

FUNCTIONAL MEDICINE UPDATE
AUGUST 2009
ISSN 1092-1761
Vol. 29, No. 8

Gut Microbiota and a Gluten-Free Diet

The topic of this month's issue is the gut microbiota. Having just completed a two-part series on gluten sensitivity and celiac disease, Dr. Bland begins with a discussion of 2009 article published in the *British Journal of Nutrition* titled "Effects of a Gluten-Free Diet on Gut Microbiota and Immune Function in Healthy Adult Human Subjects." In this article the authors state that most recent studies indicate that celiac patients treated and untreated with a gluten-free diet have unbalanced microbiota that can play a pathogenic role or constitute a risk factor for this disorder. The possible effect of a gluten-free diet on the gut ecosystem remains largely unknown, and the objective of the study described in the article was to analyze the impact of a gluten-free diet on the composition and immune function in healthy subjects to gain further insights on interactions between diet and gut microbes. The results of this preliminary short-term intervention study suggest that a gluten-free diet may influence the composition and immune function of the gut microbiota in healthy individuals, without the influence of any underlying disease, parallel with reductions in polysaccharide intake. The authors state that as intestinal bacteria constitute a constant challenge of antigens to their host that modulate immunity, the gluten-free diet should be considered as a possible environmental factor that may shape the microbiota composition and gut health in treated celiac disease patients.

REF #1

Modulation of the Immune System by Food

Dr. Bland discusses a review by Harry Wichers of Wageningen University and Research Center in The Netherlands called "Immunomodulation by Food: Promising Concept for Mitigating Allergic Disease?" Dr. Wichers writes that diet and nutrition can affect the functioning of various immune parameters, and this concept can be utilized in attempts to prevent or mitigate allergic reactions via the development of targeted food products or ingredients. His review describes recent findings with respect to food products and ingredients that show potential in this respect. Special attention is given to pro- and prebiotics, β -glucans, and fungal immunomodulatory proteins, all of which appear to strengthen Th1-mediated immunity. REF #2

The Metagenomics Era and Gastroenterology

Researchers from the Interdepartmental Program in Translational Biology and Molecular Medicine at Baylor College of Medicine recently published an article in *Gastroenterology* that is titled "Targeting the Human Microbiome with Antibiotics, Probiotics, and Prebiotics: Gastroenterology Enters the Metagenomics Era." In this article the authors state, "As our understanding of microbial variation and corresponding genetic parameters is refined, this information can be applied to rational remodeling or 'tailoring' of human-associated functions." They suggest that the specialty of gastroenterology will be affected profoundly by the ability to modify the gastrointestinal microbiota through

the rational deployment of antibiotics, probiotics, and prebiotics. As the science of metagenomics continues to move forward, combinations of these approaches might provide synergistic and effective therapies for specific disorders. REF #3

Probiotics and Gastric Bypass Surgery

Dr. Bland discusses potential clinical implications of the research that is now being done on the gut microbiota. He highlights an article recently published in the *Journal of Gastrointestinal Surgery* titled “Probiotics Improve Outcomes After Roux-en-Y Gastric Bypass Surgery: A Prospective Randomized Trial.” The article describes a novel study in which 44 patients undergoing Roux-en-Y gastric bypass (RNYGB) surgery were randomized to either a probiotic or control group. Postoperatively, patients in the probiotic group were instructed to take one probiotic supplement each day, with each pill containing 2.4 billion live cells of *Lactobacillus* species. At 6 months, a statistically significant reduction in bacterial overgrowth was achieved in the probiotic group. This group also had significantly higher postoperative vitamin B12 levels than the control group. At the conclusion of the study the researchers found that probiotic administration improves bacterial overgrowth, vitamin B12 availability, and weight loss after RNYGB. REF #4

Altered Gut Flora and Systemic Inflammatory Response

According to a 2009 article published in *Cancer Research*, inflammatory bowel disease, including ulcerative colitis and Crohn’s disease, substantially increases the risk of colorectal cancer. The article goes on to describe an animal study conducted by researchers from the UCLA School of Medicine designed to test whether genotoxicity is elicited systemically by acute and chronic intestinal inflammation. In this study, genotoxic endpoints were assessed in peripheral leukocytes and normochromatic erythrocytes during chemical or immune-mediated colitis. At the conclusion of the study the researchers proposed that mucosal inflammation, by eliciting substantial and ongoing systemic DNA damage, contributes early on to genetic instability necessary for progression to inflammatory bowel disease-associated dysplasia and the development of cancer. REF #5

Altered Gut Flora and Pain

Abdominal pain is common in the general population and, in patients with irritable bowel syndrome, is attributed to visceral hypersensitivity. A group of French researchers recently published an animal study in *Nature Medicine* in which they found that oral administration of specific *Lactobacillus* strains induced the expression of μ -opioid and cannabinoid receptors in intestinal epithelial cells and mediated analgesic functions in the gut. These researchers state that the results suggest that the microbiology of the intestinal tract influences visceral perception and suggests new approaches for the treatment of abdominal pain and irritable bowel syndrome. REF #6

Whole-Organism Metabolism: Does It Really Change As a Consequence of Gut Microbiota?

A 2009 article published in the *American Journal of Clinical Nutrition* states that recent reports suggest that the metabolic activity of the gut microbiota may contribute to the

pathogenesis of obesity and hepatic steatosis. The article describes a study conducted on both mice and weanling pigs over 21 days in which the objective was to determine whether the fat composition of host tissues might be influenced by oral administration of commensal Bifidobacteria previously shown (by the same research group) to produce bioactive isomers of conjugated linoleic acid (CLA). The results of the study showed that feeding different animal species a CLA-producing Bifidobacterium of human origin (*B. breve* NCIMB 702258), in combination with linoleic acid as substrate, results in modulation of the fatty acid composition of the host, including significantly elevated concentrations of *c9,t11* CLA in the liver. The same strain is also associated with an apparent anti-inflammatory effect on cytokine production that is pertinent to the proinflammatory cytokine profile that characterizes obesity. The researchers state that the results of this study confirm that the metabolic activity of the enteric microbiota and the dietary manipulation thereof represent a realistic target for modification of the fatty acid composition of host tissues. REF #7

Researchers of the Month

Nathalie Delzenne, PhD
Associate Professor

Patrice Cani, PhD
Postdoctoral Researcher

Division of Biochemical Toxicology
Université catholique de Louvain
School of Pharmacy
Division of Biochemical Toxicology
SFAR 7360
Avenue Mounier 73
B-1200 Brussels
Belgium

Professor Nathalie Delzenne received her degree in pharmacy and her PhD from the Université catholique de Louvain where she is now an Associate Professor. She also spent time studying at the Université de Lausanne in Switzerland. Professor Delzenne obtained a grant from NATO and spent time at INSERM (the French National Institute for Health and Medical Research), where she was involved in studies relative to the nutritional modulation of gene expression. Dr. Patrice Cani also graduated from the Université catholique de Louvain and is now a Postdoctoral Researcher there. Both Professor Delzenne and Dr. Cani are part of the Division of Biochemical Toxicology, where they work alongside well-known researcher, Dr. Marcel Roberfroid.

Dr. Bland, Professor Delzenne, and Dr. Cani have a group discussion about their ongoing research on nutritional modulation of the gut microbiota, and their specific focus on probiotics and prebiotics. They have published a number of important papers over the last several years, a number of which Dr. Bland specifically asks about and they discuss in

greater depth and detail. These articles include: “Metabolic Endotoxemia Initiates Obesity and Insulin Resistance” (*Diabetes*, 2007); “Selective Increases of Bifidobacteria in Gut Microflora Improves High-Fat Diet-Induced Diabetes Through a Mechanism Associated with Endotoxemia” (*Diabetologia*, 2007); “Gut Microflora as a Target for Energy and Metabolic Homeostasis” (*Current Opinion in Clinical Nutrition and Metabolic Care*, 2007); “Changes in Gut Microbiota Control Inflammation in Obese Mice through a Mechanism Involving GLP-2-Driven Improvement of Gut Permeability” (*Gut*, 2009); and “A Place for Dietary Fibre in the Management of Metabolic Syndrome” (*Current Opinion in Clinical Nutrition and Metabolic Care*, 2005). REF #8-12

References

1. De Palma G, Nadal I, Collado MC, Sanz Y. Effects of a gluten-free diet on microbiota and immune function in healthy adult human subjects. *Br J Nutr*. 2009 May 18;1-7. [Epub ahead of print]
2. Wichers H. Immunomodulation by food: promising concept for mitigating allergic disease. *Anal Bioanal Chem*. 2009 May 20. [Epub ahead of print]
3. Preidis GA, Versalovic J. Targeting the human microbiome with antibiotics, probiotics, and prebiotics: gastroenterology enters the metagenomics era. *Gastroenterology*. 2009;136:2015-2036.
4. Woodard GA, Encarnacion B, Downey JR, Peraza J, Chong K, et al. Probiotics improve outcomes after Roux-en-Y gastric bypass surgery: a prospective randomized trial. *J Gastrointest Surg*. 2009;13(7):1198-1204. Epub 2009 Apr 18.
5. Westbrook AM, Wei B, Braun J, Schiestl RH. Intestinal mucosal inflammation leads to systemic genotoxicity in mice. *Cancer Res*. 2009;69(11):4827-4834.
6. Rousseaux C, Thuru X, Gelot A, Barnich N, Neut C, et al. *Lactobacillus acidophilus* modulates intestinal pain and induces opioid and cannabinoid receptors. *Nat Med*. 2007;13(1):35-37.
7. Wall R, Ross RP, Shanahan F, O'Mahony L, O'Mahony C, et al. Metabolic activity of the enteric microbiota influences the fatty acid composition of murine and porcine liver and adipose tissues. *Am J Clin Nutr*. 2009;89:1393-1401.
8. Cani PD, Amar J, Iglesias MA, Poggi M, Knauf C, et al. Metabolic endotoxemia initiates obesity and insulin resistance. *Diabetes*. 2007;56(7):1761-1772.
9. Cani PD, Neyrinck AM, Fava F, Knauf C, Burcelin RG, et al. Selective increases of bifidobacteria in gut microflora improves high-fat diet-induced diabetes through a mechanism associated with endotoxemia. *Diabetologia*. 2007;50(11):2374-2383.
10. Cani PD, Delzenne NM. Gut microflora as a target for energy and metabolic homeostasis. *Curr Opin Clin Nutr Metab Care*. 2007;10:729-734.
11. Cani PD, Possemiers S, Van de Wiele T, Guiot Y, Everard A, et al. Changes in gut microbiota control inflammation in obese mice through a mechanism involving GLP-2-driven improvement of gut permeability. *Gut*. 2009;58(8):1091-1103. Epub 2009 Feb 24.
12. Delzenne NM, Cani PD. A place for dietary fibre in the management of the metabolic syndrome. *Curr Opin Clin Nutr Metab Care*. 2005;8:636-640.

The information given and discussed in these materials is for research and education purposes only and is not intended to prescribe treatment.