The Making of the Microbial Body, 1900s-2012

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Abstract

This dissertation examines how the relationship between microbes and the human body has been reconfigured over the course of the twentieth century and into the first decades of the twenty-first century. It presents a counter-narrative to the ways in which we have tended to view microbe-human relations to make sense of the emergence of twenty-first century microbial selves by focusing on the normal microbiota.

This dissertation investigates why the notion of a microbial framework for the body gained cultural, scientific and medical force in the twenty-first century. It tracks the prehistory of this development and ends with the National Institutes of Health's Human Microbiome Project, which marks the mainstreaming of an appreciation for the importance of the microbes that live in and on the body as a scientific area of study, as an important aspect of biomedicine, and as a cultural phenomenon.

I argue that there was a reorientation of medicine, science and culture that engendered a new appreciation for and shed new light on the kinds of problems and questions that researchers in marginal microbiologies were struggling to make sense of earlier. I argue that these kinds of questions and concerns came to matter more broadly with the rise of the environmental movement and the ecological sciences in the mid- to late twentieth century because they were ecological and environmental in orientation.

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Introduction

"…our most sophisticated leap would be to drop the Manichaean view of microbes: "We good; they evil."… Perhaps one of the most important changes we can make is to supersede the 20th-century metaphor of war for describing the relationship between people and infectious agents."

-Joshua Lederberg, 2000[1]

When the Human Microbiome Project (HMP), the National Institute of Health's initiative to study the microbes that live in and on the human body, announced its first results to the world in summer 2012, *Nature* hailed the work as a milestone in understanding "our microbial selves."[2] The cover of the journal presented a mirror image of a photographed flesh-and-blood woman's profile and her outline, filled with swarms of microbes teeming within her.[3] *The Economist*, along with a number amount of other popular magazines, newspapers, websites and blogs, also welcomed the announcement that summer.[4] For their microbiome-themed cover, *The Economist*

[1] Lederberg, Joshua. "Infectious History." *Science* 288 (2000): 287-293.

[2] *Nature* 486 (2012): cover.

[3] Ibid.

[4] For example, see *Scientific American* June 2012; Leroy Hood, "Tackling the Microbiome," *Science*, 336, 1209; Aw, James, "Are Bacteria Going to Be a Magic Bullet for Fighting Disease?" *National Post*, July 10, 2012. Accessed July 1, 2013. http://life.nationalpost.com/2012/07/10/are-bacteria-going-to-be-a-magic-bullet-for-fighting-disease/. Zimmer, C. "How Does Your Body's Microbial Garden Grow?" *International Herald Tribune*, June 20, 2012; Winslow, Ron and Jonathan D. Rockoff. "Gene Map of Body's Microbes is New Health Tool," *Wall Street Journal*. Accessed February 15, 2014. http://online.wsj.com/news/articles/SB10001424052702303410404577464961870114758.

redrew the Vitruvian Man as a somewhat grotesque human-microbe chimera.[5] "Microbes Maketh Man," the cover proclaimed, and described the implications of this new vision of the human as "things you'd rather not know before breakfast." The flurry over the HMP did not fade away after an initial celebratory moment. The *New York Times Magazine* ran a cover article a year later, suggesting extended cultural fascination with the human microbiome.[6] This article, written by cultural critic Michael Pollan, was titled "Some of My Best Friends Are Germs," and paired with an image of a baby smeared in dirt and licking an equally dirty toy car.

The framing of the HMP by these publications indicated the scope of the HMP's impact. The HMP was provocative in that it provided a strong contrast to dominant attitudes towards microbes and their relationship to our bodies. *Nature* provided the most straightforward and dispassionate contrast, in word and image. Its portrayal of the body as comprised of a panoply of microbes posed the question in neutral terms: What are we to make of our microbial "fellow travelers"? Are they part of our selves? How can *a self* be multiple? *The Economist* presented a more graphic and disturbing image of a microbe-comprised man as a monstrous entity—a bug-human hybrid. The notion of a body overrun by bacteria and of the things associated with such a thing were the sort of things "you'd rather not think about before breakfast," a nod to our cultural disgust with the notion of *anything* covered with microbes. For the *New York Times,* the framing of the discussion was broader, suggesting to the idea of germs as we have been culturally conditioned to see them, as associated with dirt. The image of the dirt-smeared baby immediately brings up all the ways in which we would think to respond---grab the toy truck out of the baby's

[5] *The Economist*, August 18-24, 2012.

[6] *New York Times Magazine,* May 13, 2013.

mouth, grab some mouthwash, bathe baby. The title of the article plays with the cultural status of microbes as well—"Some of my best friends are…". It's a clever take on the historically negative view of microbes that suggests both that the speaker is guilty of holding such views and that the view is a recognizable prejudice against a group. These images capture what the Microbiome Project presents to the 21st century: a recalibration of old and deeply held ideas about microbes and consequently, I argue in this dissertation, about human beings.

This dissertation asks how this recalibration happened, and explores the scientific, medical and cultural histories that shaped it. It examines the changing status of microbes in science, medicine and culture over the course of the twentieth century and into the twenty-first century, and how their relationship to our bodies has been reconfigured. It presents a counternarrative to the ways in which we have tended to view microbe-human relations to make sense of the emergence of twenty-first century microbial selves.

The 20th century was in many ways the antibacterial century. Joshua Lederberg, Nobel Prize winning microbiologist, molecular biologist and leader in the fight against emerging infectious disease, has described the dominant cultural view of microbes and their relationship to us over this period in simple terms: "We good; they evil."[7] For many, that was essentially the end of the story and the extent of the narrative about microbes in an age that saw the advent of antibiotics and a scrupulously antibacterial hygiene. In the sciences, microbes were not considered evil, but were denigrated in other ways. Microbes were extremely productive in 20th century biology, but interesting for the most part as model organisms. They were simple enough to be manipulated in the lab, but not particularly interesting in their own right for many

[7] Lederberg (2000), 292.

biologists. Their value lay primarily in what they could say about other kinds of organisms. The microbe was relegated to an object of fear and denigration in medicine and in culture--and in biology as experimental infrastructure to be disciplined in the laboratory for the investigation of Life. In short, microbes in the twentieth century were stand-ins for something else—as avatars of disease, as avatars of dirtiness and its associated negative connotations (low class, low culture), and as experimental exemplars of Life. I argue that the emergence of the microbial body championed by the Human Microbiome Project and celebrated by the culture required a transformation in this view of microbes on these three fronts.

In the first decades of the 21st century, the microbe has undergone an image makeover. Scholars have begun to explore this shift in the status of the much maligned microbe in recent years. Anthropologists have been among those first to the table, examining emerging networks and cultures built around a newly positive approach to microbes and building a subfield of multispecies ethnography that includes microbes as important nonhuman actors entangled with human life.[8] Anthropologists of science Heather Paxson and Stefan Helmreich have jointly described how representations of microbes have moved from an "idiom of peril" to an "idiom of promise."[9] They describe this new view of microbes as "plenteous, promising and full of potential" in different zones.[10] Heather Paxson has examined microbes in the artisanal and raw milk movement; seeing a new "microbiopolitics" centered on microbes in the production and regulation of food. Paxson's foodies, farmers, cheese makers, scientists and sellers claim

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[8] See Kirksey, S., and Stefan Helmreich, "The Emergence of Multispecies Ethnography," *Cultural Anthropology* 25.4 (2010): 545-576 for an overview of this emerging field.

[9] Paxson, Heather, and Stefan Helmreich. "The Perils and Promises of Microbial Abundance: Novel Natures and Model Ecosystems, from Artisanal Cheese to Alien Seas." *Social Studies of Science* 44 (2014): 165-193.

[10] Paxson and Helmreich (2014), 166.

microbes as allies rather than as enemies to be aligned against. Paxson calls those in this newly forged network of microbial allies "Post-Pasteurians," in contrast to Latour's Pasteurians, who claimed, she writes, "the hygienist's right to be everywhere" in the face of the ubiquitous threat from microbes.[11] Stefan Helmreich examines a different set of microbial allies in his ethnography of deep sea microbiology. He describes the productivity of marine microbiology for various scientific fields, from astrobiology to evolutionary biology.[12]

The promise of microbes in this new period is anchored by two core attributes that are characteristic of microbial life: the tendency of microbes to form consortia or communities in natural settings, and the dizzying diversity of microbial forms. This cooperative mode of living and the value placed on biodiversity resonate in an increasingly connected and complicated world. Microbes are being looked to as productive not only with an eye towards what bioprospecting for what they can do and make, but also for how they do it. As Paxson and Helmreich argue, microbes are increasingly being viewed "as *model ecosystems* in a prescriptive sense, as tokens of how organisms and human ecological relations with them *could*, *should*, or *might* be."[13] They note that this is an increasingly broad vision that includes "**even** the human body."[14]

I highlight the "even" in this article because it suggests a slight incredulity that the human body could be viewed through this microbial lens. This is because this kind of microbial

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[11] Paxson, Heather, "Post-Pasteurian Cultures: The Microbiopolitics of Raw-Milk Cheese in the United States," *Cultural Anthropology* 23.1 (2008): 18.

[12] Helmreich, Stefan. *Alien Ocean: Anthropological Voyages in Microbial seas*. Berkeley and Los AngeleS: University of California Press, 2009.

[13] Paxson and Helmreich (2014), 165.

[14] Ibid, 166. Emphases mine.

perspective presents a challenge to well-entrenched ideas about the human body. Philosophers of science have been piqued by the problems raised by the relationship between the body and its companion microbes as it is viewed through this lens. Some have asked how the notion of a microbial self might offer ontological challenges to old ideas about the body. John Dupré and Maureen O'Malley see a challenge to the entrenched ideas about biological ontology, noting that previously the individual organism has been "the prima facie most unproblematic concept of all" in biology.[15] For them, the notion of a microbial self not only problematizes the notion of biological individuality, but also presents an emerging cooperative model of life for biology, of organisms as ecosystems embedded in the larger ecosystems that we are more used to.

But this is not just a question engaged by philosophers. Bioethicist Eric Juengst has explored the metaphors used in microbiome research and finds that these philosophical moves—against biological individuality and towards a new ecological model of Life in the biological sciences are made explicitly by the scientists engaged in this research.[16] These investigators claim that the human is a superorganism by virtue of the fact that it incorporates multiple organisms to create what we call "the human." They claim that the body is best understood as an ecosystem, the product of the relations between the organisms that comprise it.

Anthropologists of science are beginning to engage with these microbiome researchers, taking the human microbiome as a social actor. Anthropologist Amber Benezra argues for a

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[15] Dupré, John, and Maureen A. O'Malley, "Metagenomics and biological ontology." *Studies in History and Philosophy of Science Part C: Studies in History and Philosophy of Biological and Biomedical Sciences* 38.4 (2007): 834-846.

[16] Juengst, Eric T, "Metagenomic Metaphors: New Images of the Human from 'Translational' Genomic Research," *New Visions of* Nature: Complexity and Authenticity, edited by Martin Drenthen, James Proctor, and Jozef Keulartz, 129-45. Berlin: Springer, 2009.Springer Netherlands, 2009.

collaborative approach to the human microbiome, arguing that the microbial communities of the human body are social and biological entities that require tools from both the biological and social sciences to be studied comprehensively.[17] They see this interdisciplinary effort as having a global health imperative—it could provide a way to make the links between communities, environments, diet and culture legible because of the extent to which microbes are embedded in the cultural and social relations of an increasingly mobile human population. The claim here is that truly understanding the microbial body and its impact cannot only be a biomedical project or even an epidemiological project because of the ways in which culture and the biologies of the body shape each other.

These anthropologists, scientists and philosophers present this new view of microbes in general and of the body's companion microbes in particular as an emerging twenty-first century phenomenon. I argue here that this rehabilitation of microbes and the human microbiota has deep roots in the twentieth century. Microbes have always been spoken of in an "idiom of promise," to use Paxson and Helmreich's phrase, though the voices of those doing so have tended to be much quieter than those claiming otherwise. These voices did not entirely reject the Pasteurian vision that dominated the last century, but like Paxson's Post-Pasteurians, recognized the threat of microbes and adopted a "Yes, but…" stance. These Post-Pasteurians had different agendas that either required or engendered a broader view of microbes which was obstructed by the dominant view of microbes as threatening. For some, the study of bacteria could not and should not be dictated by pathogens--nor be limited by the tools and techniques that had largely been developed around this unrepresentative slice of the microbial world. For others, the Pasteurians

[17] Benezra, Amber, Joseph DeStefano, and Jeffrey I. Gordon, "Anthropology of Microbes," *Proceedings of the National Academy of Sciences of the United States of America* 109.17 (2012): 6378.

had overreached their mandate to protect and had begun to do damage—both physical and spiritual.

Microbes were extremely productive for molecular biology, in the development of antibiotics in soil science, in agriculture and in the development of an understanding of nutrient cycling in the twentieth century.[18] These stories have been told elsewhere. Here I focus on those strange, intransigent microbes, the human microbiota, that have garnered so much attention recently and to which Paxson and Helmreich referred to with a slightly raised brow. I show that these microbes, too, had their defenders and boosters before they became cover story material for *Nature* and the *New York Times*. And while microbiome researchers have appealed to ecological concepts and communal visions to frame this ascendant view of the microbe-human relationship, similar appeals were made by various communities in a bid to make sense of the relationship of the human to its microbiota throughout the twentieth century. The nature of those appeals changed as did conceptualizations of that relationship. But what they shared was a rejection of the dominant microbial narratives which underestimated their value, either for the provision of health, the development of science or the understanding of Life. What was also different about those historical moments and now is who is making these sorts of claims, and the kind of weight given to them.

While this dissertation is not a comprehensive account of those voices and communities, it does attempt to account for where some of them came from, the ways in which they framed the relationship between the human microbiota and the body, and what was at stake in making these

[18] See, for example, Ackert, Lloyd, *Sergei Vinogradskii and the Cycle of Life: From the Thermodynamics of Life to Ecological Microbiology, 1850-1950*, Vol. 34. Springer, 2012; Spath, Susan. *C. B. van Neil and the Culture of Microbiology, 1920-65*, (PhD diss., University of California, Berkeley, 1999)*;* Eric D. Kupferberg, "A Field of Great Promise: Soil Bacteriology in America, 1900-1925," *Endeavour* 27 (2003): 16-21.

claims. They tended to come from marginal or marginalized corners. They came from the edges of medicine (and the history of medicine)—fields like dentistry and dermatology; and the edges of biology (and the history of biology) ---fields like intestinal bacteriology, gnotobiology and microbial ecology. They also came from self-consciously oppositional spaces. These include the subfields listed above, all of whom set their work against the dominant microbiology of the day, as well as from counter-culturalists and feminists in the 1960s and 1970s, and those who began to call for a change to the status quo of antibiotics use. All tended to appeal to ecological or environmentalist language and concepts to make their cases.

What happened in the 21st century was that the voices challenging the old dominant views of microbes came from some of the loudest and most powerful cultural, medical and scientific voices: the NIH, the National Research Council, Harvard, MIT, the Institute of Medicine and from the pages of *Nature*, *Science*, *The Economist* and the *New York Times*. This dissertation investigates various ecological visions of the body over the twentieth century and how the current one came to matter in this one. This dissertation asks why the notion of a microbial framework for the body gained cultural, scientific and medical force when it did. My dissertation ends with the NIH's Human Microbiome Project because of the fanfare it received and what it represents—the mainstreaming of an appreciation for the importance of the microbes that live in and on the body—as a scientific area of study, as an important aspect of biomedicine, and as a cultural phenomenon.

The making of the microbial body, then, is a story about how ideas about the body and about science move from the periphery to the center—and how they are transformed in that process. I argue that there was a reorientation of medicine, science and culture that engendered a broad appreciation for and shed new light on the kinds of problems and questions that people in marginal fields were struggling to make sense of earlier. I argue that these kinds of questions and concerns came to matter more broadly with the rise of the environmental movement and the ecological sciences in the mid to late 20th century because they were ecological and environmental in orientation. They came to be framed as such as these agendas were being developed and gaining power. It was, in a way, about finding allies and explanatory frameworks that could adequately make sense of the relationship and why it mattered. These disparate threads came into conversation with each other and were generative of new kinds of and attitudes towards science, medicine and cultural forms.

In the early 20th century, bacteriology as a field tried to find a way to define itself as a science that was separate from the applied fields that it was allied with. While soil and agricultural bacteriology by necessity looked to build a microbiology that could account for the interactions between microbes and their natural habitats, the study of microbes on the body was dominated by pathogen hunting and articulation for infectious disease management. There were various attempts in the first half of the century to investigate the human microbiota in this way. Some bacteriologists looked to intestinal bacteria to build a "proper" science of medical bacteriology that was based on the normal conditions of the human body as an environment for its microbes.[19] The goal of the field was two-fold, to create "rational" therapies for intestinal ills and to develop a proper understanding of intestinal bacteria by creating a science based on their dynamics within the intestinal habitat. Other fields that needed to deal with complex microbial environments as a matter of course were found in marginal corners in the biomedical specialties

[19] Intestinal bacteriology was a short-lived bacteriological subfield that was developed to be its own subfield of medical microbiology, unattached to the formal field of gastroenterology.

community—fields like dentistry, where the normal or healthy state included a large population of microbes that could not conform to Pasteurian vision of hygiene. The bacteriologists in these fields aimed to find a way to rationalize their specialty in an age of scientific medicine. Bacteriologists working in dentistry appealed to the young science of ecology to provide a scientific framework that could address the needs of their work on microbes in the mouth and their relationship to health. For them, the mouth could be treated as an environment for the microbial drama that they were interested in.

For the most part, microbes have been villains in histories of medicine, cast as archenemies in the war on disease. [20] Histories of disease have in large part been histories of infectious disease; histories of public health have often focused on campaigns to eradicate and control the microbial agents of disease and the creation of public health infrastructure driven by the issue of infection and contagion. [21] My dissertation extends historical examination of the microbes in the history of medicine to a few corners often not investigated. Dentistry has long been involved in ecological approaches to the study of the microbes and has pioneered much work on the microbial flora. Dental bacteriologists had been at the forefront of human microbial ecology research for most of the 20th century; and they continued to be pioneers in the new

[20] See for example, Tomes, Nancy, *The Gospel of Germs: Men, Women and the Microbe in American Life*, Cambridge, MA: Harvard University Press, 1999 and Rosenberg, Charles. *The Cholera Years: The United States in 1832, 1849, and 1866*, Chicago: University of Chicago Press, 1962.

[21] See for example, Tomes (1999); Rosenberg (1962); Worboys, Michael, *Spreading Germs: Disease Theories and Medical Practice in Britain, 1865-1900*, Cambridge, UK: Cambridge University Press, 2000; Spink, Wesley, *Infectious Diseases: Prevention and Treatment in the Nineteenth and Twentieth Centuries*, Minneapolis: University of Minnesota Press, 1978; Hammonds, Evelynn Maxine. *Childhood's Deadly Scourge: The Campaign to Control Diphtheria in New York City, 1880-1930*, Baltimore: Johns Hopkins University Press, 1999; Packard, Randall, *The Making of a Tropical Disease: The History of Malaria*. Baltimore: Johns Hopkins University Press, 2007; Teller, Michael E. *The Tuberculosis Movement: A Public Health Campaign in the Progressive Era*, New York: Greenwood Press, 1988; Farley, John, *Bilharzia: A History of Imperial Tropical Medicine*, Cambridge: Cambridge University Press, 2003.

genomic era. The Forsyth Institute, the leading dental research institute in the United States had begun work on an Oral Microbiome Database Project years before the Human Microbiome Project and had been investigating the microbial ecology of the mouth for decades before the human microbiota gained the broader attention of the biomedical world.[22] The field of oral microbiology was in many ways the leading edge of human microbial ecology and developments in dental bacteriology were central to the development of ecological perspectives in the study of the body's microbial flora.[23] The depth of oral microbiology as a field was a legacy of the history of research on the oral microbiota, which had begun to be framed in ecological terms as early as the 1930s.

In the early investigations into the relationship between microbes and the body, the body was usually framed as background despite the bearing of these microbes on the health and disease states of the body. The assumption for the most part was that microbes might be implicated in the body. But the interest in them came from microbiologists narrowly concerned about a particular area of the body. Even in the case of dental bacteriology, where the goal was the provision of human health, the focus was on relations and actions of microbes *within* a

[22] "The Human Oral Microbiome Database: a web accessible resource for investigating oral microbe taxonomic and genomic information," Tsute Chen, Wen-Han Yu, Jacques Izard, Oxana V. Baranova, Abirami Lakshmanan, Floyd E. Dewhirst, *Database* (Oxford) 2010, Accessed October 26, 2013, doi: 10.1093/database/baq013; Holden, Constance, "Random Samples: It's in His Kiss," *Science* 320 (2008): 27; Floyd E. Dewhirst, Tuste Chen, Jacques Izard, Bruce J. Paster, Anne CR Tanner, Wen-Han Yu, Abirami Lakshmanan, and William G. Wade, "The Human Oral Microbiome," *Journal of Bacteriology* 192 (2010): 5002-5017.

[23] As Dr. Dwayne Lundsford of the National Institute for Dental and Craniofacial Research Institute, one of the scientist-administrators involved in the HMP noted about the HMP's reception and findings, "[There were] no real surprises for us. [Though it was] getting all this cool press—this stuff has been around for decades, just like the oral microbiome has been around for decades. I still have to remind my colleagues that hey, we were doing this stuff a long time ago." Interview with Dr. Dwayne Lundsford, 7/9/2012.

particular kind of habitat. Their appeal to ecology had been a bid to study microbes as microbes impacted by particular environmental conditions.

In mid-late 20th century, attention shifted to the microbial body. Germ-free science and related techniques provided a look at how microbes shaped the animal body by producing bodies created in their absence; and researchers described germs as part of the “biological environment” of the body. This reframing produced various visions of the microbial body in the 1950s through 1970s that saw the development of on an environmentalist perspective on the relationship between the body and its microbes. Casting microbes as part of the biological environment of the body made them legible within the environmentalist and ecological discourses of the day.

The 1960s and 1970s saw the rise of the environmental movement and the concurrent rise in prestige, resources, and reach of the ecological sciences. Microbiology underwent a major shift in this period through a soil and environmental bacteriology reinvigorated by the development of new, extremely productive techniques and the development of new research agendas that were allied with the ecological sciences. The history of ecology has been handled by several historians--most notably Sharon Kingsland, Robert Kohler, Peder Anker, Paolo Palladino, Gregg Mitman and Linda Nash.[24] The rise in status of the ecological sciences has also been covered by Toby Appel, who describes tensions between molecular biologists and

[24] Sharon Kingsland’s *Modeling Nature: Episodes in the History of Population Ecology* (Chicago: University of Chicago Press, 1995) and *The Evolution of American Ecology: 1890-2000* (Baltimore: Johns Hopkins University Press, 2005)*;* Peder Anker’s *Imperial Ecology: Environmental Order in the British Empire, 1895-1945* (Cambridge: Harvard University Press, 2009), and Robert Kohler’s *Landscapes and Labscapes: Exploring the Lab-Field Border in Biology* (Chicago: University of Chicago Press, 2002), Linda Lorraine Nash’s *Inescapable Ecologies: A History of Environment, Disease and Knowledge* (Berkeley and Los Angeles: University of California Press, 2006), and Paolo Palladino, “Defining ecology: Ecological theories, mathematical models, and applied biology in the 1960s and 1970s," *Journal of the History of Biology* 24:2 (1991): 223-243; see also Stephen Bocking, "Ecosystems, ecologists, and the atom: Environmental research at Oak Ridge National Laboratory," *Journal of the History of Biology*, Volume 28:1 (1995), 1-47; and Chunglin Kwa, "Representations of Nature Mediating between Ecology and Science Policy: The Case of the International Biological Programme," *Social Studies of Science* 17 (1987): 413-442.

ecologists in the 1960s and 1970s as funding shifted towards ecological departments and projects.[25] However, all of these historians neglect both microbial ecology as a field in its own right and the role of microbes in the development of ecology.[26] Lloyd Ackert tracks the development of an ecological microbiology through the 1950s, centered on soil science pioneer Sergei Winogradsky's work and influence.[27] However, he does not cover developments after the 1950s, nor does he address research on microbes living on or in bodily environments.[28] While ecological concepts and ecological language were co-opted by various research communities working on the body's microbes over the course of the twentieth century, the field of microbial ecology has its own distinct history, that is part of the rise of the ecological sciences in the 1960s and 1970s, and that extends Ackert's history of Winogradsky's ecological microbiology into the formal and distinct field of microbial ecology that coalesced in the late twentieth century.

Consequently, my dissertation is in part a history of bacteriology and microbiology. Most scholarship on these fields focuses on the 19th or mid-20th century developments.[29] Susan Spath has addressed the development of general microbiology in mid-century America.[30] Eric

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[25] Appel, Toby A., *Shaping Biology: The National Science Foundation and American Biological Research, 1945-1975,* Baltimore: Johns Hopkins University Press, 2000.

[26] Kingsland is the exception—she briefly treats Gause in *Modeling Nature*—who applied traditional population ecological methods to protozoa and yeast in the 1930s.

[27] Spath (1999) and Ackert (2012).

[28] He does spend a few pages on Winogradsky's influence on Rene Dubos' medical microbiology and environmental medicine approaches. See Ackert (2012), 148-52.

[29] William Bulloch's *The History of Bacteriology* (NY: Dover Publications, 1938); for later 20th century history of medical and general microbiology, see Robert Kohler, "Bacterial Physiology: The Medical Context" *Bulletin of the History of Medicine* 59 (1985): 54-74 and Robert Kohler, "Innovation in normal science: bacterial physiology," *Isis* 76 (1985): 162-181.

[30] Spath (1999) examines Cornelius B. van Neil, the key figure in the exportation of the Delft School of microbiology to the United States at Stanford and the development of general microbiology in the United States. Bert Theunissen takes another look at the Delft School in the Netherlands in "The beginnings of the "Delft Tradition" revisited: Martinus Beijerinck and the genetics of microorganisms," *Journal of the History of Biology*,

Kupferberg has argued that agricultural bacteriology provided an alternative to the dominant "hygienic vision" of microbiology; soil and dairy bacteriologists focused on the exploitation of "useful" bacteria. He describes how this agricultural approach to managing microbes became institutionalized in the discipline of bacteriology, the tools and techniques that constituted the approach, and its impact on the field through the 1930s.[31] Keith Vernon and Robert Bud have also written about "useful" bacteria in agricultural and industrial contexts. [32] While these works do not deal with the human microbiota, they provide context for the disciplinary landscape of microbiology. Closer to the mark, Scott Podolsky and James Whorton have written about "health germs" and investigations into the management of colon health with Elie Metchnikoff's Bacillus Bulgaris and the popularity of Lactobacillus Acidophilus in pre-WWII America.[33] I place their work within the context of the science developed in the early twentieth century to rationalize and understand "health germs" through proper scientific experimentation.

Bacteriology has been addressed to some extent by historians of biology. But for the most part, microbes have been supporting players in the history of biology. In the history of molecular biology, microorganisms have been exemplary model organisms; and the work gone into making

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Volume 29 (1996), and philosopher of science Maureen O'Malley, examines the Delft school in order to trace the roots of the emerging epistemological shift in contemporary biology in "The nineteenth century roots of 'everything is everywhere'," *Nature Reviews Microbiology* 5 (2007), 647-651.

[31] Eric D. Kupferberg (2001), *The Expertise of Germs: Practice, Language and Authority in American Bacteriology, 1899-1924 (*PhD diss., Massachusetts Institute of Technology, 2001) and Eric D. Kupferberg (2003).

[32] Bud, Robert, *The Uses of Life*: *A History of Biotechnology.* Cambridge: Cambridge University Press, 1994; and Keith Vernon, "Pus, sewage, beer and milk: microbiology in Britain, 1870-1940." *History of Science* 28 (1990): 289-325.

[33] Whorton, James C, *Inner hygiene: constipation and the pursuit of health in modern society*. New York: Oxford University Press, 2000 and Podolsky, Scott H., "Cultural divergence: Elie Metchnikoff's Bacillus bulgaricus therapy and his underlying concept of health," *Bulletin of the History of Medicine* 72.1 (1998): 1-27.

them "the right organisms for the job" has been explored in recent scholarship.[34] Indeed, histories of twentieth century biology have focused on genetics and molecular biology almost to the exclusion of all else.[35] These studies deal tangentially with microbes as parts of the experimental apparatus of the laboratory; microbiology became essentially a handmaiden science inn service to molecular biology. I show in this dissertation how microbes became of interest in their own right beyond the confines of microbiology with the advent of microbial ecology. Microbial ecology became an interesting, frontier science for biology itself in the late twentieth century and set the stage for the current enthusiasm for microbes. I claim that the development of microbial ecology in the late twentieth century became as a resource for conceptual and

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[34] For more on model organisms, See *Journal of the History of Biology* 26.2 (1993) Special Section "The Right Organism for the Job," 235-381; especially Lederman, Muriel, and Richard M. Burian, "Introduction," *Journal of the History of Biology* 26.2 (1993): 235-237. See also Smith, Barbara Herrnstein, and E. Roy Weintraub. *Science without Laws: Model systems, cases, exemplary narratives*. Eds. Angela NH Creager, Elizabeth Lunbeck, and M. Norton Wise, Duke University Press, 2007; Rader, Karen Ann, *Making Mice: Standardizing Animals for American Biomedical Research, 1900-1955*, Princeton, NJ: Princeton University Press, 2004; Fujimura, Joan, and Adele Clarke, Eds. *The Right Tools for the Job: At Work in Twentieth-Century Life Sciences*, Princeton, NJ: Princeton University Press, 1992; *The Microbial Models of Molecular Biology: From Genes to Genomes.* New York, NY: Oxford University Press, 2003, by Rowland Davis; Robert Kohler treats the fungus *Neurospora* in *Lords of the fly: Drosophila genetics and the experimental life* (Chicago: University of Chicago Press, 1994); Angela Creager's *The Life of a Virus: Tobacco Mosaic Virus as an Experimental Model, 1930-1965* (Chicago: University of Chicago Press, 2002), treats a virus, but virology is part of microbiology. See also, Hans-Jorg Rheinberger, "Comparing experimental systems: Protein synthesis in microbes and in animal tissue at Cambridge (Ernest F. Gale) and at the Massachusetts General Hospital (Paul C. Zamecnik), 1945–1960," *Journal of the History of Biology* 29 (1996); Michel Morange, "What History Tells Us IV. Ciliates as models…of what?" *Journal of Biosciences* 31 (2006):27-30.

[35] See for example, de Chadarevian, Soraya, *Designs for Life: Molecular Biology after World War II*, Cambridge: Cambridge University Press, 2002; Rheinberger, Hans-Jörg. *Toward a History of Epistemic Things: Synthesizing Proteins in the Test Tube*, Stanford: Stanford University Press, 1997; de Chadarevian, Soraya and Harmke Kamminga, eds., *Molecularizing Biology and Medicine: New Practices and Alliances, 1910s-1970s*, Amsterdam: Harwood Academic Publishers, 1998; Kay, Lily E. *Who Wrote the Book of Life? A History of the Genetic Code*, Stanford: Stanford University Press, 2000; Keller, Evelyn Fox, *The Century of the Gene*, Cambridge, Mass.: Harvard University Press, 2000; Beurton, Peter et. al. Eds. *The Concept of the Gene in Development and Evolution: Historical and Epistemological Perspectives*, *Cambridge Studies in Philosophy and Biology*, Cambridge: Cambridge University Press, 2000; Appel, Toby A. *Shaping Biology: The National Science Foundation and American Biological Research, 1945-1975*, Baltimore: Johns Hopkins University Press, 2000; Benson, Keith Rodney, Ronald Rainger, and Jane Maienschein. *The American Expansion of Biology*, New Brunswick: Rutgers University Press, 1991; Borrell, Merriley. *Album of Science: The Biological Sciences in the Twentieth Century*, New York: Charles Scribner's Sons, 1989; Kay, Lily, *The Molecular Vision of Life: Caltech, the Rockefeller Foundation, and the Rise of the New Biology*, New York: Oxford University Press, 1993.

methodological innovation in way that was markedly different from the ways in which microbes were viewed and used in biology in earlier years.

But the scientific and technical innovations and productivity of microbial ecology are not the sole reasons for our current microbial moment. I argue that the same period that saw methodological and conceptual breakthroughs in microbial ecology saw the other entrenched narratives surrounding microbes questioned. The challenges to these narratives shared a similar theme—an appeal to and elevation of "the natural." I describe a "natural turn" in medicine and culture as well as in science in the mid to late twentieth century to characterize these shifts. In this period, the notion of how to define what "clean" was in a society where the destruction of germs with antibacterial agents had become a part of the cleansing regimen came under threat as a reevaluation of what "dirty" meant and signified occurred in the counterculture, and then beyond. This change in the meaning of clean and the status of "dirty" marked a reevaluation of the body's relationship to the natural world. In medicine, it meant a reevaluation of the proper way to conceptualize infection as concerns about antibiotic resistance broadened. The problem of antibiotic resistance became framed as an ecological problem created by the disruption caused to natural microbial communities by antibiotic overuse. In biology, it meant the rise of microbial vision of biological boundaries and biological identity once microbes were recognized as interestingly different from other kinds of organisms—not simple, just different, based on a science of microbes in their natural environments.

The mid-late 20th century natural turn gave legitimacy to the sorts of questions that earlier marginal voices people were interested in—dynamics and communities, microbes as interesting entities in their own right, "rational" therapeutics that recognized the body's companion microbes as part of the body's normal functioning. The current microbe-friendly period values those things that first came to be valued in this period—natural environments and ecological thinking as core values of the society, its medicine and its science.

Organization

This dissertation is divided into three parts. In the first, **Germs and Bodies**, I describe how the relationship between microbes and the body was articulated in the first half of the 20th century through the 1960s. In the **Prologue, "The Making of the Pasteurian Body"** I describe the dominant negative narrative of germs in this period. This is well-covered terrain, but I extend this story into the 1960s to show the continuing pervasive influence of this narrative on American culture.

In **Chapter 1, Gut: The Gospel of Good Germs, 1900-1940s**, I track one narrative of "good germs" that flourished in the first half of the twentieth century, dietary "health germs" for digestive health, and the related field of intestinal bacteriology. I argue that both provided a contrast to a pathogen-centric medical bacteriology in terms of science and culture. In **Chapter 2, Mouth: Dental Bacteriology and the Sciences of the Normal Flora, 1900s-1950s**, I describe how the disparate field of body ecology came into being in bacteriological subfields in marginal medical fields. This tracks how these bacteriologists appealed to ecology as a way to rationalize and thus legitimize the study of the microbes that live on and in the body. I use dental bacteriology as a case study. In **Chapter 3: The Microbial Body 1.0, 1950s-1970s**, I argue that in the mid-century, attention turned towards the idea that germs could be considered part of the biological environment of the body in contrast to the germs being the focus—with the body as environment for the germs in the first two chapters.

In **Part II: The Natural Turn**, I describe how the rise of environmentalist concerns and the ecological sciences shaped attitudes towards microbes in the 1960s-1980s. In **Chapter 4, Natural Hygiene and the Rejection of Chemical Cleansing,** I argue that the notion that germs needed to be eliminated from the body through chemical cleansing came under scrutiny. In this period, the American ideal of hyper-hygiene came under attack from a variety of angles. Hippies opposed it on the grounds that this particular hygienic regime was part of the dominant culture that needed to be questioned and challenged at all levels; feminists saw feminine hygiene sprays as a patriarchal imposition on the female body and psyche; eco-consumers embraced natural hygiene products that eschewed synthetic chemicals. In addition, dermatologists defended the bacteria of the body targeted by the chemicals in antibacterial soaps and products as harmful to the natural ecology of the body against the Hygiene Industry.

In **Chapter 5, The Limits of Pure Culture**, I examine the natural turn in microbiology through the development of a new field, microbial ecology, in the 1970s and 1980s and illustrate how it contrasted with conventional microbiology which focused on microbes in isolation, grown in pure culture, to different ends—most importantly here as a model system for molecular biology. The orientation of microbial ecology towards the "field" was not new--soil and agricultural bacteriology of earlier decades were also focused on microbes in the natural environment—but the rising ecological tide brought the core questions of these fields from the periphery to the center of microbiological science, and towards a more prominent role in biology more generally.

Part III, **The Microbial Turn,** focuses on the 21st century development of microbiome science. **Chapter 6** describes the birth of the Human Microbiome Project. It explores how it was shaped by the Human Genome Project, the development of a new technique in microbial ecology called metagenomics, and the role of galvanized interest in antibiotic resistance in the biomedical community. This chapter describes the launch of the HMP, the biggest collaborative biology project in history and its first phase, which attempted to define the normal microbial body.

PART I: GERMS AND BODIES

In the first half of the twentieth century, bacteriologists in various marginal fields were concerned with understanding nonpathogenic relationships between germs and bodies. The dominant narrative cast germs in a negative light and conventional medical bacteriology did not lend itself to the investigation of the nonpathogenic microbes that lived in and on the human body. In this Prologue, I describe the pro-hygienic narrative, how it changed and its impact on the human body through the 1960s. In chapters 1 and 2, I show how research on the nonpathogenic human microbiota presented counternarratives to the Pasteurian vision of the microbe-human relationship. These counternarratives presented microbes as either good for the body or not harmful to it. In these chapters, I present two case studies that track how this relationship was configured in the first half of the twentieth century. I argue that researchers in dental and intestinal bacteriology framed the body as an environment for the investigation of microbes in this period. In Chapter 3, I describe how that narrative was inverted in the mid-late twentieth century as microbes came to be described by biomedical researchers as part of the body's environment.

Prologue: The Making of the Pasteurian Body

Introduction

In *The Pasteurization of France,* Bruno Latour describes how the discovery and disciplining of microbes in the laboratory transformed medicine and society.[36] Microbes were invisible and ubiquitous threats to the stability of the body and society because of their potential to disrupt the health of individuals and populations—and thus all social relations. Consequently, the control of microbes became essential to the creation and maintenance of a well-ordered society. Bacteriology was developed towards the facilitation of this vision, and came to be dominated by it.[37] The hygienic program that bacteriologists increasingly subscribed to had three core tenets: "isolate, identify and eliminate."[38] The goal was straightforward: destruction of germs. This goal became gospel as the Pasteurian vision spread through all corners of society.

In "Post-Pasteurian Cultures: The Microbiopolitics of Raw-Milk Cheese in the United States," anthropologist Heather Paxson claims that "Pasteurian practices configure microbes as elements to be eliminated so that human polities might be cultivated." [39] I argue here that these Pasteurian practices extended to the care of body towards the cultivation of a mid-century American cultural ideal. First I describe how the germ theory shaped the science of medical bacteriology and the medical body that was the target of its application. Then I show how the

[36] Latour, Bruno, *The Pasteurization of France*, Cambridge, MA: Harvard University Press, 1993.

[37] See Kupferberg (2001) and Tomes (1999).

[38] Kupferberg (2001), 156.

[39] Paxson, Heather, "Post-Pasteurian Cultures: The Microbiopolitics of Raw-Milk Cheese in the United States," *Cultural Anthropology* 23.1 (2008): 15-47.

Pasteurian vision of the body became attached to cultural anxieties beyond the infectious disease threat.

Pasteurian Medicine & Science: Medical Bacteriology and the War on Germs

While there had been acknowledgement of the non-pathogenic bacteria on and in the body from the earliest days of medical bacteriology, the focus of field was on pathogens and their role in infectious disease. [40,41] Pathogens were to be isolated, identified and eliminated. For some medical bacteriologists, this hygienic program was inadequate because it neglected core scientific and medical principles. For Theobald Smith, eminent Harvard pathologist, it was a peculiar science that went straight from identification to elimination. In 1905, Smith argued that bacteriologists needed to "analyze phenomena rather than attempt to suppress or crush them" as the hygienist program dictated.[42]

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[40] For example, two pioneers of bacteriology were key voices to this end. In 1885, Pasteur speculated that life could not exist in the absence of microbes from food: "For several years… I have spoken of feeding young animals from birth with…nutritive products that have been artificially and totally deprived of common microorganisms. If I had the time, I would undertake such a study, with the preconceived idea that under such conditions life would have become impossible." Louis Pasteur, "Observations relatives à la note précédente de M. Duclaux," *Comptes Rendus de l'Academie de Sciences* 100 (1885): 68. The same year, pediatrician and bacteriologist Escherich, soon after characterizing the intestinal microbe *E. coli* which would bear his name and which became the most productive and common microbial model organism, described the relationship between man and microbe in terms of the manipulability of the microbes living in man and their potential for the treatment of intestinal disorders: "The fact that through designed changes in the food supply the character of the bacterial vegetation … can be altered opens to us a broad and remunerative perspective … the first and most important thing is a thorough study of bacterial processes in the normal intestine. May the views put forth here not be without practical value in the treatment of that murderous pestilence of the first year of life, diarrhea." As quoted in Hill, Lewis Webb. *Practical Infant Feeding*. Philadelphia and London: WB Saunders Company, 1922.

[41] See Gradmann, Christoph. *Laboratory Disease: Robert Koch's medical bacteriology*, Baltimore: Johns Hopkins University Press, 2009. See also Bulloch (1938).

[42] Smith, Theobald, "Medical Research: Its Place in the University Medical School," *The Popular Science Monthly* 66 (1905), 520. See also Smith, Theobald, "Some problems in the life history of pathogenic microorganisms," *Science* 20.520 (1904): 817-832.

Furthermore, a focus on pathogens created a peculiar medicine. In his treatment of medical theory, Georges Canguilhem stressed the importance of the normal with respect to understanding and addressing disease: "to govern disease means to become acquainted with its relations with the normal state …to establish a scientific pathology by linking it to physiology."[43] What medical bacteriology had done by adopting the hygienic program was to forego a careful investigation of the normal state by neglecting to characterize the normal bacterial flora's activities as part of it.

Bacteriologists in the early 20th century recognized here were two kinds of bacteria—nonpathogenic and pathogenic—that engaged with the body. They were very different in character. This would become increasingly evident as researchers investigated the normal flora of the body over the next few decades. The techniques of the medical bacteriological laboratory were geared towards the identification of pathogens. But it was clear that many of the nonpathogenic bacteria in the body could not be characterized in the same ways as pathogens. As one of the few early 20th century bacteriologists to develop a research program to study these bacteria noted, the normal flora were distinguished by their physiological or chemical behavior and their resistance to conventional culture media.[44] They were identified by their ability to "bring about well-marked changes in their nutritive environment,"[45] while pathogenic bacteria

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[43] Canguilhem, Georges. *The Normal and the Pathological*. *NY: Zone Books*, 1991, 11-13

[44] Kendall, Arthur I. "Certain Fundamental Principles relating to the Activity of Bacteria in the intestinal Tract. Their Relation to Therapeutics," *The Journal of Medical Research* 25 (1911): 117.

[45] Kendall (1911), 125.

were for the most part "relatively inert" in this respect.[46] Pathogens created lesions in host animals; the normal flora, well-adapted to the conditions of their hosts, did not.[47] But largely the normal flora were neglected in medical bacteriology and were not rigorously investigated as part of the normal state of the host. Instead, medical bacteriologists applied the Pasteurian vision to the body--health could be defined as and achieved by the elimination of pathogens set against a particular physiological view of normal function.

Medical bacteriology limited the study of bacteriology to pathogens and neglected the study of the normal bacterial flora as medical and scientific objects. Their liminal status made them essentially invisible as the hygienic program became more entrenched. The relationship between germs and bodies was cast in adversarial terms as they were defined primarily as external, foreign invaders that targeted the body. The language of war dominated characterizations of the relationship between the body and bacteria as the Pasteurian vision of medical bacteria flourished.

Pasteurian Culture: American Bodies under Bacterial Threat

The overwhelming framing of bacteria as germs that caused disease set up an adversarial relationship between bodies and germs in the public consciousness. The body was under threat from germs; Pasteurian practices were protection against them. Because germs were invisible and could be everywhere, the protection of the body from them required constant vigilance.

[46] Ibid.

[47] Ibid.

Prevention was the best medicine, and in an age of epidemics and outbreaks, it was the only sane option. It was because of this very real fear of disease and infection that the vigorous sanitary practices of the public health reformers and domestic scientists were adopted with such zeal and application.

In *Clean: A History of Personal Hygiene and Purity*, historian Virginia Smith describes how germ theory "reinforced every single lesson of the old gospel of cleanliness."[48] To be clean had become an article of faith in American life before the germ theory took hold. Health reform movements of the 19th century emphasized cleanliness as a goal in the protection against disease. Germ theory elevated the stakes for cleanliness as germs became clearly articulated, if invisible, enemies of human health and a target for cleaning practices alongside dirt. The relentless barrage of education and advertising from public health authorities, reformers and companies hawking products for the home during the first half of the 20th century established the eradication of germs as an essential part of American cleaning practices.[49] The germ theory became the basis for the vigorous domestic science movements in the United States that revolutionized everyday practice for American women.[50] The techniques of the hygienic laboratory came to be applied to every room in the house as the ever present threat of germs. A heightened vigilance against them manifested as an obsession with cleanliness in the home.

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[48]Virginia Smith, *Clean: a History of Personal Hygiene and Purity*, Oxford University Press, 2007, Location 4288, E-book.

[49] Hoy, Suellen. *Chasing Dirt: the American Pursuit of Cleanliness.* New York: Oxford University Press, 1995.

[50] See Tomes (1998), Chapter 6 "The Domestication of the Germ," 135-56.

Cleanliness did not only signify freedom from or protection against disease, it also signified social order and moral rectitude. [51]The germ theory put a new spin on attitudes towards cleanliness. As the Pasteurian vision spread and became part of the public health infrastructure of everyday life, disease could be seen as personal or familial failure to adhere to modern hygienic practices.[52] It follows that people had a vested interest in *displaying* modern hygiene as a mark of good moral character and civic duty. Over time, these behaviors became cemented in the everyday life.

This hardening of Pasteurian practices occurred in the midst of a wave of immigration and the fear of the diseases that the new immigrants might bring with them.[53] As Suellen Hoy writes in *Chasing Dirt: The American Pursuit of Cleanliness*, the wave of immigrants from southern and eastern Europe who came and the Black Americans who migrated into cities during this period were abhorred as reservoirs of disease and "vast masses of filth."[54] This dichotomy—of the old and the new, the foreign and the American, and the white and the black--served to reinforce the American obsession with cleanliness. The new arrivals were the target of Americanizing campaigns which carried the gospel of germs into the slums and ghettos of the cities as a means of public health control, but also as a means of civilizing the new arrivals into the American way of life.[55] This fear of the influx of potentially diseased bodies was often paired

[51] See Smith (2007), Chapter 8: "Civil Cleanliness."

[52] Rogers, Naomi, *Dirt and Disease: Polio before FDR,* New Brunswick*:* Rutgers University Press, 1992, 4.

[53] Hoy (1995). See Chapter 4: "The American Way."

[54] Hoy (1995), 92; also see Chapter 4.

[55] Ibid.

with distrust and skepticism about the character of these incoming populations; the new immigrants had a vested interest in adopting hygienic practices to counter that stereotype.

Pasteurian Bodies and Hexachlorophene

Pasteurian practices did not end in the home or the clinic or in public spaces. They also included the care of the body. Antibacterial agents were increasingly incorporated into personal hygiene products in the twentieth century. Germicidal products made the transition from hospital to home to body as "antisepticonsiousness" spread.[56] The first generation antiseptic soaps----carbolic soaps like Lifebuoy—made the transition from surgery to home in the early 20th century.[57] But in the middle of the twentieth century, there was an explosion in the usage of antiseptic and antibacterial products just as the antibiotic age began to quell fears about infection. I track how Pasteurian practices aimed at the elimination of germs became associated with a new set of threats to the body and, I argue, the self.

<u>Hexachlorophene and the Making of the Pasteurian Body</u>

In 1937, William Gump, a gifted perfume chemist at the company Givaudan-Delawanna started to investigate halogenated bisphenols in search of new antibacterial compounds and

[56] See Tebbe-Grossman, Jennifer, and Martha N. Gardner. "Germ Free: Hygiene History and Consuming Antimicrobial and Antiseptic Products," in *Innate Immune System of Skin and Oral Mucosa: Properties and Impact in Pharmaceutics, Cosmetics, and Personal Care Products*: 1-42. (2011), p. 10. See also Tomes (1999).

[57] See Matulich, Erika. "Stronger than Dirt: A Cultural History of Advertising Personal Hygiene in America, 1875 to 1940." *Journal of Product & Brand Management*11.7 (2002): 483-485 and Sivulka, Juliann. "Odor, Oh No! Advertising Deodorant and the New Science of Psychology, 1910 to 1925." *Journal of Macromarketing*. Vol. 28. No. 1. 2455.

several years later patented a compound called hexachlorophene as a skin disinfectant and germicide.[58] It was uniquely suited to this use because it was stable in soap, had strong antibacterial properties and could be *retained in the skin for extended activity*.[59] [60] Gump wasted little time in patenting the compound and promoting it to the hygiene sector as a possible agent for use in the household and personal hygiene markets—"Why should not every person be using this germ-killing soap every time he washes his hands, for bathing, for shaving, for laundering, and on other occasions?," Gump asked in 1945 the trade journal *Soap and Sanitary Chemicals*, "There is no reason why not; there is every reason why."[61]

The personal hygiene industry agreed. Gump's compound was added to a wide variety of lotions, creams, pharmaceutical products, deodorant products and soaps as a key ingredient, led by Armour's Dial Soap in 1948.[62] The success of Dial quickly expanded the market for hexachlorophene and hexachlorophene-like products in personal hygiene products.[63] The new compound soon found its way into other hygiene products and began to edge out the old germicidal products.

Like those earlier germicides and antiseptics that had made the transition from hospital to home, hexachlorophene was originally a hospital scrub used in surgical hand cleaning

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[58] Horsey, R. E., "William S. Gump: The Man and the Scientist," *Journal of Cosmetic Science* 11 (1960): 304-6.

[59]Emphasis mine. See Chapter 26: "The First Synthetic Drugs and their Analogues: Hexachlorophene," in *Drug Discovery: A History* by Walter Sneader, New York: John Wiley & Sons, 2005, 362-3.

[60] Horsey, R. E., "William S. Gump: The Man and the Scientist," *Journal of Cosmetic Science* Vol. 11, No. 5 May 1960, 304-6.

[61] Gump (1945), 85. See also Tebbe-Grossman, Jennifer, and Martha N. Gardner (2011), 19.

[62] Lawrence C. A., "Germicidal Soaps and Cosmetics," *Journal of the Society of Cosmetic Chemists 3* (1952): 125.

[63] See Tebbe-Grossman, Jennifer, and Martha N. Gardner (2011), 1-42.

products meant to help surgeons and medical professionals prep for surgery. What was different about hexachlorophene was that it was uniquely suited to be added to a broad variety of products because it was compatible with the dyes, deodorants and other ingredients of cosmetic and deodorant creams, lotions, powders and tonics. It had been *proven* effective in the laboratory in ways that the older germicides had not been.[64] [65]

By the mid-1960s, the commodification of germophobia had become central to American life. The *New York Times* reported in 1959 that the American obsession with germophobia had become very big business.[66] What the *New York Times* called "a hygienic web" had expanded five-fold in the late 1950s ($200 million to $1 billion in two years)—with products getting "antiseptic finishes" from chemical companies like Sanitized, Inc. and American Cyanamid (Cyanamid crowed that its new odor combating "purifying finish" could withstand fifty washings).[67],[68] At least fourteen different chemical companies were producing the chemicals for these consumer products by the mid-1960s.[69] The soap market was also shifting towards an antiseptic imperative—in the 1960s antibacterial soaps took over the personal soap market,

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[64] "[T]he rise and fall in popularity of "germicidal" soaps during the past several decades may be in part attributed to some lack in agreement as to whether, or not, the products were actually effective against micro- organisms in the test tube, and in particular to the questionable effects of these medicated soaps when applied to the skin." 124-5, Lawrence (1952):124-5. See also Hamilton, H. C., and Thistlethwaite, F., "A Method for the Germicidal Assay of Soaps," *Lab. Clin. Med.,* 16 (1931): 391. See also Lawrence (1952), 125.

[65] William S. Gump, "Development of a Germicidal Soap," *Soap and Sanitary Chemicals* 21 (1945): 37-8; 50

[66] See "Germ retardants making gains in consumer items," *New York Times,* October 12, 1959.

[67] Alexander R. Hammer, "Asepsis Spreads to Host of Items," *New York Times* 19 April 1959: F10

[68] *American Cyanamid Company Annual Report* 1958, 9.

[69] Theodore Irwin, "Bye-bye, bacteria!" *Popular Mechanics,* June 1966, 91.

accounting for over 50% of the market by the end of the decade.[70] The big sell for products was the marketing potential of having them “treated” for “hygienic protection” in to a hygiene-obsessed society.[71] Products with such finishes announced it on their tags—either by noting the chemical used for the finish—often the ubiquitous hexachlorophene—or by noting the trademarked name of the process itself (Sanitized, Permachem, Corobex, Purofab).[72]

In 1966, an article in *Popular Mechanics* described just how much of an impact germ killing had come to have on the everyday lives of Americans. “The clothes we wear, the rooms we live in, the bed we live in are now being made with built-in germ resistance” blared a sub-headline in the June issue.[73] “Almost everywhere you turn nowadays,” Theodore Irwin wrote, “a silent built-in war is going on against unfriendly bacteria.”[74] Irwin chided Americans for their cleanliness obsession—calling them “fanatics on cleanliness”—and bemoaned how Americans were now aggressively buying up anything marked “germ-proof,” ”sanitized,” “antiseptic,” or “bacteriostatic.” Such was the gold rush mentality to the sector that the USDA’s biologicals unit had to step in to crack down on excessive claims from manufacturers of some of these products by 1966.[75]

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[70] See Krause, Charles C. "Recent developments in the toilet-bar market." *Journal of the American Oil Chemists’ Society* 45.7 (1968): 505-509 and Herrick, A. B., and Eric Jungermann, "The new toilet soaps." *Journal of the American Oil Chemists’ Society* 46.4 (1969): 202-204.

[71] Irwin (1966), 93.

[72] “Germ retardants making gains in consumer items,” *New York Times* October 12, 1959.

[73] Irwin (1966), 90.

[74] Ibid.

[75] Ibid.

The action was achieved in these new products with microbe-resistant chemicals—which had been added to everything from bras to wigs to diapers to carpets. These products were treated or coated with chemicals that provided a "germ retardant" barrier, much like Gump's hexachlorophene did with skin. There was some concern about the safety of these chemicals and some evidence of danger—both economic and medical--but the general public did not raise much of an eyebrow and there was governmental sanction for them.[76] For example, Leander S. Stuart, the veteran director of the bacteriological department at the USDA's Pesticide Regulation Unit, which was tasked with enforcement of the federal regulations of germicides, had found no ill effects in its extensive testing of the chemical finishes. [77] Stuart was skeptical of the efficacy of the new products—"the most you can expect is a mitigating effect that reduces the chances of infection to some degree," he told a reporter.[78] But he did not see any cause for alarm and denied that there could be any danger from the new products because of the tight regulation and extensive testing that companies needed to go through before any new germ retardant chemical could be put to market.[79]

The achievement of American clean came to be associated with the chemical agents required to do so. To be clean, was no longer just about the absence of dirt or even the absence of bacteria, but it was to be *literally* covered with chemicals—in the mouth, on the skin, in the vagina, in all aspects of everyday life—treating the body and its accoutrements to a chemical

[76]For example, germfree men's underwear was removed from the market after law suits were filed against a manufacturer whose men's underwear had caused "intolerable skin irritations." Irwin (1966), 91.

[77] See "Germ retardants making gains in consumer items," *New York Times* Oct 12, 1959.

[78] Irwin (1966), 93.

[79] Irwin (1966), 203. Companies were required to hire a research lab to do "patch tests" on skin and submit them to the USDA for approval.

process to keep germs at bay. This was a Pasteurian vision of the healthy and protected body. But beyond this, it was a uniquely American clean, and a uniquely American innovation--during the 1964 Tokyo Olympics, the US team's warm-up suits were made from germ-repelling material, casting germ-free "treatment" as a cultural accomplishment and marker on the international stage.[80] The goal was to achieve a "whiter-than-white" sense of security."[81] But that sense of security was not just about protection from disease. Pasteurian practices were undergoing a shift in meaning in this period.

Pasteurian Practices and the Social Order of Odors

One of the key imperatives for the mid-century boom in antiseptic soaps and "purifying finishes" was their very invisibility. The old antiseptic products that had become institutionalized in domestic life in the early part of the century had strong smells as clear markers that screamed "clean!" This had been, as one cosmetic chemist explained, a selling point--"Much of the feeling of a sense of security following the use of early "germicidal" soaps was the direct result of the "antiseptic" odors that were imparted to these products."[82] But this began to shift as "antiseptic odors" became undesirable. This shift was evident in the marketing and discussions around antiseptic soaps. What had been a selling point in the 1920s and 1930s—the "fine antiseptic smell" of Lifebuoy would make boys feel "peppier," as one ad crowed; later ads of the consequences of not using Lifebuoy to stop the dreaded and often invisible to oneself ("Our

[80] Irwin (1966), 19.

[81] Irwin (1966), 203.

[82] Lawrence (1952), 125.

sense of smell becomes so used to this familiar odor that we don't notice it in ourselves. *But others do*." Threatened one ad targeted at women) B.O. its "extra-clean scent" was proof that it "purifie[d].""—became a point of contrast by the 1950s.[83] Lever relaunched Lifebuoy in the early 1950s with a new germ-fighting agent called puralin, whose action was similar to hexachlorophene. The ads celebrated in bold type and all caps that that "THE "MEDICINAL" ODOR IS GONE!" and literally underlined the fact that it has a "new, pleasing fragrance" that could do more than the old Lifebuoy, and built on the old B.O. campaign which had been launched with great success in the early 1930s. The old Lifebuoy could "stop B. O.;" this new formulation could, in a marriage of its old tag line and its main competitor Dial, which was the first antiseptic toilet soap on the market ("Stop odor before it starts"), "stop B. O. before it starts."[84]

Skeptical consumers were addressed directly in ads that voiced the concerns of a public that was trained to see the medicinal smell as proof of action: "It smells so good now, it makes me wonder...," asked one typical ad in bold type.[85] "Maybe you've been wondering, too," the ad continued, ""Does Lifebuoy still protect against B.O. now that its medicine smell is gone?"" The ad stressed that the new Lifebuoy, infused with the "remarkable new deodorizing discovery Puralin" worked even better than the old Lifebuoy even though "you can't see, feel or smell it."[86]

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[83] See Lifebuoy Ad, *Boys' Life*, May 1926, 49; and Lifebuoy Ad, *Chicago Daily Tribune*; January 5, 1930, D3.

[84] See Lifebuoy Ad, *Daily Boston Globe*, August 31, 1952, 4.

[85] Display Ad 191, *Los Angeles Times*; August 1, 1954, L11.

[86] Ibid.

By the 1960s, the new antibacterial soaps had become common place and had displaced the old ones in the category. Distinguished business consultant Lou Allen could distinguish between the early antiseptic soaps and the new ones—"Twenty years ago, a "clean, antiseptic smell" had a pronounced germicidal odor. Today...it has the light fragrance of an afternoon breeze wafted from spice-laden fields."[87] To smell clean was to *not* smell antiseptic at all. It was not to smell of medicine and hospitals and cleaning products, but to have a "light fragrance" that was indistinguishable from a light perfume. This was what hexachlorophene had meant for the industry and the public at large, which was distinct from the main scientific imperative or claims—that it could actually do what it was claimed it could do biochemically.

Hexachlorophene and its imitators were so powerful because they were invisible; because their effects could seem naturalized. In a post antibiotics world, the goal also shifted from protection against disease to protection against social *dis-ease*—the germs that caused body odor. This was evident in the ways in which everyday people thought about deodorant soaps and products.

This desire of the public—regardless of whether it was created by the advertising or driven by consumers—to escape the strong odors of the early antiseptic products was not purely aesthetic. When asked to evaluate antibacterial soaps, regular people could give a clear insight into what this was about. In the mid-1950s and 1960s, famed marketing guru Ernest Dichter's market research company the Institution for Motivational Research conducted focus groups on deodorants and soaps. These focus groups were commissioned by hygiene manufacturers looking

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[87] Allen, Louis A., *The Management Profession*, New York: McGraw-Hill, 1964, 256.

to help shape advertising and marketing strategies.[88] As one participant in a deodorant focus group from the mid-1950s explained, strong deodorant smells had come to be suspect:

"If I smell someone with an odor that can be associated with deodorants, I begin to feel queasy, and I think that that person is dirty—too lazy to bathe, and is using that stuff to cover up her dirt."[89]

In a research report prepared by Dichter's Institute for Motivational Research commissioned by Armour Dial on Dial soap, Dichter summed it up as follows: "Aristocrats do not smell."[90] One woman in the focus group convened for the report was even blunter in describing the class politics of soap:

> "Once, a long time ago, my husband came home with Lifebuoy. I had to throw it out. I was afraid that someone might see it in the bathroom. They would have smelled it; it had a pungent odor. They would have thought that we were too poor or too dirty to be able to afford a nice soap."[91]

Dial soap and the invisibility of its odor had become markers of social and income status.

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[88] Dichter, widely referenced in Vince Packard's Mad Men era advertising classic, *The Hidden Persuaders*, was *the* leading motivational research expert in the 1950s and 1960s. For more on Dichter, see Schwarzkopf, Stefan and Gries, Rainer, ed. *Ernest Dichter and Motivation Research: New Perspectives on the Making of Post-war Consumer Culture.* London: Palgrave Macmillan, 2010 and Ernest Dichter Papers, Finding Aid, Hagley Library Archives.

[89] "A Motivational Pilot Study on Deodorants" Norman, Craig & Kummel, Inc. 1956, 17. Ernest Dichter Papers, Box 29 790D.

[90] "Report on Focus Group Sessions Findings on the New Armour-Dial Soap," The Armour-Dial Company and Daniel J. Edelman, Inc. n.d. Ernest Dichter Papers, Box 121 2869B.

[91] Ibid.

Furthermore, carbolic soaps came to be associated with foreign bodies, as they remained popular in the colonial, and post-colonial world and favored by upwardly mobile colonial subjects and post-colonial citizens. This was quite explicitly clear in the third world, and leaked over into the United States as new immigrants trickled into the United States. It is telling that Lifebuoy and other carbolic soaps, with their hallmark strong medicinal odors, remained popular in the third world for decades after the United States had made the shift to Dial and less strong smelling germicidal soaps in the 1950 sand 1960s. Lifebuoy in the colonial world was "presented as a "strong" soap suited for washing particularly dirty bodies."[92] Given the racial and ethnic politics of foreign bodies, the fact that "a soap connoting cleanliness was thought by white manufacturers to be particularly suited for use by Africans" and other "others."[93] As Timothy Burke writes in *Lifebuoy Men, Lux Women*, in South Africa, Lifebuoy's strong odor seemed particularly suited to the working man.[94] In the 1950s and 1960s, in India, the association between carbolic soaps and the working and rural classes persisted through the 1990s.[95]

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[92] Burke, Timothy. ""Sunlight Soap Has Changed my Life:" Hygiene, Commodification and the Body in Colonial Zimbabwe," in ed. Hildi Hendrickson, *Clothing and Difference: Embodied Identities in Colonial and Post-Colonial Africa*, Duke University Press, 1996, 200.

[93] Ibid.

[94]Burke, Timothy. *Lifebuoy Men, Lux Women: Commodification, consumption, and cleanliness in modern Zimbabwe*. Durham, NC: Duke University Press, 1996.

[95] Pande, Shamni, "Heed those jingles," *Business Today*, November 16, 2008. "…his picture of a sweaty, hardworking man bathing with a hard, red carbolic soap, on the tandorosti (health) platform somehow stood the test of time and continued till well into the 1990s. Hindustan Unilever (HUL), which owns the Lifebuoy brand, changed the product as well as its imagery only in the early 2000s."

It is no surprise, then, that the people in Dichter's 1957 focus group "reserve[d] their strongest condemnation not for those who had some degree of body odor, but for those who tried to cover up the smell by using a deodorant."[96]

By the end of the 1950s, the use of strong antiseptic smelling soaps then had come to be associated with poorer bodies as well as browner ones. Americanization in the first half of the 20th century included the degermification of the waves of new immigrants; and attaining middle class status was also mediated through the degermification of working class bodies.[97]

By the mid-1950s, 90% of American women and 60% of American men used deodorants.[98] The market penetration of antiseptic soaps was also quite deep. Soaps and deodorants and other personal hygiene products could be used as a literal way to demarcate bodies.[99] The shift away from products that obviously signaled "antisepsis" was a further development in the demarcation of bodies by social and racial status. It was a counterpoint to the idea of the democratization of American life—to buy Dial instead of Lifebuoy or other carbolic soaps at mid-century was a means of distinguishing oneself from the lower classes quite literally—it *cost* more to buy Dial—but also as a means to present an odorless body.

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[96] "Report on Focus Group Sessions Findings on the New Armour-Dial Soap," The Armour-Dial Company and Daniel J. Edelman, Inc. n.d. Ernest Dichter Papers, Box 121 2869B, 17.

[97] See Tomes (1998).

[98] "A Motivational Pilot Study on Deodorants Norman, Craig & Kummel, Inc. 1956," Ernest Dichter Papers Box 29 790D, 12.

[99] In much the same way that table manners had been used to distinguish rising bourgeoisie from old elites. See Elias, Norbert, *The Civilizing Process: The History of Manners: Changes in the Code of Conduct and Feeling in Early Modern Times*, translated by Edmund Jephcott. Urizen Books, 1978.

On the one hand, the adoption of the new hexachlorophene-laced soaps meant a further pathologization of the body—by trying to do its work invisibly, without leaving a mark, it naturalized the antiseptic body by making it invisible—obliterating body odor by eliminating it without calling attention to the fact that it had been eliminated. The goal was to present a "Pasteurized" body as a natural one. To paraphrase Dichter, it would perhaps be more accurate to say that particular kinds of bodies did not smell; and did not *need* to be deodorized. Troublesome bodies needed more obvious disciplining; less problematic bodies did not. The goal was to achieve an innocuous body that belied the scientific and cultural work that went into maintaining and creating it. In chapter 4, I will describe the revolt against this constructed version of the American body.

Conclusion

By the 1950s, the hygienic practices that domestic reformers had sought fervently to implement—and the consumer industries that depended on the adoption of these practices—had become part of American life. To be American was to be fastidiously clean in the domestic and personal spheres. The quintessential image of the 1950s was "a new *americaine*…who exported the ideals of the affluent American suburbs." [100] The Pasteurian vision encapsulated in the hyper white, spotless, scrubbed and chemically treated surfaces of the suburban kitchen and the fastidious attention to personal hygiene of the American middle class.[101] This was the image of

[100] Smith (2007) location 4678; See Chapter 10: The Body Beautiful."

[101] It was a uniquely to American "myth of hygiene" that Barthes observed in 1969. Barthes, Roland. "Un cas de critique culturelle," *Communications* 14 (1969): 97–99.

America that was exported across the world on movie screens and in magazines and became emblematic of the age.[102]

Historian Nancy Tomes has described how the new hygienic vision became part of an emerging vision of a particularly American modernity. "The rising gospel of germs coincided with the emergence of a new style of cultural modernism," Tomes writes. "[It] offered a vision of hygienic modernism that was perfectly suited to "cult of the new" and its "perfectionist project.'"[103] This hygienic modernism began as a rejection of the unhygienic and thus dangerous and unscientific cultural practices of the Victorian era and came to dominate American life as constitutive of it. It reached its pinnacle in the 1950s, an exceptionally optimistic and sanitized age.

In the post war period, the astonishing success of antibiotic "wonder drugs" and other scientific and technological innovations made Americans optimistic about technology's—whether scientific or medical—role in shaping modern life. The visions of the future that proliferated in this technofuturistic age were without question extremely clean—microbe-free, fresh scrubbed, smooth surfaces and fabrics and synthetic materials that would not be traps for microbes. The future was sanitary; science fiction writers and futurists rarely mentioned the problem of germs. It seems to belong to a different era—a diseased, unscientific and blighted past.[104] This optimism was echoed by the medical establishment. By 1969, the Surgeon General

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[102] Historian Virginia Smith describes the 1950s as such: "the visual image of the 1950s is that of an exceptionally sanitized decade." Smith (2007). See Chapter 10.

[103] Tomes (1998), 158. She uses historians William Leach's and Jackson Lears's terms here respectively.

[104] Dregni, John and Erick, *Follies of Science: 20th century Visions of Our Fantastic Future*, Speck Press, 2006, 66.

announced that “it was time to close the book on infectious diseases” since they were no longer a threat to modern American life.[105]

The discovery and rapid adoption of antibiotics in the post-War period did nothing to stem the hygienic fervor of the first half of the century. Though the threat from germs had seemingly diminished in this period, the practices remained as part of the fabric of everyday life. Tomes describes the situation in the 1960s as follows:

> “By the mid-1960s, customers at roadside diners did not connect their paper cups to the old fear of the common drinking cup and the “loathsome” diseases that might be contracted from using it, nor did people blowing their noses into a Kleenex tissue realize that the “crepe napkin” had once been seen as an indispensable sanitary aid for the consumptive.”[106]

But they did these things anyway, and these behaviors became more associated with *etiquette* than with disease prevention—with the *correct* way of behaving in society. Pasteurian practices became a way of displaying good behavior. These rules were taught as part of the battery of requirements for bringing up children *well*. These became more explicitly technologies of the self: technologies of social mobility, technologies of Americanization, and technologies of modernization. The story of antibacterial cleansing products illustrates how Pasteurian practices of the body became a tool of social ordering and self-fashioning rather than as protective measures against disease.

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[105] Quoted in Tomes (1998), 254.

[106] Tomes (1998), 255.

This chapter has examined how the gospel of bad germs shaped bacteriology, medicine and the cultural orientation towards the human-microbe relationship. In the next chapter, I describe a bacteriological science built on nonpathogenic microbes in the early twentieth century and how the relationship between good "health germs" and human bodies was configured.

Chapter 1: Gut: The Gospel of Good Germs, 1900-1940s

Introduction

While the dominant view of bacteria in the pre-WWII era was the disease-causing villain, a counternarrative that stressed the beneficial aspects of bacteria ran alongside it in this era. The gospel of good germs flourished in different spaces than those that embraced the Hygienists' imperative and attitudes. While the notion that bacteria had many positive roles to play had been acknowledged by scientists from the late 19th century, public discussion of the positive aspects of germs—sewage, digestion, food production, soil--occurred only sporadically as articles on "friendly bacteria" or "good microbes" popped up occasionally in the popular press.[107]

One of the counternarratives that did have an extensive cultural and scientific life in this period centered on intestinal bacteria and "health germs." The science of intestinal bacteriology, upon which these positive claims came to be staked in this period, took a different approach to the microbe as a biomedical and scientific object from conventional medical bacteriology. The relationship between germs and the body was framed in this instance in beneficial terms; the nurturing of that relationship was the problem around which investigations of these microbes were based. I argue in this chapter that this particular gospel of *good* germs was linked to a distinct scientific approach to the study microbes. This approach viewed the body as a setting or set of conditions for microbial action rather than as an organism under threat from an invading pathogen. Those scientists who engaged in this work claimed that it required a more "scientific"

[107] For example, see Professor Lewis McLouth's *Science Notes* column from September 29, 1901: "Microbes: Good and Bad," *Detroit Free Press*, C1, "Friendly bacteria: Some of their Uses for the Benefit of mankind," *New York Times*, July 29, 1909, 5.

approach to studying microbes because of the inadequacy of traditional medical bacteriology in providing a framework and methods to study them.

For these researchers, their approach could draw dividends for therapy. A proper science of bacteriology would approach microbes as organisms in an environment, they claimed, and consequently needed to investigate and understand the conditions within which they lived. Conventional medical microbiology, with its focus on isolating and eliminating pathogens and the battery of techniques developed with this goal in mind, was a potentially faulty experimental approach for dealing with other kinds of bacteria that did not fit the infectious disease model. These researchers insisted that in order to provide a solution to a medical problem--in this case, of putrefactive microbes accumulating in the gut--one needed to understand the relations of bacteria within the gastrointestinal tract. Effective therapies would only come from an understanding of these relations. This contention provided the rationale for the short-lived field of intestinal bacteriology which flourished in the 1910s through the 1930s. Intestinal bacteriologists sought to provide a counterbalance to the traditional microbiology of the hygienic laboratory through the study of intestinal microbes.

I argue that the approach that intestinal bacteriologists took to bacteriology was based on a different vision of what a science of bacteriology should be and how microbes were related to health. I also claim that this work led to the creation of a scientifically principled acidophilus milk therapy.

Good and Bad Germs

In the late 19th and early 20th centuries, bacteria were characterized in two ways: as either good or bad for humankind. The relationship between good and bad bacteria was cast as a war between good and evil, both within the body and without. In the body, the germs of disease and decay were ever threatening to ravage the human body while "our microbe friends" staved them off.[108] The same war that was waging in human bodies was going on in the countryside, as farmers struggled to keep the bad bacteria at bay with the help of the good ones. This war between microbes was cast in elemental, Manichaean terms. The friendly bacteria in the body were part of an eternal and eminently *natural* struggle between the light and the dark, in philosophical, social, agricultural, moral and medical terms.

As Dr. Henry S. Gabbett had argued in his article "Beneficent Germs," the public image of the germ had been so maligned in the minds of the American public that it "a veritable incarnation of the principle of evil."[109] Health practitioners and scientists were at pains to combat the "many libels" that had been targeted at bacteria.[110] There were "more good microbes than bad ones," scientists, doctors and newspapers began to argue, running down lists of all of the positive things that bacteria did.[111] Microbes had been unfairly tarnished by the sensational events tied to bad actors. "The eminently respectable citizen…who wishes all microbes were dead, little appreciates how indebted not only for the comforts of life but for life itself to this

[108] "Science Notes: Microbes Good and Bad," Detroit Free Press, September 29, 1901, C1. By Prof. Lewis McLouth.

[109] Gabbett, H. S. "Beneficent Germs," *The Nineteenth Century: A Monthly Review 45* (1899): 938.

[110] "Good Points of Microbes," *Chicago Daily Tribune*, April 2, 1899, C2. See also "Science Notes: Microbes Good and Bad," Detroit Free Press, Sept 29, 1901, p. C1. By Prof. Lewis McLouth.; "Medicine: Good Germs," Time Magazine, October 15, 1923; *Civilization and the Microbe* by Arthur Isaac Kendall, Boston and New York: Houghlin Mifflin Company, 1923.

[111] "Good Points of Microbes," *Chicago Daily Tribune*, April 2, 1899, C2.

modest and uncomplaining little infusorial toiler."[112] At first this push back came from industries like the dairy industry, in which researchers like bacteriologist Dr. Herbert W. Conn of Middleton Wesleyan University, who would later co-found the American Society of Bacteriologists, demonstrated the usefulness of bacteria in the production of staple foodstuffs like butter.[113] Bacteria, Conn claimed in *Scientific American* in 1892, were "our enemies but also [were] our closest allies."[114] They were essential for the brewing, bread and cheese industries, and for agriculture writ large through soil enrichment. Greater appreciation for the myriad roles of bacteria would, Conn hoped, bring about a change in public opinion and public discourse with respect to bacteria: "we will recognize that the power of bacteria for good far outweighs their power for evil."[115] This sentiment could be found everywhere in the public discourse, even though in all cases, those making the point felt the need to counter the dominant narrative about bacteria. Everywhere this sentiment was voiced, the disclaimer was made—that yes, there were many bad bacteria, and yes, bacteria were a matter of life and death—but, these medical, agricultural and scientific men argued in the press, these bad bacteria were not the *whole* story. Throughout the 1890s and into the first decade of the new century, this sentiment was repeated. For example, it was claimed in the *Chicago Daily Tribune* in 1900, "hitherto it has been claimed that all bacteria were injurious, but now the opinion is maintained by many…medical men…that most of them are harmless, although many are decidedly injurious,

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[112] "Good Points of Microbes," *Chicago Daily Tribune*, April 2, 1899, C2.

[113] "Utilizing a friendly bacillus," *New York Times*, June 13, 1896, 4

[114] "Importance of Bacteria," *Scientific American* June 11, 1892; Vol. LXVI., No. 24, 375.

[115] Ibid, 375.

and a few are perhaps beneficial."[116] In an article titled "Indispensable Bacteria" in *Everybody's Magazine,* Dr. William Hanna Thomson argued that bacteria were essential for the earth to be habitable because of their role in the cycle of life—by decomposing dead animals and plants they allowed for the making of room for successive generations.[117]

But defenders of bacteria's myriad positive qualities were overshadowed by the hygienist's vision of bacteria. There were several reasons for this beyond the productivity of the germ theory and the fear of epidemic disease. The United States was undergoing a massive shift in the late 19th and early twentieth centuries period as urbanization accelerated and the rural population declined.[118] While the gospel of bad germs was not only preached to an urban congregation—it extended to rural households and regions as well—it was propagated to and through an increasingly urban population. Glowing defenses of the role of bacteria in agriculture and in soil enrichment resonated less with a population that was less connected to farm life. The role of microbes in the production of food also had less impact on a population that was increasingly removed from producing food for itself. Furthermore, it was the educated urban middle class that determined the public discourse and thus shaped the culture; they were even further removed from the production of food and the tilling of the soil than the general population. The fear of infection was much more relevant for them, especially in a period that saw a massive wave of immigrants from strange new places in Europe, and as African Americans flocked to cities across the United States. This disparity in engagement with

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[116] "Bacteria Good and Bad," *Chicago Daily Tribune*, June 4, 1900, 4.

[117] "Friendly Bacteria: Some of their uses for the benefit of mankind," *New York Tribune*, July 22, 1909, 5.

[118] According to the 1920 census, more than half of Americans lived in urban areas; the shift from rural to urban accelerated in the 1920s. See William G. Flanagan's *Urban Sociology: Images and Structure,* Rowman & Littlefield, 2010, 209-11.

microbial life helps explain why the dominant image of the microbe became the big, bad germ in the public sphere, as the taste makers, opinion writers and media class focused on the microbial threat rather than the productivity of microbes for everyday life.

Good Germs and Bacteriology

Those domains in which bacteria were not seen as pathogens to be destroyed but organisms to understand or to encourage had a different rationale for their study. Consequently soil bacteriology and agricultural bacteriology looked markedly different from medical bacteriology. The scientists who studied bacteria from these perspectives needed bacteria to be productive; the isolate and eliminate rationale of pathogen-focused medical bacteriology did not suit the sort of questions they were driven to ask by the practicalities of their fields.[119] Soil bacteriologists looked for ways to study bacteria in within the natural matrices within which they would need to be put to use. The ability to harness these microbes depended on their ability to manipulate them, not on their elimination.

What these bacteriologists had in common--rumen microbiologists, soil bacteriologists and intestinal bacteriologists--was an appreciation for the ways in which bacteria functioned in natural habitats and under different environmental conditions. They modeled the body as a literal set of changing conditions within which one could understand the behavior of *in vivo* bacteria. For intestinal bacteriologists, the intestinal tract could be seen as just another environment to be modeled, a backdrop for the intricacies of bacterial interaction in a particular kind of habitat. The

[119] See Kupferberg (2001). .

science of intestinal bacteriology would lead to a theory of intestinal therapy based on the transformation of the intestinal flora with ingested "health germs." While there were other narratives around "good" germs in this period, the phenomenon of "health germs" was the one with the greatest visibility in the culture.

Good Germs and the Body: Metchnikoff's Bacillus Bulgaris Therapy

The gospel of good germs was first spread most successfully in the public sphere by Pasteur Institute scientist and Nobelist Elie Metchnikoff. Metchnikoff's sour milk therapy caused a huge sensation in the early 1900s.[120] In the case of the intestinal bacteria, he argued for the introduction into the body of lactic acid bacteria that could fight the "germs of decay," or putrefaction. Metchnikoff championed the Bacillus Bulgaris, a lactic acid bacterium purportedly found in Bulgarian yogurt, as the cornerstone of his therapy. By 1910, Metchnikoff's therapy had, according to the *Washington Post,* "achieved a notoriety hardly excelled by the most famous and dreaded of the pathogenic bacteria whose names have become household words." [121] The article described Metchnikoff's therapy to the public as an example of the struggle for existence seen throughout Nature:

> "The struggle for existence extends to the world of microscopic elementary plant life, and … nature, if left alone, maintains a balance of forces. It would follow from this that just as the best way to keep field and garden insects down is to let small birds alone, so the

[120] Scott H. Podolsky, "Cultural Divergence: Elie Metchnikoff's Bacillus Bulgaricus Therapy and His Underlying Concept of Health," *Bulletin of the History of Medicine* 72:1 (1998): 1-27.

[121] "Science and Sour Milk: How the bacteriologists confirm the ancients in their use of curds and whey," *Washington Post*, May 29, 1910, MS2

best way to deal with harmful germs is to encourage their natural enemies. The lactic acid therapy makes a step in this direction."[122]

The sour milk therapy took off among the public, and quickly became a fad in the 1900s. Its popularity could be attributed to three things. First, Metchnikoff introduced it with respect to a perennial issue—the fear of aging, using suggestive anecdotal evidence to indicate the efficacy of his therapy. The bacterium touted by Metchnikoff had been found in Bulgarian yogurt; Metchnikoff claimed that it was the key to the longevity of Bulgarian peasants.[123] Second, the idea resonated with both ancient and modern ideas—the notion of the balance of nature was an ancient idea, and Darwin's impact had made the struggle for existence a core modern concept.[124] Finally, the popularity of the therapy can be explained by the cultural authority that Metchnikoff enjoyed as a celebrated scientist attached to the Pasteur Institute and later, from 1908, as a Nobelist. The popularity of Metchnikoff's theory lasted through the first two decades of the 20th century.[125]

Ultimately, it was other scientists that discredited Metchnikoff's therapy. The efficacy of Metchnikoff's Bulgaris Bacillus therapy was challenged by the medical establishment in the 1910s and finally condemned in 1924 by the American Medical Association's Council on Pharmacy and Chemistry.[126] The Council had established a Committee on Lactic Acid Ferment

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[122] Ibid.

[123] Metchnikoff, Elie, and Ilya Ilyich Metchnikoff. *The Prolongation of Life: Optimistic Studies*. Springer Publishing Company, 1908.

[124] For the history of the balance of nature concept, see Egerton, Frank N. "Changing concepts of the balance of nature." *Quarterly review of biology* 58 (1973): 322-50.

[125] For more about the fad, see Podolsky (1998) and Whorton (2000), 167-194.

[126] The American Medical Association's Council on Pharmacy and Chemistry had been established in 1905 to "set standards for drug manufacturing and advertising and fight the war on quack patent medicines and nostrum trade."

Preparations in the wake of the Bulgaris therapy's popularity. The Council rejected Metchnikoff's theory based on the failure of the Bacillus Bulgaris to implant itself within the intestines experimentally--the bacterial action upon which his therapy needed to be based.[127] In short, the reason for the fall of the therapy was that it was based on a faulty and incomplete knowledge of bacteria and how they functioned in a particular context. The experimental investigations of the bacterium in the laboratory undertaken by Metchnikoff had not adequately taken into account the bodily environment within which these bacteria needed to function.[128] The limitations of culturing and then analyzing the chemical properties of the bacterium were not sufficient tools to investigate the therapy. It was, in short, a case of *bad science*. The Five person Committee included the bacteriologists Arthur Isaac Kendall and Leo Rettger. Both insisted that Metchnikoff's theory of bacterial implantation as therapy could work if it was based on *good science*. It was largely their work in the 1920s that led to the supplanting of Bulgaris therapy with another sour milk therapy--Acidophilus milk therapy.

The Committee contrasted the therapies in the Council on Pharmacy and Chemistry's "New and Nonofficial Remedies" report in the *Journal of the American Medical Association* in 1924:

Quoted from the American Medical Association's History Timeline, http://www.ama-assn.org//ama/pub/about-ama/our-history/ama-history-timeline.page. See also Stewart, Francis E. "Origin of the council on pharmacy and chemistry of the American Medical Association." *Journal of the American Pharmaceutical Association* 17.12 (1928): 1234-1239.

[127] See Council on Pharmacy and Chemistry, "The Present Status of Bacillus Acidophilus and Bacillus Bulgaricus Therapy," *Journal of the American Medical Association* 87 (1926):172.

[128] See Herter, C. A., and A. I. Kendall. "An Observation on the fate of B. bulgaricus (in Bacillac) in the digestive tract of a monkey." *Journal of Biological Chemistry* 5.2 (1908): 293-302 for a critique of Metchnikoff and his followers' studies on Bulgaris bacteria.

"Recent observations seem to indicate that Bacillus Bulgaris cannot be implanted or made to proliferate in the intestine even when administered in large numbers. Much doubt is cast, therefore, on any alleged physiologic action of this organism in the intestine. For this reason, and because Bacillus acidophilus, according to reports, can be successfully implanted, the preference is now given by many to lactic acid bacillus cultures prepared with Bacillus acidophilus."[129]

Rettger would become the key proponent of this new therapy and a key figure in the science of intestinal bacteriology in the 1920s; Kendall had established himself as a leader in the field already in the 1910s.[130] Rettger and Kendall both believed that Metchnikoff had been right in principle but not method; a proper therapy of the intestinal flora depended on a *proper science* of bacteriology that was suited to the bacteria of the intestines. It was not enough to understand the biochemical properties of the bacteria in pure culture in the laboratory as lactic acid producing entities. It required a proper understanding of bacteria in their own right, as biological objects, behaving under a specific set of conditions.

This call for a proper science of bacteriology had been part of the conversation in the field since the turn of the 19th century. Below I track this history and then describe how Kendall and Rettger's search for a proper bacteriology led to Kendall's intestinal bacteriology and Rettger's acidophilus milk therapy.

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[129] Ibid; the 1926 article quotes the 1924 article on p. 172.

[130] See for example, Kulp W.L., Rettger Leo F. "Comparative study of *Lactobacillus acidophilus* and *Lactobacillus bulgaricus*," *Journal of Bacteriology* 9 (1924):357–95.

A Proper Science of Bacteriology

This issue of what bacteriology should be plagued the field. Bacteriologists disparaged their field as too disparate, too unorganized and not rigorous or systematic enough to be a proper science. Medical bacteriology focused too narrowly on the problem of elimination; and its infrastructure reflected the conceptualization of what a bacteria was for in this context—an organism to be identified, isolated and eliminated.

Bacteria were not only relevant to medicine as either pathogens or nonpathogens, they were also a unique class of *organisms* and consequently belonged to the biological sciences as an object of pure biological study like all other forms of life. The question of what a true science of bacteriology should look like was actively debated and discussed in the early 20th century as is typical of young sciences. But bacteriology was unique in that it was so tightly tangled up with various other sciences and applications. To be a bacteriologist could mean a variety of professions and affiliations. As Charles Rosenberg has observed, "at the end of the 19th century, indeed, bacteriology was not a field at all."[131] There were simply too many different kinds of institutional contexts, research agendas and goals that could fit under its umbrella. It could only loosely be defined by a set of basic techniques and a collection of similar organisms that were the target of those techniques. The question of what a *proper* science of bacteriology should look like was addressed repeatedly by those interested in systematizing bacteriology.

The Society of American Bacteriologists was founded in 1899 explicitly to deal with this issue of identity. As medical bacteriology became more and more closely allied with pathology,

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[131] Rosenberg, Charles "Towards and Ecology of Knowledge," in Rosenberg, Charles E. *No Other Gods: On science and American social thought*, 230. Baltimore: Johns Hopkins University Press, 1997.

it was under the auspices of the Society that bacteriologists attempted to define a pure bacteriology, concerned with bacteria for their own sake.

Theobald Smith

Theobald Smith, born in 1859, was one of the leading scientists of the first generation of American bacteriologists. He was the first professor of bacteriology in the United States, earning that title at the tender age of 24 in the 1880s. He came to bacteriology and pathology from the biology of Darwin-Huxley; and earned acclaim by the end of the 1880s as the first person to show the transmission of an infectious disease by an external parasite.[132] In 1899 he signed on as one of the charter members of the Society of American Bacteriologists, by then a professor of Comparative Pathology at Harvard. The Society tried to define bacteriology as a fundamental science while also acknowledging and fostering the needs and goals of the diverse subgroups of bacteriologists from different fields—dairy science, sanitation, pathology, soil science, agriculture, botany—working in different kinds of institutions—industry, farm, experimental agricultural station, hospital, biology departments, medical schools—that comprised the membership of the society.[133] The goals were explicit; the founders of the society described it to prospective members as such: “the unification of methods and aims” and to “emphasize the position of bacteriology as one of the biological sciences.”[134] The society was very much

[132] See “Charter Members of the Society of American Bacteriologists: Theobald Smith,” Jeff Karr and Eric Kupferberg, American Society for Microbiology Archives.

[133] See Kupferberg (2001), Chapter 4: The Society of American Bacteriologists and the Search for Identity,” 251-326.

[134] Conn, Herbert Joel, "Professor Herbert William Conn and the founding of the Society." *Bacteriological reviews* 12 (1948): 275.

concerned that bacteriology become a true science, in contrast to a handmaiden to other fields—a set of technical tools placed at the service of more important or legitimate sciences or activities. The society urged their diverse community to take a more fundamental approach to their work and to consider more fundamental questions. Over the next few decades, this tension between the applied versions of bacteriology and the broader goal of Bacteriology would be productive as researchers tried to negotiate between these two ends and mark out a proper place for their own endeavors within the field—and to contribute to the broader shape of the field. This tension was captured by Theobald Smith just a few years after the founding of the Society.

In a talk at the Bacteriology Section of the International Congress of Arts and Sciences in 1904, Smith described how bacteriology was unique in the history of biological sciences.[135] Smith was a proponent of a more nuanced view of disease in the midst of the increasingly cloistered views of the microbe hunters that dominated the field. In this address, Smith argued for a broader concept of disease—and the more *scientific* bacteriology that it would require. Bacteriology was unique among the sciences because of the degree to which it was driven by urgent practical ends in agriculture and medicine.[136] Its was animated by economic, sanitary and medical imperatives rather than by the goal of the pursuit of pure knowledge about this class of organisms. Unlike other biological fields of study which focused on one object of inquiry, like physiology, Smith argued, bacteriology was "essentially a study of two realms, that of the parasite and that of the host, of two organizations, widely different, acting upon one another and entering into complex, reciprocal relation."[137] There was no interest in bacteria *in and of*

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[135] One could argue that sciences like biochemistry had a similarly practical imperative.

[136] Smith, Theobald, "Some problems in the life history of pathogenic microorganisms." *Science* 20 (1904): 818.

[137] Ibid, 818.

themselves as a target of investigation: "it is what bacteria do rather than what they are that commanded attention, since our interest centers in the host rather than in the parasite."[138]

Smith sounded a note of caution about medical research more generally in urging caution with respect to trying to turn medical research into therapy or to put it to use too quickly.[139] As what was of interest with respect to the host was maintaining its integrity; studies were geared towards this end: "as soon as bacteria could be handled in pure culture, the study prosecuted most actively was how most quickly to destroy them."[140] Thus, "the first impulse of the youthful branch of bacteriology was…to destroy rather than to study and analyze."[141] While Smith went on to claim that this first destructive impulse was tempered in time as more neutral studies focused on the relationship between host and parasite "in their mutual relation," this tendency still shaped the field of bacteriology, especially bacteriology as it was practiced in medicine, which, as Smith claimed, is where bacteriology "in its scientific form" was largely developed as a result of the momentum, money and prestige attached to microbe hunting.[142] This focus on the identification and destruction of pathogens had shaped the agenda, the language and the research methods that came to define the science of bacteriology in the late 19th and early 20th century.

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[138] Ibid, 818.

[139] Smith, Theobald (1905), 515.

[140] Ibid.

[141] Ibid.

[142] Smith (1904), 818.

Historian Warwick Anderson has described Smith a leading figure in the study of disease as a biological rather than more narrowly medical problem.[143] Smith pushed against the reductionist tendencies of scientific medicine towards a narrow and utilitarian view of bacteria that had followed from the development of the science under the peculiar pressures outlined above. Smith's critique of bacteriology was a challenge to the field to resist the imperatives of the clinic or the wallet and to treat bacteriology as a true biological science. While he spoke broadly to the diverse field of bacteriologists, who were working in a variety of contexts as he acknowledged, he was speaking from his perch as a comparative pathologist at Harvard's medical school. He presented his ideas for the public and broader medical community the following year in an article on ""Medical research: Its Place in the University Medical School," written for *The Popular Science Monthly*:

> "…we must not look too closely at the immediate practical value of research… The tendency to make research directly prove pet theories, find cuts to health and cure diseases hitherto unsuccessfully treated continue to give the investigator trouble for some time to come. What is needed is that at least a small number of scientists work at problems of disease as we would at the other phenomena of the world around us. They should look them over from all sides calmly and objectively to get at the lessons expressed in them. They should look upon pathological manifestations as the normal sequences of operating under special conditions and for certain periods of time. They

[143] Anderson, Warwick. "Natural histories of infectious disease: ecological vision in twentieth-century biomedical science," *Osiris* 19 (2004): 43-7.

should endeavor to analyze phenomena rather than attempt to suppress or crush them. That function should belong to health officer and the practicing physician."[144]

This is what a true science of bacteriology would look like, for Smith: focusing on studying bacteria under well-define conditions. It should be was concerned with understanding "dynamic biological processes" and not "suppress[ing] or crush[ing]" phenomena as was the imperative for medical bacteriology. Smith's challenge was explicitly accepted by a young bacteriologist named Arthur Isaac Kendall by the end of the 1910s. Kendall would develop an experimental and theoretical program in bacteriology in response to Smith's challenge over the next two decades. He took as his starting point the bacteria that had been neglected in the juggernaut of pathogen-centered medical bacteriology. He would focus on nonpathogenic bacteria that lived in the body, not the pathogens that invaded it, to build a more general (medical) science of bodily bacteria.

Arthur Isaac Kendall & Intestinal Bacteriology

Arthur Isaac Kendall was born in Somerville, Massachusetts in 1877. He came of age during the exciting days of the germ theory's rise to prominence. Kendall's career trajectory began fairly typically for someone of his training and institutional affiliation. His undergraduate thesis, done at the Massachusetts Institute of Technology, was on bacterial fermentation. He built on that work at Johns Hopkins, earning the first PhD in bacteriology from the school in

[144] Smith (1905), 520.

1904. His wrote his dissertation on the fundamental aspects of bacteriology.[145] Kendall's interest was in pure bacteriology as a science in its own right; and he took Smith's challenge seriously, often quoting him at the beginning of papers and articles throughout the next few decades of his career.

Kendall had a broad range of experience as a bacteriologist working in a variety of contexts.[146].By 1909, Kendall had had broad experience working with bacteria in different contexts and from different angles. He was not purely trained in bacterial pathology and not only familiar with bacteria as they pertained to infectious disease research. But it was his work as a research fellow at the Rockefeller Institute starting in 1909 that really shaped his outlook and career. At Rockefeller, he worked under the direction of Dr. Christian Herter, a fellow graduate of Johns Hopkins, who had studied pathology under William H. Welch in the 1880s. Herter had established a private practice in New York but was also committed to laboratory medicine. Independently wealthy, he established a laboratory at his home to conduct research on the

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[145] A. I. Kendall, "A Proposed Classification and Method of Graphical Tabulation of the Characters of Bacteria," *Public Health Papers and Reports* 1902, 28: 481–493.

[146] After graduating in 1904, Kendall was hired to join the Isthmian (Panama) Canal Commission's first medical department, under the direction of William C. Gorgas Kendall served first as the Pathologist's assistant, and was eventually promoted to bacteriologist, and finally finished his tenure with the ICC as Acting Chief of the Board of Health Laboratory in 1906. While in Panama, he worked on autopsies of malaria victims (showing his interest in classification by focusing an article published in *JAMA* in 1906 on the classification of different types of parasites), trypanosomes in rats and mice, and on mosquito fumigation. After his time with the ICC, Kendall moved to New York and took a job as a bacteriologist with the NY Department of Health's Research Laboratory for a few years, working on projects like the bacterial examination of milk. See Arey, Leslie B. (1979), *Northwestern University Medical School 1859-1979*. Northwestern University Medical School., Kendall, Arthur I. "Malarial infection in certain native villages of the canal zone." *Journal of the American Medical Association* 46.16 (1906): 1151-1154; Kendall, Arthur I. "An apparatus for testing the value of fumigating agents." *Biological Studies by the Pupils of William Thompson Sedgwick: Published in Commemoration of the Twenty-fifth Anniversary of His Doctorate* (1906): 313; Kendall, Arthur I. "A new species of trypanosome occurring in the mouse Mus musculus." *Journal of Infectious Diseases* 3.2 (1906): 228-231, and Minton, Richard, Sigfrid Muller, and Gene Cohen. "Fifty Years of American Medicine on the Isthmus of Panama." *The American Journal of Tropical Medicine and hygiene* 3.6 (1954): 951-963; Kendall, Arthur I. "The significance and microscopical determination of the cellular contents of milk." *Coll. Stud. Research Lab. Dept. Health City of New York* 3 (1907): 169-81.

diseases of his patients, doing pioneering work in intestinal pathology, diseases of the intestinal tract, and on what became known as celiac disease.[147] It was in Herter's lab and under his direction that Kendall became intrigued by the nonpathogenic bacteria of the intestines.[148]

Kendall went on to do a doctorate in Public Health at the Department of Preventative Medicine and Hygiene at Harvard to explore questions first raised in Herter's lab. Smith's challenge had stayed with him: What would a proper science of bacteriology looked like? His doctoral thesis was not just the culmination of several years of work on the question of intestinal bacteria, it was also a manifesto for a new bacteriology. In 1911, Kendall, published a version of his thesis for the *Journal of Medical Research* on the relationship between intestinal bacteria and therapeutics. He stressed that his work was innovative; it would address a "new and hitherto practically neglected" area in medical bacteriology.[149] Though he was most concerned with the nonpathogenic bacteria living normally in the gastrointestinal tract, he broadened his scope by bringing all bacteria—including pathogens—under the purview of the new approach he had developed:

> "The present unsatisfactory state of our knowledge concerning the ways and means by which bacteria enter the host, gain and maintain a foothold there, and bring about

[147] "Christian Archibald Herter, M.D. (1865-1910)," by Hawthorne, Robert M, Jr. *Perspectives in Biology and Medicine* 18. 1 (1974): 24-39.; Abel, Emily K. "The Rise and Fall of Celiac Disease in the United States," *Journal of the History of Medicine and Allied Sciences* 65 (2010): 81-105.

[148] They co-authored several papers together in Herter's *Journal of Biological Chemistry*. For example, see Herter, C. A., and A I. Kendall. "The Influence of Dietary Alternations on the Types of Intestinal Flora." *Journal of Biological Chemistry* 7 (1910): 203-236., Herter, C. A., and A. I. Kendall. "The use of the fermentation tube in intestinal bacteriology." *Journal of Biological Chemistry* 5 (1908): 283-292.

[149] Kendall, Arthur I. "Certain Fundamental Principles relating to the Activity of Bacteria in the intestinal Tract. Their Relation to Therapeutics." *The Journal of Medical Research* 25, (1911): 117. (formerly the *Journal of the Boston Society of Medical Sciences* and now the *American Journal of Pathology*).

conditions more or less unfavorable to the patient's wellbeing was the incentive to the making of these studies."[150]

At stake here was a general understanding of bacterial behavior. This was different, he claimed, following Smith, than so much of bacteriology which was tied to ends that were not focused on the bacteria as an object of study in their own right:

> "The most potent factor which underlies the incompleteness of our knowledge is not difficult to determine: bacteriology, " the handmaiden of medicine," as it has been drolly expressed, besides contributing many of the most brilliant chapters of medicine, enters into so many fields of human activity and interest that it has been neglected as a pure science."[151]

What would a "pure science" of bacteriology entail? Kendall looked at biology more broadly to lay out his approach. As historian William Coleman has written, biology was undergoing a transition at the turn of the 19th century as experimental physiology became the model for the biological sciences and natural history and classificatory biology lost its status as the dominant form of biology.[152] Kendall saw this shift as "the widespread transition from the static or morphologic contemplation of biologic science to the dynamic or causative aspect," and believed that bacteriology was in need of the same kind of transformation.[153]

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[150] Ibid, 117.

[151] Ibid, 118.

[152] See Coleman, William. *Biology in the Nineteenth Century: Problems of form, function and transformation*. Cambridge University Press, 1971.

[153] Kendall (1923), 438.

Bacteriology was special, he wrote, because the simple morphology of bacteria was not distinct enough for classification to work as in other branches of biology, so bacteriologists had to rely on different markers, mediated by techniques and laboratory tools like dyes and stains, and most importantly, responses to culture media, as a means to distinguish bacterial types from each other.[154] Though, bacteriology was in a way kind of physiological chemistry because of its reliance on such methods, this battery of laboratory techniques belonged to the morphological tradition whose purpose was classification and identification of different forms of life.[155] The new biology was a laboratory biology as well, but built along the lines of the physiological laboratory in which studies of organic form and process replaced studies of biological form as the main purpose of biology.[156] Kendall wanted a bacteriology that conformed to the same modern principles: a bacteriology "approached from the dynamical rather than the cultural [i.e. morphological] standpoint."[157] He returned again to Smith's question: "mere isolation and morphological study of microorganisms will add but little to the real question, 'what bacteria do, not what bacteria are.'"[158] This was a *physiological* question, and not a cultural question; and

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[154] Kendall often quoted Smith on this: "Though their investigation may require careful morphological researches, yet the unmistakable monotony of form, combined with a considerable variation of physiological activity, has compelled the bacteriologist to pay much attention to means by which such physiological variations may be more or less accurately registered in order that they may serve as a supplementary basis for classification. Again, with the unicellular organisms the manifestations of cell activity become the most important phenomena for study." Quoted in Kendall, Arthur Isaac. "Bacterial metabolism." *Physiological Reviews* 3 (1923): 438 and Kendall (1911), 117. From Theobald Smith, "The Fermentation Tube," *Wilder Quarter Century Book*, 187-243. Ithaca, NY: Comstock Publishing Company, 1893 and reused by Smith in Smith (1905).

[155] Ibid.

[156] Coleman (1971).

[157] Kendall, Arthur I. "Some observations on the study of the intestinal bacteria, *"Journal of Biological Chemistry* 6, no. 6 (1909): 501; quoted by Kendall in Kendall (1911), 126.

[158] Kendall (1911), 137.

attempting to answer it would bring bacteriology into the realm of modern experimental biology in Kendall's estimation.

What would this "dynamical" approach look like? For Kendall, it meant leaning more heavily on the techniques of physiological chemistry which had brought bacteriology to the classification stage.[159] This biochemical perspective and approach formed the central philosophy and methods for a pure scientific bacteriology that could account for both pathogens and the nonpathogenic "normal" flora that lived in the intestinal tract that were the focus of his research.

Bacteriology, as Kendall had described, was not only being ill-served as a pure science by the status quo; it was serving medicine poorly as well. Kendall, following Smith, believed that medical research into bacteriology should start with an understanding of the normal. Thus, bacteriological medicine should have the same starting point as experimental medicine. Physiology was the science of the normal function of the body against which pathology could be read and calibrated; the normal relations of the bacteria of the body needed to be understood to begin a scientific understanding of pathogenic microbes. Medical bacteriology, Kendall charged, had gotten side tracked by the remarkable discoveries of Koch and others, and the "study of the normal and abnormal relations of bacteria" in the body was neglected.[160] This had led to a microbe-hunting rush, in which investigators turned "their full attention to attempts to isolate an organism from some hitherto "refractory" disease which should be the etiological agent.[161]" The result of this had stunted medical bacteriology, and in particular the study of the bacteriology of

[159] Kendall (1923), 439.

[160] Kendall (1911), 124.

[161]Ibid.

the intestines which had been off to a promising start in the 1880s with the extensive research of Theodor Escherich, discover of *E. coli*.[162] Kendall described the present state of knowledge as follows:

> "at the present time we are practically in the dark concerning the normal intestinal bacteria and their relations to each other, and we are equally uninformed of the laws which underlie their presence and significance in the alimentary tract, points of the greatest importance in the study of the ways and means whereby exogenous or endogenous bacteria gain and maintain themselves and cause disturbances in the alimentary canal."[163]

The fashion for microbe hunting had more consequences than just diverting the interest of scientists towards discovering and isolating disease-causing pathogens; it also led to bacteriology being dominated by a set of techniques and tools to support that goal. This, as Kendall approach was fine for pathogenic bacteria, but did not lend itself to the study of the normal bacteria in the body. These two classes of bacteria—the normal and the pathological—were very different in character. While the pathogens identified seemed to be better suited to culturing and to creating specific lesions in a host animal, many of the more important normal intestinal bacteria were distinguished by their physiological or chemical behavior. They were identified by their ability to "bring about well-marked changes in their nutritive environment."[164]

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[162] For a biographical treatment of Escherich and overview of his work, see Friedmann, Herbert C. "Escherich and Escherichia." *Advances in applied microbiology* 60 (2006): 134-196.

[163] Kendall (1911), 124.

[164] Kendall (1911), 125.

Pathogenic bacteria were for the most part "relatively inert" in this respect.[165] Instead researchers depended on their cultural characteristics for identification as well as their ability to create characteristic lesions in a host animal and specific serum reactions. [166]

These chemical and physiological characteristics of the normal bacteria could be used to build a research program, and that is what Kendall tried to do. These bacteria produced "a definite microbic response to calculable stimuli, notably the food of the host."[167] This characterizable and measurable response was "so marked" that one could experiment with these bacteria by altering the stimuli. In other words, one could map the responses of the normal bacteria by manipulating the diet of the host. This theoretical and methodological innovation brought metabolism and bacteriology to bear on each other through the language of biochemistry. Bacteriology had, after all, formally begun with questions about fermentation and putrefaction—which were the purview of biochemistry until Pasteur (a *chemist* by training) challenged Liebig's theory of fermentation.[168] The processes of fermentation and putrefaction would provide for an accounting of bacterial action; and defining the diet in metabolic terms would provide a way to bring the two into experimental conversation. By varying the diet—either carbohydrate, which brought about fermentation—or protein—which brought about putrefaction, one could alter the character of the bacterial population or "flora" in the intestines by manipulating the diet. Experimental study of such bacteria needed to depend on the

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[165] Kendall (1911), 125.

[166] Kendall (1911), 125.

[167] Kendall (1911), 137.

[168] See Debré, Patrice, *Louis Pasteur*. Baltmore: Johns Hopkins University Press, 2000, Chapter 5: "Fermentation and Life," 82-114.

manipulation of the nutrient environment to determine how the bacteria responded. This, for Kendall, was in line with the new, modern style of science—the “dynamic” approach that he felt was needed in bacteriology.

Kendall tried to institutionalize his new field. He built on the battery of papers he’d published in biochemistry and medical journals about his new methods and science in the 1910s with a larger statement of his approach. In 1916, he published a textbook on bacteriology with the renowned publishing house Lea & Febiger; it sold well enough to receive a second edition on 1921.[169]

Kendall dedicated his book to his inspiration, Theobald Smith, and quoted him again as he often did with his articles, as a way to declare his purpose and his stance on bacteriology as a field. To that end, Kendall’s book was unique from the others on the market at the time because it treated intestinal bacteriology as a subfield in its own right. For Kendall, intestinal bacteriology was a self-contained branch of bacteriology, with its own methods, rationale and theory. His book title reflected this; it was called *Bacteriology: general, pathological and intestinal*.

While the section on Intestinal Bacteriology was presented with equal weight in the title, it was a much slimmer section of the book. Lea and Febiger’s ads for the book made sure to stress that the book fully covered the basics of medical bacteriological practice-- morphology, staining, diagnosis and culturing techniques –but also highlighted the intestinal section as a unique selling point of the book—as well as the more general philosophical approach that

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[169] Kendall, Arthur Isaac. *Bacteriology: General, Pathological and Intestinal*. New York: Lea & Febiger, 1921.

Kendall was pushing on the field; i.e. the importance of "the chemistry of bacterial activity" for a thorough understanding of the nature of bacteria.[170]

Kendall's bacteriology textbook was initially well-received, though some in the medical community did not think that the section on intestinal bacteriology merited such attention. *The Journal of the American Medical Association* dismissed it as a harmless indulgence, noting that the chapter, based so heavily on Kendall's own work, would be welcomed in the field.[171] The second edition of the book, published just five years later in 1921, was met with a less kind reception. The *American Journal of Public Health* chided Kendall for not keeping up with the field that he had been so instrumental in creating. While "much knowledge [had] been gained, and much doubt has been thrown on some matters on which we thought we had definite knowledge," the references in the book were "exceedingly old" and the book was dismissed as unreliable and "not well balanced."[172] "One gets weary of the frequent references to the author, who quotes himself 76 times," lamented the reviewer.[173] Obviously in the period between the mid-1910s and the early 1920s, others had taken up the call to study intestinal bacteriology; researchers were interested in the questions that Kendall was asking, and the methods that he had elaborated.

While Kendall's work was acknowledged by the behemoth that was pathological bacteriology, it also impacted medical and scientific researchers in other fields. These included

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[170] Ad for book, *American Journal of the Medical Sciences* 153 (1917), 14.

[171]"Book Notices: Review." *JAMA* 68, (1917): 393.

[172] "Books and Reports Reviewed," *American Journal of Public Health,* 952, 1922. Review by MP Ravenel.; p. 952-3. The reviewer was Dr. Mazyck Ravenel, prominent bacteriologist and later editor of the *American Journal of Public Health*.

[173] Ibid.

pediatricians like Langley Porter at the UCSF Medical School's Hoover Foundation who were interested in the relationship between intestinal flora and infantile diarrheas (a position first advocated by Escherich in the late 19th century) and biochemists like Conrad Elvehjem at Wisconsin's school of agriculture, who was interested in the ability of intestinal bacteria to transform their nutrient environment and thus impact nutrition and diet for their animal host. Most visibly, it impacted researchers like Leo Rettger, medical and agricultural bacteriologist at Yale, who were interested in the intestinal flora and its potential general health benefits with respect to diet for animals and humans.[174] This new field flourished in the 1920s as researchers sought to find a way to turn the insights of intestinal bacteriology into a rigorously studied and scientific therapy that could succeed where Metchnikoff's Bacillus Bulgaris therapy had failed.

Leo Rettger and "The Science of Bacteriology"

Leo Rettger born in Indiana in 1874, earned a PhD in physiology and physiological chemistry from Yale in 1902 and then turned his attention towards the then quite new field of bacteriology. He started out asking fundamental questions from a physiological standpoint, writing about the antagonisms between bacteria and their products, and doing biochemical studies of putrefaction.[175] He became an eminent bacteriologist by the 1910s, ascending to the presidency of the American Society of Bacteriologists by 1917. In that year, he laid out his

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174 See Porter, Langley, and Charles Hunter Dunn. "Some studies on sugar in infant feeding." *American Journal of Diseases of Children* 10.2 (1915): 77-86 and Nath, H., et al. "Microorganisms in the cecal contents of rats fed various carbohydrates and fats." *Journal of Bacteriology* 56.6 (1948): 783.

175 Rettger, Leo F. "The Antagonism of Bacteria and their products to other bacteria." *The Journal of Infectious Diseases* 2 (1905): 562-568.

vision of what bacteriology should be—a close colleague of his would call it his "creed,"—at the American Society of Bacteriologists' annual meeting in 1917 in his presidential address. The point was to determine just what bacteriology should be as a science in its own right and on the same level as more established sciences. In his speech, "The Science of Bacteriology and Its Relation to Other Sciences,"[176] he praised applied bacteriology for leading to many developments and successes, but argued that the science of bacteriology was still in its infancy, and just starting "to emerge from its peculiarly chaotic state."[177] In his address, he made a case for bacteria as worthy of their own science:

> "To study bacteria as the ornithologist does birds, or the geologist, rock formations--in other words, to learn nature's secret in so far as it is revealed by this large group of living organisms is indeed as truly a scientific inquiry as the most profound investigation into the structure of the protein molecule. Nor need such a study be limited to organisms which are of no interest to the student of medicine. The general student of bacteriology is just as much entitled to a knowledge of the typhoid bacillus in its relation to environment and natural habitat as he is to a full understanding of the character of Bacillus subtilis, what its common places of residence are, and what its economic role may be."[178]

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[176] Rettger, Leo F. "The Science of Bacteriology and its Relation to Other Sciences," *Journal of Bacteriology* 3, no. 2 (1918): 103.

[177] Rettger (1918), 113.

[178] Rettger (1918), 104.

Bacteriology, he argued, had “been holding itself in bondage” to pathology for too long.[179] Despite its usefulness to other fields and sciences, from botany to hygiene, Rettger stressed that like any science, it required *its own* methods as well as *its own* subject matter. Furthermore, bacteria needed to be studied with the same depth and breadth as any other biological class of organisms. And finally, bacteriology deserved the same respect and rigorous training as any other science. He took the poor state of training in the field to task.[180] He wanted bacteriology to be considered with the same seriousness as chemistry or physics--as a *fundamental* science.[181] Being a bacteriologist should not, he insisted, be the same thing as being a laboratory technician; it needed to require more than the ability to “pour gelatin and agar plates and to count colonies.”[182]

Like his predecessor Smith, Rettger was interested in bacteriology as a science rather than as a technical tool for pathologists. Rettger was part of the larger discussion happening in the bacterial world around what a proper science of bacteriology should be and echoed some of the concerns that Smith and Kendall had voiced. He would build on the Kendall’s work to develop an intestinal therapy.

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[179] Ibid, 103.

[180] Ibid, 104

[181]Rettger stated it as follows: “How can a bacteriologist be made in three or six months, when it takes at least as many years to produce a chemist, a physicist or an electrical engineer? It is my firm conviction that we cause irreparable injury to our science when we recommend for positions men or women who have not had the same advanced training that is as a rule required of the chemist, for example.” Rettger (1918), 104.

[182] Ibid, 104.

Lactobacillus Acidophilus Therapy

Rettger believed that a proper science of bacteriology built along the lines of Kendall's intestinal bacteriology could be leveraged for intestinal therapy. For Rettger, the intestinal bacteria that were the target of Metchnikoff's therapy needed to be understood from a scientific perspective. Kendall, his colleague on American Medical Association's Council on Pharmacy and Chemistry's Committee on Lactic Acid Ferment Preparations, shared this view.

Rettger was based in the Department of Bacteriology at Yale and at the Storrs Agricultural Station. He began investigations into the "so-called *bulgaricus* product," referring to the Metchnikoff sour milk treatment skeptically, and other lactic acid bacteria at Storrs.[183]

Rettger wrote two books that exemplify the transition that Kendall was hoping for in medical bacteriology—from pure intestinal bacteriology to a therapy built on its principles. The first, *A Treatise on the Transformation of the Intestinal Flora: With Special Reference to the Implantation of Bacillus Acidophilus*, he co-wrote with his collaborator Dr. Harry Cheplin and was published in 1921.[184]

The "treatise" was a comprehensive investigation of how to correct the bacterial balance in the intestines and based on an extensive set of studies at Yale. It echoed Kendall's contention that "reformation rather than annihilation of the intestinal flora" was the goal for maintaining

[183] Rettger, Leo F. "The influence of milk feeding on mortality and growth, and on the character of the intestinal flora." *The Journal of Experimental Medicine* 21 (1915): 365.

[184] Rettger, Leo Frederick, and Harry Asher Cheplin. *A Treatise on the Transformation of the Intestinal Flora: With Special Reference to the Implantation of Bacillus Acidophilus*. New Haven: Yale University Press, 1921.

good intestinal health.[185] This "reformation" could be accomplished through the "implantation" of Lactobacillus Acidophilus. It could do what Metchnikoff's bulgaris could not—implant itself in the intestines as plants in the soil, and thus transform the bacterial population.

Acidophilus Milk in the Public Sphere: A Scientific Cure for Modern Life

In the interim between this book and its follow up (1935's *Lactobacillus acidophilus and its Therapeutic Application)*, the acidophilus milk industry flourished. With the proof of a "treatise" behind them and sensing a ready marketplace, Rettger and Cheplin wasted no time in moving from research to therapeutic product. They applied for a patent on the production of acidophilus milk in 1921, the same year that they published their work on the intestinal flora. [186] In anticipation of the patent's approval, Cheplin opened Cheplin Biological Laboratories in Syracuse NY in 1923 to sell Acidophilus Milk to the medical community. The patent was granted in August 1924 for a new "beverage" that the pair named "acidophilus milk."[187] In the patent application, Cheplin and Rettger were at pains to distinguish it from Bacillus bulgaris milk, indicating that their product was completely new, if similar to other sour milks already on the market. They stressed its "therapeutic property" in the patent as the beverage's ability to become implanted in the human intestinal track, and thus to transform the bacterial flora there.[188]

[185] Kendall, (1911), 151. There were many who believed that removal of the colon completely was the best way to solve intestinal ills. See Whorton (2000), Chapter 8.

[186] Rettger, Leo F. and Harry Asher Cheplin. "Beverage." U.S. Patent 1,506,501 August 26, 1924.

[187] Ibid.

[188] Ibid.

Cheplin Biological Laboratories did not market their newly patented product directly to the public. Instead, they marketed their product to the medical community for a variety of medical ills (mucous colitis, chronic diarrhea, intestinal toxemia or constipation) in professional journals like the *American Journal of Medical Sciences* and the *Journal of the American Medical Association*.[189] For mucous colitis, constipation, intestinal toxemia and chronic diarrhea, the benefits were variously bowel movement regulation, the relief of abdominal pain and intestinal gas; fatigue, as well as a change in the mucous-y and bloody stools into healthy stools.

Scientists were increasingly concerned about dosage in commercial preparations of acidophilus, like pills, as indicated by bacteriologist Nicholas Kopeloff's 1924 article in *Archives of Internal Medicine*.[190] Tablets were available to the medical profession as early as 1917 as Bacid, through the Arlington Chemical Company, a Yonkers, NY based producer of medicines.[191] Bacid, which was advertised throughout the medical and drug dispenser

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[189] Cheplin's acidophilus milk was not the only acidophilus milk product being advertised in the American Journal of the Medical Sciences. Lederle Antitoxin Laboratories also advertised there beginning in 1924. Lederle's acidophilus milk had also been accepted by the Council on Pharmacy and Chemistry of the American Medical Association in January 1922 and went about targeting physicians in the *American Journal of the Medical Sciences* in January 1924. It began by taking the same approach as Cheplin Biological laboratories did, specifying what conditions could be treated with acidophilus milk in bold headline (e.g. intestinal toxemia), describing the symptoms that could be relieved (gas, aching limbs, fatigue), and noting the scientific principle of the treatment—"bacteriological simplification of the intestinal flora." It also noted that it was Council accepted in the ads, as Cheplin did, and offered information and physician's sample upon request. But unlike Cheplin, the ads were smaller and less aggressive. Lederle was a large company that had been around for a long time, a well-respected producer of antitoxins for decades. Cheplin was at pains to set itself apart, hence the repeated references to Cheplin's own expertise as the scientist/clinician involved in the research and the details. Lederle seems to have won this little ad war—Cheplin ceased advertising in the journal in September of 1924 while Lederle continued at least through the end of the year.

[190] Kopeloff, N. "Clinical Results Obtained with Bacillus Acidophilus," *Archives of Internal Medicine* 33(1924):47-54.

[191] See ad for Bacid tablets, capsules and liquid cultures in the *American Journal for Medical Sciences* 163 (1922): 15; *American Journal of Clinical Medicine* 29 (1922): 2.

professional press in everything from *Science* to the *Medical Woman's Journal* to *National Drug Clerk*, to *The American Physician*, sold well.

The liminal status of acidophilus products was indicated in the trade magazine *Printer's Ink* in 1928 in its description of acidophilus milk: "It is not a drug, though it is sold in drug stores. It is scarcely a medicine, though it is prescribed by physicians. It is simply a scientific means for re-implanting in the intestinal tract healthful bacilli which nature intended to be there."[192] Acidophilus milk producers switched their advertising strategy in 1927 to educate, what Printers Ink (the advertising industry trade magazine) called "Mr. and Mrs. Everybody" about the wonders of acidophilus milk.

Walker-Gordon Laboratory Company, a producer of certified milk products with "scientifically operated" farms was purchased by The Borden Company in 1929 as Borden moved to expand its dairy businesses with a rash of acquisitions of fourteen dairies.[193] Walker-Gordon targeted the public. Like Lederle and Midwest-based Brook Hill, which provided acidophilus milk for Walgreen Drug Store (it was available for 20 cents a glass at Walgreen's fountains), the central argument of the ads was about "vitality." Before the purchase, the character of the advertising for their acidophilus milk product, which launched several years after Cheplin and Lederle, emphasized the lack of vitality characteristic of modern Americans. In one ad, from the New York Times in October 1927, the ad characterizes modern life and illustrates its point with an image of spectators at a boxing match: "Exercise by proxy, soft, rich foods,

[192] *Printer's Ink*, 143 (1923): 1.

[193] The Borden Company Annual Report, 1929.

sedentary work."[194] The effects of these conditions could be prevented, the ad argues; "vitality and vigor" could be "restored" through the use of acidophilus milk. The effects of these conditions are specified as well—chronic fatigue, depression, shattered nervous systems—these manifested in "modern city life's most baffling ailment—intestinal sluggishness." Another ad reinforces the consequences of this new sedentary life ("minutes for meals, hours for movies, an empty gym" its headline laments) and again links "sluggish intestinal tracks" with "lowered vitality."[195] Yet another ad spells out the connection: "soft, rich foods" and "sedentary indoor lives" encourage "germs of decay" to "take possession" of our digestive tracts; these germs produce poisons that are absorbed by the blood and carried "to every part of the body" resulting in generalized symptoms.[196] These germs of decay are "driven out and replaced by" the "healthful bacillus Acidophilus" to restore health.

This new strategy placed Acidophilus milk beside a host of other popular health products available to the layman or laywoman that would revitalize and reinvigorate their bodies and lives. It was a peculiar product in that it was both a scientific and a natural remedy. As an ad from 1928 claimed, the "rush of modern life," "our faulty diet," and "the lack of proper exercise" were causing American nerves to fray and bodies to slump.[197] These "artificial conditions" could be combated with Acidophilus milk.[198] It would precipitate "a remarkable return of physical

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[194] Walker-Gordon Acidophilus Milk ad, October 27, 1927, *New York Times*, 25.

[195] Walker-Gordon Acidophilus Milk ad, November 10, 1927, *New York Times*, 16.

[196] Walker-Gordon Acidophilus Milk ad, December 9, 1927, *New York Times*, 18.

[197] Walker-Gordon Acidophilus Milk ad, *Daily Boston Globe*, June 6, 1928, 21.

[198] Walker-Gordon Acidophilus Milk ad, June 19, 1928, *New York Times, 15.*

vigor, … buoyancy and well-being" that would provide the energy needed to succeed in modern life. [199]

As one ad put it, the action of these germs of health enabled you to "win back your lost heritage." [200] The key thread in these ads during 1927 is that acidophilus milk could be a cure for modern life; a way *back* to "optimism, mental ease, and physical vitality."[201] This was about restoring the *natural order of things* through a scientifically mediated natural remedy—a point stressed in many ads, which often noted that their product was produced under the "closest supervision by highly trained bacteriologists" or the laboratory that they collaborated with.[202] Ads also appealed to scientific authority more generally in their pitch to the public with ads picturing scientific figures and 17th and 18th century engravings indicating "characteristic stages in the development of medicine from early speculations to the scientific achievements of modern medicine."[203] Drs. Elie Metchnikoff and Christian Herter made appearances in the new ads, along with photomicrographs of acidophilus bacilli next to a bottle of the milk. In these ads the biological origin story of bacillus acidophilus is told. In previous ads, it was enough merely to say that acidophilus milk provided friendly bacteria to combat and crowd out "the germs of decay." Now the story of these "wholesome, friendly organisms"" was explained: they were the benign "bacteria of infancy" which thrived on the "natural diet of infancy," milk, which was

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[199] Walker-Gordon Acidophilus Milk ad, June 6, 1928, 21; *Daily Boston Globe*; Walker-Gordon Acidophilus Milk and July 2, 1928, *Daily Boston Globe*, 21

[200] Walker-Gordon Acidophilus Milk ad, November 29, 1927, *New York Times*, 20.

[201] Walker-Gordon Acidophilus Milk ad, December 16, 1927, *New York Times*, 20.

[202] Walker-Gordon Acidophilus Milk ad, *New York Times*, October 3, 1929, 19.

[203] Walker-Gordon Acidophilus Milk ad, *New York Times*, February 24, 1930, 13.

"nature's most nearly perfect food"[204] But as you grew to adulthood and began to eat "all sorts of foods," the "germs of decay" took over, produced poisons and caused the plethora of common digestive disorders. Acidophilus milk was a means to "Renew the youth of your digestion" by "correct[ing]" your digestion.[205] It was not your fault if your digestion was faulty; rather, the ad claimed, modern diet was to blame. We are "below par;" one ad reasoned, because "our food is 'below par' in certain nutritive elements."[206] Acidophilus milk could help "correct" that deficiency. The ads aimed to educate as a means to sell.

In the 1940s, Acidophilus milk advertising dropped off as interest in acidophilus milk as a health food product diminished as well. In ads, the focus on the rhetoric of good germs also diminished by this time as the focus became regularity and constipation. The link between digestive health—and taking this regularly for that purpose and good bacteria was lost or at least buried. The war marked an end of an era, as exemplified by Cheplin Laboratories. In 1943, Bristol Meyers purchased the company and converted into a penicillin production site because its fermentation processes and infrastructure which were used for acidophilus could be transferred to penicillin production fairly easily.[207] The therapeutic, good germs of the intestine came to be overshadowed in the antibiotic revolution by good germs who could be harvested and extracted to kill bad ones.

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[204] Walker-Gordon Acidophilus Milk ad *New York Times* April 6 , 1929, 16; Walker-Gordon Acidophilus Milk ad *New York Times* June 24, 1929, 8; Walker-Gordon Acidophilus Milk ad *New York Times* May 12, 1930, 13.

[205] Walker-Gordon Acidophilus Milk ad *New York Times* Mar 6, 1929, 14; Walker-Gordon Acidophilus Milk ad *New York Times* April 16, 1929, 16.

[206] Walker-Gordon Acidophilus Milk ad, *New York Times* October 3, 1929, 19. This ad notes "promotes regular elimination" and "hence the tremendous public interest in corrective foods."

[207]See "The Pharmaceutical Sector," by John Northrup, in *The Business Of Healthcare Innovation*, ed. Lawton R. Burns, Cambridge University Press, 2005, 38.

Conclusion

World War II marks the end of the "health germ" narrative as a cultural and scientific phenomenon until the recent explosion in enthusiasm for probiotics in the 21st century.[208] The overwhelming cultural force of antibiotics reshaped the narrative around germs in such a way as to crowd out virtually everything else. Acidophilus milk and acidophilus products became a tiny, specialty market until the emergence of the animal and dairy probiotics and prebiotics industry in the 1980s.[209]

Theobald Smith's call for a pure science of bacteriology would eventually be answered by the 1940s, when the field of "general bacteriology" acquired the hallmarks of an institutionalized science—societies, training programs, journals and professional networks.[210] The general bacteriologists approached bacteria as objects of study in their own right, as Smith had argued for. Consequently, general bacteriology bridged the narrow silos of agriculture, industry and medicine to address fundamental questions about bacteria; bacterial nutrition, bacterial metabolism, bacterial physiology—and bacterial ecology were all included under the auspices of general bacteriology. General bacteriology, however, would be come under fire for

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[208] The probiotics industry is a huge global industry today; hitting $28 billion in 2011 and expected to double by 2018. "Probiotics Market – Global Industry Analysis, Market Size, Share, Trends, Analysis, Growth and Forecast, 2012 – 2018" August 30, 2013. http://www.prweb.com/releases/2013/8/prweb11077944.htm. There is also an explosion of literature claiming a probiotics revolution. See, for example, Huffnagle, Gary B. *The Probiotics Revolution: The Definitive Guide to Safe, Natural Health Solutions Using Probiotic and Prebiotic Foods and Supplements*. Random House LLC, 2008.

[209] See also Floch, M. H., and A. S. Kim. "Intestinal microecology," *Probiotics: A Clinical Guide*. SLACK Incorporated, 2010.

[210] See Kohler, Robert E. "Innovation in normal science: Bacterial physiology." *Isis* 76 (1985): 162-181 and Spath (1999).

its own limitations as it became more and more focused on particularly productive model organisms like *E. Coli* in the middle of the twentieth century.[211]

Kendall's intestinal bacteriology was, as he had indicated in his research papers and in his book, to a large extent a study of bacterial metabolism. His study of intestinal bacteriology was part of a broader research program into bacterial metabolism that he began with his intestinal bacteriology studies, and continued through the mid-1940s (Parts 1 through 121!) primarily from his perch as Professor of Bacteriology, Dean and then Research Professor of Bacteriology at Northwestern University Medical School, publishing primarily in the *Journal of Infectious Diseases*.[212] Kendall virtually abandoned the term "intestinal bacteriology" after the second edition of his book was panned, and spent much of his remaining career investigating similar terrain as "studies in bacterial metabolism."[213] By the time he retired in 1942 and finished his series in 1945, general microbiology had subsumed and surpassed his work.[214]

But the intestinal bacteriology research had established a framework for the relationship between bacteria and body. The intestinal bacteria were the stars of this field, and their machinations were important in order to manage the ill-effects of first putrefactive bacteria and secondly to transform the population of the bacteria living in the gut through implantation of

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211 See Spath (1999). .

212 See his series of articles on bacterial metabolism, started in 1913 and extending through the 1930s, beginning with Kendall, Arthur I., and Chester J. Farmer. "Studies in bacterial metabolism. I." *Journal of Biological Chemistry* 12 (1912): 13-17; ending with Kendall, Arthur Isaac. "Contagiousness of Poliomyelitis: Studies in Bacterial Metabolism: CXXI." *Southern Medical Journal* 38 (1945): 593-595.

213 Kendall stops using the term "intestinal bacteriology" in his published work after the second edition of his textbook was published in 1921. Afterwards, "bacterial metabolism" is his characterization of choice for his work, linking his work to the emerging scientific field of bacterial metabolism.

214 See "The Deans: Arthur Isaac Kendall, Dean 1916-1924," *Northwestern University Medical School, 1859-1979,* by Leslie B. Arey (published by Chicago: Northwestern Medical School). 461-5.

microbes into the soil of the intestinal tract. The body, though the beneficiary of such therapy, was very much background, an environmental setting and set of conditions for the unfolding of a bacterial drama.

But his early research on intestinal bacteriology became part of the conventional wisdom in medical bacteriology. It was incorporated into Hans Zinsser's popular bacteriology textbook, which became the gold standard in the field. This text exemplified the typical treatment of the body's bacterial flora in medical bacteriology in the 1920s.[215] In the fifth edition of the Zinsser book, published in 1922, the section on the bacterial flora was added, relying heavily on Kendall's research, textbook and papers. Unlike in Kendall's book, there was no section on intestinal bacteriology. Instead, the bacterial flora of the human body was treated in a chapter on the "bacteriological examination of material from patients" in the first section of the book, which was on the general biology of bacteria and bacteriological technique--in other words, the fundamentals chapter.[216] It was not treated as a special case which required special attention or a particular approach, like in the following chapters which treated well defined fields like immunity and infection, or pathogenic bacteria, which unsurprisingly took up the lion's share of the book.

The primary concern in Zinsser's book with regard to the bacterial flora was the importance of identification for correct diagnosis and identification of pathogenic bacteria. In Zinsser, it is the intestinal bacteria that receive special attention because of their relation to diet and the close resemblance between nonpathogenic intestinal microbes and pathogens that may

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[215] Zinsser, Hans (1922). *A Textbook of Bacteriology*. (5th edition). New York: D. Appleton & Company.

[216] Ibid, 206.

invade there.[217] It was primarily an exercise in identification and classification—the very things that Kendall was attempting to move medial bacteriology beyond. But in the 1930s, Zinsser's treatment of the microbes that lived in and on the body changed. The concept of "bacterial ecology" became part of the medical bacteriological cannon. In the next chapter I examine how ecological concepts changed ideas about the relationship between bodies and their germs.

[217] Zinsser (1922), 224.

Chapter 2: The Ecology of the Mouth: Dental Bacteriology and the Sciences of the Normal Flora, 1900s-1950s

Introduction

The bacteria flora in the gastrointestinal canal, on the skin, in the mouth and elsewhere on and in the body were collectively called the "normal flora." This category of bacteria occupied a marginal status in bacteriology. Medical microbiology's focus on pathology meant that they were given short shrift, and as discussed in the last chapter, the infrastructure of the medical bacteriology laboratory did not lend itself to the study of the kinds of microbes that dominated the normal flora. These flora were different in kind from the foreign invaders who came in, established themselves and through proliferation created a pathogenic state in the body that could destroy the host. The normal flora were bacteria that were well adapted to the conditions in the body, and in fact, whose lives depended on their ability to work *within* the system. These bacteria tended to not be amenable to the culture media and cultivation techniques of medical bacteriology.

Furthermore, in an age of pathogen hunting, there was little prestige or reward attached to studying them what were considered innocuous and harmless parasites that were not implicated in infectious disease. As with the intestinal bacteria, the normal flora were seen as living within or on particular environments of the body. They were described in terms of geographical zones—categorized by the bodily environments in which they lived and often classified as such.[218] Though this notion of the body as environment for the flora would suggest that soil

[218] Theodor Rosebury, who wrote the first comprehensive treatment of the normal flora in 1962, described the state of the field in the earlier twentieth century as follows: those studying the normal flora "dealt with the subject piecemeal, as though the various inhabited loci in man are ecologically different continents." Rosebury, Theodor,

bacteriology in particular would be an apt resource for methods and approaches to the environmentally situated flora of the body, agricultural or soil bacteriologists, who investigated the basic processes of productive as well as destructive microbes in real environments, did not investigate the normal flora.

Consequently, there was no community of bacteriologists focused on the normal flora as a whole in the early twentieth century. Beyond the intestinal bacteria, the bacteria on the rest of the body were studied, for the most part, by bacteriologists in those clinical specialties that were centered on a particular body area or organ.[219] These were essentially bulwarked fields, and developed at different rates.[220]

Microorganisms Indigenous to Man, New York. McGraw-Hill Book Company, 7 and see chapter 6 for taxonomic practice.

[219] The vaginal flora, sharing as it did some characteristics with the intestinal flora in terms of the prominence of lactobacilli, were studied by those trained in intestinal bacteriology. See for example, Louis Weinstein, who co-authored Rettger's 1935 book on acidophilus therapy, and who later became a prominent infectious disease specialist and one of the leading figures in the study of the impact of antibiotics on the normal flora. See Weinstein, Louis, "The Bacterial Flora of the Human Vagina." *The Yale Journal of Biology and Medicine* 10 (1938): 247-60; *Lactobacillus Acidophilus and Its Therapeutic Application* from 1935. Leo F. Rettger, Maurice N. Levy, Louis Weinstein, and James E. Weiss, *Lactobacillus Acidophilus and Its Therapeutic Application* (New Haven: Yale University Press, 1935); Weinstein, Louis. "The complications of antibiotic therapy." *Bulletin of the New York Academy of Medicine* 31.7 (1955): 500 and Weinstein, Louis. "Superinfection: A complication of antimicrobial therapy and prophylaxis." *The American Journal of Surgery* 107.5 (1964): 704-709.

[220] For example, skin bacteriology began to flourish in the 1940s and 1950s, as dermatologists investigated the flora of the hands of doctors and how to prepare them for surgery, and later investigated the production of bodily order by bacteria and the sweat glands for the army and the hygiene industry. Skin bacteriology would also adopt ecological framework, but as part of the general ecological moment of the 1960s and 1970s, which I address in Chapter 4. For surgical scrub work, see work of Philip Price, a leader in the field. See Price, Philip B. "The Bacteriology of Normal Skin; a new quantitative test applied to a study of the bacterial flora and the disinfectant action of mechanical cleansing." *Journal of Infectious Diseases* 63.3 (1938): 301-318 and Price, Philip B. "New Studies in Surgical Bacteriology and Surgical Technic: with Special Reference to Disinfection of the Skin." *Journal of the American Medical Association* 111.22 (1938): 1993-1996. For body odor work, see Shelley, Walter B., Harry J. Hurley Jr. and Anna C. Nichols, "Axillary odor: experimental study of the role of bacteria, apocrine sweat, and deodorants," *Archives of Dermatology* 68 (1953): 430. Interestingly for what follows, University of Pennsylvania was a leader in dermatological bacteriology.

But there were pockets of medical bacteriology that required their own version of bacteriology based on the habitats they were studying. We saw this in the last chapter with intestinal bacteriology. Smith and Kendall had both operated within the context of medical schools (Smith at Harvard and Kendall at Northwestern), but in medical schools pathology-focused medical bacteriology overshadowed any other perspectives with respect to the body's microbes. Dental schools, however, were a different matter. The mouth was teeming with microbes, and dental infection was complex. The nature of disease in the mouth and the nature of a healthy or hygienic mouth made dental bacteriology particularly ill-suited to conventional medical bacteriology. The institutional location of dental bacteriology, ensconced as it was within dental schools and not medical schools, provided an opportunity for a different approach to bacteriology to flourish and to have lasting and broad impact on the field. Dental bacteriology developed a strong vision of itself and its place within bacteriology. Dental bacteriology, like aquatic bacteriology or soil bacteriology, was particular to its place—and the characteristics of this bodily zone defined its questions and its concepts. Instead of looking to physiological chemistry for models and methods as the intestinal bacteriologists had, dental bacteriologists looked to the emerging science of ecology to provide a framework for their subfield. Like the intestinal bacteriologists, the goal was to create a proper science of bacteriology that studied microbes in a particular environment as biological organisms in their own right. Like Rettger, the goal of these researchers was also to eventually get to therapy--or in their words, a "rational hygiene"--based on a legitimate science of oral bacteriology. This rational hygiene would be distinct from the hygienic vision of conventional medicine because of the nature of microbes in the mouth. But for these researchers, who were located in an already marginalized field—dentistry—and were a marginalized subfield within dentistry, more was at stake. Here I argue that dental bacteriologists appropriated ecological language and concepts to frame their work as scientific and more productive—but also more legitimate--and as distinct from traditional medical bacteriology. It was about developing a better bacteriological science and a more rational hygiene, but also about attaining a higher status for dental bacteriology and dentistry. To do this, in an age of scientific medicine, meant adopting a scientific rationale for an applied field. I argue that the appeal to ecology reinforced the notion that the mouth was a particular kind of environmental context for microbes, and required its own methods and concepts that were distinct from conventional medical microbiology.

Ecology and the Normal Flora: Zinsser's *A Textbook of Bacteriology, 1920s-1930s*

Conventional medical bacteriology as a field, focused as it was on the pathogen, gave short shrift to the normal flora. In textbooks like Hans Zinsser's essential *A Textbook of Bacteriology: a practical treatise for students and practitioners of medicine and public health*, the normal flora chapter—if there was one at all--was largely about how to identify its members at different body sites so as to distinguish them from disease-causing bacteria. Studying the nonpathogenic bacteria was an exercise in collecting, categorizing and naming. But that was the extent to which they were considered important or worth examination.

Through the first six editions of his textbook, Zinsser housed the normal flora in a chapter on bacterial examination called "The Bacteriological Examination of Material from Patients and Outline of Flora of the Normal Human Body," in the fundamentals section of the book ("General Biology and Bacteriological Technique,"). The takeaway was as follows: "In studying bacteria in disease it is of considerable importance to have a clear idea of the morphological and cultural characteristics of forms which are frequently encountered in different parts of the human body under normal conditions. … [Lack of this knowledge can lead to] many erroneous etiological conclusions and …render[s] the investigation of the causation of diseases in the mouth, intestines and other locations extremely difficult."[221] Zinsser then went on to catalogue the normal bacterial flora according to "individual locations," giving spare descriptions of each "habitat" and describing the bacteria present by shape and cultural characteristics.[222] He covered only mouth, nose, and the intestinal tract. The sixth edition followed suit, published with the same chapter structure in 1927. But in the seventh edition, published in 1934, something had changed. In this edition, Zinsser merged two of his foundational chapters: the chapter on the normal flora described above, and "The relation of bacteria to environment, and their classification," which had described relationships between bacteria (antagonism and symbiosis) and relationships between bacteria and its hosts (e.g. parasites and saprophytes).[223] The new chapter was called "Bacterial Ecology and the Flora of the Normal Body." In the ensuing seven years, the science of ecology had become an established field.[224]

Zinsser's textbook was arguably the most authoritative bacteriology textbook for medical students, as is evidenced by the number of editions that it went through (eight in his lifetime; at

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[221] "Zinsser, H. (1922), 216-7.

[222] Ibid., 217. For example, for the mouth subsection he described saliva as a poor culture medium but a good "fluid medium" for many kinds of bacteria, which he then describes.

[223] The definitions given are different than the current definitions; Zinsser described all bacteria living in or on a host as parasites; and all those living elsewhere as saprophytes. He did allow for a category of bacteria that could flourish under either condition: "facultative parasites."

[224] The premiere journal *Ecology* was founded in 1920. The 1920s and 1930s was a critical period in the history of ecology. See Kingsland (2005) and Foster, J. B. and B. Clark, "The sociology of ecology: ecological organicism versus ecosystem ecology in the social construction of ecological science, 1926–1935," *Organization & Environment* 21 (2008): 311–352.

least twelve posthumous ones), the foreign language editions (including Chinese), the numerous printings (38 from its initial 1910 edition through his death in 1940), and Zinsser's stature in the field (he was a member of the National Academy of Sciences and served as President of the American Society of Bacteriologists).[225] His text was a key reference on bacteriology for medical doctors and medical researchers in a variety of specialties for the greater part of the 20th century. So the shift in the presentation of the normal flora from essentially the periphery--"general knowledge" for "bacteriological technique"--to the center—i.e. the basis of a bacterial ecology—had potentially broad impact. It framed the study of the normal flora as a biological entity of interest in its own right.

The language Zinsser used was significant. First, he defined the term "ecology," introducing what may have been a new and foreign concept for medical students and practitioners--"Ecology is the study of the mutual relation between organisms and environment." Then, he *argued* for the term's suitability for medical bacteriology: "The environment of an organism is as much a product of the presence and activities of other living things as it is of nonliving chemical substances and physical forces. It is natural and logical therefore, to apply the term ecology to the study of the general and special phenomena of the mutual relations between bacteria and living organisms and to the mutual relation between bacteria and their non-living environment."[226]

[225] Wolbach, Simeon Burt. "Hans Zinsser." *Biographical Memoirs* 24 (1947): 321; *Zinsser's Microbiology* (1995); ed. Wolfgang Jofklik, Wolfgang. *Zinsser's Microbiology*. New York: Appleton & Lange, 1995.

[226] Zinsser, H. and Stanhope Bayne-Jones. *A Textbook of Bacteriology*. Seventh Edition. New York: D. Appleton-Century Company, 1934, 126.

Over the course of a few years, then, the ground had shifted in the study of the normal flora. The term "bacterial ecology" became increasingly prevalent in medical research and bacteriology and came to denote the normal flora and its relationships; with the host as habitat. The normal flora and its relationships was the target of investigation as researchers began to want to do more than catalogue what was there for the purposes of bookkeeping or taxonomy. This application of ecology to the normal flora was particularly evident early on in dental bacteriology.

Oral Bacteriology and Ecology

Those studying the bacteriology of the mouth had the luxury of being able to approximate the *in vivo* conditions easily in the laboratory and thus could characterize the living system more easily than those studying other parts of the body, like the gastrointestinal tract. Unlike microbes in the gastrointestinal tract which could really only be accessed through fecal matter, those in the mouth were easy to access through saliva samples and swabs. Because they lived in constant contact with the air, they tended to be aerobes or facultative aerobes and so did not present the technical problem that anaerobes did to the laboratory. Anaerobes were notoriously difficult to cultivate; most aerobes were not. The diversity of microbes in the mouth was a given by the 1930s and research into their roles in oral diseases and disorders drove investigations in dentistry departments. Research thrived in dental bacteriology along these lines, with researchers aiming to determine the pathological characteristics of the many microbes found in the mouth. Ecology offered something new to the haphazard quality of this research just as dental training was undergoing a transformation. One of the key figures and sites in both the transformation of dental education and in oral microbiology was Professor Joseph Appleton and his institution, the University of Pennsylvania's School of Dental Medicine. For Appleton, an esteemed bacteriologist who would go on to become Dean of Penn's Dental School as well as head of the Philadelphia branch of the American Society of Bacteriologists, ecology offered a means to make both dental bacteriology and dentistry more scientific.

Joseph L. T. Appleton's "Biologic Viewpoint" and Dentistry

Joseph Luke Teasdale Appleton had been brought up by amateur naturalists, and developed an orientation towards his work that reflected that. Upon graduating from Hamilton College in 1909, he studied invertebrate anatomy at Woods Hole and taught chemistry and biology at Pennsylvania State University. He later turned from basic science to dentistry, following in the footsteps of his dentist father. He had inherited his father's love of biology and enthusiasm for the dental profession, and they drove his passion to bring what he called a "biologic viewpoint" to the field of dentistry.[227] By 1914 he had graduated from University of Pennsylvania's prestigious dental school and become an Instructor in its Bacteriopathology and Microbiology Department. In 1924, he attained a full professorship in the department. He would become a leading voice in the debate over dental education over the next few decades, and implement his "biologic viewpoint" for dentistry as Dean of the dental school (appointed in 1941) and at Penn's Graduate School of Medicine.

[227] Levy, Barnet M. "In Memoriam: Joseph Luke Teasdale Appleton September 18, 1888-January 10, 1980." *Journal of Dental Research* 60.5 (1981): 866-866.

For Appleton, a "biologic viewpoint" was required for a "fundamental approach to oral microbiology."[228] In the 1920s, the first few years after attaining his professorship, Appleton was adamant that dentistry not remain a merely "technical procedure."[229] Dental research was a neglected field waiting to be explored, he believed. He sought to ensure that it would find an institutional place and that a scientific approach would become enshrined in dental training.[230]

But in the first decade of his tenure, Appleton feared the future from his perch at the University of Pennsylvania. He yearned to teach "proper bacteriology" to the dental students under his purview; but was not sure if he would be able to find a way to do so because of the practical orientation of dental training.[231] Proper bacteriology for Appleton meant the same kind of approach to bacteriology that had been championed by bacteriologists like Theobald Smith and Rettger in previous decades: a bacteriology that was scientific and not just a "handmaiden to medicine," or in this case, dentistry. He and his likeminded friend and colleague at Yale, A. Leroy Johnson, kept each other abreast of developments in the field in that direction and lamented the state of affairs in private, sending encouraging notes when one or the other brought their concerns publicly to the profession.[232]

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[228] Letter to Johnson 12/3/51; UPC4.11 archives Joseph Luke Teasdale Appleton Personal Papers: Box 18 folder 34: Correspondence with A. LeRoy Johnson, 1928-56.

[229] Johnson to Appleton, 1/8/29: UPC4.11 Joseph Luke Teasdale Appleton Personal Papers: Box 18 folder 34: correspondence A. LeRoy Johnson, 1928-56.

[230] Letter 5/25/28 from Johnson: notes that "I agree with you that the urgent need is for clinical teachers with the biological viewpoint. That is the thing we are aiming at. The more boys we can get into scientific laboratories, that is, boys of the right sort, the sooner the scientific point of view will reach the clinic. I do not feel that there is a shortcut. The biological p.o.v. is none too evident in medicine so we cannot bank too strongly on the way the med sciences are being presented at present."

[231]Letter to Johnson, 3/6/29 Joseph Luke Teasdale Appleton Personal Papers Box 18 folder 34: Correspondence with A. LeRoy Johnson, 1928-56.

[232]For example, Johnson noted the following with respect to an editorial in the *New York Journal of Dentistry*: "I see where you have been doing some missionary work. It is the best thing of McCall's I have ever read." Letter from

It was a fortuitous time for Appleton and Johnson as dental education was undergoing a general reassessment in the 1920s. Dental schools had been rocked by what became known as the Carnegie Report. The report, *Dental Education in the United States and Canada*, was a five-year study conducted by William J. Gies, a Yale-trained biochemist who founded Columbia University's School of Dentistry (in 1899), and funded by The Carnegie Foundation. The 1926 report examined dental programs and the dental profession in the United States and Canada. Gies visited *every* dental school in Canada and the United States and critiqued each one extensively. He argued that dental education should follow in the footsteps of medical education. He recommended that here should be a two year-college requirement for incoming students for dental students as there was for medical students and that the dental degree should be on par with a medical degree and prepare students for general practice instead of specialties (something he felt should be left to post-graduate specialized training programs). Furthermore, and as was no surprise based on Gies's scientific background, he wanted dental schools to focus more on basic science training and basic biomedical research. Gies had founded the *Journal of Dental Research* in 1919 and was a leading voice in the push to make dentistry a more scientific profession.

Gies's report was controversial—but it sparked debate in the field about how best to reform dental education. Reform was debated vigorously in dental journals in the late 1920s and 1930s. In response to the report, the field took action. Initiatives for dental research at Yale's and the University of Rochester's medical schools were established. There was also discussion of a new dental section at the American Association for the Advancement of Science, and money for new fellowships and positions for dental research created in medical schools. Schools also

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Johnson to Appleton 10/4/33 Joseph Luke Teasdale Appleton Personal Papers Box 18 folder 34: Correspondence with A. LeRoy Johnson, 1928-56.

moved to implement stricter admissions requirements and standards in accordance with the report. [233], [234],[235]

Appleton may not have agreed with all of the recommendations that Gies had made, but he was fully committed making dental schools more research focused and dental training more scientific. [236] Appleton was a vocal enough advocate of dental research that he was named president of the International Association for Dental Research in 1933, an association that was co-founded in part by Gies in 1920. Like Gies, he wore two hats, engaging with both the bacteriology and dentistry communities.[237] In 1936, he finally had the opportunity to implement his vision of a "biologic" dental bacteriology in his department. He had already been engaging in "exploratory surveys" of some of these issues he would set before the school in the past few years on his own recognizance; he now aimed to ramp up the research efforts. Appleton prepared a proposal for a research program with the goal of constructing a "rational hygiene" for the

[233]Letter from Johnson to Appleton, 1/8/29, Joseph Luke Teasdale Appleton Personal Papers Box 18 folder 34: Correspondence with A. LeRoy Johnson, 1928-56.

[234] Letter from Appleton to Johnson 3/9/29, Joseph Luke Teasdale Appleton Personal Papers Box 18 folder 34: Correspondence with A. LeRoy Johnson, 1928-56.

[235] Letter to Johnson from Ernest Goodpasture, a Professor of Pathology at Vanderbilt that he passed on to Appleton. Joseph Luke Teasdale Appleton Personal Papers Box 18 folder 34: Correspondence with A. LeRoy Johnson, 1928-56.

[236] Letter from Johnson 5/22/28: "[Dr. S. H.] Whipple [Dean of Rochester School of Medicine] believes that reform in dentistry cannot come from the present dental schools but must be built up in the way that you and I have often expressed, training young men in science and slowly evolving a new type of teacher and leader. He has absolutely no faith in [William J.] Gies [of Columbia University]. He said that the only man who thought that [Gies'] Carnegie Report was worth a *New York Times* thing was Prichett, and there may be some doubt there." Joseph Luke Teasdale Appleton Personal Papers Box 18 folder 34: Correspondence with A. LeRoy Johnson, 1928-56.

[237] In 1938, Appleton served as president of the Philadelphia Chapter for the American Society of Bacteriologists.

mouth.[238] Appleton detailed his research program to the administration, requesting research as well as administrative support.

"The recognition and evaluation of the factors controlling the kinds and numbers of bacteria in the human mouth constitute a basic problem underlying a rational hygiene of the mouth," he argued in his report.[239] He went on to detail the many ways in which the oral flora varies—over the course of the day, with age, depending on individual—and ways to investigate this variation in the clinical laboratory "systematically and comprehensively." Characteristics of saliva, effect of diet on the flora, and antibiotic effects of oral bacteria were some of the lines of research that he suggested. He stressed the importance of doing the research *in vivo* on human subjects to glean the most accurate—and directly clinically and therapeutically relevant—information. Appleton would later get much of his research program funded through Office of Naval Research, which had a strong dental division, after the war, and the funding would make provision for Ned Williams, who would go on to become a leading oral microbiologist of the next generation and be Appleton's successor as head of the Bacteriology department.

"Rational Hygiene" and Ecology

But what was a "rational hygiene" of the mouth? In this early formulation, Appleton described it in terms of "factors" that affected the types and abundance of bacteria in the mouth,

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[238] "A Prospectus of a Research Program at the School Of Dentistry, University of Pennsylvania." Dated 3/2/36. Joseph Luke Teasdale Appleton Personal Papers Box 19, Folder 6: "Notes on Mouth Bacteria" 1936-9.

[239] Ibid.

Just a few years later he would recast this "rational hygiene" in ecological terms. These factors were the environmental conditions of the mouth.

In the spring of 1940, the year before becoming Dean of University of Pennsylvania School of Dental Medicine, Appleton gave a speech at the Dental Centenary Celebration in Baltimore. The event, billed as "The Greatest Meeting in the History of Dentistry" by its organizers (the American Dental Association was the main sponsor) brought together thousands of dentists and dental researchers from all over the country and beyond to Baltimore, the "birthplace" of American professional dentistry.[240] Appleton made a sweeping case for the value of dental research, and the necessity of an "ecologic" approach in his address. He titled it "The Problems of Oral Microbiology as Problems in Ecology." In it he argued that the focus on pathogens in dental bacteriology had been limiting; and that his "biologic" viewpoint, now rebranded as an "ecologic" approach, offered much to the field:

> "The ecologic approach to the problems of oral microbiology does not mean loss of interest in the actual or potential pathogenicity of particular biotas. But it does mean much more. It means to search for a background or a perspective or a frame of reference in which or from which we can form a juster estimate of the significance of a particular biota; and further, it alone can guide us to that basic knowledge upon which to build a rational hygiene of the mouth in so far as this hygiene is related to the micro-organisms which, from our birth to our death, struggle for existence in our mouths… Only by this broad biologic approach, shall we see in true perspective the activities—not only in

[240] Anderson, George McCullough. *Proceedings, Dental Centenary Celebration: Baltimore-Maryland, March 18, 19, 20, 1940*. Baltimore: Waverly Press, 1940.

relation to human health and disease, but also in relation to the purely intellectual understanding of nature, to which pure science aspires."[241]

Appleton was after a "rational hygiene." What, then, was an "irrational hygiene"?[242] Oral microbiology had suffered from a lack of a systematic, scientific orientation, Appleton argued, because of its focus on pathogens:

"The pathological significance of the organisms found has all but monopolized our interest and attention. This orientation leads at most to a recognition of isolated and unrelated facts."[243]

This focus on the pathological that had dominated the field could not be the basis of a *rational* hygiene. Oral bacteriology had to move away from the focus on pathological bacteria of the mouth if it were to become a true science—and reap the benefits of that—prestige, basic knowledge, and practical developments. An "attempt in the spirit of pure biology" to truly "understand the nature" of the mouth flora would lead to much greater dividends.[244]

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[241] Appleton, J.L.T. "The Problems of Oral Microbiology as Problems in Ecology," In *Proceedings, Dental Centenary Celebration: Baltimore-Maryland, March 18, 19, 20, 1940,* edited by George McCullough Anderson, 282-93. Baltimore: Waverly Press, 1940, 282.

[242] Furthermore, an "irrational hygiene" had broader consequences than just the failure of the field. In the 1930s and 1940s, mouth hygiene products had exploded onto the scene making a variety of unsubstantiated claims about their ability to clean and safeguard the mouth based on the haphazard scientific record. This research, then, had a direct impact on the health of the public. See for example, Van Der Merwe, S. W. "Some aspects of modern dentifrices," *Journal of Dental Research* 7.3 (1927): 327-336.

[243] Appleton (1940), 282.

[244] This was is an old story in the history of science and medicine—Francis Bacon had railed against the empirical study of "particulars" in the 18th century in the establishment of science; and to take a much closer example Harvey McGehee details how "becoming scientific" came to signify the maturation of medical clinical specialties in *Science at the Bedside: Clinical Research in American Medicine, 1905-1945,* Baltimore: Johns Hopkins University Press,

Studying the ecology of the mouth was a means to provide a scientific framework for dentistry. It was important not just as a scientific investigation into nature, it was also essential for *practice*. At stake here was not just the intellectual question of understanding oral microbiology in deeper and more comprehensive terms. This was also about the position and status of dentistry itself in the academy, and within that, the status of Appleton's sub-specialty, oral bacteriology, within dental science. Just the previous year, eminent professor Basil G. Bibby had opined that "Oral bacteriology has fallen into disrepute because it has contributed nothing to the prevention of dental disease."[245] Appleton believed was that the problem lay in its empirical, haphazard approach. If oral microbiology was tp prove its worth to the larger field, it would need to become scientific.

What was needed was a framework, a philosophy of bacteriological dentistry that could only be found through a "biologic" approach that acknowledged the scientific nature of the problem. As Appleton had said in his address in Baltimore, creating a rational hygiene of the mouth required a thorough understanding of the struggle for existence of microbes in the mouth. This was a biological problem, not a technical one. The science most suited to the job, he argued, was ecology. The mouth's microbiota was in a state of dynamic equilibrium, and the science best suited to understand it was the science of relationships—ecology. For Appleton, a rational hygiene of the mouth *required* an ecological approach.

1981. In all of these cases, the concern was the same—how to create a systematic study out of "particulars" gleaned from practical motivations?

[245] Bibby, B. G. "Oral bacteriology: basic considerations bearing on disease and therapy." *Journal of the American Dental Assocaition* 26 (1939): 629.

Ecology was a natural fit for the dental bacteriologist. While other clinical specialties looked to other sciences upon which to model their scientific approach, oral bacteriology chose a science that was predicated on the idea of a complex set of relationships. Appleton kept files on ecology, including articles usually culled from *Science*, and referenced ecology articles and concepts in his work.[246] He fine-tuned his language as the field of ecology progressed. By the early 1950s, he was describing his work in terms that could be taken straight from any contemporary ecology textbook: "the basic approach was ecologic, trying to study the nature and dynamics of microbial populations in their interrelations with a changing environment."[247]

Under Appleton's direction, "ecologic studies" in oral bacteriology were initially undertaken at Penn's School of Dental Medicine in an unsystematic fashion due to lack of funds and staff. His proposal did not reap dividends until he was able to secure outside funding after the war. His pre-war studies comprised studies in three interrelated fields: exploration of factors influencing the number and type of bacteria in the human mouth, interrelations between bacterial populations in the nasal, oral and pharyngeal cavities, and finally the effects of the saliva on the microbes of the mouth.[248] Appleton now wanted to systematize these research interests into a comprehensive program. He was adamant that these three related areas of pure research were" essential" to a "rational hygiene of the oral cavity."[249] The dividends, he believed, would be a

[246] UPC4.11 J.L.T. Appleton Personal Papers: Boxes 20 & 21; various folders.

[247] Letter to Johnson 12/3/51. UPC4.11 J.L.T. Appleton Personal Papers: Box 18 folder 34: correspondence with A. LeRoy Johnson, 1928-56.

[248] Appleton, J.L.T., "A Program of Research in the Department of Bacteriopathology," submitted for Naval Research Grant in October 1946. Joseph Luke Teasdale Appleton Papers, Box 22: Folder 36: "Research project, Navy NR 183-333, contract N6 onr-249, Task Order 5.

[249] Ibid, 1.

direct ameliorative effect on not just oral disease, but also respiratory and gastrointestinal disease, and a "lessening of the reservoirs of airborne infection."[250] Furthermore, this fundamental knowledge was, he claimed, "potentially important" for the defense against and the "effective use of" bacteriological warfare.[251] This bid to show military relevance to the grant-giving body he was appealing to—the U. S. Navy was also an appeal to the broad repercussions of a proper science of dental bacteriology. In order to implement the program, he needed money for minds and hands—technicians—but most importantly, an assistant professor in the department who would spend half his time teaching and the other half on these particular research programs. Appleton already had someone in mind—Ned Williams, a PHD who was newly on the market.

Appleton was interested in a long list of particular research problems and kinds of studies that would be included in the research program. He wanted to do a series of surveys, for example, on the effect of seasonal change on the oral microbiota of different groups of people (by age, sex, economic status, and race) to see if changes correlated with seasonal fluctuations in disease among different populations; the effect of development on the oral microbiota, the effect of diet on oral microbiota (by looking at bottle and breast fed babies). He wanted to determine the "natural hygiene" of the mouth by studying the survival length and rate of bacteria in the mouth in humans and in animal models (only in vivo studies)—and how this varied depending on diet (e.g. carbohydrate heavy), under "normal" conditions, among other conditions. He wanted to study the symbiotic and antibiotic character of oral microorganisms experimentally

[250] Ibid, 1.

[251] Ibid, 2.

through the use of sulfonamides and antibiotics, building on research that had suggested that antibiotics like penicillin disturbed the "microbiotic balance" of the mouth, resulting in "unpleasant local sequellae" like thrush and black tongue.[252] With respect to saliva, he was interested in understanding its effects on various properties of oral bacteria. The Navy's Office of Naval Research granted Appleton about ten thousand dollars for his ambitious research program and funded him through mid-1950s. By 1951, Appleton's program had worked on the quantitative relationships among oral bacteria, done comparative studies of bacteria in the nose, mouth and pharynx, and studies how bacteria can move from one location to another. He now proposed to extend these studies and to focus on a few new questions that could be related to biological warfare.[253]

In April 1953, Appleton and Williams requested another two year extension of his research grant, at $35,000 total, with the Office of Naval research, this time giving his studies a new name—"microbial ecology of the oral cavity."[254] At this time he explained confidently what he meant: "My field is bacteriology, or ecology of the oral cavity, that is, the study of the oral microorganisms and what influences them."[255] He proposed to expand their research to ask questions about the relationships between the bacteria that could be cultivated from saliva under a variety of conditions; how saliva might affect microorganisms of importance in biological warfare with *in vitro* studies, and using "tracer" organisms in a "field study" to see whether and

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[252] Ibid. 9.

[253]"Proposal for extension of the longevity of the study of oral micro-organisms," 1951. Joseph Luke Teasdale Appleton Papers, Box 22: Folder 36: "Research project, Navy NR 183-333, contract N6 onr-249, task Order 5.

[254] "Proposal for an extension of the studies on oral-micro-organisms," April, 13, 1953. Joseph Luke Teasdale Appleton Papers, Box 22: Folder 36: "Research project, Navy NR 183-333, contract N6 onr-249, task Order 5.

[255] Levy (1980): 866.

how it spread among a closed group of individuals.[256] They analogized their studies of the "strategic" areas of nose, mouth and pharynx, as either filters or reservoirs for microbes, with water reservoirs and filtration plants.[257]

The Institutionalization of Appleton's "Biologic Viewpoint" for Oral Microbiology

In 1944, Appleton put out the third edition of his textbook, *Bacterial Infection with Special Reference to Dental Practice.* In this edition, Appleton added a chapter on the ecology of the microorganisms of the mouth. He stressed the importance of oral hygiene and declared that the goal of the book was to improve oral hygiene. The *American Journal of the Medical Sciences* described it as having two purposes: "to give a comprehensive concept of infectious disease" and to provide a reference for practicing dentists.[258] The target audience was both researchers and for practitioners working on patients. The *American Journal of Public Health* also reviewed the book and pushed it towards nurses, doctors and public health administrators. [259]

The fourth edition of the book, which came out in 1950, was widely and positively reviewed. Reviewers noted the ecology chapter as a core part of the text; and in some cases highly praised the discussion of it as fundamental to the study of dental infection.[260] A thorough

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[256] Ibid, 4. They did not receive the full grant, and submitted their final report in January of 1954. "Final Report to Office of Naval Research, Dental branch," January 31, 1954. Joseph Luke Teasdale Appleton Papers, Box 22: Folder 36: "Research project, Navy NR 183-333, contract N6 onr-249, Task Order 5.

[257] Ibid, 1.

[258] Review of J. L. T. Appleton's *Bacterial Infection with Special Reference to Dental Practice*, *The American Journal of the Medical Sciences* 208 (1944): 416.

[259] Wisan, J. M. Review of J. L. T. Appleton's *Bacterial Infection, With Special Reference to Dental Practice*, *American Journal of Public Health and the Nation's Health* 35.10 (1945): 1091-1092.

[260] Letter to FW Hancock, Lea and Febiger from M. D. Appleman, Chairman of the Department of Bacteriology and Harrison Kurtz, instructor, Department of Bacteriology at USC 11/28/51. They had been sent complimentary copies

review in the *British Dental Journal* suggests how much impact Appleton's approach to dental training had become institutionalized. "According to some authorities," the reviewer wrote, "the dental curriculum is too overloaded with academic subjects and such people, might think that this book contains more info than is required by the dental student. Whether this criticism is justified is open to question."[261] The reviewer then went on to defend Appleton's approach, lauding his goal of presenting ""comprehensive concept" of infection via "general principles." Special attention is paid to the question of the oral flora: "In the chapter labeled the ecology of the oral cavity the author rightly stresses that a complete census of the micro-orgs present is as yet impossible. The variation of the flora and fauna in health and disease is well brought out."[262]

Appleton was involved in the transformation of dental education. By the time he stepped down as dean of the Dental School, things had changed dramatically in dental education. In 1950, the Commonwealth Fund put out a report which claimed that students were not getting adequate technical and practical training to be general practitioners.[263] This was in stark contrast to the state of dental schools as described by Gies' Carnegie report of 1926. That report had lamented the unscientific state and overly technical training orientation of dental schools earlier in the century. Just twenty-five years later, the field lamented the opposite problem. But by the late 1950s, dentists were congratulating themselves on having achieved Appleton's goal:

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of book. They opted to use it (135 copies for dental students and hygienists). They "particularly like[d] the way in which the bacteria of the mouth are discussed beginning with the ecology of the oral cavity and in stepwise manner taking up the newer knowledge of caries…" Box 18 Folder 33: Lea and Febiger 1926-56 correspondence.

[261]Review of fourth edition of the book, *British Dental Journal* 88 (1950), 644.

[262] Ibid.

[263] "Integrated Teaching in the Basic Sciences: Report on 5 Years' Experience," *Journal of the American Medical Association* 147 (1951): 1221-3.

establishing dentistry as a full branch of medicine. In 1958, the University of Pennsylvania School of Dental Medicine opened its own research building, celebrating Appleton at the dedication. By 1959, Alfred Asgis, organizer of the first "dentomedical meeting" in the United States in the 1920s, could confidently claim that dentistry had gained "prestige and dignity" as a clinical and research specialty.[264]

Conclusion

In the case of dental bacteriology, attention to the ecological was as much about scientific research as it was about professional standing. The production of knowledge and the scientific framework that that came who had a specific goal in mind to increase the status of not only their subfield—clinical microbiology in a medical specialty—but also to make their *clinical specialty* more scientific—and thus to elevate its and their status. They looked to new approaches to their field to do so, based on the practical problems that they faced in the laboratory and clinic. Dental bacteriologists adopted an ecological framework to redefine and elevate their clinical specialty and discipline (medical bacteriology) as scientific and cutting edge (as opposed to merely rote technician's work); this research helped created the foundation for a mapped bacterial ecology of the body.

The focus of this bacteriology was on bacteria within a particular kind of environment, and the research agenda Appleton developed investigated how varying conditions within the mouth impacted the bacterial population within it. The saliva of the mouth was proxy for the

[264] Alfred Asgis, "Oral Medicine: Foundation of Oral Dental Science and Practice," *Annals of Dentistry* 19 (1960): 2.

environmental conditions of the mouth in the laboratory. Here, as with intestinal bacteriology in the previous chapter, the focus was on the microbes within particular bodily environments.

The sciences of the normal flora looked to ecology as a source for concepts and a framework for the normal flora at different body sites throughout the twentieth century. For example, in skin bacteriology, Professor Mary Marple's 1965 treatment of the skin flora, *The Ecology of the Human Skin*, would bring ecological approaches to the field in the 1960s and revolutionize it.[265] But oral bacteriology was the first to make a case for the productivity of this framework, and to try to build a discipline based on it.

The past two chapters have described how researchers sought to approach the bacteria that lived in and on the body in their own terms, insisting that these bacteria required different scientific approaches and frameworks to study them and to build an effective and "rational" medicine for those parts of the body where they thrived. In oral microbiology, the question of a "rational hygiene" based on a scientific approach to the normal flora was framed in professional status terms with respect to a marginal sub-discipline within a marginal discipline. In the next chapter, I shift focus to the body in this investigation of the microbe-human relationship, to researchers that saw the flora of the body as part of the body's environment.

[265] Noble, W. C. "Skin microbiology: coming of age." *Journal of Medical Microbiology* 17.1 (1984): 1-12.

Chapter 3: The Microbial Body 1.0, 1950s-1970s

Introduction

In this chapter, I describe how researchers in the mid-late 20th century described the relationship between the human microbiota and the body. In this work, microbes were treated as part of the environment of the body conceptually and experimentally in contrast to earlier approaches which treated the body as an environment for microbes. As in previous chapters, these developments occurred at the edges of mainstream science and medicine, but had lasting impact in various domains. Here I examine three approaches to human microbiota through the work of gnotobiologist (i.e. germ-free scientist) Thomas Luckey, medical bacteriologist Rene Dubos, and oral bacteriologist Theodor Rosebury. These three individuals were successful to various extents in shaping broader views of the body and its relationship to the human microbiota. In the 1950s-1970s, their complementary visions of a microbial body focused on the body itself as a cultural, biological and medical object and defined the relationship between microbe and body in environmental terms. Gnotobiology, or germ-free science, extended the pure culture ideal of bacteriology to animals; Thomas Luckey used it to define the human microbiota as part of the body's "biological environment." René Dubos studied the impact of the intestinal flora on the body's normal physiology as part of his larger project to reform biomedicine. And finally, Theodore Rosebury presented the normal flora as a natural environment under cultural and chemical threat to the public. I argue that these three contrasting versions of the relationship between microbes and the human body redefined the human microbiota as an "environment" that shaped the body in intimate ways. These new visions of the body saw microbes as integrally implicated in its normal function, and viewed the human microbiota as important for medicine, biology and culture.

Gnotobiology: Microbes as "The Biological Environment" of the Body

James Reyniers and the "Pure Culture" concept

James Reyniers was a bacteriologist who had created the first germ-free laboratory at the University of Notre Dame in the post-war years. He had spent the 1920s and 1930s on the problem of creating and maintaining germfree life and successfully reared and maintained microbe-free animals in the 1940s to some fanfare.[266] Though there had been attempts to investigate whether life could exist in the absence of germs--a speculative question first asked by Pasteur in the 1885--, Reyniers was not initially interested in answering this question.[267] He was investigating a bacteriologist's questions about bacterial variation in an *in vivo* context (i.e. What are the distinguishing characteristics of a bacterial type in an animal? How can you identify different types of bacteria by their physiological effects and behaviors?).[268] After a few years of investigation, his question about bacteriological experimental methods morphed into a question about experimental animals and spaces. Creating germfree animals and a germfree environment

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[266] Life without Germs," *LIFE*, September 26, 1949, 107-13.

[267] "For several years… I have spoken of feeding young animal from birth with…nutritive products that have been artificially and totally deprived of common microorganisms. If I had the time, I would undertake such a study, with the preconceived idea that under such conditions life would have become impossible." Pasteur (1885). For a history of such attempts, see Kirk, Robert, "Life in a Germfree World: Isolating Life from the Laboratory Animal to the Boy in the Bubble," *Bulletin of the History of Medicine* 86 (2012): 242.

[268] Trexler, Philip P. and Roger P. Orcott, "Development of Gnotobiotics and Contamination Control in Laboratory Animal Science," in *50 Years of Laboratory Animal Science*, edited by McPherson CW, Mattingly SF, Memphis: American Association for Laboratory Animal Science,1999), 122.

within which to maintain them became Reyniers' new goal.[269] The field would bring the "microbial variable" in biological systems under the auspices of the experimenter.[270] Achieving this control would make biology a more "*exact"* science.[271] The goal was to strip biological organisms down to their essentials.

Reyniers saw his new science as an extension of the pure culture concept in bacteriology.[272] Pure culture depended on the complete isolation of a bacterium in a known medium in order to define it and to manipulate it in the laboratory. This was a requirement for a biological object that could not easily be seen or characterized without the technical tools of the laboratory and whose morphological characteristics were not as variable as other kinds of organisms. The creation of germfree life followed the same bacteriological principle—the germfree laboratory was a means to study organisms in isolation as scientific objects in a well-defined environment.

The term that Reyniers chose for the new field clarified his philosophy of "pure units": gnotobiology means *known life* ("gnos") + ("bios"). For Reyniers, to know a biological phenomenon completely was to study it in isolation—"free from all life," and in an

[269] Ibid.

[270] Luckey, Thomas D. *Germfree Life and Gnotobiology*, NY: Academic Press, 1963, 19.

[271] Ibid.

[272] Reyniers (1959), 4.

"uncontaminated environment."[273] It meant the creation of "biological *tabula rasa,"* and the infrastructure necessary to maintain it.[274]

Gnotobiologists saw their science as sharing the philosophy of modern experimental science. As Reyniers explained at a conference in 1959,

> "[t]he need for isolating "pure units" from the natural complex in which they exist forms the basis of analysis . . . [w]hether these pure units are compounds, physical particles, bacteria, animals, or mathematical symbols does not alter the philosophy."[275]

"Pure units," divorced from any kind of natural context, was what a true scientific object was; gnotobiologists wanted to bring this kind of experimental and conceptual precision to the animal body.

James Reyniers' new science captured the imagination of the scientific world in the 1950s and 1960s.[276] By the early 1960s, the study of germ-free life had had acquired all of the trappings of a fledgling science—a battery of methods, dedicated research centers around the world, a government laboratory in the National institutes of Health (the Laboratory of Germfree Animal Research at the National institute of allergy and Infectious Disease), conferences, and a comprehensive textbook.[277] It had moved from a marginal technique to an emerging field with an

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[273] J. A Reyniers, "The Pure Culture Concept and Gnotobiotics," *Annals of the New York Academy of Sciences* 78 (1959): 4.

[274] Reyniers (1959), 4.

[275] J. A. Reyniers, "The Production and Use of Germ-Free Animals in Experimental Biology and Medicine," the *American Journal of Veterinary Research* 18 (1957): quotation on 678.

[276] See Robert Gannon, "Life in a Germfree World," *Popular Science,* August 1962, 90; "Life without Germs," *LIFE*, September 26, 1949, 107-13.

[277] See Reyniers (1959), Gannon, (1962), 90, and Luckey (1963).

increasingly sought after set of techniques that were being applied to problems in chemistry, physics and experimental biology.[278] Reyniers, recognized as the founder of the field, had become an internationally celebrated scientist.[279] Germ-free research enjoyed positive press throughout the 1950s and 1960s and brought a measure of public fame to the field, though it never gained the status of a major biological or biomedical field like, for example, molecular biology would. But gnotobiological animals would become part of the standard battery of experimental animal models for a various kinds of research into the indigenous microbiota through the present day.[280]

But what Reyniers' science did was, as scholar Matthew Weinstein has described it in *Bodies out of Control: Rethinking Science Texts,* was to reveal the normal through the pure.[281] Reyniers' germfree animals could live, but they were not *normal*--for good and for ill. Though their bodies did not decay and they had perfect teeth, they had distorted physiological and morphological characteristics in those parts of the body exposed to the microbiota, like an enlarged cecum (rodents) and lesser variability among animals in those flora-facing organs (chickens).[282] Studying a germ-free animal provided insights into the ways in which its

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[278] Reyniers (1959), 3.

[279] "Notre Dame Scientist to Lecture in Europe," *New York Times*, August 30, 1953, 56.

[280] See for example, Falk, Per G., et al. "Creating and maintaining the gastrointestinal ecosystem: what we know and need to know from gnotobiology," *Microbiology and Molecular Biology Reviews* 62.4 (1998): 1157-1170. In 2008, the International societies for gnotobiology and for microbial ecology held a joint conference, indicated the extent to which they were in conversation by the 2000s. See Midtvedt, Tore. "XVI Symposium of the International Association for Gnotobiology (IAG) & XXXI Congress of the Society of Microbial Ecology and Disease (SOMED) Stockholm, Sweden, 28-30 May 2008." *Microbial Ecology in Health and Disease* 20.3 (2008): 121-121.

[281] Weinstein, Matthew. *Bodies Out of Control: Rethinking Science Texts*. New York: Peter Lang, 2010, 17-28.

[282] Gordon, Helmut A. "Morphological and Physiological Characterization of Germfree Life." *Annals of the New York Academy of Sciences* 78 (1959): 208-220. See p. 219 in particular: "Germfree chickens and rats, in comparison to normal-stock controls, were found to display reduced weight, water, reticuloendothelial tissue and connective tissue content in such organs as are normally in contact with the flora. The same findings, although less extensively

microbiota shaped it. The strange bodies of the germ-free animals and the work needed to maintain them suggested that microbes were not innocuous inhabitants of the body that only mattered when an infectious pathogen loomed, but that they impacted the body's physiology, metabolism and morphology, and thus were implicated in the creation of a "normal" body. Consequently germfree animals were experimental tools that could be used to answer questions about the ways in which the "biological environment" impacted the body.

"Gnotobiology is Ecology": T. D. Luckey's Intestinal Microecology

Reyniers had declared that gnotobiology at its core was about separating an organism from "the natural complex in which it normally exists."[283] Thomas Luckey, author of the first gnotobiology textbook, *Germfree Life and Gnotobiology* (1963), called this "natural complex" "the biological environment" of the body.[284] Luckey joined Reyniers at Notre Dame in 1946 as an assistant research professor in the Laboratory of Bacteriology to work on germ free studies.[285] Luckey, would rebrand gnotobiology as a necessary part of the broader project of ecology in the 1970s with his work in an emerging field that he called "intestinal microecology."

In the late 1960s and the 1970s, a research community focused on intestinal microecology—a successor to the short-lived field of intestinal bacteriology of the 1920s and

tested, were made also in germfree mice. It is assumed that these characteristics of the germfree animal are caused primarily by the lack of the stimulation that would be caused by flora."

[283] Reyniers (1959), 4.

[284] Luckey (1963).

[285] Luckey, T. D. "Sir Samurai TD Luckey, PhD." *Dose-Response* 6.1 (2008): 97-112.

1930s that focused on the microbiota of the gastrointestinal track—coalesced around Luckey. For Luckey, this was an *ecological* project rather than a bacteriological project because microbes were part of the "total environment" of the body in the gnotobiological conceptualization of the animal body. Consequently, gnotobiology was an environmental science that offered an experimental approach for the "biological component of the environment."[286]

For Luckey, the marriage of ecology with gnotobiology created a space for a new subfield centered on the work of researchers investigating the intestinal flora with gnotobiological methods. The goal was to articulate the "microenvironment" of the body through an exploration of that part of the body in which the microbes were most clearly implicated and congregated in greatest numbers--the gastrointestinal tract. For Luckey, an agricultural biochemist by training, the context of the gut made the most sense to focus on as the seat of metabolism and because of the findings of gnotobiology which had shown the extent to which microbes were part of the digestive process.[287] Luckey had been involved in the creation of diets meant to compensate for the lack of microbes in germ free animals.

Luckey organized the inaugural International Symposium on Microecology in 1970 at his home base, University of Missouri, Columbia. It was an apt setting for such a conference because of the interdisciplinary nature of the conference. It brought together researchers in agriculture, animal science, space science (space diets) and medicine, and the University had divisions that spanned this broad range of disciplines. The conference involved the agricultural

[286] Gnotobiology could "open the biological component of the environment to exact qualitative and quantitative description." Luckey, T. D. "Gnotobiology is Ecology." *The American Journal of Clinical Nutrition* 23.11 (1970): 1533.

[287]Luckey had done his doctoral work on vitamin synthesis in germ-free chicks at the University of Wisconsin, Madison under eminent agricultural biochemist Conrad Elvehjem.

school, the veterinary school and the medical school, as well as the Space Sciences Research Center.[288] As an interdisciplinary effort, the symposium received a good deal of support from the school.[289] The conferences focused on metabolism as a way to structure the relationship between the body and its microbial environment. Studies about how the metabolic by-products of the intestinal flora impacted host metabolism, how intestinal flora may be implicated in the immune mechanisms, and how intestinal bacteria may produce carcinogens in the presence of certain host diets were some of the ways in which the body took center stage in these symposia.[290] The proceedings of the first five conferences, all held and UMC were published as special section in the *American Journal of Clinical Nutrition* in a nod to its focus on host metabolism.

Luckey and attendees of the symposia saw great potential for this new field. They imagined what would be needed to properly study the "microenvironment" of the body and called for a Microecology Institute that would help foster the new science. They saw the institute as a "force for environmental control."[291] This institute's purpose would be to study "microbes in our intimate environment" in order to understand how our "interrelationship" with them shaped us and to find means to exploit and control this relationship to improve our health and more broadly, "our quality of life."[292] Luckey imagined the work that the Microecology Institute

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[288] Luckey, T. D. "Introduction to intestinal microecology." *The American Journal of Clinical Nutrition* 25.12 (1972): 1294 and Floch, Martin H., and David J. Hentges. "Preface." *The American Journal of Clinical Nutrition* 27.11 (1974): 1265.

[289] Luckey (1972), 1294.

[290] See Luckey (1972), 1294; Floch and Hentges (1974), 1265 and Luckey, T. D. "5th International-Symposium on Intestinal Micro-Ecology-Preface," *American Journal of Clinical Nutrition* 32 (1979): 108 for descriptions of work; especially Floch & Hentges. See also, Abrams, G. D. "Microbial effects on mucosal structure and function," *American Journal of Clinical Nutrition* 30.11 (1977): 1880-1886.

[291] Luckey (1972), 1294.

[292] Ibid.

would do: defining “microbic environments” under varying conditions, characterizing “host ecologic niches” and the microbes that dwelt there, developing model systems based on these microbes, and investigating host-microbe interactions.[293] These basic studies would have broad impact in his vision: “applications in bioengineering and biocontrol” would be coordinated with “theoretical and philosophic concepts of microecology.” The real world applications of such integrated work would be vast for biomedicine, food production and for space exploration.[294]

At the tail end of the spring term in 1978, University of Missouri, Columbia held the fifth international symposium on microecology. The symposium was deemed important and expansive enough to be published as a special issue of the *American Journal of Clinical Nutrition*. The papers of the symposium comprised the whole January issue of the quarterly journal, with Luckey serving as guest editor for the special issue. Again, most of the papers focused on biochemistry and metabolic investigations (though a session on electron microscopy suggested the broadening of the field’s scope). The conference so well-attended and intellectually vigorous that the conference attendants planned to extend the two day conference to a third day for its sixth occasion.[295] Luckey took the opportunity to reflect on the future of the field in his keynote address.[296] He argued that the field should aggressively investigate medical

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[293] Ibid.

[294] The following details Luckey’s vision: “The institute would pioneer applications of the knowledge of microecology that are so desperately needed to guide innovative activities in such areas as infection-free health centers for aged persons, new parameters for hospital management systems, development of clinical gnotobiology facilities for cancer, transplantation and immune incompetence centers, microflora control for prolonged space flights, positive microbic control for public health practices in under- and overdeveloped areas, and biocontrol in food production.” Luckey (1972), 1294.

[295] Luckey, T. D. (1979), 108.

[296] Luckey, T. D. "Whither, intestinal microecology?." *The American journal of clinical nutrition* 32.1 (1979): 109-112.

topics. Of paramount importance for the field in Luckey's eyes, was the extent to which the articulation of the microecology of the body could be manipulated to improve human health. To this end, he stressed that the field needed to incorporate gastroenterology or "intestinal physiology" if the field was to truly yield a proper understanding of the intestinal microecology and its impact on the body. He illustrated this with an example from his own laboratory (a study on "alimentary kinetics").[297] In short, intestinal microecology had a biomedical imperative, and served to improve the storehouse of biomedical knowledge that could be used to improve human health. He was arguing for the importance of the biological environment of the body for established biomedical fields.

Luckey had given his most lucid description of his view of the relationship between the microbiota and the body at the 1976 Symposium. It was the American bicentennial; Luckey took the historic opportunity to think big about the field and to put it in historical context. "Philosophically an organism is composed of its nature, or genetic potential, which develops in time according to its nurture or environment,"[298] he observed. Luckey broke down the "environment" into three categories--the physical, chemical and biological, and defined "nurture" as any interaction with these types of environmental forces. The biological environment of the body included all forms of life with which a biological organism had come into contact with. The biological microenvironment (as opposed to the "macrobic" environment), was to be assessed both in terms of the number and variety of microbes and their diverse metabolic activities in the intestinal tract. Because the body itself was of primary

[297] Ibid.

[298] Luckey, T. D. "Bicentennial overview of intestinal microecology," *American Journal of Clinical Nutrition* 30.11 (1977): 1753-1761.

importance, Luckey stressed the important of gnotobiological animals as experimental tools that would aid in the investigation of the human-microbe relationship. He contrasted this with knowledge gained from studies of microbes cultured from the intestinal flora in the laboratory. Understanding the dynamics and the metabolic activities of the microbiota was important because this would produce knowledge about how the microbiota impacted the body, not just how the microbes themselves functioned as individual organisms.

The symposium met biannually into the 1980s. [299]In the 1980s, the field of intestinal microecology became subsumed into the emerging research community focused on probiotics, providing much of the scientific basis for the lactobacillus milk, capsule and yogurt industries.[300] But in the 1970s, intestinal microecology what framed as a science offering a new way to understand the body's microbial environment rather than as a resource for industry.

René Dubos: Environmental Medicine and the Indigenous Flora

Renowned microbiologist René Dubos also studied the relationship between bodies and their microbiota in the middle of the century. Luckey and René Dubos mingled in the same communities and were familiar with each other's work on intestinal microbes and gnotobiotic animals.[301] Like Luckey, Dubos saw the microbes of the body as an important and impactful part of the body's environment. Dubos and his colleagues demonstrated that the microbiota shaped

[299] Thomas D. Luckey Papers, University of Missouri, Columbia Archives Box A85-6.

[300] Luckey (2008); see also Floch, M. H., and A. S. Kim.Chapter one: "Intestinal microecology." *Probiotics: A Clinical Guide*. SLACK Incorporated, 2010.

[301] They cited each other's work and attended some of the same conferences on gnotobiological animals.

host physiology and morphology in discrete ways. For Dubos, the indigenous flora and their impact on the body became the experimental basis for his larger project to reform both biological science and medicine.

In the late 1950s, Dubos was comfortably ensconced at the Rockefeller Institute of Medical Research and headed up the well-established Bacteriology and Pathology laboratory. But Dubos was chafing under the constraints of traditional microbiological research. He had come to the conclusion that "the very success of the reductionist approach [in biomedicine] has led to the neglect of some of the most important and probably the most characteristic aspects of human life."[302] In his book *Mirage of Health*, published in 1959, Dubos elaborated on his critique of this reductionist approach, grounding it on a unique perspective on germs. Dubos' book stressed how the eradication of bacteria living peacefully with humans through the use of antibiotics could lead to "a power vacuum into which far more dangerous invaders would be pulled."[303] In the mid-1950s, Dubos had given several of talks and wrote several papers on the relationship between infection, antibiotics and the companion microbes that lived in and on the body. [304] He noted how most humans carry within them microbes that were capable of becoming virulent pathogens, and argued that there was not enough attention paid to the conditions that turned peaceful coexistence into disease. He stressed that a focus on microbe hunting and

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[302] Quoted in Carol Moberg, *René Dubos: Friend of the Good Earth, Microbiologist, Medical Scientist, Environmentalist,* Baltimore: ASM Press, 2005, 122.

[303] Leonard B. Berman, "Different Viewpoint on Germs," review of *Mirage of Health* by René Dubos, published in 1959, publication unknown. RU René Dubos Collection, 450 D851 Box 51, Folder 11. Dubos, René Jules. *Mirage of Health: Utopias, progress, and biological change*. New York: Harper, 1959.

[304] See, for example, René Dubos, "On Living at Peace with Infection," (Address before American Foundation, Nov 15, 1955), RU René Dubos Collection, 450 D851 Box 26, folder 3; René Dubos, "The Germ Theory Revisited" (Lecture given at University of California, Berkeley in March 25, 1954), RU René Dubos Collection, 450 D851 Box 118, folder 4, "Conferences and Lectures;" and "Infection into Disease" (manuscript from ca. 1956), RU René Dubos Collection, 450 D851 Box 26, folder 6.

pathogen eradication had dangerous consequences that resulted in a “mirage of health” that could not last. The achievement of true health would require a different approach to the relationship between microbes and human bodies that examined the nature of that relationship in normal as well as pathological states. Dubos argued that a new way of conceptualizing the germ-body relationship was needed to produce a proper model of the body that could better address the problem of infectious disease. In short, the achievement of health could not proceed from a flawed model of the body. A proper model of the body would need to include its indigenous microbiota.

Dubos took his *Mirage of Health* musings argument into the laboratory in the 1960s. In 1961, Dubos renamed his laboratory at the Rockefeller Institute of Medical Research from “Bacteriology and Pathology” to “Environmental Medicine.” Dubos’ environmental medicine was built on the idea that states of health and disease were essentially the adaptive responses of organisms to environmental conditions, a vision he had laid out in *Mirage of Health*.[305] He expanded upon these ideas in 1965’s *Man Adapting*, which was based on a series of lectures given at Yale.[306]

For Dubos, biology itself needed a reconceptualization. Medicine suffered from its inadequate framework and the limitations of its fundamental orientation to life. The problem with biology was its narrow focus and reductionist method:

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305 Dubos described it as focused on “the effect of environmental factors on the development, health and disease of human beings.” “Annual Report 1969-1970,” RU René Dubos Collection, 450 D851 Box 26, folder 6.

306 Dubos, Rene Jules, *Man Adapting*, Yale University, New Haven, 1965.

“…scientific biology has been identified from its very beginning with the concept that the body is a complex but otherwise ordinary machine, and that detailed analysis of its elementary structures and energy mechanisms is the only valid approach to the understanding of the living organism. Such an attitude had discouraged the scientific study of the biological problems which do not lend themselves to the reductionist analytic methods now in vogue among experimental scientists. In particular, it has inhibited the study of the biological phenomena which are the consequence of the organism's evolutionary history--for example, … the reactions elicited by physicochemical stimuli and various life situations.” [307]

This vision had restricted the possibilities of medicine to engage more successfully with the body because it had limited itself to this narrowly conceived model of the body.

Dubos he had begun to develop his version of *non*reductionist research programs in the 1960s. He aimed to open up the normal functions of human life in order to get a proper picture of health. Dubos’ study of the indigenous microbiota was one of the first domains within which he translated this antireductionist perspective into a research program. It made sense for him to started his environmental medicine research program in his own unquestioned area of competence—microbiology. What, then, would an environmental medical microbiology look like? Dubos’ work investigated this question by placing the indigenous microbiota of the body within the category of environmental impacts that shaped it—in its health as well as disease states.

[307] Dubos, René Jules. “Man’s Nature and Man’s History,” *American Scientist* 53 (1965): 4 - 19.

Soil Bacteriology in the Biomedical Laboratory: Dubos' Environmental Medical Bacteriology

Dubos did not come to the study of the bacteriology from medicine, but rather from agriculture. What would be called his "holistic habit of mind" could be explained by that early training in agricultural and soil bacteriology.[308] Dubos earned his PhD in microbiology under Selman Waksman, the esteemed soil microbiologist, in the department of Biochemistry and Microbiology at Rutgers, and had studied scientific agriculture before then at the Institut National Agronomique in Paris.[309] Waksman, who had come to soil microbiology through a background in farming, had been hugely influenced by the agricultural microbiologist Sergei Winogradsky. Both Winogradsky and Waksman were interested in the chemical processes of living systems, and developed different ways to investigate bacteria in the context of the field from the traditional medical microbiology. Indeed, Dubos had found microbiology boring, with its focus on taxonomy, until he read an article by Winogradsky on his methodological approach to soil microbiology in 1924 which suggested a whole new approach to microbiology to the young Dubos.[310] In that article and in his later work on soil microbiology through the early 1950s, Winogradsky chided microbiologists for focusing so heavily on the technique of pure culture, insisting instead on the importance of studying bacteria *in context*—shifting the focus to their relations in nature and their interactions with their environment. This became a central

[308] Ackert (2012), 149-52; and Gerard Piel and Osborn Segerberg, *The World of René Dubos*, New York: Holt, 1990, xx.

[309] Dubos, René Jules, "The Infinitely Small: Microorganisms in Human Life and in Science," prepared for *Scientists Speak: Biology* (Harcourt Brace and Co., 1959), RU René Dubos Collection, 450 D851 Box 26, Folder 22.

[310] Sergei Winogradsky, "Sur la methode directe dans l'étude microbiologique du sol," *Chimie et Industrie* 11 (1924): 1-8. Winogradsky's "Direct Method" will be addressed in Chapter 5, as an important precursor to the modern field of microbial ecology.

principle in Dubos' work for the rest of his career; he claimed later that his intellectual life had begun with these ideas.[311] When Dubos turned to medical microbiology on the advice of Waksman and took a job at Rockefeller, he brought this orientation with him.

He knew from his training in soil microbiology that the microbial world the extent to which microbes were embedded in environmental relations. He needed to figure out a way to study these microbes and their impact on the body. Dubos spent increasing energy and time on the indigenous flora studies in the 1960s, despite the misgivings of his colleagues at the Rockefeller Institute.[312] Denied adequate funding for these studies from the Institute, he obtained outside funding from the Health Research Council of the City of New York in 1962 and from National Research Council in 1963.[313] Both grants would support the indigenous flora work through the 1960s and into the 1970s.

The studies focused on the impact of the microbiota on the production of health and normal states in experimental organisms. First, he sought to determine whether the microbial flora had a role to play in the susceptibility of experimental organisms to infection and second, he sought to determine whether the indigenous microbiota played a role in shaping their physiological, morphological and metabolic characteristics.[314]

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[311] René Dubos, "Pasteur's Dilemma: The Road Not Taken" (American Society of Microbiology Lecture, Diamond Jubilee Symposium, April 2, 1974). RU René Dubos Collection, 450 D851 Box 28, Folder 13. Also see Hirsch, James G., and Carol L. Moberg. "Rene Jules Dubos: February 20, 1901-February 20, 1982." *Biographical Memoirs. National Academy of Sciences (US)*58 (1988): 135.

[312] Moberg (2005), 123.

[313] RU René Dubos Collection, 450 D851 Box 54, Folder 1, Health research Grant 1962-1975 and RU René Dubos Collection, 450 D851 Box 54, Folder 2, National Research Council, Health, Education and Welfare Grant 1963-74.

[314] RU René Dubos Collection, 450 D851 Box 54, Folder 1, Health research Grant 1962-1975 and RU René Dubos Collection, 450 D851 Box 54, Folder 2, National Research Council, Health, Education and Welfare Grant 1963-74.

Though Dubos did not use germfree animals in his research, he used mice that had been bred and reared in Rockefeller Institute of Medical Research to be free of common mouse pathogens.[315] These mice had defined microbial profiles and were maintained in the Rockefeller Laboratory. Dubos studied the distortions made by the lack of normal microbiota on the bodies of these mice in his lab.

Dubos laid out his perspective and his project in an essay, "Man's Nature and Man's History," published as the introductory essay to his acclaimed book *Man Adapting* in 1965 and on its own in *The American Scientist* that same year.[316] In it he used his research on the indigenous microbiota as evidence for his vision for environmental medicine. His experimental investigations had shown that these microbes were implicated in both the development and maintenance of the health of both anatomical and physiological features of experimental animals.[317] This was proof that environmental stimulation shaped the body in distinct and measurable ways. He extended his research program into the early 1970s before turning from research to become a cultural leader in and proselytizer for the environmental movement.[318]

But in the 1960s, Dubos was focused on the relationship between germs and bodies, and how it could impact the practice of medicine. The changes wrought on the bodies of

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[315] These were the New Colony Swiss Mice, derived from Standard Swiss mice in the 1950s. Dubos, René, Russell W. Schaedler, and Richard Costello. "Lasting Biological Effects of Early Environmental Influences I. Conditioning of Adult Size by Prenatal and Postnatal Nutrition." *The Journal of Experimental Medicine* 127.4 (1968): 783-799; Savage, Dwayne C. "Microbial biota of the human intestine: a tribute to some pioneering scientists." *Current Issues in Intestinal Microbiology* 2.1 (2001): 1-15.

[316] Dubos, René, "Man's Nature and Man's History," *American Scientist*, Vol. 53, 1965, 4 - 19.

[317] Dubos (1965), 23.

[318] See Moberg, Carol L. *René Dubos, friend of the good earth: microbiologist, medical scientist, Environmentalist*. Zondervan, 2005. It was Dubos that coined the phrase "Think Globally, Act Locally."

experimental mice, most drastically viewed in the cecum, suggested that the body flora had a morphological role to play as well as an immunological, protective and nutritional role in the host. The key idea was the adaptation of the individual in its environment; the ecological present produced by host and microbiota was an "evolutionary equilibrium" that was implicated in the health of the body.

He took his views to the medical community in the 1960s. For example, in 1966, Dubos delivered the Louis J. Hirschman Memorial Lecture on the indigenous flora of the gastrointestinal tract to a meeting of the American Proctologic Society in Cleveland. He argued for the importance of the indigenous flora in the maintenance of health and the prevention of disease as a practical imperative. He claimed that medicine had limited its therapeutic potential by focusing only on pathogens. Medicine had missed the fact that "the symbiotic species [of the indigenous microbiota are of at least equal importance" to pathogenic bacteria because they were "essential to the well-being of the host."[319] These microbes, Dubos claimed, "elicit[ed] histologic and physiologic responses which constitute the normal healthy state of the gastrointestinal tract."[320] This impact needed to be incorporated into the study, practice and theory of medicine. This seemingly esoteric knowledge about the nature of the body was important for proper therapy.

But Dubos made an argument about the importance of the intestinal microbiota for understanding the nature of biology as well. He noted the vast number of symbiotic relationships found in nature, placing the indigenous microbiota of the body alongside other *biological*—in

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[319]René Dubos, Russell Schaedler, and Dwayne Savage, "The Indigenous Flora of the Gastrointestinal Tract," *Disease of the Colon and Rectum* 10 (1966): 23. Delivered June 21, 1966.

[320] Ibid. 23.

other words, not just *medical*--phenomena. These symbiotic relationships were of two kinds, he claimed. There were those microbes that pointed to a well-established association with the host developed over a long period of co-evolution. There were also microbes that could *become* pathogenic as long as there was a biological equilibrium in the body that kept them at bay. Dubos was providing a biological definition and rationale for the study of the indigenous microbiota in infectious disease medicine—and for the study of the microbiota itself for the development of the body.

Towards the end of his talk, Dubos placed this research on the microbiota within an even broader context that he would expand upon in his next popular book, 1968's *So Human an Animal: How We Are Shaped by Surroundings and Events*.[321] "Man becomes what he is through his responses to the forces of the environment in which he functions."[322] That environment included the microbes that lived in and on the body, which shaped not only the normal physiology and morphology of the body, but which also served a protective role for the body with respect to pathogens.

Dubos's Environmental Medicine project could be placed alongside a broader movement that would coalesce under the term medical ecology that developed during the same period. These approaches at root shared an orientation to disease and to health. This new approach spread across the medical field as interest in a new model of medicine that would move beyond the narrowly physico-chemical model of the body and include environmental, social and cultural

[321] Dubos, Rene Jules, *So Human An Animal: How we are shaped by surroundings and events*, New York: Scribner, 1968.

[322] Dubos et. al. (1966), 29.

factors grew.[323] This movement gathered steam in the 1960s and 1970s as calls for a new approach to medicine that went beyond the old reductionist biomedical model that sought causes—and therapies—for disease in the physico-chemical processes of the body grew louder.[324] A flurry of books, articles that articulated new ecologically informed approaches to medicine flourished in this period.[325] But Dubos deserves a privileged place in this history because he was one of the first to outline a broad vision for an ecological medicine and to popularize it. Even if, as his critics charged, he pushed too far beyond his competence in trying to establish an environmental or ecological medicine research program and practical methods, he is still to be recognized for offering what he claimed was, and what was received as "a new way of understanding health and disease."[326]

What Dubos saw in the laboratory at Rockefeller led Dubos directly to ideas that he expounded upon in *Man Adapting* in 1965, and then later in its sequel, *So Human an Animal: How We Are Shaped by Surroundings and Events*, which won him the Pulitzer in 1969. In this book, the lessons of his indigenous flora work had been absorbed as part of a broader argument that Dubos made in increasingly social terms. But in this same period another microbiologist took the normal flora as a starting point for a broader cultural project and brought his arguments to the public. But instead of turning away from the normal flora to make an argument about the

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[323] As scholar William Arney describes this change, "the rise of ecological medicine expands the realm of medical discourse beyond the body." Arney, William Ray. *Medicine and the Management of Living: Taming the last great beast*. Chicago: University of Chicago Press, 1984, 63.

[324] These new approaches looked to systems science as a conceptual tool—Arney describes how "without exception" the proponents of ecological medicine, like George Engel and his biopsychosocial model, looked to systems theory for a framework for the new approach. Arney (1984), 70-1.

[325] For more on ecological medicine and medical ecology in the 1950s-1970s, see Arney (1984), Chapter 5: "The New Medical Logic: Relationships, Information Flows, Systems," 62-77.

[326] Arney (1984), 70.

need for an ecologically informed cultural change, this microbiologist leaned into it, and took aim at a set of cultural practices regarding and attitudes towards the body's flora and its relationship to the body.

Theodor Rosebury and *Life on Man*

While Dubos and Luckey explored the microbe-body relationship in the laboratory in the 1960s, Theodor Rosebury was winding down an illustrious research career in the same period, retiring from his position as chair of the Department of Microbiology at Washington University Dental School in 1967. Rosebury had been doing pioneering work in oral microbiology both technically and theoretically from the 1930s.[327] As became typical in oral microbiology, Rosebury was focused on the interactions of the flora in the mouth, and took a special interest in the mouths' indigenous flora.[328] He had written a chapter on the bacteriology of mucous membranes for the first edition of Dubos' classic textbook *Bacterial and Mycotic Infections* (1948), and contributed a chapter called "Bacteria indigenous to man" to the third edition of the book (in 1958). He expanded upon this chapter to write the first comprehensive account of what he called "microorganisms indigenous to man" in 1962.[329] It had been the work of decades; and was a milestone in the study of the indigenous microbiota. Like Dubos and Luckey, Rosebury considered these microbes as integral parts of the biological environment. But the point he was

[327] Fine, Daniel H. "Dr. Theodor Rosebury: Grandfather of modern oral microbiology." *Journal of Dental Research* 85.11 (2006): 990-995.

[328] Rosebury, Theodor, David Gale, and Duane F. Taylor. "An approach to the study of interactive phenomena among microorganisms indigenous to man." *Journal of Bacteriology* 67.2 (1954): 135.

[329] Rosebury, Theodor, *Microorganisms Indigenous to Man*, New York: McGraw-Hill, 1962.

making was both broader and simpler than either scientist. He saw his book as a stepping stone, an opening salvo in the search for a "general theory of the indigenous microbiota."[330] Beyond this, he argued that the *cultural* orientation to the indigenous microbiota needed to change. He appealed to a cultural rather than scientific ecological framing of the microbial body in his popular treatment of the topic, *Life on Man* in 1969. Here, he took the notion of microbes as bodily environment further into ecological and environmentalist discourse by using similar tropes to defend them. He described the normal flora as under threat from the culture. To achieve a proper cultural and scientific orientation to the normal flora would mean a re-evaluation of our relationship to it in both arenas.

Rosebury's *Microorganisms Indigenous to Man* was a singular project and a milestone in the study of the indigenous microbiota. It was the first time that the scattered world literature on the normal flora had been pulled together in one place. Rosebury had spent thirty years pulling together research from disparate sources in order to present as complete a picture of the normal flora as possible—drawing on the work of intestinal bacteriologists, dental bacteriologists, dermatologists, studies on vaginal bacteriology and more. Rosebury criticized the bulwarked nature of studies on the normal flora and hoped to overcome this compartmentalization with his book. He lamented that researchers had "all dealt with the subject piecemeal, as though the various inhabited loci in man are ecologically different continents."[331] This had led to a "tacit assumption" that the flora at each site was distinctive--and belonged under the purview of those medical specialties who exclusively investigated a particular body site. This was reinforced by

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[330] Rosebury (1962), 7.

[331] Ibid.

the use of “habitat” as a taxonomic tool.[332] The problem was that this overlooked possible similarities between the different floras of the body--and precluded the possibility of the development of a whole body approach to the relationship between man and his microbes that would interrogate the basic relationship between microbes and the body and lead to the articulation of overarching principles about it. What was needed, he argued, was “a general theory of the indigenous microbiota.”[333]

Rosebury did not think that it was possible to delineate a general theory yet--the state of contemporary knowledge was too “insufficient” and not well organized enough to allow it.[334] Rosebury’s call for a general theory of the indigenous microbiota, coming at the end of his career, was a challenge to the next generation of microbiologists to find a way to develop one---to find a way across the artificial boundaries that had been erected by the organization of the bacteriology(ies) of the medical specialties. It was a call for a total-body approach to the problem. He outlined its importance in medical terms as well that echoed Dubos’ and Luckey’s orientation to the normal flora as an environmental factor that could be therapeutically (and otherwise) productive:

> “Our indigenous biota is, in fact, part of the environment in which we live. …the biota is no less subject than the rest of our environment to manipulation for human benefit.”[335]

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[332] Ibid, Chapter 6.

[333] Ibid, 7.

[334] Ibid, 7.

[335] Ibid, 352.

But he went further than either of them by stressing the necessity of working towards a greater and holistic understanding of the indigenous flora: “We need to accept its existence.”[336]

But what did Rosebury mean by this statement? *Who* was it that needed to accept its existence? Not, presumably, the expected readership of the book--most likely medical researchers and bacteriologists looking for a textbook or handbook for the normal flora; and those eager to look across the clinical divides that Rosebury had dismissed. Even though the book was an attempt to highlight their importance, the problem in medicine and biology was not their acceptance, but their neglect. More language that hinted at a broader project or goal could be found in his Preface:

> “It seems conceivable that deep-seated inhibitions--Victorian vestiges not entirely abolished by the efforts of Freud and his followers--may have played a hidden role in shaping the manner in which this subject has come to be handled. If this be true, perhaps the effort made in this book … will serve another end besides the more obvious ones--as a contribution, however small, to human emancipation.”[337]

How could a comprehensive study of the indigenous flora lead to “human emancipation”? And what did he mean by “Victorian vestiges” that cast a shadow over the study

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[336] Ibid, 352.

[337] Ibid, 7. Full quote: “It seems conceivable that deep-seated inhibitions--Victorian vestiges not entirely abolished by the efforts of Freud and his followers--may have played a hidden role in shaping the manner in which this subject has come to be handled. If this be true, perhaps the effort made in this book to deal with the subject as a unit, not overlooking differences but searching for similarities, on the premise that we are dealing with a single aspect of human biology, will serve another end besides the more obvious ones--as a contribution, however small, to human emancipation.”

of the normal flora? These were cultural questions, and Rosebury would provide answers to them for the general public in Life *on Man*. In the book, Rosebury would call for a new attitude towards the microbes that lived in and on the body that resonated with countercultural and environmentalist critiques of mainstream culture and practices, and which targeted hyper-Pasteurian visions of the healthy body.

Life on Man: Respecting Our Environment

After retiring from the bacteriology department of the Washington University in Saint Louis in 1967, Rosebury turned to popular science books as a means to supplement the income from his pension. [338] The first one was 1969's *Life on Man,* based on a general interest lecture he had been giving and fine-tuning over the previous years (called "Life on the Planet Man") and as a development of ideas he had only hinted at in *Microorganisms on Man*.[339] [340]

The book took aim at the Pasteurian body and cultural ideals that I described in the Prologue with the sciences of the human microbiota as ammunition. The sciences of the normal flora were concerned with a "rational hygiene" based on appropriate scientific principles that made sense for the care of those parts of the body where bacteria lived normally. This had become central to the ethos of dental bacteriology through Appleton's work to develop an ecological bacteriology of the mouth since the 1930s. At issue was what a hygiene not based on

[338] Letter to Norbert Slepyan, Harper and Row, 6/27/1968. Theodore Rosebury papers, Box 6: *Life on Man* Correspondence.

[339] Letter to Winifred Burhop, 11/23/1966. Theodore Rosebury Papers, Box 2.

[340] Speech announcement, Washington University of Saint Louis Department of Bacteriology, 9/10/1964. Theodore Rosebury papers, Box 6: *Life on Man* Correspondence

the eradication of bacteria looked like. In the case of the normal flora, the conventional hygienic framework would not work, as Rosebury, as an oral bacteriologist, well knew. Rosebury's book criticized and took aim at a society obsessed with antibacterial products and hyperactive hygiene. His book brought the human microbiota squarely into the cultural combat zone of the late 1960s and 1970s.

Rosebury's book was the first popular book to explicitly translate the sciences of the normal flora to the masses. The original tentative subtitle conveyed the gist and broad range of the book: “"the impolite subject of our normal microbes; where and how they live on us; and what they do; their influence through history on our manners and prejudices; what Rabelais, Leeuwenhoek, Freud, Lenny Bruce and others have had to say about it all; and what we ought to do about it."[341] For him, the body's microbes were part of a larger narrative about things and practices designated as “dirty”—in the bodily as well as the cultural sense. Rosebury saw germs as straddling both categories and drew a circle around them for the public.

As in his academic treatment of the subject, he had described the human microbiota as part of the body's environment. In this book he argued that the human microbiota needed to be protected from ubiquitous hygienic practices that were harmful to it. He argued that the hygienic practices and the urge to eliminate bacteria from the body were rooted in faulty cultural ideas about what the nature of a healthy was because of a confusion about what it meant to be clean in an antibacterial age.

It was a book that could resonate with the times—and indeed, Rosebury gave a nod to the new youth culture at the start of the book: “The hippies… see cleanliness as part of the sham

[341] Draft manuscript, “Life on Man,” 10/17/1968. Theodore Rosebury Papers, Box 5.

of a hypocritical world."[342] The hygiene industry had created a culture in which the human microbiota were too often associated with disgusting things and viewed with disgust; Rosebury wanted people to claim their microbes without shame. As he wrote, his book was a challenge to "a particular set of prejudices" in the hope that "science might shine a light on [these] prejudices and show how foolish they are."[343]

Rosebury saw his project as part of the general atmosphere of the day in which youth were challenging the status quo on a variety of fronts. They too, had "already decided that some… accepted ideas… are foolish and have abandoned them or are in the process of abandoning them."[344] Rosebury's book was part of a general movement in the late 1960s and early 1970s that challenged the traditional orientation to hyper-clean culture. For hippies and counterculturalists, this critique was a broad critique usually framed in dirty/cleanliness terms—a rejection of hygienic modernism through a questioning of "the natural" normal.[345]

Rosebury saw the problem of the relationship between bacteria and humans as the culturally created attachment of shame to healthy and normal bodily functions and characteristics. He hoped that his book would lead to a new definition of the obscene that was not grounded in cultural prejudices—"The new notion of obscenity will take over where health stops and disease begins."[346] Microbes were not, as Rosebury knew and which he explained in

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[342] Rosebury, Theodor. *Life on Man*, New York: Viking Press, 1969, 11.

[343] Rosebury (1969), 228.

[344] Ibid.

[345] I explore this in Chapter 4.

[346] Rosebury (1969), 231.

his book, always associated with disease; they were, in fact, necessary for the provision of health.

The human microbiota had been unfairly maligned because people had grouped all microbes together.[347] They had painted all microbes that mingled with the body with those ones that caused disease and those that teemed in feces.[348] The confusion between "clean" and "healthy" was to blame. If one defined "clean" in terms of the absence of microbes as had occurred with the extension of hygienic modernism throughout the culture, then the vagina and the mouth, for example were always at risk of being "filthy" because confusion over the status of the human microbiota.[349] Healthy, he argued was about the absence of disease—not the absence of microbes. The principle that mattered was "Not filth, but disease" because "filth" as generally thought of with respect to microbes was not an adequate basis for determining health for these parts of the body.[350] He warned that extreme cleanliness could have harmful consequences because microbes who were implicated in health could be eliminated along with those that needed to be targeted. The proper approach to microbes was to live with the microbes and to minimize our intervention into it: "We need to live with life on man, and we ought to leave well enough alone.[351]

His final chapter expanded on this point. He condemned American society for becoming "too fastidious" about odors and sweat. He attacked the hygienic routines that Americans

[347] Ibid, 238.

[348] Ibi, 239.

[349] See my discussion of cleanliness in the Prologue.

[350] Ibid, 243.

[351] Ibid, 243.

engaged in faithfully that seemed to have the imprimatur of scientific authority.[352] As research for the this chapter, entitled "The Shell Game," Rosebury collected tons and tons of magazine and newspaper ads for cosmetics, deodorants, feminine hygiene products, soaps, beauty creams, douches, antiperspirants from the 1960s and 1970s.[353] These ads, he argued, "are turning us all into compulsive hand-washers, and face and body washers."[354] These were the tools used to create and enforce a clean culture that he deemed illogical and oppressive, and which he equated with the other social pressures that shaped everyday life. Rules for hair, nails, teeth and dress: "Dress and smell like aristocrats, look affluent whether you are or not; it is the image that counts not the man or the woman beneath, that counts."[355] He decried how the principle of "total cleanness" had come to be "equated with minimal social acceptability."[356] He accused the advertising industry and its alliance with the personal hygiene products industry of creating such an atmosphere and wanting to create consumers based on a fear of dirt: A consumer who "underneath the façade he so anxiously offers to the world' believes that s/he is "hopelessly dirty, fighting in a sea of filth and decontamination he can never achieve."[357]'

This was a somewhat gender neutral problem—offending body odors were a hygiene industry target for both men and women. But Rosebury saw the impact on women and girls as

[352] Ibid., 10

[353] "Shell Game Clips" Folder, Box 6. Theodore Rosebury Papers.

[354] Rosebury (1969), 255.

[355] Ibid.

[356] Ibid, 155. Also Alexander Kira. *The Bathroom: Criteria for Design*, Center for Housing and Environmental Studies, Ithaca: Cornell University Press, 1966.

[357] Rosebury (1969), 256.

particularly pernicious and harmful, and reserved his most pointed critique for the feminine hygiene products industry:

> "The girls have a fearsome lot of problems all their own, the advertisements say—all, of course, the work of microbes, or germs as the huckster likes to call them, those nasty little things which, he is sure you know, need to be exterminated, like vermin, trod on like cockroaches on the kitchen floor. … Unless you heed the huckster's friendly counsel you are sure to give off these unpleasant if not loathsome stinks from your skin and your mouth; but far worse is something abhorrent which he delicately calls "feminine odor." And then localized and details for you….The smell…comes from the curse of menstruation, abetted by that other evil always delicately called perspiration; both of course…befouled by those despicable germs….Here are douches, sprays, powders, suppositories in bountiful array…Benevolent antiseptics, deodorants, antiperspirants, especially designed to substitute for careless nature, saviors of femininity."[358]

Rosebury's passionate screed against the hygiene industry and the feminine hygiene products in particular was both an indictment of an obsessively clean culture and a defense of the human microbiota. Which, he asked to close the book, was worthy of censure: "Is it normal microbes or perverted men?"[359] Rosebury brought the sciences of the normal flora squarely into the history of feminine hygiene at the moment when the women's movement was taking off, and when skepticism about the traditional approach to the body and its microbes, and the humans and

[358] Ibid, 256-9.

[359] Ibid, 259.

their environment was beginning to come under fire in medical and cultural spheres. Rosebury brought these concerns together.

Rosebury framed the abhorrence of microbes on the body in social, cultural and psychological terms. For him, these practices were problematic not just for what they did to the body—but for what they did to the mind—and the soul. Rosebury made clear in *Life on Man* what he meant by his cryptic references to "Victorian vestiges"' and Freud in his dry, academic book on accounting of the bacteria of the body—that the obsession with the elimination and fear of germs and dirt on the body was an impediment to "human emancipation." [360]

<u>Reception of *Life on Man*</u>

*Life on M*an resonated broadly. The *New York Times* saw the book that had been written "not to entertain, but to protest." [361] Rosebury, the *New York Times* reviewer claimed, was protesting ""civilized" man's fetishes about cleanliness."[362] Rosebury became a fashionable public intellectual on the subject of germs and clean culture in the 1970s.

The book was an immediate success. Viking Press, which published the book in June 1969, thought the book had tapped into something in the air and moved quickly to capitalize on

[360] Rosebury (1962), 7. Full quote: "It seems conceivable that deep-seated inhibitions--Victorian vestiges not entirely abolished by the efforts of Freud and his followers--may have played a hidden role in shaping the manner in which this subject has come to be handled. If this be true, perhaps the effort made in this book to deal with the subject as a unit, not overlooking differences but searching for similarities, on the premise that we are dealing with a single aspect of human biology, will serve another end besides the more obvious ones--as a contribution, however small, to human emancipation."

[361] Stock, Robert. "About Fleas and Feces," *New York Times*, July 13, 1969, BR8.

[362] Ibid.

the project. They sent out more review copies of Rosebury's book than any other book that year, and as the accolades poured in, they more than doubled the advertising budget for the promotion of the book.[363] Thomas Guinzburg, the president of Viking praised Rosebury for the "marvelous press" Rosebury had garnered on his debut.[364] From the start, his book garnered interest across the media spectrum. Big media wanted him on their programs-- Rosebury did interviews with "The David Frost Show," "the Today show, and a radio interview with Chicago radio giant Studs Terkel.[365] Terkel liked the interview so much that he re-ran it soon afterwards. Even Marshall McCluhan wrote Rosebury personally to let Rosebury know that he would have "many occasions to use your book in my studies with my students of communication."[366] Rosebury's *Life on Man* made an impact into the 1970s he was asked to appear on a public affairs show in Montreal in 1974 to discuss the "origin of our compulsive attitudes towards cleanliness."[367] It was added to the syllabus in a sociology course on marriage and Family at Point Park College in Pittsburgh.[368] Letters poured in from readers who found that the message of the book resonated with their experiences and attitudes. One navy corpsman writing from Gibraltar who had done some medical research at the Naval Medical Research Institute would not "go so far as to say "dirt is good for you,"…but "one thing which is certain is that the "cult of cleanliness" in America is

[363] Letter from Thomas Guinzburg, 10/15/1969. Theodor Rosebury Papers, Box 6.

[364] Ibid.

[365] Letter to Gerald Piel, 8/29/1969, Letter to Beatrice Rosenfeld 10/24/1969, and Letter from Naomi Sterling. 7/10/1969. Theodore Rosebury papers, Box 6: *Life on Man* correspondence.

[366] Letter from Marshall McLuhan 9/18/69. Theodore Rosebury papers. Box 6: *Life on Man* correspondence.

[367] Letter from Anne Dychtenberg. 8/12/74. Theodore Rosebury papers, Box 2.

[368] Letter from Professor Phyllis C. Martin, 1/31/1970. Box 6: *Life on Man* correspondence.

really a waste and a burden to the average individual."[369] One Ronald L. Kaiserman of Philadelphia wrote vowed to by Rosebury's book "in great quantities" for friends and relatives "as my duty to their sanity." He analogized the problem of the body to the problem of the environment: 'You write as someone concerned about ecology, for surely we are doing to our environment what we do to ourselves, like putting runways through everglades and pipelines through Alaska "for our benefit," Just as ladybird Johnson's program of beautifying the highways meant plantings in front of junkyards, not removal of them, like a deodorant."[370]

His book was received favorably in the scientific, popular and countercultural spaces. The book won a special commendation in the Science category of the 1971 National Book Awards. He was invited to speak at universities in an activist context in the late 1960s and early 1970s.[371]

Rosebury's book and its broad defense of germs on the personal hygiene front resonated with other defenses of germs and attacks on chemicals. Organic farming looked to reject the pesticide-heavy practices of farming and promote natural, microbe-friendly and useful practices.[372] The food culture of the new hippies also looked to get away from the mainstream food of the 1950s in favor of foods that were often fermented.[373] While Rosebury sympathized with the counterculture, he was not of it—for example, Rosebury poo-pooed the organic farming

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[369] Letter from Alec Quackenbush, 2/10/1970. Box 6: *Life on Man* correspondence.

[370] Letter from Ronald L. Kaiserman. 12/18/1969. Theodore Rosebury papers. Box 6: *Life on Man* correspondence.

[371] For example, He was invited to participate in the East Bay Women For Peace's teach in at Berkeley Letter to East bay Women for Peace, 12/23/1969. Box 6: *Life on Man* Correspondence.

[372] See Case, Andrew S., *Looking for Organic America: J.I. Rodale, the Rodale Press, and the Popular Culture of Environmentalism in the Postwar United States*. (PhD dissertation, University of Wisconsin-Madison, 2012).

[373] See Belasco, Warren, *Appetite for Change: How the Counterculture Took on the Food Industry*, Ithaca: Cornell University Press, 2006, for an in depth exploration of countercultural food habits and attitudes.

and health food movements as illegitimate and irrational. Rather, he saw all of them as manifestations of a rising anti-scientism in the culture at large.[374] He even defended hexachlorophene as one of the few antiseptics that actually worked before it came under scrutiny and was eventually banned by the FDA. As he wrote, "my sympathies are with the young but my objective is rationality."[375] He was concerned with "irrational hygiene" and urged a hygiene not based on the sciences of the normal flora. His placed the microbes of the body within the discourse of *environment under threat* as a way to defend them against biomedical and scientific neglect and cultural opprobrium. This threat was cultural as well as medical with respect to the normal flora, and embodied in conventional hygiene practices.

Conclusion: Germs as Environment

Their framing of the human microbiota as "environment" led these researchers to different conclusions. While Rosebury and to some extent Dubos saw the cultural potential of this reframing of the relationship between the body and microbes, Dubos and gnotobiologist Thomas Luckey focused on the potential of the microbial body to shape biomedicine. Rosebury placed his defense of the microbial environment of the body within environmentalist discourses of protection and respect. Dubos and Luckey used the characteristics of the microbiota-less body they saw in the laboratory to argue that biomedicine needed to take this natural "biological environment" seriously.

[374] Rosebury, (1969).

[375] Rosebury (1969), 228.

All three of these researchers saw the normal flora of the body in environmental terms. These versions of the microbial body did not carry any particularly expansive cultural force though they made waves within different fairly marginal communities in this period. Luckey's intestinal microecology became the basis for the emerging probiotics field in the 1980s; Rosebury's book became a cult classic among microbiologists, and Dubos' work on the flora was largely eclipsed by his earlier pioneering work on antibiotics and his later celebrity as an environmentalist icon.[376]

But the appeal to ecology and the reframing of germs as environment of the body paid dividends with respect to the reevaluation of germs in medicine, science and culture that would allow for the possibility of the Human Microbiome Project to have such resonance in recent years. It would take the Human Microbiome Project to make a real stab at transforming the body through even bolder claims about human-microbe relationship. In the next section, I explore how ecological vision permeated through cultural, scientific and medical spaces—and how it impacted the conceptualization of the relationship between the body and its microbes.

[376] See Moberg (2005).

PART II: THE NATURAL TURN

The section investigates what I will call the "natural turn" in the second half of the 20th century. In this period, a greater appreciation of "the natural" spread throughout the culture as an ecological sensibilities intensified. This increased attention to "the natural" could be seen in cultural, medical and scientific spheres. In the sciences, ecology rose in status and institutional power as anxieties about pollution, contamination and synthetic chemicals grew and government and society looked for ways to understand and manage the new threats. The second half of the twentieth century has been called the "Age of Ecology" for good reason.[377] In culture, it meant an increasing adoption of attitudes that embraced an environment-under-threat narrative and more "natural" approaches to everyday life. In medicine, it meant a proliferation of perspectives that critiqued and problematized a dominant biomedical model because of its limited attention to environmental factors.

With respect to microbes, this natural turn saw the elevation and strengthening of pre-existing narratives to contrast with the three dominant narratives about microbes—the dominance of pure culture in microbiological science, the focus on microbe hunting and pathogen elimination in medicine, and the antibacterial imperative in culture (the "hygienic modernism" described in the Prologue). In contrast, these counternarratives were centered on a bacteriology that looked more to agricultural and soil bacteriology than to conventional medical bacteriology, an infectious disease medicine that was not based on eradication, and a cultural

[377] See Part 6: "The Age of Ecology: Science and the Fate of the Earth" of Donald Worster's *Nature's Economy: A history of ecological ideas*, Cambridge University Press, 1994. The book was originally published in 1977.

sensibility that rejected the notion that germs were inherently dirty and needed to be eliminated at all costs.

But the appeal of and to “the natural” was a reaction to the *not*-natural; a challenge to dominant themes in each domain which meant different but complementary things in scientific, medical and cultural spaces. In science, it meant attention to natural units rather than laboratory created and enforced ones. In medicine, it meant a concern about the impact of the environment on the body that contrasted with a narrow focus on the body as a physiological machine. In culture, it meant a rejection of mainstream cultural modes as inauthentic, artificial and poisonous, all which came to be conflated in an ecological age and eschewed in favor of “the authentic” writ broadly.

These three changing scientific, cultural and medical narratives impacted the status of the indigenous flora of the body and the general relationship between germs and humans. The three threads discussed in the last chapter provide entry points into each of these developments. Gnotobiology was an instantiation of a particular 20^{th} century ideal of science (isolate, reduce, purify) that the new ecological microbiology rejected; Dubos’s environmental medicine insisted on a different, interactionist view of pathogenic and nonpathogenic microbes in the body; Rosebury’s *Life on Man* brought the normal flora of the body into conversation with countercultural attitudes of the 1960s and 1970s by framing its protection in environmentalist, feminist, and ideological terms.

The Natural Turn in Culture

The first narrative about germs that was refuted in new ways in this period was the notion that germs needed to be eliminated from the body through chemical cleansing. In this period, the American ideal of hyper-hygiene came under attack from a variety of angles. Hippies opposed it on the grounds that this particular hygienic regime was part of the dominant culture that needed to be questioned and challenged at all levels; feminists saw feminine hygiene sprays as a patriarchal imposition on the female body and psyche; eco-consumers embraced natural hygiene products that eschewed synthetic chemicals. In addition, dermatologists defended the bacteria of the body targeted by the chemicals in antibacterial soaps and products as harmful to the natural ecology of the body against the Hygiene Industry. This was a multi-pronged attack on the Pasteurian body.

The Natural Turn in Science

Ecology came of age in the post war years and by the mid-1960s had come to be seen as subversive—providing a critique of society as well as science.[378] Its position as critic of mainstream thinking and approaches, aligned with other movements that aimed to do the same thing in this period.

While post-WWII ecology embraced the concept of ecosystem and mathematical tools and concepts as a way to make them "harder" and more predictive—and thus to gain the status of a serious science, it also provided a different perspective from the other dominant sciences of the

[378] See Kingsland (2005), Chapter 7: "A Subversive Science?".

day. In biology, the reductionist approach was essential. The notion that one could understand life by looking at it in the most simplified form provided a counterpoint to the argument that ecology implicitly made—that one needed a science of relationships—of interaction between organisms and environment to understand life. It brought biology out of the laboratory and into the real world—it was a means to discuss and to study the impact of humans on the natural world—and vice versa. This was a counterpoint to the reductionist science of the molecular biological laboratory that insisted on highly artificial conditions to get at constituent and elemental parts or organisms. Ecological sciences focused on the natural context and relationships between organisms in "nature" and on natural units of study. The most important innovation of ecology in counterpoint to the other kinds of biology was the unit it was based on—the ecosystem. It was "a natural unit including living and nonliving parts that interacted to produce a stable system."[379] What ecology did by this period was to provide a way to translate the natural world into units that were not based on individual organisms—and to insist on their legitimacy and importance for scientific investigation.

Eugene Odum published the first edition of his influential textbook, *Fundamentals of Ecology* in 1953, and described the ecosystem as the central unit of ecology. The concept of ecosystem became a central foundational concept in ecology over the next twenty years.[380] The ecosystem was the counterpoint to the molecular biology's focus on molecule, genes and organisms. This tension was philosophical as well as practical—the rising cultural and political power of ecology was such that the molecular biology "establishment" was worried about the

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[379] Kingsland (2005), 189.

[380] The International Biology Program a global effort to coordinate large-scale ecological initiatives from the mid-1960s through the mid-1970s played a large role in propagating the ecosystems concept. Indeed, this was considered its main achievement by historian Donald Worster. See Worster (1994), 373.

new upstarts' increasing competitiveness for government funding.[381] Indeed the 1960s was a period of crisis for biology which saw the rise of ecological science alongside the environmental movement as competing visions clashed.[382] By the late 1960s, molecular biologists had begun to loudly lament the proliferation of ecological research which to them had come to their detriment. Ecology received an increasing share of NSF funding as environmental concerns gained broad support throughout the country in the 1960s and 1970s.[383] By 1968, the NSF's program director for genetic biology would lament the "disproportionate emphasis given to environmental biology" over what he considered the more fundamental molecular and genetic biological sciences.[384] The ecological sciences were intertwined with a new powerful political and social agenda which transformed the status of environmental science in this period as people looked for ways to manage environmental problems that were increasingly salient to the society.

The ecological sciences could be contrasted with the molecular sciences in that they approached their object in different ways. Ecology, as a scientific tool for managing real world problems—was focused on the interrelations and context; the molecular sciences were concerned with fundamental units and processes. The rising power of ecology in the 1970s could be seen in the shift in framing of gnotobiology from its birth in the 1940s to the 1970s, in which Luckey would argue that gnotobiology—the science of pure types—was *actually* ecology.

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[381] Worster (1994), 372.

[382] See Appel (2000), Chapter 8: "Allocating Resources to a Divided Science."

[383] Ibid.

[384] Appel (2000), 1921.

I will examine the natural turn in microbiology through the development of a new field, microbial ecology, in the 1970s and 1980s and illustrate how it contrasted with the old, traditional microbiology which focused on microbes in isolation, grow in pure culture, to different ends—most importantly here as a model system for molecular biology. The orientation of microbial ecology towards the "field" was not new--soil and agricultural bacteriology of earlier decades were also focused on microbes in the natural environment—but the rising ecological tide brought the core questions of these fields from the periphery to the center of microbiological science, and towards a more prominent role in biology more generally.

The Natural Turn in Medicine

The third dominant narrative was a medical one. This period saw the birth of environmental medicine and medical ecology, which saw an increasing concern with environmental impacts on the body. Medical microbiology and its focus on the elimination of the pathogen from the body meant that infectious disease medicine was focused on a very narrow disease model and biomedical model of the body. In this period, ecological approaches to the relationship of microbes to the body became the concern of an increasingly broad community of biomedical researchers who decried an overly aggressive antibiotics-centric culture that reduced fighting infectious disease to pathogen whacking and medical bacteriology to pathogen articulation and destruction.

In infectious disease medicine, the natural turn could be seen in attitudes towards antibiotics. They were discussed as part of a technological overreach narrative almost from the beginning of the antibiotics age, as antibiotics pioneers warned about the dangers of antibiotic resistance and the impact of the new drugs on the normal flora. Dubos, for example, had begun writing about antibiotic resistance in the early 1940s and continued in this vein through his later work on the ecology of the indigenous flora in the 1950s and 1960s.[385] There were a proliferation of other apprehensive voices as well in the 1940s and 1950s. Infectious disease specialists diligently worked on and discussed these problems to as their field saw a decline in the prestige and resources for their scientific work in an age that believed infectious disease to be largely conquered.[386] Along with the evolution of antibiotic resistance, the phenomenon of superinfection, infection resulting from the decimation of the body's normal flora due to antibiotic therapy, was also a topic of much concern in this community during this period.[387] The study of these phenomena in the 1950s-1970s was part of an ecological strain in modern medicine that focused on the impact of antibiotic usage on the microbial population in and on the body and in the environment—and the repercussions of these ecological changes for human health. While René Dubos pioneered an ecological approach to medicine that aimed to apply ecological framework to medicine, infectious disease ecology, which focused on an ecologically informed approach to infectious disease, had its roots in the golden age of antibiotics, with researchers lamenting the *ecological* effects of the use of antibiotics on the body's flora and beyond. These ecological effects were the target of many in the infectious disease *specialty* from the 1940s, but garnered broader attention in the 1970s when it was shown that antibiotic

[385] Moberg, C., "René Dubos: A Harbinger of Microbial Resistance against Antibiotics," *Microbial Drug Resistance* 2 (1996):287-297.

[386] See Kass, Edward H. "History of the specialty of infectious diseases in the United States," *Annals of internal medicine* 106.5 (1987): 745-756 and Kass, Edward H., and Katherine Murphey Hayes. "A History of the Infectious Diseases Society of America," *Reviews of Infectious Diseases* (1988): 1-158.

[387] See for example Weinstein, Louis, "The Complications of Antibiotic Therapy." *Bulletin of the New York Academy of Medicine* 31.7 (1955): 500 and Weinstein, Louis, "Superinfection: A complication of antimicrobial therapy and prophylaxis," *The American Journal of Surgery* 107.5 (1964): 704-709.

resistance could impact the normal intestinal flora and could be transferred between animals, environment and humans.[388]

Stuart Levy, who led the 1970s work on antibiotic resistance and the intestinal flora on farms, brought the old concerns of the infectious disease community about the transfer of resistance among microbes into conversation with early biotechnologists looking to engineer microbes with new recombinant DNA techniques. Historian Robert Bud describes the birth of a new consensus around antibiotic resistance between those working on plasmids in the cutting edge recombinant DNA world and those infectious disease specialists who had been worrying about antibiotic resistance for over two decades.[389] The thing that the biologists feared creating by mistake in the laboratory—mutant, malicious microbes and genes that could escape into the body or the wild—were actually being created by the medico-pharmacological complex and propagated by the medical profession.[390] The combination of cutting edge science with a cautionary tale about a medical establishment gone astray was a potentially compelling story—and Levy knew how to make the world listen—by enlisting celebrity scientists, holding simultaneous press conferences around the world, and issuing statements about the global problem of antibiotic misuse.[391] It was a masterful move, and garnered lots of media attention—and brought the problem of antibiotic resistance out of the periphery and towards the center of

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[388] See Levy, Stuart B., George B. FitzGerald, and Ann B. Macone, "Changes in intestinal flora of farm personnel after introduction of a tetracycline-supplemented feed on a farm," *New England Journal of Medicine* 295.11 (1976): 583-588, and Levy, Stuart B., "Emergence of antibiotic-resistant bacteria in the intestinal flora of farm inhabitants," *Journal of Infectious Diseases* 137.5 (1978): 688-690.

[389] Bud, Robert, *Penicillin: triumph and tragedy*. Oxford University Press, 2007, 189.

[390] Levy, Stuart B. *The Antibiotic Paradox: how miracle drugs are destroying the miracle*. New York: Plenum Press, 1992.

[391] Bud (2007), 188-90.

medical and societal attention.[392] By the 1990s, Levy would frame the problem of antibiotic resistance as an explicitly ecological problem—in his popular book *The Antibiotic Paradox* (1992) and for the biomedical and pharmaceutical community a few years later, in a Ciba Foundation Symposium paper entitled "Antibiotic Resistance: An Ecological Imbalance."[393]

This story is beyond the scope of this dissertation, but the aftermath of the developments sketched here will be discussed in broad outline in the beginning of the next section. Concerns about antibiotic resistance plays a key role in the shaping of the microbial turn that I discuss in Chapter 6.

From the Natural Turn to the Microbial Turn

These developments began to redefine the relationship between microbes and man in ways that would bear fruit in the twenty-first century with the Human Microbiome Project and the perceived biomedical, scientific, philosophical and cultural productivity of bacteria in this period. The natural turn set the stage for what I will call the Microbial Turn, in which microbes have settled squarely into, in the words of anthropologists Heather Paxson and Stefan Helmreich, "an idiom of promise" after being primarily ensconced in "an idiom of peril" throughout the twentieth century. I argue that this natural turn saw important, parallel developments in the reframing of germs and their relationship to the body that were necessary for the

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[392] Bud (2007), 189.

[393] Levy, Stuart B. "Antibiotic Resistance: An Ecological Imbalance," in *Antibiotic resistance: origins, evolution, selection and spread,* CIBA Foundation Symposium 207, 1-14. New York: Wiley, 1997.

conceptualization and construction of much more compelling and culturally resonant Microbial Body, version 2.0 at the beginning of the twenty-first century.

Chapter 4: Natural Hygiene and the Rejection of Chemical Cleansing

Introduction

The "natural turn" in culture saw the dislodging of the Pasteurian body as a cultural ideal. This was just one thread in a general "natural turn" that could be seen in virtually all aspects of American culture in this period.[394] The rise of organic farming, homeopathic medicine, influences of ethnic food, clothing and music all aimed for authentic approach to life that was closer to Nature. This cultural change was, in the words of sociologist Todd Gitlin, a "turn from straight to curved, from uptight to loose, from cramped to free—above all, from contrived to natural."[395] The "contrived" covered all those aspects of life that were deemed inauthentic or artificial; the "natural" encompassed behaviors, self-presentation, etc. as well as *Nature* itself—i.e., the environment. The culture of antibacterial cleansing came under fire in three arenas in the 1960s and 1970s—the countercultural, in which conventional ideas about cleanliness and the management of the body came to be questioned by feminists and hippies; the consumerist, in which a natural products industry emerged as what historian Virginia Smith calls "ecological puritans" opted to forego conventional cleansing and use products that resonated with their ecological sensibilities; and the scientific, which saw dermatologists pitted against the same "hygiene freak" companies that counterculturalists railed against.

This appeal to "the natural" meant different things to these different (in some cases overlapping) communities. For the counterculturalists, it meant a rejection of the hegemony of

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[394] See Belasco (2007) and Braunstein, Peter, and Michael William Doyle, eds. *Imagine Nation: The American Counterculture of the 1960's and 70's*. Routledge, 2013 and also Miller, Timothy, *The Hippies and American Values*, University of Tennessee Press, 1991.

[395] Gitlin, Todd. *The Sixties: Years of hope, days of rage*, Random House LLC, 1993, 215.

mainstream values and patriarchal culture in favor of less contrived and more authentic values. For the ecological puritans, it referred to concerns about protecting the body and the environment from chemical pollution; for the dermatologists, it was about defending their vision of the natural biological body and its normal function.

Conventional Hygiene and Counterculture

Theodore Roszak describes the counterculture in his seminal book *The Making of a Counterculture* which reflected on the contemporary movement in 1969. In his preface to the 1995 edition, Roszack reflects again on the times with the benefit of distance. He described the counterculture he had tried to make sense of in the 1960s as less an explicit movement that a general atmosphere of protest in which "[e]verything was called into question: family, work, education, success, child-rearing, male-female relations, sexuality, urbanism, science, technology, progress. The meaning of wealth, the meaning of love, the meaning of life—all became issues in need of examination."[396]

Historians Peter Braunstein and Michael William Doyle echo this assessment in their edited volume, *Imagine Nation: The American Counterculture of the 1960s and 1970s*. It was "an inherently unstable collection of attitudes, tendencies, postures, gestures, "lifestyles," ideals, visions, hedonistic pleasures, moralisms, negations, and affirmations." [397] Furthermore, "These

[396] Roszak, Theodore. *The Making of a Counter Culture: Reflections on the technocratic society and its youthful opposition*. University of California Press, 1995, xxvi.

[397] Braunstein, Peter, and Michael William Doyle, "Historicizing the American Counterculture of the 1960s and 1970s," in Braunstein, Peter, and Michael William Doyle, eds. *Imagine Nation: The American Counterculture of the 1960's and 70's,* New York: Routledge, 2013.

roles were played by people who defined themselves first by what they were not, and then, only after having cleared that essential ground of identity, began to conceive anew what they were."[398] Indeed, as historian Timothy Miller has claimed, the hippies did not see themselves as just another subculture; they saw themselves as "the Disloyal Opposition to Establishment culture."[399]

As social scientists trying to understand counterculture in the early 1970s described it, "its members have consciously and deliberately rejected the value system of the larger society within which they exist and have attempted to substitute in the place of this dominant set of priorities 'a series of inverse or counter values in face of serious frustration or conflict.'"[400]

In 1969, Roland Barthes wrote a short piece for the journal *Communications* about hippies that took stock of their cultural positioning and self-fashioning. Barthes described several points of contrast between cultural norms and the hippie subculture--collective eating vs. individual meals; itinerant living vs. sedentary life--and poor cleanliness as opposed to "the American myth of hygiene" among other oppositions.[401] Barthes saw this rejection of hygiene as part of an ideological stance, a pointed critique of the bourgeois ideals of the times and a rebellion against the values of their parents' generation. Hygiene had come under attack as one of the targets of this inversion.

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398 Ibid.

399 Miller (1991), 103.

400 See for example, Spates, James L., and Jack Levin. "Beats, Hippies, the Hip Generation and the American Middle Class: An Analysis of Values," *International Social Science Journal* 24 (1972): 328.

401 Barthes, Roland. "Un cas de critique culturelle," *Communications* 14 (1969): 97–99.

Rosebury's assessment of the new youth culture in *Life on Man* reinforced this outsider view: "They see cleanliness as part of the sham of a hypocritical world."[402] For Rosebury, this new view of conventional American hygiene was a lesson for everyone else: "If this […"total cleanness" …equated with minimal social acceptability"…] is something the hippies are rebelling against, swinging all the way to the other sides, are they perhaps trying to say something we ought to listen to?"[403]

To be a "dirty hippie," the common epithet hurled often hurled at hippies, was the point. It may have begun as teenage rebellion—a way to signal a chafing against parental and social order through self-presentation. But, as Todd Gitlin writes, what may have begun as "symbols of teenage *difference* or *deviance* were fast transformed into signs of cultural *dissidence*."[404] Rejecting it was a disruptive and pointed critique of what hippies saw as the hypocrisy of an establishment that was responsible for what was *truly* dirty—pollution, Vietnam, racism. As Thane Gower Ritalin wrote in *Seed*, a Chicago-based newspaper that was a member of the Underground Press Syndicate in the 1960s, "That a few Hippies appear dirty punctuates the fact that in a crucial sense, all adult non-Hippies are filthy."[405] Rejecting the culture of cleanliness was a symbolic rejection of what hippies saw as the materialism, hypocrisy and consumerism that had become hallmarks of the idyllic suburban America of the 1950s.[406] It meant to reject the

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[402] Rosebury, (1969), 11.

[403] Rosebury (1969), 255-6.

[404] Gitlin, (1993), 215.

[405] Thane Gower Ritalin, "The Hippies and the Hypocrites," *Seed* 11, August 25, 1967.

[406] For more on hippies and cleanliness, see Hoy (1995), 176-7.

class consciousness, racism and ethnic fear of white suburban society. The “the hygiene freak companies,” as they were referred to in The *Great Speckled Bird*, Atlanta’s underground newspaper, were just one more institution to be questioned.[407]

Hygienic modernism, which had been on the rise throughout the twentieth century had reached its peak in the 1950s, came to be seen as an artifact of an overly sanitized and oppressive society by the 1960s. To reiterate Nancy Tomes own assessment of the period from the perspective of her Baby Boomer peers, the germophobic rituals of her childhood came to be seen as “old-fashioned” and “uptight” by the late 1960s.[408] They were ripe for questioning and revision in this period of cultural upheaval and questioning.

Natural Women and Chemical Clean

Hippies were not the only ones with an ideological complaint against the dominant culture; and they were not the only ones who sought to reclaim their bodies—and minds—from the “purifying finishes” and germicides the marketplace championed in pursuit of total cleanliness. While their politics were not purely oppositional, as those described above, they did take issue with the hygiene industry on other terms. Rosebury had aimed his most pointed critique in *Life on Man* at feminine hygiene products; this critique was echoed in the feminist literature of the time.

Feminists attacked conventional hygiene with a more focused and explicit critique. While adolescent bodies and the young bodies of the hippies were under threat from a mainstream culture that aimed to make them conform to the American ideal, women’s bodies were even

[407] “Woodstock—3 Days of Peace?,” *Great Speckled Bird*, July 28, 1969, 7.

[408] Tomes (1999), xiv.

more so. Women's bodies have always been some of the most troublesome bodies—and in a body odor conscious age, the site of the most anxiety producing odors.[409] It was no surprise that women's bodies were the focus of the most aggressive marketing and advertising for antiseptic products, and had been for decades by the time the feminists confronted the concept of feminine hygiene or "cunt deodorant," as on underground paper called it in 1969.[410],[411] Germaine Greer's groundbreaking *The Female Eunuch*, published in 1970, addressed "the great vaginal odor story," as she called it in an interview the following year, and laid out how it was "a clear example of the exploitation of the inner female mind through advertising"[412]:

> "Nowadays it is not enough to neutralize perspiration and breath odors; women are warned in every women's magazine of the horror of vaginal odor, which is assumed to be utterly repellant. ... [T]he huge advertising campaigns for deodorants...deliberately play on female misgivings about the acceptability of natural...odors."[413]

For Greer, the antiseptic body was essentially a female one—she contrasted the modern male body, which could even encompass the new "ecological male"—"some men...take pride in smelliness and hairiness, as part of their virile rejection of prettiness"—with her take on the mainstream feminine ideal: "the glabrous odourless body of the feminine toy."[414] The achievement of this ideal was not just about "cunt hatred" as Greer called it, and its implications

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[409] See "Woman as Body" section in Price, Janet, and Margrit Shildrick, eds. *Feminist Theory and the Body: a reader*, New York: Taylor & Francis, 1999, for scholarship on women's bodies and culture.

[410] See Ferranti, Michelle. "From Birth Control to that "Fresh Feeling": A Historical Perspective on Feminine Hygiene in Medicine and Media." *Women & Health* 49 (2010): 592-607.

[411] "Woodstock—3 days of peace?," *Great Speckled Bird*, July 28, 1969, 7.

[412] Excerpt from Interview with Greer by *off our backs*, "The Female Eunuch," *Great Speckled Bird*, July 5, 1971, 5.

[413] Germaine Greer, *The Female Eunuch*, Harper Perennial Modern Classics, 2008, 43 & 290.

[414] Ibid.

for women's psychological health and integrity, it was also about physical *health*. While those who rejected chemicals for their own bodies in the 1960s tended to describe that opposition in ideological terms. The threat to women's health was immediate and familiar. These chemicals were not just theoretically sick, they were psychologically harmful, and could be physically harmful. "The excessive use of douches with chemical additives is actually harmful to the natural balance of organisms existing in the vagina," Greer wrote, "and yet no doctor has dared to denounce it openly."[415]

These attitudes towards feminine hygiene products and sprays were evident across the feminist literature. The "Do It Yourself" attitude that the women's health movement of the early 1970s embraced encouraged women to take active charge of their bodies and their health, and to educate themselves about how best to care for themselves and their vaginal health.[416] Articles like *Everywoman's* widely syndicated "Self-Examination" article stressed the point that Greer had made about vaginal health, bacterial balance and germicides:

> "The vagina has a delicate balance of bacterial and fungal growth which can be easily upset and result in an infection, really an overgrowth of one or the other."[417]

The Boston Women's Health Collective classic *Our Bodies, Ourselves* (1971) raised the issue in its first edition with an indictment of the hygiene industry's insistence on "such obscene

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[415] Ibid, 290.

[416] The west coast sisters, "DO It Yourself," *Great Speckled Bird*, September 13, 1971, 12; reprinted from *Everywoman*. Morgen, Sandra, *Into Our Hands: The Women's Health Movement in the United States, 1969-1990*, New Brunswick, New Jersey, and London: Rutgers University Press, 2002. Ruzek, Sheryl Burt, *The Women's Health Movement Feminist Alternatives to Medical Control*, New York: Praeger Publishers, 1978.

[417] Peggy Grau/Everywoman, "Self Examination," *Great Speckled Bird*, September 27, 1971, 9.

things as deodorants for our vaginas."[418] In later editions, *Our Bodies, Ourselves* expanded upon the issue of feminine hygiene sprays, douches and vaginal bacterial balance. In 1973's edition (more widely available edition because it was published by major publishing house Simon and Shuster), a new chapter on women and healthcare discussed hygiene, douching and vaginal infections. It educated the public about the normal vaginal flora: "Many bacteria grow in the vagina of a normal, healthy woman. They help keep the vagina acid, which kills yeasts, fungi and other harmful organisms. Anything that upsets this balance may cause some organisms to multiply all out of proportion…." [Infections can happen] "when your system is out of balance…"."[419] It advised women to "avoid irritating soaps and sprays" and to douche with baking soda and vinegar or yogurt as opposed to using the antibacterial douches on the market.[420] They endorsed the use of unpasteurized yogurt to prevent infections and to treat mild symptoms, noting that it contained ""good" bacteria normally found in the vagina and often destroyed when we take antibiotics."[421] They warned about antibacterial medications for vaginal infections: "all the good bacteria are destroyed along with the bad. If the [bad bacteria] grows back faster than the friendly bacilli, then we can become re-infected."[422]

The underground papers that lambasted the "hygiene freak companies" were the same ones that provided a forum and megaphone for the burgeoning women's movement. Articles about women's health from publications like *Everywoman*, a feminist near-monthly paper out of

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[418] Boston Women's Health Collective, *Our Bodies, Ourselves*, Boston: New Hogtown Press,1971, 4.

[419] Boston Women's Health Collective, *Our Bodies, Ourselves*, New York: Simon and Shuster, 1973, 260.

[420] Boston Women's Health Collective, (1973), 259.

[421] Boston Women's Health Collective, (1973). See chapter on "Prevention."

[422] Boston Women's Health Collective, (1973), 138.

California, and *off our backs*, a radical feminist collective's publication were distributed through the Liberation News Service and through less formal networks to alternative newsweeklies across the country.[423] Announcements for the openings of women's health centers, classes and presentations were also publicized in these papers as women aimed to educate themselves about their bodies—and reclaim them from a paternalistic medicine that relied too heavily on pharmaceuticals for the new ecological youth, and from the purview of a marketplace that looked to exploit women's bodies by playing on their psyches.[424] Consequently, the discussion of feminine hygiene was an issue for the broader counterculture, and the discussion about it played out in that context—alongside discussions about ecology, organic farming, pesticides, Vietnam, gay rights, and civil rights in the early 1970s.

Ecological Attitudes: The New Consumer and the New Regulatory Atmosphere

The feminist movement saw the issue of cleanliness as a political as well as a health issue. Their view of the hygiene industry and its insistence on chemical clean was both about opposing the "obscene" nature of the products they pushed (echoing the inversion of hippies seen adult non-Hippies as "filthy") and about health concerns about the impact of the chemicals in hygiene industry products on the body's ecology.[425]

[423] For example, see "Do It Yourself," *Great Speckled Bird* September 13, 1971, 12, and "Self-Examination," *Great Speckled Bird*, September 27, 1971, 9 and "Fragrant Vulvar Inflammations," *Great Speckled Bird*, November 16, 1970, 21. For more on the underground press, see Leamer, Lawrence, *The Paper Revolutionaries: The rise of the underground press,* New York: Simon and Schuster, 1972 and McMillian, John, *Smoking Typewriters: the Sixties underground press and the rise of alternative media in America*, New York: Oxford University Press, 2011.

[424] See "Do It Yourself," *Great Speckled Bird* September 13, 1971, 12; reprinted from *Everywoman*. See also Morgen, Sandra. (2002) and Ruzek, Sheryl Burt (1978).

[425] Boston Women's Health Collective, (1971), 4.

Concerns about the encroachment of synthetic chemicals was not limited to the hygiene industry. It could be seen in various arenas. These concerns were galvanized in the early 1960s by Rachel Carson's watershed book *Silent Spring* (1962), in which she raised concerns about DDT and its environmental impact.[426] In *Crabgrass Crucible: Suburban Nature and the Rise of Environmentalism in Twentieth-century America*, historian Christopher Sellers describes how concerns about the synthetic chemicals used to create and maintain the suburbs became another oppositional point in the general cultural upheaval of the countercultural shifts of the 1960s.[427] Sellers focused on the problem of industrial hazardous waste from synthetic chemicals seeping into places where they should not be. Concerns about the toxicity to the body and chemical exposure grew alongside concerns about the impact of chemicals on the environment. Historian Virginia Smith calls those who first called attention to the problem of pollution in the 1960s, "ecological puritans," but these concerns were broader—and became a strong and enduring sensibility in the counterculture.[428]

For Roszak, the environmental movement was one of the legacies of that moment of deep and broad questioning of the status quo that was at the root of the Counterculture. What they had done was "found a new ecologically grounded reading of the myth of the noble savage."[429] This was evident in the food, the clothing and the music that the counterculture embraced.[430] All

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[426] See for example, Sellers, Christopher C. *Crabgrass Crucible: Suburban Nature and the Rise of Environmentalism in Twentieth-century America*, University of North Carolina Press, 2012.

[427] Ibid.

[428] Virginia Smith (2007), 130.

[429] Roszak (1995), xxviii.

[430] For more on how the counterculture embraced ethnic foods, see Warren Belasco (2007); for more about the counterculture's explicit embrace of pre-industrial ideas/non-Western cultures, see Braunstein, Peter, and Michael William Doyle, eds. (2013).

eschewed artificiality in favor of the natural and authentic—a reading for them that meant anti-corporate—and very specifically anti-chemical. Ecological perspectives infused the counterculture in the late 1960s and 1970s; it could be seen in the extent to which articles on ecology proliferated in virtually edition of the collection of papers that constituted the underground press. Articles like poet Gary Snyder's "Ecology Manifesto: the Four Changes" published in various underground publications in 1969, and "An Ecological Conscience" from 1966 issue of SANITY which was a response to an article from earlier in SANITY called "Man the Measure of All Things?".[431] Though "ecology" was still fairly ill-defined at the time, what it meant to invoke it was clear--a respect for the environment and a privileging of what could be construed as "natural." They embraced organic farming, which rejected the pesticide-heavy practices of conventional and industrial farming and promote natural, microbe-friendly and useful practices.[432] The food culture of the ecologically inclined also looked to get away from the highly industrialized and chemically processed foods of the 1950s in favor of authentic and ethnic foods.[433]

The ecological sensibility that threaded through society of the times led to a broad concern with the over-chemicalization of everyday life, and had broad implications.

First, it created a new kind of consumer. Those who embraced an ecological ethos wanted to live that ethic. To so do, they would need the means to do so—they would either have to make what they needed or buy it to opt out as much as possible from a conventional consumerism that depended heavily on synthetic chemicals across the board. By the late 1960s, they could browse

[431] For example, see *The Fifth Estate,* Dec. 11-24, 1969, 94, Underground Newspapers Collection.

[432] See Case, Andrew S. (2012).

[433] Belasco (2007).

the Whole Earth Catalogue to find products that suited an ecological lifestyle and could shop at their local food co-op to find the unprocessed foods they wanted.[434]

[435] Concerns about the impact of chemicals on the body became the impetus for the birth of an alternative to the hygiene industrial-chemical complex: a burgeoning natural products industry, which sprang up cross the globe. The new consumer provided an opportunity for natural cosmetics and hygiene entrepreneurs. In the 1960s and 1970s, new natural hygiene companies forged in the counterculture sprang up to meet this demand. [436] By the 1980s, their products came to sit alongside the antiseptic products in drug stores across the country as the sector gained more adherents.[437]

Tom's of Maine, one of the first to become an established company in the sector, launched in 968 with phosphate-free laundry detergent and expanded into the natural personal hygiene market by the mid-1970s.[438] These new products did not proclaim their "germ killing" powers and chemical, technical prowess as earlier personal hygiene products had, instead they

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[434] See Cox, Craig. *Storefront Revolution: food co-ops and the counterculture*. Rutgers University Press, 1994.; See also Belasco (2007).

[435] Deese, Richard S. "The Artifact of Nature: 'Spaceship Earth' and the dawn of global environmentalism." *Endeavour* 33.2 (2009): 70-75. Deese describes it as follows: "By the summer of 1969, a different aesthetic of technology was gaining ground, as indicated by the success of R. Buckminster Fuller's book *Operating Manual for Spaceship Earth*. Displacing the old Promethean vision of dominating nature, this aesthetic stressed forming a symbiotic relationship between human civilization and the natural world. This new aesthetic would become paramount in the early 1970s as evidenced by the success of Stewart Brand's *Whole Earth Catalogue*, which offered countercultural consumers an opportunity to purchase geodesic domes, solar water heaters and other artifacts of 'appropriate technology', and E.F. Schumacher's 1973 book *Small is Beautiful* which extolled the virtues of decentralized, small-scale economies."

[436] For more about the emergence and growth of the natural beauty industry and green entrepreneurship in the 1970s, see "Entrepreneurship in the Natural Food and Beauty Categories before 2000: Global Visions and Local Expressions," Geoffrey Jones, Harvard Business School Working Paper 13-024 August 28, 2012.

[437] Jones (2012).

[438] See Tom's of Maine corporate website: "Heritage" http://www.tomsofmaine.com/company. Accessed August 12, 2013.

asked the following: “Why do we have to put up with things like...artificial bactericides in our deodorants? ... Has America forgotten how it feels to live without [them]?”[439] The new consumer wanted, these new companies claimed, products that “contain the things people used before we got so fancy and technical.”[440] As the founder Tom Chappell told the Boston Globe in 1980 in a glowing article about his growing company, “Tom’s is committed to the person who chooses natural living.”[441]

Dr. Bronner’s Magic Soap and Hippie Hygiene

The most popular and iconic hygiene product for the eco-sensitive counterculture was Dr. Bronner’s Magic Soap. It had the right politics and ingredients. Its iconoclastic founder, Emil HeilBronner, was a scion of a famous Orthodox Jewish family of master soap makers and emigrated from Germany to the United States in 1929. He made a living as a soap consultant based on his familial and education experience in the field and saw the transformation of the soap industry by the synthetic chemical age.[442] The rise of Nazism and the extermination of his parents in the Holocaust further radicalized the already eccentric Bronner, who dropped the “Heil” from his name in the 1930s as Hitler rose to power. He gained notoriety for his broad-ranging philosophy in the 1940s—calling for interfaith peace and understanding, and selling soap on the side. He married his philosophy with his product, literally. Snippets from his obscure

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[439] Early Ad for Tom’s of Maine, from Tom’s of Maine website. Accessed August 12, 2013. http://www.tomsofmaine.com/business-practices/heritage/early-history

[440] Ibid.

[441] “Even toothpaste is back to basics,” Kay Longcope, *Boston Globe,* February 28, 1980, 15.

[442] “Our Story,” Dr. Bronner’s Magic Soap corporate site. https://www.drbronner.com/our-story/timeline/. Accessed August 12, 2013.

philosophy were written in tiny type on the label of each bottle. It was an ideology embodied in soap. Hippies and counterculturalists responded to it as a complete counterpoint to the corporate, chemical "hygiene freak" industry—in distribution, in marketing, and in presentation.

They liked that it came packaged with a cryptic philosophy "All-One" that argued for world peace and an ecological worldview that co-opted Buckminster Fuller's "Spaceship Earth."[443] It was an integrated philosophy—the soap had multiple uses and the label argued cryptically for a "we're all in this together" worldview that he had been hawking in speeches before slapping it onto soap labels. Dr. Bronner's natural soap saw its sales grow in the late 1960s. The soap was popularized through word of mouth, passed along at communes and happenings and concerts. In became particularly popular in 1968 at Haight Ashbury and found its way by word of mouth onto the shelves of health food stores and food co-ops across the country that were the meccas of countercultural lifestyle management.[444] Everything about the soap—its mode of transmission and creation, the explicit ideology that its maker embraced, even the fact that Dr. Bronner printed his phone number on the label and accepted calls from all comers at all hours of the day—were a completely radical departure and a rewriting of what hygiene could mean, and how it could be done, and how it could be sold. Dr. Bronner's soap had multiple uses, as laid out on the label. It was used to clean clothes, cars, pets, hair and bodies—a rejection of market segmentation as well as a rejection of the idea that bodies were different than other kinds of things that needed cleaning.[445] It was literally embodied ideology.

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[443] Dr. Bronner's Magic Soap labels.

[444] Cox (1994).

[445] For more on Bronner, see Pat Sherman, "In the Spirit of Soap," *San Diego Magazine* February 2007, 106-109; 200; Japenga, A., "A Philosopher and his Soap," *Los Angeles Times,* July 28, 1987; "Dr. Bronner's Castile Soap and `Full truth' religion," December 10, 1995, National Public Radio, Washington, D.C., United States, Washington, D.C.:; Sullivan, R., "Vogue beauty: Soap salvation," *Vogue,* September 1. 1997. 546-546, 548.

But beyond its seemingly perfect instantiation as the anti-commodity commodity, it was the composition as well that served as a selling point. As Dr. Bronner himself recalled, “They liked the “No synthetics! None!” notation on the label.”[446] They also liked that it was biodegradable. As his grandson who now runs the company recalled about his grandfather’s mid-century philosophy, “The mantra of the day was *Better living through chemistry*. ...They were making pesticides and plastics and artificial fertilizers and here’s my grandfather saying, “you’ve gotta watch out for this stuff.”[447] Dr. Bronner’s was a counterpoint and an eagerly embraced counterpoint to the “hygiene freak companies” on bodies that had been disciplined to consider themselves problematic and in need of chemical processing and “purifying finishes” to be acceptable. Dr. Bronner’s soap and its adoption provided a product for the new eco-friendly, anti-chemical ethos of the 1960s.

The New Consumer and the Hygiene Industry

The possibilities of this new consumer were not lost on the marketing world or on the hygiene industry, who tried to co-opt it in short order. By the early 1970s, the 1960s youth were maturing into a powerful new demographic block, with a new set of values. Madison Avenue and the market were eager to respond.

Ernest Dichter, the marketing guru and motivational research pioneer lent an increasing amount of time and space to try to characterize the new post-hippie consumer of the 1970s and how best to market to them, and to divine their values. In his newsletter *Findings*, for example,

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[446] Hillinger, C., “This Man's Soapbox is a Bottle of Soap,” *Los Angeles Times*, February 9, 1977.

[447] Quoted in *The GORT Cloud: The Invisible Force Powering Today's Most Visible Green* Brands By Richard Seireeni, Chelsea Green Publishing, 2008, see “Case Study No. 1: Marketing Magic: Dr. Bronner’s Magic Soap,” 33.

he advised his subscribers on how to monetize the “anti-establishment” attitudes of the youth market (“Fads: Serious Business”[448]), chided corporations for attempting to display a social conscience to more ecologically sensitive consumers (“waterfalls rushing down the faces of detergent boxes...sparkling rivers flowing over chemical manufacturers’ logos.”) and analyzed the effectiveness of their strategies.[449] He presaged the coming of the new eco-conscious consumer in his newsletter with articles like “Back to Nature Cosmetics,”[450] “How Can advertisers bridge the generation gap?” which tried to decode the new countercultural youth attitudes and sensibilities to Madison Avenue.[451] He speculated on the idea of an emerging “Body ecology”—and “mouth ecology” in a report for Lever Brothers on toothpaste in 1971, suggesting a new era in hygiene:[452]

> “It seems to us that this country may be entering the beginning phase of what may be called "body ecology." With increased attention being focused on the impact of pollutants on the environment, Americans are likely to start seeking out individual ways of expressing their fears and anxiety. One possible way in which such concern may be manifested is in the development of new body care practices designed to limit the real and imaginary pollutants. “[453]

[448] “Fads: Serious Business,” *Findings* Nov-Dec 1970, 6, No. 10. 2. Ernest Dichter Collection, Box 128.

[449] “Advertisers and their “Social Consciences,” *Findings* 1971, 7 No. 9, 2-3. Ernest Dichter Collection, Box 128.

[450] “Back to Nature Cosmetics,” *Findings*, February 1972, Ernest Dichter Collection, Box 128.

[451] “How Can advertisers bridge the generation gap?” *Findings*, March 1969, Vol 5. No. 3, 1. Box 127, Ernest Dichter Collection.

[452] “Oral Hygiene - The Psychology of the Mouth -- A Proposal for a Motivational Research Study Lever Brothers Company” 1971. P. 10 Ernest Dichter Collection 26. 108 2470A.

[453] Ibid, 10.

His motivational research take was right on—except that the pollutants that these new consumers feared were in the products themselves that Dichter was trying to help sell to them. The new ecological sensibility was not lost on the hygiene industry and it tried to co-opt it by creating product lines to appeal to this new disaffected consumer. One company, Mennen aimed to do so by marrying ecological sensibility with the tried and true strategy of scientific authority.

Mennen and Natural Body Ecology

In the summer of 1972, the Mennen Company announced to more than thirty journalists the launch of a new, revolutionary product. It was a new underarm deodorant—by then an old category—but a truly new kind of deodorant that embodied the values of the times. Unlike the harsh chemical products of the past, Mennen's new deodorant was laced with a so-called natural deodorizing agent, Vitamin E. Vitamin E was riding a wave of interest in the late 1960s. [454] After the FDA formally recognized it as essential for human nutrition in 1969, the market eagerly used it for various products. Vitamin E was the latest miracle vitamin; it could allegedly cure varicose veins, heart disease, impotence, and alleviate the signs of aging. [455] It was pushed as a natural remedy that had extensive cosmetic benefits without itself being a cosmetic. As one advertorial crowed, "Vitamin E Oil is a non-cosmetic product that gives amazing cosmetic results. This organic fluid is not a "cover-up"...it is absolutely natural... [and will] give you better

[454] "Debating Face Value of Vitamin E" by Beth Ann Krier, *Los Angeles Times*, September 19, 1972, D1; "The Vitamin E Boom: 4 Experts Sift Fact From Fantasy," Voltz, Jeanne, *Los Angeles Times*, February 3, 1972; 11.

[455] Krier (1972), D1.

results than you ever dreamed possible from a fine beauty product."[456] Mennen's research scientists claimed that the all-purpose remedy could be used in the elimination of underarm odor, which by then had grown to a half a billion dollar industry in the US. The announcement was sufficiently important to the company that the president, George Mennen himself, gave the introduction to the sciences director of the company before he gave his presentation to the press. Dr. Harold Schwartz had been working on the new product for five years, and confidently unveiled it to the world. Using flip charts, he broke down the science behind the new product into bite sized bits: "How Perspiration Odor is formed," and then: "Change in Bacterial Population, and finally, "Maintenance of Body Ecology."[457]

The problem with underarms, Dr. Schwartz explained, was not *sweat*. Sweat didn't cause odor. Rather, the problem was the combination of "resident bacteria" living on the underarms and oxygen. Vitamin E, an antioxidant, could solve the problem, Dr. Schwartz explained, because it could prevent the biochemical reaction that created the offending odor. But more than that, it would do so without destroying the bacteria as the aggressive chemicals in traditional deodorants would. Mr. Mennen stressed this point, the raison d'etre of the product: Mennen E preserved "the natural body ecology," and would not "upset the balance of nature."[458] This was what was revolutionary about the new product: a deodorant that acknowledged the anti-chemical orientation of the times and which leveraged a natural solution that respected the natural flora of the body.

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[456] VITALE advertorial, "Vitamin 'E' Oil Gives Skin New Beauty in Days," *Los Angeles Times*, November 26, 1972, 14.

[457] "Advertising: Vitamin E Underarm Assault," Philip H. Dougherty, *New York Times* June 9, 1972, 47.

[458] Ibid.

The product was a big deal. Mennen was so sure that it was a sure thing that they hadn't even test marketed it and hadn't even done market research on the advertising. Instead, small, hotshot agency Martin Landey, Arlow Advertising had been working for 2 years on the project in virtual secrecy. Mennen put a massive 12 million dollars behind the introductory marketing campaign and dropped the project just a few weeks after it unveiled it to journalists with ads in magazines and newspapers and a 2.5 million dollar TV advertising budget.[459] Mennen, the innovator behind antiperspirant and aerosol deodorant was poised to launch "a new era of deodorant protection," as the ads proclaimed. This era would be in tune with the times—an ecologically sensitive product for an ecologically sensitive time.

Less than a year later, after selling 10 million units and after the FDA had received an "unusual number"--7 times as many complaints--about the product as normal due to underarm rash (contact dermatitis) and other adverse reactions, Mennen stopped shipping the product.[460] The debacle became a textbook case for failure of a product launch in marketing departments.[461] But what was important was what Mennen and Schwarz and Martin Landey tried to do—and what certain markets embraced. The full page magazine ads in *McCall's*, *Newsweek*, *Reader's Digest*, *Psychology Today*, *Good House Keeping* and *Art Direction* honed in on the message:

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[459] *Broadcasting* 85, (1973), 20

[460] "Psst…The End of Mennen E," *Washington Post*, April 7, 1973, D2.

[461] For example, see *Essentials of Marketing*, by Joel R. Evans and Barry Berman, New York: Macmillan Publishing Co., 1984, 45 and William M. Pride, O. C. Ferrell, *Marketing: Basic concepts and decisions*, Houghton Mifflin, 1980, 218. In most cases, marketing specialists agree that the problem was the lack of research, though some scholars have claimed that the problem was that consumers were perplexed about the relationship of Vitamin E to their armpits. (See *The Making of a Name: The Inside Story of the Brands We Buy* by Steve Rivkin and Fraser Sutherland, Oxford University Press, 2005, 85. This seems unlikely, however, given the popularity of Vitamin E at the time and its status as a cure-all for a wide variety of conditions.

"Unlike other harsh, chemical-based deodorants, Mennen E does not significantly intrude on **the balance of nature on the body**."[462]

But beyond the complaints that the product precipitated, it did not find the instant reaction from the public and the "new consumer" that Mennen assumed it would. It was the general consensus of the advertising and marketing world that "the advertising stressed a product attribute that was not salient to the consumer."[463] In analyzing the product's failed launch, Ernst Dichter noted that the uniqueness of the product—the Vitamin E as a selling point—did not go far enough. "Mennen...was more successful initially with shampoo based on protein—than with [Mennen E]. ...Overemphasis on ascertaining "uniqueness" rather than filling a need... [could be a problem]."[464] But the more important point was that those to whom they wanted to appeal--hippies, environmentalists, counterculturalists--were not ready to listen to or look to Mennen, a "hygiene freak company" for an ecological solution to the problem of body care. Mennen was advertising in the wrong places and to the wrong people.

The people who were looking for this kind of product were not looking to Madison Avenue to solve this problem or address it. The market was growing, but Mennen missed it—it was about an ideology, not just an ingredient. And the youth was highly skeptical of Madison Avenue and the products they sold—in particular hygiene companies like Mennen. They were on to "the hygiene freak companies" and their attempts to use the counterculture as an advertising

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[462] For example, see Mennen ad in *McCall's,* December 1972.

[463] See "Advertising and the consumer," Engel, James F. *Journal of Advertising*, Summer (1974): 8 and T. G. N. Chin, "New Product Successes and Failures: How to Detect Them in Advance," *Advertising Age*, September 24, 1973, 61.

[464] Ernest Dichter, "When a "Checked Out" new Product Poops Out," *Findings*, February 1973, Vol. 9, No. 2, 1. Box 128, Ernest Dichter Collection.

angle.[465] In 1970, the exasperation and disgust of some in the counterculture was explicit: "You kin start a movement to Liberate Womens an Zap in two Weeks here comes Look magazine with a Cover Story an sells a million dollars in Advertisin to deodorant manufacturers with it. What I am sayin is that Almos Anything is cooptable by the Establishmen."[466] It was Tom's of Maine and Dr. Bronner's that were sought out by the new consumer and which were available in the right spaces-- shelved in local co-ops and "marketed" via word of mouth.

Environmental Concerns and Regulation in the 1970s: Hygiene and Human Health

This concern with the over-chemicalization of life inaugurated a period of increased regulation in the 1970s focused on chemical containment and environmental protection. The Environmental Protection Agency was founded in 1970 to strengthen and consolidate environmental policy and regulation regarding chemical pollution and its impact on the environment and human health.[467] While the EPA focused on policies governing chemical releases in the environment, the Food and Drug Administration addressed those chemicals which were part of everyday bodily use. The FDA's Over-the-Counter Drug Review was begun as a follow up to the Drug Efficacy Study Implementation that had been initiated by the Kefauer-Harris Amendments of 1962. DESI assessed prescription drugs, while the OTC Review was focused on those drugs and chemicals that were not subject to DESI regulations. However, the OTC Review can be seen as a continuation of the efforts to control industrial pollution and

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[465] "Woodstock—3 days of peace?," *Great Speckled Bird*, July 28, 1969, 7.

[466] Og, "Foible of the End of the Revolution, No. 67," *Great Speckled Bird*, February 23, 1970, 2.

[467] For more on EPA in the 1970s, see Collin, Robert W. *The Environmental Protection Agency: Cleaning Up America's Act*. Greenwood Publishing Group, 2006 and McMahon, Robert. *The Environmental Protection Agency: Structuring Motivation in a Green Bureaucracy: The Conflict between Regulatory Style and Cultural Identity*, Sussex Academic Press, 2006.

protect the human safety by managing the toxicity of chemicals used on the body. Over-the-counter drugs were regulated differently from prescription drugs; they were the province of hygiene and cosmetics industries as well as drug companies in the business of nonprescription drugs. The OTC Review, was, in effect, about the management of risk and the protection of the health of the body with respect to extensive exposure to chemicals through repeated daily use. Here, the hygiene industry was pitted against a governmentally empowered cadre of biomedical experts who tried to characterize the dangers of hygiene products to the body. Their concerns echoed those of the hippies, feminists and eco-consumers described above: they were concerned with defending and protecting "the natural" body from the hygiene industry.

This Review included the hygiene products eschewed by ecologically conscious consumers, counterculturalists and feminists as avatars of chemical cleansing. In the investigation of these particular chemicals, the status of the germs of the body became central—and the extent to which they should be considered part of the "natural" body to be protected was at issue.

The FDA's Over-the-Counter Drug Review: "Body Ecology" and the Hygiene Industry

In the 197s' OTC Review, the question of whether or not the microbes that live on the body should be subject to regulatory protection from the antimicrobial ingredients in soaps and deodorants used by the hygiene products industry came to be hotly debated in the halls of the FDA.[468] The controversy lined up in classic terms—Industry vs. Academic Science—and at

[468] The FDA has opened up this front on antimicrobial soaps just recently after finally issuing its final report on triclosan in December 2013—after opening it in 1972. See FDA Consumer Updates: "FDA Taking Closer Look at 'Antibacterial' Soap," December 16, 2013. http://www.fda.gov/forconsumers/consumerupdates/ucm378393.htm and "Five Reasons Why You Should Probably Stop Using Antibacterial Soap," Smithsonian Magazine.com, January 3, 2014. Accessed January 5, 2014. http://www.smithsonianmag.com/ist/?next=/science-nature/five-reasons-why-you-should-probably-stop-using-antibacterial-soap-180948078/..

stake for both was who had the authority to direct policy. But this was not only about the demands of big business's clout in government against a disinterested cadre of scientific experts, it was fought out over who had Good Science on their side. Did industry, with its long years of established protocols and massive resources, know how best to make a scientific determination about risk and safety—or did the academic doctors and scientists who were the leading lights of a field that had fairly low status in the biomedical firmament? Was their tough stance on what came to be referred to as the "body ecology theory" about doing Good Science or was it an attempt to defend a framework which had provided a scientific basis and theoretical grounding for the field? This controversy over whether or not the microbial body needed protecting and what the consequences of a decision might be were played out in the eco-conscious 1970s. It is no surprise who "won" the debate at the FDA over body ecology, but what was interesting is that there was a debate at all—that at this period in time there was public visibility for this kind of science and these kinds of concerns.

The OTC Review

In 1972, the Food and Drug Administration began the Over-the-Counter Drug Review as a follow up to the Drug Efficacy Study Implementation (DESI). FDA Commissioner Charles Edwards, who had not started DESI but oversaw its implementation from his appointment by Nixon in 1969, decided to expand the drug review functions of the FDA and assess nonprescription drugs as well. His proposal to do so was announced in the *Federal Register* in January 1972. It was a wildly ambitious proposal—Edwards proposed to review the "safety, efficacy and labeling" of *all* nonprescription drugs by independent advisory committees.[469]

[469] Yingling, Gary L. "The OTC Drug Review," *Food, Drug and Cosmetics Law Journal* 28 (1973): 273, p. 273.

Because of the vast number of products that this would entail reviewing, Edwards and his top lawyer Hutt organized the review around "active ingredients"—grouping products according to the drugs that provided the effect of the product. The first two categories were announced the same day as the announcement of the project in the *Federal Register* with a call for data about active components of antacid products—and a call for information about antibacterial agents in products meant for "repeated daily human use."[470] Edwards and Hutt moved fast; Hutt drafted the regulations and Edwards signed the final regulations for the review in May.[471] Both were eager to create a smooth process—Hutt was quite candid about not wanting to create another DESI, and so organized the process to be as a streamlined and efficient as possible.[472]

The advisory panels reflected the changing times and the changes that Edwards had brought to the FDA. The panels were comprised of seven appointed voting members who had technical expertise to scientifically assess the drugs under review—academics and clinicians in addition to at least one toxicologist and one pharmacist. The experts were all hired as consultants to the government and could not have any conflict of interest in evaluating the drugs under review. The three nonvoting liaison members were comprised of an FDA employee from the Bureau of Drugs (to allay, in part inter-administration politics over where the OTC should live—in the Commissioner's office or in the Bureau of Drugs), a consumer advocate appointed by the barely new Consumer Federation of America and an industry representative appointed by the consumer health products trade association, the Proprietary Association.[473] In an era in which the

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[470] *Federal Register* 37, p. 4. January 5, 1972.

[471] *Federal Register* 37, p. 9464, May 8, 1972.

[472] J. Richard Crout FDA Oral History, p. 19-20, FDA History Office.

[473] Yingling (1973), p. 274.

consumer movement was having a major impact on government, the FDA wanted to open up its processes to public view—"the advisory committees were set up on purpose to open up decision making and expose FDA decision making to a more public view, with scrutiny and participation by major academic figures," as J. Richard Crout, the Director of the Bureau of Drugs at the time recalled.[474]

Change at the FDA: A New Openness

The early 1970s were a tumultuous period for the regulatory structure in the United States and in particular for the FDA. Charles Edwards, an MD brought in from Booz Allen Hamilton by Nixon's administration to run the FDA in 1969 revolutionized the agency. He doubled the budget in two years, using his connections and political skills, and streamlined its functions.[475] He created the expert advice system—institutionalizing the use of expert committees and vastly increasing the number of expert committees involved with FDA decisions. They expert committees brought in cutting edge researchers—and many of leading researchers--"the best people in the country," as Edwards' successor as FDA Commissioner, Alexander Schmidt recalled— agreed to join them.[476] Meetings with industry leaders became a regular occurrence and consumer advocates were brought to the table and met with FDA on an official basis, if less frequently than industry leaders.[477] Edwards and his administration opened up the FDA to the public view and public participation.

[474] Crout Oral History, p. 22.

[475] Hilts, Philip J. *Protecting America's health: The FDA, business, and one hundred years of regulation*. New York: Alfred A. Knopf, 2003, p. 195.

[476] Schmidt Oral History, FDA History Office, p. 65.

[477] The consumer movement had opened up the doors of government in other ways—1967's Freedom of Information Act made meetings and records accessible to the public and the Advisory Committee Act of 1972 ensured that

Industry was not surprisingly nervous about the new openness and the new power of the consumerist movement. The trade associations for both the Proprietary (personal hygiene) industry and for the Pharmaceuticals Manufacturers industry both issued statements to express their vehement opposition to the OTC regulations being "substantive" rather than "interpretive."[478] It was the general consensus that a court challenge from a trade association or a company would be forthcoming, challenging the FDA's authority to issue "substantive regulations"—which had the force of law versus "interpretive" regulations, which were essentially guidelines.[479] But the FDA would not back down, and this opening salvo set the tone for the OTC Review, with industry feeling under threat and defending itself aggressively.

Hexachlorophene and the Antimicrobials I Panel

The Antimicrobial Panel seemed urgent—there had been controversy in recent years about hexachlorophene, the antimicrobial ingredient that had come to be used in a vast number of hygiene products over the previous two decades, and its safety. Despite a 1969 report by William Gump, the creator of hexachlorophene himself, claiming that hexachlorophene "presented no problems for its topical use for humans" despite its "fairly high oral and systemic toxicity" for animals, reports about its dangers for human use accumulated by the early1970s.[480]

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consumer representatives could attend expert committee meetings and that most of these meetings were open to the public. Prior to the Edwards era, an estimated 90% of FDA files were secret. Hilts (2003), p. 196. Note about the lawsuit (birth control, Morgan) that led to Edwards' top lawyer Hutt to set rules that made 90% of FDA files open to public.

[478] "FDA's effort to invest OTC/Proprietary Monographs with Substantive Regulatory Status Faces Court Challenge" *FDC Reports* 34, January 10, 1972, p. 30.

[479] Ibid, p. 29.

[480] Gump, W. S. (1969), "Toxicological properties of hexachlorophene." *Journal of the Society of Cosmetic Chemists*, 20:173.

It is perhaps not surprising that Gump, who had first suggested that hexachlorophene be brought into the personal hygiene market and made a fortune off it, would discount the dangers. However, FDA studies, prompted by a proposed move to expand the use of hexachlorophene, showed something troubling.[481] FDA studies showed a link to both brain seizures in infants and paralysis in rats, and the issue sparked public concern.[482] The controversy spilled out into the public sphere in March 1971, when the FDA announced that it was studying the issue and considering action on hexachlorophene. [483]

By November, Ralph Nader and his organization Public Citizen's new Health Research Group (founded that same year) was calling for the FDA to classify all soaps, deodorants and feminine hygiene sprays as drugs to be available through prescription only.[484] Nader and his army of acolytes leveled a sustained attack on federal regulation starting in the late 1960s, in part by generating numerous reports and books in the late 1960s and early 1970s that attacked particular agencies' shortcomings as the consumer movement saw them, and were able to effect real change.[485] Nader chided the FDA for protecting industry because of its refusal to act, despite the clear scientific evidence of and the clear concerns of FDA scientists over the toxicity of hexachlorophene. Just two months later, in January of 1972, the FDA offered new limits on hexachlorophene's use in products. The following month, the FDA issued a joint statement with

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481 Gump, W. S. (1969), "Toxicological properties of hexachlorophene." *Journal of the Society of Cosmetic Chemists*, 20:173.

482 Graham, Ellen, "Government Studies Neurological Effects of Hexachlorophene: Widely Used Disinfectant Tied To Brain Seizures, in Infants, Paralysis, Lesions in Rats," *Wall Street Journal*, 30 Mar 1971: 12.

483 Ibid.

484 "Nader Urges Curb on Use of Hexachlorophene in Soap," Special to The *New York Times* 29 Nov 1971: 27; "Nader asks for controls on hexachlorophene," *The Baltimore Sun* (1837-1987), 29 Nov 1971: A10.

485 For history of consumer activism in the United States, see Hilton, Matthew. *Prosperity for all: Consumer activism in an era of globalization*. Cornell University Press, 2009.

the American Academy of Pediatrics and the National Center for Disease Control which declared that "there is a firm basis for concern about the indiscriminate or prolonged exposure of humans to hexachlorophene."[486] And by September of 1972, it was front page news when the FDA banned nonprescription sales of hexachlorophene outright after thirty infants were killed in France due to hexachlorophene-laced talcum powder.[487]

For industry, the writing had been on the wall for some time, so many companies had already moved to remove hexachlorophene from their products. Purex, Proctor and Gamble, Noxell, and Gillette swapped out hexachlorophene for other less controversial and less well-known antibacterial agents.[488] Other companies, like Colgate, gave up on the antibacterial segment altogether and removed antibacterial agents from products that had previously had them. But it would hit three of the major hygiene products companies quite hard. First, New Jersey-based and Swiss-owned Givaudan—for whom Gump had developed hexachlorophene, and who was its only producer in the United States, would be hit hard enough financially that it was considering legal action in light of the "hysterical" overreaction of the FDA.[489] Armour-Dial, which would have to redo the formula for its very popular Dial Soap, was looking at a $3 million dollar net loss, and was caught off guard by the scope of the ban. PhisoDerm, a leading acne wash producer was facing a major recall in light of the September decision. This was would

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[486] Lockhart, Jean D. "How toxic is hexachlorophene?" *Pediatrics* 50.2 (1972): 229-235.

[487] "FDA to curb sales of germ-fighter," *The Baltimore Sun*, 23 Sep 1972: A1.

[488] Many of these were those same companies that had jumped on the hexachlorophene band wagon in previous years. See the Prologue.

[489] "U.S. Hexachlorophene Curbs Will Hit Hard At 3 Firms, Have Little Effect on Others," *Wall Street Journal*, 25 Sep 1972: 4.

have a huge impact on the American hygiene industry; an estimated four million pounds of hexachlorophene were used annually in the United Stated by 1972.[490]

The hygiene industry's experience with the hexachlorophene incident primed it to defend its bottom line when the OTC Review's Antimicrobials section got underway. Armour Dial in particular—which had been forced to write off $6 million dollars in Dial Soap inventory and had to shut down production for two weeks while it reformulated its soap with triclocarban, was primed for a fight and took a leading industry role in the debates over the OTC Antimicrobial Panel's findings.

The Antimicrobials I Panel

The panel was comprised of leading experts in their field. The first experts to be appointed to the panel were announced in late March of 1972. They were Harvey Blank, MD, chairman of the dermatology department at the University of Miami School of Medicine, Walter Lobitz, Jr., head of dermatology at University of Oregon Medical School and Raymond Hopponen, the Dean of South Dakota College of Pharmacy and author of the Anti-Acne chapter in the 1971 edition of the American Pharmaceutical Association's Handbook of Non-Prescription Drugs.[491] By June, the complete panel had been named, adding Howard Maibach, associate professor of Dermatology at UCSF Medical Center, Paul Stolley, MD, of the Hopkins School of Public Health, U Mississippi Dean of Pharmacy Wallace /Guess, PhD, Frank B. Engley Jr., PhD, Dean of U of Missouri School of Medicine's microbiology department, Dr. Florence Kinoshita of the University of Chicago's toxicology lab, and Dr. Faye Arundell, a

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[490] Ibid.

[491] "Hopponen, Lobitz, Blank on FDA HCP-Antibacterial Panel." *FDC Reports* 34, March 27, 1972, p. T&G1-2.

physician from Menlo Park, California.[492] Maibach was replaced with a colleague from UCSF Medical Center's dermatology department, William Epstein.[493] When Arundell was dropped because of a potential conflict of interest in June, the FDA offered her spot to a researcher whom industry trade magazine *The Pink Sheet* (also known as FDC *Reports*) referred to as "world famous English dermatologist" Mary Marples.[494] Because of the vital importance of the panel's purview to the cosmetics and personal hygiene industries, industry representatives from each of those industry's trade associations (the Proprietary Association and the Cosmetic, Toiletry and Fragrance Association) were named.[495] There was concern in the industry about Engley being named to the panel because of his allegedly strong anti-industry bias.[496] The Proprietary Association was nervous from the start about the whole advisory panel set up, and in meeting with the FDA to outline the liaison's participation, insisted on being able to contest the OTC regulations if any company opposed them. Generally there was concern about what the OTC Review would entail; the first panel that met, the Antacid Panel, had gotten off to a rocky start—Edwards had to try to "close" the credibility gap" between the PA and the FDA after the first

[492] "FDA's Antimicrobial/Hexachlorophene Advisory Panel," *FDC Reports* 34, p. 2. June 5, 1972.

[493] "FDA Antimicrobial/Hexachlorophene Panel May Get International," *FDC Reports*, July 3, 1972. Vol. 34, p. T&G2.

[494] Ibid. *FDC Reports* was the Drug and Cosmetics industry/regulatory trade journal that covered industry and government regulatory activity.

[495] "FDA's Antimicrobial/Hexachlorophene Advisory Panel," *FDC Reports* 34, p. 2. June 5, 1972. Dr. Joseph Pisani was the PA's rep and Gillette's Robert Giovacchini for cosmetics.

[496] *FDC Reports,* March 27, 1972, p. T&G2.

meeting of the antacid panel “got off track” and to allay their concerns about the review and its process.[497],[498]

Industry perhaps should have also worried about the possible appointment of Dr. Mary Marples. Dr. Mary Marples had published a seminal book about skin bacteria called *The Ecology of the Human Skin* in 1965.[499] Her “monumental opus,” as leading dermatologists were calling it by the mid-1970s, had revolutionized the field of dermatology and had become a key reference point and core document for the dermatological subfield of skin bacteriology.[500] Such was the impact of and interest in the book that she was invited to write an article about it for *Scientific American* in 1969.[501] The famous poet WH Auden even wrote a poem inspired by the article.[502] Retired by the 1970s, Marples was considered *the* authority on the bacteriology of the human skin. She was highly esteemed by the panel—the panel’s chair Dr. Harvey Blank had nominated her for honorary membership to the society of investigative dermatologists in 1967, the year she retired.[503] Her 1,000 page book was well-reviewed outside of the specialist bacteriological and dermatological press in major journals like *JAMA* and the *British Medical Journal*. Both reviews

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[497]“Naming of advisory panel on HCP & Antibacterials,” *FDC Reports* 34, March 20 1972, p. T&G1-2.

[498] “Feb 22 Meeting of FDA Antacid Advisory Panel,” *FDC Reports* 34, Feb 28, 1972, p.T&G1. That inaugural meeting had “degenerated” so quickly into such “a government talkfest” about process and FDA procedures that one panelist turned off his hearing aid shortly after the meeting started

[499] Dr. Marples (MD) was based in New Zealand’s Otagu University microbiology department, where she taught and researched medical mycology and bacteriology. “1946: Molly Marples Joins department,” “A Brief History of the NZMS,” 2005. http://micro.otago.ac.nz/history/1946/molly-marples-joins-department

[500] Kligman et. al. (1976), “Bacteriology,” *Journal of Investigative Dermatology* 67: 160-68.

[501] Marples, Mary J. "Life on the human skin." *Scientific American* 220.1 (1969): 108.

[502][502] WH Auden, “A New Year Greeting, after an article by Mary J. Marples in Scientific American. January, 1969. (For Vassily Yanowsky).”

[503] “The Society for Investigative Dermatology, Inc. 28th Annual Meeting” (1967): *Journal of Investigative Dermatology* 49, 337-47, P.342.

praised her innovative "microbe's eye view" approach to skin as soil."[504] The reception of her book moved her from merely distinguished in the field of medical mycology to world famous in dermatological circles. It was her work that would be a key piece of evidence and source of scientific authority for the position of the dermatological experts on the panel.

Marples' *The Ecology of the Skin* was the founding text for the new direction in skin bacteriology in the 1970s, framing as it did skin health and disease as an *ecological* problem. It provided a contrast with older approaches to health and disease, with the focus on "bacteria killing" of conventional medicine. This was important because, as a prominent skin bacteriologist noted in the 1970s, "We are just beginning to learn that there are other approaches to the prevention and control of bacterial disease,…that there are "good" as well as "bad" bacteria, and that wanton policies of destruction only create new problems."[505] The research of the day had "strong ecologic overtones,"—focusing on "cutaneous habitats, the factors regulating the composition and density of the microflora and the interactions among them, [and] the effects of artificial dispossession of native organisms…"[506] This "new emphasis," he stressed, was in line with the concerns of the day—the research orientation was happening "at a time when ecology is a dominant theme of modern life."[507] Researchers insisted that this new theory was not just "an academic sport," but a research direction that had produced, and would

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504 JAMA called her ""microbe's eye view" of the skin" not just "entertaining" but perhaps more importantly, "valid." Fite, George L. "The Ecology of the Human Skin." *JAMA: The Journal of the American Medical Association* 192.5 (1965): 428-428. The British Medical Journal called her skin-as-soil approach "unusual" and the book itself "impressive," "necessary and scholarly Rook, A. J. "The Skin's Inhabitants." *British Medical Journal* 1.5447 (1965): 1427.

505 Kligman et. al. (1976), p. 160.

506 Ibid.

507 Ibid.

continue to produce clinical and therapeutic dividends.[508] This was cutting edge science in the dermatological world.

The "Body Ecology" Theory

The Antimicrobial Panel released its preliminary report to the public and controversy exploded. It played out in the popular and trade press.

In its proposal for a monograph on the antimicrobials, the Panel was quite clear on its rationale for determining rules about the usage and composition of antimicrobial soaps. *The Pink Sheet* highlighted the panel's concern with normal flora in a section called "Natural Ecological Balance: Normal Skin Flora."[509]

They discussed their concerns by invoking ecological science. "Classic ecological studies have shown only too clearly the dangers of altering a stable community of any type, including microorganisms." The trade journal found it an emphatic enough statement to highlight it: the panel had "declared" this as such.[510]

The Pink Sheet continued it summation as follows:

> "The panel said that clinical studies submitted to show effectiveness of antimicrobial soaps in prevention of minor skin infections were "insufficient to support" a favorable

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[508] Ibid.

[509] "No Ingredients Cleared For Antimicrobial Soaps in OTC Panel Report to FDA But Some Can Be Used for One Year, Pending Studies for More Data: Tough Report Clears Only 5", *FDC Reports* vol. 36, July 1, 1974, p. 10-16, p. 14.

[510] Ibid. p. 16.

conclusion. Considerable data received by the panel, the report indicates, show that the skin is not the natural barrier it had been previously considered to be, that chemicals absorbed through the skin can adversely affect the brain, the kidneys, and the testicles, and that high doses of topical ingredients Basically, the panel seems to feel that the majority of antimicrobial ingredients now in use may not only be ineffective for claims if preventing disease, but may cause worse infections and be toxic systemically.[511]

And most importantly:

"Panel's basic view apparently is tied to the belief that the normal human skin has an ecological balance which is self-protective and should not be disturbed except for medical need such as surgery or health care personnel who come into contact with pathogenic organisms."[512]

The problem with these products was that their action was excessive: "The deodorant effect from reduction of normal skin flora, particularly gram positives, was recognized by the panel. The effect, how-ever, could be achieved by a 70% reduction in the microbial flora, where as some antimicrobial soaps cause a reduction of up to 90% of the flora, the report indicated. "[513]

The report made a statement that was read in the press as a direct challenge to industry:

"Reduction of the cutaneous population of gram positive microorganisms for a deodorant effect "may be disadvantageous to the host, since not only is there no conclusive evidence

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[511] Ibid, p.14.

[512] Ibid, p. 14.

[513] Ibid, p. 15.

that the antimicrobial reduces or prevents infection, but its action may even enhance the growth of potentially pathogenic microorganisms. … The view of the panel is that perhaps some bar soaps, which achieve a 90% or more reduction of gram positive organism, may be so active as to be harmful. *Until definitive data are available, it is prudent to avoid significant alterations in normal flora*."[514]

The structure of the OTC review was that the panels would designate active ingredients as one of three statuses—Category I, which meant "safe and effective," Category II, which meant dangerous, and Category III, which meant further study was needed. Being labeled as anything but Category I could upend the industry for products already on the market. The Panel was suggesting these antibacterial agents be designated as Category III.

Armour-Dial sent a furious telegram to Commissioner Schmidt on July 18, claiming that the company and the soap industry more broadly could suffer "irreparable damage" if the Panel's draft report was proposed as is, without changing what the company called an "unproven scientific concept."[515] The president of the company, David Deunsing, attacked the scientific validity of the panel's draft report as follows:

"[the report] clearly indicates and suggests that the use of antimicrobial products on a daily basis will increase certain bacterial infections due to gram negative i.e. pseudomonas and streptococcal (sic), organisms." [516]

[514] Ibid, p. 16 Emphasis mine.

[515] "T&G: Antimicrobial I: TCC & TFC Revisions; Armour-Dial Telegram," p. T&G2, *FDC Reports*, July 29, 1974.

[516] Ibid.

This position, which was "repeatedly emphasized throughout the panel's report" was "drawn from conjecture" he claimed, and was "*unsupported by any adequate, controlled studies*."[517] Furthermore, it "totally ignores the fact that billions of bars of antimicrobial soaps have been sold for three decades without an increase in cutaneous infections due to streptococcal or gram negative bacteria."[518]

The expert panel convened via conference call less than a week later to settle on a response to Duensing's strong statement. They spent hours mulling over how to respond, and came back with a forceful response. They refused to change the document or their position—and bolstered their scientific standing by adding additional references to defend what Duensing had referred to as an "unproven scientific concept."[519]

Duensing, decided to go straight to the top with his complaints—and asked Commissioner Schmidt to change the report before publishing it, stressing again the danger to the industry and what he saw as the shoddiness of the science—and issuing a thinly veiled legal threat.[520] The panel was not playing by the rules of good science—"conjecture and theories" should be presented as such, and not, in his view, as "Statements [made] "in a repeated and

[517] Emphasis mine.

[518] Ibid.

[519] Ibid, p. T&G2.

[520] Ibid, p. T&G2. "We feel that remaining moot on an issue which could significantly damage our entire marketing franchise and place the FDA in a position of having to reverse unfounded allegations made by the panel would be a disservice to our company and to the agency."

biased manner which could lead one to conclude that their position is established by scientific fact."[521]

What was at stake was the definition of scientific fact—how you establish it, and what it means—and who has the authority to make them. It was a battle over what kinds of evidence should be relevant for the protection of the public—as well as a more conventional power struggle over who had greater influence at the FDA, especially in the midst of changes that saw it aim for higher scientific credibility and distance from industry.

President Deunsing worried that the publication of the report "followed by a press conference with panel members present," would in all likelihood "precipitate the publication and distribution of information to the American consumer which is false and misleading, thereby causing irreparable harm" to Armour-Dial and the whole industry.[522]

Duensing's fears were not far off—the press did pick up on the story and frame it from the cautionary and anti-industry perspective of the panel's scientists. In August, *The Washington Pos*t ran an article entitled "Attacking Germicidal Wisdom," and noted that Americans had bought into the idea that "nothing but good" would come from killing germs on the skin and had spent countless millions on germicidal soaps and products aimed at destroying the bacteria on the skin.[523] But this "Germicidal Wisdom" had come under fire from the FDA's Over the Counter [commission], the article claimed. "A growing body of data" indicated that killing skin bacteria indiscriminately could have a deleterious and counter-intuitive effect: "the potential to allow

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[521] Ibid. , p. T&G2

[522] Ibid, T&G2.

[523] "Attacking Germicidal Wisdom," by Morton Minz, August 23, 1974, *Washington Post*, p. B1.

“more dangerous organisms to thrive and cause potentially serious infections.” The “harmless bacteria” on the skin was not so innocuous, the scientists on the government panel were claiming; rather they had a protective function to play in the maintenance of health. *The Boston Globe* warned that such familiar brands such as Lifebuoy, Dial, Irish Spring and Safeguard may be forced to change their chemical formulas to contend with the fact that some naturally occurring skin bacteria served a “protective function.”[524] The Chicago Tribune was more sensational, noting the potential of the study to “burst the bubble of the $190 million a year deodorant/antimicrobial soap industry.”[525] The panel was adamant that this was a major problem—and declared that if the FDA could not act to enforce new guidelines, then Congress should get involved and pass legislation to that effect.[526]

Armour-Dial, still smarting from the hexachlorophene ban, aggressively defended itself against regulatory moves that could potentially impact its bottom line again, just a few short years after the hexachlorophene hit. They were tenacious. They attacked the panel again in January 1975, this time with support from Proctor and Gamble, who also called for a disavowal of the body ecology theory on scientific grounds, calling the body ecology concept a “hypothesis” and calling again for the FDA commissioner to disavow it.[527]

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[524] “FDA study says deodorant soaps may be killing “good” germs, too,” by Michael J. Conlon, Sept 7, 1974. *Boston Globe*, p. 2.

[525] “Deodorant soaps—a big stink behind all the clean?” by Karen Peterson, *Chicago Tribune* Nov 14, 1974, p. B1.

[526] Ibid.

[527] “P&G and Armour-Dial Challenge Antimicrobial I Panel’s Gram Negative Hypothesis; …Criticize One Year Category III test,” 21-2; 21. *FDC Reports* 37, January 6, 1975.

Industry vs. the Academy: Whose science? Whose Authority?

For industry microbiologists, the body ecology "hypothesis" was not proven. But for the experts on the panel, it was the cutting edge of their science. This was a fundamental distinction that led to the industry representatives and the dermatologists to butt heads. For the industry, their clinical tests and the proof of the marketplace provided the right kind of evidence to defend their products. For the expert dermatologists on the panel, working in the academy but not entirely of it—part of the medical firmament and the biomedical research community, but working on its margins as one of the less well-respected science was about a legitimizing framework that made sense of the biological object that it targeted. Much like Appleton and the dental microbiologists a few decades earlier, ecology provided a scientific framework and theoretical orientation for skin bacteriology to claim, and a research agenda for the community to pursue.

In all cases, each player appealed to the authority of science. The FDA sought the imprimatur of scientific authority through its expert panels to provide legitimization for the agency and its policies. For experts on the Antimicrobials Panel. Industry rejected this—insisting that they had accumulated scientific authority over their products. Industry insisted that the standards of evidence remain on their terms—based on the kinds of tests and research they did in their industrial laboratories or that were outsourced to often friendly academics.

At stake in this controversy was whether the FDA could issue a rule based on the *threat* of danger, not proven danger—a pre-emptive strike based on a new biological model of the body that saw microbes as implicated in the provision of health.[528]

Closing the controversy and the FDA

Schmidt had become commissioner of the FDA as the DESI was winding down and after the beginning of the OTC Review. He had been appointed in July 1973 by HEW Secretary Caspar Weinberger from his position as Dean of the University of Illinois Medical School. Schmidt stated on until December 1976. He replaced Charles Edwards, who had organized the OTC and gotten it off the ground. And who had been commissioner since 1969 and appointed by Nixon to be Assistant Secretary for Health in the Department of HEW. Last stages were boring to Schmidt because the exciting early phase work had been done already. But the OTC review was something else entirely. It was new and Schmidt had the opportunity to really shape its form. Schmidt was very proud of the work that went into the review and sought out—and got—the best people to staff its advisory committees.[529] Schmidt originally signed off on the Antimicrobials panel report on September 6, 1974, despite the outcry from industry.[530] Schmidt, a notoriously meticulous and careful reader of documents that were to be released to the public, had taken great pains to read the report carefully, perhaps even more so in this case in the face of industry

[528] For history of regulation at the FDA, see Carpenter, Daniel. *Reputation and power: organizational image and pharmaceutical regulation at the FDA*. Princeton University Press, 2010*;* Hilts (2003), and Daemmrich, Arthur A., and Joanna Radin, eds. *Perspectives on Risk and Regulation: The FDA at 100*. Chemical Heritage Foundation, 2007.

[529] Alexander Schmidt Oral History, FDA History Office Oral Histories Collection, p. 65.

[530] "OTC Antimicrobial I Report Signed by FDA's Schmidt," *FDC Reports* September 9, 1974, T&G3-4.

pressure. Upon sending the report back to his FDA staff for revisions to the preamble, the FDA's administrative/official introductory statement for the report, he warned his staff to stress the preliminary nature of the report and to stress that it did not represent official FDA policy. But he ignored Armour-Dial's demands for revisions to the report and left it virtually untouched. This was an effort to ward off brewing controversy and to thread the needle between the experts on the panel and the industry voices that were pressuring the FDA to disavow the theory in strong terms.

Though consumer activists had been involved in the Antimicrobial Panels, there was no outcry about the outcome of the Panel. Law Professor Joseph Page, a leading consumer rights lawyer who was heavily involved in OTC drug regulation and had been involved in the OTC Review over the years, did claim that Schmidt's preamble was proof that the FDA had caved to industry pressure.[531] But Nader's Raiders did not write a monograph indicting the FDA over its shameful genuflecting to Big Soap, nor did they try to educate the public about body ecology as a means to better manage their own health in daily life as they did in other arenas. The book was effectively shut on the "body ecology" theory and the OTC's review of antibacterial agents dragged on in obscurity through the next few decades, until it was reopened in 2013.[532]

Conclusion

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[531] "Professor Page Links Antimicrobial I Preamble to Industry Pressure," p. T&G4. *FDC Reports* 37, /January 20, 1975. Schmidt had previously rejected the notion of putting a disclaimer on each OTC category monograph that would not bind the FDA commissioner to enforce the rules determined by panels.

[532] "FDA Taking a closer look at 'Antibacterial soap,'" Dec. 16, 2013. FDA Consumer Updates http://www.fda.gov/forconsumers/consumerupdates/ucm378393.htm

In the end what did this moment matter? The “body ecology” theory fell out of regulatory sight with respect to the personal hygiene companies until December of 2013, when the FDA finally issued its proposed rule on triclosan, a popular replacement for hexachlorophene in hygiene products in the 1970s.[533] The skin bacteriology community continued to use an ecological framework to think through and shape their small field; and the hygiene companies continued to use many of the controversial chemicals in their products and saw the antibacterial products industry grow.

But the natural products industry could point to a scientific rationale for their products that could complement their ecological approach; and as the eco-consumer movement grew in the ensuing decades, the urge to move away from chemical cleansing expanded, as the expansion and increased market share of natural hygiene products companies proved.[534] It anticipated the acceptance that the hygiene hypothesis, first suggested in the late 1980s, would have with a variety of communities who were wary of hyper-cleansing through chemicals and the appeal to the protection of the normal flora was used as a rationale for opting to use alternatives to hygiene industry products.[535] Antibacterial cleansing came under fire as excessive—and potentially harmful to the body because of its derangement of the normal flora—and its potential to create antibiotic resistance. Antibacterial clean culture became a cultural marker for mainstream disaffection and a biomedical threat—punk band X-Ray Spex would blast in the late 1970s as an

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[533] “FDA Taking a closer look at ‘Antibacterial soap,’” Dec. 16, 2013. FDA Consumer Updates. Accessed February 24, 2014. http://www.fda.gov/forconsumers/consumerupdates/ucm378393.htm

[534] See Jones (2012).

[535] See, for example, Strachan, David P. "Family size, infection and atopy: the first decade of the ‘hygiene hypothesis'," *Thorax* 55 (2000): S2 and Weiss, Scott T. "Eat Dirt--the hygiene hypothesis and allergic diseases." *The New England Journal of Medicine* 347.12 (2002): 930.

image of what was wrong with consumerist society on the album an in the song “Germ Free Adolescents” in the late 1970s; the hygiene hypothesis would target it as one of the reasons for the rise of certain kinds of chronic allergies by the 1990s.

Chapter 5: The Limits of Pure Culture: The Natural Turn in Microbiology

Introduction

The turn towards "the natural" in science was evident in the growing prominence of ecology in the 1960s and 1970s. Increased societal attention to the environment led to an explosion in investment in and a rise in status of the ecological sciences as new branches of ecology asserted themselves in this period.[536] Ecology stood in obvious contrast to molecular biology, which had become the dominant and most celebrated biological science in this period.[537] While molecular biology focused on elucidating fundamental mechanisms shared by all living organisms, ecology aimed to characterize the nature of the relationships between organisms and their natural context. The competing visions could be boiled down to a few key differences: For ecology, the ecosystem became the fundamental unit of investigation and organization as ecosystem ecology grew to dominate the field from the1960s.[538] For molecular biology, it was the molecule that mattered most. For ecology, it was the *relationships and interactions* between organisms and environments that were fundamental to its approach to the living world. For molecular biology, it was the biochemical pathways within an organism that were fundamental to understanding life. These two sciences provided contrasting visions of the unity of life—one based on the similarity of biological processes and molecular components within organisms; the other based on webs of connections and processes between organisms. It

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[536] See Appel (2000), Chapter 8: "Allocating Resources to a Divided Science."

[537] For history of molecular biology, see Morange, Michel. *History of Molecular Biology*. John Wiley & Sons, Ltd, 1998.

[538] See Kingsland (2005), chapters 7 & 8.

was the difference between emphasizing *withness* as opposed to *likeness* in the investigation of life.

Likeness and withness suggested an old division in the sciences: between lab and field. In *Landscapes and Labscapes: Exploring the Lab-Field Border in Biology*, Robert Kohler defines the laboratory as a foil for field sciences. Unlike in the field, in which environmental factors are a central aspect of the investigation, laboratories "eliminate the element of place."[539] Theirs is a "logic of placelessness."[540] They are "invariant and generic environment[s]." [541] For molecular biology (and other dominant experimental biological sciences like biochemistry) the *point* was to eliminate context to explore the essential processes of life in a generic and thus universal setting; the point of the field was to investigate connection and context.

In microbiology, there was tension between these two visions of the investigation of life. At issue was where you looked at microbes and how: cultivated in the laboratory or through direct observation in the natural world. The study of microbes incorporated both approaches. In the 1940s and 1950s, however, advancements in general microbiology—microbial physiology, metabolism and genetics came to overshadow the work that had been done in soil microbiology as it became more and more about finding antibiotics. What has been called a "new dynamism" in microbiology centered on microbial genetics, which would depend upon cultivation techniques required to articulate basic information about microbes in the laboratory.[542] The study

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539 Kohler (2002), 6.

540 Ibid.

541 Ibid.

542 Spath (1999), 260.

of microbes in the environment was overshadowed in this period because of the successes of studying particular microbes that were not necessarily important to soil science and environmental processes, like *E. Coli,* in the laboratory. The productivity of this work in bacterial metabolism and bacterial physiology created a knowledge base about particular microbes that would make them ideal model organisms for investigations about broader biological questions. It followed that these microbes became a key part of molecular biological experimental systems; and microbiology became a kind of handmaiden science for what came to be seen as the *real* work of 20th century biology by the 1950s: molecular biology.

The concerns about context and interactions between microbes and between microbes and their environments had been of interest to microbiologists studying environmental microbes from the beginnings of the field of microbiology. Since the 19th century, there had been subfields of microbiology that focused on microbes and their function in natural environments. In the 1960s, their questions and priorities garnered new scientific and societal interest because of the rise of environmentalist concerns and the increasing institutional power of ecological approaches.[543] These old questions and priorities of soil and agricultural bacteriologists would be reframed as ecological in this period under the banner of "microbial ecology."

Microbial ecology took off as a formal, self-conscious field in late 1960s as part of the broader rise of ecological perspectives and thinking in science.[544] Despite the increased attention in the 1960s, this was essentially a rebranding of a soil microbiology old agenda tied to some new methods, but with one fundamentally powerful change: the focus on ecosystems as

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[543] See Appel (2000), Chapter 8 and Kingsland (2005), Chapters 7 and 8.

[544] See Shepard, P., and D. Mckinley. *Subversive science: essays toward an ecology of man*. Houghton Mifflin, 1969.

experimental units rather than individual microbes. The old agenda had been extraordinarily productive with respect to shaping ecology and soil science in the early 20th century— the new microbial ecology insisted on its societal relevance as part of the ecological turn and framed itself in direct opposition to the dominance of pure culture and laboratory cultivation techniques. For these new microbial ecologists, they were opposing a dominant narrative about how to study microbes by insisting on "direct studies" of the environment. But "direct studies" had been championed since the 1880s by soil microbiologists.[545] I argue in this chapter that in the 1960s-1990s, a counternarrative was constructed in opposition to a microbiology dominated by laboratory cultivation and pure culture, which stressed ecological frameworks (the natural environment vs. the laboratory environment), ecological units (the ecosystem vs. the organism; the consortia s. the individual), and ecological approaches (characterizing inter-organismal transformations vs. intra-organismal transformations) and the limitations of pure culture. The productivity of this new approach produced a paradigm shift by bringing these perspectives, allied with new conceptual and methodological tools, to the center of microbiology and biological science.

The result of this transformation was a revitalized microbiology that focused on and highlighted the peculiarities of microbes as a class of living things. This was a stark contrast to the ways in which microbes had come to be treated in the scientific landscape--as experimental tools for the articulation of a molecular vision of life and as a stand-ins for a universal, reductionist vision of life. Rather than being valued mostly as tools (in experimental biology) or targets (in medicine), they became objects of knowledge in their own right in this period. In an

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[545] Ackert, Lloyd. "The Master of Brie-Compte-Robert and His "Direct Method:" Translating the Cycle of Life into Ecology," *Sergei Vinogradskii and the Cycle of Life*. Springer Netherlands, 2013. 107-124.

interesting inversion, it was the tools of the molecular biological laboratory that enabled this shift.

Pure Culture

The development of pure culture techniques were enormously productive for the biological sciences and for medicine. Pure culture permitted microbes to be seen through the experimental eye—and to be characterized and catalogued accordingly. In medicine, pure culture allowed for the identification and neutralizing of pathogens. In an age when fighting infectious disease was essentially a matter of microbe hunting and destruction, the pure culture laboratory provided the necessary tools and conceptual framework for this kind of approach. It was a foundational technique for the science of microbiology, and first developed with a medical imperative in mind. But it is the role of microbes and pure culture in basic biological research that I focus on here.

Pure culture was an obstacle because it set the terms of what counts in the scientific biological landscape of microbiology. While in practice it was a question of representation—if you could not see something, then you could not investigate it or include it in your actionable theory of the world, in theory it became an existential question—if it could not be cultured, *then it did not exist* in the science of microbiology. The organizational manual—the institution of the Bergey Manual of Deterministic Bacteriology, the Society of American Bacteriologists' bible, one of its only and most essential organizing and foundational tools/documents, stated so categorically in 1923—by proclaiming that a bacterium that could not be cultured could not be classified.[546] This had an impact on the field and biased research towards those bacteria that *could* be cultured—and thus classified. The repercussions from that decision persisted for decades in microbiology, providing a biased view and much more meagre picture of the diversity and richness of microbial life. While soil bacteriologists, intestinal bacteriologists, and rumen bacteriologists pushed beyond these confines by necessity-- many of the bacteria they were interested in were not amenable to pure culture and the biochemical articulation of the basic processes of microbes in the laboratory--, the field remained for the most part a science built on the technique of pure culture, with peripheral communities of practices trying to push beyond that vision.[547]

Microbes in Molecular Biology

Microbes became important model organisms in biological research early in the 20th century. *E. Coli*, an intestinal microbe that had named for and discovered by German Pediatrician Theodor Escherich in healthy feces in 1885, became the microbe of choice for laboratory research early in the 20th century because it was harmless, easy to obtain, isolate and to grow in the laboratory via pure culture techniques. It played a foundational role in molecular biological research because it had been so well-characterized and disciplined for the laboratory by the 1940s. It became the most popular bacterium for biological research in the world, and

[546] Society of American Bacteriologists, *Bergey's Manual of Determinative Bacteriology*, Baltimore, MD: Williams and Wilkins, 1923.

[547] See Kupferberg (2001) and Ackert (2012).

played a central role in the development of molecular biology.[548] For example, Jacques Monod used *E. Coli* in his foundational work in molecular biology.[549] His much quoted encapsulation of the philosophy of molecular biology used *E. Coli* to make the point— "[What is] true of *E. Coli* must also be true of elephants."[550] This was already a well-known axiom by the early 1960s. What it meant for a biology founded on shared basic principles was that a bacterium could tell us everything we needed to know about the basics of life.[551] What was most important was elucidating the fundamental processes of the building blocks of biological organisms.

This vision of Life emphasized the importance of similarities among organisms rather than their relationships to each other and their natural environments. It placed the mechanics of the body-machine and its biochemical pathways and its constituent parts at the center of knowledge-making about Life.

But microbiologists, and in particular, soil microbiologists, knew that what was true of *E. Coli* was not necessarily true of other microbes. *E. Coli* had been one of the key experimental organisms for the study of microbial metabolism and physiology, but it was not truly representative of the microbial world. Most microbes could not be cultured because they had a

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[548]For example, it was *E. Coli* that Joshua Lederberg and Edward Tatum used for their Nobel Prize winning work on bacterial genetics in the 1940s Lederberg, Joshua, and Edward L. Tatum. "Gene recombination in Escherichia coli." *Nature* 158.4016 (1946): 558-558; Meselson, Matthew, and Franklin W. Stahl. "The replication of DNA in Escherichia coli," *Proceedings of the National Academy of Sciences* 44.7 (1958): 671-682.

[549]Burian, Richard M. "Technique, task definition, and the transition from genetics to molecular genetics: Aspects of the work on protein synthesis in the laboratories of J. Monod and P. Zamecnik," *Journal of the History of Biology*26.3 (1993): 387-407; Rheinberger, Hans-Jörg. "Internationalism and the History of Molecular Biology, *"Annals of the History and Philosophy of Biology 11 (*2006): 249.

[550] See Monod and Jacob, "General Conclusions: Teleonomic Mechanisms in Cellular Metabolism, Growth, and Differentiation," *Cold Spring Harbor Symposia on Quantitative Biology 21* (1961): 389–401.

[551] Burian, Richard. *The Epistemology of Development, Evolution, and Genetics*. Cambridge University Press, 2005.

different metabolism. *E. Coli* was essentially similar to animals because its metabolic processes were essentially the same—they were organotrophs—meaning that their metabolism was based on the reduction of organic compounds as energy and carbon sources. Most microbes were not organotrophs—and thus their metabolism was not represented by *E. Coli* in significant ways. As such, while the molecular biological maxim could say that, in truth, whatever was true of *E. Coli* was also true of elephants, it was *not true* that whatever was true of *E. Coli* had to be true of other microbes. Microbial ecology as a field set itself against such notions of the microbe in the 1970s and beyond, targeting pure culture and the experimental organisms that were amenable to the conventional laboratory cultivation techniques as an artificial bacteriology. They developed new perspectives and methods to circumvent these limitations in order to create a *true* science of microbiology. For these microbial ecologists, creating a true science of microbiology was by necessity a microbial ecological effort because so much of the microbial world lay beyond the limits of traditional techniques. A laboratory cultivated E. Coli may be an adequate model organism for an elephant, they essentially argued, but there were too many other kinds of microbes that behaved differently to make this a credible claim for microbial ecology. At issue was always whether or not the ways in which they differed mattered—for microbial ecologists, who were interested in understanding natural process in the environment and not the fundamental characteristics of individual organisms, it mattered very much.

For microbes, a science of life without nature proved extremely limiting as it became clear that the majority of the microbial world could not be cultured and that microbes in natural environments lived in communities with distinct roles to play within this natural ecological unit. For microbes, whose deceptively simple biology had made them great model organisms for reductive approaches to life, the community and the context were just as important as the individual microbe itself. A true understanding of microbial life would require an ecological perspective. In short, a perspective that took the ecosystem as its fundamental unit, and which emphasized *withness* over *likeness* in its conceptualization of the unity of life.

Winogradsky's "Ecological Microbiology"

In microbiology, the increasing prominence of the sciences of natural environments exposed a long-standing tension in the field. From the beginnings of the field, in the 19th century, there was an acknowledgement of the limitations of culturing microbes to capture the microbial world by those working on environmental settings. [552] The microbial ecologists of the 1960s and 1970s looked to the 19th century for their origin story: naming as founding fathers Dutch microbiologist and botanist Martinus Beijerinck (1851-1931), who had developed enrichment culture for microbes, and Russian soil scientist Sergei Winogradsky (1856-1953), who developed the Winogradsky column, which used environmental samples layered in one column to grow a variety of microbes at once in close proximity. [553] As early as 1897, Winogradsky had insisted on the diversity of microbes and their importance in nutrient cycling in the biosphere. The modified culture techniques and microscopy that he and others developed allowed some insight into

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[552] For agricultural and environmental bacteriology in the early 20th century see Ackert (2012), Spath (2000), and Kupferberg (2001).

[553] His most famous dictum, which has become fundamental in microbial ecology, "everything is everywhere, but the environment selects While this is often attributed to Beijerinck, it actually belonged to another Dutch microbiologist, Louerns Gerhard Baas Becking (1895-1963). See de Wit and Bouvier (2006) "'Everything is everywhere, but, the environment selects'; what did Baas Becking and Beijerinck really say?" *Environmental Microbiology* 8:4 755-758.

microbes *in situ*, but were limiting.[554] Enrichment culture became a classic technique for soil bacteriologists, but even though it allowed for soil microbiologists to "see" and to study a broader range of microbes than the limited culture media that had been defined for conventional laboratory microbiology, enrichment cultures could be biased towards particular kinds of microbes that were most fit for that particular environment—and thus would change the composition of the enrichment culture. However, the microbes that flourished in enrichment culture were often not the microbes most important in natural ecosystem. Their approach still focused on attempting to culture and isolate microbes, and assuming that the microbe of the laboratory would essentially function the same way as it did in the natural environment as long as one could provide the proper nutrient environment. Indeed, Winogradsky saw pure culture and cultivation techniques as the only means to get at the metabolic and physiological potential of a microbe despite his doubts about their reliability for capturing the natural dynamics of microbes in soil.[555] For Winogradsky, there was a fundamental difference between soil microbiology and what had come to be known as general microbiology (i.e. microbial metabolism, morphology and physiology)—soil microbiology was, he wrote, "principally speaking a microbial ecology."[556]

Winogradsky's version of microbial ecology grew out of his experimental work on microbial nutrition. It led him to see microbes as central to a "cycle of life" that included

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[554] Winogradsky S. N., "On the role of microbes in general circulation of life." Lecture to a meeting at the Imperial Institute of Experimental Medicine, 1896, 27, Printing House of Imperial Academy of Sciences, Sankt-Peterburg, 1897.

[555] Ackert,, Lloyd T. "The "Cycle of Life" in Ecology: Sergei Vinogradskii's Soil Microbiology, 1885–1940." *Journal of the History of Biology* 40.1 (2007): 137.

[556] Ibid, 137.

chemosynthesis, autotrophy and global nutrient cycling.[557] This broad vision was an ecological framing of Life as nutrient cycling, the exchange of matter and the transformation of energy and exchange influenced ecologists in the 1920s and 1930s as well as agricultural scientists. Winogradsky had attempted to study “free nature” in the laboratory by collecting samples in the wild and then approximating the sometimes exotic natural environments where his experimental organisms lived (e.g. sulfur springs) in a bid to understand the role of microbes in the economy of nature. He called his approach the “direct method.”[558] His described his direct method in the early 1920s; it consisted of a) avoiding laboratory cultivated cultures in favor of microbial strains freshly isolated from the soil with as little interference as possible; b) “feeding” them with nutrients that approximate as closely as possible those used by them in the soil; c) including soil in solid media used to study microbes in the lab and d) studying the soil population as a whole because of the importance of competition in determining the roles of microbes in the soil.[559] In short, Winogradsky thought that the proper way to study microbes was not in artificial laboratory cultures, but in as close to a natural state as possible; and in their natural environments in competition with other microbes.

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[557] See Ackert, Lloyd T, "The Role of Microbes in Agriculture: Sergei Vinogradskii’s discovery and investigation of chemosynthesis, 1880–1910," *Journal of the History of Biology* 39.2 (2006): 373-406 and Ackert, Lloyd T. "The “Cycle of Life” in Ecology: Sergei Vinogradskii’s Soil Microbiology, 1885–1940," *Journal of the History of Biology* 40.1 (2007): 109-145.

[558] For more on Winogradsky’s “direct method,” see Ackert, Lloyd. *Sergei Vinogradskii and the Cycle of Life: From the Thermodynamics of Life to Ecological Microbiology, 1850-1950*. Vol. 34. Springer, 2012; chapters 7-10.

[559] Winogradsky S. “Sur la méthode directe dans l’étude microbiologique du sol,” *Comptes Rendus de l'Academie des Sciences*, 177 (1923): 1001–1004; also published here: Winogradsky, Sergei. "Sur la méthode directe dans l’étude microbiologique du sol." Chimie **et Industrie** (1924): 1-8.

This technique was developed more as an agricultural tool to assess the quality and health of soil rather than as a means of studying the biological nature of soil and its microbes.[560] But it served both purposes—and Winogradsky's insistence on a "Direct Method" resonated with later microbial ecologists for whom the direct study of nature was the central rationale for their work.

Winogradsky's Direct Method may have begun as an investigation into the health of the soil, but became the cornerstone of Winogradsky's vision of Life and the proper way of studying it with respect to microbes. He insisted that a proper understanding of a microbe required that the microbe be studied under conditions that were as close to its natural environment as possible.

To this end, he used fresh soil ("sifted and reduced to a convenient degree of humidity and density") and induced the microbes there to reproduce ("germs, already there, were made to proliferate") and then introduced to a variety of media containing natural nutritional materials of animal and plant origin to create "auxiliary cultures."[561] He observed the results directly with microscopes and compared the "biological reaction" of the microbes in these auxiliary cultures with the "microbiological state" of natural soil experimentally through chemical analysis. Historian Lloyd Ackert describes Winogradsky's method as the "transform[ation] [of]] the natural microbiological state of the soil into a series of reactions in gelatin plates."[562] Winogradsky had tried to create a new soil science in the 1920s that would go beyond the previous two strands—the isolation and cultivation of species of microbes from the soil in pure culture, using the enrichment techniques that he had pioneered in the 1890s (along with Bejeirnik

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[560] Dworkin, Martin. "Sergei Winogradsky: A founder of modern microbiology and the first microbial ecologist," *FEMS microbiology reviews* 36.2 (2012): 364-379.

[561] See Ackert (2004), 158-9; quoting Winogradsky.

[562] Ackert (2004), 160.

separately), and secondly, the biochemical analysis of the soil. His tool kit consisted of three things: direct microscopy of the soil microbes, growing cultures from natural soils and then enriching them in accordance with the questions under investigation; and finally, “auxiliary cultures” to approximate natural conditions as closely as possible in the laboratory.[563] Winogradsky had encapsulated his new vision for soil microbiology as Ecological Microbiology, in the late 1930s in *Annales Agronomique*. The goal was “establishing by laboratory experiments the conditions of existence and the activities of the microbes within their habitats” with the requirement that the researcher should “avoid as much as possible all that is artificial, or conventional, in the contemporary methods of general microbiology.”[564]

Winogradsky died in 1953, but his work deeply influenced microbiology more broadly in agricultural experiment stations, ecology departments and microbiology departments and institutes across the world.[565] For example, Salman Waksman (1888-1973) and René Dubos were both acolytes of Winogradsky and took his direct method and ecological approach as central aspects of their own work.[566]

Soil microbiologists and rumen microbiologists made strides through the 1950s in expanding the purview of culture techniques, like building way to culture anaerobes in the laboratory and building continuous culture systems to approximate rumen microbial

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[563] See Ackert (2004), 160-1.

[564] Ackert (2004), 196-7. See also Winogradsky, S. "Principes de la Microbiologie Oecologique." *Antonie van Leeuwenhoek* 12.1 (1947): 5-16 and Winogradsky, S. "La microbiologie oecologique. 1." *Congres de Microbiologistes françaises Paris*, 1938.

[565] See Ackert (2012).

[566] See Ackert (2012), Chapter 9, “Science is Ecological an Ecology is Scientific: The Uptake of Vinogradskii’s Direct Methods,” 141-60; in particular, 143-152.

environments, but these subfields and their experimental approaches did not permeate microbiology very broadly because of their difficulty; and more strides were not made in the field in earlier years because of technical limitations.[567] In a broader research context in which fundamental processes could be elucidated arguably by any organism, there was not a broader push to investigate those microbes whose biology made them less amenable to the laboratory except in soil microbiology, which offered few career prospects to recent graduates in the late 1920s-1940s.[568] Many of these graduates, like René Dubos, moved from soil microbiology to medical microbiology or to agricultural bacteriology. Those with expertise in soil bacteriology were rewarded with dividends after René Dubos discovered antibiotic properties in soil microbes in 1939 and inaugurated the antibiotics era. Soil bacteriology now had a broad mandate and raison d'etre, but it was not for the older reasons that had been established by Winogradsky and other early pioneers in the field. It was not for the elucidation of larger biological processes and the "cycle of life" or even about the health of the soil (where as Winogradsky had started). Instead, it was about microbe prospecting for medicinal purposes. These were where the resources for soil microbiology were directed in the 1940s and 1950s as researchers sought medical miracles in the soil.

From Winogradsky's Direct Method to Brock's "Direct Studies of the Natural Environment"

[567] Brock, T. D. *Principles of Microbial Ecology,* Prentice-Hall Biological Science Series, 1966.

[568] See Cooper, Jill Elaine. *Of Microbes and Men: A scientific biography of Rene Jules Dubos*, (PhD. Diss. Rutgers University, 1998), 83-86.

Microbial Ecology in the 1960s and 1970s

Microbial Ecology as a field coalesced in the 1960s and aligned itself with the broader ecologizing of the sciences. Thomas Brock wrote the first textbook of the field in 1966 (*Principles of Microbial Ecology*); two more textbooks followed in the early 1970s (Sheldon Aaronson's *Experimental Microbial Ecology* (1970) and Martin Alexander's *Microbial Ecology* (1971). Strides had been made in the 1960s and early 1970s to expand upon the methods available to study microbes in natural environments.[569] Disciplinary activity followed soon afterwards—the International Commission of Microbial Ecology was established in 197l; it then established the International Society for Microbial Ecology, which launched a journal *Microbial Ecology* in 1974. *Microbial Ecology* provided the outlines of the field in its policy for paper submissions:

We "will accept papers in those branches of ecology in which microorganisms are involved. Articles describing significant advances in the microbiology of natural ecosystems will be considered as well as those describing new methodology. In addition, the journal will accept reports describing microbiological processes associated with environmental pollution..."[570]

This vision of the field encapsulates how microbial ecology set itself against an old laboratory focused microbiology by providing three fundamental points of contrast: natural ecosystems vs. individual microbes; techniques for studying these systems vs. old culture methods; and environmentally relevant microbiological processes vs. medical or molecular

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[569] See for example, Rosswall, T.H., (ed.): *Modern Methods in the Study of Microbial Ecology.* Bulletin No. 17 of the Ecological Research Committee, Swedish Natural Science Research Council, (Stockholm). 1973.

[570] "Description of the Journal," *Microbial Ecology* 1 (1974), i.

biological microbiological processes. Microbial ecological research of this period demonstrated this difference. Researchers often explicitly described their work as challenging the dominance of pure culture and laboratory cultivation techniques. For these researchers, the rationale for microbial ecology was that it could revitalize the field of microbiology. An ecological approach, for them, meant circumventing the laboratory and the cultivation techniques that it required through direct studies of microbes in their natural environments.

This insistence on direct studies in opposition to pure culture techniques took on a different valence for these microbial ecologists than with Winogradsky's Direct Method. For these microbiologists it was about the nature of their field—how it should be conducted, as well as what it was for—and what kind of knowledge it could produce about microbes. These approaches would lead to the production of knowledge about microbes as a unique class of organisms, rather than as simplified versions of more "complex" or "higher" organisms.

In microbiology this was especially true—the seemingly simple biology of microbes that had made them amenable to becoming model organisms in the molecular biological and genetics laboratory made this approach inadequate to studying them as a class of organism—"complex microbial processes" required a different unit, unlike complex physiological or molecular ones. Microbial ecologists were clear that pure culture was inadequate to the job because microbes in natural habitats were present in mixed cultures, not pure ones. As one piqued microbial ecologist wrote, "mixed culture phenomena are not merely composites of the pure culture behavior of organisms present."[571] While early pioneers in environmental microbiology had made this very point, the limitations of the tools available had allowed for only limited success in studying

[571] Bungay, H. R., and Mary L. Bungay, "Microbial interactions in continuous culture," *Advances in Applied Microbiology* 10 (1968): 269-290.

microbial communities. In the 1960s, computers helped provide a means to capture the complexity of the processes through simulation and data analysis. Earlier approaches had recognized the theoretical interest in the population but had stopped at figuring out how to investigate them—they had just isolated and characterized the constituents of a mixture from a natural environment. But pure culture studies were "of limited relevance" to understanding natural bacterial populations because of the degree to which they were implicated in those environments and how those environments shaped their behavior.[572]

But why now and not earlier? And where was Winogradsky's Ecological Microbiology, so eloquently described and so revered just 20 years earlier?

Thomas Brock

Thomas Brock, author of the first textbook on microbial ecology (1966), has been described as the father of modern microbial ecology. Brock had earned a PhD in mycology in 1952 from Ohio State University and learned bacteriology from a stint in the Antibiotic Research Division at The Upjohn Company in Michigan. By the early 1960s, he was a professor at Indiana University who was beginning to earn notice, first with very well-received work on the marine microbe *Leucothrix mucor*, and then with work that would make his career—his studies on a microbe he discovered in the Hot Springs at Yellow Stone National Park, *Thermus Aquaticus*.[573]

[572] Bungay & Bungay (1968), 270.

[573] The work on L. mucor was exciting enough to be make the cover of *Science* and to be featured in the *New York Times* in 1964. Brock, Thomas D. "Knots in Leucothrix mucor," *Science* 144.3620 (1964): 870-872; Brock, Thomas D. "The Road to Yellowstone-and beyond," *Annual Reviews in Microbiology* 49.1 (1995): 8. L. mucor was amenable to direct light microscopic observation and as a result could be tracked and quantified in nature.

Brock's forays into environmental microbiology with *L. mucor* and then at Yellow Stone provided the foundation for his vision of microbial ecology. Brock spent the early 1960s reflecting on what microbial ecology *should* be while working on his textbook and working at Yellow Stone. He reached out to ecologists to discuss the nature of ecological science, and reflected on his own background in plant ecology and determined that microbial ecology's distinguishing and organizing principle needed to reflect the same sensibility.[574] He presented a unified view of the field: it was about microbial interactions with macrobes, each other and their natural environment. Thus, he decided, what set microbial ecology apart from microbiology was the centrality of the natural environment over cultivation in the laboratory. For Brock, "the proper approach to microbial ecology was through direct studies of the natural environment."[575]

But the notion of "direct studies of the natural environment" was an idea that already had purchase within soil microbiology through Winogradsky's Direct Method, developed in the 1920s, and articulated as a vision for an Ecological Microbiology in the late 1930s and 1940s. Brock, coming a generation later and earning his PhD in mycology just the year before Winogradsky's death, embraced Winogradsky's insistence on a "direct method," but found it wanting. He rejected the standard enrichment culture technique that had been used to isolate microbes from nature as "unecological" and claimed an even *more natural* bacteriology for himself—declaring that he taught himself how work directly from and in nature.[576] Winogradsky had tried to bring the natural environment into the laboratory for study under controlled

[574] Brock had started his graduate career in botany before switching to mycology at Ohio State University.

[575] Brock (1995), 9.

[576] Ibid, 8. "I taught myself how to isolate pure cultures directly from nature, instead of using the accepted but unecological enrichment culture technique."

conditions; for Brock, the microbial ecologist needed to work *in nature*, not just directly from it or to approximate it as closely as possible.

Brock had started reading up on ecosystems ecology as well in the early-mid 1960s, and determined that this kind of approach would be suited to a an environment-based microbial ecology. He reasoned that many natural systems were steady state systems, and thus they could be studied as relatively simple ecosystems because they had constant variable features (temperature and pH, for example). Ecosystems ecology could thus be applied to natural systems that exhibited steady state properties and were thus sufficiently simple and well characterized for experimentation.[577] This provided another contrast to laboratory cultivation of microbes and a new way of studying microbes directly in nature.

Brock set up temporary laboratory facilities in a cabin at Yellow Stone Park in 1966 to study microbes in the Hot Springs, with a grant from the NSF to study cyanobacteria and thermal springs as model ecosystems. The Hot Springs were a suitable steady-state ecosystem for his purposes. Brock immersed microscope slides into the spring for various amounts of times and then examined them microscopically with fluorescent tracers.[578]

He brought equipment to the field and set up experiments in the springs themselves. Here was the key contrast with Winogradsky's Ecological Microbiology—this was a field microbiology first rather than second, that aimed not to approximate the natural environment under controlled laboratory settings, but to conduct experiments directly in the natural

[577] Brock, Thomas D. "The ecosystem and the steady state." *Bioscience* 17.3 (1967): 166-169.

[578] Bohlool, B. B., and T. D. Brock. 1974, "Immunofluorescence approach to the study of the ecology of Thermoplasma acidophilum in coal refuse material," *Applied Microbiology* 28:11-16; Bott, T. L., and T. D. Brock. 1969. "Bacterial growth rates above 90 degrees C in Yellowstone hot springs," *Science* 164:1411-1412.

environment. The goal was to seek natural settings that were amenable to experimentation rather than to bring the natural environment into the laboratory to be made amenable for laboratory experimentation. Instead of bringing nature into to the laboratory, he brought the laboratory to nature.

Brock was at pains to distinguish his work from the old kind of ecological bacteriology—his work was truly ecological, he claimed, as he was not just culturing microbes from natural samples. The environmental context was essential to his work—and the productivity of his approach.

Brock found traces of organisms who could not be cultured on conventional culture media because of their temperature growth requirements, and other microbes which did not exhibit the same characteristics *in situ* as they did in the laboratory when examined microscopically.[579] Brock's work was lauded in the scientific community; he was asked to write a lead feature on microbial ecology for science in 1967 and focused on his Hot Springs work.[580] In subsequent years, after the excellent reception that his article, "Life at High Temperatures," received, Brock sought out thermal springs to investigate around the world—traveling (in some cases more than once) to Italy, Iceland, New Zealand, Japan, Central America, and the Caribbean from 1968 to 1972.[581] He was looking for more natural environments to study—they would provide the experimental conditions to explore—higher temperatures, different altitudes and

[579] Ibid.

[580] Brock, Thomas D. "Life at high temperatures," *Science* 158.3804 (1967):1014.

[581] Brock (1995), 17.

pHs, etc. It was in the natural world that one could extend the definition of life—his work showed that there was no "upper temperature limit of life."[582]

Brock was unequivocal about what had led to this innovation in reflecting on his work. "The study of microbes directly in the natural habitat led to the discovery of extreme thermophiles, he declared. "A reliance on enrichment culture techniques and standard incubation temperatures of 55°C had caused investigators working up to that time to miss them."[583] Again, it was the limits of conventional, laboratory bacteriology were the culprit for this limited understanding of the microbial world.

Brock's new class of organisms—the extremophiles—was testament to the productivity of direct studies for microbiology. The race was on to find more microbes that could exist in what had been considered environments too hostile for life—and thus expand the definition of what life could be.[584] Furthermore, Brock's proved just how productive microbial ecology could be for biology more broadly—a decade after his discovery of *Thermus aquaticus* in the Hot Springs, its taq polymerase would become the basis of the Polymerase Chain Reaction (PCR) that would facilitate a biotechnological and molecular biological revolution.[585]

Brock's commitment to direct studies of microbes in natural environments had uncovered a new class of organisms that expanded the limits of where life could exist and how organisms might function. It had, as Brock argued, implications for basic understanding about the basic

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[582] Brock (1967), 1014.

[583] Brock (1995), 12.

[584] For more on this, see Stetter, Karl O. "History of discovery of the first hyperthermophiles." *Extremophiles* 10.5 (2006): 357-362.

[585] Rabinow, Paul. *Making PCR: A story of biotechnology*, Chicago: University of Chicago Press, 1996.

processes and necessities of life. It provided a rationale for such studies. Brock's work had been possible because of the increased funding provided to microbial ecological projects in an increasingly ecological age. Brock's work also garnered interest from major scientific journals that were paying more attention to the findings of the environmental sciences. Brock's work emphasized the importance of microbes in their own right—as arguments about the nature of life and its limits; not just as model organisms that could be stand ins for other organisms. Model environments could be chosen based on their own unique qualities that made them amenable to experimentation—and they could reveal new aspects of life that laboratory studies on their own could not.

Natural vs. Cultured Microbes: Direct Microscopic Studies

Direct studies of microbes in their natural environments led to other insights about the nature of microbial life and its peculiar features. Microbes from the soil had been cultivated in the laboratory and their morphology and physiology detailed in depth by the 1960s, using conventional techniques. It had been the general belief that, as soil microbiologists at Pennsylvania State's University's Agricultural Experiment Station observed in 1972, that "…microorganisms, as they naturally reside in soil, would have a morphology and physiology similar to that of their laboratory-cultivated counterparts."[586] But, they argued, there were some

[586] Bae, H. C., E. H. Cota-Robles, and L. E. Casida, "Microflora of soil as viewed by transmission electron microscopy," *Applied Microbiology* 23.3 (1972): 637-648.

indications from the 1960s that cultivated versions of microbes were not quite the same as they were found in their native state.[587]

This story was not true, though it suited the narrative of the times—Winogradsky had suggested that laboratory cultivation changed microbes out as early as 1949 in his soil microbiology textbook *Microbiologie du Sol: Problèmes et Méthodes*: "one cannot challenge the notion that a microbe cultivated sheltered from any living competitors and luxuriously fed becomes a hot-house culture, and is induced to become in a short period of time a new race that could not be identified with its prototype without special study.'[588] While this could have been placed within a narrative including Winogradsky, it was not. The authors settled on a counternarrative attack on laboratory cultivation—and used a tool that Winogradsky had included as one of the key legs of his Ecological Microbiology. Microbiologists turned to comparative microscopic studies to try to characterize the differences between microbes that had been cultivated in the laboratory and those that were found in nature.

The Penn State Group had begun to investigate this question in the late 1960s and early 1970s using a variety of visual techniques.[589] They used incandescent and ultraviolet transmitted-light microscopy, bright-field microscopy, ultraviolet-fluorescence microscopy (using a light-diffraction microscope), time-lapse photography and Transmission Electron Microscopy to study microbes directly from soil so as to avoid any influence of laboratory preparation on the natural

[587] Often this work was found in Soviet Soil Science journals. See footnotes to Bae (1972): (2, 3, 5, 10, 12, 20-22, 24, 34, and 35.

[588] Winogradsky S., *Microbiologie du Sol. Problèmes et Méthodes,* Paris*:* Masson, 1949. Translation from Dworkin (2012): 364-379.

[589]See Casida, L. E., "Observation of microorganisms in soil and other natural habitats," *Applied Microbiology* 18 (1969):1065-1071, Casida, L. E., Jr.,. "Microorganisms in unamended soil as observed by various forms of microscopy and staining," *Applied Microbiology* 21 (1971):1040-1045, and Bae et. al. (1972).

versions of the microbes under study.[590] The goal was to preserve the character of individual cells from their natural habitat in order to view them as they actually were. The Penn State Group was confident enough in its studies to declare categorically in 1969 that "*in situ* indigenous soil microorganisms differ from similar organisms grown in the laboratory."[591]

The next step was to explore the ways in which this mattered and why it occurred.

Transmission Electron Microscopy and Freeze-Etching techniques were first applied to soil and marine microbiology in the early 1970s.[592] Direct microscopic studies, using ever more powerful and sophisticated scanning and transmission electron microscopes brought more detail to microbial mats and biofilms from the from the 1970s onward.[593] The even more powerful microscopes developed in the second half of the 20th century showed the importance of microbial communities, biofilms and microbial mats in the natural world—and that these were the natural conditions under which microbes tended to exist there.

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[590] They outlined the problems as such: "Most of the available techniques require that growth be initiated on laboratory media or by adding nutrients to the soil, or that in situ microflora be examined by various forms of bright-field or ultraviolet-fluorescence microscopy. The use of medium or nutrient additions usually upsets the climax community balance and causes a relatively quick enrichment for certain segments of the population, although much of the population may not respond at all. In addition, those cells that do respond by germination or multiplication may no longer be in their natural soil state. The various forms of light and ultraviolet-fluorescence microscopy often are hampered by the apparently small size of many of the indigenous cells and, at times, of the difficulty in distinguishing the microbial cells from other components of the habitat." They argued in this paper that Transmission Electron Microscopy would solve some of the technical problems inherent in trying to do this; they would just need to physically extricate the cells from their natural habitats. Bae (1972), 637.

[591] Casida, L. E. "Observation of microorganisms in soil and other natural habitats." *Applied Microbiology* 18.6 (1969): 1065.

[592] See Bae et. al. (1972).

[593] See for example, Geesey, G. G., W. T. Richardson, H. G. Yeomans, R. T. Irvin, and J. W. Costerton, "Microscopic examination of natural sessile bacterial populations from an alpine stream." *Canadian Journal of Microbiology* 23.12 (1977): 1733-1736; Cheng, K.-J., Stewart, C.S., Dinsdale, D. & Costerton, J.W., "Electron microscopy of bacteria involved in the digestion of plant cell walls," *Animal Feed Science and Technology*, 10 (1984): 93-120; Costerton et. al. (1994), "Biofilms, the customized microniche," *Journal of Bacteriology* 176 (1994): 2137.

J. William Costerton, the so-called "father of biofilms," received a PhD from the University of Western Ontario in 1960 and went on to teach microbiology at the University of Calgary in 1970, from which perch he essentially founded biofilm microbiology.[594] Costerton began collaborating with K. J. Cheng, a researcher at the Canada Department of Agriculture Research Station in Alberta, Canada on rumen bacteria and their cell walls.[595] Costerton became an expert in electron microscopy along with microbiology, and used electron microscopy to investigate microbes in natural habitats in the late 1970s.[596] They turned to the ruminant digestive system, which had been studied from an ecological perspective in some depth for over two decades, in the early 1970s.[597] Soon they turned to electron microscopy to study the ultrastructure of the rumen bacteria cell walls and expanded their studies in this domain. They used the microscope to study this ecosystem directly as well—and decided to compare what it looked like to the same microbes in cultured form in the laboratory. When they purified them in the lab, they behaved just like "ordinary" bacteria, or the standardized *E. Coli* and other bacteria that were grown in the laboratory.

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[594] "In Memoriam: John William Costerton," Memorial Announcement, Kaloomps Funeral Home http://www.inmemoriam.ca/view-announcement-296198-john-william-costerton.html; Montana State University Center for Biofilm Engineering website profile, https://www.biofilm.montana.edu/costerton. Accessed March 3, 2014.

[595] Cheng, K-J., and J. W. Costerton. "Localization of alkaline phosphatase in three gram-negative rumen bacteria." *Journal of Bacteriology* 116.1 (1973): 424-440.

[596] See for example, Geesey, G. G., et al. (1977).

[597] See Hungate, Robert. *The Rumen and Its Microbes*, Academic Press, 1966. Hungate was a pioneer in rumen bacteriology and is considered by some to be the "first truly modern microbial ecologist" because "he and his colleagues dealt directly with the ecosystem of these microorganisms. Instead of limiting their efforts to isolating and identifying microorganisms of the rumen, Hungate and his collaborators also measured their activities in situ." From Konopka, Allan. "Microbial Ecology: searching for principles," *Microbe* 1.4 (2006): 175-179. See also Chung, King-Thom, and Marvin P. Bryant. "Robert E. Hungate: Pioneer of anaerobic microbial ecology," *Anaerobe* 3.4 (1997): 213-217.

Microbes in their natural environments developed features that made sense for that particular context. Therefore, a proper understanding of bacteria required one to respect the fact that isolating and purifying bacteria types in the lab would not provide a "true" or accurate account of the biology of a bacterium because it could be context dependent.

By the mid-1980s, they were ready to make broader statements about this technique and about its attack on pure culture. In 1985, Costerton and Cheng wrote a long treatment of this in a book *Bacterial Adhesion*, and tracked the differences between them.[598] And two years later, they published a monograph called "Bacterial Biofilms in Nature and Disease" in the Annual Reviews of Microbiology.[599]

The gist was that living in biofilms or consortia, and that bacteria living in communities "usually have significantly different properties form free-floating bacteria of the same species"—that the context determined essentially what a bacterium does, then if one wanted to understand the bacteria's role in a natural system or setting, or in the real world, one needed to take the environment, the context, as well as the bacterium into account when characterizing a biological phenomenon. [600] For Costerton, biofilm bacteriology meant "the end of the pure culture era" and was a direct rebuke, he joked, to the "Teutonic reductionist tendencies of Robert Koch" which

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[598] Costerton, J. William, Thomas J. Marrie, and K-J. Cheng. "Phenomena of Bacterial Adhesion," in *Bacterial Adhesion*, eds. Dwayne Savage and Madilyn Fletcher, 3-43, Springer US, 1985.

[599] Costerton, J. William, K. J. Cheng, Gill G. Geesey, Timothy I. Ladd, J. Curtis Nickel, Mrinal Dasgupta, and Thomas J. Marrie. "Bacterial biofilms in nature and disease," *Annual Reviews in Microbiology* 41.1 (1987): 435-464.

[600] Costerton, J. William, Z. Lewandowski, D. DeBeer, D. Caldwell, D. Korber, and G. James, "Biofilms, the customized microniche," *Journal of Bacteriology*, 176 (1994): 2137.

had provided the pure culture and isolation framework for conventional microbiology since the late 1880s. [601]

Microscopy could provide a way to investigate microbes in their natural habitat and demonstrated the extent to which cultivation changed microbes. It further reinforce the importance of direct environmental studies, and the extent to which microbes were contextual creatures. If one wanted to understand natural, environmental, inter-organismal processes, the starting point for knowledge making about the microbial world could not be the cultivation techniques of pure culture and conventional microbiology. But again, this vision of microscopy as a tool to wield against the legacy of Koch's "reductionist tendencies" was not necessarily a new thing. Winogradsky had turned to microscopy as a tool for studying natural organisms.

Microscopy had revealed the extent to which microbes in natural ecosystems were different than their laboratory incarnations. What it could not reveal, however, was the richness of the diversity of microbes in natural settings. Laboratory cultivation and pure culture isolation limited not only what kinds of microbes that could be seen, as Brock's discovery of thermophiles had shown, but also changed the nature of the microbes that could be cultivated in the laboratory. At issue, then, was how to characterize what was there—and to try to understand the genetic basis for the different manifestations of microbes in the laboratory vs. natural settings.

Ecosystem vs. Organism: Choosing Experimental Units for Analysis

[601] Costerton, J. William. "A short history of the development of the biofilm concept," *Microbial Biofilms,* eds. Hilary M. Lappin-Scott and J. William Costerton, Washington DC: ASM Press, 2004, 4.

The next technique was extremely productive way in which microbial ecology embraced "direct studies" of the environment was in turning molecular biology into a tool for the articulation of microbial diversity. This technique was originally developed as a means to investigate evolutionary questions with respect to microbes and was co-opted for the study of microbes *in situ*. Here "direct study" meant to bypass cultivation completely and to make the undetectable visible without the powerful but limited visual tools of the biofilm bacteriologists. It also led the way to a different approach to studying the physiological and metabolic characteristics of microbes that microscopic study could also not reveal.

One of the main problems of the microbial world had always been the fact that they could not be seen or made visible easily. Identification of microbes essentially required with pure culture because of the lack of defining and particular enough morphological characteristics of microbes. This problem was as much a problem for the microbial ecologist, who wanted to know what was there. As it was a problem for the taxonomist, who also wanted to know the extent of what was there and how to make sense of it. It was this concern about the classification of microbial life that led to another "direct approach" to studying microbes that would become a central tool of the microbial ecologist.

Classifying Microbiology through Molecular Means: Carl Woese and ribosomal RNA

Carl Woese came of intellectual age in the 1950s, right as the molecular biological age was dawning. He received his PHD in biophysics from Yale in 1953, the year of Watson and

Crick's triumph over the structure of DNA.[602] Woese embraced the molecular paradigm in his early career and the "cryptographic" approach, as he called it in retrospect, to the problem of gene expression.[603] But he began to question the point of such investigations—the endpoint was not, he decided, to crack the genetic code, which had become the Holy Grail and raison d'etre of the new biology, but to understand evolution. Deciphering the code could not be an end in itself, for him; instead he aimed to find a universal biological principle linked to evolution. His approach was to take the techniques of molecular biology and apply them to the most classical of biological problems—evolution. His used microbes as a tool to investigate evolution, by comparing ribosomal RNA sequences and cataloguing their differences to build a phylogenetic tree based on those differences. This way forward had been laid out as early as 1965 by Linus Pauling, who had thought through "Molecules as Documents of Evolutionary History" in the *Journal of Theoretical Biology*."[604] Woese realized that in order to do this new kind of phylogeny correctly, you would need to track a universal molecule. He surmised that ribosomal RNA, required to make proteins, would be a good choice because ribosomal RNA had the "phylogenetic 'reach'" to capture all of living things since it participated in an essential cellular function.[605]

[602] Watson, J. D., and F. H. C. Crick, "Genetical implications of the structure of deoxyribonucleic acid," *Nature* 171 (1953):964-966.

[603] See for example, Carl Woese, "Nature of the Biological Code," *Nature* 194 (1962), 1114 – 1115.

[604] Zuckerkandl, E., Pauling, L., "Molecules as documents of evolutionary history," *Journal of Theoretical Biology* 8 (1965):357-66

[605] Woese, Carl R., "A new biology for a new century," *Microbiology and Molecular Biology Reviews* 68.2 (2004): 173-186.

Woese collected species of bacteria from other researchers and sequenced their ribosomal RNA in order to test the haphazard classificatory schemes of traditional microbiology—and unsurprisingly found them wanting. But what the technique allowed was a new way of describing microbes without using the standard microbiological techniques that were built on old organismic biological classificatory schemes—the need to identify a difference that could be *seen* based on some physiological or biochemical characteristic of an *in vitro* or *in vivo* bacterium or microbe (the shape, the stain, some biochemical property, etc.). These all required that the microbe be isolated and captured—it needed to be cultured to characterize it properly, especially since the old morphological methods of classification did not work on microbes. Woese found a way to characterize microbial difference and identity that did not depend on what he deemed artificial classification (shape, stains, etc.) or classifications of convenience (disease, location, etc.). He insisted that in order to understand biological problems—one needed a framework that reflected the order of the natural world—a natural classification of organisms.

Woese took the question into the laboratory—and argued that what the evidence he could marshal showed was that the ordering of the living world as had been accepted was wrong.[606] He strongly rejected the classification of microbes into eukaryotes and prokaryotes as a basis for phylogeny—“eukaryote/prokaryote is not primarily a phylogenetic distinction, although it is generally treated so” he wrote in a now classic 1977 paper that introduced his theory to the

[606] Woese, Carl R., and George E. Fox. "Phylogenetic structure of the prokaryotic domain: the primary kingdoms." *Proceedings of the National Academy of Sciences* 74.11 (1977): 5088-5090. See Woese, Carl R. "Bacterial evolution." *Microbiological reviews* 51.2 (1987): 221-271 for an extensive treatment.

world.[607] His new classificatory scheme was initially controversial but eventually came to be accepted and mainstreamed by the 1990s.[608]

The first step to understanding the living world for Woese was to see it properly—to understand how to map it *in time.* Woese described how biological organization was linked on a molecular level to deep evolutionary history through a new microbial phylogeny. Microbial ecologists took his approach and adapted it for their field. It provided a way to circumvent cultural methods to investigate the diversity of the microbial world that microbial ecologists aimed to characterize.

“A Field of Genes:” Norman Pace and rRNA

Microbiologist Norman Pace[609] took the methods that Woese developed and applied them environmental contexts. It was Pace’s application of Woese’s new rRNA analysis method that provided a new method of “direct study” to the microbial ecologist.

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[607]Woese and Fox, (1977). Woese claimed that there were 3 kingdoms, not five—and that microbial diversity was much greater than previously believed.

[608] Evidence for mainstreaming includes his awards: Macarthur Genius Grant as an innovator in 1984 when he was still controversial but beginning to be acknowledged as a visionary. He received the Leeuwenhoek Award, microbiology’s greatest honor in 1992, the Salman Waksman Award for Microbiology from National Academy of Sciences in1995, the National Medal of Science in 2000; and in 2003, the Crafoord Prize from Royal Swedish Academy of Sciences.

[609] Pace has become a leading figure in microbial ecology, but beyond that he has also become recognized more broadly in the scientific and intellectual realms. He was awarded a MacArthur Genius grant in 2001, the same year he was awarded the National Academy of Sciences’ Selman Waksman Award for Microbiology, the highest honor for a microbiologist in the United States.

Norman R. Pace earned his PhD at the University of Illinois, Urbana a few years after Woese had been hired as a molecular biologist in the department of microbiology after a chance meeting with Pace's advisor, eminent molecular geneticist Sol Speigelman, at the Pasteur Institute (Woese had been working for a few months with Monod and Jacob).[610] Pace did his dissertation on viral RNA replication, and continued his work on RNA upon leaving Illinois.[611]

It was literally "a field of genes"—Woese's favorite term—that Pace turned his attention to. [612] Pace described his technique in contrast to the classical technique of pure culture and its increasingly stifling limitations for the environmental microbiologist:

> "The description of pure cultures is a foundation of experimental microbiology. It seems possible, however, that much of the biological diversity of the earth has not been, or cannot be, brought into pure culture. We are developing technical strategies for analyzing fundamental aspects of naturally occurring microbial populations without the need for their cultivation."[613]

This time, the problem with conventional cultivation techniques was not that they did not present a real picture of how microbes functioned in their natural habitats, but limited what could even be seen. Brock's work on extremophiles had demonstrated a whole class of microbes that had been missed by conventional cultivation techniques; and their identification had helped

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[610] Sapp, Jan. "The iconoclastic research program of Carl Woese." *Rebels, Mavericks, and Heretics in Biology*, New Haven: Yale University Press, 2008, 309.

[611] Pace, N.R., "In vitro studies of viral RNA replication," (Ph.D. Thesis, the University of Illinois, Urbana, 1967).

[612] Pace, Norman R., Jan Sapp, and Nigel Goldenfeld. "Phylogeny and beyond: Scientific, historical, and conceptual significance of the first tree of life," *Proceedings of the National Academy of Sciences* 109.4 (2012): 1018.

[613] Stahl, David A., D. J. Lane, G. J. Olsen, and N. R. Pace. "Characterization of a Yellowstone Hot Spring Microbial Community by 5S rRNA Sequences." *Applied and Environmental Microbiology* 49.6 (1985): 1379-1384.

change the shape of the Tree of Life through Woese's molecular phylogeny technique. The cultivation techniques provided a skewed picture of the microbial world that had implications for phylogeny and for ecology. The present state of knowledge was incomplete, but Woese's methods offered a way to address this problem. Pace reasoned that Woese's molecular techniques could solve this problem and present an "unbiased" view of the microbial world by bypassing the artificiality of the general microbiological laboratory and going directly to the natural world:

> "The methods use recent advances in nucleic acid sequencing and recombinant DNA technology to determine nucleotide sequences of 5S or 16S rRNA genes from microbial communities containing multiple organisms. By comparing these sequences with known ones, we can define the phylogenetic status of any organism residing in the communities. Because only the naturally available biomass is required for these methodologies, the analyses project a relatively **unbiased picture** of an in situ microbial community. …
>
> The direct isolation and sequencing of the 5S rRNAs from environments of reasonably plentiful biomass and limited complexity offers a relatively convenient determination of the dominant community members. "[614]

The short article—just five pages—was published in the specialized *Journal of Applied and Environmental Microbiology* in summer 1985. Pace had gone to Yellowstone National Park to investigate microbes in one of the Hot Springs whose visible microbial "inhabitants" had resisted cultivation (which as Pace and his collaborators noted, was typical of "natural microbial

[614] Stahl, et. al. (1985). Emphasis mine.

populations)."[615] While earlier attempts at cultivation were unsuccessful, Pace's sequencing method uncovered a complex microbial community with a few dominant members that could be characterized phylogenetically according to similarities in the ribosomal DNA to microbes in the existing ribosomal RNA library that Woese had begun with his excursions in the 1970s.[616]

The following year, Pace and his collaborators provided a more extensive take on their new method in the *Annual Reviews of Microbiology*. Their thirty page treatment of the technique included a nod to Woese in the title and declared that the technique could address place as well as time—the two great and central problems of biology, linked with a molecular method: "Microbial Evolution and Ecology: An Ribosomal RNA Approach." From the start they make a strong, unequivocal statement about the importance of the new technique for microbiology:

> "There is no more fundamental and straightforward way to classify and relate organisms than by appropriate nucleic acid sequence comparisons. The simple morphology of most microbes provides few clues for their identification; physiological traits are often ambiguous. The microbial ecologist is particularly impeded by these constraints, since so many organisms resist cultivation, which is an essential prelude to characterization in the laboratory."[617]

For Pace and his collaborators, finding a way to characterize the uncultured majority of microbial species was necessary for microbiology as a field, but also for the goals of microbial

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[615] Brock, T. D., *Thermophilic Microorganisms and Life at High Temperatures*, New York: Springer-Verlag, 1978.

[616] Lane, David J., Bernadette Pace, Gary J. Olsen, David A. Stahl, Mitchell L. Sogin, and Norman R. Pace, "Rapid determination of 16S ribosomal RNA sequences for phylogenetic analyses." *Proceedings of the National Academy of Sciences* 82.20 (1985): 6955-6959.

[617] Olsen, Gary J., David J. Lane, Stephen J. Giovannoni, Norman R. Pace, and David A. Stahl. "Microbial Ecology and Evolution: A ribosomal RNA approach." *Annual Reviews in Microbiology* 40.1 (1986): 338.

ecology. These uncultured microbes were doing something—and their fundamental processes could provide crucial insight into environmental processes. These new techniques provided a means "to tease apart the complexity of the natural microbial world and ascribe the chemical basis of environmental transformations to the activities of specific organisms."[618]

Molecular tools provided a way for the uncultured world to be seen and to hint at the ways in which microbes shaped their ecosystems. What molecular biology did was to overcome the limitations of culturing microbes—it provided a new frame through which to think about and to see microbes. It became a tool for microbiology in an inversion—that allowed one to see the environmental more clearly by sidestepping the historical baggage that culture techniques had created in the articulation of microbes. These new method made molecular biology a tool for the elucidation of fundamental microbiological questions, rather than making microbes a tool for the elucidation of general biological questions as they were in molecular biology.

For microbial ecology, the point of experimental investigation from this perspective was to provide insights into how microbes functioned in natural environments, and not as self-contained exemplars of living systems. In short, the experimental control of an organism for its manipulation in the molecular biological laboratory or for its destruction in the biomedical laboratory was not the point. These are different goals, require different approaches—and presented a different view of what microbiology *was* and *should be*. It was a broad vision in which biodiversity was central, rather than having one exemplary microbe, disciplined by the laboratory to provide the essential insights into microbial biology.

[618] Pace, N. R. "Microbial Ecology and Diversity," *American Society of Microbiology News*, 65 (1999), 328-333.

Conclusion: A Science of Life without Nature

In *Controlling Life: Jacques Loeb and the Engineering Ideal in Biology,* historian Philip J. Pauly described how biologists in the 20th century began to "decide that nature was fading away."[619] This was a direct result, he argues, of the increasingly important role of the laboratory in biology: "As biologists' power over organisms increased, their experience with them as "natural" objects declined." The laboratory does two things that transform a natural object—decontextualizes it and simplifies it--to make it suitable for experimentation. Thus laboratory science dispenses with aspects of a natural object that make it *natural* to transform it into a scientific object. Furthermore, as Knorr-Cetina tells us, laboratory work depends upon the traces, parts, "extractions," or "'purified' versions" of natural phenomena.[620] The laboratory was increasingly artificial—it created, as Knorr-Cetina writes, a new "social order" for natural objects quite different from the natural order from which they had been extricated. As biological work—or more accurately, the most high status biological work—became more and more laboratory based, the circumstances of that work came to change how biologists understood and viewed the natural world. Microbes, then, were increasingly valued for their laboratory incarnations and not for their role in natural environments.

If nature was fading away, then the epistemological status that the natural had was also fading away. Pauly has described how Jacques Loeb took the programmatic goals for

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[619] Pauly, Philip J. *Controlling Life: Jacques Loeb and the engineering ideal in biology*. New York: Oxford University Press, 1987, 200

[620] Knorr-Cetina, Karin. *Epistemic Cultures: How the sciences make knowledge*, Cambridge: Harvard University Press, 1999, 27.

experimental physiology—the unity of living nature and the development of general techniques for the manipulation of organisms—as a starting point for his new experimental biology.[621] Biological entities in the laboratory came to be viewed as "technologies of living substance" more than windows onto the nature of life.[622] Experimentalists who were wedded to the notion of the laboratory as essential in making the most important knowledge about life increasingly came to see Nature as "trivial," in Pauly's terms. Biology could be improved upon or co-opted and put to use. For Pauly, Loeb created a new ideal for the 20th century experimental biologist—the biologist as *engineer*. This engineering approach to biology shaped the biological sciences in profound ways in the 20th century, and is the philosophy undergirding modern biotechnology and experimental biology.[623]

Implicit in this approach is the notion of biological objects as constituent parts. To understand their function is essential; the rest become just particulars—parts that can be put to use for other ends as technologies. But the rise of the ecological sciences saw increasing interest in defending the "natural"—and to bring it back into science, and to insist that managing and manipulating life could be—and needed to be—considered in terms of natural systems and not just organism's molecules. The management of systems required a different kind of biological knowledge—of organisms *in situ* rather than organisms' component parts.

In this kind of biology, organisms could become tools in the service of rather than the objects of knowledge production. The establishment and use of a model organism is similar to

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621 Pauly (1987), 36.

622 Landecker, Hannah. *Culturing Life: How cells became technologies.* Harvard University Press, 2007.

623 See Landecker (2007) and Bud (1994).

setting controls: the more you know about an organism the more suitable it is to be a model organism because you can sharpen the focus of an experiment without being distracted or having to account for outside effects.[624] They could become the "right tools for the job" by virtue of the experimental control that a researcher would have over them, based on the accumulated knowledge about that organism or experimental set up as an experimental system. The organism could become an instrument in the experimental apparatus. Bacteria, with their seemingly simple biology, took on a new role in this new biological landscape—as well characterized and easily cultured microbes like *E. Coli* became experimental systems for molecular biology and genetics. They became an emblem for modern biology—the new biological sciences just as they had become emblems for medicine in the 20th century when infectious disease was the most important part of medicine.

But what does it mean to contextualize a de-natured object in the laboratory? Knorr Cetina surmises that this attempt to disappear context makes laboratories "epistemically advantageous" for science.[625] But it is "epistemically advantageous" according to a particular kind of knowledge order that promotes certain values. Placelessness is an epistemic virtue, to use Galison's and Daston's phrasing, that is part of the core values of experimental laboratory science.[626] Placelessness speaks to the universality of an experimentally produced piece of knowledge.

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[624] For more on model organisms, See *footnote* 34.

[625] Knorr-Cetina (2009), 27.

[626] See "Epistemic Virtues" section in *Objectivity*, Lorraine Daston & Peter Galison. Published: New York: Zone Books; Cambridge, Mass. MIT Press, 2007, 39-42.

But in taking nature at face value, microbial ecologists were eager to understand the nature of place as a first principle. It was a field science that rejected the decontextualization of microbes in the laboratory as anathema to their research agenda and knowledge project. For Brock, microbial ecology had meant working in the natural habitat and with natural model systems. Brock's work had uncovered a new category of microbe; the microscopic studies of Costerton and others had shown the ways in which microbes differed in lab and in field by focusing on the field; and the molecular techniques that Pace modified from Woese provided a way to bypass the microbiological laboratory and see the diversity and richness of the microbial world in a way that required attention to place. It provided another avenue with which to investigate microbial function, starting from the environment rather than the laboratory. This was the point of the natural turn in microbiology, animated by concerns about pollution control and management: the environmental control of the activities of populations in the natural world.[627]

In their study of objectivity, Galison and Daston describe how scientific objectivity has changed over time and meant different kinds of things at different periods. These historically specific and contingent kinds of scientific objectivity embody a set of "epistemic virtues" that are manifested in the practices of a particular scientific culture, period and setting. There is an ethical component to these ideals that shape the subject of knowledge production. This ethics implies an ordering of the kind of knowledge produced—some knowledge is better or more virtuous than other kinds of knowledge. The natural turn saw the rise of a competing vision of epistemic virtue that could be contrasted with the molecular biological version—one that privileged environmental context and natural relationships between organisms as core targets of

[627] See for example, Bungay (1968) and Hawkes, Herbert Aubrey, *The Ecology of Waste Water Treatment*, Pergamon Press, Headington Hill Hall, 1963.

scientific investigation. This could be seen in the rise of microbial ecology and its insistence on denigrating conventional microbiology on the grounds that it did not present a good enough picture of the microbial world or provide reliable knowledge about microbes.[628]

The microbe that pure culture techniques produced was an excellent model organism for the kinds of investigations required to ask the core molecular biological questions—a perfect object for the "social order," to use Knorr-Cetina's phrase, of the molecular biological laboratory. The pure culture techniques that were so amenable to fighting pathogens and to studying the newly dominant biological sciences of the mid to late 20th century, molecular biology and genetics, had placed undue limits on microbiology itself. Microbiologists were aware that traditional culture techniques missed a vast number of microbes in the natural world because they could not be cultured. The hidden diversity of the microbial world was a large question mark; the natural turn made this question mark less and less tenable for a scientific world more and more interested in understanding natural environments and environmental processes.

The natural turn saw the advancement of the idea that microbes were perhaps best understood in natural settings. In the natural world, microbes congregated in communities, consortia and mats—and were markedly different from their laboratory incarnations. The innovation of the natural turn was in looking to ecosystems as the proper way to understand and investigate microbes. It used on the ecosystem as a functional unit, and natural environments as the starting point for producing a particularly microbial form of knowledge about the world—that could reshape our basic understandings about biology more broadly.

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[628] See Daston & Galison (2007), 39-42.

Increased interest in other microbes that were unculturable and on the relationships between microbes and their environments set the stage for paradigm shift in microbiology that tilted more towards the old questions that had animated soil and agricultural bacteriology. The field of microbial ecology, which emerged as a distinct field within microbiology in the 1970s became part of the broadening and strengthening network of ecological sciences more broadly. This field's attempt to build a science around the unit of the ecosystem as opposed to the individual microbe—and to attempt to study microbes in natural context set the stage for the microbial turn in the twenty-first century, which I discuss in the next section.

PART III: THE MICROBIAL TURN

According to anthropologists Stefan Helmreich and Heather Paxson, microbes have found themselves ensconced in an "idiom of promise" at the beginning of the twenty-first century, in marked contrast to the "idiom of peril" that dominated microbes in the last century.[629]

In the Part I of this dissertation, I argued that this "idiom of promise" was always there albeit as an often marginalized counternarratives to the dominant "idiom of peril" surrounding microbes. In the last section, I argued that the natural turns in science, culture and medicine reshaped the narratives around microbes in ways that raised their status in these domains. The twin poles that defined them culturally—germs as filth and germs as disease—were problematized as the solutions to both problems were re-evaluated as excessive technological overreactions that could be harmful to the balance of nature—a culture obsessed with cleanliness that had distorted society's values and unloaded chemicals on the body and the environment; and an antibiotics arms race that had severe ecological fallout. In science, microbes were no longer viewed as only simple, representative and easily disciplined model organisms for more interesting or allegedly complex organisms, but became generative and important biological objects, worthy of study in their own right. These changes in the status of the microbe transformed what it could mean to have a microbial *body*—a cultural, medical and biological concept--and who might be interested in building one.

[629] Paxson and Helmreich, (2014).

In the next chapter, I explore the context, creation and impact of the National Institutes of Health's Human Microbiome Project and the development of human microbial ecology in the twenty-first century.

Chapter 6: The Human Microbiome Project

"We are 10 parts microbe, and one part human. We are clearly outnumbered."

--David Relman, 2005 Kinyoun Lecture, National Institutes of Health[630]

Introduction

The Human Microbiome Project was launched in 2007 by the National Institutes of Health. The point of the project was to discover what microbes lived in and on the human body and to investigate how these microbes are impacted by—and impact—human health and disease states. The HMP was conceived as a biomedical, microbial and biological project. Not only would it provide insight into the microbial world and the health of the human body, it had the potential to, as National Human Genome Research Institute Director Francis Collins claimed at the outset of the HMP, "reshape the way we think about and approach human biology."[631]

Investigations into the body's microbes had been undertaken throughout the 20th century, and explicit microbial visions of the body had been put forth before, as discussed earlier in this dissertation. This new vision of the body differed in several ways. First, it was backed by real institutional heft, by one of the major arbiters of the shape and direction of biomedical research in the United States and beyond. It was a massive effort, involving multiple National Institute of

[630] "Human Endogenous Microbial Ecosystems: The Next Frontier," 2005 Kinyoun Lecture, National Institutes of Health. Videocast at http://videocast.nih.gov/summary.asp?Live=4261&bhcp=1.

[631] "NIH Launches Human Microbiome Project," Press Release, *NIH News*, December 19. 2007. Accessed February 12, 2012. http://www.nih.gov/news/pr/dec2007/od-19.htm.

Health, four major sequencing centers and two university medical centers. It is the largest *ever* collaborative biology project. It was not the product of one lab conducting a series of experiments in service to a larger environmentalist vision of biomedicine (Dubos), or one man bringing together disparate research into one book to build a sourcebook of the entirety of microbes on the body (Rosebury), or a small research community making a pitch for the importance of their work (Luckey, gnotobiology and intestinal microecology). The endgame here was nothing short of the creation of a new science with the resources of the federal government, the imprimatur of the NIH, and the prestige of the Human Genome Project. It brought the microbial body to the forefront of the biomedical universe—and consequently the culture.

Those earlier versions of the microbial body cast microbes as part of the biological environment of the body. The HMP's version describes the relationship between the body and its associated microbes in a different way. In "Metagenomic Metaphors: New Images of the Human from 'Translational 'Genomic Research," scholar Eric Juengst analyzed the language used by HMP scientists in the planning stages of the project.[632] For these researchers and administrators, the HMP, the human genome should be considered as part of a human "metagenome" that includes the genomes of all the microbes associated with the body; the human body should be thought of as an ecosystem, and the human being should not be considered as a single species bound individual but rather as a "superorganism" that incorporates multiple organisms to produce the self. In short, the Human Microbiome scientists insist that the *I* needs to be recast as a *We*—and that the human body is an ecological human-microbial complex.[633] The audacity of

[632] Juengst (2009).

[633] This new orientation includes within it previous perspectives that had been used to frame this relationship--the body can be cast as environment for microbes and microbes as environment for the body experimentally, but the main innovation in this version of the microbial body was to redefine the body ontologically as part microbial.

this ontological claim was enough to attract cultural attention; that the biomedical establishment was making it attracted much more. This was clear evidenced by the HMP making the covers of the most influential cultural and scientific magazine and journals in the world upon completing its first phase.[634]

In this chapter, I argue that the institutional nature of this investigation and its broad collaborative scope made the Human Microbiome Project a crucial part of the establishment of a new microbial narrative about the body. I track the why, the what and the how of the Human Microbiome Project, and how it came to be. I argue that the HMP tracked with the changes in the three dominant narratives of the microbe in culture—as pathogen, as experimental tool, and as the avatar of unhealthiness. In this new era, the war on germs as it had been conducted since the advent of antibiotics was rejected; the microbe became a conceptual model for life (as community) rather than an experimental model for life (a thing to think with rather than to experiment on), and the microbe became a component part of a healthy body.

Antibiotic Resistance and the Microbial Body

2001 was a watershed year for concerns about antibiotic resistance. The WHO named it as one of the three major disease threats for the 21st century and developed a global plan to address the issue.[635] Antibiotic resistance and the fallout from antibiotics was an old problem, but it gained new urgency at the turn of the 20th century. The antibiotic resistance community of

[634] It made the covers of various publications in the summer of 2012: *Science, Nature, The Economist, Scientific American* and major newspapers like the *New York Times*, for example.

[635]Levy, Stuart B. *The Antibiotic Paradox: How the misuse of antibiotics destroys their curative powers*. Da Capo Press, 2002, viii.

microbiologists saw this in broader, ecological terms that looked beyond a narrow focus on the pathogen. Microbiologists engaged in the fight against antibiotic resistance were some of the main voices calling for a broader project to study the body's microbiota at the turn of the twentieth century. For them, the problem of antibiotic resistance was intimately related to the human microbiota. They saw both problems as at root about the ecological and evolutionary relationship of microbes with each other, with the bodies within which they lived and with antibiotic drugs.

In 2000, Nobel Laureate Joshua Lederberg reassessed the old idea of eradication as the core ideology of infectious disease medicine in *Science*. Lederberg had become a leading voice in the fight against emerging infectious diseases by this time. Lederberg had won his Nobel in the 1950s for work on bacterial genetics and had been a prominent molecular biologist since the 1950s. However, the re-emergence of intransigent infectious diseases in the 1980s and 1990s shifted his attention to the problem of antibiotic resistance. Joshua Lederberg spent the 1990s as a major voice in the gathering emerging infectious diseases movement, first as chairman for the Institute of Medicine's study *Emerging Infections: Microbial Threats to Health in the United States* and then as the founding chair and organizer of the Institute of Medicine's Forum on Emerging Infections (also Forum on Microbial Threats) (a position he held from 1996-2001).[636], [637]

[636] Joshua Lederberg, Robert E. Shope, and Stanley C. Oaks, Jr., eds., *Emerging Infections: Microbial Threats to Health in the United States*, Washington, D.C.: National Academy Press, 1992.

[637] For more on this, see *Microbial Evolution and Co-Adaptation: A Tribute to the Life and Scientific Legacies of Joshua Lederberg*, Institute of Medicine (US) Forum on Microbial Threats, Washington (DC): National Academies Press (US); 2009 and "Joshua Lederberg (1925-2008)," Stephen S. Morse *Science* 319 (2008), 1351.

By the end of the decade, he had developed a new vision of infectious disease that was informed by an "increased awareness of the microbial environment" that had been garnered over the previous two decades.[638] Reflecting on the history of infectious disease medicine in a review article for *Science*, he presented this new vision as follows:

> "…our most sophisticated leap would be to drop the Manichaean view of microbes: "We good; they evil."… Perhaps one of the most important changes we can make is to supersede the 20th-century metaphor of war for describing the relationship between people and infectious agents."[639]

This "Manichaean view" of microbes was a core tenet of scientific medicine of the 20th century. To reject it was not, then, just about trying on a different metaphor—it was about reconceptualizing the biomedical infrastructure and ideology that had been built on this view of the pathogenic relationship. This Manichaean approach had led to the wild successes of the antibiotic era and a widespread optimism by the 1960s that infectious disease had been conquered.

The antibiotic industry had initiated an arms race with pathogenic microbes that was a contest between, as Lederberg phrased it, "our wits" and "their genes."[640] That the industry was losing the infectious disease arms race was proof for Lederberg that the metaphor was flawed, or had perhaps reached its limits. The biomedical research and industrial complex had reified the war metaphor by creating this arms race in two ways. First by creating new pathogenic strains

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[638] Lederberg (2000), 290.

[639]Ibid, 293

[640] Ibid, 290.

that were a reaction to the antibiotics used to treat the old strains, and second by shaping the research lab to conform to the requirements of the antibiotics industry. Experimental animal models of infection, as Lederberg wrote, were "superb for *in vivo* testing of an antibiotic, but [bear] little relation to the dynamics of everyday human disease."[641] He argued that having an effective model of infection required more than a model that reduces infectious disease to a single pathogen—a model built more for the development of antibiotics than for the understanding of the disease. No wonder, then, to Lederberg, that we were losing the *long* war. Instead medical experts were focused on the battles at hand instead of looking for a long term solution. We were losing a war we thought was over; Lederberg argued that we needed a new strategy to win. The solution to getting better at dealing with infectious disease, would begin, Lederberg wrote, with "the simple recognition that humans, animals, plants and microbes are co-inhabitants of the planet."[642] This would require a re-conceptualization of disease as "instabilities within this context of cohabitation... [which] arise from...ecological and evolutionary...sources."[643]

This new infectious disease strategy also would require, according to Lederberg, a re-conceptualization of the body. Rather than a self-contained bounded organism under threat from invading microbe, "we should think of each host and its parasites as a superorganism with the respective genomes yoked into a chimera of sorts."[644] This "sociological development," as he termed it, regarding the "collaboration between hosts and infecting microbes" would challenge

[641] Ibid., 292.

[642] Ibid., 291.

[643] Ibid., 291.

[644] Ibid., 292.

old ideas about infection.[645] “The infected host is in fact at metastable equilibrium,” he wrote, and “[the] balance could tip toward favorable or catastrophic outcomes.”[646]

For Lederberg, a deeper understanding of this framework for disease and for this model of the body would require a “germs’ eye view.”[647] Doing this opened up what microbes were of interest to infectious disease medicine. The nonpathogenic microbes that were part of the body’s normal flora were thus implicated in disease in a new way, and became salient in a new way. They became central to the problem of infectious disease. Lederberg argued that the most effective and successful parasites don’t kill their hosts, but rather find a way to live with them. What was needed was a way to better understand and manage the parasitic relationship between infectious agent and host. What was needed was a new metaphor and a new approach that would investigate “the physiology of homeostatic balance in the infected host qua superorganism.”[648] This new view of disease required a reconceptualization of disease as instability and health as homeostasis; and a reconceptualization of the biomedical body from physiological machine to multispecies collective, or superorganism.

This vision was an ecological one. Lederberg believed that using an ecological model could subvert the arms race and provide a real way to achieve “long lasting security” for human health and which would leverage the protective role of the body’s microbial flora.[649] It would be

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[645] Ibid., 292.

[646] Ibid., 292.

[647] Ibid., 293.

[648] Ibid., 288.

[649] Ibid., 293: “For example, domestication of commensal microbes that bear relevant cross-reacting epitopes could afford the same protection as vaccines based on the virulent forms.”

based on a cooperative imperative: how to live together in the best way possible rather than how to destroy one's enemies.

This new vision of disease and of the body required new kinds of knowledge. If you wanted to understand disease as a "homeostatic balance" in a superorganism, you needed to know what organisms *comprised* that superorganism. The microbes lived in and on the human body were in natural habitats—and were part of the uncultured majority in the microbial world. To characterize these organisms would require the tools and approaches developed by microbial ecologists to bypass the limitations of laboratory culture.

If disease states were essentially "instabilities within this context of cohabitation... [which] arise from...ecological and evolutionary...sources," then you needed to know how to characterize *stability* within this context in ecological and evolutionary terms. This meant capturing the community as it existed in state of health within the body. This was a problem that could not be solved, again, by conventional microbiology methods dependent on culturing microbes in isolation in the laboratory. It would require an understanding of how those microbes functioned in the context of a functioning human body. Cohabitation, in microbial mats biofilms and consortia was the natural state of most bacteria—and they did not necessarily function in the same way outside of this context.

Making the superorganism legible required microbial ecology; it required a way to characterize communities rather than isolating the pathogen and understanding its metabolism and physiology in order to neutralize it. But it would also need a way to make the "human" and "nonhuman" parts of this biological chimera legible. This would require not just scientific tools that could deal with these disparate kinds of organisms, but the institutional will and heft to do this. Genomics and the success of the Human Genome Project provided both. The problem of defining the superorganism was framed as a genomics problem—and as a problem of defining human biology rather than just an innovative conceptual move aimed at dealing with the growing problem of antibiotic resistance.

Microbes in the Aftermath of the Human Genome Project

For those involved in antibiotic resistance research, the issue of an ecological view of infection required a different view of the human body. It was evident to them that a body conceived as a superorganism could not be adequately described by the Human Genome Project, which had been described in to great fanfare as “the blueprint for human life.”[650] They weighed in on this signature development shortly after the announcements of the first results in 2001.

Julian Davies, who had been working on antibiotic resistance since the 1960s, wrote a letter to *Science* to comment on the publication of the first draft of the human genome in 2001.[651] The sequencing of the human genome was, he wrote, “without question, a crowning achievement in biology.”[652] But he called the claims being made in the lay and scientific spheres that the HGP had uncovered the “blueprint for human life” or had decoded the “Book of Life” exaggerated. “We depend on more than the activity of some 30,000 genes encoded in the human genome,” Davies wrote. Human life was “critically dependent on the presence of upwards of 1000 bacterial

[650] Davies, Julian (2001), “In a Map for Human Life, Count the Microbes, Too,” *Science* 291 (2001), 2316.

[651] For example, Davies, Julian E. "Studies on the ribosomes of streptomycin-sensitive and resistant strains of Escherichia coli," *Proceedings of the National Academy of Sciences of the United States of America* 51.4 (1964): 659.

[652] Davies (2001), 2316.

species living in and on us."[653] This accompanying community of microbes meant that "human life depends on an additional 2 to 4 million genes." Consequently, he argued, until the "synergistic activities" between humans and their "obligatory commensals" were understood, our comprehension of human biology would be inadequate. Davies' letter came to be cited in founding and central documents of the Human Microbiome Project and what came to be MetaHIT, the EU's similar initiative and is noted as a kind of ur-text for the project.[654]

While Davies chastised the scientific community for its narrow view of the human; microbiologist David Relman, Lederberg's successor as chair of the Institute of Medicine's Forum on Microbial Threats (he took the position in 2002), took the publication of the draft Human Genome sequence as an opportunity to chastise the scientific community for its myopic focus on the human genome with respect to the biological world. He both extolled the microbial world for what it could offer to the investigation of human biology, but also for what it could offer to the understanding of life more broadly.

In an editorial for *Trends in Microbiology* in March 2001, Relman called for a "second human genome project" focusing on the body's microbes.[655] Relman, Stanford Medical School Professor of Microbiology and Immunology, and his Stanford colleague and co-author Stanley

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[653] Davies (2001), 2316.

[654] "The Human Metagenome Project – Recommendations from the Paris Workshop," 2005, Accessed October 15, 2013. http://www.human-microbiome.org/index.php?id=55; Peterson, Jane, the NIH HMP Working Group, Susan Garges, Maria Giovanni, Pamela McInnes, Lu Wang, Jeffery A. Schloss, Vivien Bonazzi et al., "The NIH Human Microbiome Project." *Genome Research* 19.12 (2009): 2317-2323. Interview with Dr. Lita Proctor 7/6/12.

[655] David A. Relman, Stanley Falkow, "The Meaning and Impact of the Human Genome Sequence for Microbiology," *Trends in Microbiology* 9 (2001), 206-208.

Falkow addressed themselves to the microbiology community in a bid to galvanize it to capitalize on the Human Genome Project.

Relman saw it as an opportunity to challenge the view that the HGP encapsulated at the institutional level: “For much too long, science policy decisions have reflected a human-disease-oriented perspective, and an unspoken philosophy of human ‘genomic supremacy’. As part of this belief system, the size of one's genome and the number of predicted genes determine one's relative importance in the biosphere.”[656] This notion of human genomic supremacy was severely challenged when the relative paucity of the human genome was discovered upon comparing the human genome to others. The advances in microbiology—the complexity of the deceptively simple organisms was an interesting challenge to the whole notion of “genomic supremacy” based on genome size. Instead, here was a model of flexibility based on diversity, plasticity, and transferability. ”The discoveries of unimagined functional diversity, genomic plasticity and lateral gene transfer in the microbial world significantly expanded our understanding of biological systems far beyond the boundaries defined by studies in the mammalian world…,’ he argued. While he was preaching to the crowd—speaking as he was in a microbiology journal, he pointed out that the merits of microbiology had been neglected by other kinds of biologists: “To the surprise of some,” Relman and Falkow noted, “recent findings suggest that microorganisms are extremely effective instructors about the natural world.”[657] But it went beyond benign neglect, to dismissal couched in a human-centric biological perspective: “…although we microbiologists celebrate this diversity [of the microbial world], many other biologists look on

[656] Ibid., 206.

[657] Ibid.

with barely disguised amusement and will insist that the human genome is the ultimate example of successful evolution."[658] This was a defense of microbiology and a call for it to move to the center of discussions of biology more broadly—but also human biology as well.

Relman went further than Davies, describing just to what extent human biology could be viewed in microbial perspective. There were already indications of a "host-microbe cross-instructional process" in which microbes and human cells spoke to each other and shaped each other's actions; and the human genome sequence had uncovered over 200 human genes that had homologs only found in microbes.[659] Microbiologists new that there were many microbes in the human microbiota that were so closely tied to the human body that they could not exist without it; they depended on the body for their survival. The blurring of the lines in terms of metabolic processes and evolutionary processes between human and microbe was more ammunition for the view that humans should be viewed as superorganisms.

For Relman, the HGP presented an opportunity for microbiologists to explore a portion of their field of which they were still "woefully ignorant."[660] The time was ripe to capitalize on the excitement of surrounding the HGP and to lobby for its complement, "a comprehensive genomic inventory of the large portion of cellular life within the human body that has been ignored so far…"[661] It would not only provide a more accurate and clearer look at the entirety of human life, but also would be a source for broadening the knowledge of the amazing functional diversity of

[658] Ibid., 207.

[659] Ibid.

[660] Ibid., 209.

[661] Ibid.

the microbial world, in the tradition of microbial ecological investigations since Brock's globe-trotting excursions to hot springs in the 1960s and 1970s: "The human biome is as much an unexplored frontier as the collection of life found at deep-sea thermal vents, if not more so."[662]

While Davies and Relman framed the need for an investigation into the body's companion microbes in terms of understanding the biology of the body and biological life, Joshua Lederberg expanded upon these questions and spoke in terms of human identity in 2001. He built on the infectious disease ecology theme in his *Science* article from the previous year in a Law School symposium titled "DNA: Lessons from the Past—Problems for the Future."[663] Lederberg's Keynote Address had two titles—speaking both to the central issue of DNA and the "obligatory commensals" that Davies had stressed: "Beyond the Genome" and "Whose Germs are they Anyhow?"

Lederberg argued that the issue of human microbiota was a problem that reached beyond the purely technical or biological; it had implications beyond the laboratory and the clinic. It opened up big questions about the nature of human life and would have an impact in the social (legal etc.) sphere. "Is human identity all in the genes?"[664] He asked. He sidestepped the old nature-nurture controversy that this question tended to be associated with and asked instead: "how much biology and how much, if any, "nature" is there beyond the genome, beyond the instructions inscribed in the chromosomal DNA." There was of course evidence that the notion of DNA as a blueprint could not account for differences of expression of the same DNA—there

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[662] Ibid.

[663] Lederberg, Joshua, "Beyond the Genome," *Brooklyn Law Review* 67 (2001), 7-12.

[664] Lederberg (2001), 10

were too many “exceptions that blur the once rigorously enforced boundaries between heredity and epigenesis” to make that claim.[665] He laid out the epigenetic phenomena that had been discussed in the realm of molecular and developmental biology so far to round out the picture of cellular phenotypes: beyond the nucleic sources of information; there were also the “epinucleic”—methylation—and he added an additional speculative category--the “extranucleic—protoplasm. But even this list was not comprehensive. To round out what he described as “our contemplation of sources of individual identity,” one needed to include the “obligatory commensals” that Davies had discussed in his letter to *Science*. Lederberg called this collection of microbes “the microbiome.”[666] He defined his new term as “the microbes that share our body space and that inhabit our skin, our mucous membranes and our gut.”[667] These impacted our health because they were implicated in our normal functioning.

He spoke in terms of bodies and not disease: “each one of us is a small ecological community that operates in some balance with competitors within its various components.”[668]

This was not a uniquely human phenomenon, Lederberg noted—symbiotic phenomena could be found throughout the biological world. The notion of a microbiome, of companion microbes in the animal world, then, was not only an explanatory framework that could work for the human body, but for all bodies. It suggested a new perspective on the whole panoply of animal life.

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[665] Ibid., 10

[666] Ibid.

[667] Ibid.

[668] Ibid,. 11

Davies, Lederberg and Relman placed the problem of companion microbes within the context of the Human Genome Project. But addressing the body's flora in the same way as the HGP presented one very clear problem—how to investigate multiple genome of multiple organisms that were not readily accessible? How to extract the DNA from the body's microbes? The majority of microbes in any habitat were unculturable; the same was true of the human body's microbes. Microbial ecology had provided means to assess microbial diversity in natural environments with Norman Pace's innovative use of Woese's 16s rRNA techniques, but this technique did not provide much insight into the metabolism, physiology and ecology of these diverse uncultured microbes. But the development of new techniques to place the genomes of the body's microbes alongside the human genome at least made this *possible*.

Metagenomics and the Human "Superorganism"

The term "metagenome" was coined by a group of soil researchers from the Department of Plant Pathology and Cornell's Chemical Biology Department in 1998. It meant the collective genomes of the soil microflora. The method developed by these researchers to investigate the untapped chemistry of the soil microflora married molecular biology and genomics and came to be known as metagenomics. This group was not primarily focused on the issue of microbial diversity, but was looking to find new chemical products in the soil that could be of applied in medicine and elsewhere.[669] The goal was functional analysis of the uncultured microbial components of the soil. Soil microbiology had been extremely productive in earlier years, but the

[669] Handelsman, Jo, Michelle R. Rondon, Sean F. Brady, Jon Clardy, and Robert M. Goodman. "Molecular Biological Access to the Chemistry of Unknown Soil Microbes: A New Frontier for Natural Products." *Chemistry and Biology* 5.10 (1998): R245-R249.

screening for antibiotic activity and other properties had yielded little in the late 20^{th} century because soil had been screened over and over again using the same culturing techniques and essentially everything that could be recovered had been.[670] A new approach was needed.

Their method was fairly straightforward. First they extracted DNA directly from the soil using "gentle" methods to preserve it. Next, they cloned it using a restriction enzyme and cloned it into a bacterial artificial chromosome which was able to carry long DNA fragments in *E. Coli*. Finally, the clones were screened for biological activity that could lead to "the production of novel natural products."[671]

Microbial ecologists recognized the limitations of Pace's innovation for recognizing microbial diversity in natural environments, but were eager to push beyond this to get at characterization of the uncultured world. The new metagenomic technique was adopted widely and quickly in the next few years. The power of metagenomics for human microbial ecology was realized soon afterwards as well because it provided a means to investigate biological activity and functionality for microbes that were inextricably linked with their hosts. As Jo Handelsman, one of the scientists that did the initial work on the soil metagenome explained in her much cited review of metagenomics in 2004,

"Many bacterial symbionts that have highly specialized and ancient relationships with their hosts do not grow readily in culture. Many of them live in specialized structures… in host

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670 Ibid., R245.

671 Ibid., R247.

tissues, making them ideal candidates for metagenomic analysis because the bacteria can be separated readily from host tissue and other microorganisms."[672]

In 2006, the National Research Council recognized the growing importance of metagenomics and convened the Committee on Metagenomics. The NRC released a report from the committee in 2007 called *The New Science of Metagenomics: Revealing the Secrets of Our Microbial Planet*, which promoted metagenomics as a revolutionary and exciting new field. Metagenomics had brought "the dawning of a new microbial age" and had provided proof that "Microbes run the world."[673] The report looked briefly at the Human Microbiome Project, which in 2007 was just launching, and saw huge potential for the project. They doubled down on Lederberg's vision: it was now an "inescapable" fact that "we are superorganisms composed of both microbial and human parts."[674]

The language of "superorganism" was increasingly used in the mid-2000s by researchers aiming to show the joint nature of basic metabolic processes, especially in the gut, via metagenomic analyses.[675] The first metagenomic study of the human microbiota was conducted on the human gut.[676] The study indicated that the digestive process is a joint microbial and

[672] Handelsman, Jo. "Metagenomics: application of genomics to uncultured microorganisms." *Microbiology and Molecular Biology Reviews* 68.4 (2004): 669-685.

[673] Handelsman, J., J. Tiedje, L. Alvarez-Cohen, M. Ashburner, I. K. O. Cann, E. F. Delong, W. F. Doolittle et al. "The New Science of Metagenomics: Revealing the Secrets of Our Microbial Planet." *National Research Council Report* 13. Washington, DC: The National Academies Press, 2007, 1.

[674] Handelsman et. al. (2007), 57.

[675] See for example, Turnbaugh, Peter, Ruth E. Ley, Michael A. Mahowald, Vincent Magrini, Elaine R. Mardis, and Jeffrey I. Gordon. "An Obesity-associated Gut Microbiome with Increased Capacity for Energy Harvest," *Nature* 444 (2006): 1027-131.

[676] Gill, Steven R., Mihai Pop, Robert T. DeBoy, Paul B. Eckburg, Peter J. Turnbaugh, Buck S. Samuel, Jeffrey I. Gordon, David A. Relman, Claire M. Fraser-Liggett, and Karen E. Nelson. "Metagenomic Analysis of the Human Distal Gut Microbiome." *Science* 312 (2006): 1355-1359.

human effort, and concluded that "humans are superorganisms whose metabolism represents an amalgamation of microbial and human attributes."[677] Jeff Gordon of Washington University in Saint Louis, who would be deeply involved in discussions leading up to and in the early stages of the HMP, had been working on intestinal microbial ecology of mice with germfree mouse models in the 1990s.[678] With the advent of metagenomics, his collaborators had begun to marry his gnotobiological (germfree) studies of mice models to comparative microbial genomics of human-gut microbe symbiosis in an attempt to characterize the complex dynamics of host-commensal bacteria relations in humans.[679] In the years right before the HMP's launch, his lab had established itself as a leader in the field, with much-cited publications in high impact journals like *Science* and *Cell*[680]*;* and his paper on the relationship between obesity and gut microbial ecology garnered a coveted spot in *Nature* and splashy press coverage.[681] This work framed the animal-microbial relationship in the language of "superorganism" as well:

> "Our study in mice demonstrates the feasibility and utility of applying comparative metagenomics to mouse models of human physiologic or pathophysiologic states in order

[677] Ibid.,1355.

[678] Bry, Lynn, Per G. Falk, Tore Midtvedt, and Jeffrey I. Gordon. "A model of host-microbial interactions in an open mammalian ecosystem." *Science* 273 (1996): 1380-1383; Falk, Per G., Lora V. Hooper, Tore Midtvedt, and Jeffrey I. Gordon. "Creating and maintaining the gastrointestinal ecosystem: what we know and need to know from gnotobiology," *Microbiology and Molecular Biology Reviews* 62 (1998): 1157-1170.

[679] Xu, Jian, and Jeffrey I. Gordon. "Honor thy symbionts." *Proceedings of the National Academy of Sciences* 100.18 (2003): 10452-10459.

[680] Bäckhed, Fredrik, et al. "Host-bacterial mutualism in the human intestine." *Science* 307.5717 (2005): 1915-1920.; Ley, Ruth E., Daniel A. Peterson, and Jeffrey I. Gordon. "Ecological and evolutionary forces shaping microbial diversity in the human intestine." *Cell* 124.4 (2006): 837-848.

[681] Ley, Ruth E., Peter J. Turnbaugh, Samuel Klein, and Jeffrey I. Gordon. "Microbial Ecology: Human Gut Microbes Associated with Obesity." *Nature* 444 (2006): 1022-1023; See Henig, Robin Marantz, "Fat Factors," *New York Times*, August 13, 2006. Accessed August 13, 2012. http://www.nytimes.com/2006/08/13/magazine/13obesity.html.

to understand the complex interplay between host genetics, microbial community gene content and the biological properties of the resulting *'superorganism'*."[682]

When the proposal for the Human Microbiome Project was produced in 2007, it, too, married the language of the superorganism with the technique of metagenomics: "the human [is] a "superorganism" whose genetic and metabolic landscape is an amalgamation of microbial and human components."[683] Human metagenomics researchers began to argue for breaking the division between environmental and medical microbiology.[684] For Jeff Gordon and his collaborators, that understanding the new body, the new medicine and our new deep understanding of ourselves in evolutionary time would depend on breaking down old barriers in microbiology: "It is time to breach the institutionalized dichotomy between environmental science and biomedical research, and to study ourselves as an integral and dependent part of our microbe-dominated world."[685]

Exploring Collaborative Metagenomics Projects

The potential of metagenomics for human microbiota quickly caught fire in the scientific community globally. There was interest and excitement about the possibility of an international

[682] Turnbaugh, Peter J., et al. (2006). Emphasis mine.

[683] Weinstock, George, Richard Gibbs, Human Genome Sequencing Center, Richard Wilson, Jeffrey Gordon, Sandra Clifton, Genome Sequencing Center, Bruce Birren, and Chad Nusbaum, "Pilot Project to Expand the Number of Sequences of Culturable Microbes from the Human Body," (2007), 4. Accessed March 13, 2014. http://www.genome.gov/pages/research/sequencing/seqproposals/hmpp_proposal.pdf

[684] Ley R.E., Knight R. and Gordon, Jeffrey I. (2007) "The Human Microbiome: Eliminating the biomedical/environmental dichotomy in microbial ecology," *Environmental Microbiology* 9 (2007): 4.

[685] Ibid.,4.

collaborative project built around the human superorganism. At the Human Metagenome Workshop, held in Paris and organized by the French National Institute for Agricultural Research in October/November 2005, 80 participants from Europe, North America and Asia eagerly discussed sequencing the Human Intestinal Metagenome, funding the project and its impact on health and industry. The Paris workshop saw the human metagenome as essential to the understanding of human biology. They described it as having "a profound influence on physiology, nutrition, immunity and development and disruptions in these human-associated microbial communities are a significant factor in many diseases."[686] The meeting participants stressed the cutting edge nature of such a project, seeing it as the next frontier of genomics.[687],[688] The workshop resulted in the creation of the International Metagenome Consortium, a "broad international consortium of laboratories and other concerned institutions" committed to investigating the Human Intestinal Metagenome. The thinking was that coordination between institutes would allow for a more efficient approach to the goal. The consortium aimed to do the following: allow standardization of procedures and quality control of the data; coordinate the analyses and ensure the free and rapid flow of data and resources throughout the scientific community, and manage the reference data set and maintain its currency throughout all stages of development of the project.[689]

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[686] "The Human Metagenome Project – Recommendations from the Paris Workshop," (2005).

[687] "Understanding the dynamic and variable nature of human microbial communities is a critical aspect of the challenge before us. Defining this dynamic diversity represents the next frontier of genomics."

[688] INRA (2006), "Mapping the Human intestinal metagenome." Press kit for the International Agricultural Show — Microflora of the Digestive Tract. Accessed April 1, 2010. http://presse.inra.fr/en. See also, "The Human Metagenome Project – Recommendations from the Paris Workshop" (2005).

[689] "The Human Metagenome Project – Recommendations from the Paris Workshop," (2005).

Just two months after the INRA-led meeting, the NIH convened its own workshop and began to investigate the possibility of a Human Microbiome Project within the NIH. Discussions about the Human Microbiome Project began with an informal brainstorming session in February 2006, at a hotel in Maryland. The meeting was open to any interested institutes and some invited external researchers who had expertise or an interest in investigating the human microbiome.[690] In addition to representatives from the National Human Genome Research Institute, there were staff from the National Institute of Arthritis and Musculoskeletal and Skin Diseases, the National Institute of Allergy and Infectious Disease, the National Heart, Lung and Blood institute, the National Institute of Diabetes and Digestive and Kidney Diseases, National Institute of Dental and Craniofacial Research. Extramural representatives included Genome Sequencing Center directors from Washington U. School of Medicine, Washington University in St. Louis' Center for Genome Sciences, Baylor College of Medicine and Craig Venter's Institute for Genomic Research. David Relman, who had called for a "Second human genome project" for the human microbiota just a few years earlier, also attended.[691] Jeff Gordon, now Director of Washington University's Center for Genome Sciences also attended.[692]

The chair of the meeting, George Weinstock, had attended the Paris meeting along with some of the other participants. Weinstock described the enthusiasm at the Paris workshop and

[690] "Human Microbiome Project "Brainstorming" Session," February 14, 2006. Accessed September 12, 2013. http://commonfund.nih.gov/hmp/brainstorming0206/index.

[691]Relman had become an authority in the field of human microbial ecology by the mid-2000s. See for example, Eckburg, P. B., Bik, E. M., Bernstein, C. N., Purdom, E., Dethlefsen, L., Sargent, M. & Relman, D. A., "Diversity of the human intestinal microbial flora," *Science*, *308*(2005), 1635-1638.

[692] See for example, Hooper, Lora V., Tore Midtvedt, and Jeffrey I. Gordon. "How host-microbial interactions shape the nutrient environment of the mammalian intestine," *Annual Review of Nutrition* 22.1 (2002): 283-307. And Xu, and Gordon (2003).

willingness of European and American sequencing institutes to commit to sequencing reference genomes. Despite the enthusiasm, however, he and his fellow brainstormers noted that despite the enthusiasm, there was no clear sense of how nor solid discussion about how to approach so large a project. One of the goals of the brainstorming meeting was to address those organizational issues more clearly, and to even attempt an estimate of costs to launch a pilot program—and perhaps to gain an American advantage in setting the course for and leading the international effort.

Framing a Human Microbiome Project

At the meeting, everyone was invited to describe their work in human microbiome research and how they saw the key challenges to a Human Microbiome Project. Jeff Gordon asked the fundamental question: Why would we want to sequence the human microbiome? Gordon, channeled his recent more heady work on human-symbiont relationships that he had explored in depth in an article for the *Proceedings for the National Academy of Sciences* in 2003.[693] There he had argued that the microbiome was necessary for us to acquire "a comprehensive view of ourselves as a life form."[694] Understanding the human microbiome would provide us with "an extended view of ourselves" and shed light on the evolutionary history of humans, since the microbiome was deeply implicated in it.[695]

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[693] Xu and Gordon (2003).

[694] Ibid, 10452.

[695] Human Microbiome Project "Brainstorming" Session." February 14, 2006. Accessed September 12, 2013. http://commonfund.nih.gov/hmp/brainstorming0206/index.

The variables at issue with the microbiome would need to be addressed, the participants noted—temporal, genetic, environmental, seasonal and individual factors would all need to be taken into account. And furthermore, the question emerged of whether there was such a thing as a "normal" or "core" microbiome—or perhaps "several modes of health" related to "A spectrum of normalcy."

The meeting convened with next steps towards creating a plan to build a trans-NIH project and to plan for possible coordination with an international initiative. But the final point made was about how to communicate to the public *why* the project was worth funding and why it was important to do. It was, after all, not an investigation into a specific disease or set of disease, but an investigation, first and foremost, that was "looking at the "normal" or healthy state."[696] This was very much a reality for the NIH and for many of the institutes that attended; the importance of branding of an agency or its initiatives for the public tastes could impact funding.[697] This project, would be about understanding "the nature of health" in an attempt to "more thoughtfully" define the target for therapy. They framed is at such: Instead of "remov[ing] the signs of illness" the underlying framework for the project to be presented to the public would stress "actually restoring people to health." The Brainstorming meeting participants made a further point about the nature of the kinds of disease this would speak to: "Many illnesses are ecological diseases rather than the result of exposure to a rare pathogen." But even in the field of

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[696] Ibid.

[697] For example, the National Microbiological Institute was renamed the National Institutes of Allergy and Infectious Disease by Congress in 1955 to capitalize on rising concerns about allergies in the public as concerns about infectious disease waned. See Kass (1987), 752, and Harden, Victoria Angela. *A Short History of the National Institutes of Health*, Dewitt Stetten, Jr., Museum of Medical Research, 1998.

infectious disease, the nature of the relationship between host and pathogen was being reconceptualized; infectious diseases were being cast as "ecological" as well.[698]

This was a strategy they would stick to, though it was not the only possible one, and certainly not the only once that had been raised. Gordon had looked at how microbiome research could grow dividends: "Future studies of the molecular foundations of human-bacterial symbioses in the intestine will require tools and concepts from many disciplines. In turn, the results of such studies should have broad implications that cross traditional disciplinary boundaries."[699] He outlined possible projects and gains for cellular microbiologists, biochemists, genome scientists, and systems biologists, anthropologists, nutrition scientists, plant molecular biologists, microbial ecologists and evolutionary biologists. If the project was geared towards these human-microbe symbioses, it would impact a plethora of fields even further afield from the biological and biomedical:

> "studying the molecular strategies used by symbionts for defining scarcity in their environment, for managing access to crucial resources when they are limiting, and for making decisions about sharing goods with others to ensure societal stability (concepts of cooperation and reciprocity…) could yield operating principles of interest to systems and environmental engineers, mathematicians (including those that study game theory),

[698] "Human Microbiome Project "Brainstorming" Session." February 14, 2006. Accessed September 12, 2013. http://commonfund.nih.gov/hmp/brainstorming0206/index.

[699] Xu and Gordon (2003), 10458.

ecologists, economists, business managers, and perhaps those who study, organize, and even govern our human communities."[700]

But rather than framing the project as a rich site for biomedical and other knowledge production, the meeting participants focused on a message more palatable to the public, and that could gel with conceptions of health and disease in the public sphere. The project's worth was in its approach to the following: "ecological diseases," "restoring" health," and "the nature of health." This was language that made sense in a world where the old infectious disease paradigm was under attack and whose costs were becoming salient (superbugs); and it was language that spoke to the concerns of a society that had incorporated alternative and complementary approaches to health into its mainstream—"restoring" health rather than "removing the signs of illness"—this was a different approach to disease and therapy in contrast to a model of destroying a pathogen or therapy that managed symptoms rather than addressed a deep cause. The HMP would address "ecological disease," which could mean a holistic disease that spoke to the whole body—something that the multiple body site nature of the HMP could address, it could mean an ecosystem disruption, or a disease model that spoke to environmental and host factors.[701] Consequently, in order to explain the importance of a concerted effort spent towards defining the "normal" or 'healthy' state, a new model of health was appealed to—an ecological one that relied on the restoration of health rather than the eradication of a "rare pathogen," or the mere management of symptoms.

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[700] Ibid, 10458.

[701] "Human Microbiome Project "Brainstorming" Session." February 14, 2006. Accessed September 12, 2013. http://commonfund.nih.gov/hmp/brainstorming0206/index.

The Human Microbiome Project: Collaboration at the NIH

The HMP was part of the NIH's new Roadmap for Medical Research and funded by the new NIH Common fund to the tune of $115 million dollars over five years. The NIH's Roadmap for Medical Research had been created out of conversations in 2002 that the NIH conducted with scientists, health care providers, the public and policy makers to determine problems that could be approached through a coordinated effort across NIH silos. It was an attempt to leverage a less bulwarked approach to biomedical research in order to promote and invest in interdisciplinary and collaborative research. The old NIH structure had excelled in fostering advancements within the individual institutes and centers; but there was a recognition that twenty-first century biomedical science required "functional integration of Trans-NIH interests."[702] Inherent in the Roadmap's approach was the sense that the new biomedical research was a collaborative enterprise; it sought ways to nurture this. This new sensibility was sparked in part by the success of the HGP and the recognition of the role of bioinformatics and computational biology in reshaping the way in which biological research was increasingly being done. The need to coordinate research around the common resources, like databases and tools that could be shared was central to the motivation for this move. In 2006, Congress created the NIH Common Fund by law to fund cross-NIH initiatives, institutionalizing a collaborative approach to government-sponsored biomedical research with guaranteed funding. The microbiome project fit into this new framework smoothly—it was relevant to various institutes and could help allocate resources to address the broad data overload problem that was increasingly being seen as an issue as

[702] "Fact Sheet: NIH Roadmap for Biomedical Research," August 2006. Accessed February 2, 2014. http://opasi.nih.gov/documents/NIHRoadmap_FactSheet_Aug06.pdf.

sequencing technologies became cheaper and faster since the project would require tools to deal with massive amounts of data.

The steady decline in price and time needed for sequencing made the idea of sequencing the microbial cohort of the body seem possible; and the increasing genomification of biological research more broadly seemed to make the time ripe for a coordinated effort regarding the microbiome—a clearly huge project.[703] It was based in part on the multi-institutional and collaborative HGP, but would build upon it. As the National Human Genome Research Institute asserted in 2003, "large resource data sets are becoming an increasingly critical component of biomedical and biological research" and the need for what the Institute termed "community resource projects" for this new kind of data-heavy biology was paramount.[704] A "community resource project," defined at a January 2003 meeting of genome scientists, database producers, journal editors and funding bodies by the Wellcome Trust about public sequence databases and the future of data-driven biology, was "a research project specifically devised and implemented to create a set of data, reagents or other material whose primary utility will be as a resource for the broad scientific community."[705] From the start the HMP would be shaped in the image of the HGP and with an eye to providing microbiome researchers with tools and resources to center research around. This would be a project for the 21st century—backed by the NIH Common Fund and the NIH Roadmap.

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[703] For a treatment of Data-driven genomics research, see Stevens, Hallam, *Life Out of Sequence: A Data-driven History of Bioinformatics*, Chicago: University of Chicago Press, 2013.

[704] "Reaffirmation and Extension of NHGRI Rapid Data Release Policies: Large-scale Sequencing and Other Community Resource Projects" National Human Genome Research Institute, February 2003. Accessed March 2, 2014. http://www.genome.gov/10506537.

[705] Ibid.

The meeting participants noted that the question of technology was of course essential and a major task. New analytical tools that could search the inevitably huge datasets would need to be developed; databases would be needed to link meta-data like clinical annotation to the microbial sequences produced.

Launching the Human Microbiome Project

In April 2007, the first real planning meeting of the project was held by the NIH to see whether such a project could work under the auspices of the Roadmap program. There was still a question as to whether the project was feasible; the assembled attendants were tasked with giving shape to a potential project. The meeting was chaired by George Weinstock again, but this time in concert with Jo Handelsman, metagenomics pioneer. The meeting brought together over fifty experts in a range of fields--metagenomics, microbial ecology, computational science, genomics, microbiology, medicine and bioethics. The workshop recommended that the HMP focus on sequencing and annotating reference microbial genomes needed for the analysis of metagenomic samples. The creation of a data set of reference microbial genomes would from cultivable organisms would be required for metagenomic analysis of uncultivable organisms to be taken from human samples.[706] Second, the project would attempt to characterize microbiome complexity at a variety of body sites (skin, vagina, gut, mouth) using 16srRNA sequencing across a large number of body sites and individuals and then a smaller sequencing of sites and individuals as a means to address the question of whether there was a shared core microbiome at

[706] NIH Roadmap Human Microbiome Project Workshop April 22-23, 2007. Accessed June 14, 2012. http://commonfund.nih.gov/hmp/workshop0407/index.

each body site. Third, the project would attempt to understand the relationship of the microbiome to human diseases—funding individual/lab-led investigations into the relationship between microbiome and particular diseases.

Finally, technology development was needed—the challenge of developing sampling and cultivation techniques were immediate needs; longer term, the need for very rapid and very cheap sequencing methods to handle the sheer volume of data that would be generated. The bioinformatics challenges were seen as substantial but not impossible to manage. The creation of metadata standards and a policy of immediate release of data would be built into the project from the start as part of the new collaborative and open ethos of data-drive biology. Furthermore, the HMP would need to build data sharing and management resources for the HMP data. These decisions would define the economy of the new science: a set of protocols would normalize how the community would share and present results and shape the development of the new science. The meeting attendants also included Ethical, Legal and Social Issues in their recommendations—looking at the clinical and health applications, such as probiotics, microbiome "profiling" for use in forensics, microbiome transplants and the relationship between the microbiome and behavior.

Defining Health for a Microbial Body

This rewriting of the body as an ecological entity, or "superorganism" had implications for basic biomedical notions of the normal and pathological. If a disease could be reframed as an ecological disturbance or imbalance; then health was ecological balance or stability. But what was a "healthy" or "normal" ecosystem? Are they the same thing? This was both a philosophical and a practical question for the first big study to come out of the HMP—the healthy cohort study. It was also the topic of discussion from the earliest planning meetings of the HMP. The participants in those meetings asked the following: What did a healthy body look like in microbial terms? Was there such a thing as a core microbiome? What was the difference between the microbiome in health and disease? These questions, central to the practicalities of research and study design, came down to a deceptively simple question that had deep cultural resonance: what did it mean to be normal? And what were the boundaries of health? The very question of how to choose subjects spoke to this—and the old issues of natural/normal emerged in the selection of HMP participants.

The problem of how to go about selecting subjects to participate in the study proved complicated. A planning meeting to hash this out was held in July 2007. At issue was how to design sample collection and the sequencing of the collected samples.[707] The workshop was chaired by David Relman, who had, as discussed earlier in this chapter called for a "second human genome project" that would focus on the microflora in 2001.[708] Relman's vision of a microbiome-focused project was prescient—he had called for a collaborative body site approach that would focus on flora-rich sites.

Relman charged the group with taking into account the characteristics of their proposed sample population—the variability of the donor, where to sample and when, over what period of time to sample, the importance of "rare" donors within the sample population, and how to

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[707] Human Microbiome Project Sampling Workshop. July 25, 2007. Accessed July 24, 2012. http://commonfund.nih.gov/hmp/workshop0707/index.

[708] Relman and Falkow (2001), 206-208.

conduct appropriate statistical analyses for the project. But the first question he raised was at the heart of the study itself—and the most difficult one to grapple with: How does one determine "the definition of a normal or healthy human being?" This question had been raised in the brainstorming meeting from the previous year. It had led to a philosophical discussion about whether there was such a thing as "normal" with respect to the microbiome among the experts gathered. But these speculations were moot now when it came to implement the study design. They had to have a rationale for their baseline and for the reference data set the HMP aimed to generate—to study the role of the microbiome in health and disease on needed a picture of them in health. The goal of the first phase was to create an experimental and actionable definition of the healthy microbial body.

The meeting gathered experts based on the body areas to be sampled: gut, skin, vagina and mouth. Each expert team consisted of a clinical doctor and a genomic scientist and/or microbial ecologist. The discussions focused on sampling and patient recruitment. Jeff Gordon and gastroenterologist Peter Mannon, a representative from the national Institutes of Allergy and Infectious Diseases led the gut discussion; The "Vaginal Site" discussion was led by Larry Forney, an environmental microbial ecologist who had recently expanded his ecological purview to the vagina, using the new culture-independent methods to define a "normal" vaginal flora and Jack Sobel, a vaginal health expert and Chief of Infectious Diseases at Wayne State who had published widely on the vaginal flora since the 1980s. [709] The "Skin Site" discussion was led by

[709] Zhou, Xia, Stephen J. Bent, Maria G. Schneider, Catherine C. Davis, Mohammed R. Islam, and Larry J. Forney, "Characterization of vaginal microbial communities in adult healthy women using cultivation-independent methods." *Microbiology* 150.8 (2004): 2565-2573.

Julie Segre, a skin biologist at the National Human Genome Research and Maria L. Turner, a dermatologist at the National Cancer Institute.[710]

Each expert team discussed the state of knowledge in their respective fields and offered suggestions that addressed Relman's initial concerns. Each team had a different take on what was needed for the study to capture the "normal" or "healthy" for their respective body sites—and in some cases distinguished between these two concepts completely. But each brought to bear the accumulated knowledge that had shaped investigations into those spheres over the twentieth century and into the present day.[711]

The oral cavity experts began their workshop with the issue of the relationship of "normal" to "healthy." They stressed that most Americans suffered from some kind of oral disease; "perfect oral health" was abnormal, if anything. This put the difference between the two into relief—did normal mean typical or did it mean healthy? Was it an idealized norm or a statistical one? What was the goal of the HMP in defining the microbiome? The expert team suggested focusing on typical individuals rather than the atypically healthy (as defined, of course, by dental experts). They insisted on the need for sampling by a dental specialist because of the complex geography of the oral microbiome.

The gut discussion emphasized the gut microbiota's consistent composition over time despite short term fluctuations in relative abundance. They suggested the standard sampling techniques for analysis of the gut microflora—stool sampling. Because of simplicity of this

[710] Human Microbiome Project Sampling Workshop. July 25, 2007. Accessed July 24, 2012. http://commonfund.nih.gov/hmp/workshop0707/index.

[711] Ibid.

sampling method, the approach championed by the gut experts was to sample a large number of people to get a broad sense of microbial diversity. The best way to determine the normal microbiome of the gut would be to determine it statistically across many individuals.

The vaginal microbiome session emphasized different issues. Sobel and Forney favored a less direct sampling approach in contrast to the gut experts—they suggested first identifying representative samples after an initial high level statistical analysis and focusing on those as the basis of "the normal." They also noted how for them a salient issue was the challenge of determining who healthy individuals were since clinical measures of vaginal disease often did not correlate with symptoms reported by women to their gynecologists.[712] These experts noted that self-sampling was suitable in the clinic, but not for the HMP because the study should aim to characterize different regions of the vagina that required gynecological expertise. The question of whether individual patients should be used for oral/vaginal/gut sampling was also raised since

[712] The disconnect between the medical profession and the patient in terms of how to define healthy or normal vaginal health—and who could--had been politicized in the 1970s. See Chapter 4. This discussion also revisited some of the same questions that had been raised by vaginal bacteriologists over the course of the 20th century. The question of how to define vaginal cleanliness in purely biological terms was contested in the 1930s by those investigators that were investigating it to establish what a healthy vaginal flora *should* look like, and how to achieve it. But there was an acknowledgement among these elite medical researchers that the flora played a role in the health of the normal vagina. At issue was what the relationship was between the normal and the natural was; and how to define "clean" in a zone where the elimination of bacteria may not be the equivalent of a healthy or nonpathogenic state. Over the next few decades, the question of how to define "normal" was at stake as researchers tried to establish a "baseline" for the normal bacterial population of the healthy vagina and how new products like tampons, oral contraceptives and antibiotics—and hexachlorophene-- affected it. See Weinstein, Louis. "The bacterial flora of the human vagina." *The Yale journal of biology and medicine* 10 (1938): 258. For example, see Hite, K. and Hesseltine H., "A study of the bacterial flora of the normal and pathologic vagina and uterus," *American Journal of Obstetrics and Gynecology* 53 (1947): 233, Brand, Elizabeth N. "Bacteriology of vaginal flora after use of internal tampons." *British Medical Journal* 1.4748 (1952): 24, Morris, C. A., and Delia F. Morris. "Normal' vaginal microbiology of women of childbearing age in relation to the use of oral contraceptives and vaginal tampons," *Journal of Clinical Pathology* 20 (1967): 636.

these sites' microbiota were more strongly linked to and implicated with each other than the skin.[713]

The final body site session was on the skin. The skin team emphasized the diversity of the microbial habitats of the skin on and between individuals, echoing Mary Marples' 1965 foundational text *The Ecology of the Skin*.[714] They also linked the skin microbiome to environmental settings and routines—people working in different professions had different microbial profiles as did people who lived in different kinds of habitats/climates. Of the three standard methods for dermatological sampling—punching, swabbing and shaving, Segre and Turner suggested the least invasive—swabbing—and pushed for the consideration of geographic location and profession in choosing study subjects.

It had been clear to the organizers of the conference that each community of experts would have its own preferences and traditional approach to clinical research. In order to figure out the best way to design a multi-site project that made sense for each body site and community of experts, the conference broke into two moderated breakout sessions in order to hash out sampling plans for a whole-body project. What to collect? How to collect the samples? And how many?

Most of the recommendations were practical and explicit—they covered suggestions for how to structure sampling, who should do the sampling (experts or subjects), number of subjects, sample storage, and what kinds of "metadata" (i.e. age, race, occupation) to collect. But the same

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[713] Human Microbiome Project Sampling Workshop. July 25, 2007. Accessed July 24, 2012. http://commonfund.nih.gov/hmp/workshop0707/index.

[714] Marples (1965).

underlying tension that had been first raised in the brainstorming meeting the previous year back was noted here--distinction between “normal” and “healthy” considered “critical” to the HMP. That tension remained unresolved. It would need to be resolved for the first phase of the HMP and its first major initiative—what came to be known as the “normal cohort study.” The study asked whether there was a core microbiome shared by humankind and aimed to provide a reference set against which future human microbiome research could be calibrated against. These recommendations shaped the protocols for sampling and specimen collection for the HMP.

Over 11,000 samples were collected from 300 volunteers. The volunteers were recruited from the two sequencing sites that were also part of medical school campuses that could provide the dental and medical expertise needed to collect the samples and which consequently had expertise and experience in doing clinical studies---Washington University, Saint Louis and Baylor College of Medicine. The Genome centers at those sites recruited men and women between the ages of 18 and 40—looking to focus on adults post-adolescence and pre-menopausal subjects since hormonal changes were known to impact the microbiome. A significant portion of the cost of the HMP went to the specialists needed to take the samples—dental, dermatological, gynecological and gastrointestinal expertise needed to do the examinations of subject candidates and to take samples as well. Lita Proctor, coordinator of the Human Microbiome Project, described the challenges as follows:

> “So, imagine doing this. You go to your doctor maybe on an annual basis to get a checkup, I mean, every single body site, if you were a volunteer for this study, every single part of your body that was going to be sampled would have to be clinically examined and to be verified free of disease before you could participate. It turns out for example, most of us, healthy otherwise, have oral disease of some kind, it can be

gingivitis, caries, so 80% of people who were actually healthy everywhere else had oral disease. So they had to be sent to their dentist, and get all that cleared out, then get re-recruited for the program… there's so many inclusion and exclusion parameters because the whole idea was this gold standard…[a] healthy population…I don't know if there is a such a thing."[715]

But this construction of the normal did not stop at the collating and conceding of different definitions of "healthy" among these experts. It also required the proximate preparation of the body—to minimize the "interference" of personal hygiene products on these "normal" bodies. The HMP Working Group developed a Core Microbiome Study Protocol that listed what kinds of products were acceptable and what were not—and the extent to which study subjects needed to stop using them.[716] These products had been designated as ecological disrupters. There was an insistence here that "normal" needed to be "natural"—and that "healthy" did not necessarily line up with products meant to promote "healthiness."

The study participants needed to fill out the "Eligibility Verification Checklist" to determine whether or not they could participate in the study. The checklist was to be filled out at the first sampling visit, prior to specimen collection. The information requested was about the usage of medications before for 7 days prior to the study.[717] They asked if women had taken vaginal or vulvar medications; and everyone if they had taken any topical antibiotics or steroids,

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[715] Dr. Lita Proctor Interview, 7/6/12.

[716] "NIH Human Microbiome Project - Core Microbiome Sampling Protocol A." Accessed January 25, 2014. http://www.ncbi.nlm.nih.gov/projects/gap/cgi-bin/study.cgi?study_id=phs000228.v1.p1.

[717] McInnes,Pamela and Mary Cutting. "Manual of Procedures for Human Microbiome Project Core Microbiome Sampling Protocol A." July 29, 2010. Accessed June 12, 2012. http://www.ncbi.nlm.nih.gov/projects/gap/cgi-bin/GetPdf.cgi?id=phd003190.2.

and whether they had any acute diseases. A portion of the study participants were sampled up to three times over the course of two years. This study design reflected the flexibility of the microbiome and the desire to capture a picture of a "natural" population of microbes on the body that was ecologically at balance—without the interference of antibacterial agents or other chemicals as well as infections.

The "normal body" was constructed out of the negotiation over what kinds of people to include in the study and accumulated knowledge from these different fields of what might disturb the normal flora of that site. To find suitable subjects for the study, parameters of "healthy" had to be shifted. For example, they had to increase the blood pressure criteria and the BMI in order to find a viable study population.[718] Proctor describes it in ecological terms as a "shifting baseline"—a concept originally developed in coral reef systems. "The idea is, what's a pristine coral reef? At what point do you say the system is starting to degrade…what do you call normal or healthy, or reference? Because if the system is continually degrading, what are you calling it? Can you actually get to the pristine or normal condition?"[719]

This solution to this problem was clear for the microbiota of the body---the notion of a core microbiome. As metagenomics pioneer Jo Handelsman described it:

"Identifying the core species … is essential to unravelling the ecology of microbial consortia because it has been proposed that these commonly occurring organisms that appear in all assemblages associated with a particular habitat are likely critical to the function of that type

[718] Proctor Interview, 7/6/12.

[719] Ibid.

of community. Thus, identifying a core is the first step in defining a 'healthy' community and predicting community responses to perturbation."[720]

This was an ecological vision of what would constitute health in bodily terms—a healthy community could be determined by seeing what was particular microbes were shared across a clinically healthy population. It would answer show what was required for normal function. Determining a healthy microbial body required linking clinical markers of healthiness with microbial communities shared across bodies.

Conclusion

The end of Phase I of the HMP in 2012 was met with much fanfare in the scientific world. *Nature* published the associated papers and put the HMP on its cover; *Science* did a special issue on the gut microbiota the week before, which provided context and perspective for the coming HMP articles in *Nature* if not the results themselves with think pieces, reviews and classic articles that strayed from the more narrowly defined issue and addressed the whole microbiome.[721] *Nature* published three articles—an introductory overview article to the microbiome from David Relman and two articles authored by "the Human Microbiome Project Consortium." The first laid out a "framework" for human microbiome research that outlined the way in which the science would be done. The second presented the results of the healthy cohort study. Papers that addressed the microbiological and microbial ecological implications of the

[720] Shade, Ashley, and Jo Handelsman, "Beyond the Venn diagram: the hunt for a core microbiome," *Environmental Microbiology* 14.1 (2012): 4.

[721] See cover; *Science* June 8, 2012.

study followed shortly in additional publications.[722] Consequently, the HMP was a truly big event for the scientific world.

Nature chose to highlight the healthy cohort study on its cover with a focus on the healthy cohort study: “First results from the Human Microbiome Project highlight the healthy variation in our microbial selves.” It was this study that really captured the imagination of the scientific community rather than the reference genome database or the other community resources that the HMP had built. Not even the framework—this forward leaning attempt to define a new science and the collection of technical and organizational tools to structure is—was as suggestive and exciting as the idea of a study of the microbial self and its parameters. The HMP’s revelation was that it offered a new way to conceptualize the human—“a microbial self” that required a new approach to health and to disease, and a new science.

The Human Microbiome Project was borne in part out of long held concerns about antibiotic resistance and their impact on the body’s microbes—both as a broader concern about infectious disease, but also out of the methodological and institutional innovations made possible by the Human Genome Project. It was a big, collaborative biology project that needed to be governmental in scope and animated by the changing vision of and rising status of a microbes as interesting biological objects in their own right—and a rising concern about that dangers of infectious disease. The notion of the body as an ecosystem gave more heft to considerations of how microbes were impacted by human intervention and everyday practices—and the realization that the changing collectivity of microbes had an impact on human health.

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[722] Human Microbiome Consortium, “A Framework for Human Microbiome Research,” *Nature* 486 (2012): 215–221. 6; See footnote 4 of this paper for additional papers.

It required enough people to *see* bacteria in a new way and the ability to *characterize* them in a new way—but it also required the institutional space to implement a project of such scope. It required the broad interest of the scientific community and the institutional wherewithal to attempt such a large project. The new vision of the body has more in common with the functional units of microbes in their natural environments--microbial mats and biofilms, ecosystems that shape each other—rather than individuals defined by a genetic inheritance.

The microbial body required a collaborative approach—the very nature of the knowledge required specialist knowledge from a variety of fields—a unified approach to building a new model of the body. It required a big biology approach—and a common language or technique to bring all of these into conversation. Genomics permitted a whole organism approach; metagenomics permitted an approach that could investigate microbes in the natural context of the body. It defined the body in new terms that were equal parts old and new—the old ecological ideas and knowledge base about the vagina, the gut, the mouth and the skin but rewritten in the language of cutting edge genomic science.

Conclusion: The Microbial Body 2.0

"We are living in this cultural project that's rarely talked about. We hear about the war on terror. We hear about the war on drugs. But the war on bacteria is much older, and we've all been indoctrinated into it. We have to let go of the idea that they're our enemies."[723]

--Sandor Katz, "fermentation revivalist" and author of *The Revolution Will Not Be Microwaved,* 2010

Microbes and Science, Medicine and Culture in the Twentieth and Twenty-first Centuries

At the beginning of the twentieth century, the microbe was fixed in a deeply adversarial relationship with humans as medicine, science and culture centered on the elimination of microbial life from the human body and human relations. At the beginning of the twenty-first century, this hygienic vision of human-microbe relations has been re-evaluated as microbes have become important actors in the provision of human life and generative of new approaches to medicine, biology and everyday life.

If bacteriologists in the early twentieth century struggled with how to define their field as scientific--"[t]o study bacteria as the ornithologist does birds, or the geologist, rock formations," 21st century microbial ecologists have garnered the respect and interest of the scientific world. [724]

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[723] Quoted in "Nature's Spoils," by Burhard Bilger, *New Yorker,* November 22, 2010.

[724] Rettger (1918), 104. E. O. Wilson expressed admiration and excitement for the field of microbial ecology in the 1990s: "If I could do it all over again, and relive my vision in the twenty-first century, I would be a microbial ecologist. … Into that world I would go with the aid of modern microscopy and molecular analysis. I would cut my way through clonal forests sprawled across grains of sand, travel in an imagined submarine through drops of water proportionately the size of lakes, and track predators and prey in order to discover new life ways and alien food webs,:" from E. O. Wilson's biography, Wilson, Edward O. *Naturalist*. Washington: Island Press, 1994, 364.

If they lamented the extent to which their field was dominated by technicians that "pour gelatin and agar plates and … count colonies," microbiologists in the early 21st century have found themselves as the forefront of conceptual, philosophical and technological developments in biology.[725]

Michel Morange and Joan Fujimura describe how 21st century biologists are moving beyond the reductionist research programs that dominated the last century in favor of new holistic programs that ask questions about the complexity of biological systems.[726] Those old reductionist biology(ies) focused on the structure of the molecular components of organisms. The limitations of this approach became clear in the wake of the Human Genome Project. Fujimura describes the HGP as the "final straw" in the growing disillusionment that biologists had with the 20th century molecular vision of life: it "left us with too few genes to account for the complexity of bodies, diseases, and therapeutics."[727] Postgenomic approaches looked for ways to account for the complexity of life. This was partly about how to makes sense of the massive amounts of data that had been produced by the HGP. These new biological problems birthed a new style of biology—a collaborative, multidisciplinary science that incorporated the expertise of computer scientists, engineers, mathematicians, physicists and myriad types of biologists in

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Stephen J. Gould described the current moment as follows: "This is truly the "age of bacteria" – as it was in the beginning, is now and ever shall be." In Stephen J. Gould, "The Evolution of Life," *Scientific American*, October 1, 1994, 85-6.

[725] Rettger (1918), 104.

[726] Fujimura, Joan H., "Postgenomic futures: translations across the machine-nature border in systems biology." *New Genetics and Society* 24.2 (2005): 195-226 and Morange, Michel. "Post-genomics, between reduction and emergence."*Synthese* 151.3 (2006): 355-360.

[727] Fujimura (2005), 196.

contrast to the old “benchside biology” of the last century.[728] The new style of data-driven biological work, analyzed in depth in Hallam Stevens’ *Life Out of Sequence: A Data-driven History of Bioinformatics*, co-produced tools and problems in biology.[729] Metagenomics, a method born out of this new approach to biology, made the problems of microbial ecology legible as “Big Data” problems. More than this, because of the sheer vastness of the microbial world and the nature of the problem—not one genome, but multiple fragments of genomes to make sense of--, the problems of microbial ecology became a source of one of the most interesting problems to consider in the postgenomic landscape of biology (i.e. The Human Microbiome Project).[730]

Bioinformatic approaches are not the only hallmark of the postgenomic age. The new holistic research programs see the problems of complexity in biology as concerned with the integration and association of biological components as well as with the integration of data. In both cases, a research problem need not be circumscribed by an organism (or limited to a molecule); but was based on a collective or *system*. Microbial life lent itself to these programs because so much of it functioned as systems in biofilms, microbial mats and the microbial consortia of the human body.

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[728] Ibid, 197.

[729] Stevens (2013).

[730] See Pollack, Andrew. "DNA sequencing caught in deluge of data." *New York Times*, November 30, 2011. Accessed February 1, 2014. http://www.nytimes.com/2011/12/01/business/dna-sequencing-caught-in-deluge-of-data.html?pagewanted=all&_r=0; Singer, Emily, “Our Bodies, Our Data,” *Quanta Magazine*, October 7, 2013, Accessed March 3, 2014. http://www.simonsfoundation.org/quanta/20131007-our-bodies-our-data/; Alexander Gelfand, "The Microbiome: Dealing with the Data Deluge," *Biomedical Computation Review*, October 22, 2012, Accessed March 4, 2014. http://biomedicalcomputationreview.org/content/microbiome-dealing-data-deluge; Sagoff, Mark, "Data Deluge and the Human Microbiome Project," *Issues in Science and Technology* 28.4 (2012): 71-78.

In the new holistic approaches, systems could be conceived broadly—the National Science Foundation defined biocomplexity as "dynamic interactions among the biological, physical and social components of the Earth's diverse environmental systems" in 2000.[731] Microbes, implicated in all of "Earth's diverse environmental systems," could be placed at the center of biological research as important players in biological networks and as models for complex and integrated living systems. In short, the holistic research programs of the 21st century aimed to characterize relations between biological components in a system, with the system itself as a functional unit. Microbial ecology could become a paradigmatic science for this approach to life.

If early 20th century bacteriologists had fretted over the extent to which bacteriology had "been holding itself in bondage" to pathology, it had now pulled itself out from under this yoke to shape new visions of and researchers agendas for the study of human health and disease. [732] The relationship between microbes and disease in the early 21st century was conceived of in terms of one-germ/one-disease; the new vision of both transforms this view and broadens the purview of what a microbial disease can mean. The management and control of that old relationship engendered a medical culture focused on microbe hunting and the search for magic bullets that could pin-point and eliminate the threat. In the 21st century, this relationship has been reconfigured from a "germs' eye view"--infection as ecological disturbance as opposed to an

[731] Quoted in Fujimura (2005), 197.

[732] Rettger (1918), 103.

attack of a pathogenic agent.[733] This new model of disease opens up the way for new methods of management and control of infectious disease.

This new microbial ecological vision of disease and microbe-human relations can encompass both infectious and chronic disease. Chronic diseases are increasingly being seen as having a microbial component or reconceptualized wholesale as having a microbial cause.[734] For example, allergy. In its most recent incarnation, allergy was a disease caused by exposure to allergens.[735] It has been turned in recent years into a condition caused by *lack of* exposure to microbes.[736] In both cases, the ultimate cause was changes to the bodily environment wrought by modern life. But instead of targeting new synthetic chemicals and materials produced by a culture increasingly reliant on chemicals as the culprit, it was Pasteurian practices that could be blamed. This theory, called the Hygiene Hypothesis was first devised in 1989, and has become the basis for clinical and laboratory research into allergies. Microbiome researchers are investigating how the development of the immune system might be compromised by the impact of hygienic practices and antibiotics on the microbiome.[737]

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[733] Lederberg (2001), 293.

[734] These conditions run the gamut from inflammatory bowel disease to cardiovascular disease. See for example, Ordovas, Jose M., and Vincent Mooser. "Metagenomics: the role of the microbiome in cardiovascular diseases," *Current opinion in lipidology* 17.2 (2006): 157-161; Damman, Christopher J., Samuel I. Miller, Christina M. Surawicz, and Timothy L. Zisman. "The Microbiome and Inflammatory Bowel Disease: Is There a Therapeutic Role for Fecal Microbiota Transplantation?" *The American Journal of Gastroenterology* 107.10 (2012): 1452-1459; Ehlers, Stefan, and Stefan H.E. Kaufmann. "Infection, inflammation, and chronic diseases: consequences of a modern lifestyle," *Trends in Immunology* 31.5 (2010): 184-190.

[735] Jackson, Mark. *Allergy: The History of a Modern Malady*. Reaktion Books, 2007.

[736] Velasquez-Manoff, Moises. *An Epidemic of Absence: A New Way of Understanding Allergies and Autoimmune Diseases*, New York: Simon and Schuster, 2012.

[737] For microbiome research and allergy, see Hooper, Lora V., Dan R. Littman, and Andrew J. Macpherson. "Interactions between the microbiota and the immune system," *Science* 336 (2012): 1268-1273; Huffnagle, Gary B. "The microbiota and allergies/asthma," *PLoS pathogens* 6.5 (2010); Cernadas, Manuela. "It takes a microbiome: commensals, immune regulation, and allergy," *American Journal of Respiratory and Critical Care Medicine* 184.2

This vision of allergy articulated a critique of modern life on microbial terms. The institutionalization of Pasteurian practices--one of the hallmarks and triumphs-- of the American Century, had negative consequences that society was just truly coming to terms with. Implicit in this new Post-Pasteurian vision of disease was a critique of modern American culture: they ways in which we managed our bodies, our living spaces, and our children's bodies and lives were making us sick. Antibiotics and clean culture were preventing the body from developing alongside its old bacterial friends and divorced the body from its evolutionarily determined context. To produce a healthy individual, the body needed microbial training and components. Microbes were required for the body to be able to function properly *in the world*. These new conditions were the consequences of the ecological disruption of microbe-human relations wrought by ingrained cultural practice.

In the twentieth century, cultural attitudes towards microbes were dominated by the war on germs. Today there are competing narratives that surround germs in everyday life. The antibacterial age has been explicitly described as "a cultural project that… we've all been indoctrinated into" by Sandor Katz, food activist and self-proclaimed "fermentation revivalist" with an explicitly pro-bacterial agenda.[738] But this subcultural explicit re-framing of our relationship to microbes is implicit in the changing behaviors of the public. The probiotics industry is now a multi-billion dollar industry; and its products stock the shelves of virtually

(2011): 149-150. For the Hygiene Hypothesis, see Wills-Karp, Marsha, Joanna Santeliz, and Christopher L. Karp. "The germless theory of allergic disease: revisiting the hygiene hypothesis," *Nature Reviews Immunology* 1.1 (2001): 69-7.

[738] Quoted in Bilger (2010), 102.

every supermarket in the country.[739] The ready availability and popularity of these pills, shakes, yogurts, and powders demonstrate the extent to which the notion that bacteria can produce *health* has become naturalized in the culture. To use Heather Paxson's term, we are increasingly becoming Post-Pasteurians who recognize the importance of the old hygienic narrative, but embrace the new.

For Katz, bacterial cultivation of the body is a moral imperative and ideological stance.[740] It is about organizing one's life—through cooking, composting, and other practices around the principle of a microbial ethics. Katz and his acolytes see bacterial cultivation of the body as a rejection of corporate technoscientific food and antibacterial culture in favor of a more natural, ecologically coherent approach to living. This is one possible direction that a microbial culture may develop in the future: as an ally to the various natural and artisanal food movements that have emerged in recent years.[741] The probiotics industry is also a growing part of the functional food and supplement markets; bacterial cultivation of the body consequently is seen as part of the culture of bodily optimization through supplements, vitamins and health- and performance-enhancing foods.[742]

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739 "Probiotics Market to Reach $31 Billion by 2015," July 12, 2011. MarketResearch.com. Accessed May 5, 2012. http://www.marketresearch.com/corporate/aboutus/press.asp?view=3&article=2204&g=1

740 Katz, Sandor Ellix. *Wild Fermentation: The Flavor, Nutrition, and Craft of Live-culture Foods*. Chelsea Green Publishing, 2003; Katz, Sandor Ellix. *The Revolution Will Not Be Microwaved: Inside America's Underground Food Movements*. Chelsea Green Publishing, 2006.; Bilger, B. (2010, Nov 22). Bilger (2010), 102.

741 See Paxson (2012) for artisanal food movement; Kera, Denisa, and Marc Tuters. "Social Stomach: Performative Food Prototypes." Presented at Creative Science 2011, Nottingham 25-26th July 2011. Available at http://dces.essex.ac.uk/Research/iieg/papers(2011)/CS11_Kera(16).pdf and Parkins, Wendy, and Geoffrey Craig. *Slow Living*. New York: Berg Publishers, 2006 for slow food movement.

742 For probiotics as functional foods, see Granato, Daniel, Gabriel F. Branco, Filomena Nazzaro, Adriano G. Cruz, and Jose A.F. Faria, "Functional foods and nondairy probiotic food development: trends, concepts, and products." *Comprehensive Reviews in Food Science and Food Safety* 9.3 (2010): 292-302 and Granato, Daniel,

Microbial Bodies

In "Living differently in time: Plasticity, temporality and cellular biotechnologies," Hannah Landecker notes that bioethicists often ask how new biological sciences "[change] what it means to be human." She argues that they do more than this; new biological approaches "[change] what it is to be biological." [743] As different biological approaches rise to prominence, the emphasis they place on particular features of life become salient. Their particular visions of life begin to matter more; they gain more explanatory force and cultural power in myriad domains.

This past decade has seen various calls for "a new biology for a new century." This "new biology" has been conceptualized primarily in two distinct ways: first, as a "Synthetic Biology," which moves beyond the genome and aims to take the reductionist paradigm in molecular biology one step further and engineer "biological machines" out of molecular components; and second, as a "Systems Biology" that moves beyond the genome towards a complexity-focused and computationally driven holistic biology.[744] Each of these "new" biologies can be described as an extension of hegemonic biological styles that have been examined by historians of

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Gabriel F. Branco, Adriano Gomes Cruz, José de Assis Fonseca Faria, and Nagendra P. Shah, "Probiotic dairy products as functional foods." *Comprehensive Reviews in Food Science and Food Safety* 9.5 (2010): 455-470.

[743] Landecker, Hannah. "Living differently in time: Plasticity, temporality and cellular biotechnologies." *Technologized Images: Technologized Bodies,* edited by Jeanette Edwards, Penelope Harvey, and Peter Wade, 213. New York: Berghahn Books, 2010.

[744] For systems biology outlook, see "The Century Beyond the Gene," by Evelyn Fox Keller in *Journal of Biosciences 30* (2005), 3-10; for synthetic biology outlook, see "Beyond the Genome: The Challenge of Synthetic Biology," an interdisciplinary roundtable discussion with Craig Venter, Sarah Franklin, Peter Lipton held as LSE, in *Biosocieties* 3 (2008), 3-20.

science—systems biology keeps the biology-as-information framework described by Lily Kay intact; and synthetic biology takes the "engineering ideal" in biology to its logical conclusion.[745] The bodies that these sciences envision are different—they change what it means to be biological in different ways that have been and will continue to be incredibly powerful and productive in the coming years. Microbiome research relies on both of these biologies to present another new way of being biological in the 21st century. Microbiome research offers a cooperative and collaborative vision of biological function that depends on the ability to investigate and identify life through molecular tools, and the ability to make sense of its collaborative functioning through computational means. But this new vision is distinct because of its environmentalist and ecological orientation. Carl Woese provides a description of what a microbiologically-led 21st century biology should be:

"Our task now is to resynthesize biology; put the organism back into its environment; connect it again to its evolutionary past; and let us feel that complex flow that is organism, evolution and environment united."[746]

It is this ecological vision of life that grounds microbiome science's new conceptualization of the biological and the human. In this biological approach to life, the body becomes an ecosystem and the human becomes a superorganism.

But bodies are more than biological. They clarify connections between the scientific, the cultural and the social in a particular historical period because they are constituted at the nexus of

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745 See Lily Kay, *Who Wrote the Book of Life? A History of the Genetic Code*, Stanford, California: Stanford University Press, 2000; Philip J. Pauly (1987).

746 Woese (2004), 173.

particular scientific, cultural, and social practices and concerns. They bind particular kinds of discourses and practices together. For example, in *The Human Motor,* Rabinbach describes how the body as motor became the site for labor power and productivity in a 19th century world focused on optimization, efficiency and energy, with physiology and thermodynamics as its animating sciences.[747] Catherine Walby's describes a bioinformatic body implicated in an increasingly virtual and computational society.[748] It follows that the consequences of the Pasteurian practices of the last century have also played a role in the emergence of a microbial body. The legacy of the cultural adoption of these practices have created problems and concerns and given them weight beyond the laboratory and clinic. Concerns about antibiotic overuse in an age of emerging infectious diseases are part of the constitution of this new vision of the body, as are the spread of chronic conditions that could be framed as diseases of microbial underexposure. Cultural and social developments have made it possible to implicate microbes in the functioning of a normal, healthy body and to frame their absence as threat to human health and human social relations.

Microbial Selves

Nikolas Rose has described how human beings have become "somatic individuals," people who "increasingly come to understand ourselves, speak about ourselves, and act upon

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[747] Rabinbach, Anson, *The Human Motor: Energy, fatigue, and the origins of modernity*. Berkeley and Los Angeles: University of California Press, 1992.

[748] Catherine Walby, *The Visible Human Project: Informatic Bodies and Posthuman Medicine, Biofutures, Biocultures,* New York: Routledge 2007.

ourselves—and others—as beings shaped by our biology."[749] Consequently, as our conceptualization of our biology changes, so too must our understanding of our selves change. For Rose, new forms of personhood emerge from the institutionalization of new kinds of biological regimes.[750]

In the early 21st century, microbiome research has produced a microbial body---and is in the process of producing a microbial self.[751] What this microbial self entails will become clearer as the microbial body is more clearly articulated. How will a microbial self shape our sense, as Rose asks, of "understanding, fashioning and managing ourselves in the everyday conduct of our lives"?[752] These developments are already underfoot in ways that can be seen in different corners of the culture.[753] These are questions that we will have to grapple with as we address how to heal microbial bodies, how to optimize them, how to leverage them and how to govern them.

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[749] Rose, Nikolas, *The Politics of Life Itself: Biomedicine, Power and Subjectivity in the 21st Century*, Princeton University Press, 2007, 188.

[750] Rose (2007), 106-130.

[751] This is, of course, not a one-way process; changing concerns about the relationship between the body and its microbiota shaped the tenor and direction of microbiome research as well.

[752] Rose (2007), 257.

[753] In addition to the discussions of probiotics, Katz's fermentation movement, and new perspectives on infection and chronic disease, see also the American Gut Project. The American Gut Project is part of the personal genomics boom that the last few years have seen, with companies like Knome, deCODEme, and 23abndMe popping up, in addition to the Personal Genome Project. It is a crowd-sourced project that offers a glimpse at a person's microbiome. The emphasis of the project with respect to its presentation to the public is the comparative and flexible possibilities for reports: on what may be shared between pets, family members and how similar or different your microbiome might be from a foreign one, and how the microbiome tracks with your dietary changes over time. There are several tiered packages more expensive than the basic one—package deals of the basic analysis for 2, 3 or 4; family package for $1500 for 4 people or pets that tracks similarities and differences in a family; a package that tracks the changes in your microbiome over the course of a week ("A Week of Feces,"; a global package for $129 that analyzes your microbiome and a "foreign" microbiome (Asian, African, Latin American), all through the premium packages. The $15,000 package gets into deep analysis and links that analysis to dietary habits and changes. See American Gut Project FAQs. http://americangut.org/?page_id=104

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