The Road Taken: René Dubos' journey from microbiologist to ecologist

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In May 1977, René Dubos composed a letter to the University of Georgia biologist Eugene Odum. Then aged 76, Dubos was at the height of his fame as a popular medical and scientific thinker. In a 50-year-career that had taken in a PhD in soil microbiology at Rutgers University, the isolation of the first antibacterial agents in Oswald Avery's laboratory at the Rockefeller Institute for Medical Research in New York, and pioneering studies of turberculosis and the role of intestinal microflora in the regulation of health and disease, the French-born medical researcher had increasingly decried short-term technological fixes that he feared might upset the delicate balance between humans and microbes. In this way, Dubos had come to be regarded as an apostle for the burgeoning environmental movement and a defender of the view of the earth as a delicate ecosystem. It was a view that he shared with Odum, not least because it was Odum who had brought the ecosystems concept to wider popular audiences through his 1953 book *Fundamentals of Ecology,* and who had helped establish ecology as a scientific discipline in American universities. In theory then, the researchers had much in common. However in 1977 when Dubos discovered that Odum was to be presented with the Tyler Award for thinkers who had made a significant contribution to ecology and environmental science – the same award that Dubos had been presented with the previous year – the Frenchman blanched. "You are for me Mr Ecology," he informed Odum. "Although I know *I am not an ecologist*, I have repeatedly been involved in scientific problems which have ecological components. This is happening once more in an enterprise that will certainly be my last professional activity."[1] [italics inserted]

The last line appears to be a reference to Dubos' to attempts to draw out the ethical dimensions of his vision of human ecology, an enterprise that in 1978 saw him using the phrase, "Think globally, act locally," for the first time and touring lecture theatres and television studios to drive home his message of the "symbiosis of earth and humankind".[2] If so, however, it begs the question why Dubos was so reluctant to take credit for other currents in ecological thought that were assuming programmatic importance in American universities and medical research departments by the late 1970s? As Dubos' biographer and former

research assistant, Carol Moberg, acknowledges, Dubos sometimes denigrated ecology as "the vaguest word" in the English language.[3] Yet in a "philosophical sense," at least, she says he considered himself an ecologist.[4]

Moberg's assessment is supported by a manuscript Dubos prepared in 1981, the year before his death from pancreatic cancer. In it Dubos acknowledged that he had never taken a course in ecology and had "few occasions to use the word until the 1960s." Nevertheless, he continued: "I now realize that, ever since I began my professional life as an experimental biologist in 1924, I have always looked at things from an ecological point of view by placing most emphasis *not* on the living things themselves but rather on their interrelationships and on their interplay with surroundings and events." [italics in original].[5]

In invoking the centrality of ecological perspectives to his medical career and thought, Dubos no doubt hoped to explain – perhaps to himself as much as to others – his quixotic research choices and why he had come to eschew a narrow programme of biochemical research for a broader, holistic approach to the problems of infection and disease. Instead, as Dubos put it in a 1974 article reassessing the career of Louis Pasteur inspired by Robert Frost's poem "The Road Not Taken," he had opted for the "road 'less traveled by' – namely, the road that will lead to physiological and ecological studies."[6]

In so doing, Dubos presented his flowering as an ecological thinker as a story of linear progression – the inevitable product of the intellectual seeds planted in his youth when, as a 23-year-old editor working in Rome, he had chanced on an article by the Russian soil microbiologist Sergei Winogradsky and became "entranced" by the idea that even the smallest living organisms were influenced by environmental conditions, in this case, the chemical composition of soil.[7] It was this insight that Dubos claimed had led to his discovery in 1932, together with Avery, of a soil enzyme that decomposed the polysaccharide capsule of pneumococcus, the major cause of lobar pneumonia, and his isolation in 1939 of the first commercial antibiotics, gramicidin and tyrothricin.[8] And it was this that

in turn had led him to emphasize the relationship between health, disease, and the environment in his popular writings.

But to what extent can we trust Dubos's account of "the road taken," to paraphrase the title of his essay on Pasteur? And what exactly did he mean by ecology?

As Anderson has pointed out, Dubos was not the only medical researcher to begin thinking along ecological lines in the 1930s: the Australian immunologist Frank Macfarlane Burnet was also adopting ecological perspectives in this period and by the 1960s was making similar claims to originality and intellectual priority for such ideas.[9] Yet while in 1940 Burnet had published a hugely influential book (*Biological Aspects of Infectious Disease*) expounding his "ecological point of view," and four years later Dubos had recommended Burnet as the Dunham Lecturer at Harvard University, Dubos almost never cites Burnet in his writings.[10] In this respect at least, Dubos conforms to the pattern of other pioneers in the field, each of whom, according to Anderson, "tended to represent himself … as the sole author of the idea, and rarely cited others, even those linked by education and friendship."[11]

One of the difficulties with judging the reliability of Dubos' retrospective assessment of his career is that prior to 1970 his practice was to discard his laboratory notebooks, correspondence, and personal papers, so we do not have a record of his thinking at the time. It was only with the establishment of the Rockefeller University Archives in 1974 that he was persuaded to save important correspondence and manuscripts. It is possible that searches in archives of other medical researchers with whom Dubos corresponded will turn up letters from an earlier date, but until then the best guide to the evolution of his thinking are his own writings.

In this paper, I present a close reading of his papers, lectures, interviews, and books in an attempt to trace the evolution of his thinking about disease ecology and reconstruct his intellectual influences. In particular, I concentrate on the

post-war period when Dubos returned to the Rockefeller Institute from Harvard University. Prior to departing for Harvard in 1942, Dubos had considered himself an experimental biologist and had only been incidentally interested in infectious disease. Though recruited by Avery to work on lobar pneumonia his focus was adaptive biological processes and the physiochemical environment of soil bacteria. This changed, however, with the death in 1942 of his first wife Marie Louise – a tragedy that Dubos attributed to stress and strain in her personal life and which awakened his interest in the phenomenon of latent infections and the environmental conditions governing virulence and host susceptibility to disease. Characteristically, Dubos not only pursued these questions in the laboratory, where he used novel media to encourage the growth of homogenous tuberculosis bacilli in order to study virulence on a physiochemical level; he also pursued the question through a study of the history of tuberculosis and attention to the relationship between the epidemiology of the disease and wider social and environmental conditions. In short, he became both a medical researcher and a scientific and environmental thinker. The result was the birth of a broader biological and ecological sensibility, but one that, arguably, owed as much to the veterinary pathologist and Rockefeller researcher Theobald Smith as it did to Burnet.

I then shift to the post-1961 period when Dubos changed the name of his laboratory from Bacteriology and Pathology to Environmental Biomedicine and began studying the indigenous microbial flora of the gastrointestinal tract and their role in host susceptibility to disease and the regulation of healthy physiological function. Working with germ-free mice, Dubos increasingly extrapolated from his laboratory observations into the role of diet and nutritional changes in rodents' susceptibility to infection to wider conjectures about the importance of microbes to human health and the ways in which states of disease could be seen as failures to adapt to environmental insults. At the same time, Dubos adopted the language of ecosystems. However, while aware of Odum's use of the term and its meaning within scientific ecology, Dubos employed it in a much looser sense to signal his interest in "human ecology" and ecological

feedback loops due to the interplay of environmental forces and the economic and ethical decisions of human actors. In this way, I argue, he sought to associate himself with ecological currents that by the late 1960s were acquiring programmatic importance in American universities and also becoming central to the teaching of medical epidemiology and public health

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On returning to the Rockefeller in 1944, Dubos had decided to focus on the metabolism of the tubercle bacillus with a view to better understanding the disease's pathogenesis. While visiting the sanatorium in the Adirondacks where Marie Louise was treated in 1942, Dubos had observed that fatty substances on the outer parts of the tubercle bacilli caused them to clump together. In order to study the bacilli, microbiologists ground these clumps, or pellicles, into smaller particles, resulting in the mixing together of bacteria that had grown under "extremely different environmental conditions."[12] The result was a heterogeneity of cultured strains, whereas what was needed was a way of fostering the diffuse growth of homogenous bacilli, i.e. either entirely virulent or avirulent bacilli. Dubos solved this problem by adding a commercial detergent, Tween, to the growth media, enabling the production of uniform cultures of young mycobacteria that he separated into virulent and avirulent groups based on observable morphological and chemical differences (virulent bacilli grew in serpentine cords and bound to neutral red dyes, whereas avirulent bacilli grew without any orientation).[13] Dubos further demonstrated that certain substances present in the *in vivo* environment, such as short chain organic acids, inhibited the growth of bacilli, whereas other substances, such as serum albumin, promoted it. In this way, Dubos was able to show that the "physiochemical environment prevailing in and around the tuberculosis lesion is of paramount importance in determining the course of the infectious disease process."[14] In studies using germ-free mice, Dubos and his colleagues also showed that the composition of diets markedly affected the survival of mice infected with the mycobacterium by causing "non-specific stresses."[15]

At the time, Dubos' studies of the physiochemistry of tuberculosis was hailed as a major breakthrough in the understanding of the disease's pathogenesis, leading to the award in 1951 of the Trudeau Society Medal. More recently, Dubos' studies of tuberculosis have been seen as opening up the "ecological facets of virulence."[16] But a close reading of Dubos' writings from the period show that he explicitly contrasted his insights into the physiochemical factors governing the virulence of tubercle bacilli with an ecological approach to disease. Dubos' first statement of this position came at the O.T. Avery Lecture at the *Society of American Bacteriologists* in 1948. Dubos opened the talk by praising Smith's writings on parasitism and disease, quoting Smith's insight that disease was a manifestation of a "delicate equilibrium between invader and invaded host."[17] However, in the very next sentence Dubos explained that although "this broad biological and ecological point of view has been extremely useful in the analysis of epidemiological problems… it has contributed little to the understanding of the mechanistic aspects of parasitism." The problem, as Dubos saw it, was that:

> Little is known of the mechanisms by which tubercle bacilli become established in a new host, and cause disease, or of the processes used by the infected host to overcome the infection. In other words, we know much of the ecological aspects of host-parasite relationships in tuberculosis, hardly anything of the means used by the bacillus to behave as a parasite.[18]

Dubos concluded that whatever the true nature of the mechanisms that retarded the growth of tubercle bacilli in infected individuals, "this equilibrium is extremely unstable, and it is well known that many changes in the host or his environment can bring about reactivation of a dormant tuberculosis infection." The passage, which reappears in a paper Dubos published on tuberculosis the following year in the *American Scientist*, is the first use of the term "ecological" I can find in his writings. However, it is significant that he applies it to what might more properly be termed Smith's biological view of host-parasite interactions, not the sense in which Burnet uses the term when referring to ecological climax

states and competition for resources within ecological niches.[19] Second, it is clear that, as much as Dubos respects and admires Smith's insights, he does not think that Smith's "ecological view" of disease is particularly relevant to his work on tuberculosis. The reason appears to be that, unlike Smith and other medical microbiologists in the period, Dubos was not interested in immunological explanations for the phenomenon of latent infections. Instead, he privileged biochemical explanations for these states of infection without disease.

For a more detailed account of this approach and to understand the sense in which Dubos was happy to be called an ecologist we must turn to *Biochemical Determinants of Microbial Disease*.[20] Although two years previously Dubos and his second wife, Jean Porter Dubos, had published *The White Plague*, a historical survey of tuberculosis, this was Dubos' first scientific book since *The Bacterial Cell* and the clearest signal yet that he now considered himself a medical researcher.[21] The book took the form of a series of linked essays based on material that Dubos had presented at the Warren Triennial Lectures in Boston in 1953 and refined during his visiting professorship at the University of California, Berkeley, in the spring of 1954. It was there that Dubos had met Karl Friedrick Meyer, the professor of experimental pathology at the University of California, Berkeley, who had been a close friend of Smith, and became familiar with Meyer's research on psittacosis and his famous survey of latent infections.[22] Dubos cites Meyer's survey early in the first chapter, "Infection into Disease". He also draws on Smith's writings on parasitism and for the first time cites Burnet's *Virus as Organism*, the book which emerged from Burnet's Dunham Lecture series.[23] However, it is to the French physiologist Claude Bernard that Dubos turns to for an antecedent for his ideas about the importance of the physiochemical environment of the host to the pathogenicity of microbes and to Winogradsky for an ecological methodology that will shed light on these interactions. Usually, Dubos explains, parasites exist in a state of latent infection. "Only when something happens which upsets the equilibrium between host and parasite does infection evolve into disease. In other words, infection is in many cases the normal state; it is only disease which is abnormal."[24] Traditionally,

microbiologists had offered an immunological explanation of latent infections. However, Dubos argued, it was not enough to analyze the "host-parasite relationship" in terms of antibodies and acquired immunity; the *in vivo* biochemical environment was just as important:

> As one tries to discover a metabolic basis for pathogenicity, it soon becomes apparent that the first question to be answered is not why pathogens can cause disease, but rather why saprophytes do not proliferate as well – or at all – *in vivo*... The answer to this riddle will certainly be found in one aspect of the problem which is rarely mentioned and never studied, namely, the very special types of environment which microorganisms find in animal tissues.[25]

Dubos argued that microbiologists needed to pay attention to two kinds of *in vivo* environments. One was "the extracellular environment in which blood and tissues are bathed under normal conditions" – in other words, the homeostatic physiological systems described by Bernard and captured in his concept of the "milieu interieur".[26] The other was the intracellular environment microbes encountered *within* phagocytes. Dubos argued these were probably just as important to infectious disease processes, but due to a paucity of knowledge of these intracellular environments it was difficult to know what role they played in pathogenicity. Just as Winogradsky had shown that soil microbes could only be understood in their natural environment, so, Dubos argued, the study of infectious disease must be placed on a similar "ecological basis".

> no metabolic analysis of infectious disease is possible until an ecological concept is introduced to formulate the problem. It is because this ecological concept has been lacking almost completely heretofore that bacterial biochemistry has contributed so little to the understanding of pathogenesis.[27]

The significance of this passage cannot be overstated as it points to the essential contrast that Dubos sees between his approach to infectious disease and those of other medical microbiologists who, for all their insights into the biology and ecology of host-parasite interactions, have yet to apply ecological methods to the study of bacterial biochemistry. It is in this narrow methodological sense, I believe, that Dubos was happy to describe himself as an ecologist.

Dubos' ambivalence about ecological terminology is perhaps nowhere better illustrated than in the change of name of his laboratory in 1961 from Bacteriology and Pathology to Environmental Biomedicine. According to Moberg, Dubos selected the prefix "environmental" because he was worried that as a science ecology "ignored the role of human beings."[28] Yet this was the same Dubos who by 1964 was describing the digestive tract a "highly integrated ecosystem."[29]

Sangodeyi has convincingly argued that Dubos' interest in the role of intestinal microflora in the regulation of health and disease prefigured the interest in the human microbiome.[30] It also sparked Dubos' interest in other human adaptive responses, but, crucially, this was now no longer confined to the microbial level. Instead, Dubos' subject increasingly became the interaction between humans and their total environment and the ways in which states of ill-health could be seen as failures to adapt to wider environmental insults. Best described as an organismic or humanistic biology, Dubos' new vision found its first expression in *Man Adapting* and was subsequently elaborated for a popular audience in his Pulitzer Prize-winning *So Human an Animal*, but now with a focus on the dangers that environmental changes posed to human health.[31] It was a theme that Dubos would continue to explore in different iterations until his death in 1982, leading him to coin such slogans as "Think globally, act locally" and to focus increasingly on what he termed "human ecology." In her biography, Moberg argues persuasively that for Dubos "human ecology" primarily designated "an attitude or matter of conscience… not… a predictive science" and that a value-driven, humanistic concern for the planet required, as he put it in *The Wooing of the*

Earth, an "understanding of ecological systems."[32] However, rather less attention has been paid to Dubos' employment of the term ecosystem.

The term is usually traced to the English plant ecologist Arthur Tansley who first used it in an article in 1935 in *Ecology*, the same journal that, coincidentally, had published Dubos' first scientific paper a few years earlier.[33] However, it was not until the 1950s that it began to gain wider currency as a result of the publication of Odum's *Fundamentals of Ecology*. It was this that brought the ecosystems concept to the wider world and helped establish ecology as an independent scientific discipline. As Golley has argued, part of the reason for the success of Odum's book, which went through several reprintings and was translated into numerous foreign languages, was that Odum defined ecosystems extremely broadly as "any entity or natural unit that includes living and non-living parts interacting to produce a stable system in which the exchange of materials between the living and non-living parts follows circular paths."[34] In this way, the concept encompassed both the biosphere of a pond and the biosphere of the earth. By providing an integrated way to view the environment, Golley argues Odum's book also informed the "growing realization that humans were destroying their environment," hence the uptake of the term by the public.[35]

Perhaps it was this aspect that made the term similarly attractive to Dubos, but if he thought that humans and their interactions with natural systems could be studied with the scientific methods described by Odum, his 1977 letter suggests that this was not something that he felt lay within his field of expertise. Instead, the ecological vision Dubos expounded in his twilight years cleaved closely to the themes of his 1969 Jacques Parisot lecture, "Human Ecology," sponsored by the World Health Organization, and had little to do with Odum's ideas of ecosystems. Summing up his new philosophy as the "five Es – ecology, economics, energy, esthetics and ethics," Dubos explained that:

> ….human history and the *countless ecosystems* in which it has developed are… largely the consequences of choices and decisions made either at the individual or the social level… Although the word ecology is now chiefly used to denote control of pollution and elimination of rubbish, its real and much larger scientific meaning has to do with the interplay between organisms and their total environment [italics inserted].[36]

It is clear from the passage that for Dubos ecosystems, or as he prefers it, ecology, signals something very different from Odum's scientific usage: not the study of the interplay of biological and environmental forces, but the ecological feedback loops implicit in social systems and ethical decisions taken by human actors exercising free will, hence his claim in the same lecture that human ecology is "qualitatively different from orthodox ecology because human beings make choices and thereby influence profoundly the course of natural events." The result was that by the 1970s, ecology had become a compendium term for Dubos. As he explained at a symposium, entitled "Ways of Healing: Ancient and Modern" held at the University of California San Francisco in January 1977, human life was shaped by "three different classes of determinants": genes, environmental forces evoking adaptive responses, and what he called the "human ability to choose among alternative courses of action". "The most important aspects of adaptation are not the homeostatic responses – which are essentially passive," he explained, "but the creative responses that depend upon the deliberative choice of surroundings and conscious cultivation of one's potentialities."[37] In a note appended to the draft of one of his lectures from this period, Dubos summarized his humanistic ecological even more succinctly:

> Orthodox, professional ecologists are primarily interested in natural environments, unaffected by human intervention. In contrast, I have concerned myself with the interplay between humankind and the Earth.[38]

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To conclude, in this paper I have sought to understand Dubos's unease with ecological terminology and ask to what extent we can trust his account of his transition from microbiologist to ecologist. To do so, I have resisted retrospective readings that portray Dubos as a reluctant ecologist or as an ecologist all along. Instead, my account has stressed the divergences between his ecological thought and that of other medical researchers and scientists in the period.

By the 1940s, Dubos' interest in natural microbial environments and *in vivo* studies had led to his disillusion with germ theory and an embrace of Smith's concept of host-parasite interactions and balanced biological states. At the same time, he became aware of Burnet's "natural history" approach to the study of infectious disease and his integration of neo-Darwinian ideas into medical microbiology. However, rather than embrace Burnet's "ecological point of view," Dubos stressed the importance of physiochemical factors and the environment of the host to the regulation of virulence and resistance to infection in animal models. In the early years of his career, this preoccupation led Dubos to focus on the physiological environment of microbes *within* the human body, but in later years Dubos increasingly expanded his vision to consider the macro forces operating on these microbial environments from *without*. However, for Dubos, talk of ecosystems meant little more than an attention to the interplay of organisms and the total environment, plus the feedback loops between these systems due to human interventions. The result was that to the end of his life Dubos remained wary of the claim that ecology deserved to be regarded as a scientific discipline on a par with biology. Instead, the value of ecology to Dubos lay in its methodology – the way it drew medical researchers' attention to conditions pertaining in nature, as opposed to conditions in the laboratory – as well as to man's esthetic and moral responsibilities.

One of the values of tracing Dubos' transition from microbiologist to ecologist is that it forces medical historians to confront important historiographical and

definitional questions and reflect on our own use of ecological terminology in the context of medical research. In particular, Dubos' career returns us to the question first posed by Mendelsohn in 1998, namely "where did the modern, ecological understanding of infectious disease come from?" and his answer that it must have come "from within" bacteriology.[39] To the extent that Dubos spent most of his career at the Rockefeller, a leading international center for microbiological research, he would seem to fit Mendelsohn's thesis. However, many of Dubos's formative ideas about biological and ecological processes can be traced back to his early studies of soil microbiology and his engagement with the ideas of Winogradsky.

Perhaps a more fruitful way of thinking about Dubos deployment of ecological language is Anderson's suggestion that it may have been a rhetorical device, allowing researchers working at the intersection of biology and medicine to pursue parasites across institutional, disciplinary and discursive boundaries.[40] Certainly, Dubos corresponded with many medical researchers who shared his preoccupations, including Burnet's protégé Frank Fenner, who had worked briefly with Dubos at the Rockefeller and whose research in the 1950s into the rabbit virus, myxomatosis, greatly impressed him.[41] Archival research may turn up further correspondence between Dubos and other proto-ecologists working at the intersection of biology and medicine in the period. In the meantime, one of the values of subjecting Dubos's account of his intellectual journey to closer scrutiny is it that it allows us see more clearly his own road taken.

[1] Dubos to Odum, May 24, 1977. RU 450 D639 Box 18, Folder 16, René Jules Dubos papers, Rockefeller Archive Center.
[2] C. L. Moberg, *René Dubos, Friend of the Good Earth: Microbiologist, Medical Scientist, Environmentalist* (Washington, D.C: ASM Press, 2005), 162; 1978. "Symbiosis of Earth and Humankind," lecture American University, Washington D.C., May 6, 1978, RU450 D851, Box 119, Folder 5, René Jules Dubos papers, Rockefeller Archive Center.
[3] Moberg, *Friend of the Good Earth,* 122.
[4] Moberg, *Friend of the Good Earth,* 137.
[5] René Dubos, "The Effects of Events, Surroundings and Personal Choices on the Scientific Interests and Attitudes of René Dubos at age 81", unpublished manuscript, 1981, RU450 D851, Box 31, Folder 14, René Jules Dubos papers, Rockefeller Archive Center.
[6] René Dubos, "Pasteur's Dilemma – The Road Not Taken." *ASM News*, 40, 9 (1974): 703-709.
[7] Ibid, 703. In the article, Winogradsky attacked laboratory procedures that sought to grow soil microbes in pure cultures, labelling such procedures "greenhouse ecology" and argued that the kinds and number of microbes in a particular sample of soil at any given time are determined by the physical characteristics of the soil and its chemical composition. S. Winogradsky, "La méthode directe dans l'étude microbiologique du sol." *Chimie et Industrie*, 11 (1924): 215-222.
[8] M. Honigsbaum, "Antibiotic Antagonist: The Curious Career of René Dubos." *The Lancet*, 387, 10014 (2016):118-9.
[9] Warwick Anderson, "Natural Histories of Infectious Disease: Ecological Vision in Twentieth-Century Biomedical Science." *Osiris*, 2, 19 (2004): 39–61.; F. M. Burnet, *Biological Aspects of Infectious Disease* (Cambridge: University Press, 1940).
[10] A. N. Zabusky, "Ecological Odyssey: The Intellectual Development of René J. Dubos." BA thesis, Harvard University, 1986, 69-71. A rare exception comes in a note appended to a talk Dubos gave at Reed College in 1959, where under "further reading," he described the 1953 edition of Burnet's book, *Natural History of Infectious Disease*, as "rather technical, but nevertheless highly readable and exciting." R. J. Dubos, "Post Prandial Musings on Resistance to Infectious Diseases," symposium paper, Reed College, Frederick, Maryland, September 1959, RU 450 DA51, Box 26, Folder 25, René Dubos Papers, Rockefeller University Archives.
[11] Anderson, "Natural Histories," 41.
[12] S. Benison, "Reminiscences of René Jules Dubos: Oral history, 1957." Volumes 1-10, Colombia University Libraries, Special Collections, II, p. 11.
[13] R. J. Dubos and B. Davis, "Factors Affecting the Growth of Tubercle Bacilli in Liquid Media." *Journal of Experimental Medicine*, 83 (1946): 409-423.; R. J. Dubos and G. Middlebrook, "The Effect of Wetting Agents on the Growth of Tubercle Bacilli.' *Journal of Experimental Medicine*, 88 (1948): 81-88.; G. Middlebrook, R. J. Dubos, and C. Pierce. "Virulence and Morphological Characteristics of Mammalian Tubercle Bacilli." *Journal of Experimental Medicine,* 86 (1947): 175-184.
[14] R. J. Dubos, "Discussion of Treatment of Tuberculosis Meningitis and Survival of Bacilli in Tuberculous Lesions." *American Review of Tuberculosis*, 65 (1952): 638-40.
[15] R. J. Dubos and C. Pierce, "The Effect of Diet on Experimental Tuberculosis of Mice." *American Review of Tuberculosis*, 57 (1948): 287-293
[16] Moberg, *Friend of the Good Earth*, 82.
[17] T. Smith, *Parasitism and Disease* (Princeton: Princeton University Press, 1934).; R. J. Dubos, "Cellular Structures and Functions Concerned in Parasitism." *Bacteriological Reviews*, 12 (1948): 173-194.

[18] Ibid.
[19] F. M. Burnet, *Biological Aspects of Infectious Disease* (Cambridge: University Press, 1940), 28, 31.
[20] R. J. Dubos, *Biochemical Determinants of Microbial Diseases* (Cambridge, MA: Harvard University Press, 1954).
[21] R. J. Dubos and J. Dubos, *The White Plague: Tuberculosis, Man and Society*. (New Brunswick: Rutgers University Press, 1987 [1952]).; R. J. Dubos, *The Bacterial Cell in Its Relation to Problems of Virulence, Immunity and Chemotherapy* (Cambridge, MA: Harvard University Press, 1945).
[22] M. Honigsbaum, "'Tipping the Balance': Karl Friedrich Meyer, Latent Infections, and the Birth of Modern Ideas of Disease Ecology." *Journal of the History of Biology*, 49, 2 (2016): 261–309.; K. F. Meyer, "Latent Infections." *Journal of Bacteriology* , 31, 2 (February 1936): 109-135.
[23] F. M. Burnet, *Virus as Organism: Evolutionary and Ecological Aspects of Some Human Virus Diseases* (Cambridge, MA: Harvard University Press, 1945).
[24] Dubos, *Biochemical Determinants,* 2.
[25] Ibid, 13.
[26] Ibid, 14.; Frederic L. Holmes, "Claude Bernard, The 'Milieu Intérieur' and Regulatory Physiology." *History and Philosophy of the Life Sciences* 8, 1 (1986): 3–25.
[27] Dubos, *Biochemical Determinants* 22-23.
[28] Moberg, *Friend of the Good Earth*, 122.
[29] R. J. Dubos and R. W. Schaedler, "The Digestive Tract as an Ecosystem." *American Journal of the Medical Science*s, 246 (1964): 267-271.
[30] F. Sangodeyi, "René Dubos and the Emerging Science of Human Microbial Ecology." Research Reports, Rockefeller Archive Center, 2012.
[31] R. J. Dubos, *Man Adapting* (New Haven, CT: Yale University Press, 1965); R. J. Dubos, *So Human An Animal* (New York: Charles Scribner, 1968).
[32] Moberg, *Friend of the Good Earth*, 14, 137-140.R. J. Dubos, *The Wooing of Earth* (New York: Charles Scribner's Sons, 1980), 156-157.;
[33] R. J. Dubos, "Influence of Environmental Conditions on the Activities of Cellulose-Decomposing Organisms in the Soil." *Ecology*, 9 (1928): 12-27.
[34] F. B. Golley, *A History of the Ecosystem Concept in Ecology: More Than the Sum of the Parts* (Yale, NH: Yale University Press, 1996), 66.
[35] Ibid, 68-69.
[36] R. J. Dubos, "Human Ecology." *WHO Chronicle*, 23, 11 (1969): 499-504.
[37] R. J Dubos, "Homeostasis and Creative Adaptations," lecture at UCSF Institute for the Study of Human Knowledge, January 25, 1977, RU450 D851, Box 119, Folder 1, René Dubos Papers, Rockefeller University Archives.
[38] R. J. Dubos, "Ecological Philosophy". MSS Lectures, September 1975, RU450 D851, Box 28, Folder 6, René Dubos Papers, Rockefeller University Archives.
[39] J. A. Mendelsohn, "From Eradication to Equilibrium: How Epidemics became Complex after World War I," in C. Lawrence and G. Weisz (eds), *Greater Than The Parts: Holism in Biomedicine, 1921-1950* (Oxford: Oxford University Press, 1998), 303-331.
[40] Anderson, "Natural Histories," 41
[41] R. J. Dubos, "The Evolution of Infectious Diseases in the Course of History." *Canadian Medical Association Journal*, 79, 6 (1958): 45-451.