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Hookworms Make Us Human: The Microbiome, Eco-immunology, and a Probiotic Turn in Western Health Care

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[rh]Hookworms Make Us Human

[ab]Historians of science have identified an ecological turn underway in immunology, driven by the mapping of the human microbiome and wider environmentalist anxieties. A figure is emerging of the human as a holobiont, composed of microbes and threatened by both microbial excess and microbial absence. Antimicrobial approaches to germ warfare are being supplemented by probiotic approaches to restoring microbial life. This article examines the political ecology of this probiotic turn in Western health care. It focuses on *Necator americanus*—a species of human hookworm—and its relations with immunologists. The analysis moves from a history of human disentanglement from hookworm, to contemporary anxieties about their absence. It examines the reintroduction of worms for helminthic therapy and explores emerging trajectories for probiotic health care involving the synthesis, modification, and/or restoration of worms and their salutary ecologies. The conclusion

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differentiates these trajectories and identifies an emerging model of “post-paleo” microbiopolitics.

[microbiome, hookworm, political ecology, immunology, probiotic]

## [h1]Immunology in the Anthropocene

Historians have long noted how knowledge about nature is co-produced alongside ideas about the natural organization of society. Extensive literatures document how shifting ideas about what is normal, natural, and right shape science in both lab and field, and how in turn scientific ideas come to shape the realities they purport to represent. Scholars have demonstrated this to be especially true for immunology and ecology, two of the most ‘social’ of the natural sciences. For Donald Worster (1994), these sciences are social in that they describe the organization and dynamics of living actors and use sociological models.

For example, historians of immunology have linked the emergence of binary metaphors of the “immune self” at war with hostile “non-self” invaders to Western notions of the individual self (Cohen 2009; Napier 2012), to gendered ideal of the male body (Martin 1990), and to the colonial encounter with exoticized others (Anderson 1996). They explain how these imaginaries were co-produced alongside militaristic approaches to public health and practices of germ warfare. Further work has tracked the persistence of these military models through the Cold War (Anderson 2014), and their gradual displacement by more ‘flexible’ models of immunity co-incident with the rise of postmodern and neo-liberal models of subjectivity in the 1980s (Martin 1994). Here immunity becomes a story of accommodation and adaptation. In a recent contribution, the historian Alfred Tauber (2017) identifies an ecological turn in 21st-century immunology. He links this to “the collective experience that the earth is facing an environmental crisis, if not a catastrophe” (2017, 218) and suggests that:

the ether of environmentalism has enveloped all of us, and immunology is finding its own expression in response. The environmental movement has heightened awareness of human dependence on intricate ecological balance, so, as opposed to only a generation ago, the immune system is now being firmly placed in an environmental context in which immunology and ecology have formed a new disciplinary amalgam (2017, 218).

Tauber is especially interested in the rise of what has become known as eco-immunology. This field of science takes as its starting point a figure of the human as a “holobiont” (Bordenstein and Theis 2015): a dynamic ecology composed of a multitude of microbial organisms. Eco-immunologists explore how the holobiont maintains homeostasis in the face of enormous organismal diversity and relational complexity.

The scientific origins of the holobiont and of eco-immunology can be traced back to the writings of Lynn Margulis in the 1980s (Gilbert et al. 2012). But the growth of ecological thinking in the last 20 years of immunology has been propelled by a broader “microbiomania” (Helmreich 2015) that has gripped the life sciences and medicine (for a general introduction, see Yong 2016). The diminishing cost of high-throughput DNA sequencing has enabled scientists to begin to map the myriad microbial lifeforms that live in the human body and to trace their ecological interactions. Research on this human microbiome suggests that many core bodily systems and functions have a microbial signature. Metabolism and immunity have been rethought as multispecies processes (for an introduction, see Velasquez-Manoff 2012) and a story is emerging of how mood and cognition are shaped by microbes along a gut–brain axis (Cryan and Dinan 2012).

This ecological, microbial turn is driving a fundamental reappraisal of the prevalent negative associations of microbes in immunology. There is a growing interest in the pathologies that are understood to result from “missing microbes” (Blaser 2014). It is suggested that the antimicrobial

focus of modern health and hygiene—informed in part by martial models of immunity—might have engendered globally “dysbiotic” human microbial ecologies. These are resulting in “epidemics of absence” (Velasquez-Manoff 2012), manifest in the dramatic recent increase in non-communicative inflammatory diseases—like inflammatory bowel disease (IBD), allergy, diabetes, depression, and autism. Heather Paxson and Stefan Helmreich (2014) note how, in response, microbes are emerging as model ecosystems for a wide range of restorative endeavors. These include much speculation about and investment in a new round of “probiotics 2.0” (Maxmen 2017; Relman 2015).

In some parts of the world, the focus of health care is beginning to shift from wholesale microbial eradication toward differentiating microbial agencies and curating encounters with beneficial microbes. There is a probiotic turn underway here, which encompasses a growing interest in finding ways of managing human microbial composition and colonization by modulating life course infection pathways and intensities. New modes of evolutionary or Darwinian medicine have been proposed (Rook 2009), inflected as Tauber and others would have it, by wider anxieties about planetary health and a desire to find ways of living well with our micro as well as macroecological kin. This enthusiasm for the microbiome can also be detected in the social sciences—most notably in recent work by Donna Haraway (2016). Haraway reads an affirmative ontostory for multi-species relations in (or beyond) the Anthropocene out of Margulis’s science of symbiogenesis and the figure of the microbial human (see also Hird 2009).

Although he explores the varieties of ecology that inform eco-immunology, Tauber (2017) is rather vague about which forms of environmentalism are coming to shape the discipline’s ecological turn. But historians and political ecologists have long made clear that there is no universal environmentalism. Environmentalism is a heterogeneous political practice, as much as ecology is a heterogeneous science. To understand the character and consequences of the probiotic turn in health care, we therefore need to attend in more detail to its political ecological specificities. This

article takes up this task. It aims to place ecological immunology and its practices of microbiome management in their political and ecological contexts.

To do so, it focuses on *Necator americanus* (*N. americanus*)—a species of human hookworm—and its relationships with immunologists, both lay and scientific. Humans coevolved with *N. americanus*, and it is still a common part of the human microbiome in the Global South. The article tells this story of hookworm and its immunologists in four parts. It first develops work in history and anthropology that traces the public health campaign that *disentangled* humans from *N. americanus* in much of North America and Europe in the early 20th century. A second section draws on scientific literature and interviews with immunologists, who since the late 1980s have suggested that *N. americanus* might be an “old friend” microbe, whose absence was causing an epidemic of inflammatory disease. A third section analyzes data gathered from interviews with scientists, *N. americanus* users, and retailers to provide an overview of contemporary projects to *reintroduce* *N. americanus*. It focuses on clinical trials to reintroduce worms and the DIY activities of a network of patients who sourced their own worms and began using them therapeutically to treat their conditions. A final section identifies three emerging directions of the probiotic turn in Western health care. These involve the molecular *synthesis*, genetic *modification*, and/or *restoration* of helminths and their human microbiome.

[h1]Post-Pasteurianism

To specify the types of ecology and environmentalism at work in the probiotic turn I draw on and develop work by Heather Paxson (2012) on the “ecologies of production” of raw-milk cheesemaking in the United States. Paxson describes these practices as “post-pastoral” (rather than simply pastoral or antipastoral) in that they maintain a commitment to elements of modern urban life—like capitalism, science, technology—even as they promote a return to valued premodern

social and ecological relationships. In an account of the role afforded bacteria in cheesemaking, Paxson (2008) identifies the linked emergence of what she terms “post-Pasteurian” approaches to the management of microbial life (or microbiopolitics). Here, she is riffing off of Bruno Latour’s (1988) famous account of the *Pasteurisation of France*—in which he traces the rise of modern, antibiotic approaches to public health and hygiene. For Paxson, post-Pasteurians: “work hard to distinguish between ‘good’ and ‘bad’ microorganisms and to harness the former as allies in vanquishing the latter. Post-Pasteurianism takes after Pasteurianism in taking hygiene seriously. It differs in being more discriminating” (Paxson 2014, 118). Elsewhere, Paxson (2014) differentiates post-Pasteurianism from “anti-Pasteurianism”—as expressed, for example, in the anti-vaccine movement—in that it maintains epistemic and political faith in (some forms) of science and state activity.

I develop Paxson’s analysis of post-Pasteurian forms of microbiopolitics by exploring the claims made by some helminthic therapists that they are engaged in both the domestication of worms and the restoration or “rewilding” of their microbiome. To better specify the types of political ecologies involved in going probiotic, I link the concept of microbiopolitics to literature on domestication and some of its synonyms and antonyms. Domestication is both a slippery and a weighty term in anthropology. Rebecca Cassidy and Molly Mullin (2007) caution that a genealogy of its meanings tells us as much about the discipline as it does the phenomena it purports to describe. This article deploys an expansive understanding that ranges beyond prevalent conceptions of domestication as an index of human control (Clutton-Brock 1999). It includes more mutualistic approaches in which nonhumans—like *N. americanus*—can also be agents of domestication (Tsing 2012), and ecological understandings in which the domus of domestication comes in spatial forms other than the domestic home and its immediate environs (Leach 2003).

In so doing, the article opens out to writing that expands the discussion of both dysbiosis and microbiopolitics to the scale of the planetary (Landecker 2015; Tsing 2014). Hannah Landecker suggests that the global prevalence and promiscuity of antibiotic drugs, and the resistance they inevitably select for, has created an Anthropocene signature in the microbiome. Past efforts toward microbial control are now written into the historic and contemporary microbiome and all microbial life, now and in the future, will bear the hallmarks of antibiotic biochemistry. If we follow Landecker, then the domus for our analysis of human–microbial relations and health must expand in ways that cut across any micro–macro scalar bifurcation. As Anna Tsing makes clear in her work on mushrooms, there is no pure, primitive microbiome or set of premodern human-microbial relations to which we might imagine a return. The emerging forms of microbiopolitics for human–microbial health are to be found amid the “ruins” of the Anthropocene (Tsing 2015) and must be conceived of in such terms.

## [h1]Disentanglement

Worms are brilliantly co-evolved criminals, exploiting their hosts, harming them, holding them back. Our goal is their extinction—to reclaim our species, body by body, until we have achieved “the eventual helminthic defaunation of man,” as Stoll said in 1962. “For only in a society made up of parasite-free individuals will we know of what the *human* being is capable.” (Klass 2015, no page numbers; *emphasis in the original*)

The life cycle of *N. americanus* (Figure 1) requires that eggs excreted in human faeces are deposited in warm, moist soil. Once hatched and in the presence of a naked foot, the larvae crawl through the skin and travel through blood vessels, heart, lungs, mouth, and throat to return to the gut. Successful reproduction therefore requires situations with suitable climate and soil, frequent human defecation, and opportunities for skin contact.

[FIGURE 1 ABOUT HERE]

*N. americanus* first became known to Western science in the 19th century in the context of growing concerns about its effects on plantation labor productivity (Farley 2003). High levels of hookworm infection lead to anemia and lethargy and affect child development (Loukas et al. 2016). Colonial administrators and their medical researchers were finding great intensities of pathological hookworm infection in situations where malnourished bodies were concentrated in squalid conditions with poor health care and sanitation (Couacaud 2014; Palmer 2009). *N. americanus* became known as the “germ of laziness” (Ettling 2013) and was the subject of one of the first American public health programs.

The hookworm eradication campaign was led by the Rockefeller Sanitary Commission (c. 1910–15) and is well recorded in the history of medicine (Farley 2003; Palmer 2010). These accounts relate a Pasteurian program for microbial control that involved significant investments in public administration, education, and deworming drug delivery across large areas of the U.S. South, and subsequently in the Caribbean and Central America. As Norman Stoll, a parasitologist at the Rockefeller Institute, explained, the aim was “the eventual helminthic defaunation of man” (Stoll in Klass 2015). The Rockefeller campaign targeted the worm as a germ, deploying martial practices to reconfigure the ecology of the host and their wider environment. Deworming drugs make the ecology of the host hostile to worms, while public health interventions worked politically and ecologically to target breeding sites and vectors of reinfection. The aim was to liberate the human body through microbial disentanglement.

Continued deworming coupled with urbanisation and improved sanitisation led to the 20th-century control of *N. americanus* in the United States and Europe. But global *N. americanus* control remains a distant prospect. *N. americanus* is endemic in many rural areas of the Global South, as



well as in poor parts of the United States (McKenna et al. 2017). Hookworms remain a cause of debilitating disease, and anti-helminth, germ warfare programs have been reinvigorated under the banner of Global Health. With new and increased funding from the Gates Foundation, they are directed toward school-based deworming programs using out of patent or freely provided deworming drugs (For critical discussion of the politics and efficacy of these interventions, see Parker and Allen 2014). Significant investments have also been made into the development of hookworm vaccines (Hotez et al. 2013). These interventions aim to prime the human immune system to attack hookworm larvae and make the gut a less hospitable location. Researchers think it unlikely they will be able to engender sterilising immunity and achieve the permanent exile of hookworm. But they hope to modulate infection intensity without requiring expensive and politically and ecologically challenging sanitary interventions.

## [h1]Blowback

In the 1980s, researchers tracking the consequences of these successful efforts to disentangle human bodies began to notice important changes in immunological relations. Concerns began to be expressed that (however incomplete) antibiotic, Pasteurian approaches might be excessive, causing new pathologies or forms of blowback (Wallace and Wallace 2015). Epidemiologists and immunologists correlated the growth in autoimmune, allergic and inflammatory disease with the rise of Western health and lifestyle practices (Bach 2002). In 1989, David Strachan (1989) offered a “hygiene hypothesis” to account for these trends. Strachan pointed to the success of Pasteurian approaches to germ warfare in changing microbial exposures. This thinking resonated with those working on successful helminth eradication projects in places like Papua New Guinea. Those workers had begun to notice marked increases in allergy and autoimmune disease (Flohr et al. 2009). While deworming programs continued apace, some of those involved began to question their desirability.

By the early 2000s, Strachan's hygiene hypothesis had been refined by other eco-immunologists and microbiologists into a "biome depletion" hypothesis (Rook 2009). This theory pushes back against Stoll's ideal of the "defaunated man" best assisted by antibiotic germ warfare. While agreeing that the developing human body can be threatened by microbial infection, it argues that the vast majority of the human microbiome is benign or beneficial. Graham Rook and others suggest that from birth the body and the immune system are also enabled and calibrated by encounters with microbes. In particular, they argue for the salutatory role played by a small number of microbial "old friends." These are microbes with which humans originally co-evolved that can be differentiated from undesirable "crowd infections" (like typhoid or cholera) that emerged after the agricultural revolution and subsequent urbanization. Rook and his collaborators suggest that in the absence of old friend microbes, the immune turns against itself, and other functions go awry.

*N. americanus* (and a few other helminths) have been proposed as potential old friends. Immunologists have begun to develop a more sophisticated understanding of *N. americanus*'s evolutionary history and its internal ecological relations with its host. Helminths are known to have parasitized hominids since the Pliocene (5.3–2.6 MA) (Perry 2014). Parasitologists suggest that *N. americanus* likely evolved into its current form as a result of a long history of antagonistic relations with small mammals, our hominid ancestors, and then modern humans. Theories of parasite evolution suggest that over time, successful parasites tend to become less aggressive and pathological, as those that kill or significantly harm their host run the risk of not completing their life-cycle (Parker and Ollerton 2013). As a result, many contemporary infections with *N. americanus* are unknown and asymptomatic: Many people can tolerate a moderate "worm burden" without obvious consequence. Eco-immunological research suggests that during their long, co-evolutionary history, *N. americanus* have learned to train, modulate, or calibrate the human immune system to achieve host tolerance (Allen and Maizels 2011; Wammes et al. 2014). Immunologists posit that

hookworms can communicate with the commensal bacteria that are in contact with the human gut. This enables them to disguise their presence and suppress the host's normal immune response (Zaiss et al. 2015). One group of immunologists have borrowed a popular metaphor from macroecology to present *N. americanus* as a “keystone species” (Bilbo et al. 2011). This describes an organism—like a wolf or a beaver—that has a disproportionate influence on its ecology relative to its abundance. Set in the context of their long history of incorporation, *N. americanus* come to figure as ghosts; former keystone species whose demise creates microbial dysbiosis that drives cascading or self-reinforcing conditions of autoimmunity and inflammation.

This science offers a new grand narrative of human–microbial co-evolution that departs from the post-war antibiotic celebration of the end of infectious disease (and more recent counter-narratives of the “coming plague” of emergent infectious diseases). We are told that worms have made a home in us, developing mutualistic relations through our long history of pre-agricultural movement. Hookworms were tailored to the pre-Neolithic domus. In these situations, hookworm is an old friend. But these amicable relations began to become unsettled with the rise of sedentary agricultural systems. They reached conditions of dysbiosis with the high infection intensities of colonial plantations. Here, hookworm crosses a political ecological tipping point and becomes a crowd infection. But the modern absence of worms can also push the human holobiont over an auto-immune threshold, resulting in microbial dysbiosis and amplified host inflammation. A dystopic figure emerges in this narrative of the defaunated modern human, bereft of its microbial kin and living itchy, depressed, overweight lives that are chronically dependent on expensive and unpleasant regimes of immunosuppressant and anti-inflammatory drugs. As I explore below, the parallels between this story and ecologists' diagnoses of the environmental crisis are clear to see.

[h1]Reintroduction

The diagnosis of biome depletion and the recognition of the potential therapeutic properties of helminths like *N. americanus* have inspired a range of scientists and patients to begin to experiment with the reintroduction of worms. These interventions come in many different forms, but they are linked by a common ecological approach to health care that takes as its starting point the therapeutic possibilities of managing the human as a microbiome. David Pritchard is an immunologist at the University of Nottingham in the United Kingdom, who worked on the deworming research project in Papua New Guinea (PNG) mentioned above. He was inspired by the data emerging from this study and wanted to explore a hypothesis that *N. americanus* have therapeutic potential. He sourced some worms from PNG and self-infected to demonstrate safety to his Institutional Review Board. In 2004, he conducted the first clinical trial using *N. americanus* as a treatment for asthma. A range of pre-clinical and clinical trials have since followed, exploring the therapeutic potential of *N. americanus* and some other helminths for a range of conditions (Elliott and Weinstock 2017; Wammes et al. 2014). So far, the results from phase two human trials have been inconclusive. The results allow immunologist to paint a complex picture in which the efficacy of helminths seems to vary according to the type of autoimmune disease, host genetics, the current and past composition of the host microbiome, and the history of microbial loss and colonization (Rook 2012).

In spite of these uncertainties and apparent clinical setbacks, a growing number of citizens have begun sourcing their own worms and conducting DIY experiments. A patchy, but nonetheless global, network of commercial providers now sells *N. americanus* and four other helminths online. As a mode of microbiopolitics, this “hookworm underground” (Velasquez-Manoff 2012) has much in common with the craftiness, regulatory uncertainties, and counter-cultural ethos of Paxson’s post-pastoral raw-milk cheese production systems. For instance, as of 2018 it is illegal to import live *N. americanus* larvae that are outside the human body into the United States, (FDA 2016). The U.S.

Food and Drug Administration prohibits shipments and regularly intercepts parcels at the border. Clients of one commercial provider travel to Mexico to get infected, while two others use cryptocurrencies and encrypted email to prevent tracing and to ensure anonymity. But larvae are easy to produce, hard to detect, and can withstand long journeys in the mail. Circulation is widespread, and prosecutions are rare. Domestic experiments in helminthic therapy have fast overtaken clinical trials in terms of numbers of participants (Cheng et al. 2015).

Helminthic therapy is made possible by social media groups, which operate alongside the commercial providers to offer advice and support. Users tend to come to helminthic therapy online, often as a last resort. They take worms to treat a wide range of chronic autoimmune and inflammatory conditions (including IBD, asthma, and psoriasis). They feel that their conditions are often poorly understood and that treatment through immunosuppressant drugs is often ineffective and debilitating (Cheng et al. 2015). John Scott is the main custodian of the Facebook helminthic therapy support groups. Scott was one of Pritchard's initial trial participants and has long suffered from a range of autoimmune conditions. He is retired and has led the creation of a helminth care manual, which is free and open source, and presented and regularly updated as part of an extensive helminthic therapy wiki.<sup>1</sup> This is an impressive resource that introduces the field, collates scientific papers, and details more than 500 testimonials of personal success and failure.

The wiki and the discussions on the support groups shed insight into the mundane lay eco-immunological practices (see Enticott 2003) through which users have domesticated worms—taking them into their homes and accommodating them into their bodies. Sustaining and caring for their *N. americanus* involves close inspection of diet, medicines, and other commonplace lifestyle exposures. It also involves frequent reinfection to maintain the desired number and age of worms, and thus the intensity of immunosuppression. This takes time and experimentation. Different people require different numbers of *N. americanus* and different frequencies of reinfection. Helminth care also

involves attuning to the corporeal presence of the worms. Some users claim to be able to feel their worms working, others only know they are there by the absence of symptoms of their prior conditions.

A few users have developed incubation systems for growing their own *N. americanus*. The wiki collates a range of detailed protocols that list the materials, skills, and precautions necessary to live well with worms (and warm faeces) in domestic settings. Some users employ microscopes to detect *N. americanus* eggs in their feces and thus check the health of their colony. Some have refined methods for identifying and counting larvae and enabling reinfection. Some persuade family members or friends to host a backup colony. Domestic incubation cuts the costs of using commercial suppliers, ensures a reserve supply for swift reinfection, and allows users to maintain and modify their desired colony. Users I spoke to explained how they overcame their initial revulsion and learnt to value their helminths as “gut buddies” or “colon comrades” (Lorimer 2016).

# [h1]Synthesis, Modification, and Restoration

Can modern science use naturally occurring helminths as a starting point, and improve them?

The use of transgenic helminths and longer-lived helminths are examples that might be considered. Biotechnology to improve production of helminths, including in vitro culture of helminths or cultivation of human specific helminths in genetically modified animals (e.g., humanized or immunosuppressed mice) might also be considered. In addition, irradiation of organisms to achieve sterility and eliminate the possibility of transmission is a possibility. As a specific example, a “designer helminth” might be envisioned which has many of the properties of the bovine tape-worm (long life span, self-limiting colonization) but which is substantially smaller in size, thus eliminating much of the inconvenience when the organism dies and is eliminated from the body (Parker et al. 2012, 1200).

The growing scientific and popular interest in *N. americanus*'s salutary properties has prompted a range of speculation, and research and development, on the futures of helminthic therapy. Three prominent futures can be identified, which I have termed synthesis, modification, and restoration. These link developments among those involved with helminth reintroduction with those who continue to seek human disentanglement and helminth control. These futures are differentiated on ecological and political grounds according to the status they afford the living organism and its ecology in the delivery of health, and by their relationship to prevalent models of drug development within the pharmaceutical industry. Together, they offer a typology for specifying the different modes of post-Pasteurian microbiopolitics emerging within the probiotic turn in Western health care.

## [h2]Synthesis

Scientists who were involved in decoding the hookworm genome speak of a “veritable pharmacopoeia” of synthetic molecules that will soon become available for new phases of drug development (Navarro et al. 2013). There is excitement that new drugs will be able to replicate and even enhance hookworms’ mutualistic abilities to train and calibrate the human immune system (Harnett and Harnett 2017). These immunologists aim to simulate the agencies of the hookworm in pill form to provide a standardized therapeutic without the initial discomfort of infection or the risks of accidental release. This model also helps maintain the financial returns for the pharmaceutical industry currently associated with chronic dependency on immunosuppressant drugs (Tilp et al. 2013).

At the same time, information provided by the hookworm genome, and conceptions of helminths achieving immune suppression by dialogue with other microbes, are also informing a new round of antihelminth drug development. New pharmaceuticals might target the

bacteria that make the body hospitable to parasitic helminths, reconfiguring the gut microbiome to make it harder for worms to take up residence. These pharmacological interventions turn the dialogical character of the hookworm and the embodied history of its human conversation against the organism (see Beisel [2017] on the malaria vaccine). Those promoting this future would have few qualms if such interventions enabled the eradication of the worm, so long as it could be recapitulated in molecular form. This model of developing “drugs from bugs” is now well established in the pharmaceutical industry, and its products are familiar to clinicians and general practitioners. It represents a likely trajectory in which 20th-century visions of pathway-targeted small molecule therapeutics are co-opted into the idea of perfectly engineered hookworm therapeutics. As I discuss in more detail below, this model largely stays within the Pasteurian tradition and does not challenge the idea of therapeutics or shift the status of the worm and its microbial ecology.<sup>2</sup>

## [h2]Modification

Such molecular and antibiotic futures are contested by prominent figures involved with helminthic therapy. They suggest that it will be impossible to recapitulate in pill form all the work done by a whole organism (Villeneuve et al. 2017). They point to the inevitable side effects of single molecule therapeutics and the continued risks of anti-helminth drug resistance (Bilbo et al. 2011). They also argue that a hookworm vaccine or future eradication might commit those living asymptotically with hookworm to drug dependency and to an epidemiological transition toward elevated autoimmune conditions (Wammes et al. 2014).

Instead, they defend the use of whole organisms and propose expanding and refining the choice of species or modifying the helminths that are currently in use (Lukeš et al. 2014). There are at least 340 species of helminth that are known to infect humans (Crompton 1999). In 2007, the



immunologist David Elliot and his coauthors published the following list of the properties of an ideal therapeutic helminth (Elliott et al. 2007):

- has little or no pathogenic potential
- does not multiply in the host
- cannot be directly spread to close contacts
- produces a self-limited colonisation in humans
- produces an asymptomatic colonization in humans
- does not alter behavior in patients with depressed immunity
- is not affected by most commonly used medications
- can be eradicated with an anti-helminthic drug
- can be isolated free of other potential pathogens
- can be isolated or produced in large numbers
- can be made stable for transport and storage
- is easy to administer

The director of the helminth retailing company Biome Restoration explained how these criteria informed his review of the human parasitology literature and the choice of the cysticercoids (or larval stage) of the rat tapeworm (*Hymenolepis diminuta*) as an alternative to *N. americanus*. *H. diminuta* cysticercoids (or *HDC*, Figure 2) are easily harvested from grain beetles (*Tenebrio molitor*), which are their intermediate hosts. These beetles were commonly found in flour and would frequently have been consumed by people before the industrialization of grain processing and baking. *HDC* are promoted as a preferable alternative to *N. americanus* as they are cheap to produce, cannot spread between people, are taken orally, remain inside the gut, and do not take up

residence. *HDC* pass through the body in two weeks and can be grown in lab animals (see production cycle in Figure 3). *HDC* have become popular as an alternative or supplement to *N. americanus*.

[FIGURES 2 AND 3 ABOUT HERE]

In promoting *HDC*, the manufacturer suggests that *H. diminuta* should be “considered domesticated, since we control its reproduction for our own benefit” (Biome Restoration 2016). Although they shape the breeding of *HDC* and have limited its vectors for infection, there is no deliberate selection for desired characteristics and thus no likely differences between free-ranging and laboratory populations. William Parker is a prominent immunologist whose work informs Biome Restoration. In the commentary that is quoted at the start of this section, he has proposed more ambitious trajectories for engineering a designer helminth. He imagines the genetic manipulation of a bovine tapeworm. This worm is long-lived and unable to colonize other parts of the body. He suggests that it might be shrunk, modified so that it does not secrete its usually motile egg sacs from the user’s anus, and installed to perform low-maintenance and dependable human immune system calibration. [h2]Restoration

Many of the scientific, commercial, and amateur proponents of helminthic therapy present such acts of selection and modification as part of a broader project of biome restoration. Biome restoration is understood to be the logical outcome of a Darwinian or evolutionary approach to medicine, that involves the diagnosis of evolutionary mismatches and the promotion of remedial interventions (Parker and Ollerton 2013; Rook 2009). Proponents of this approach to microbiopolitics have identified a wide range of contemporary medical and lifestyle practices that are understood to debilitate the microbiome. They implicate some of the most significant developments associated with modern diets, hygiene and health care, including birth by Caesarean section, infant formula, antibiotics, and other antimicrobials, and water treatment (Blaser and Falkow 2009). There has a

been a proliferation of popular science books from prominent microbiologists promoting probiotic diets and lifestyles, with titles such as *Let Them Eat Dirt* (Finlay and Arrieta 2016), or *Dirt Is Good* (Gilbert and Knight 2017).

These restorative post-Pasteurian recalibrations are based on a profound reconsideration of the very idea of a therapeutic microbe. As Villeneuve et al. suggest:

Humankind eventually needs to move beyond the idea that helminths are best used as a drug or a therapy. Rather, we need to embrace the view that helminths are a necessary component of the ecosystem of a healthy body, and that helminths should be cultivated for population-wide biota restoration. Attempts to develop helminth-derived drugs are, by intent, designed to treat disease, not to restore health to the population. As such, efforts to produce helminth-derived drugs will not help achieve the long-term goals of disease prevention, and may indeed provide a distraction from such goals as they divert resources that could be used for biota-based restoration and maintenance. (Villeneuve et al. 2017, 6).

In this context, *N. americanus* figure in a more holistic ecological guise. They are valued for their role as an old friend keystone species with the ability to reorganize or rebalance dysbiotic bodily ecologies, in a similar fashion to the promotion of wolves or beavers for rewilding in the wider countryside (Lorimer 2017b). This example offers a microbial manifestation of the long-standing tensions in ecology between reductionist and holist approaches to both scientific explanation and ecological management (Worster 1994).

Much of the discussion of biome restoration is pragmatic and future orientated, but there is a strand of enthusiasm for helminthic therapy (and microbiome modification more generally) that is deeply antipathetic to modern, urban life. Some enthusiasts align biome restoration with a broader shift toward paleo lifestyles, which valorize dietary, exercise, hygiene, and health practices

associated with life before the agricultural revolution. This movement is perhaps best exemplified in the complex character of Jeff Leach. Leach is an anthropologist and microbiologist who works with the Hadza in Tanzania. He helped found the American Gut project, a citizen science–led human microbiome initiative. Leach is the author of *Rewild* (Leach 2015), which actively promotes the salutary benefits of aligning one’s microbiome with those living in the wild. As far as I am aware, he does not use helminthic therapy, but he has undergone a fecal microbiota transplant donated by a Hadza man of his own age. In the blog article reporting this event—entitled “(Re)becoming human” (Leach 2014)—Leach is careful to protect against accusations of neo-primitivism. But there are many in the emerging microbial rewilding community who are less wary. John Scott explained how he frequently needs to caution and police the more gung-ho contributors to the helminthic therapy support groups. In other online microbial rewilding self-help groups, users and self-declared microbial experts articulate a new version of the long-standing narrative around the margins of Western science about “domestication-induced deficiencies” among modern human populations (see H. M. Leach 2003; Leiper 2017).

## [h1]Hookworms Make Us Human?

This article has traced a history of Western relations with hookworm. It has followed shifting paradigms of immunological thought and the ways in which these have come to inform the discourse and practice of health care. It examined how an early 20th-century binary immunological understanding of the ideal human as parasite-free informed martial, antibiotic campaigns of germ warfare dedicated to global hookworm eradication. It identified a shift away from this model among some immunologists seeking to understand situations of auto-immunity engendered by the absence of the worm. Here the hookworm as foe is supplemented by a figure of the hookworm as ghost, sparring partner, and guide. Immunity becomes a story of communication and diplomacy.

The metaphors of immunity shifted again as the wider microbial messmates caught up in this multispecies conversation became visible. A more ecological and less anthropocentric discourse comes to the fore, in which immunity for the human holobiont involves the pursuit of homeostasis through the careful differentiation of old friends and crowd infections. In moderation, hookworms become keystone species, capable of orchestrating a gut ecology. The presence of worms is attributed a profound effect on (hitherto) human bodily process like metabolism, immunity, and even cognition. The worm moves from foe, to partner, to agent of history: an evolutionary force capable of securing its own longevity through the careful manipulation of its host's ecology. In some circles, hookworms make us human in a stunning reversal of the modern antibiotic model. But elsewhere, the war on worms continues. These paradigms of immunology are coexistent. One has not replaced the other.

Nonetheless, this radical reappraisal of the pathological and therapeutic potentials of *N. americanus* appears to confirm the claims made by historians and sociologists of science that immunity and microbiology in the Anthropocene are undergoing a profound environmentalist epiphany, which is driving an ecological turn in thought and practice. The figure of the microbial human (or *Homo microbis*) emerges as a victim of mismanagement and dysbiosis, in line with the Anthropocene zeitgeist (Helmreich 2015). Both the body and the planet are pushing up against or have crossed irreversible tipping points that might bring to an end the very ecological conditions in which human life evolved and flourished. In response, specific models of ecological management are emerging similar to those well established in the macroecological fields of wildlife conservation and restoration. These seek to manage ecological dynamics by recalibrating the composition, circulation, functions, and intensities of a target ecology. Reintroducing worms is presented as akin to rewilding with wolves or beavers.

To conclude I would like to draw out what this analysis tells us about the specific forms of ecology and of environmentalism at work in the probiotic turn. To do so, I will return to the work of Heather Paxson on microbiopolitics. There are similarities between the approaches to microbial management of DIY helminthic therapists and those of Paxson's post-Pasteurian cheesemakers. Those using worms also seek to differentiate between the good and bad microbe through a close attention to the ecological relations in which worms do their work. They know that worms can be parasites and ghosts—pathological in both their excessive presence and their absence—and with the potential, in the right circumstances, to make a good life possible. There are also similarities between some parts of the helminthic therapy movement and the post-pastoral epistemic, political, and economic norms of Paxson's cheesemakers. There is a place here for science, for technology, and for some modes of modern capitalism and its necessary state action.

Where the ecological turn in helminthic therapy and the wider field of evolutionary medicine differs from Paxson's post-pastoral is in its imagined historical ecological reference baseline. Biome restoration is not commonly presented as a return to premodern pastoral ecologies. Instead, advocates like Graham Rook push their reference further back to a prehistorical point before the agricultural revolution. While both share in the Arcadian tradition of ecology (Worster 1994), for helminthic therapy the fall happens not with the rise of industry, but with the earlier adoption of sedentary lifestyles, animal and human domestication, population concentration, and the rise of crowd infections. Biome restoration might better be described as a post-paleo model of microbiopolitics. There are some on the margins who frame biome restoration as an authentic return, finding therapy in idealized wild relations found out there, in places perceived as removed from Western civilization. There are forms of "paleofantasy" (Zuk 2013) at play here. But the majority are post-Pasteurian—they want to keep the bad bugs at bay—but the good germs (or old friends) are to be found further back in time.

A specific version of microbial ecology thus characterizes the immunology of the hookworm underground and those using live *N. americanus* in clinical medicine. Here the wildness of *N. americanus* is understood in a systemic context in terms of functions and processes. In their efforts to select, modify, and even engineer *N. americanus*, these worms are not primarily valued as authentic components of a past primitive state. Instead, they are promoted for their self-willed ability to train, modulate, and balance a human ecology. When William Parker speculates about the future engineering of a designer helminth, he hopes to tame the worm while securing the functional potential of its salutary wildness. His is a fundamentally future-orientated and techno-optimistic model of biome restoration. But tensions are beginning to arise in this movement over the best economic model to value this wild potential and to secure the future of hookworm (and other microbial) therapies. Important questions are surfacing that are beyond the scope of this article. Should worms be held in common, available for free, or at cost in a fashion akin to blood banks? Should the future of this therapy be left to the entrepreneurs who first brought worms to market? What would happen if big pharma got involved, patenting a modified worm and lobbying for the removal of all competing organisms?

The most likely scenario is presented by those synthesising *N. americanus*'s secretions to recapitulate the organisms' functions in pill form, and to enable its eradication. This model is well funded, firmly Pasteurian, and maintains the status quo models of molecular drug development. Drugs from bugs fits with the antibiotic orthodoxy that remains prevalent in approaches to One Health and Global Health. But the lively debate that is developing around the translation of microbiome science suggests that the ecological turn in immunology and clinical microbiology will need to grapple with questions of political economy (Slashinski et al. 2012, Stallins et al. 2018). Such questions are also prominent when we consider the stark geography as to where the hookworm is encountered as a parasite, a ghost, or a mutualist (Lorimer 2017a). This makes painfully visible how

the probiotic turn is patchy, localized, and configured by familiar, if nonetheless important, socioeconomic disparities. A recognition of our microbial constitution does not, by necessity, engender the more humane treatment of other humans.

As with the diagnosis of the Anthropocene, it is clear that responsibility for microbial ecological change and the ability to respond to its consequences is unequally distributed. In keeping with the rich vein of work in medical anthropology and geography, we should conceive of paradigms of immunological thought, variations in human–microbial health, and modes of microbiopolitics as the outcome of specific disease configurations (Hinchliffe et al. 2016). There is no linear epidemiological transition at work here and the presence, absence and return of *N. americanus* serves as an index of levels of social, economic, and ecological security.

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#### [h1]Notes

1. See <http://helminthictherapywiki.org/>
2. I am grateful to one of the reviewers of this article for this observation.



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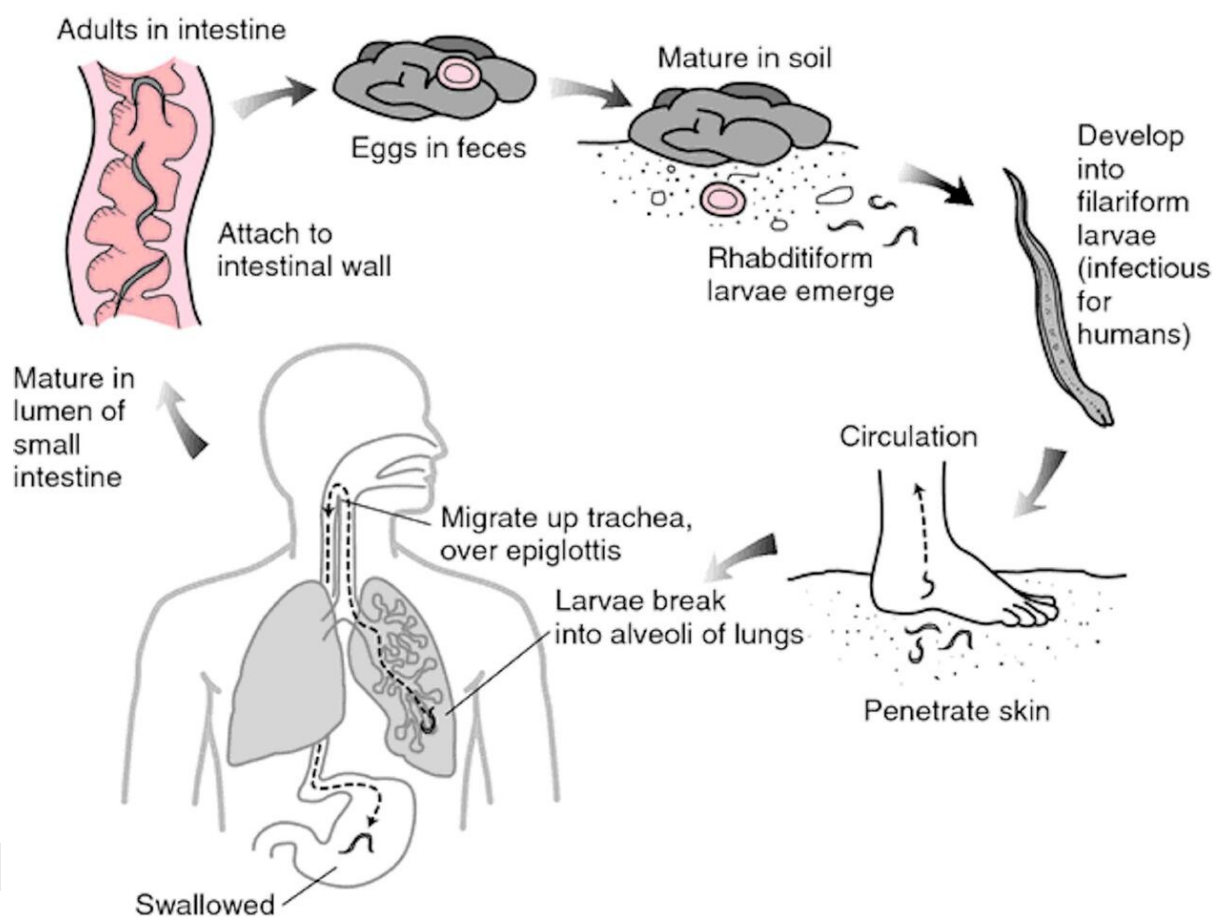


Figure 1. Lifecycle of *N. americanus*



Figure 2: *Hymenolepis diminuta* cysticercoids or HDC.

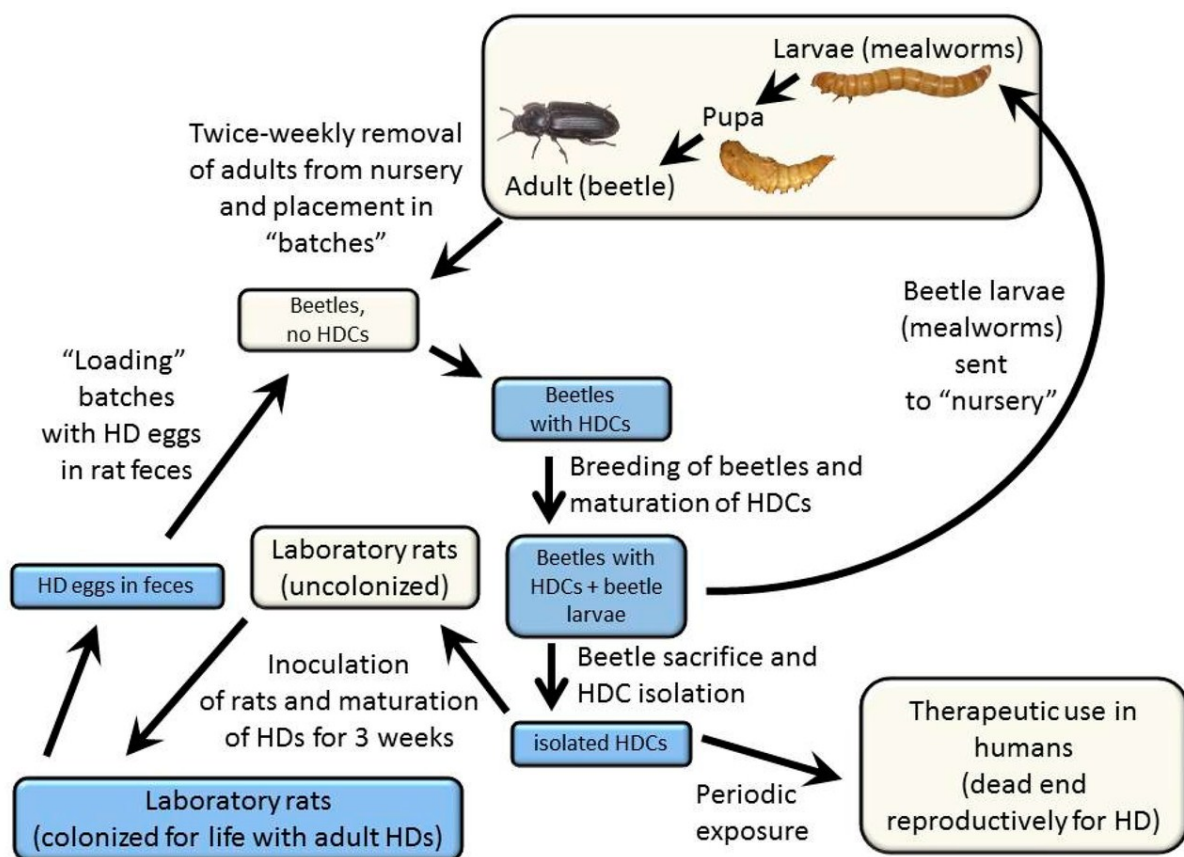


Figure 3: The maintenance of *HDC* in laboratory rats (primary hosts) and grain beetles (secondary hosts). Source (Smyth et al. 2017, 5).