



## EDITORIAL

## MEDICAL IMPORTANCE OF HUMAN MICROBIOTA

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Microorganisms are always considered as pathogens but it is now estimated that less than 1% of known microbial species are pathogenic to humans. The most microbes either coexist 'peacefully' with humans and they are good microbes. Human microbiota inhabits the body, living on the skin, in the mouth, gut, nose, and genital tract. Although the importance of gut microbiota for digestion of foodstuffs is widely recognized, additional roles for the body's microbes in nutrition, immunity, and other functions is being recognized now. Human microbiota regulates brain, liver, and lung health via bidirectional pathways like the microbiota-gut-brain axis, influencing mood, cognitive function, and systemic inflammation. Modern medicine is increasingly targeting the microbiome to treat diseases by using probiotics, and prebiotics to restore balance, and by using faecal microbiota transplantation.

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We used to think about the microbes as 'bad' for humans. This was because of the popular 'germ theory' of disease which states that microorganisms can invade living hosts and cause a disease. Robert Koch made the discoveries that led Louis Pasteur to describe how small organisms called germs could invade the body and cause disease. Germ theory replaced the 'miasma theory' (bad air) during the late nineteenth century. This resulted in development of stringent sanitation measures and development of very effective vaccines and antibiotics. Microorganisms are always considered as pathogens but it is now estimated that less than 1% of known microbial species are pathogenic to humans. The most microbes either coexist peacefully with humans or are essential for life on Earth.<sup>1</sup> Now we recognize that there are 'good microbes', or commensal microbes also, that provide required help to the human and similarly would provide benefit to the environmental source.<sup>2</sup>

Although the first scientific evidence that microorganisms are part of the normal human system emerged in the mid-1880s, the concept of the human microbiome, and thus the intensive study of it, was developed primarily in the first decade of the 21<sup>st</sup> century. The Human Microbiome Project (HMP) was started in 2007 and in the first three years of the project, scientists discovered nearly 200 different bacterial member species of the human microbiota.<sup>3</sup> Now, it is known that the human body is home to trillions of microorganisms, including bacteria, viruses, and fungi. In a healthy adult, this is called microbiota which collectively has a biomass equal to the human brain.<sup>4</sup> The human microbiota consists of approximately 100 trillion microorganisms that is about three times more than the human cells. Human microbiota weighs around 1.1 Kg and occupies 1.4 litres of space. Their highest density is found in the intestines. These microorganisms interact with the host and profoundly influence physiological homeostasis and immune mechanisms.<sup>5</sup>

Human microbiota inhabits the body, living on the skin, in the mouth, gut, nose and genital tract. The gastrointestinal tract normally contains a complex, dynamic population of 400 to 1,000 species of microorganisms that outnumber human cells. Communities of microorganisms that inhabit the body can cause diseases, but most of the times they live in harmony with their human hosts and provide vital functions that are essential for survival of their hosts. Although the importance of gut microbiota for digestion of foodstuffs is widely recognized, additional roles for the body's microbes in nutrition, immunity, and other functions are just beginning to be appreciated and this represents an intensive area of biomedical research. In healthy humans, most gut microbes are strictly anaerobic and about 90% belong to the phyla *Bacteroidetes* and *Firmicutes*, although there are many different types of bacteria in each of these phyla.<sup>6</sup>

Some scientists consider human microbiota as a 'virtual organ' because it performs essential functions that the human genome cannot perform. Human microbiota synthesizes essential vitamins, e.g., Vitamin K, B12, folate, biotin. They break down indigestible fibres into short-chain fatty acids (SCFAs) like butyrate which is an energy source for colonic cells. Human microbiota regulates lipid and glucose metabolism. Human microbiota trains the immune system to distinguish between harmless and pathogenic microbes. It regulates inflammatory responses, and supports the integrity of mucosal barriers.

Commensal microbes prevent the overgrowth of pathogens by competing for nutrients and space and by producing antimicrobial substances called bacteriocins. Interestingly, human microbiota regulates brain, liver, and lung health via bidirectional pathways like the microbiota-gut-brain axis, influencing mood, cognitive function, and systemic inflammation.<sup>7</sup>

Although the gastrointestinal tract is essentially sterile at birth, microorganisms living in

symbiosis with one another and with the host rapidly colonize the gut after birth. The composition of the microbiota in infants is influenced by multiple factors, including the birth modality (Caesarean section versus vaginal delivery), diet (breast milk versus formula feeding), and the use of antibiotics. With the cessation of breastfeeding and the start of a more diverse diet, there is rapid diversification of gut microbiota. The concentration of these microbes increases steadily along the gastrointestinal tract, with relatively small numbers in stomach and extremely large numbers in colon.<sup>6</sup>

In patients with inflammatory bowel disease (IBD), there is a decrease in the number of bacteria from the phylum *Firmicutes*. Various environmental factors often trigger dysbiosis, so broad-spectrum antibiotics used to treat infections significantly impact the microbiota. Dysbiosis is of three types: Loss of beneficial bacteria, Overgrowth of potentially pathogenic bacteria, Loss of overall bacterial diversity.

The majority of doctors are not aware of the rapidly developing science of microbiome and they are not also trained to give evidence based nutritional advice. Western-style diet is associated with gut dysbiosis and inflammation, which in extreme cases, may result in a leaky gut and translocation of gut-derived bacteria that promote liver inflammation and non-alcoholic steatohepatitis (NASH).<sup>5</sup> A diet that is high in plant-based carbohydrates, fats, grains, fish and naturally fermented foods is the healthiest diets around the world. Certain lifestyle changes and novel approaches including Faecal Microbiota Transplantation (FMT) and nutritional supplementation with probiotics, prebiotics, and symbiotics have offered solutions for dysbiosis management and paved the way towards restoring a healthy microbiome, with only minimal long-term unfavourable effects.<sup>9</sup>

Modern medicine is increasingly targeting the microbiome to treat diseases by the use of probiotics (live beneficial microbes) and prebiotics (fibre that feeds them) to restore balance; by using faecal microbiota transplantation which is now an established treatment for recurrent *C. difficile* and it is an investigational therapy for IBD and metabolic disorders. Developing personalized nutrition and ‘metabolism-based editing’ is to strengthen host functions that control the microbial environment.

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