2016 VOLUME XLVI NUMBER 2

CHRISTIAN SCHOLAR'S REVIEW

Deeply Connected to God's Good World, the Human Microbiome

By Michael Kunnen and Clayton Carlson

We worship a relational God. In Genesis 1:26 God is already "us" ("Let us make man in our image") providing an intriguing word from which the Christian tradition sees evidence of the Trinity, God as three in one, in perfect relationship with Godself.[1] New advances in science have revealed that individual humans should also be considered "us" for each person is actually a vast community of species living a remarkably interconnected and interdependent existence. The story of the creation of human beings in Genesis 1 and 2 highlights the role of relationships in the lives of humans. In Genesis 2 humans have a relationship with God, each other, and with God's creation. By Genesis 3 all of these relationships are disrupted so that Adam and Eve are barred from the Garden, the man rules over the woman, and food comes from the ground through toil. The relationships are not severed; by grace we can still be in relationship with God, we still relate with each other, and we still connect to God's world. However, nothing is as it could be. Today it is still possible to find new ways in which we are in relationship with each other and God's world and, as we might expect, we find that these relationships are crucial to who we are but are at the same time twisted into something less than they could be.

From Germs to Community

By the year 1683 the field of microscopy had advanced to the point that Anton van Leeuwenhoek was able to visualize bacteria that were dwelling in tartar scraped from his teeth.[2] From this new advance in technology we learned that

Advances in DNA sequencing technologies are revolutionizing our understanding of microbial populations on and within human beings. The goal of this article is to evaluate some of these discoveries in light of the story of scripture. The early chapters of Genesis make clear the relational nature of human being in regards to our connections to God, to each other, and to God's creation. Research into the human microbiome reveals new levels of connectedness that could have been expected theologically and the new connectedness revealed by science can begin to shape our theology. **Michael Kunnen** is the Coordinator of the Bridge Street House of Prayer in Grand Rapids, MI and **Clayton Carlson** is an Associate Professor of Biology at Trinity Christian College in Palos Heights, IL.

our bodies are homes to microbes. The fields of microbiology and microscopy developed in tandem over the years since, and the role of these microbes in causing disease became clear in the 1870s.[3] Incredible advances in treating human diseases with antibacterial antibiotics in the 1930s – 1950s had an unintended consequence of teaching the public that bacteria are an enemy. Those first-observed bacteria from the tooth scraping could have led to an understanding that bacteria are a natural part of the human makeup, but instead we learned that diseases are caused by germs. We created a logical fallacy: diseases are caused by germs, bacteria are germs, and therefore all bacteria cause disease. It has taken another technological advance to help us to appreciate the breadth and depth of bacterial communities that reside on and in human beings. While it was once necessary to grow, isolate, and then characterize microbes in order to identify them, it is now possible to read the DNA inside each species directly. Next-generation sequencing and its ability to read DNA sequences from complex populations has turned the DNA within each microbe into an identifying bar code.[4] As an analogy, the historical technique would be similar to identifying those in attendance at a large festival by personally interviewing each person. The new sequencing techniques are more like reading the driver's license number of each attendant as they walk through the gates. It is now possible to identify rapidly the diversity and quantity of microbes residing in until-now indecipherably complex communities. The complex population of microbes within the human environment is called the microbiome, and microbiome research has now revealed what we as Christians should have expected all along; human beings are intimately connected to this world.

Humans are Ecosystems

The human body provides a number of unique, but interconnected, ecosystems for microbial life. The human skin, mouth, throat, colon, and vagina are richly inhabited by vast populations of organisms living in balanced harmony. These ecosystems are occupied by different species that are each well adapted for the nutrients available there, the immune system responses present, and other selective pressures found in each location. The diversity in any single human body ecosystem is still being determined by groups like the Human Microbiome Consortium, known by the National Institutes for Health as the Human Microbiome Project,[5]

[1]John Calvin, "Commentaries on the First Book of Moses Called Genesis, Vol 1", trans. John King (Grand Rapids, MI: Wm. B. Eerdmans, 1948), 86 (1847).
[2]M. Karamanou, E. Poulakou-Rebelakou, M. Tzetis, and G. Androutsos, "Anton van Leeuwenhoek (1632-1723): Father of Micromorphology and Discoverer of Spermatozoa," *Revista Argentina de Microbiología* 42.4 (2010): 311-314.
[3]Joshua Lederberg, "Infectious History." *Science* 288.5464 (2000): 287-93.
[4]Michael L. Metzker, "Sequencing Technologies—the Next Generation," *Nature Reviews Genetics* 11.1 (2010): 31-46.
[5]Peter J. Turnbaugh, Ruth E. Ley, Micah Hamady, Claire Fraser-Liggett, Rob Knight, and Jeffrey I. Gordon, "The Human Microbiome Project: Exploring The Microbial Part of Ourselves in a Changing World," *Nature* 449.7164 (2007): 804.

but the bacteria that make up the human microbiome seem to come primarily from six main phyla.[6] Which phyla is the most common will depend on which bodily ecosystem is being analyzed. There is a large but finite pool of bacterial species that have ever been identified as part of the human microbiome, but any individual human bears only a subset of these species.[7] Within an individual, the collection of microbes that reside on their skin will be more similar to the microbes that live on a neighbor's skin than the microbes that live within their own mouth. In fact, interpersonal differences in microbiota within a particular ecosystem (such as skin) could be smaller even than the differences one person has on their own skin at different body parts.[8] In all the total number of bacteria in the human microbiome could be 10^{14} individuals with a human lifespan representing up to one million bacterial generations.[9]

The richest and most complicated microbial population living on or in humans is found within the large intestine, the colon. This community, typically referred to as the gut microbiota, likely houses 70% of the human microbiome[10]. The makeup of the gut microbiota depends on individual genetics, physiology, diet, and environment in which the human lives. While more than 1,000 different species have been found living in human colons, any individual human will house around 150 species.[11] Microbes living in the human gut are granted a warm, moist, nutrient-rich environment, while humans with a diverse and balanced gut microbiota receive a number of health benefits. The gut microbiota serves as a digestive complement to the human digestive systems providing perhaps 20 – 30% more calories from carbohydrates typically indigestible using human enzymes alone.[12] The gut microbiota also protects its host from pathogenic bacteria. Any gut pathogen would need to thrive in an environment already filled with rapidly-growing, well-adapted members of the microbiota.[13]

The interactions between the gut microbiota and the human immune system are extensive and remarkable. After birth the T regulatory cells (T_{reg}), cells that sup-

[6]Ilseung Cho and Martin J. Blaser, "The Human Microbiome: At The Interface of Health and Disease," *Nature Reviews Genetics* 13.4 (2012): 260-270.

[7]Elizabeth K. Costello, Keaton Stagaman, Les Dethlefsen, Brendan J. M. Bohannan, and David A. Relman, "The Application of Ecological Theory Toward an Understanding of the Human Microbiome," *Science* 336.6086 (2012): 1255-1262.

[8]Elizabeth A. Grice, Heidi H. Kong, Gabriel Renaud, Alice C. Young, Gerard G. Bouffard, Robert W. Blakesley, Tyra G. Wolfsberg, Maria L. Turner, and Julia A. Segre, "A Diversity Profile of the Human Skin Microbiota," *Genome Research* 18.7 (2008): 1043-1050.

[9]Ilseung Cho and Martin J. Blaser, "The Human Microbiome: At The Interface of Health and Disease," *Nature Reviews Genetics* 13.4 (2012): 260-270.

[10]Inna Sekirov, Shannon L. Russell, L. Caetano, M. Antunes, and B. Brett Finlay, "Gut Microbiota in Health and Disease," *Physiological Reviews* 90.3 (2010): 859-904.

[11]Craig L. Maynard, Charles O. Elson, Robin D. Hatton, and Casey T. Weaver, "Reciprocal Interactions of the Intestinal Microbiota and Immune System," *Nature* 489.7415 (2012): 231-241.

[12]Valentina Tremaroli and Fredrik Bäckhed, "Functional Interactions Between the Gut Microbiota and Host Metabolism," *Nature* 489.7415 (2012): 242-249.

[13]Craig L. Maynard, Charles O. Elson, Robin D. Hatton, and Casey T. Weaver, "Reciprocal Interactions of the Intestinal Microbiota and Immune System," *Nature* 489.7415 (2012): 231-241.

press immune response, are "trained" in the colon where they learn which bacterial species in the gut are to be tolerated.[14] The T_{reg} cells will prevent an inflammation response in the gut from the normal microbiota but are still able to permit a full immune response if those same bacteria are found elsewhere in the body. These T_{reg} cells are found in higher numbers in the gut than in any other body location and ingestion of probiotics can stimulate an increase in the number of these anti-inflammatory cells. While the microbiota is shaping our immune system, our immune systems are certainly shaping the gut microbiota. The inner layers of the colon are lined with thick mucus in which comparatively fewer bacteria reside. Bacteria that are able to penetrate this mucus layer are more likely to be pathogenic and are therefore killed by the immune system. In essence, the immune system selects for bacteria that only interact with human tissue minimally. Some of these beneficent bacteria will even ferment gut carbohydrates into simple molecules like butyrate that then become the primary energy source for the human cells that make up the inner lining of our colons.[15] Our bodies select which species thrive, and those bacteria in turn support the health of our bodies.

Community Matters

A healthy and balanced relationship with a diverse microbiota is important for each human ecosystem. Like in the colon, the skin microbiota is shaped by and shapes the immune system.[16] The skin microbiota is made up of bacteria, viruses, phage (viruses that infect bacteria), fungi, and even multicellular organisms like mites. Our skin microbiota is shaped by factors out of our control like sex, age, and immune history but it is also responsive to influences we can control like clothing choices, hygiene, and the climate in which we live. Examples of benefits of a healthy skin microbiota come from the well-characterized skin microbe, *Staphylococcus epidermidis. S. epidermidis* can produce molecules that are inhibitory to dangerous skin pathogens like Group A Strep or *Staphylococcus aureus*. Additionally *S. epidermidis* is able to repress the inflammation response of the immune system at the skin. On the other hand, some skin conditions like psoriasis are characterized by reduced microbiota diversity.[17] A patch of skin inflamed with psoriasis has much less microbial diversity than the healthy skin

[14]C. H. Hansen, Dennis Sandris Nielsen, Miloslav Kverka, Zuzana Zakostelska, Klara Klimesova, Tomas Hudcovic, Helena Tlaskalova-Hogenova, and Axel Kornerup Hansen, "Patterns Of Early Gut Colonization Shape Future Immune Responses of the Host," *PLoS One* 7.3 (2012): e34043.

[15]Craig L. Maynard, Charles O. Elson, Robin D. Hatton, and Casey T. Weaver, "Reciprocal Interactions of the Intestinal Microbiota and Immune System," *Nature* 489.7415 (2012): 231-241.

[16]Elizabeth A. Grice and Julia A. Segre, "The Skin Microbiome," *Nature Reviews Microbiology* 9.4 (2011): 244–253.

[17]Alexander V. Alekseyenko, Guillermo I. Perez-Perez, Aieska De Souza, Bruce Strober, Zhan Gao, Monika Bihan, Kelvin Li, Barbara A. Methé, and Martin J. Blaser, "Community Differentiation of the Cutaneous Microbiota in Psoriasis," *Microbiome* 1.1 (2013): 31.

immediately beside it. Because of its constant exposure to the environment, the skin microbiota is very dynamic. This can make it more difficult to study, but could potentially make it easier to manipulate once we learn which members are necessary for a healthy skin ecosystem.

Clearly the microbiota is necessary for health of the digestive system as well. Classic work by Maier and Hentges showed that bacteria-free mice, which have no microbiota, are highly susceptible to pathogens of the digestive system, at least in part because of the lack of normal microbiota with which to compete.[18] However many studies have shown that common chronic digestive conditions also have an apparent role for the microbiota.[19] Inflammatory Bowel Disease (IBD) includes ulcerative colitis and Crohn's disease. IBD has become a global epidemic. Both conditions within IBD involve a damaging immune response against the normal microbiota. Patients with IBD, like those with psoriasis discussed above, have reduced microbial diversity as compared to those with a healthy digestive tract, in part due to a decrease in numbers from the group Bacteroidetes.

Strikingly, gut biodiversity not only affects digestive health, but appears to have consequences for psychological health as well. There is now enough evidence that the gut microbiota can impact brain development and brain behavior that the interaction is referred to as the microbiota-gut-brain axis.[20] Germ-free mice have been shown to display antisocial behaviors consistent with autism. Some, but not all, of the behaviors were reversible once the mice were populated with typical gut bacteria.[21] Gastrointestinal disorders are a common co-condition for those with autism, and interestingly, the severity of these two conditions tends to correlate. Hsiao and colleagues at the California Institute of Technology may have identified a partial mechanism behind the microbiota-gut-brain axis.[22] Using a mouse model of autism it was shown that treatment of mice with bacteria known to be beneficial for digestive health in humans can improve the social symptoms of the condition. Treatment of these mice with *Bacteroidesfragilis*, commonly found in healthy human colons, was able to improve digestive health, reduce gut inflammation, correct abnormal levels of various molecules in the blood, and decrease the social ailments. They claim that "microbiome-mediated therapies may be a safe and effective treatment for neurodevelopmental disorders." Whether we are

[18]Bruce R. Maier and David J. Hentges, "Experimental Shigella Infections in Laboratory Animals I. Antagonism by Human Normal Flora Components in Gnotobiotic Mice," *Infection and Immunity* 6.2 (1972): 168–173.
[19]Tadakazu Hisamatsu, Takanori Kanai, Yohei Mikami, Kazuaki Yoneno, Katsuyoshi Matsuoka, and Toshifumi Hibi, "Immune Aspects of the Pathogenesis of Inflammatory Bowel Disease," *Pharmacology & therapeutics* 137.3 (2013): 283-297.
[20]John F. Cryan and Timothy G. Dinan, "Mind-Altering Microorganisms: The Impact of the Gut Microbiota on Brain and Behaviour," *Nature Reviews Neuroscience* 13.10 (2012): 701–712.
[21]L. Desbonnet, G. Clarke, F. Shanahan, T. G. Dinan, and J. F. Cryan, "Microbiota is Essential for Social Development in the Mouse," *Molecular Psychiatry* 19.2 (2014): 146.
[22]Elaine Y. Hsiao, Sara W. McBride, Sophia Hsien, Gil Sharon, Embriette R. Hyde, Tyler McCue, Julian A. Codelli et al., "Microbiota Modulate Behavioral and Physiological Abnormalities Associated with Neurodevelopmental Disorders." *Cell* 155.7 (2013): 1451-1463.

to this point or not, the makeup of our microbial communities has substantial effects on our health and quality of life. Study of the microbiome has revealed that the cause of some serious physical, mental, and developmental conditions may be, at least in part, distorted relationships.

Establishing Community

The microbial communities of the various human ecosystems are all established and developed after birth. In the womb, the developing fetus is thought to be in an essentially microbe-free environment, but from the breaking of the embryonic sac through birth and infanthood the newborn is exposed to an unimaginable number of microbes. In vaginal childbirth, the mother's body undergoes an incredible series of physiological and microbial changes that may influence her child's microbiota for years to come. Throughout pregnancy, a woman displays high estrogen levels. This has numerous impacts on the mother's body, but one somewhat unexpected response is the release of glycogen into the vagina. Glycogen is an energy storage molecule reserved en mass within the liver and muscles. Release of glycogen, essentially stored energy, into the vaginal canal just when a woman will need a great deal of stored energy seems counterintuitive. However this glycogen is rapidly metabolized by a common group of vaginal microbes, those of the genus *Lactobacillus.* The influx of glycogen leads to an explosion in the *Lactobacillus* population and a decrease in microbial diversity which in turn has two important consequences. First, the fermenting *Lactobacillus* produce lactic acid reducing the pH of the vagina to a degree of acidity that inhibits, or even kills, most pathogens likely to be present there. The second is that while in the birth canal, the newborn is covered with huge numbers of bacteria from this beneficial genus. As the child grows and is exposed to more and more species of bacteria from contact with parents, the environment, and later other foods, the colonization is controlled by the *Lactobacillus* that are already present in each location. The *Lactobacilli* may only reside in a certain ecosystem within the child temporarily (remaining dominant on the skin for only months), but its presence from the beginning can have long-term consequences on microbiota.[23]

The mother's ability to shape her child's microbiota does not stop at birth. She will continue to shape which microbes colonize her infant through the act of nursing. Breast milk has long been known to include antibodies. What has only recently been appreciated is that in addition to containing antibodies against a wide variety of pathogens to which the mother has been or is being exposed, breast milk passes on the same set of antibodies that the mother uses to groom her own microbiota. As discussed above, our immune systems shape which microbes thrive in environments like the colon by attacking and clearing any bacteria that

[23]M. Grönlund, O. P. Lehtonen, E. Eerola, and P. Kero, "Fecal Microflora in Healthy Infants Born by Different Methods of Delivery: Permanent Changes in Intestinal Flora after Cesarean Delivery," *Journal of Pediatric Gastroenterology and Nutrition* 28.1 (1999): 19–25.

interact too aggressively with human tissue. The mother does this, at least in part, by secreting antibodies against known problem species into the mucus that lines her colon. The set of antibodies used are the accumulated wisdom from a lifetime of relating to gut microbes. When nursing she is able to share this wisdom by filling her infant's digestive tract with nutritious milk that contains antibodies that are able to mark for destruction any microbes her body has found to be problematic. This process may provide time for beneficial bacteria to become established in the colon so that they may become robust competition for pathogens the child will encounter later in life. It appears that through the beautiful and intimate act of nursing a child, one of the closest forms of relationship in which humans can participate, a mother can biologically shape the future relationships her child will have with the broader world.

The makeup of the human microbiota is much more dynamic among children than it is among adults, but even adults help shape their microbiota every day. One substantial mechanism by which the gut microbiota is shaped is through diet. As reviewed by Graf and others,[24] the makeup of the gut microbiota is substantially different depending on whether the host consumes a standard Western diet (rich in protein, fat, and refined carbohydrates), a vegetarian diet, or a more whole foods diet common in rural areas of developing countries. One study comparing the gut microbiota composition of individuals from 0 to 70 years old from Venezuela, Malawi, and the United States found that at every age the diversity of microbes clustered according to country of host. The effect of particular foods on the gut microbiota has been observed in a broad range of studies. These groups have assessed changes caused by fruits, vegetables, nuts, whole grains, red wine, and beans. As a whole, these studies reinforce an idea that is perfectly logical. The microbes that thrive in our digestive tract must tolerate our immune system and thrive on our diet. Any drastic change in diet is likely to have a corresponding change on the gut microbiota. Perhaps the lesson then for individuals suffering from a damaging relationship with their gut microbiota is to change their diet in some way that they can sustain. A shift away from a damaging relationship in almost any direction is likely to bring an improvement. Like our mothers did for us long ago, we now have the ability to shape our most important microbial population with every bite we take.

Our microbiota is not only shaped by what we bring into our bodies but also by where we go and with whom we spend time. A study published in *Science* analyzed the microbiota of houses.[25] They measured the microbial communities that dwell on various surfaces of six homes inhabited by six different families. In

[24]Daniela Graf, Raffaella Di Cagno, Frida Fåk, Harry J. Flint, Margareta Nyman, Maria Saarela, and Bernhard Watzl, "Contribution of Diet to the Composition of the Human Gut Microbiota," *Microbial Ecology in Health and Disease* 26.0 (2015) doi:10.3402/mehd.v26.26164.
[25]Simon Lax, Daniel P. Smith, Jarrad Hampton-Marcell, Sarah M. Owens, Kim M. Handley, Nicole M. Scott, Sean M. Gibbons et al., "Longitudinal Analysis of Microbial Interaction between Humans and the Indoor Environment," *Science* 345.6200 (2014): 1048–1052.

the course of the study, three of the families moved into new houses. The findings reveal that a huge portion of the microbes that live within our homes come from the human beings that live within them. The researchers were able to predict accurately which home a given sample came from based on the microbes common to members of that family. For the families that moved, their new homes begin to have a microbial fingerprint similar to that of the family within just days. What was particularly interesting in this work is that the individuals that lived nearly within the home shared a common skin microbiota like they shared a common home microbiota. This was true whether the residents were related, in a relationship, or only cohabitating. Our human relationships shape our microbial relationships. Other work[26] has shown that the sharing of microbes influences the microbiota of skin, mouth, and colon and the sharing can be with whomever we live. Even animals that live within our homes can shape our microbial communities. Furthermore our pets' microbiota is influenced by living with us. Given the importance of microbial diversity in the various human environments, it is striking that our relationships with place, others, and even animals can have impactful biological consequences. In our every relationship, be it with others, with animals, or even with locations, we undertake a biological exchange. In a very real way the mega-organism we are is a biological consequence of every relationship we have ever had. Likewise, everywhere we go, and to everyone we meet, we leave behind part of who we are.

A Community at War

From the early chapters of Genesis, it is clear that all of the highly interwoven relationships of creation were originally "very good." However with the choice to disobey God and the resulting entry of sin into the world, brokenness has pervaded all aspects of creation, including relationships. This is evidenced in Genesis 3:7-8:

> Then the eyes of both of them were opened, and they realized they were naked; so they sewed fig leaves together and made coverings for themselves. Then the man and his wife heard the sound of the LORD God as he was walking in the garden in the cool of the day, and they hid from the LORD God among the garden.

Sin also caused disunity within humanity. Disunion between humans is illustrated in verse 12 when Adam accuses God and Eve of causing him to sin: "The man said, 'The woman you put here with me – she gave me some fruit from the tree, and I ate it.'" Finally, there also exists a brokenness between humans and creation as shown in the curse God speaks against Adam in verses 17b-18: "Cursed is the ground because of you; through painful toil you will eat of it all the days of your

[26]Se Jin Song, Christian Lauber, Elizabeth K. Costello, Catherine A. Lozupone, Gregory Humphrey, Donna Berg-Lyons, J. Gregory Caporaso, Dan Knights, Jose C. Clemente, Sara Nakielny, Jeffrey I. Gordon, Noah Fierer, and Rob Knight, "Cohabiting Family Members Share Microbiota with One Another and with Their Dogs," *ELife* 2 (2013), doi:10.7554/elife.00458.

life. It will produce thorns and thistles for you, and you will eat the plants of the field." Not only are the humans now at odds now with the earth itself, but they are in conflict with all creatures over which they were to rule. Living in a broken world it is no surprise that there is evidence of brokenness in our relationships with our microbes.

Disruption to our microbiota can begin at the moment of birth. While Caesarian section is certainly a gift from God which has made routine the kinds of births that once would have threatened the lives of mother and child, it is also a severe interruption of the "very good" process established originally. Children born by C-section, which may be up to one third of all American newborns,[27] are not given the opportunity to be inoculated with *Lactobacillus* in the birth canal. Dominguez-Bello and colleagues[28] reported that children born by C-section have skin, mouth, and fecal microbiota that more closely resemble their mothers' skin microbiota than their mothers' vaginal environment. This includes large numbers of the potentially dangerous streptococcus and staphylococcus groups. There is some data to support the notion of long-term consequence of birth by C-section including increased rate of asthma[29] but the full consequences of this new microbial foundation are not yet known. After the child is born it is possible to support the baby on formula, and while nutritious when needed, formula cannot pass on a lifetime of accumulated biological wisdom based on real-life experiences like a mother is able to do through nursing.

Antibiotics, tools of redemption that are able to protect us from suffering and death, are not able to do so without also effecting our beneficial relationships. An American child may take 10 – 20 courses of antibiotics before adulthood.[30] Long-term antibiotic use has been shown to have lasting consequences on the microbiota. One study showed that infants who took amoxicillin for respiratory infections had massive changes in the gut populations. These infants had total elimination of some beneficial species (*Bifidobacteriumadolescentis*) of bacteria and a significant reduction in others (*Bifidobacteriumbifidum*). Troublingly, children that have had long-term antibiotic treatments harbor larger numbers of bacteria that are antibiotic resistant in all human ecosystems tested. It is likely that these antibiotic strains were able to thrive in the various human environments once the

[27]Joyce A. Martin, Brady E. Hamilton, M. J. Osterman, Sally C. Curtin, and T. J. Matthews, "Births: Final Data for 2013," *National Vital Statistics Reports: From the Centers for Disease Control and Prevention, National Center for Health Statistics, National Vital Statistics System* 64.1 (2015): 1-65.

[28]Maria G. Dominguez-Bello, Elizabeth K. Costello, Monica Contreras, Magda Magris, Glida Hidalgo, Noah Fierer, and Rob Knight, "Delivery Mode Shapes the Acquisition and Structure of the Initial Microbiota across Multiple Body Habitats in Newborns," *Proceedings of the National Academy of Sciences* 107.26 (2010): 11971–11975.

[29]Mette C. Tollånes, Dag Moster, Anne K. Daltveit, and Lorentz M. Irgens, "Cesarean Section and Risk of Severe Childhood Asthma: A Population-Based Cohort Study," *The Journal of Pediatrics* 153.1 (2008): 112–116.

[30]Martin Blaser, "Antibiotic Overuse: Stop the Killing of Beneficial Bacteria," *Nature* 476.7361 (2011): 393–394.

resident microbiota had been weakened by the drug treatment.[31] In each of these cases we see a technological advancement (C-section, formula, and antibiotics) that is able to protect and foster life but comes with unintended consequence of disrupting and breaking relationships.

Stewards of a Relationship

We live now in a time between the resurrection of Jesus Christ and His return. The work of redeeming all of creation, every relationship, has already been accomplished but is also still being completed. We have been given understanding about the relationships we have to our microbiota and now have a responsibility to determine how to be wise stewards of our bacterial communities.

A first responsibility is simply to recognize the value of these relationships. It has been argued by Steven Bouma-Prediger,[32] and more recently by Pope Francis,[33] that the start of proper stewardship of God's creation is appreciation of the interconnectedness of all of creation, great and small. By recognizing our mutual dependence on the microbes that live on and in us we begin to ascribe them some of the value God has held for them all along. Putting an end to the practice of seeing all bacteria as germs and enemies allows us to begin the task of maintaining these small patches of garden within God's larger creation.

Our next response should be to attempt to cultivate mutualistic microbial communities. From the very beginning of life, making birthing plans, all attempts should be made for a child to be born vaginally if the birth will be safe for both mother and child. As discussed above, C-section is certainly a redemptive gift, but that does not mean it should be used interchangeably with vaginal birth. C-section is far superior to a high-risk birth, but from a microbiome perspective it is *not* equivalent to a vaginal birth. In high-risk birth, when C-section is prudent to protect the mother or infant, perhaps it would be advisable to inoculate the baby after birth with vaginal secretions in order to promote a robust *Lactobacillus* population.

Likewise during childhood and even into adulthood there are steps that can be taken to ensure a healthy, diverse microbiome. The effect of diet on the gut microbiome has been established, showing that culture-dependent food choices largely determine diversity, but the most diverse microbial community should grow in response to the most diverse diet. A diet that ranges from high to low protein with a variety of carbohydrates, whole grains, and fruit and vegetables should

[31]R. K. Shrestha, S. K. Rai, L. K. Khanal, and P. K. Manda, "Bacteriological Study of Neonatal Sepsis and Antibiotic Susceptibility Pattern of Isolates in Kathmandu, Nepal," *Nepal Med Coll J* 15.1 (2013): 71-73.

[32]Steven Bouma-Prediger, *For the Beauty of the Earth: A Christian Vision for Creation Care* (Ada, MI: Baker Academic, 2010).

[33]Pope Francis and the Catholic Church, *Encyclical Letter Laudato Si'of the Holy Father Francis: On Care for Our Common Home,* http://w2.vatican.va/content/francesco/en/encyclicals/documents/papa-francesco_20150524_enciclica-laudato-si.html, 2015.

foster a rich, diverse, beneficial gut microbiota. Some foods can act as a *prebiotic* serving as a food source for desired microbes. For example inulin, an indigestible carbohydrate found in bananas and other fruits, serves as a food source for some Bacteroidetes species which are present in huge numbers in those with a healthy gut. For others that suffer from a dysbiosis, an antagonistic relationship with their microbiota (for example those with IBD), perhaps treatment should include not only immune suppressants and anti-inflammatory drugs but also probiotics. The standard treatments attempt to mitigate the immune system's attack on the gut microbiota while a probiotic treatment aims to restore beneficial relationships that will stop the need for an immune response. One example of this treatment is the Food and Drug Administration–regulated VSL#3 which is considered a medically prescribed food. Each dose includes 900 billion microbes that are common in those with a healthy gut microbiome and rare in those with IBD. Research shows the probiotic treatment is similarly effective as the entry-level drug mesalamine.[34]

Possibly the most important response of people of faith to the science of metagenomics is to become advocates for wise use of antibiotics. Every exposure to antibiotics has an impact on our microbiota. As discussed above, exposure in infancy and early childhood may have particularly strong and lasting effects on later microbial communities. The Get Smart About Antibiotics program from the CDC has recommendations for patients and healthcare professionals that help guide decisions regarding when it is appropriate and necessary to prescribe an antibiotic. Antibiotics have traditionally been viewed as treating very distinct groups of bacteria but it is important now to view this treatment in light of the whole microbiota. Treatment with antibiotics can disrupt up to a third of gut bacteria for as long as six months.[35] Positively, the CDC reports that antibiotic treatment for acute bronchitis decreased only from 75% to 57% between 1995 and 2005. This progress is insufficient considering it has been known for 40 years that antibiotic treatment has no effect on acute bronchitis.[36] More troublesome than mis-prescribed antibiotics is the use of antibiotics in non-medical settings. In the United States most antibiotics are used in the meat-producing industry to speed the rate of growth in farm animals. Other antibiotics are used in products ranging from hand soap to deodorant to socks. If we start with an understanding that microbial communities are important for health of ecosystems it is easier for patients, physicians, and those making these products to consider how the miraculous gift of antibacterial antibiotics can best be used.

[34]Richard N. Fedorak, Paolo Gionchetti, Massimo Campieri, Karen Madsen, Kim Isaacs, Claudio Desimone, and Balfour Sartor, "VSL3 Probiotic Mixture Induces Remission in Patients with Active Ulcerative Colitis," *Gastroenterology* 124.4 (2003), doi:10.1016/s0016-5085(03)81909-1.

[35]Les Dethlefsen, Sue Huse, Mitchell L. Sogin, and David A. Relman, "The Pervasive Effects of an Antibiotic on the Human Gut Microbiota, as Revealed by Deep 16S RRNA Sequencing," *PLoS Biology* 6.11 (2008), doi:10.1371/journal.pbio.0060280.

[36]Michael L. Barnett and Jeffrey A. Linder, "Antibiotic Prescribing for Adults with Acute Bronchitis in the United States, 1996-2010," *JAMA* 311.19 (2014): 2020–2022.

Finally, we should be conscious of the sharing of microbes that occurs with those with whom we interact. There is a biological component to every interaction. This certainly should be understood as a warning when interacting with the weak and sick who could be harmed by otherwise innocuous members of our microbiota. It should also be a reminder that we cannot be in any human relationship without being fundamentally changed by the encounter. We should foster healthful microbiota not only for our own health but also so that we can share that physical health with others through relationships as brief as a handshake or as intimate as cohabitation.

Theology from the Microbiome

When interpreting the science of the human microbiome in light of the story of God's work in creation there are multiple conclusions possible. The first is that humans are deeply connected Earthlings, part of the broader ecosystem of life on Earth. God, with wisdom, created humans that are not on top of or beyond creation, but who are fully embedded in the messy web of life that exists on this planet. This world is our home. Second, we are completely interdependent on the smallest inhabitants of our world. Our health and wellbeing is dependent on the health and wellbeing of the last and the least within us. And finally, we need to use humility as we consider the claims from microbiome research. It has already shown that it has the ability to reframe how we think of ourselves and our health, but like all other corners of creation, this very science is fallen, too. Frequently the wrong experiments are done, coming to the wrong conclusions. Consequently there are substantial gaps in our understanding of which microbes must be present for health in any human ecosystem. The details of how seemingly benign microbes set off a chain of events that leads to a full immune response are not yet known. While we wait for science to progress, we should expect to continue to find that these relationships are critical to who we are and that they are frequently broken versions of what they could be.

From these conclusions come a series of logical practices. First, since we are fundamentally connected to all other life on this planet it is imperative that we care for that life. Christians must appreciate the web of relationships that allows us to flourish and must work to protect those relationships from systems that may prioritize efficiency or economy instead of mutual beneficence. Second, because we depend on the microbes within we must foster healthful microbiomes. Self-care should include care for all our systems, including cardiovascular, respiratory, neurological, and microbiological. A diverse diet will aid the digestive system and the microbial system. Finally, as this area progresses, Christians should continue to seek signs of God's good creation in the results published while fully expecting to find evidence of relationships that are strained and broken. Microbiome research, like all areas of research that explore creation, can present opportunities to know our Maker more clearly.

The study of microbiomes gives us another view of God's story in scripture: Human beings were created in right relationship with the microbiota living both on and inside them; however, when humans chose to sin and disobey God, these relationships were disrupted by the corruptive effects of the fall. Nevertheless, Christ came to reconcile these relationships to their rightful existence, and He also welcomed His Church to join Him in this ministry of reconciliation. Now Christians can take action, making wise choices to restore all relationships that have been broken by the fall and are now redeemed by Christ.