

Opinion: Conservation and stewardship of the human microbiome

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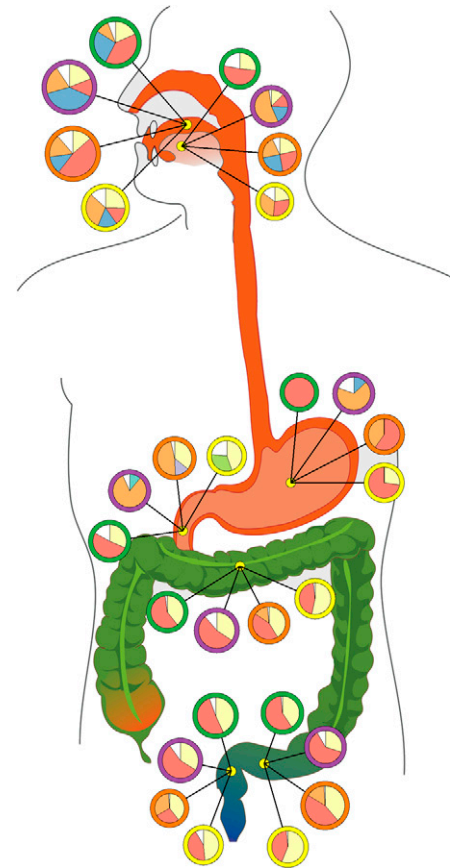
Many studies have shown how the human gut microbiome can be altered by diet, antibiotics, and other factors. All of these factors can contribute to dysbiosis, where the services typically provided by symbiotic microflora are disrupted because of shifts in function or diversity. Just as humans have impacted many large animal species in the environment, drastic changes in human lifestyle over the past century may have altered the global pool of human-associated microbes; if so, these shifts may pose substantial threats to individual and public health. Hardin (1) defined “The Tragedy of the Commons” as a situation where each individual benefits from overexploitation of a public resource, and we argue that there is benefit to regarding the global human microbiome as a collective good (i.e., a Microbial Commons).

Many practices, some of which confer health benefits, can influence the composition of the human microbiome. These practices include modes of infant delivery (2), broad nutritional trends (e.g., the “Western diet”), and exposure to pollutants and environmental toxins. The prevalence of excessive hygienic practices and widespread antibiotic use may also have immediate negative impacts on health, including obesity, type 1 diabetes, and functional bowel disorders (3). Conversely, greater exposure of infants to dust and some household pets may improve childhood responses to allergic and airway diseases through distinct gut microbial communities mediating immune system responses (4). How do these impacts map from the individual to the regional or global microbiome? The dispersal of strains and communities via physical contact between hosts offers opportunities for recruitment of

healthy and resilient microbial communities during development, but this transmission may be of limited value if communities are locally depleted. Such contact may also facilitate the establishment of certain opportunistic pathogens, such as *Clostridium difficile* and *Pseudomonas aeruginosa*, and more complex communities associated with dysbiosis.

Recent studies have identified regional changes in disease incidence that may be associated with alterations of the microbiota in the affected region. To date, most of these changes have been documented in urbanized Western countries. For example, there has been as much as a fivefold increase in the incidence of atopic diseases over the past 30–50 years (5), and similar increases in the incidence of type 1 diabetes, multiple sclerosis, and inflammatory bowel disease. Interestingly, the offspring of recent immigrants acquire the disease risk of their adopted country (6). Industrialization and health care are transforming developing countries and leading to significant microbiome impacts there as well (7). Elucidating correlation and causation between practices that are linked to microbiome changes, identifying the scales (local, regional, and global) at which these influences are felt, and exploring consequences for public health will all be vital foci for future research. We must address the role of factors, including host genetics, population substructure, strain-level differentiation, evolutionary process, and environmental passage on the microbial diversity we observe. We must also consider the impacts of sharing space in built-environment settings, such as daycares, hospitals, and retirement homes.

A growing understanding of the consequences of altering the microbiome is beginning to inform the choice of treatments. For



Graphical representation of phylum-level bacterial taxonomic distributions (pie charts) associated with four healthy individuals (color-coded outer circles) at multiple digestive tract locations, including (from top to bottom) teeth, tongue, stomach, duodenum, transverse colon, sigmoid colon, and rectum. Figure generated with GenGIS (13) using data from (14).

example, the prophylactic administration of antibiotics during birth to pregnant women who test positive for Group B *Streptococcus* is

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usually favored over other possible strategies, based on risk analysis relative to immediate health outcomes. This approach, however, has a negative impact on the symbiotic microbes that are crucial in early infant development. Newer approaches, such as the introduction of probiotic strains or entire microbial communities (8), or highly targeted species-specific antibiotics, offer new opportunities to fight pathogens without subjecting an individual to the unintended consequences of antibiotic treatment, and may be favorable from a public health point of view as our knowledge of pathogens and healthy microbiomes increases, and as new, viable therapeutic strategies emerge. Health practices and the environment influence not only the current composition of the microbiome, but the selective pressures on its constituents. Lateral gene transfer, the “sharing” of genes between organisms, appears to occur at very high rates in the microbiome (9), even affecting critical functions, such as butyrate synthesis (10). Changes in antibiotic use and dietary patterns can rapidly change the selective pressures operating on gut microflora, and these increased environmental stresses have long been associated with increased rates of mutation and genetic exchange (11, 12).

New initiatives provide opportunities for supporting microbiome conservation and stewardship. For example, the world’s first fecal transplant bank (www.openbiome.org)

heralds the beginning of organizations that preserve global microbiome samples, spanning cultures and continents. Engagement with health-care professionals, policymakers, and the general public should focus on the importance of maintaining a healthy microbiome, and evaluate the potential costs and benefits of current therapies. As we learn more about the long-term health impacts of practices that damage the microbiome, and the spatial scales at which these impacts can be felt, the risks of microbiome mismanagement can be expressed as a broader public health concern. Cohort studies, such as the Genetics, Environmental, and Microbial project, (www.gemproject.ca)

and large citizen science surveys, such as American Gut (<http://americangut.org>), offer unique opportunities for public engagement. Such initiatives can help assess and communicate how measurably different management practices are linked to regional disparities in microbiome composition. By drawing on knowledge and techniques from conservation biology, we will be better able to understand and protect our Microbial Commons.

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- 1 Hardin G (1968) The tragedy of the commons. The population problem has no technical solution; It requires a fundamental extension in morality. *Science* 162(3859):1243–1248.
- 2 Azad MB, et al.; CHILD Study Investigators (2013) Gut microbiota of healthy Canadian infants: Profiles by mode of delivery and infant diet at 4 months. *CMAJ* 185(5): 385–394.
- 3 Blaser M (2011) Antibiotic overuse: Stop the killing of beneficial bacteria. *Nature* 476(7361):393–394.
- 4 Fujimura KE, et al. (2014) House dust exposure mediates gut microbiome *Lactobacillus* enrichment and airway immune defense against allergens and virus infection. *Proc Natl Acad Sci USA* 111(2): 805–810.
- 5 Bach JF (2002) The effect of infections on susceptibility to autoimmune and allergic diseases. *N Engl J Med* 347(12): 911–920.
- 6 Söderström U, Aman J, Hjertqvist A (2012) Being born in Sweden increases the risk for type 1 diabetes—A study of migration of children to Sweden as a natural experiment. *Acta Paediatr* 101(1):73–77.
- 7 Smith MI, et al. (2013) Gut microbiomes of Malawian twin pairs discordant for kwashiorkor. *Science* 339(6119): 548–554.
- 8 van Nood E, et al. (2013) Duodenal infusion of donor feces for recurrent *Clostridium difficile*. *N Engl J Med* 368(5): 407–415.
- 9 Smillie CS, et al. (2011) Ecology drives a global network of gene exchange connecting the human microbiome. *Nature* 480(7376): 241–244.
- 10 Meehan CJ, Beiko RG (2014) A phylogenomic view of ecological specialization in the Lachnospiraceae, a family of digestive tract-associated bacteria. *Genome Biol Evol* 6(3):703–713.
- 11 Foster PL (2007) Stress-induced mutagenesis in bacteria. *Crit Rev Biochem Mol Biol* 42(5):373–397.
- 12 Stecher B, et al. (2012) Gut inflammation can boost horizontal gene transfer between pathogenic and commensal Enterobacteriaceae. *Proc Natl Acad Sci USA* 109(4):1269–1274.
- 13 Parks DH, et al. (2013) GenGIS 2: Geospatial analysis of traditional and genetic biodiversity, with new gradient algorithms and an extensible plugin framework. *PLoS ONE* 8(7): e69885.
- 14 Stearns JC, et al. (2011) Bacterial biogeography of the human digestive tract. *Sci Rep* 1:170.