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How Probiotics and the Microbiome Will Change Medical Practice

Gregor Reid
Lawson Health Research Institute, gregor@uwo.ca

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Gregor Reid, PhD, MBA, ARM, CCM, Dr. HS, FCAHS, Director of the Canadian Centre for Human Microbiome and Probiotic Research, Lawson Health Research Institute, Professor, Departments of Microbiology and Immunology, and Surgery, The University of Western Ontario

The Bell Wing at Toronto General Hospital has long gone, but in the Fall of 1982, that was where I began my journey into human microbiome and probiotic research. Stimulated by mentor Dr. Andrew Bruce, Head of Urology, I asked the question: "Were there beneficial bacteria in the urogenital tract and if they help prevent infection, could they be replenished to reset an infectious state back to normal?" Thirty-three years later, this is arguably the hottest field of medicine, and one that will transform its practice for years to come.

Humans have evolved from microbes, so it should be no surprise to find these organisms playing a key role in health. But, who would have thought they would be living in the brain,[1] breast tissue,[2] stomach,[3] in some sort of suspended state, and, through the gut, influencing metabolism,[4] cardiac health,[5,6] anxiety[7] and bone density,[8] to name a few? Who would have imagined being able to identify over 200 species present in any given niche within hours using a device the size of a Mars Bar?[9] And to be able to detect disease through metabolic by-products from these microbes?[10] A mere eleven years ago, the word probiotic was barely in the medical language, and viewed by some as snake oil: today, its market size is around $30 billion. The transfer of feces from human donor to recipient was unimaginable not long ago, but to find that it has a 90% cure rate of deadly *Clostridium difficile* infection[11] and to consider doing this to prevent obesity or delay mental illness[12] would have seemed draconian just ten years ago. Yet, here we are today recognizing that microbes play an integral part in health and disease. Indeed, potentially in the determinants of health and their developmental origins. Where could the future possibly take us?

These discoveries are playing havoc with traditional practices and systems we established within our society. From the early 20th Century, regulatory agencies were set up and instructed to adjudicate that drugs could prevent, treat and cure disease. Fast forward to the present, it seems absurd to suggest that microbial-containing food and supplements need to be defined as drugs that must be prescribed to treat, prevent and potentially even cure some diseases. The FDA, for example, clearly demands that this should happen.[13] Not only that, the system of registering bacterial strains as part of regulatory procedures does not allow for depositing strain combinations, even though once separated from each other, such strains die, thereby defeating the whole purpose of deposition.

The education of medical doctors and other healthcare professionals has been streamlined in recent years, with teaching the importance of beneficial microbes all but deleted. If our healthcare specialists don't understand this area, how can we ask them to manage health issues associated with microbes, and recommend interventions and approaches outside of drug prescriptions? Continual medical education and conferences might help, but they often convey opinions rather than establish guidelines and basic training. With companies creating diagnostic systems to relay microbiome and metabolome data,[10] practitioners must be able to interpret them and consider the ethical implications of disclosing the information.[14]

If the composition of the gut microbiome influences drug adsorption,[15] should all drugs not be re-tested against a patient's microbes? The implications are enormous, but this aspect of personalized medicine is clearly on the horizon. Probiotics have been shown to augment the effects of some drugs,[16,17] but how do physicians write a script for a probiotic food? The creation of Guidelines that outline probiotic products that have been at least clinically tested[18] certainly helps consumers plod through the multitude of products available, and recognize those that have not been tested for effectiveness in humans.

As the microbiome appears to form into an 'adult' composition by around age three, and as many diseases are already conditioned by then, the question of 'programming' the microbiome during fetal and early life must be considered. The best way of doing this is far from understood, but manipulation of one form or another is already taking place through the placenta,[19] breast milk,[20] and probiotic infant formula.[21] Longitudinal studies are needed to understand this crucial stage in life, yet Canada, the European Union and USA have ceased funding large microbiome programs, and pay lip service to the funding of probiotic research and indeed research on what makes people healthy. This is ironic considering the funders are institutes of 'health'.

Corresponding Author:
Gregor Reid
Lawson Health Research Institute F3-106
268 Grosvenor St.
London, Ontario N6A 4V2
519-646-6100 x65256
gregor@uwo.ca

While surgery and other invasive interventions will be necessary long into the future, many other aspects of medicine will change dramatically in the next twenty years. Interpretation of data, whether acquired in centres or by individuals, will become paramount, and a holistic understanding of anatomy and physiology, nutrition and the microbiome will be essential. Metchnikoff directed us to ask why Bulgarian peasants lived so long[22] and how fermented foods were associated with it. The key to a long, healthy life likely does lie in our food and microbes - we just need to understand how best to align them, in some cases also taking into consideration our genetic endowment. Time will tell how quickly we embrace the future.

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