Emerging Topics in Gastroenterology

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KEYWORDS

• Microbiome • Probiotics • Fecal transplant • Cyclic vomiting
• Eosinophilic esophagitis • Microscopic colitis

KEY POINTS

- Genetic variations, diet, stress, and medication use have all been demonstrated to affect the composition of the microbiota in the gastrointestinal tract. Aging may lead to changes in physiology that impact gastrointestinal bacteria, potentially resulting in somatic symptoms related to a disordered microbiome.
- Fecal microbiota transplantation (FMT) has been shown to significantly alter the composition of the recipient's gut microbiome.
- Cyclic Vomiting Syndrome episodes are often triggered by emotional stress or antecedent viral illnesses. CVS is a diagnosis of exclusion, as it lacks any identifying radiological or laboratory abnormalities.
- Eosinophilic esophagitis(EE) is an increasingly-recognized cause of dysphagia and food impaction as well as infant feeding problems.
- Microscopic colitis(MC) is microscopic inflammation of the colonic mucosa that can cause chronic, watery, non-bloody diarrhea, abdominal cramping, and pain. The cause of MC is unclear and it can only be diagnosed through biopsy of the colonic mucosa.

GASTROINTESTINAL MICROBIOME AND PROBIOTICS

Researchers estimate that more than 100 trillion bacteria representing more than 600 different phylotypes can be found within a healthy human gut.[1] Additionally, more than 30 different fungal species may also be found in humans, depending on gender and stage of life.[2] These bacteria and fungi make up a community of microorganisms that lives in symbiosis with humans, engaging in numerous diverse interactions that influence health. Though the gastrointestinal (GI) microbiome undoubtedly interacts with the human body, there is much that is unknown about the formation, maintenance, and impact that the microbiome has on health and disease.

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New evidence suggests that the microbiome begins forming during the fetal period either through translocation of bacteria from maternal circulation or colonization via bacterial ascension from the vagina.[3,4] The method of delivery and the first few days of life significantly modify the microbiome composition.[4] Early diet plays a key role in establishing a colony of good bacteria as human milk oligosaccharides found in breast milk stimulate the growth of key bacteria. Interestingly, randomized trials have demonstrated that the consumption of human milk oligosaccharide analogues, even by adults, can improve the microbiome by stimulating the growth of bifidobacteria.[5]

After establishment, the microbiome continues to evolve in composition and function throughout the first few years of life. During this period, enteric neurons, immunologic factors, and the microbiome itself interact through complex signaling pathways to establish a homeostatic environment in the GI tract.[6] By age 3 years, the microbiome takes on a composition with characteristics that remain generally consistent through much of adulthood.[4] However, many events can shift microbiome composition and function in ways that may ultimately affect health. For example, exposure to antibiotics in early childhood may lead to lifelong changes in the composition of the microbiome.[7,8] Also, as individuals choose a more restricted diet that eliminates specific animal or plant sources of food, the substrates available for bacteria within the GI system can change dramatically. Changing substrates may create new patterns of bacterial growth and changes in the diversity of the microbiome.[9] Genetic variations, diet, stress, and medication use have all been demonstrated to affect the composition of the microbiota in the GI tract.[8] Aging may lead to changes in physiology that affect GI bacteria, potentially resulting in somatic symptoms related to a disordered microbiome.[10,11]

Research is now focusing on the impact that an altered microbiome has on an individual's health and symptomatology. When the composition of the microbiome shifts, individuals may begin to experience specific pathologic symptoms. For example, in patients with irritable bowel syndrome, studies suggest that alterations in bacterial composition are associated with changes in epithelial barrier dysfunction, visceral hypersensitivity, and GI motility.[12,13]

However, GI symptoms, such as diarrhea, constipation, bloating, and abdominal pain, are no longer thought to be the only manifestations of a disordered microbiome. Dysbiosis, a condition wherein the healthy microbial structure of the GI tract is disturbed, has been postulated to be an inciting event or contributing factor to the development or worsening of metabolic disease, mental health, neurologic disease, and cancer, among other conditions.[12,14,15] For instance, children who are raised in homes with pets have alterations in their microbiome that may be a link to protection from developing allergic diseases and respiratory virus infections.[7] Furthermore, studies of individuals with atherosclerosis demonstrate that those with and without disease have significantly different bacterial species that predominate in their GI microbiome.[16] The combination of a specific microbiome composition with a diet that provides a specific digestive substrate may result in the synthesis of trimethylamine-N-oxide, which has been identified as a risk factor for major cardiovascular events.[16] Similarly, in 1 study, the gut microbiome composition was found to be more predictive of type 2 diabetes disease severity than the body mass index.[17] The microbiome is also different in obese and lean individuals.[18–20] These observations raise interesting questions for future research. Does the composition of the microbiome drive disease or does the disease state alter the milieu of the environment such that the microbiome composition changes? What is the clinical significance of knowing about an alteration? Can diagnostic strategies or treatment options be developed that allow clinicians to partner with the microbiome to improve disease outcomes?