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Effect of Overgrowth or Decrease in Gut Microbiota on Health and Disease

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Abstract

Context: The composition and function of the gut microbiota develop with their host from birth. The human microbiome, especially the gut microbiota, plays a critical role in a myriad of health and normal activities. However, the increase or decrease in number of gut bacteria may cause several disorders. This review aimed to assess the importance of human gut microflora and their roles in the health and possible diseases caused by fluctuations in the number of these bacteria.

Evidence Acquisition: For the current review, we searched for the terms "bacterial gut flora", "role," "number," and "increase" and "decrease" on the Google scholar, PubMed, Science Direct, SciVerse, and Scopus search engines and databases. The exclusion criteria were "genetic factors," "veterinary flora," "protozoal flora," "mold," "fungal," and "yeast flora".

Results: The gut microbiota is accompanied by the regulation of several host metabolic pathways, giving rise to interactive host-microbiota signaling, metabolic, and immune-inflammatory responses that physiologically connect the gut, muscle, liver, and brain. A more thorough understanding of these axes is an early essential for reaching therapeutic strategies to use the gut microbiota for combating disease and improving health. Bacterial species of Bacteroides, Clostridia, and Bifidobacterium consist of a large proportion of the gut bacterial flora. Increase in the proportion of these genera in the gut could cause abscess formation, sepsis, inflammatory bowel disease (IBD), Crohn's disease, toxicity, infection, and malnutrition. However, the decrease in the proportion of these species is accompanied by allergies in infants, inflammation, malabsorption syndrome, carbohydrate/fiber intolerance, atopic eczema, and IBD.

Conclusions: The results showed that although the human gut microbiome plays a pivotal role in health in a normal concentration, fluctuation in their number (increase or decrease) is a possible factor in the appearance of major diseases.

Keywords: Gut Flora, Health, Clinical Disorders

1. Context

The composition and function of the gut microbiota develop with their host from birth. The human microbiome, particularly the gut microbiota, plays a critical role in a myriad of health and normal activities (1). These include immune system function and prohibition of pathogen propagation, nutrition, and several other health-related situations (2). However, the increase in the number of gut bacteria may cause several disorders. There is an interplay that depends on the host genetics, nutrition, and lifestyle (3). The gut microbiota is extremely diverse, varies between individuals, and may fluctuate over time, such as during disease and early development (4). The gut microbiota is accompanied by the regulation of several host metabolic pathways, giving rise to interactive host-microbiota signaling, and metabolic and immune-inflammatory responses that physiologically connect the gut, muscle, liver, and brain. A more thorough understanding of these axes is an early essential for reaching therapeutic strategies to use the gut microbiota for combating disease and improving health (1).

2. Evidence Acquisition

For the current review, we identified studies using the search terms "bacterial gut flora," "role," "number," "increase" and "decrease," and "health" on the Google scholar, PubMed, Science Direct, SciVerse, and Scopus databases and search engines. We tried to include abstracts from conferences as well.

The terms "genetic factors," "veterinary flora," "protozoal flora," "mold," "fungal," and "yeast flora" were used as the exclusion criteria. Among the results, publications published from 1997 to 2015 were selected and used for data collection.

3. Results

The most numerous gut bacterial flora include of different species of Bacteroides, Clostridia, Bifidobacterium, and non-pathogenic Enterobactereaceae. The increase in number of these genera could cause abscess formation, sepsis, inflammatory bowel disease (IBD), Crohn's disease, toxicity, infection and malnutrition (5-8). However, a decrease in the number of these bacteria is accompanied by allergies in infants, inflammation, malabsorption syndrome, carbohydrate/fiber intolerance, atopic eczema, and IBD. This review was performed with the aim of assessing the importance of bacteria in the human gut and to determine their roles in health and possible diseases due to fluctuations in the bacterial populations. Tables 1 and 2 describe the functions and effects of gut bacterial flora under healthy and diseased conditions. Tables 1 and 2 (9-37) describe the roles of some important gut bacteria and their effects on health and disease.

Several studies have determined that obesity is associated with an increase in the phylum Firmicutes and a relatively lower abundance of the phylum Bacteroidetes (38-41). Research into Crohn's disease has revealed that patients with Crohn's disease exhibit a significant reduction in the overall diversity of the gut microbiota (42, 43) and changes in microbial composition (44). A study on type 2 diabetes (T2D) showed that the proportions of the phylum Firmicutes and the class Clostridia in the gut of patients was significantly reduced among patients with T2D (45).

In addition, acidification of colonic secretions attenuates the absorption of ammonia by non-ionic diffusion. Treatment with fermentable fiber alone has also been reported to be beneficial. There is a risk of fecal carriage of fluoroquinolone-resistant strains (46). Moreover, high levels of genetic flux may occur between gram-negative Enterobacteriaceae (47). The intestinal microbial communities are actively regulated by epithelial Paneth cells via their secretion of antimicrobial peptides or α-defensins. α-Defensins can selectively kill non-commensals while increasing the growth of commensals. A study showed that Paneth cells targeted by graft-versus-host disease (GVHD) resulted in increased Escherichia coli growth and septicemia (48). On the other hand, various perioperative treatments were found to affect the number and proportion of gut flora in SD rats (49).

4. Conclusions

The results showed that although the human gut bacterial species play a pivotal role in health, immunity, and nutrition in normal concentrations in the intestine, fluctuations in their number (increase or decrease) is a possible factor in the appearance of major health disorders. Furthermore, gut microflora induce disease even in the normal state, for instance inflammation and invasion of the epithelium may occur. Several factors such as age, hormonal changes, and immune suppression are among the major factors causing the disorders in the gut microbial population.

Footnotes

Authors' Contribution: Abdolmajid Ghasemian and Farshad Nojoomi performed the study and data collection.

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Table 1. [Part 1] Approximate Number and Normal Roles of Gut Bacteria

Bacterial Genus	Number/g	Normal Effects/Roles
Bacteroides	10^{10-11}	Vitamin production; barrier; production of carcinogens; immune activation and modulation; Paneth cell protein production; degrading and de-conjugation of bile acids; production of biotin, cobalamin, folic acid (5, 6), pantothenic acid, pyridoxine, and riboflavin; *E coli* sepsis
Bifidobacterium	10^{3-4}	Hydrolysis of (7), barrier, liver damage, cancer, immune activation and modulation, anti-allergic, metabolism of xenobiotics/toxins, degradation of N-nitrosamines, degradation of polycyclic aromatic hydrocarbons, generating a Th2 cell population, sepsis by *E. coli* (8, 9)
Escherichia coli	10^{2} - 10^{3}	Diarrhea, barrier impeding the growth of pathogens, degradation of N-nitrosamines and polycyclic aromatic amines and N-hydroxyl aryl amines, reduction of blood (10) ammonia levels and reversal of MHE , reduction of endotoxemia, improvement of liver functions
Enterococcus	10^{2}	Immune modulation, inhibition of pathogens and opportunistic species, attachment to epithelial cells, IBD prevention and treatment (11, 12)

Table 1. [Part 2] Approximate Number and Normal Roles of Gut Bacteria

Bacterial Genus	Number/g	Normal Effects/Roles
Lactobacillus	10^{2-3}	Blockage of adherence receptors, prevention of colon cancer, produce organic acids, production of H202, degradation of N-nitrosamines, anti-tumor glycopeptides, stimulating balanced immune responses, prevention of food allergy in infants, reduction in blood (13) ammonia levels and reversal of MHE, suppression of the expression of proinflammatory cytokines IL-6 and IL-17 and promotion of the expression of the major tight junction proteins claudin-1 and occludin (14), bacteriocin production (15)
Streptococcus	10^{3} - 10^{4}	Fermentation of sugars and lactic acid production (16), barrier function
Peptococcus	ND	Immune modulation
Peptostreptococcus	ND	Immune modulation, short-chain fatty acids
Ruminococcus	ND	Blockage of adherence receptors, sulfur degradation, gut barrier protection (17), anti-inflammatory effects (18)
Clostridia	104	Vitamin production, degradation of proteins and polysaccharides, anti-inflammatory effects (18)
Micrococcus	ND	Barrier function, short-chain fatty acids
Veillonella	ND	Propionic acid from lactic acid; NO production; anti-inflammatory properties; production of biotin, cobalamin, folic acid, pantothenic acid, pyridoxine, and riboflavin (19)
Proteus	10^{2}	Inhibition of pathogen attachment
Eubacterium	10^{2} - 10^{3}	Short-chain fatty acids, anti-inflammatory properties, metabolism of xenobiotics/toxins, prevention of colonization by pathogens, conversion of dietary flavonoids to active aglycones
Fusobacterium	10^{2}	Prevention of colonization by pathogens, propionic acid

Abbreviation: ND, not detected.

Table 2. [Part 1] Effects of Overgrowth and Decrease in the Gut Bacterial Species on Health and Disease Conditions

Bacteria Genus	Effect of Overgrowth	Effect of Decrease
Bacteroides	Bacteroides infections, capsule, abscess formation, sepsis, inflammatory bowel disease (IBD), Crohn's disease (20), achlorhydria/hypochlorhydria, malnutrition, auto-immune disorders, disruption of cellular adhesion molecules by proteases (21)	Inflammation, IBD, Crohn's disease, malabsorption syndromes (22)
Bifidobacterium	Cancer: colon/breast inflammatory bowel disease, irritable bowel syndrome, achlorhydria/hypochlorhydria, malnutrition, autoimmune disorders, increased paracellular permeability, colorectal cancer (CRC) (23)	Allergies in infants, inflammation, malabsorption syndrome, carbohydrate/fiber intolerance, atopic eczema, IBD (22), Crohn's disease (22), obesity (24), visceral hypersensitivity, contractile hyper-responsiveness, intestinal permeability, and inflammation (14)
E. coli	Intestinal giardiasis, malnutrition, vitamin B12 deficiency, impaired formation of micelles, bile salt dehydroxylation, formation of hydroxy fatty acids (25), bile salt deconjugation, increased colonic water secretion, inhibited monosaccharide transport, inhibition of folate conjugases, increased fecal nitrogen, hypoalbuminemia Lamina propria: Increased mononuclear cells, mucosal damage by bacterial enzymes, loss of brush border, endotoxemia/antigenemia Liver damage Joint disease, cystic acne: endotoxemia, ulcerative colitis, colorectal cancer (CRC), increased paracellular permeability, Crohn's disease, intestinal inflammatory disorders (26), obesity, eczema (1)	Inflammation

Table 2. [Part 2] Effects of Overgrowth and Decrease in the Gut Bacterial Species on Health and Disease Conditions

Bacteria Genus	Effect of Overgrowth	Effect of Decrease
Enterococci	Rheumatoid arthritis, formation of hydroxy fatty acids Bile salt deconjugation, increased colonic water secretion Inhibition of monosaccharide transport, mucosal damage by bacterial enzymes Loss of brush border	Atopic eczema, lower gut flora, health of pet rabbits (27)
Lactobacilli	Intestinal giardiasis, vitamin B12 deficiency bile salt dehydroxylation, impaired formation of micelles, Formation of hydroxy fatty acids Bile salt deconjugation, Increase colonic water secretion, inhibition of monosaccharide transport, inhibition of folate conjugases, increased fecal nitrogen, hypoalbuminemia Lamina propria: Increased mononunuclear cells, mucosal damage by bacterial enzymes Loss of brush border, severe decrease in pH (28)	Atopic eczema, IBD (34), visceral hypersensitivity, contractile hyper-responsiveness, intestinal permeability, and inflammation (14)
Streptococcus	Intestinal giardiasis; high levels of lactic acid, plasma diamine oxidase (DAO), and D-lactate; chitosan and chitooligosaccharide degradation (29)	Inflammation and pathogen growth (23)

Table 2. [Part 3] Effects of Overgrowth and Decrease in the Gut Bacterial Species on Health and Disease Conditions

Bacteria Genus	Effect of Overgrowth	Effect of Decrease
Corynebacterium	Acne	Inflammation
Eubacterium	Malnutrition, achlorhydria/hypochlorhydria, sepsis, IBD, diverticulosis, autoimmune disorders, inflammation from complement or cytokine cascades, Crohn's disease, hyperlipidemia, hypertension, disruption of cellular adhesion molecules by proteases (30, 31)	Carbohydrate/fiber intolerance, malabsorption syndrome, fatigue and maldigestion (32)
Fusobacterium	Endotoxemia/antigenemia Liver damage Joint disease, autoimmune disorders, inflammation from complement or cytokine cascades, Crohn's disease, hyperlipidemia, hypertension (33)	Inflammation and infection, tumorigenesis (32, 34)
Proteus	Rheumatoid arthritis (RA), cystic acne: endotoxemia, atopic eczema,	-
Ruminococcus	Colorectal cancer (CRC)	Decreased sulfur metabolism (23)
Clostridium	Toxicity and infection	Digestive system infections, T2D, allergy sensitization (1)
Veillonella	Endotoxin lipopolysaccharide (35)	High lactic acid, low NO production for pathogen inhibition
Prevotella	Attachment, degradation of chitosan and chitooligosaccharide	Inflammation and infection (36, 37)

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