Basic Definitions and Concepts: Organization of the Gut Microbiome

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KEYWORDS

Microbiome • Microbiota • Enterotypes • Gastrointestinal function

KEY POINTS

- New claims are frequently made for a role for the microbiome in a disease or disorder previously considered remote from the gut, not to mention its bacterial population.
- The microbiome has been linked to such seemingly unrelated entities as depression, anorexia nervosa, autism, Parkinson disease, allergy, and asthma.
- Although many of these proposals have been based on animal studies, explorations of the microbiome in human disease continue to proliferate, facilitated by the availability of a variety of technologies that rapidly and with ever-increasing economy provide a detailed assessment of the microbial inhabitants of our gastrointestinal tract, their biological activities, and metabolic products.
- With these technologies come new terminology, such as microbiota, microbiome, metagenomics, and metabonomics, which are identified in this article.

To the busy clinician the tsunami of information that hits his or her desk or computer on a daily basis relating to the science and clinical implications of the microbiome has become simply overwhelming. Not a day goes by without a new claim for a role for the microbiome in a disease or disorder previously considered remote from the gut, not to mention its bacterial population. Thus, the microbiome has been liked to such seemingly unrelated entities as depression, ^{1,2} anorexia nervosa,³ autism, ^{4–6} Par-kinson disease, ^{7–9} allergy, and asthma. ^{10–12} Although many of these proposals have been based on animal studies, explorations of the microbiome in human disease continue to proliferate, facilitated by the availability of a variety of technologies that rapidly and with ever-increasing economy provide a detailed assessment of the microbial inhabitants of our gastrointestinal tract and their biological activities and metabolic products. ^{13–16} With these technologies comes a new terminology:

Microbiota is the assemblage of microorganisms (bacteria, archaea, or lower eukaryotes) present in a defined environment, such as the gastrointestinal tract.

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- *Microbiome* is the full complement of microbes (bacteria, viruses, fungi, and protozoa) and their genes and genomes (though strictly speaking different, the terms *microbiome* and *microbiota* are often used interchangeably).
- *Metagenomics* is the study of the gene content and encoded functional attributes of the gut microbiome in healthy humans.
- *Metabonomics* is the quantitative measurement of the multiparametric (time related) metabolic responses of complex systems to a pathophysiologic stimulus or genetic modification, often used synonymously with *metabolomics*.

The term *flora*, which dates from the time when bacteria were included in the plant kingdom, has now been largely abandoned and replaced by *microbiota*. Although the focus of the review is on the possible role of the microbiota in gastrointestinal diseases and disorders, one must first briefly review what is known of the microbiota in health.¹⁷

THE MICROBIOME IN HEALTH: DEVELOPMENT, INFLUENCES, AND FUNCTIONS

Much of what we know of the composition and functions of the normal gut microbiota comes from large national or multinational consortia.^{18–22} Although the microbiome of each individual is quite distinct at the level of individual bacterial strains, data from a European consortium indicated that, at a higher level of organization, some general patterns can be identified across populations.^{19,20} They identified 3 broad groupings (enterotypes) driven by the predominance of certain species: *Prevotella, Bacteroides,* and *Ruminococcus.* Enterotype prevalence seemed independent of age, body mass index, or geographic location but might have been driven by differing dietary habits.²⁰

Although the delineation of the full range of normal variations in the composition of the gut microbiota within and between individuals continues to be defined, certain trends have emerged. Traditionally, it was thought that the intestinal tract is sterile at birth; new evidence indicates that the colonization of the infant's gut may commence in utero from the placenta.^{23,24} However, the balance of evidence indicates that most of the infant's microbiome is acquired from the mother during birth and continues to be populated through feeding and other contacts.^{25–29} Several factors influence the microbiome over these critical early months and years of life²⁵⁻²⁸. mode of delivery (vaginal birth vs cesarean delivery),29-32 diet (breast milk vs formula),^{27,33,34} geography,³⁵ and exposure to antibiotics.³⁶ By 2 to 3 years of age, the child's microbiota has come to closely resemble that of an adult in terms of composition^{17,37,38}; some further evolution through to adolescence has, however, recently been reported.³⁹ Thereafter, the microbiota is thought to remain relatively stable³⁵ until old age when changes are seen, possibly related to alterations in digestive physiology and diet⁴⁰⁻⁴²; further longitudinal studies are required to more precisely define agerelated changes in adults.

Several factors influence the composition of the microbiota in health and must be accounted for in the interpretation of findings in disease. Foremost among these is diet.⁴³ General characteristics of the diet (total calories, highly processed vs vegetable and fruit based)^{20,35,44,45} as well as the relative concentrations of specific components, such as carbohydrate,^{46–48} protein,⁴⁹ fat,^{50,51} fiber,^{51–53} and vitamins,^{54,55} have all been shown to influence the composition of the microbiota. It has been assumed that diet-related changes reflect the long-term effects of a particular dietary pattern over a lifetime^{20,35,42,56}; it is now evident that relatively acute, albeit drastic, changes in dietary habit may also result in shifts in microbial populations.⁵⁶ All of these observations are highly relevant to the study of gastrointestinal diseases given the

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