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Diet, Microbiome Ecology and Obesity

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The Microbiome and Obesity

The distal gut of humans and other vertebrates contains 10 to 100 trillion microbes, collectively called the microbiome, encoding one hundred times more genes than the human genome and playing a role in health and disease [1]. A microbiome that is disturbed due to altered health or environmental factors, has been shown to increase infections and metabolic disorders, including obesity, insulin resistance, diabetes, high blood pressure and cardiovascular disease [1-3].

The role of the microbiome in obesity was noted by observing that germ-free mice lacking a microbiome are leaner than conventionally bred mice [3]. Introducing the gut microbiome from conventionally bred mice into germ-free mice (conventionalization) resulted in a 60% increase in body fat within 14 days, despite a lower intake of food [3]. The lean state of mice lacking a microbiome was attributed to their inability to ferment polysaccharide-rich food to the short chain fatty acids, a source of energy and lipogenesis. A transfer of the microbiome from the conventional mice to the germ-free mice, reversed the situation, increasing adiposity and insulin resistance [4].

Effects of Diet

Diet modification of the gut microbiome influences obesity [5,6]. The effect is rapid, with a high fat diet changing the microbiome within a single day [7]. The effects of diet are selective. A western diet, high in both fat and sugar correlates with an increased proportion of *Firmicutes* microbes, that are highly efficient in harvesting energy from food, over the less efficient *Bacteroidetes*, resulting in increased obesity [8]. The energy is generated from otherwise indigestible polysaccharides, fermented by microbiome enzymes that are not encoded in the human genome. The fermentation products include monosaccharaides and short-chain fatty acids that are absorbed into the circulation and stimulate the synthesis of liver triglycerides and their incorporation into adipocytes, or acting as regulatory molecules [4].

The main short-chain fatty acids produced by the microbiome are acetate, butyrate and propionate [1-3]. Among the three, butyrate and propionate are predominantly antiobesogenic while acetate shows more obesogenic potential [2]. Skeletal and cardiac muscles and brain cells oxidize acetate to carbon dioxide and other metabolites while adipocytes oxidize butyrate for lipogenesis. Butyrate is metabolized to ketone bodies that provide energy to the colon epithelium. Butyrate also improves insulin sensitivity and has anti-inflammatory potential. Propionate has been found to inhibit cholesterol synthesis and inhibit the expression of resistin [2], an adipocyte-derived signaling polypeptide implicated in obesity-mediated insulin resistance.

Studies in humans show that gut differences and diet alter the microbiome and energy balance [9]. People prone to obesity may harbor a gut microbiome that transports monosaccharaides more efficiently and have a more effective extraction and storage of energy from the diet, compared with the microbiome of lean people. A study on 12 obese people assigned to a low calorie diet, either fat- restricted or carbohydrate-restricted showed after a year that 70% of the microbial species were unique to each person and remained constant, with the *Bacteroidetes* and *Firmicutes* divisions dominating the microbiome [9]. Obese people had fewer *Bacteroidetes* and

more *Firmicutes* than did lean controls. Weight loss increased the proportion of *Bacteroidetes* over that of *Firmicutes*, irrespective of diet type [10]. Caloric content also modified the microbiome. A study on 12 lean and 9 obese people on diets that varied in caloric intake (2400 vs 3400 kcal), showed that the higher caloric intake that increased body weight was linked to a 20% increase in *Firmicutes* and a 20% decrease in *Bacteroidetes* [6].

Childhood Microbiome in Relation to Later Obesity

The prevalence of certain microbiome species in early childhood may be linked to overweight and obesity in later life [11]. Normal weight infants, ages 6 and 12 months, showed higher levels of *Bifidobacteria* than children of the same ages who developed obesity at the age of 7 years. Breastfeeding played a critical role in the microbiome composition and in lowering propensity to obesity in later life [11]. *Bifidobacteria*, especially *B. breve, B. infantis*, and *B. longum*, typically colonized the gut microbiome of healthy breastfed infants, reducing the risk of these children being overweight or obese 13 - 22%. The longer an infant was breast-fed the lower the likelihood of later life obesity [11].

Manipulation of the Gut Microbiome

Prebiotics

Prebiotics are non-digestible foods that stimulate the growth and/or activity of colonic microbes [13]. They modulate the gut microbiome, predominantly increasing the concentration of *bifidobacteria*. The reported metabolic changes that take place include a reduction in hepatic cholesterol and triglyceride, a lowering of inflammation markers, enhanced satiety and reduced body fat in children with obesity [14].

Probiotics

Probiotics are live bacteria found in yogurt, kefir and standardized supplements. Probiotics modify the microbiome, but in contrast to prebiotics, probiotics persist for short periods after intake and do not become permanent members of the microbiome [15].

Probiotics have been used in agriculture to promote the growth of farm animals. Under certain circumstances selected microbes may similarly affect humans, by modifying the microbiome [16]. High levels of certain intestinal lactobacilli can increase weight and hyperglycemia in healthy adults, though the effects are strain and dose specific. Both the bacterial strain and the host are important determinants in the effects of the probiotic preparation will play a role in inhibiting or promoting weight gain and certain marketed probiotics may contain strains that favor obesity. *Lactobacillus acidophilus* intake, as well as *Lactobacillus fermentum* and *Lactobacillus ingluviei* were associate with weight gain in humans and animals, while an intake of *Lactobacillus gasseri*, or *Lactobacillus plantarum* by obese humans and animals, resulted in weight loss [16]. As most commercial probiotic preparations include *Lactobacillus* strains, it may be advisable to monitor the strains of *Lactobacillus* in the preparation.

Clinical Considerations

Diet can selectively modify the microbiome within a day. High fat diets or diets rich in calories from carbohydrates, increase the proportion of *Firmicutes* over *Bacteroidetes*, stimulating lipogenesis and weight gain. A hypo-energetic diet (either low carbohydrate or low fat), increases the proportion of *Bacteroidetes* over *Firmicutes*, parallel with weight loss. The source of fat is important. Animal studies show that saturated fats have different effects on the gut microbiome; a changed microbiome following a feeding of unsaturated fats can protect against weight-gain induced by saturated fat [5].

While small trials has shown that prebiotics and certain probiotics reduced metabolic markers associated with obesity [16], large prospective studies are needed to obtain conclusive answers. Prebiotics, such as inulin, alter the microbial composition. Probiotics must be taken regularly for an effect, as the microbes do not become permanent populations in the gut. Different sources of probiotics may increase or a decrease weight depending on their content of microbial species and the receiving host [16]. Additional studies are needed to identify gut microbes that would be most effective in reducing obesity.

Potential Future Directions

Fighting obesity by regulating the gut microbiome is of growing interest to researchers, commercial companies and government. The white House announced in May 2016 a National Microbiome Initiative to support collaborations between public and private researchers in developing technologies to generate insight and expand education on the microbiome.

In summary, a mixture of cutting edge techniques, as well as new strategies and well-designed human studies, have potential to unravel complexities associated with the microbiome, human genetics and lifestyle, helping to remedy the growing global problem of obesity.

Bibliography

1. Morowitz MJ., *et al*. "Contribution of intestinal bacteria to nutrition and metabolism in the critically ill". *Surgical Clinics of North America* 91.4 (2011): 771-785.
2. Chakraborti CK. "New found link between microbiota and obesity". *World Journal of Gastrointestinal Pathophysiology* 6.4 (2015): 110-119.
3. Arora T and Backhed F. "The gut microbiota and metabolic disease: Current understanding and future perspectives". *Journal of Internal Medicine* 280.4 (2016): 339-349.
4. Backhed F., *et al*. "The gut microbiota as an environmental factor that regulates fat storage". *Proceedings of the National Academy of Sciences of the United States of America* 101.44 (2004): 15718-15723.
5. Sonnenburg JL and Backhed F. "Diet-microbiota interactions as moderators of human metabolism". *Nature* 535.7610 (2016): 56-64.
6. Jumperez R., *et al*. "Energy balance studies reveal association between microbes, calorie load and nutrient absorption in humans". *American Journal of Clinical Nutrition* 94.1 (2011): 58-65.
7. Tilg H. "Obesity, metabolic syndrome, and microbiota: multiple interactions". *Journal of Clinical Gastroenterology* 44.1 (2010): S16-S18.
8. Ley RE., *et al*. "Microbial Ecology: Human gut microbes associated with obesity". *Nature* 444 (2006): 1022-1023.
9. Byrne CS., *et al*. "The role of short chain fatty acids in appetite regulation and energy homeostasis". *International Journal of Obesity* 39.9 (2015): 1331-1338.
10. Ley RE., *et al*. "Obesity alters gut microbial ecology". *Proceedings of the National Academy of Sciences of the United States of America* 102.31 (2005): 11070-11075.
11. Kaliomaki M., *et al*. "Early differences in fecal microbiota composition may predict overweight". *American Journal of Clinical Nutrition* 87.3 (2008): 534-538.
12. Gibson GR and Roberfroid MB. "Dietary modulation of the human colonic microbiota: in troducing the concept of prebiotics". *Journal of Nutrition* 125.6 (1995): 1401-1412.
13. Delzenne NM., *et al*. "Targeting Gut Microbiota in Obesity: Effects of Peribiotics and Probiotics". *Nature Reviews Endocrinology* 7.11 (2011): 639-646.
14. Roberfroid M., *et al*. "Prebiotic effects: metabolic and health benefits". *British Journal of Nutrition* 104.2 (2010): S1-S63.
15. Chen Jia., *et al*. "Diet effects in gut microbiome and obesity". *Journal of Food Science* 79.4 (2014): R442-R451.

16. Million M., *et al*. "Gut bacterial microbiota and obesity". *Clinical Microbiology and Infection* 19.4 (2013): 305-313.