

Parasites, ghosts and mutualists: a relational geography of microbes for Global Health

Homo microbis

Recent developments in gene sequencing have helped identify the vast diversity of microbial life in, on and around the human body. Scientists interested in this microbiome offer a figure of the human as *Homo microbis* (Helmreich, 2015), comprised of bacteria, viruses, fungi, archaea and even a few animals invisible to the naked eye. The composition and dynamics of the human microbiome are increasingly implicated in discussions of human health (Relman, 2015). We are learning more about the causes of infectious diseases, but we also increasingly hear about beneficial microbes and the consequences of their decline or absence.

‘Missing microbes’ (Blaser, 2014) have been associated with a range of metabolic, immunological, and mental health conditions – including allergy, obesity, inflammatory bowel disease and depression. These ‘epidemics of absence’ (Velasquez-Manoff, 2012) have been tied to situations of microbial imbalance or ‘dysbiosis’ (Logan et al., 2016). While causal links are not yet clear, and these claims are contested, a widespread reappraisal is underway in modern medicine of the salutary potential of the microbiome and the therapeutic use of microbes.¹

This medical microbiology of missing and beneficial microbes departs from the germ theory of disease, in which a specific malady is linked to a specific microbe. Instead it is founded on an ecological or configurational model. Here no microbe is inherently pathogenic (Méthot and Alizon, 2014): context and relations matter. Disease is presented as the emergent outcome of complex, spatio-temporal interactions between the host immune system and microbiota and the external microbial environment (Hinchliffe et al., 2016).

These developments in microbiology have some profound implications for the geography of health and disease. While there is a long history of relational and ecological work on health in geography and anthropology, this has largely been premised on a negative understanding of microbes. Spatial patterns of microbial presence and abundance have been taken as an index of socio-economic development:

fewer microbes = better places. This ‘antimicrobial’ geography informed the history of public health and is also true for Global Health, the ‘area for study, research, and practice that places a priority on improving health and achieving equity in health for all people worldwide’ (Koplan et al 2009, 1995. See also Brown and Moon, 2012; Herrick and Reubi, 2017). Global Health describes a diverse range of programmes. But they are united by an antimicrobial concern with the control and/or eradication of infectious diseases. There is currently little room in geography or in Global Health for understanding health and disease as configured by missing or beneficial microbes.

To address this gap, this paper develops a relational geography of microbes and the diseases of microbial dysbiosis. To do so it builds from recent relational approaches at the interface of more-than-human geography and political ecology. These examine health and disease as multispecies conditions configured by specific socio-ecological ‘situations’ (Hinchliffe et al., 2016). The concept of a disease situation foregrounds the political and ecological relations that shape the ‘intensities’ of human-animal-microbial interaction that might lead to pathogenesis – or the emergence of disease.

The analysis in this paper develops the prevalent concerns in this literature with infectious diseases associated with microbial excess. Here microbes are *parasites*, benefiting at the expense of their hosts. It then turns to disease situations marked by missing microbes. Here microbes figure as *ghosts* whose absent presence causes dysbiosis. The paper then attends to disease situations that are addressed through proactive microbial introduction and management. Here microbes become *mutualists* performing relations with the host of reciprocal benefit. The human-microbial relations captured by the three figures of the parasite, ghost and mutualist are those of upmost concern to medical scientists engaging with the microbiome. The three labels that describe these relations are taken from the microbiology literature.

In identifying these three figures and tracing their political ecologies the paper aims to offer geographers a more expansive conception of human microbial relations and the forms of ‘microbiopolitics’ (Paxson, 2008) that might underpin contemporary approaches to Global Health. It supplements long-standing concerns with antimicrobial or ‘Pasteurian’ approaches to healthcare, that are focused on the microbial parasite, with an attention to probiotic or ‘post-Pasteurian’ (Paxson, 2008)

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alternatives. These seek to manage and modulate human infection intensities to channel the mutualistic potential of microbes.

Hookworms

The analysis in this paper focuses on human relations with hookworms (*Necator americanus*, Figure 1). Hookworms are helminths and comprise one of the few animal components of the human microbiome. They are microscopic in their larval stage, during which they live outside of the human body. Hookworms are biologically very different to the bacteria that have become the main foci of microbiome research. Some microbiologists might even contest their inclusion in the microbiome. But, as I hope to show in this analysis, the bifurcated geographies of hookworm disease situations, and an emerging understanding of the worms’ role in configuring the human microbiome, make them ideal subjects for a relational geography of microbes.

Hookworms live in our guts and feed on our blood. They reproduce by laying their eggs in our faeces. Larvae hatch in warm, moist, shitty soil and seek to re-enter human bodies through the skin. Subsequent stages in the life cycle (Figure 2) see the larvae migrate to the heart, from where they eat their way into the lung. They are coughed up and swallowed, returning to the gut. Hookworms co-evolved with people and each worm can live in the host for several years. ‘Colonies’ tend to develop fairly slowly and a modest ‘wormload’ can be tolerated without symptoms.

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Hookworms can become pathogenic in different socio-ecological situations. Excessive hookworm infection causes significant morbidity to more than 500 million people in rural areas of low-income countries (CDC, 2016) (Figure 3). Hookworms are the second most significant parasitic infection after malaria (Hotez, 2013), and are the subject of Global Health initiatives to ‘deworm the world’ (Evidence Action, 2016). Hookworms were eradicated from North America and Europe at the start of the twentieth century through the development of antimicrobial drugs and improvements in sanitation (Ettling, 2013). The absence of hookworms has been

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3 implicated in the rise of dysbiosis. The demise of these ‘old friends’ (Rook 2009a) is
4 understood to imbalance the immune system, turning it against the self and generating
5 a range of autoimmune, allergic and inflammatory disease. Clinical trials are
6 underway to test the potential of helminthic therapy (Wammes et al 2014). These
7 trials have been overtaken by the ‘hookworm underground’ (Velasquez-Manoff,
8 2012): an international network of patients who breed worms at home and distribute
9 them through the Internet. There is growing industry interest in replicating
10 hookworm’s immunosuppression in pill form (Ditgen et al 2014).
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17 This seeming spatial paradox, of concurrent programmes to ‘deworm’ and ‘reworm’
18 the world, provides a compelling rationale for a relational geography of microbes and
19 of dysbiosis. Hookworms are not inherently pathological. They become so because of
20 shifts in the intensities of their socio-ecological relations. These shifts give rise to
21 disease situations marked by both excessive presence and by recent absence. Too
22 many or too few hookworms can cause dysbiosis. The paper details three contrasting
23 human-hookworm relations, which are described by the political-ecological figures of
24 the parasite, ghost and mutualist that were introduced above. It critically examines
25 their multispecies character, and prevalent political-economic and microbiopolitical
26 relations. The conclusion reflects on the implications of this analysis for the
27 geographies of health and disease, and for the practices of Global Health. It assesses
28 the contributions the figure of *Homo microbis* could make to developing more-than-
29 human approaches to the geographies of health. It suggests a need to recognise
30 multiple forms of microbial humans by mapping the patchiness of situations in which
31 people can live well with and without hookworms. It links these geographies to
32 prevalent patterns of inequality. It advocates for forms of healthcare better calibrated
33 to the pathological potential of microbial excess and absence, and the mutualistic
34 possibilities of living with microbes. These alternatives challenge the antimicrobial
35 orthodoxy, essentialist models of the microbial pathogen, and the magic bullet
36 solutions to disease ascendant in Global Health.
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52 **Relational geographies of microbes**

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54 Medical geographers and anthropologists have long been concerned with microbes in
55 their studies of disease ecology (Mayer, 2010). This work resonates (in often
56 underexplored ways) with more recent ethnographic research on health in more-than-
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human and multispecies studies (for a review see Nading, 2013). While these health literatures have yet to engage explicitly with the ecological ontologies of the microbiome, attention has been paid to exchanges between a wide range of viruses, bacteria and animals and human immune systems across a growing diversity of interspecies contact zones (e.g. Greenhough, 2012; Lowe, 2010; Bull, 2016; Beisel and Boëte, 2013). We can situate this multispecies turn within a wider shift towards relational understandings of disease in medicine and the social sciences (Anderson and Mackay, 2014).

Steve Hinchliffe and his co-authors (2013; 2016) develop this work in their analysis of the geographies of biosecurity. They take issue with conventional ‘Cartesian’ mappings of disease as the outcome of universally pathogenic microbes crossing borders and infecting discrete territories. They note the importance of the extensive networks of globalisation in enacting and distributing ‘socio-technical diseases’ (see also Ali and Keil, 2011), but suggest that it is more informative to think of disease in terms of topologies of intensive relations. In their reading, topology refers to the complex spatio-temporal relations and intra-actions (after Karen Barad) that configure the ‘intensities’ of any socio-ecological situation. Bodies become ecologies entangled and enfolded within a geography of more or less pathogenic landscapes. These are marked by potential disease ‘tipping points’ (2013: 538). Here infectious disease does not come from an outside, but is ‘ecosyndemic’ (Singer, 2010): immanent from particular political ecological ‘situations’ whose shifting microbiologies create conditions of dysbiosis. Pathogenicity, they argue, is best conceived ‘as a process, rather than a fixed object’ (Hinchliffe et al., 2016: 25).

Work in this vein has tended to focus on the topologies of viral ‘hotspots’ (Brown and Kelly, 2014) ‘clouds’ (Lowe, 2010) and ‘epidemic space’ (Loon, 2005). A common concern lies with the intensified socio-ecological relations of contemporary agriculture, urbanization, and globalization, which are understood to generate ‘blowback’ (Wallace and Wallace, 2015), or the *excessive presence* of undesired microbes (Shukin, 2009; Porter, 2013; Wallace, 2009). Here microbial dysbiosis takes the form of ‘crowd infections’ (Wolfe et al., 2007) and emergent infectious and zoonotic disease. To date, there has been little work exploring the topologies of dysbiotic situations generated by microbial absence, or of the proactive efforts to tip

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3 bodily ecologies out of dysbiotic relations that we will encounter in the hookworm
4 story. Indeed, there has been remarkably little research in geography or anthropology
5 on allergy and the inflammatory and autoimmune diseases that are currently being
6 associated with missing microbes (though see Mitman, 2008).
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11 The critical impulse that shapes this relational, microbial turn is inspired by theories
12 of the biopolitics of immunity, as well as more established concerns with political
13 economy. For example, Hinchliffe and his co-authors (2016) are critical of the
14 security practices – or what they term ‘disease diagrams’ – of modern intensive
15 agriculture and associated programmes for One Health (Hinchliffe 2015). These, they
16 argue, are premised on the separation and purification of animal bodies and ecologies
17 and the denigration of vernacular and non-Western forms of expertise. They suggest
18 that these generate ‘autoimmune’ tendencies, in which bodily (and by extension
19 social) ecologies tip into a disease state when the immune system turns again itself in
20 the absence of a co-evolved antagonist (Hinchliffe and Ward, 2014. See also
21 Mutsaers, 2015; Brown and Nettleton, 2017).
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31 Drawing on the writings of Roberto Esposito and Jacques Derrida, they illustrate
32 more communitarian approaches to ‘immunology management’ on the farm
33 (Hinchliffe and Ward, 2014). These are premised on the affirmative potential of
34 encounters with social and microbial difference (in this case pig shit and the
35 vernacular knowledge of the farmers who make it available. See also Law and Mol,
36 2008). They suggest that this strategic ‘mucking up’ enables tolerance, hospitality and
37 mutual flourishing. We can find resonances of these communitarian approaches to
38 immunology management in the shift from Pasteurian to ‘post-Pasteurian’ forms of
39 ‘microbiopolitics’ that Heather Paxson (2008; 2014) has identified in her work on raw
40 milk cheese production in North America. Post-Pasteurian approaches do not reject
41 Pasteurisation, but involve more targeted means of managing microbial life,
42 encouraging or living with some microbes to secure desired systemic properties.
43 There is a nascent interest here in finding ethical means – however ‘awkward’ (Ginn
44 et al., 2014) – of living well with microbes and their insect vectors.
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56 These relational understanding of pathogenicity could be better linked to established
57 writings in anthropology and political ecology on the structural violence and
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‘pathologies of power’ (Farmer, 2004) associated with colonial and capitalist forms of public health and biomedicine. There are important differences between work in this older, Marxist tradition and the new relational approaches (for discussion see Brown and Kelly, 2014; Guthman and Mansfield, 2013; Braun 2015). There is scope for a more systematic synthesis than can be offered here, but for the purposes of the analysis that follows I will identify one common concern and point of conceptual convergence. Hinchliffe et al (2016) give a ‘topological twist’ to established approaches to political economy in their analysis of campylobacter as a ‘just-in-time’ disease. In working viral agencies into theories of capitalism, they link the intensification of agriculture and its endemic dysbiosis to post-Fordist relations of labour precarity, commercial pressure and regulatory inefficacy. Their argument is that we can only understand the pathological intensification of human-microbial relations by tracing the globalising logics, practices and assemblages of contemporary capitalism. In the analysis that follows, I develop this conceptual framework by attending to the pathologies of power associated with the parasites of plantation capitalism, the inequalities amongst those facing microbial absence, and the emerging political ecologies of microbial reintroduction.

Human-hookworm relations

This account is structured to explore three types of human-hookworm relation, which are described by the ecological figures of the: *parasite*, *ghost* and *mutualist*. This analysis is informed by a close reading of scientific literatures on hookworms and interviews with a range of clinical practitioners and patients engaged with de- and re-worming. It is not exhaustive of human-hookworm relations past, present, or hypothetical. Instead it offers a heuristic for developing a relational geography of microbes.

Parasite

Parasite is a polysemous word. Recent work in the social sciences (oft inspired by Serres, 2007) has developed transgressive, or even affirmative, figures of the parasite (Lezaun, 2011; Bull, 2016; Kelly, 2012). I touch on these in the discussion of other relational figures below. But in the interests of specificity, I take a rather narrow and negative biological definition of a parasite as: ‘an organism that obtains nutrients at

the expense of the host organism, which it may directly or indirectly harm' (OED, 2016).

Mortality as a direct result of 'hookworm disease' (Necatoriasis) is rare. But hookworms can become parasitic and thus pathogenic in particular political-ecological situations. Necatoriasis hotspots are characterised by high and protracted levels of infection intensity, where bare skin frequently comes into contact with the soil and a dysbiotic worm colony accumulates. High wormloads lead to protein deficiency and anaemia. They can affect cognitive function and development, especially amongst children (Brooker et al., 2004). We can find examples of such relations in critical histories of public health. These illustrate how the political-ecological intensities of colonial capitalism created the perfect conditions for hookworms to become parasitic. Steven Palmer argues that:

Hookworm disease was a sickness of ecological, economic, and cultural displacement and recombination; its virulent appearance along these teeming trenchworks of modernity went hand in hand with the increasing density and speed of the globe's road, rail, and ocean connections. A close relative of nineteenth-century capital, the hookworm parasite thrived in heated frontier regions where vulnerable bodies were amassed for hard labor, and it became potent through accumulation (2009, 679)

Colonial mines, tunnels, railroad beds, and plantations (in India, Africa and the Americas) were ideal 'hotspots' (Brown and Kelly, 2014) for the genesis of hookworm disease, as were the settlements of indigenous peoples forcibly confined to reserves (e.g. in Australia). Hotspots were comprised of rapidly growing concentrations of displaced and poorly nourished people, suffering from high levels of reinfection as a result of bad sanitation and suitable soil (Couacaud, 2014).

Palmer suggests that in the 19th century hookworms were 'simmering among rural peoples around the world'. They 'boiled over' because of the 'intense ecosocial disruptions' (2009, 708) of world capitalist expansion. The amplified intensities of these situations 'tipped' hookworms over a threshold, shifting them from a microbial old friend (more below) to a parasitic 'crowd infection'. Necatoriasis briefly became

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an ‘industrial epidemic’ (Jahiel and Babor, 2007) – a pre-Fordist precursor to the contemporary ‘just-in-time’ diseases we encountered above. As various authors have argued, the ‘macroparasitic’ (i.e. asymmetrical and exploitative) character of plantation colonial capitalism exacerbated the ‘microparasitic’ depredations of the hookworm (see Brown, 1987).

During the early 20th century hookworms became known as the ‘germ of laziness’ because of their effects on labour productivity (Ettling, 2013; Anderson, 2006). Subsequent scientific research and public health programmes (largely funded by the Rockefeller Foundation) sought to modulate infection intensities to control necatoriasis (Palmer, 2010; Farley, 2003). In the South of the USA, sanitation, footwear, drugs and education disentangled agricultural workers from the vectors for infection. Many people left hookworm hotspots for cities, and gradual improvements in nutrition helped boost host tolerance. Worms and other microbes were killed off in large numbers. Such programmes for hookworm control have all the hallmarks of the modern, antibiotic modes of microbiopolitics documented by Latour (1988) and other, more celebratory, historians of public health (e.g Farley, 2003). They involve systematic efforts to lock down and rationalise the circulation of microbial life, separating human bodies from the environment and purifying them of their component microbes.

The application of such antibiotic approaches is globally patchy and the biogeography of hookworm prevalence and infection intensity conforms to familiar maps of uneven development – to the extent that public health experts have devised a ‘worm index’ of human development (Hotez and Herricks, 2015). Some helminth infections are still common amongst minority populations living in poverty in North America and the EU (Hotez, 2009). But hookworms are now extinct in the ‘wild’ in these regions and their prevalence and infection intensity are on the wane across much of the urban Global South (Pullan and Brooker, 2012).

Parasitic relations with hookworms persist amidst rural populations in low-income countries, especially in Africa and South Asia. Highest infection intensities are often amongst children (Hotez et al., 2005). Sanitation projects have fallen out of favour as strategies for hookworm control and World Health Organisation attention and Gates

Foundation funding is now focused on the regular distribution of deworming drugs to schoolchildren (WHO, 2016). The efficacy of school based deworming is fiercely contested (Evans, 2015), especially in areas with poor sanitation and high reinfection risk. Hookworms have also developed antimicrobial resistance and there has been limited investment in new drugs, as more affluent Northern markets have shrunk (Hotez et al., 2013).

This brief, topological analysis of hookworms-becoming-parasitical on crossing a threshold, suggests that necatoriasis is not necessary a disease of under-development resulting from the spread of a specific pathogen. Hookworms are not inherently pathological. They can be endemic and asymptomatic, but become pathogenic because of an increased intensity of exploitative, unequal or abandoned socio-ecological relations. In these situations, pathology is indexed to excessive presence and bodily dysbiosis is the outcome of the crossing of a disease threshold. Historians link the amplification of infection intensities to the pathologies of power associated with colonial capitalism, but they also caution against reading off hookworm disease as a universal outcome of systemic structural violence. The materialities of co-infection, host genetics and epigenetics, soil type, working conditions, defecation practices and sanitation investments all shape the differential emergence of infection intensities (Couacaud, 2014).

Ghost

A growing body of immunological theory, scientific evidence and vernacular experience questions the desirability of wholesale hookworm eradication. There is a concern that the absence of hookworms and other microbes could be as pathological as their excessive presence. Epidemiologists have noted an association between general declines in microbial infection and the increase in susceptibility to certain autoimmune and allergic diseases (Bach, 2002). In 1989 David Strachan offered a 'hygiene hypothesis' to account for these broad trends (Strachan, 1989). This theory has been refined by work that seeks to differentiate the salutary effects of different microbial infections. Immunologists, like Graham Rook (Rook et al., 2014), encourage a separation between harmful 'crowd infections' (which evolved recently because of urbanization) and the microbial 'old friends' with which humans co-evolved.

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Rook suggests that radical recent changes in the composition of the human microbiome have led to the loss of the ‘old friends mechanism’ (Rook, 2009b) through which resident microbiota enable and calibrate vital bodily processes like metabolism, immunity and cognition. The same service is not provided by crowd infections, which either kill the host, or to whom the host develops immunity. While scientific and public health attention remains focused on ‘targeted hygiene’ and the control of crowd infections (Bloomfield et al., 2016), the salutary effects of the absent venerable human microbiome is emerging as a hot topic in the life sciences.

Hookworms have been identified as one such old friend. The absence of hookworms and other human helminths is currently being afforded significant attention in explaining microbial dysbiosis and its effects on human health. Epidemiological research suggests that ‘allergic diseases are rare in areas with high helminth parasite exposure and common where helminth exposure is lacking or significantly reduced, such as urban areas of developing countries and industrialized nations’ (Flohr et al., 2009, 20). A long-term observation study of patients with multiple sclerosis infected with different helminths showed that disease activity improved during infection and regressed when infection was treated (Correale and Farez, 2011). Comparable, but by no means clear cut patterns have also been observed for the effects of helminths on diabetes, IBD and metabolic disease (for a review see Wammes et al., 2014).

Immunologists seeking to explain these trends suggest that hookworms produce an entirely different ‘immune response profile’ to bacterial and viral pathogens (Allen and Maizels, 2011). They argue that because of a long history of human co-evolution, ‘helminths have evolved to dampen, rather than disable, the immune system of their hosts’ (ibid, 384). Recent work in immunology identifies a ‘helminth-induced immune regulatory environment’ (Helmby, 2009) through which worms enter into a ‘continuing dialogue’ (Allen and Maizels, 2011), 385) with the human immune system to enable permanent residence. This work also suggests that in the absence of worms and other components of the microbiome, the immune system becomes poorly calibrated, is unable to differentiate harmful materials, becomes oversensitive, and ultimately turns against itself, resulting in elevated levels of allergy and inflammation (Fleming and Weinstock, 2015).

Microbiologists use mouse models to trace the complex interactions between the host, helminths and resident bacteria. They suggest that helminths can manipulate the microbial population for their own ends, in ways that explain immune modulation (Reynolds et al., 2015; Zaiss et al., 2015). One set of immunologists has drawn on concepts from conservation biology to explain helminths' calibrating potential (Bilbo et al., 2011). They suggest that hookworms figure as missing 'keystone species': 'species that play a disproportionately large role in the prevalence and population levels of other species within their ecosystem or community' (Wagner, 2010: 51). The past presence of hookworm is sensed as a contemporary absence made manifest in forms of ecosystem dysfunction and 'ecological anachronism' (Barlow, 2013). The concept of ghost keystone species was first developed to explain the 'trophic cascades' caused by the absence of apex predators, like the wolf (Eisenberg, 2010). The absence of these species is understood to tip ecologies into new states characterized by reduced diversity, functionality and resilience. Advocates of helminthic therapy speak of 'Darwinian medicine' (Rook, 2009a) that would address analogous 'evolutionary mismatches' between the ecological composition of human bodies, the immune systems they have trained, and the external environments to which they are exposed (Parker and Ollerton, 2013).

These discussions of the demise of old friends and the causes of the current epidemics of absence implicate practices that are central to the modern, antibiotic approaches to managing microbes that were encountered above (see table one).

Socio-ecological change	Microbial consequence
Clean water	Reduced faecal transmission
Increase in caesarean sections	Reduced vaginal transmission
Reduced breastfeeding	Reduced skin-to-skin transmission and a changed gut flora
Smaller family size	Reduced early life transmission
Widespread antibiotic use	Reduced vaginal transmission and selection for a changing composition
Changing diet and cooking practices	Alterations in gut flora

Diminished contact with soil and farm animals	Reduced early life transmission
Increased bathing, showering and use of antibacterial soaps	Selection for a changing composition
Increased exposure to ‘crowd infections’	Infectious disease

Table 1: Table of modern practices understood to negatively affect the human microbiome (taken from Blaser and Falkow, 2009; Bono-Lunn et al., 2016; Rook et al., 2014).

Interventions like flush toilets, antibiotics, and Caesarean sections, that have been central to Western narratives of civilisation and development, have been recast as potentially pathological. We are told that in becoming modern the human microbiome is in danger of unravelling. Immunologists and microbiologists have extended this discussion to pathologise Western urban and post-industrial life. They draw attention to undesirable processes of microbial colonization and the resulting forms of microbiome composition (Hanski et al., 2012; Rook et al., 2014). The story here is of health and safety going too far. An excessive desire to minimize risk and modulate microbial infection intensity creates a model of biosecurity that is prone to auto-immunity: ‘a self-protective syndrome whose attempts to exclude difference are ultimately self-destructive’ (Hinchliffe and Ward 2014, 143).

Early accounts of inflammatory and autoimmune conditions suggested that these are ‘Western diseases’ or ‘diseases of affluence’ (Pollard, 2008), associated with populations that have passed through a spatial epidemiological transition. But there are stark disparities in the socio-economic status of those who currently experience hookworms as a ghost in urban areas around the world (Rook et al 2014). Coping with autoimmune disease may require regimes of immunosuppressant drugs, whose availability is patchy and dependent on an ability to pay. Autoimmune diseases may well be exacerbated by the socio-ecological intensities of urban poverty that generate a perfect microbial storm of absent old friends and amplified exposure to urban crowd infections. The chances of living well without hookworms and other old friends are as strongly configured by entrenched pathologies of power as the situations in which people can live well with worms.

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4 A figure of hookworms as ghost helps extend Hinchliffe et al's (2016) topological
5 understanding of pathogenicity to explore situations in which microbial absences shift
6 ecological intensities to create dysbiosis. Many of the microbial excesses associated
7 with the emergent infectious diseases of agriculture and urban life may stem from the
8 absence of regulating microbes. But there has been little explicit attention given in
9 medical geography to the topologies of such absences and their effects on
10 autoimmunity. Understanding the immune system legacies of microbial absences
11 requires a more protracted conception of the microbial geographies of health, where
12 the focus is less on the intensities and immediate spatio-temporalities of outbreak (cf
13 Dixon and Jones 2015), and more on intergenerational microbial inheritance, the
14 accumulation of microbial exposure and immunomodulation over the life course, and
15 the cascading effects of microbial absences. Emerging relational geographies of
16 pathogenicity must also attend to the protracted and discordant temporalities of
17 microbial colonization and immune system calibration.

28 *Mutualist*

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30 Anxieties about missing microbes have informed a wide range of laboratory research
31 manipulating the microbiomes of animal models. Experiments and pre-clinical trials
32 with mouse models and murine helminths, comparable to those of humans, try and
33 simulate and explain the links between de- and reworming and the incidence of
34 allergic and autoimmune disease. Wammes et al argue that these experiments in
35 murine helminthic therapy: 'provide strong evidence that helminths can not only
36 downregulate parasite-specific immune responses, but also modulate autoimmune and
37 allergic inflammatory responses and improve metabolic homeostasis' (2014: 1150).

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39 Human clinical trials of helminthic therapy are now underway. A recent review
40 identifies 28 trials focused on ten different autoimmune diseases, including Crohn's,
41 Multiple Sclerosis and autism (Fleming and Weinstock, 2015). The USA Food and
42 Drug Administration have granted a license to use the ova (eggs) of the pig
43 whipworm *Trichuris suis* as an investigational medicinal product (Elliott and
44 Weinstock, 2009) and the Danish company *Parasite Technologies* has patented a
45 production process. In the UK the Medicines and Healthcare Regulatory Authority
46 have licensed the use of *Necator americanus* (Pritchard, 2011). Trials have
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demonstrated that it is safe to introduce these two species into human patients. But evidence of the efficacy of helminthic therapy has been mixed and inconclusive. Fleming and Weinstock note that ‘some phase 2 studies have not achieved positive results for their primary outcome measures’ and argue that ‘the jury is out as to the efficacy of helminth treatment’ (2015: 289) as many studies are in progress, and several were poorly designed. New trials are underway and many more are planned.

In parallel with these clinical developments, and in part in frustration at their slow progress, a variety of patients, citizen scientists and health providers have been reworming. In 2016, there were at least five commercial providers of hookworms and other helminths, all run by people with experience of self-treatment (see Cheng et al., 2015).² Hookworm therapy has been driven by social media, which link together a globally disparate community that operates independently of scientific researchers and commercial providers. Empowered by online resources and their own experiments, some users have learnt to grow their own. They use animals originally purchased from commercial providers, or sourced from participation in clinical trials. Some have cobbled together readily available domestic technologies to make their own laboratories. Detailed incubation protocols circulate containing instructions on how to create surrogate ecologies for incubating and nurturing worms. Making use of cheap microscopes and library images, they harvest and isolate new stock from their faeces and count larvae before self-infecting (for more information see AUTHOR REF).

A recent survey identified 6-7000 ‘self-treaters’, using four different helminth species (Cheng et al 2015). Allergies, IBD and MS were the most common reported conditions. The cost of helminth therapy varies from US\$10 000 – > US\$1000 per annum, depending on the species used, the dose required and the degree of support provided. This is a marginal economic activity, whose legality is currently unclear. In the main, this ‘hookworm underground’ involves non-profit, communitarian relations and zealous advocacy. Fellow sufferers and users gift or exchange worms at cost. They share experience to ensure reserve supplies and to build capacity. The shared aim of these ‘biological citizens’ (Rose and Novas, 2008) is to enhance the legitimacy and availability of helminth therapy (cf Epstein, 1996 on patient activism and HIV).

Here hookworms come to figure as ‘symbionts’ (Biome Restoration, 2016), ‘mutualists’ (Pritchard and Brown, 2001) or ‘mutualistic symbionts’ (Autoimmune Therapies, 2016). Patients talk affectionately of their ‘gut buddies’, or ‘colon comrades’ (AUTHOR REF). Mutualism and symbiosis were once synonymous in ecology, but the latter is increasingly used to describe a wider range of relations, including parasitism. Mutualism is more specific and describes a ‘relationship existing between two organisms of different species which contribute mutually to each other's well-being’ (OED, 2016). In accounting for the mutualistic agencies of hookworms, scientists draw on the accounts of an interspecies dialogue between old friends outlined above. Helminth providers use similar metaphors. They argue that worms initially serve to ‘calibrate’ a child’s immune system before ‘exercising’ adults’ immunity (Biome Restoration, 2016). Worms are understood to ‘restore nature’s balance’ (Autoimmune Therapies, 2016) and enable ‘symbiotic immunomodulation’ (Symmbio, 2016). They are to be enrolled in a wider project of ‘biome restoration’ (Biome Restoration, 2016).

We can position this DIY reworming within a broader probiotic turn that is taking place in the management of health in certain Western contexts (AUTHOR REF). Efforts to translate the science of the human microbiome have converged with a reappraisal and reinvention of the microbial dimensions of a range of vernacular cooking and hygiene practices. The result is a range of experiments, interventions and regulations designed to reverse the trends outlined in table 1 (see table 2). Examples would include: the proliferation of pro- and pre-biotic diets and supplements designed to work on the gut microbiome (e.g. Sonnenburg and Sonnenburg, 2015), and private sequencing services to monitor their effects (e.g. uBiome.com); probiotic hygiene products that seed the body or the built environment with good bacteria (e.g. motherdirt.com); and the use of faecal transplants to treat antibiotic resistant infections (Gough et al., 2011) and vaginal seeding to replicate microbial birth canal colonisation in babies born by C-section (Dominguez-Bello et al., 2016).

Socio-ecological change	Microbial consequence	Post-Pasteurian management of microbial intensities
Clean water	Reduced faecal	Probiotic drinks, like

	transmission	Kombucha
Increase in Caesarean sections	Reduced vaginal transmission	Discouragement of C-Sections Swabbing to replicate the microbial colonization associated with vaginal delivery
Reduced breastfeeding	Reduced skin-to-skin transmission and a changed gut flora	Breast feeding promotion New types of probiotic and prebiotic formula
Smaller family size	Reduced early life transmission	Pox parties to spread diseases like measles and chicken pox*
Widespread antibiotic use	Reduced vaginal transmission and selection for a changing composition	Ban on some antimicrobial cleaning products Discouraging use of antibiotics Promotion of probiotics
Changing diet and cooking practices	Alterations in gut flora	Probiotic, raw and paleo diets Growth in pro- and pre-biotic dietary supplements
Diminished contact with soil and farm animals	Reduced early life transmission	Children’s ‘messy play’ and ‘Nature reconnection’ projects
Increased bathing, showering and use of antibacterial soaps	Selection for a changing composition	Controls on use of antimicrobials (like Triclosan) Growth in probiotic hygiene products and practices
Increased exposure to ‘crowd infections’	Infectious disease	n/a

Table 2: Table showing post-Pasteurian responses to modern anxieties about microbial dysbiosis.
*Some of these practices shade towards the anti-Pasteurian (Paxson 2014), for example with pox parties organised by anti-vaccination movements.

In these situations, we see hookworms (and other microbes) becoming subject to Paxson’s (2008) ‘post-Pasteurian’ forms of ‘microbiopolitics’. Even the most gung-ho advocates of microbial ‘rewilding’ (e.g. Leach, 2015) are post-, rather than ‘anti-

Pasteurian' (Paxson 2014). Post-Pasteurian reworming is similar to the practices of biosecurity as 'immunity management' documented by Hinchliffe and Ward (2014) in their writings on how pig farmers 'muck-up' sterile animals with earth and faeces to boost their immune systems. But here hookworms are used strategically as a known keystone species to manage the ecological intensities of the bodies into which they are deliberately introduced. Hookworms are deployed to tip dysbiotic bodily ecologies back over the threshold, which triggered autoimmune disease. Like wolves reintroduced to rewild nature's reserves, hookworms are enrolled to modulate the intensities of a target ecology and secure desired systemic properties. Hookworms restore immunomodulation and to enhance the resilience of *Homo microbis* to prevent degenerative change (see AUTHOR REF).

The discovery of hookworms' salutary properties has prompted a range of speculation and research and development on the future of helminth therapy. While advocates speak of restoration and rewilding, there is a growing (and not necessarily incommensurable) desire to gain more control over hookworms and their mutualistic potential. Prominent advocates of helminthic therapy want to persevere with the use of whole organisms. They seek to refine their choice of species and speculate about modifying the helminths currently in use (Elliott et al., 2007; Parker et al., 2012). A very different future is currently being imagined for hookworms by figures in the pharmaceutical industry. 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).

On the one hand, there is excitement about new 'drugs from bugs' that will replicate hookworms' abilities to train and calibrate the human immune system (Ditgen et al., 2014). The hope is that the agencies of the hookworm might be simulated in pill form to secure the type of profitable returns currently associated with chronic dependency on immunosuppressant drugs. In this guise the ghostly hookworms return in molecular form to function as the immunological equivalent of a *scarecrow*: a pared down simulation that mimics a keystone's calibrating agencies.

At the same time, information provided by the hookworm genome and conceptions of helminths in dialogue with microbes, inform a new round of deworming drug and

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vaccine 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. Comparable and well-established Global Health programmes to develop a hookworm vaccine (Hotez et al., 2016) are focused on identifying antigens to chemicals secreted at key stages in the hookworm lifecycle. These pharmacological and vaccinological interventions turn the dialogical character of the hookworm, and the embodied history of its human conversation, against the organism (cf Beisel, 2017 on the malaria vaccine). Drugs would exclude hookworms’ microbial ‘messmates’ (Haraway, 2008) and increase its antagonists. While vaccines teach the body to attack on first encounter.

These proposals have been criticized by scientists who point to the cost and the difficulties of recapitulating the ecological agencies of an entire animal in molecular form (Bilbo et al., 2011). They do not believe that a keystone species can be simulated and note that worms will continue to develop drug resistance (Hawdon, 2014). Others have expressed concerns that a successful hookworm vaccine would permanently deprive immunised populations of the immunomodulation benefits of mutualistic infection and increase the risk of dysbiosis amongst already precarious groups (Wammes et al., 2014).

More broadly, critics note the differences between a drug that is designed to treat a specific illness and a live organism that acts preventatively on a bodily ecology to confer health (Bono-Lunn et al., 2016). They suggest that a focus on drugs from bugs ignores the systemic drivers of dysbiosis (Logan et al., 2016). Members of the hookworm underground contest the proprietary tendencies implicit within these developments. They are concerned that profit-centred efforts to privatize the ‘hookworm secretome’ and eradicate worms may undermine patient-centred benefits already accruing in helminthic therapy. From the perspective of the hookworm, these pharmacological futures can no longer to described as mutualistic. Benefits flow only one way, and the human has become the parasite. Some even hope that new vaccines might enable hookworm eradication.

These post-Pasteurian relations of deliberate re-entanglement with hookworms or their molecular surrogates have quite specific geographies, which are currently under

explored. Clinical trials in helminthic therapy are focused on populations living near a small number of North American and UK hospitals. The geography of the online hookworm underground is harder to establish. The gatekeepers and most active members of this network on social media, who were contacted in the conduct of this research, are concentrated in North America, Western Europe and Australia. It is likely that mutualistic human-hookworm relations map on to the more affluent regions in which hookworms currently figure as ghosts.

Geography, dysbiosis and Global Health

This paper has developed a relational geography of the microbiome and of dysbiosis through a focus on disease situations associated with human hookworms. It argues that no microbe is essentially pathogenic; pathogenesis is the outcome of political and ecological relations. The paper adds to existing work on disease situations marked by microbial excesses and offers an analysis of disease situations of microbial absence and proactive restoration. In so doing it identifies three types of human-microbial relation, which are described by the ecological figures of the parasite, ghost and mutualist. The paper maps the global occurrence of each type of relation, their multispecies composition, and their prevalent modes of political economy and forms of microbiopolitics. These are summarised in table three.

	Parasite	Ghost	Mutualist
Global occurrence	Tropical areas in the rural Global South (figure 3)	Global North and urban Global South, especially areas from which hookworm have recently been removed.	Poorly mapped. Scattered across urban areas of the Global North. Some tropical areas in the Global South with controlled infection intensities.
Multispecies composition	Excessive worms, repeated infection, co-infection with other parasites, poor nutrition, comprised immune system.	Absent worms. Dysbiotic microbiome. Overactive immune system.	Controlled worm population, ready supply of replacement worms, no inadvertent infection risk, access to good nutrition and managed diet,

			immunomodulation.
Political Ecology	Poor sanitation and healthcare, intensive plantation agriculture, poverty and inequality, limited access to effective deworming drugs	Common access to sanitation, footwear, deworming drugs and basic healthcare. Variable access to immune-suppressant drugs.	Wealthy. Good healthcare and sanitation. Worms as common property with at cost provision v. growing private interest in pharmaceutical surrogates
Microbiopolitics	Pre-Pasteurian, patchy Pasteurian based on ‘magic bullet’ drugs and vaccines	Antimicrobial. Involving toilets, sanitation and national deworming programmes	post-Pasteurian in Urban North involving controlled reintroduction by scientist and expert patients. Pre-Pasteurian in rural Global South with traditional means of controlling infection intensities.

Table 3: A summary of the key characteristics of the three types of human-microbial relation identified in the paper.

In conclusion, I will briefly reflect upon the implications of this analysis for the geographies of health and for the field of Global Health. But before doing so it is worth reiterating the limitations posed by a focus on hookworms. There are risks in taking hookworms as illustrative of the great diversity of the human microbiome. Hookworms are obligatory animals (i.e. they only reside in humans) that cannot reproduce inside their host. Unlike the bacteria that have been the main focus of recent scientific work on the microbiome, they reproduce slowly and cannot engage in lateral gene transfer. Hookworms’ sociability with bacteria and their keystone mutualistic agencies are likely relatively rare. There are plenty of other helminths, let alone viruses and bacteria, with whom such mutualistic relations are improbable (e.g. Moran-Thomas 2013). There are plenty of microbes we might not miss.

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3 Nonetheless, there are three broad contributions offered by this analysis of human-
4 hookworm relations. First, thinking with hookworms helps open up the radical
5 implications of an ontology of *Homo microbis* for conceiving the human and human
6 health. These are early days in the development of this science, and much of what is
7 outlined above may well be revised as microbiologists gain more traction on the
8 ecological and immunological dynamics of the human microbiome. But here we are
9 presented with a porous and ecological figure of the human whose life course
10 microbial exposures come to configure identity, subjectivity and health outcomes (cf
11 Meloni, 2015 on epigenetics). Only some of our microbes are inherited and the
12 microbial self is thus open to deliberate or inadvertent modification. This relational
13 ontology of the microbial human challenges how medical geography might conceive
14 space-time. Analysis must focus on life course microbial colonisation, and infection
15 hotspots and vectors. But it must also acknowledge absences and their latent
16 ecological effects (cf Anaya et al., 2016). The human as *Homo microbis* is an unstable
17 and nonlinear accumulation, marked by disease tipping points with differing degrees
18 of reversibility.
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31 Influential commentators like Donna Haraway (2016), celebrate the ways in which
32 the science of the microbiome and microbial symbiosis offer a post-foundational
33 ontology for more-than-human theory and politics that further undermines Humanist
34 dreams of the bounded individual (see also Hird 2010). Other sociologists of science
35 are more cautious about the new materialisms emerging from the ‘microbiomania’
36 (Paxson and Helmreich 2014) of the contemporary biosciences. Drawing together
37 their disparate research on astrobiology and raw milk cheese, Paxson and Helmreich
38 note the ways in which communities of microbes are coming to figure as ‘model
39 ecosystems’ for a range of hopeful political and ecological projects. They are wary of
40 taking *Homo microbis* too literally and await its encoding by established power
41 geometries of gendered, racialized and capitalist biotechnology (cf Guthman and
42 Mansfield, 2013 on the coding of environmental epigenetics). While the post-
43 genomic, vital materialism offered by microbiome science can be aligned with the
44 political projects of more-than-human geography, we should be aware of the
45 historical, political and economic conditions that shape its emergence (see Sangodeyi,
46 2014). The differentiation of microbiome science as it increasingly proliferates across
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the domains of Big Science, biotechnology, citizen science, art-science and DIY biology will be important subjects for future research.

This analysis in this paper begins to lay the foundations for this type of critical work. By identifying the geographies that come to configure the human microbiome, it pluralises *Homo microbis*, identifying different sub-species of *Homo microbi*. Tracing how hookworms make and unmake different humans adds to existing criticisms of germ theory and its essentialist understanding of disease as caused by a specific pathogen. Instead this analysis has demonstrated how hookworms, like any other microbe, take on radically different roles in different political-ecological situations. These situations are patterned. They map on to historical and contemporary geographies of colonialism, development, trade, property and urbanisation, to draw out just a few of the processes identified in this story. Hookworms become pathological as parasites in situations of agricultural and industrial intensification and/or political abandonment. The shifting intensities of these situations are familiar from existing work on the emergent diseases of colonialism, agriculture and urbanisation. What this analysis adds is an attention to the pathological potential of microbial absence and the dysbiosis it generates. While the causes of autoimmune and inflammatory disease are multivariate and still unclear, their apparent microbial signature suggests the need for a relational geography of missing microbes. The degree to which the diseases of microbial absence are ‘pathologies of power’, that can be linked to the structural violence of the unequal provision of healthcare is now an open question. Autoimmune and inflammatory diseases are neglected in medical and health geography and require further research.

Thinking with hookworms helps us begin to answer this question and in so doing to identify some of the implications of the rise of the microbiome for Global Health. While we are some way off knowing what a healthy microbiome looks like – and the answer is unlikely to be singular – there is a growing interest in cultivating the microbiome as a route to individual and public health. Thinking Global Health in terms of the microbiome requires a continued attention to situations of excessive microbial presence, coupled with a new concern for beneficial microbial colonisation and the risks of microbial absence and dysbiosis. Such thinking further complicates linear models of a modern epidemiological transition, in which development can be

1 indexed to microbial absence. It suggests a need to recalibrate the discourses inherent
2 (if not explicit) in Global Health that developed countries are healthier because they
3 are cleaner and more devoid of pathogens and microbes, whereas the Global South is
4 the geographic Mecca for bad microbes, dirt, and lack of sanitation. If the pursuit of
5 sterility can be pathological, then Global Health will need to rethink its ontological
6 foundations.³

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14 Hookworm control will remain a clear public health priority in many rural areas of the
15 Global South. But it appears that too comprehensive a shift to antibiotic relations with
16 hookworms can instigate autoimmune and inflammatory conditions in populations ill
17 equipped to manage without them. Urban populations with ghostly worms, living in
18 situations with poor sanitation, and exposed to pre-Pasteurian relations with urban
19 crowd infections and novel infectious diseases, are particularly vulnerable to
20 dysbiosis. A concern with contemporary dysbiosis does not necessarily imply an anti-
21 Pasteurian return to an Eden of universal symbiosis. Pasteurian forms of
22 microbiopolitics have made life better, and their geography is still all too patchy.

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31 Attention turns to a post-Pasteurian recalibration of hygiene that would secure the
32 mutualistic presence of old friends and calculate and manage the intensities of
33 microbial ecologies. This might involve intervening through the strategic use of
34 keystone species to maintain biological diversity and ecosystem functionality. As the
35 story of hookworms makes clear, any panoptic aspiration for a global post-Pasteurian
36 microbiopolitics are confounded by established geographies of underdevelopment.
37 Hookworms illustrate the rarity of situations in which such forms of microbiome
38 management can be achieved. The provision of sanitation, drugs and living organisms
39 is distinctly uneven (cf Braun, 2007). The current focus in Global Health on
40 deworming through vaccination and drug delivery fails to address the socio-
41 ecological drivers of infection intensity. If these programmes were successful, they
42 risk driving future epidemics of autoimmune disease. In short, the rise of the
43 microbiome raises some profound challenges to the geographies of Global Health
44 whose import has yet to be even realised.

Notes

¹ See for example the research gathered in The Translational Microbiome Forum

www.translationalmicrobiome.org/

² For more information on therapeutic helminth providers see: <http://wormswell.com>,

www.autoimmunetherapies.com, <https://tanawisa.com>, <https://biomerestoration.com>, and

<http://www.symmbio.com>.

³ I am grateful to an anonymous reviewer of this paper for the wording of this paragraph.

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Figure 1: Necator americanus (Source CDC)

140x99mm (300 x 300 DPI)

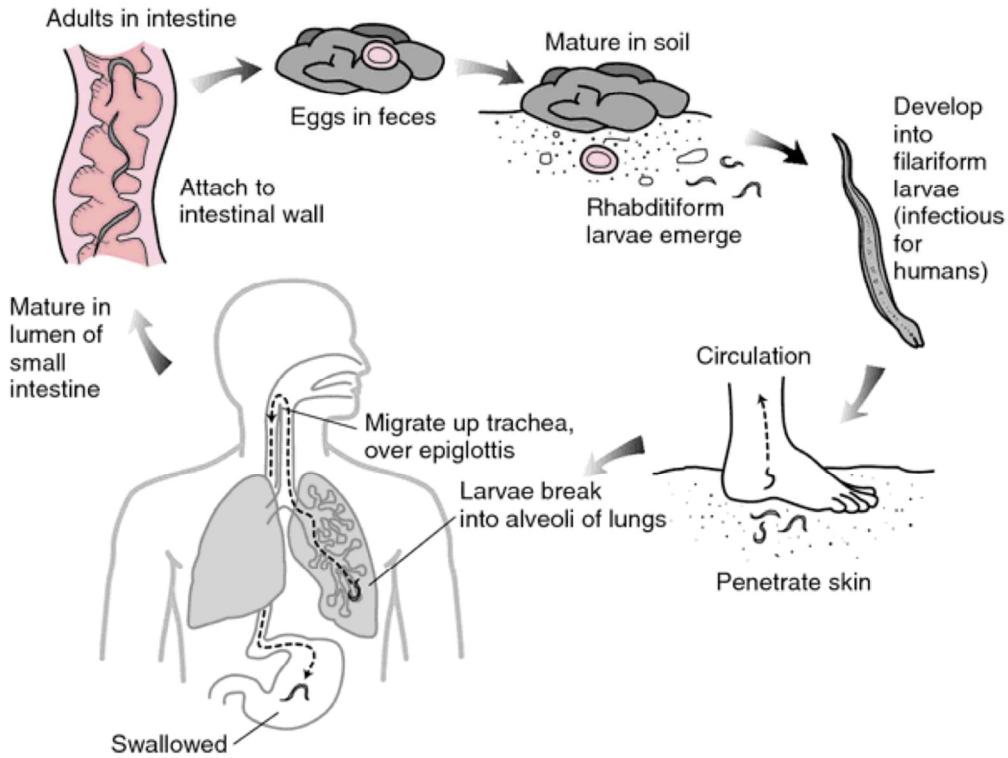
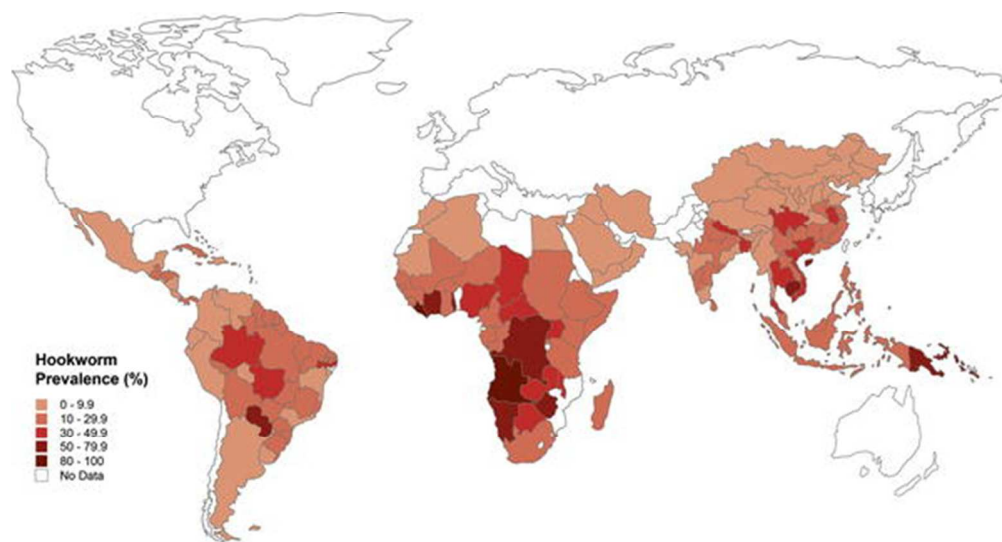


Figure 2: *Necator americanus* lifecycle (Source: CDC)

212x161mm (150 x 150 DPI)



Global distribution of *Necator Americanus* in 2003 (from de Silva 2003)

211x112mm (72 x 72 DPI)