Neu, MD

Obesity is a major public health problem in the United States and many other countries. Childhood obesity rates have risen extensively over the last several decades with the numbers continuing to rise. Obese and overweight children are at high risk of becoming overweight adolescents and adults. The causes are multifactorial and are affected by various genetic, behavioral, and environmental factors. This review aims to discuss a previously underrecognized antecedent of obesity and related chronic metabolic diseases such as heart disease and diabetes. Specifically, we highlight the relationship of the microbial ecology of the gastrointestinal tract during early development and the consequent effects on metabolism, epigenetics, and inflammatory responses that can subsequently result in metabolic syndrome. Although studies in this area are just beginning, this area of research is rapidly expanding and may lead to early life interventions that may have significant impacts in the prevention of obesity.

FIG 2. Epigenetic factors leading to obesity.
Early Microbe Contact and Obesity Risk: Evidence Of Causality?

*Erika Isolauri,* Seppo Salminen, and Samuli Rautava

**ABSTRACT**

The industrialized societies worldwide are in the middle of epidemics of diet-related chronic diseases, obesity being the common denominator. Lately, these conditions have been linked with a distinct microbiota composition in affected individuals different from that of healthy individuals. In particular, dysbiosis during critical stages of development induces lasting alterations in the immune and metabolic phenotype. The compositional development of the gut microbiota, again, is highly sensitive to environmental influences such as maternal health and nutrition, the mode of delivery, early feeding and antibiotic use. Shifts in the microbiota by high-energy diet increase energy extraction and storage, provoke a low-grade inflammatory response and impair gut barrier function, and, consequently, result in obesity and metabolic disease. A lower abundance of butyrate-producing bacteria and lower overall richness of bacteria has been associated with increased metabolic disease risk in humans. Recent reports suggest that *Akkermansia* type bacteria or butyrate producing microbes may have anti-inflammatory potential and enhance intestinal barrier function, which may both alleviate obesity and related metabolic complications. Thus we are not directly what we eat or our mother eats, but what our microbiota eat and how the collective composition of the microbiome is modified by the diet. On this basis, altering the intestinal microecosystem may be taken as a key target to attain prophylactic or therapeutic effects in metabolic and inflammatory conditions. Tools for such modulation include specific probiotic bacteria and potentially also non-digestible carbohydrate components able to modify microbiota composition and activity.
FIGURE 1. The co-evolution of the gut microbiota composition and host metabolic programming.
Reshaping the Gut Microbiota at an Early Age: Functional Impact on Obesity Risk

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Editorial

Microbiome, peptide autoantibodies, and eating disorders: A missing link between gut and brain
Fig. 1. Microbiome-gut-brain axis and eating disorders.
Conclusions:

We provide evidence of an intestinal dysbiosis in AN and an association between mood and the enteric microbiota in this patient population. Future directions include mechanistic investigations of the microbiome-gut-brain axis in animal models and association of microbial measures with metabolic changes and recovery indices.
Discussion: Sex-related response to how E. coli affects feeding and anti-melanocortin hormone antibody production may depend on the presence of these bacteria in the gut before E. coli supplementation. These data suggest that sex-related presence of certain gut bacteria may represent a risk factor for ED development.
Therapeutic manipulation of the microbiome

- Antimicrobials
- Prebiotics
- Probiotics
- Postbiotics
- Fecal transplantation
The Gut Microbiome and Probiotics

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Probiotics

• Viable organisms that have health benefits
• Nearly all probiotics are isolates from the human microbiota
• Probiotics may be administered orally for therapeutic purposes
• Common bacterial genera include: bifidobacteria, lactobacilli, streptococci, enterococci, E. coli
• Probiotics studied for their effects in various conditions
• One way to alter microbiota favorably
Prebiotics

• Nondigestible food components
• Beneficially affect the host by selectively stimulating the growth and/or activity of 1 or a limited number of bacteria in the colon
• Typical prebiotics are carbohydrates such as oligosaccharides