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Once Bitten: Mosquito-Borne Malariotherapy and the Emergence of Ecological Malariology Within and Beyond Imperial Britain

TOM QUICK

SUMMARY: This article explores the extent to which the emergence of networked conceptions of etiology and network-oriented approaches to the organization of medical practice were historically congruent. Focusing on interwar malariology, it contextualizes the development of ecological approaches to infection management and control in terms of mosquito-borne malariotherapeutic practice. In Britain, mosquito breeding programs directed toward the therapeutic infection of mental hospital patients prompted malariologists to modify and refine existing environmental approaches to malaria. Breeding mosquitoes, attending to patients, and maintaining sources of malarial blood modified malariologists' etiological presumptions, contributing to a wider breakdown of associations between race, place, and disease. Simultaneously, the emergence of an international network of malariotherapy-devoted institutions helped transform malariological practice. Examination of a collaboration between British and Romanian malariologists shows one way in which this network contributed to the transformation of malariology from a formal League of Nations–focused endeavor to one distributed along common lines of research and prevention.

KEYWORDS: malaria, mosquitoes, ecology, epidemiology, medical networks

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In recent years approaches to global public health and analysis of its conduct and emergence have converged on discussion of networks and the transmission of materials through them. It is now well established that the history and contemporary practice of public health can be characterized in terms of the emergence of and activity within biological, social, institutional, or technological networks. Whether related in terms of international communication and collaboration, flows of information and materials between actors of various kinds, or ecological "entanglements" of humans and organic nature, knowledge concerning infectious diseases such as malaria is now routinely portrayed as the outcome of multifarious connections among scientists, health officials and vulnerable groups, and their engagements with the natural world.[1] Such characterizations chime with contemporary scientific approaches to the analysis and management of pathogens: in many respects global public health has become a quintessentially ecological science, concerned with tracking distributed flows of organic material and redirecting these along pathways that minimize their potential for harm.[2]

Less well understood is how or why diseases such as malaria came to be conceptualized in terms of the distribution of organic material through networks of exchange in the first place. For example, though it is clear that ecological modes of thought have been critical to

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[1] For an indication of the range of studies of malariology that draw on these concepts compare, e.g., John R. McNeill, *Mosquito Empires: Ecology and War in the Greater Caribbean* (New York: Cambridge University Press, 2010), Rohan Deb Roy, *Malarial Subjects: Empire, Medicine and Nonhumans in British India* (Cambridge: Cambridge University Press, 2017), and Alex M. Nading, *Mosquito Trails: Ecology, Health, and the Politics of Entanglement* (Oakland: University of California Press, 2014).

[2] Franklin White, Lorann Stallones, and John M. Last, *Global Public Health: Ecological Foundations* (Oxford: Oxford University Press, 2013).

the formalization of network-centered approaches to biology (for instance through elaboration of the "food chain" concept), work on their emergence in tropical medicine has concentrated on the role of vector theory and its adoption in the context of field-based studies. Thus the constitution of ecology as the "science of vital interconnections" during the 1930s is considered by and large separately from studies that emphasize the significance of field-based knowledge of particular geographical circumstances for the control of disease.[3] Similarly, while historians of ecology have associated the conceptualization of life in terms of networks of exchange with contemporary articulations of imperial ideals, the emergence of ecological interpretations of disease transmission is often attributed to studies that sought to remain sensitive to the needs and experiences of colonized peoples.[4] How the metropole-

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[3] H. G. Wells, Julian Huxley, and G. P. Wells, *The Science of Life* (London: Cassell, 1931), esp. 946–96, quotation on 820. On the academic development of ecological epidemiology, see, e.g., Andrew Mendelsohn, "From Eradication to Equilibrium: How Epidemics Became Complex after World War I," in *Greater Than the Parts: Holism in Biomedicine, 1920–1950,* ed. Christopher Lawrence and George Weisz (Oxford: Oxford University Press, 1998), 303–31; Warwick Anderson, "Natural Histories of Infectious Disease: Ecological Vision in Twentieth-Century Biomedical Science," *Osiris* 2, no. 19 (2004): 39–61. On the emergence of ecological ideas in the tropical medical field, see, e.g., Helen Tilley, *Africa as a Living Laboratory: Empire, Development and the Problem of Scientific Knowledge, 1870–1950* (Chicago: University of Chicago Press, 2011), chap. 4 and Warwick Anderson, *Colonial Pathologies: American Tropical Medicine, Race, and Hygiene in the Philippines* (Durham, N.C.: Duke University Press, 2006), chap. 8. On climate, race, and tropical medicine during the nineteenth century, see David Arnold, *Colonizing the Body: State Medicine and Epidemic Disease in Nineteenth-Century India* (Berkeley: University of California Press, 1993).

[4] Peder Anker, *Imperial Ecology: Environmental Order in the British Empire, 1895–1945* (Cambridge, Mass.: Harvard University Press, 2001); Tilley, *Africa as a Living Laboratory* (n. 3); E. D. Carter, "Development Narratives and the Uses of Ecology: Malaria Control in Northwest Argentina, 1890–1940," *J. Hist. Geog.* 33 (2007): 619–50.

dominated world of biological theory and the colonial contexts of tropical medicine interacted at this time is as yet unclear.[5]

Building on an emerging body of literature that has begun to unpack the complex relations between practice-centered, field-based, laboratory-based, and theoretical strands of ecological medical thinking during the first half of the twentieth century, this article addresses links between the articulation of this kind of network-oriented theorization and practice and activities that centered in and around the British imperial capital.[6] In so doing, it associates its development with broader political and structural changes in the organization of imperial science before the Second World War.

The article focuses on the hitherto underexamined overlap in interwar British malariology between ecologically inflected ideas of disease transmission and distinct, previously established environmental modes of thought. Discussion of the emergence of ecological ideas in malariology at this time has centered on the growing authority of entomological science within public health, and particularly on the significance of a series of Rockefeller Foundation–funded studies conducted in Italy between 1926 and 1933. These are credited

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[5] Mark Honigsbaum and Pierre-Olivier Méthot, "Introduction: Microbes, Networks, Knowledge—Disease Ecology and Emerging Infectious Diseases in Time of COVID-19," *Hist. Phil. Life Sci.* 42, no. 3 (2020): 28.

[6] Albert G. Way, "The Invisible and Indeterminable Value of Ecology: From Malaria Control to Ecological Research in the American South," *Isis* 106, no. 2 (2015): 310–36; Rachel M. Dentinger, "Patterns of Infection and Patterns of Evolution: How a Malaria Parasite Brought 'Monkeys and Man' Closer Together in the 1960s," *J. Hist. Biol.* 49, no. 2 (2016): 359–95; and Julia R. Cummiskey, "'An Ecological Experiment on the Grand Scale': Creating an Experimental Field in Bwamba, Uganda, 1942–1950," *Isis* 111, no. 1 (2020): 3–21. These all draw in different ways on Robert E. Kohler, *Landscapes and Labscapes: Exploring the Lab-Field Border in Biology* (Chicago: University of Chicago Press, 2002).

with the identification of the "*maculipennis* complex"—the idea that the primary species of mosquito responsible for malaria transmission should in fact be understood as a range of hereditarily distinct types possessing varying capacities for pathogen transmission, whose classificatory differentiation can be achieved via careful examination of their eggs.[7] Malariologists Lewis Hackett and Alberto Missiroli's promotion of this finding is seen as a watershed moment that stemmed from their commitment to the idea that the best way to tackle the disease is to eradicate its insect hosts. Those most committed to the eradication of mosquito "vectors," it is assumed, were most motivated to understand their life cycle and typology.[8] Implied is that this in turn prompted a reconceptualization of malaria in terms of distributed processes of pathogen exchange in specific locales.

Even in the face of such developments, the older environmental idea that malaria is caused in the first instance by climatic conditions held sway longer among practitioners of British tropical medicine than elsewhere. This was in part due to an institutional separation between those responsible for the administration of British science in the imperial metropole and those who undertook field-based practice in its colonies. The concentration of research funding in London and its environs encouraged a differentiation of duties: free from the pressures of day-to-day colonial management, metropolitan theorists of disease continued to conduct studies that had no necessary relation to the sensitivities or needs of places and peoples most affected by malaria.[9] Though a cadre of self-consciously "medical"

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[7] Bernadino Fantini, "Anophelism without Malaria: An Ecological and Epidemiological Puzzle," *Parassitologia* 36 (September 1994): 83–106, 102–6.

[8] E.g., Anderson, *Colonial Pathologies* (n. 3), 209–10 and 214–15; Carter, "Development Narratives" (n. 4), 625.

[9] Douglas Melvin Haynes, "The Social Production of Metropolitan Expertise in Tropical Diseases: The Imperial State, Colonial Service and the Tropical Diseases Research Fund,"

entomologists focused on insect eradication did emerge from within British metropolitan agricultural science during the 1910s and 1920s, their professional interests remained distinct from those that predominated in the gentlemanly world of tropical medical research.[10] While both nascent disciplines were bolstered by programs of imperial "improvement" that aimed to "civilize" colonized peoples through economic development, their very different targets—agricultural yields on the one hand, and bodily capacity for labor on the other—created little motive for collective endeavor. Sustained collaborations between tropical medical researchers and biologically trained entomologists were few and far between in London or indeed elsewhere in Britain at this time.

This article shows that in the British context at least, ecological malariological ideas did not emerge from within entomological science alone but were constituted through the *interaction* of the initially separate realms of entomological and tropical medical practice. It substantiates this claim via examination of a set of circumstances that motivated British malariologist Lt. Col. Sydney Price James to engage closely with entomological concerns that had previously appeared only peripheral to his role as a leading proponent of tropical medicine. At least since his participation in a (somewhat superficial) failed attempt to control malaria solely through mosquito eradication in Myan Mir, India, between 1902 and 1909, James had been a key advocate of climatological or environmentalist approaches to

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Sci. Tech. Soc. 4 (1999): 205–38; Sheldon Watts, "British Development Policies and Malaria in India 1897–c.1929," *Past Pres.* 165, no. 4 (1999): 141–81.

[10] J. F. M. Clark, "Sowing the Seeds of Economic Entomology: House-Flies and the Emergence of Medical Entomology in Britain," *Parassitologia* 50, nos. 3–4 (2008): 321–28; Clark, "Bugs in the System: Insects, Agricultural Science, and Professional Aspirations in Britain, 1890–1920," *Agric. Hist.* 75, no. 1 (2001): 83–114.

malariology.[11] In their support of the idea that malaria incidence had more to do with the overall climatic, agricultural, and developmental conditions of specific territories than with the makeup of local mosquito populations, gentlemanly malariologists such as James, Sir Rickard Christophers, and Patrick Manson helped sustain the idea that the apparently peculiar susceptibility of colonists to malaria in the tropics was a consequence of differential rates of racial "acclimatization" to warm, humid conditions: prolonged intergenerational exposure to malaria had (they contended) caused tropically "native" races to develop constitutional resistance to it.[12] These figures considered malaria in terms of a hierarchy in which territorial, corporeal, and economic development proceeded in tandem: it could, they believed, best be tackled by "improving" housing, promoting technologically complex forms of agriculture, and administering quinine.[13] Yet despite James's initial support for this approach, his research during the 1920s and 1930s would help complicate associations between malaria

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[11] Randall M. Packard, *The Making of a Tropical Disease: A Short History of Malaria* (Baltimore: Johns Hopkins University Press, 2007), 119. On malariology and tropical medicine more generally at this time, see, e.g., Gordon Harrison, *Malaria, Mosquitoes, and Man: A History of Hostilities since 1880* (New York: Dutton, 1978); Leo B. Slater, *War and Disease: Biomedical Research on Malaria in the Twentieth Century* (New Brunswick, N.J.: Rutgers University Press, 2009); and Frank M. Snowden, *The Conquest of Malaria: Italy, 1900–1962* (New Haven, Conn.: Yale University Press, 2006).

[12] Jean Mitchell, "The War on the Anopheles Mosquito: Malaria, Labour and Race in the New Hebrides, 1925–1945," in *Health and Difference: Rendering Human Variation in Colonial Engagements*, ed. Alexandra Witmer and Veronika Lipphardt (New York: Berghahn, 2016), 68–80, esp. 71, and Randall M. Packard, "Indexing Immunity to Malaria in South Africa in the 1920s and 1930s," *Anthr. South. Afr.* 39, no. 2 (2016): 116–30, esp. 117–18.

[13] Arnold, *Colonizing the Body* (n. 3), esp. 33–34 and 282–83; Watts, "British Development" (n. 9), esp. 157–58 and 164–65.

prevalence, climatic conditions, and inherited bodily characteristics. Such complications arose in part through tensions that emerged between British tropical medical theorists' preexisting environmentalist leanings and a new, clinically motivated impulse to understand the specificities of interactions between mosquito, plasmodial, and human life cycles.

The establishment of laboratories and institutions devoted to insect breeding became a critical means by which entomological and tropical medical expertise came into contact in the British imperial metropole. In contrast to the directly malariologically motivated interest in mosquito breeding then emerging elsewhere, mosquito cultivation in Britain found its strongest rationale in a set of practical concerns relating to the clinical treatment of a form of insanity.[14] James thereby came to be involved in a breeding program that was directed in the first instance not toward the study of malaria per se but rather toward the treatment of mental hospital patients, using a new "biological" psychiatric technique known as malariotherapy. Developed by Austrian physician Julius Wagner-Juaregg, malariotherapy provided somewhat reliable (though at times deadly) relief from the effects of what was then known as General Paralysis of the Insane (GPI). While the practice has attracted considerable interest from historians of medicine, only passing attention has been paid to the significance that the utilization of mosquitoes within it had for tropical medicine.[15] Indeed the only recent study to

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[14] On motivations for mosquito breeding in other contexts at this time, see Annick Opinel, "Reconstructing an Epistemological Itinerary: Environmental Theories of Variation in Roubaud's Experiments on Glossina flies and Anopheles, 1900–1938," *Parassitologia* 50, nos. 3–4 (2008): 255–65, esp. 263n30 and Slater, *War and Disease* (n. 11), 48–50.

[15] Joel T. Braslow, "The Influence of a Biological Therapy on Physicians' Narratives and Interrogations: The Case of General Paralysis of the Insane and Malaria Fever Therapy, 1910–1950," *Bull. Hist. Med.* 70, no. 4 (1996): 577–608; Margaret Humphreys, "Whose Body? Which Disease? Studying Malaria while Treating Neurosyphilis," in *Useful Bodies:*

detail malariotherapy's considerable malariological legacy is concerned with its relevance to present-day epidemiology rather than interwar tropical medical practice.[16] As this article shows, however, the precise goals of insect breeding as well as the act of breeding itself helped redirect James's work. Specifically, the utilization of mosquitoes in clinical psychiatry motivated an increasingly careful differentiation of relations between climatic factors and interactions between human, insect, and plasmodial "types," "races," or "strains."[17] Despite the attraction that racially determined interpretations of malarial susceptibility had for James and his peers, ever-finer classificatory differentiation of the biological entities involved in malariotherapeutic practice helped rupture long-standing associations between place, race and disease in British tropical medical thought.

Finally, this article identifies a key institutional context within which ecological malariological thinking more generally was able to thrive during the 1930s. Both the apparent therapeutic success of the London-based program and the opportunities it created for the production of experimental transmission studies encouraged wider adoption of the practice.

Humans in the Service of Medical Science in the Twentieth Century, ed. Jordan Goodman, Anthony McElligott, and Lara Marks (Baltimore: Johns Hopkins University Press, 2003), 53–77; Gayle Davis, *"The Cruel Madness of Love": Sex, Syphilis and Psychiatry in Scotland, 1880–1930* (Amsterdam: Rodopi, 2008), 176–84; Nathaniel Comfort, "The Prisoner as Model Organism: Malaria Research at Stateville Penitentiary," *Stud. Phil. Biol. Biomed. Sci.* 40, no. 3 (2009): 190–203.

[16] F. Ellis McKenzie et al., "Strain Theory of Malaria: The First 50 Years," *Adv. Parasit.* 66 (2008): 1–46.

[17] On the terminological elision between "race," "strain," and "type" in malariology, see Gabriel Gachelin and Annick Opinel, "Theories of Genetics and Evolution and the Development of Medical Entomology in France (1900–1939)," *Parassitologia* 50, nos. 3–4 (2008): 267–78. I follow contemporary usage in this article.

With the establishment of mosquito-borne malariotherapy programs in Romania, Italy, the Netherlands, and the United States, an international network of malariotherapeutic institutions began to emerge. This proved particularly hospitable to epidemiological ideas that emphasized exchange of materials and interaction between bodies in specific locales. While James's principal entomological assistant Percy George Shute remained very much a junior partner during their initial research, the emergence of opportunities for international collaboration increased both his malariological authority and his intellectual independence. By the mid-1930s Shute was collaborating with malariotherapy-concerned colleagues in Romania on self-consciously ecological (rather than simply environment-focused) field studies. Working within the context of the League of Nations Malaria Commission, Shute and James helped foster new models of malariological organization that paralleled then-ascendant "new liberal" ideals of imperial management.[18] In place of the preestablished, strictly hierarchical relationship between metropolitan theorists and colonial practitioners, an approach to malariological organization emerged that, though still weighted decidedly in favor of inhabitants of colonizing lands, at least nominally privileged collaboration between equal scientific peers regardless of race or geographic origin: the elaboration of networked ideas of infection and the establishment of international networks of malariological collaboration proceeded hand in hand during the 1930s.

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[18] See, e.g., Mark Mazower, *No Enchanted Palace: The End of Empire and the Ideological Origins of the United Nations* (Princeton, N.J.: Princeton University Press, 2009), chaps. 1–2; Sunil S. Amrith, *Decolonizing International Health: India and Southeast Asia, 1930–65* (Basingstoke: Palgrave, 2006), chap. 1; and esp. re: malariology, Hughes Evans, "European Malaria Policy in the 1920s and 1930s: The Epidemiology of Minutiae," *Isis* 80, no. 1 (1989): 40–59.

The article begins then by outlining the constitution of a program of mosquito-borne malariotherapy at Horton Mental Hospital in Epsom, Surrey, during the 1920s and early 1930s. It follows James and Shute as they became immersed in the therapeutic program against GPI there. Their initially unique clinical emphasis on using mosquitoes to transfer malaria between human patients, it shows, entailed the collection of a wide variety of "types" or "strains" of both mosquitoes and malarial pathogens. This in turn contributed to a complication of associations between climatic conditions and prevalence of malaria. The second section outlines the significance that Shute and especially James found mosquito-borne malariotherapy to have for malariological science. The renewed attention that mosquito cultivation brought to the ways individuals of different species interacted, it emphasizes, helped prompt a conception of the malarial field as a place in which pathogens were transmitted by variably susceptible populations of humans, insects, and mammals. Finally, it is shown that the above developments had significant implications for the ways in which malariologists approached research and control efforts. At the League of Nations Shute and a group of similarly malariotherapy-concerned Romanian malariologists became key proponents of an explicitly ecological vision of disease control, focused on tracing networks of bodily interaction in specific locales. Addressing this international scientific collaboration foregrounds the ways in which malariotherapy-related malariology, grounded in the institutions devoted to its practice, contributed to a broader reconceptualization of public health on ecological grounds during the 1930s.

Adapting Mosquito Life to the Clinic

Over the course of the 1920s and 1930s Horton Mental Hospital became a critical site for the establishment of ecological understandings of malarial transmission and management in

Britain. GPI constituted one of the most feared and confounding mental pathologies in Western medicine at this time. Characterized by grandiose delusions, dementia, and eventually bodily incapacitation, it came to be associated with syphilitic infection during the first three decades of the twentieth century.[19] By 1918, however, a new and highly promising therapeutic technique had emerged through which the condition would it seemed finally be overcome. Developed by Austrian physician Julius Wagner-Juaregg, malariotherapy targeted recently identified syphilis-causing spirochetes, apparently by raising the temperature of patients' bodies.[20] Though the exact efficacy of malaria remained mysterious, GPI patients thereby found themselves deliberately infected with this fever-causing agent in the interwar years.

For the most part, malaria was transmitted via blood inoculation. This had been the method developed by Wagner-Juaregg, and constituted a simple means of conveying malaria-causing plasmodia between patients' bodies. Transporting syphilitic patients' blood between psychiatric wards presented few technical challenges to psychiatric professionals increasingly enthusiastic about the therapeutic potential of somatic treatment methods.[21] During its early years then, the apparent simplicity of the technique encouraged its rapid expansion.[22] From its primary site in Wagner-Juaregg's Vienna, the approach was taken up first throughout

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[19] Davis, *"Cruel Madness"* (n. 15), 201–4.

[20] Magda Whitrow, *Julius Wagner-Jauregg (1857–1940)* (London: Smith-Gordon and Nishimura, 1993).

[21] See, e.g., Deborah Blythe Doroshow, "Performing a Cure for Schizophrenia: Insulin Coma Therapy on the Wards," *J. Hist. Med. All. Sci.* 62, no. 2 (2007): 213–43.

[22] The National Archives (TNA) MH 51/697: Sydney P. James, "The Treatment of 'General Paralysis of the Insane' by Causing the Patients to Suffer from a Mild Form of Malaria" [minute], May 25, 1923.

continental Europe, then in Britain, the United States, and further afield.[23] In Britain, initial experimentation in 1922 at Whittingham Asylum in Lancashire precipitated its almost immediate countrywide adoption.

British mental hospitals' enthusiasm for malariotherapy rapidly became a matter of concern for the Ministry of Health. Somewhat panicked correspondence between the ministry and hospital superintendents, exacerbated by long-standing fears that malaria could erode the industry and civility of nations, indicates the extent to which practitioners' eagerness to experiment outstripped governmental powers of surveillance.[24] Anxiety regarding the possibility that deliberately infecting patients might result in the general reintroduction of the disease was particularly acute. Shortly after becoming aware of the initial Whittingham study the ministry thereby charged their official advisor on tropical diseases Sydney Price James with investigating the treatment's potential efficacy and associated public health risks.

James was an influential advocate of environmental conceptions of malarial etiology. He had started his career in the Indian Medical Service, participating in efforts against smallpox and yellow fever as well as malaria itself. There, he collaborated with Rickard Christophers, a leading advocate of the notion that malaria could be best combatted through agricultural

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[23] Stefan Wulf, "Malariablut in der Westentasche: Der Beginn der Malariafieber-Therapie gegen die progressive Paralyse in der Hamburger Staatskrankenanstalt Friedrichsberg (5. Juni 1919)," *Medizinhistorisches J.* 52, no. 1 (2017): 2–40; Olga Villasante, "Malaria Therapy in Spain: 100 Years after Its Introduction as a Treatment for the General Paralysis of the Insane," *Hist. Psych.* 31, no. 3 (2020): 325–40; Jesper Vaczy Kragh, "Malaria Fever Therapy for General Paralysis of the Insane in Denmark," *Hist. Psych.* 21, no. 4 (2010): 471–86; Humphreys, "Whose Body?" (n. 15).

[24] E.g., TNA MH 51/697: Letter from R. M. Clark to C. Hubert Bond, June 13, 1923; TNA MH 51/697: Letter from R. H. Steen to C. Hubert Bond, June 11, 1923.

improvement in combination with segregation of "vulnerable" colonists and indigenous populations, and fostering of the latter's supposedly greater "natural resistance."[25] In 1924, James joined the newly formed League of Nations' Malaria Commission and was also a member of the British government's 1927 Fletcher Committee, tasked with advising on the organization of medical research in India.[26] During the commission's early years he followed Christophers in his staunch support of economic development-centered approaches to malaria control, becoming the principal opponent there of both Hackett and his advocation of the prioritization of mosquito eradication measures above other strategies.[27]

James's initial investigatory findings for the ministry emphasized the potential dangers deliberately infecting patients with malaria posed to the British public. Though some hospitals had sought to control mosquitoes in the vicinity of their grounds, most were not even aware of local insect population levels. Given such ignorance, James recommended that all malarial GPI cases "should be segregated in a mosquito proof ward during their period of infectivity"—a suggestion that echoed the racially segregationist control measures then being implemented in West Africa.[28] He also recommended that hospitals without the ability to

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[25] Watts, "British Development" (n. 9), 157–60 and 164–67; Packard, "Indexing Immunity" (n. 12), 117–18.

[26] TNA MH 78/102: Letter from James to G. Buchanan, September 1, 1927; Samuel R. Christophers, "Sydney Price James, 1870–1946," *Biog. Mem. Fell. Roy. Soc.* 15, no. 5 (1947): 507–23.

[27] Iris Borowy, *Coming to Terms with World Health: The League of Nations Health Organization 1921–1946* (Frankfurt: Peter Lang, 2009), 239–55.

[28] TNA MH 55/1713: Letter from James to C. Hubert Bond, November 14, 1923; Stephen Frenkel and John Western, "Pretext or Prophylaxis? Racial Segregation and Malaria Mosquitoes in a British Tropical Colony: Sierra Leone," *Ann. Am. Assoc. Geog.* 78, no. 2 (1988): 211–28.

analyze patients' blood for parasites should refrain from the practice.[29] Nevertheless, probably mindful of general enthusiasm for the procedure, he did not condemn malariotherapy per se. Rather, he proposed to experimentally explore the extent to which patients exposed to the bites of previously uninfected mosquitoes could become vectors from which further transmission might take place.

James thus became involved in malariotherapeutic research via an exploratory study of its risks. Like other malariologists who emphasized climatic causation at this time, he paid particular attention to the human-based stage of the plasmodial life cycle, believing resistance to reflect the racial and constitutional makeup of populations in endemic areas. Just as African and Indian populations were characterized as malarious carriers that threatened the health of "advanced" white settlers, asylum patients constituted potential sources of infection and needed to be managed as such. It was above all however "necessary that we should know whether the[ir] blood . . . is really infective to mosquitoes before we draw up rules" regarding hospital practice.[30] Such investigation, he concluded, required utilization of mental hospital facilities to conduct a preliminary test of "actually conveying malaria by Nature's method."[31]

James may well have considered mental hospital patients as potential stand-ins for colonial subjects from the very start of his malariotherapeutic studies. As Mark Jackson has shown, mental incapacitation was often evaluated within the same unilinear developmental framework as racial difference at this time.[32] Moreover, the notion that both mental and

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[29] James to Bond (n. 28).

[30] James, "Treatment" (n. 22); James to Bond (n. 28).

[31] TNA MH 55/1713: Letter from James to Buchanan, January 11th 1924.

[32] Mark Jackson, "Changing Depictions of Disease: Race, Representation and the History of 'Mongolism,'" in *Race, Science and Medicine, 1700–1960*, ed. Waltraud Ernst and Bernard Harris (London: Routledge, 1999), 167–88.

physical disease could be caused by interruption to the "balance of nature" (e.g., through industrial development or urbanization) played a significant role in both psychiatry and public health in 1920s Britain.[33] Whether or not he consciously saw the ministry's request as an opportunity to replicate "tropical" infection in the relatively controlled confines of a mental hospital, using mosquitoes rather than blood injections likely appealed because it seemed closer to the circumstances accompanying malarial transmission in Britain's colonies.

Initial experiments were conducted during November and December 1923 at institutions in the vicinity of London, including Claybury and Hanwell asylums and the City of London Mental Hospital. Accompanied by Shute, James collected female *Anopheles maculipennis* from a farm ("Mugridges") on the Isle of Grain, a low-lying, marshy, historically malarious area on the Kent coast. These were then taken to patients. Each evening between six and seven o'clock, "feeding bottles" containing the mosquitoes were "fixed by means of long strips of adhesive plaster" to their bodies and remained on them overnight (Figure 1).[34] The mornings following, the bottles were removed to the ministry's laboratory in Carlyle Place.

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[33] See Mark Jackson and Martin D. Moore, eds., *Balancing the Self: Medicine, Politics and the Regulation of Health in the Twentieth Century* (Manchester: Manchester University Press, 2020), esp. Martin D. Moore, "Balance and the 'Good' Diabetic in Britain, c.1900–60," 33–63.

[34] London Metropolitan Archives (LMA) H22/HT/MTU/B/03/006: "G.P.I. and Malaria. Book A. October 31st 1923 to September 29th 1925"; TNA MH 55/1713: Letter from James to R. H. Steen, November 17, 1923. See also *Principles and Methods of Antimalarial Measures in Europe: Second General Report of the Malarial Commission* (Geneva: League of Nations, 1927), 43.

There, they were kept in an incubator for a week, after which they were dissected and examined for sporozoites (the infective stage of plasmodium development).[35]

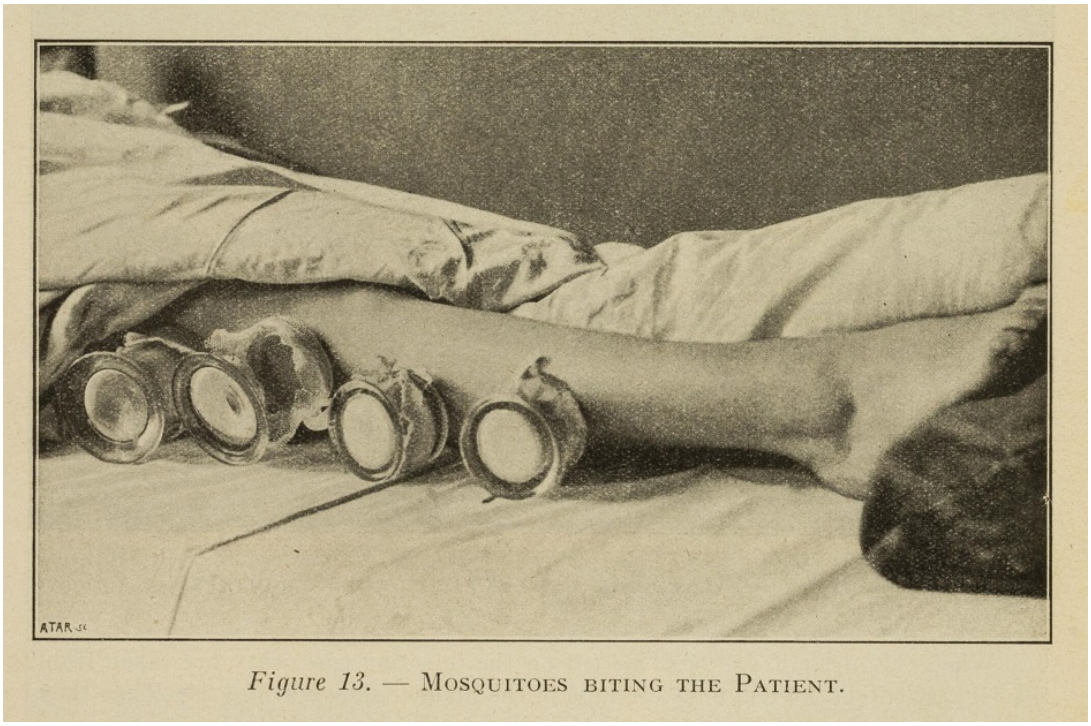

Figure 13. — Mosquitoes biting the Patient.

Figure 1. Illustration of mental hospital patient infection using mosquitoes. From *Principles and Methods of Antimalarial Measures in Europe: Second General Report of the Malarial Commission* (Geneva: League of Nations, 1927), 44, Wellcome Collection, (CC BY-NC 4.0).

Early transmission efforts proved unsuccessful, however. A number of practical problems attended the operation. For starters, batches of collected mosquitoes would begin to die off before suitable patients could be found.[36] Then, when patients did become available, it was not always possible to convey mosquitoes to them. Even when mosquitoes had been "fixed"

[35] James to Steen (n. 34); TNA MH 55/1713: Letter from [James] to [Buchanan], December 15, 1923.

[36] "G.P.I. and Malaria. Book A." (n. 34).

to a patient, it proved "difficult for them to be induced to bite,"[37] and they generally only "fed sparingly."[38] Sporozoites had as a consequence been undetectable in their dissected bodies.

Here then, despite his personal attachment to environmental conceptions of disease causation, it became necessary for James to prioritize the entomological element of malarial transmission. His and Shute's struggles with the deliberate infection of mosquitoes led the pair to pay increasing attention to the circumstances and condition not only of the patients involved in the study but also of the insects applied to them. For example, mosquitoes didn't generally bite if they had recently taken a blood meal elsewhere. It was therefore necessary to take the presence of potential food sources (such as cattle) in the contexts in which they found the insects into account.[39] They also found that temperature both played a critical role in inducing biting and (along with humidity) influenced sporozoite development—observations that initially appeared to support climatic conceptions of disease causation.[40] Infection success was forthcoming once these factors were taken into account. In their initial report on the procedure, the malariologosts considered that it had been only their entomological and parasitological ignorance that had prevented their earliest trials from succeeding.

Having established that careful mosquito care did indeed make it possible to use insects to convey malaria between patients, James and Shute began to address malariotherapeutic treatment itself. James would become an enthusiastic advocate of this clinical technique, and

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[37] James to Buchanan (n. 31).

[38]"G.P.I. and Malaria. Book A." (n. 34).

[39] Ibid.

[40] James to Buchanan (n. 31). Sydney P. James and Percy G. Shute, *League of Nations Health Organization—Malaria Commission: Report on the First Results of Laboratory Work on Malaria in England* (Geneva: League of Nations, 1926), 16.

his lobbying resulted in he and Shute coming to be identified as experts in the ministry's preferred method of malaria inoculation. Consequently, in Britain the cultivation and transportation of infected mosquitoes began to displace the collection and distribution of blood as the primary means by which malariotherapy was conducted. A dedicated malariotherapy ward and mosquito collection station were established in an isolated building at Horton. A sustained "strain" of malaria of the variety *Plasmodium vivax* was cultivated among the hospital's patients and used as the principal source for infection of those in other institutions.[41] Its success depended in large part on the competence of the malariologists as carers and cultivators of mosquitoes.

The growing popularity in Britain of mosquito-borne malariotherapy posed new problems for the conduct of the nascent therapeutic program. Scalability was the most immediate concern. James and Shute sought to respond to increasing demand for infected insects by utilizing mosquitoes' apparent sensitivity to climatic variation. When collected mosquitoes were not needed, they were placed in an "ice chest," in which it was found their life span might be extended by between one and three months.[42] Incubation would alternatively accelerate the development of the mosquito-stomach-piercing "oöcysts" characteristic of infected animals.[43] Mosquito food was also found to be critical to the insects' ability to thrive. Mosquito breeders had previously tended to rely on sugar, water,

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[41] John A. Sinton, "A Report on the Provision & Distribution of Infective Material for the Practice of Malaria-Therapy in England and Wales," in *Ministry of Health Reports on Public Health and Medical Subjects*, vol. 84 (London: Ministry of Health, 1938), 8.

[42] *Principles and Methods* (n. 34), 45; James and Shute, *League of Nations Health Organization* (n. 40).

[43] LMA H22/HT/MTU/B/03/007: "Experiments with All Species of Mosquitoes, Quinine Prophylaxis, Injections with Sporozoites"; Sinton, "Report on the Provision" (n. 41), 14–16.

and fructose-heavy foods such as raisins. James became convinced that this diet reduced insect infectivity, thinking it possible that provision of such food was "not entirely favourable to oöcyst development."[44] A reliable supply of blood food thus became another essential element of the program.

A constant, adequate supply of insects for Britain's GPI cases could not however be maintained through adult mosquito collection alone. The malariologists therefore looked to alternative approaches to cultivation. By gathering and rearing larvae, for example, it would no longer be necessary to use the insects immediately. The development of effective rearing techniques to facilitate this demanded further observation of mosquito lives in the field. Shute (who had gained his initial entry to the world of tropical medicine as a servant of Ronald Ross, tasked with duties considered relatively mundane such as mosquito dissection) noted that overly clean water and the "artificial foods such as dried yeast" relied on by previous investigators tended to produce adults that were "much smaller than normal" and did "not readily bite."[45] He believed that it was necessary instead to re-create the "natural" conditions within which larvae developed, literally carrying the malarial field into the hospital laboratory. Thus he began placing "narrow slices of grass sods . . . cut from a field or hedgerow" into his water-filled cultivation pans—a move that seemed to completely fulfil

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[44] James and Shute, *League of Nations Health Organization* (n. 40), 17.

[45] Percy G. Shute, "A Simple Method of Rearing and Maintaining *Anopheles maculipennis* Throughout the Year in the Laboratory," *J. Trop. Med. Hyg.* 39, no. 20 (1936): 233–35, 233. On Shute, see Leonard Jan Bruch-Chwatt, Percy C. C. Garnham, and Robert Killik-Kendrick, "Obituary: P.G. Shute, O.B.E. (1894–1977)," *Trans. Roy. Soc. Trop. Med. Hyg.* 71, no. 5 (1977): 456–57.

larval nutritional requirements.[46] Rearing mosquitoes according to "nature's method" could, he believed, produce adults at a far greater rate.

Yet even rearing larvae would not provide a reliable enough supply of insects to meet malariotherapeutic demand: larvae still had to be collected and were readily available only at certain times of the year.[47] New strategies of malariological research had nevertheless begun to gain prominence during the program's early years. Other experimental practitioners, including the French malariologist Emile Roubaud, Mark Frederick Boyd in Tallahassee, Florida, and Walter Kikuth of Bayer's laboratories in Germany, began to breed sustained insect populations at this time.[48] Indeed, it was at James's suggestion that Kikuth began infecting his bird model organisms using mosquitoes. Kikuth subsequently founded a breeding facility at the Bayer labs to facilitate this move to "natural" infection methods.[49] Impressed, James instigated a similar program at Horton. Up until this point James and Shute had looked to mosquitoes' already-understood behavior and environment for guidance in their cultivation. As the Horton breeding facility was established, however, it would become clear that the insects both were more diverse and possessed more complex biological capacities than the pair had previously assumed.

By 1933, part of the isolated malariotherapy ward at Horton had been converted into a dedicated mosquito-breeding center. A side room in which patients' blood had been tested was now an "incubation room" maintained at a constant temperature and humidity. Calling

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[46] Shute, "Simple Method" (n. 45), 233.

[47] Sydney P. James, "Some General Results of a Study of Induced Malaria in England," *Trans. Roy. Soc. Trop. Med. Hyg.* 24, no. 5 (1931): 477–538, 480.

[48] On Boyd, see Humphreys, "Whose Body?" (n. 15).

[49] Slater, *War and Disease* (n. 11), 48–50.

on James's colonial contacts, the pair experimented with the "carrying powers" of different mosquito types.[50] Bright, color-coded cages denoting different strains of mosquito in different states of infection lined its shelf-bestowed walls.[51] A "specially built insectory, a fairly large room with a large glass front facing south" was added outside the ward itself. This was "heated with electric bars which are thermostatically controlled" and "shaded by overhanging trees which prevent it from getting too hot in summer."[52] A 1938 report on the center noted that the facility increased both the longevity of the mosquitoes and the overall capacity of Horton as a source of insects for malariotherapy.[53]

Importation of insects and organic materials from malarious regions helped transform Horton from a national site concerned with the local production of malariotherapeutic material into an international center for the study of malaria itself. In addition to diversifying their mosquito stocks, James and Shute gathered a range of geographically distinct plasmodium strains, maintained through continuous infection of patients. Their principal therapeutic type of *Plasmodium vivax* was referred to as the "Madagascar strain" because it had initially been taken from a "Lascar [sailor] from Madagascar."[54] In addition, they experimented with *Plasmodium ovale* obtained from the Liverpool School of Tropical

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[50] "Experiments with All Species" (n. 43). The term "carrying power" was Shute's. See Percy G. Shute and Ernest Ungureanu, "Preliminary Report on the Longevity of the Races of Anopheles Maculipennis," Report to the Health Organization Malaria Commission, League of Nations, C.H./Malaria/273, Geneva, February 21, 1939.

[51] Sinton, "Report on the Provision" (n. 41), 16.

[52] Shute, "Simple Method" (n. 45), 234.

[53] Sinton, "Report on the Provision" (n. 41), 15–18.

[54] LMA H22/HT/MTU/B/03/009: "Benign Tertian Malaria, Madagascar Strain, Indexed"; *Principles and Methods* (n. 34), 39; Sinton, "Report on the Provision" (n. 41), 8.

Medicine, distinct strains of *vivax* from Italy and Romania, both Romanian and "tropical" kinds of *falciparum*, and *knowlesi* imported from India.[55] International connections thus became a critical aspect of the initial emergence of Horton as a site of malariological research. As James would later recall, between 1931 and 1933, "batches of anopheles were received alive at Horton from countries as far distant as British India, West Africa, Uganda and Trinidad, and . . . a number of countries in Europe."[56]

More generally, insectary-bound mosquitoes required constant sources of blood for consumption. This was supplied at Horton by introducing "a small pig" into the building.[57] Pigs were widely recognized as attractive to mosquitoes—James and Shute often targeted pigsties during their collecting missions, and Boyd used a pig to attract his entomological go-betweens.[58] Thus "field" conditions were again imported into the clinical laboratory setting. In the incubation room, where mosquitoes were confined to smaller cages (and malariologists and medical staff needed to move about without pig-sized impediments), feeding was more awkward. Consequently, in addition to accommodating each batch, the color-coded cages on the shelves of the incubator room were adapted to house rabbits. These would be partially shaved, placed on a metal tray, and inserted during meal times.[59]

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[55] James, "Some General Results" (n. 47), 478–79; Sinton, "Report on the Provision" (n. 41), 6–7; Percy G. Shute, "Report on a Third Visit to Roumania for the Study of Malaria—Health Organization Malaria Committee," League of Nations C.H./Malaria/250, Geneva, November 25, 1937.

[56] Sydney P. James, "Advances in Knowledge of Malaria since the War," *Trans. Roy. Soc. Trop. Med. Hyg.* 31, no. 3 (1937): 263–80, on 268.

[57] Shute, "Simple Method" (n. 45), 234.

[58] "Experiments with All Species" (n. 43).

[59] Sinton, "Report on the Provision" (n. 41), 16.

The multiplication of mammalian species, mosquito types, and plasmodium strains at Horton required that James and Shute consider an increasingly complex set of factors relating to malaria transmission. First, the utilization of pigs and rabbits as means of feeding mosquitoes recalled contemporary debates concerning the role of cattle and other animals in control efforts. Perhaps the most influential objection to those who advocated mosquito destruction above other strategies at this time was the so-called anophelism without malaria problem. From the very earliest days of the insect vector hypothesis, malariologists had encountered inconsistencies between the distribution of specific mosquito types and that of malaria. For example, despite the consistent identification of *maculipennis* in malarious areas, they were also found in places free from infection. The presence of *maculipennis* "without malaria" prompted some malariologists to return to ideas of climatic causation, reemphasizing the effects of temperature and humidity on the insects.[60] Most prominently during the 1920s, Roubaud proposed that rather than constituting a biologically uniform population of malaria carriers, races such as *maculipennis* in fact adapted rapidly to local circumstances: if a local area was heavily populated by cattle, the mosquitoes there would develop a heritable "appetite" for bovine blood and consequently stay away from humans.[61] Though James and Shute's early studies also drew on ideas of climatic influence, their use of pigs and rabbits to breed mosquitoes destined for human blood transmission implied a particular stance regarding mosquito classification. Rather than adopt Roubaud's contentions

[60] Fantini, "Anophelism without Malaria" (n. 7), 85–87 and 95–96.

[61] Opinel, "Reconstructing an Epistemological Itinerary" (n. 14), 260–64.

regarding the inheritance of acquired characteristics (and with it associated doubts regarding the biological stability of races), the pair assumed that types remained relatively fixed.[62]

A second consideration concerned the diversity of mosquito types able to carry malaria at all. After Grassi and Ross's initial association of malaria with mosquitoes, it had generally been assumed that responsibility for transmission lay with all mosquitoes of the *anopheles* type. Yet as malariologists began to pay closer attention to the insects in both infected and non-infected areas, it soon became clear both that many different types of *anopheles* existed and that these were not equally susceptible to infection. Moreover, other types were also found to be capable of transmission.[63] Between 1900 and 1930, taxonomists and entomologically oriented malariologists identified a plethora of "infectious" and "non-infectious" mosquitoes. Of these, "infectious" *Anopheles maculipennis*, *pseudopictus*, *culicifacies*, and *quadrimaculatus* were cultivated at Horton. Though the Horton studies would continue to rely on the readily available *maculipennis*, James initially hoped that varieties he presumed to be better adapted to "tropical" conditions such as *culicifacies* would prove more effective carriers.[64] Nevertheless, evaluation of the relative carrying power of each proved difficult.[65] Faced with such ambiguities, James and Shute began to consider the nature of interactions between insect carriers and pathogens, and the extent to which plasmodia from particular locales could be identified with insects from the same region. In not merely collecting and breeding different mosquito types but also attempting to turn these

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[62] On Roubaud's Lamarckism, see Gachelin and Opinel, "Theories of Genetics" (n. 17), 275–76.

[63] The other types included, e.g., *culex* and bird malaria. See Slater, *War and Disease* (n. 11).

[64] James and Shute, *League of Nations Health Organization* (n. 40), 15.

[65] James, "Some General Results" (n. 47), 490.

to practical, clinical ends, the Horton experiments thereby helped challenge any simple identification of specific insect "races" with malaria prevalence.

Finally, the expanding range of plasmodium strains maintained in the hospital brought questions relating to the geographical specificity of interactions of malarial pathogens with human bodies to the fore. During the early decades of the twentieth century, the notion that there existed human races native to the tropics that were somehow more "tolerant" of malaria had provided justification for segregation of colonizing and colonized communities. Even into the 1930s James continued to characterize "dark" Africans as more "resistant" to outbreaks of fever and therefore less in need of medical assistance.[66] Yet the precise grounds on which he made these claims underwent a significant shift after 1923. The following section details the importance that malariotherapeutic studies at Horton had for the conceptualization of both individual and population-based immunity at this time and their implications for Shute and James's recommendations regarding malaria control.

Horton's "Experimental Animals" and Their Malariological Implications

The creation of new sets of interspecies relations at Horton encouraged the elaboration of novel conceptions of the management of malaria in humans. In contrast to both environmentally determinist and mosquito-centered approaches to infection control, the clinical demands of the treatment program prompted a combination of perspectives, grounded in closer consideration of relations *between* human and mosquito bodies alongside the plasmodial life cycle itself.

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[66] Packard, "Indexing Immunity" (n. 12), 118.

As the Horton malariologists came to concern themselves with these interactions, they became increasingly circumspect about making broad statements regarding either the general nature of infection or the relative susceptibility to malaria of whole populations, species, or "races." Malariotherapy's clinical requirement that processes of infection be controlled in particular bodies at specific times helped deepen their appreciation of the pitfalls associated with unqualified malariological generalization. For example, some of their earliest studies highlighted the physiological diversity of plasmodia.[67] Despite British malariology's tendency to offer environmental explanations for changes in symptomatic progression, James and Shute's studies of disparately sourced strains supported the idea that these were at least as much due to physiological plasmodial differences.[68] Further, the previously privileged focus on preventing infection of colonizers came in their work to be supplemented by a keen awareness of the circumstances surrounding the infection of mosquitoes. Thus an early malariotherapy-related article of James's highlighted that he and Shute had emphasized "the factors which are concerned in the transmission of malaria from man to mosquitoes" as well as "from mosquitoes to man."[69]

The Horton studies thereby helped refine existing generalizations regarding the malarial susceptibility of whole insect and human populations. In the first place, James and Shute's clinical studies indicated that the capacity of individual patients to resist infection was primarily dependent on their specific life histories and present circumstances rather than more

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[67] E.g., Sydney P. James, William D. Nicol, and Percy G. Shute, "Plasmodium Ovale Stephens: Passage of the Parasite through Mosquitoes and Successful Transmission by Their Bites," *Ann. Trop. Med. Parasitol.* 26, no. 2 (1932): 139–45.

[68] James, "Advances in Knowledge" (n. 56), 270.

[69] Sydney P. James, "Epidemiological Results of a Laboratory Study of Malaria in England," *Trans. Roy. Soc. Trop. Med. Hyg.* 20, no. 3 (1926): 143–65, on 146.

general environmental or hereditary factors. The point was made most clearly in studies of GPI patient "re-infection." This was considered therapeutically necessary when initial infection resulted in only a temporary cessation of syphilitic symptoms.[70] However, it often proved difficult to induce a second malarial attack in patients using the same strain. Despite James's continuing commitment to racial differentiation in treatment programs, his and Shute's experiments with imported strains did not thereby support notions of geographic or population-based susceptibility: an individual who had gained resistance to one plasmodia type seemed to remain vulnerable to others regardless of their ancestry or living conditions.[71] Indeed, even when only one type such as *vivax* was used, simply substituting a strain of it taken from a different locale was often enough to cause the appearance of a second symptomatic bout in an otherwise "immune" patient.

These findings prompted further speculation regarding differences in mosquito carrying power. Rather than attending to the infectivity of whole races or strains of mosquito, the pair increasingly came to emphasize differences between individual insects. Variation among *maculipennis*, for example, seemed to imply that the physiological range of individuals within any one type was at least as important a factor as differences between *maculipennis* and other taxonomic varieties. Whether resistance to infection was due to the size of a mosquito's proboscis or oesophageal opening, their capacity to take on blood, or (as James suggested at one point) their ability to "absorb" plasmodial zygotes before they could "come to maturity," the pair had by 1931 arrived at the conclusion that differences in infection

[70] James, "Some General Results" (n. 47), 495.

[71] Ibid., 537.

frequency were "too great to be attributed to any other reason than that [mosquito] individuals of the same species . . . vary greatly."[72]

These observations appeared of great malariological import to the two scientists. Variable insect susceptibility became an important point of departure for James's pronouncements on malarial control during the 1930s, helping bolster his preexisting skepticism of the tendency of entomologically focused theorists to emphasize mosquito eradication campaigns to the exclusion of other strategies. Successful malaria transmission was, he argued, largely dependent on a minority of mosquitoes (such as those at Horton) that had led a "sheltered life . . . protected against sun, wind and rain . . . unfavourable changes of temperature and . . . natural enemies."[73] Investigations of "the particular and exact . . . life histor[ies] of the few individual mosquitoes" that "become . . . malaria-transmitter[s]" would open up the possibility of deploying control measures targeted only at those that led "an abnormal life."[74] Again in line with his environmentalist leanings, James initially considered unnatural "house-bound" mosquitoes to be the principal vectors and contended that eradication measures should primarily be directed within homes in the first instance.[75]

James and Shute's newfound experiences with infection in a clinical setting appeared to have significant implications for the conduct of malariological research, too. While James at least implicitly admitted that previously advanced environmental theories had failed to engage adequately with entomological science, he resisted the conclusion that the field as a whole should henceforth defer to parasitological and entomological investigation. Indeed, at a

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[72] Ibid., 487.

[73] James, "Epidemiological Results" (n. 69), 155.

[74] Ibid., 155–56.

[75] On the context for this stance see Frenkel and Western, "Pretext or Prophylaxis?" (n. 28).

1933 Royal Society of Tropical Medicine and Hygiene debate on bird malaria, he declared that such laboratory-based studies "may be very misleading as a guide to what happens in human malaria."[76] Instead, he argued, it was necessary to develop a detailed understanding of the specific developmental circumstances of those bodies (mosquito, human, or otherwise) that displayed particular vulnerability to the disease. On the one hand, this would imply recognition that clinical settings such as Horton themselves constituted more directly epidemiologically relevant "laboratory conditions" than did bird-centered studies.[77] Conventional laboratory-based scientists in Britain appeared sympathetic on this point, with renowned malariologist J. Gordon Thomson noting his professional envy of research opportunities at Horton in which "man, owing to an accident, had become an experimental animal."[78] Yet James also emphasized that his finding that the circumstances required for malarial transmission were highly specific implied a need for far more detailed, localized malariological field study than had been conducted hitherto. "One who fully appreciates the importance" of his conclusions, he claimed, would "begin at once to study the habits of the particular individual mosquitoes which get into the dangerous infective condition."[79]

A second, related strand of research at Horton seemed even more significant for the articulation and conduct of malariological epidemiology. In 1934–35, a serious epidemic swept across what was then the British colony of Ceylon, severely impacting trade and according to some estimates wiping out over eighty thousand people (around two percent of

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[76] J. Gordon Thomson, "Immunity in Malaria," *Trans. Roy. Soc. Trop. Med. Hyg.* 36, no. 6 (1933): 483–514, quotation on 506.

[77] James, "Epidemiological Results" (n. 69), 157.

[78] James "Some General Results" (n. 47), 529.

[79] James, "Epidemiological Results" (n. 69), 155–56.

the population).[80] The devastation prompted a rash of speculation on the conditions that had allowed the disease to spread: as far as malariologists were aware there had always been some level of malarial infection on the island. Why then, they asked, had there been an especially deadly outbreak at that point?

James and Shute believed that their clinical studies provided a key to the mystery. These indicated that malariologists should pay close attention to the specific circumstances of transmission and infection. Their attempts to infect especially resistant patients at Horton had led them to experiment with their exposure to increasingly large doses of plasmodia, in the hope that this would overcome any inherent bodily capacity to fight the disease. Subjecting patients to repeat mosquito feedings, it seemed, could "break down" immunity.[81] Equally, the technique could transform mosquitoes that at first seemed completely incapable of transmission into carriers.[82] Most significantly, the pair believed that through careful passing of *vivax* between mosquitoes and humans, they had created a malaria strain that induced symptoms comparable in severity to those seen in the Ceylon epidemic.[83] Contrary to the primarily economic and social causes cited in many discussions of the matter, pandemic events such as that in Ceylon could they believed be attributed in large part to changes in the extent to which human and mosquito populations were exposed to one another, alongside changes in the nature of the infective agent itself. It was therefore not so much the combination of a priori distinct "environmental" and "entomological" factors that determined

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[80] Kalinga Tudor Silva, *Decolonization, Development and Disease: A Social History of Malaria in Sri Lanka* (New Delhi: Orient Blackswan, 2014), chap. 3.

[81] Sydney P. James, William D. Nicol, and Percy G. Shute, "Clinical and Parasitological Observations on Induced Malaria," *Proc. Roy. Soc. Med.* 29 (1936): 879–94, 885.

[82] James, "Epidemiological Results" (n. 69), 148.

[83] James, Nicol, and Shute, "Clinical and Parasitological Observations" (n. 81), 879–81.

its seriousness, but rather the development, nature, and behavior of populations of man, insect, and parasite as each intersected with the others on the ground.[84]

James again made sure to hedge his and Shute's claims, suggesting that the most important conclusions to be drawn concerned the research strategies of malariologists rather than the general nature of epidemics. Above all, he argued, greater attention needed to be paid to the specificities of interactions between mosquitoes, plasmodia, humans, and other animals in malarious locales. "Intensive study of individual infants and children in a localised hyperendemic area" was particularly urgent: "Enquiry should start with the newly born, and each individual should be placed under continuous observation until the usual age of naturally acquired immunity is reached."[85] In the short term at least, such recommendations appeared influential. James proudly reported toward the end of the 1930s that it was "now generally recognized that a 'malaria survey' must include clinical and parasitological study, over a considerable period, of selected individuals."[86]

Despite James's modesty regarding the immediate relevance of his and Shute's conclusions to control efforts, it was clear that they had the potential to significantly alter prevailing malariological attitudes and beliefs. Imperialists' concern with the vulnerability of Europeans to "tropical" malaria types, for example, would be placed on a different footing once it was realized (as Christophers put it) that "those on shooting or other expeditions into the jungle" were often subjected to "massive inoculation of sporozoites."[87] If James and Shute were to be believed, any natural resistance of colonists on such expeditions would be

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[84] Ibid., 879 and 892.

[85] James "Some General Results" (n. 47), 497.

[86] James, "Advances in Knowledge" (n. 56), 269–70.

[87] James, Nicol, and Shute, "Clinical and Parasitological Observations" (n. 81), 893.

overcome far more rapidly than if they were to remain in towns or villages. The implication was clear: if all bodies were in principle equally susceptible to infection, directly racial or constitutional explanations would become increasingly redundant. In a similar vein, James began cautioning against the then-contentious proposal that quinine be administered daily as a "prophylactic" in malarious areas. This would, he warned, risk masking low-level asymptomatic infection among vulnerable populations, resulting in more individuals experiencing severe "clinical attacks" when deadlier strains appeared.[88] That this conclusion implied a continuing disavowal of medical intervention among those James had previously characterized as constitutionally "resistant" to the disease is perhaps unsurprising. Yet it was also the case that the Horton studies had rendered the contention that variable susceptibility could be attributed to inherited or climate-induced physiological difference untenable. The Northern European patients there were just as capable of acquiring "immunity" to particular strains as were those who had lived in malarious regions their whole lives.

Taken together, these conclusions helped foster a new conception of the place of malariology in the management of public health. Most obviously, the claim that small changes in the circumstances of transmission could greatly alter infection rates implied a need for finer-grained field analysis than even that envisaged by entomological theorists. It would be vital to enlist locally knowledgeable investigators wherever such surveys were to be carried out. In this regard James's recommendations implied greater authority be accorded fieldworkers with long-term connections to the places that they studied. It is notable that he cited survey work in Tanganyika (then emerging as a major center for ecology-influenced

[88] James "Some General Results" (n. 47), 515.

investigations of the Tsetse fly and sleeping sickness) in this regard.[89] Just as his and Shute's work called the concept of inherent racial differences in susceptibility into question, it also implied elevation of the scientific authority of indigenous representatives in malariological study. Their proposals thereby resonated with the then-ascendant "new liberal" conception of imperial management, in that they supported investment in the training and "improvement" of indigenous scientific capabilities rather than the direct imposition of control measures from the imperial metropole.[90] It is further notable that it was at the League of Nations—also the institution in which new liberal values gained greatest purchase—that their claims found their most enthusiastic reception.

New liberal ideals, in which the training of local elites would be supervised and encouraged by experts from more "advanced" territories, also influenced the direction of the pair's clinically focused experiments. During James and Shute's tenure, Horton was transformed from a relatively obscure mental hospital into an international center for malariological research and training. As early as 1930 James reported that plasmodia had been "successfully conveyed in [Horton] mosquitoes to Holland, Italy, Germany, Malta, Roumania and Spain for the purpose of malariatherapy in those countries."[91] Mosquitoes were also used as traveling research objects. The scientists conveyed their own breed of *maculipennis* to Missiroli's malariological laboratory in Rome, in an attempt to gauge their susceptibility to infection from the blood of Italian malaria sufferers.[92] Infected mosquitoes

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[89] James, "Advances in Knowledge" (n. 56), 270; Tilley, *Africa as a Living Laboratory* (n. 3), chap. 4. On ecology in British tropical medicine, see also Carter, "Development Narratives" (n. 4), 645–46.

[90] See n. 18.

[91] TNA MH 78/102: Letter from James to [Buchanan], June 13, 1930.

[92] "Experiments with All Species" (n. 43).

were similarly transferred to the town of Iași in Romania and used on GPI cases housed in the recently founded Socola Psychiatric Hospital there.[93]

Opening Horton up to the global community of malariologists in this way had profound effects on both the institution itself and the malariotherapeutic practices that went on inside it. For example, funding anxieties quickly evaporated with the arrival of an international scientific audience. James reported to the Ministry of Health that Horton had become a "training centre for . . . 'malariologists' in British Dominions and Colonies."[94] In addition to educating officers from as far afield as Uganda, Egypt, and the United States, "distinguished professors from France, Germany, Italy, Greece and other countries" had "made special journeys to England to visit the centre."[95] Even more encouragingly, Horton-modeled institutions were founded in Romania, Italy, the Netherlands, and the United States during the 1930s.[96] As well as further legitimating experiments at Horton in the eyes of government officials, these new sites constituted sources of scientific support and exchange. As the center of an expanding, international network of simultaneously clinically and entomologically focused malariological practice, then, James and Shute were able to extend their investigative practices into territories (such as Romania and Italy) in which malaria posed a direct threat.[97]

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[93] Shute, "Report on a Third Visit" (n. 55).

[94] James to [Buchanan] (n. 91).

[95] Ibid.

[96] James, "Advances in Knowledge" (n. 56), 267.

[97] The continued asymmetry of power relations both among malariologists and between colonizers and colonized subjects at this time should not be forgotten. Though there isn't space to elaborate the point here, James's introduction of monkeys to Horton as potential replacements for mental hospital patients offers a stark illustration of prevailing attitudes regarding racial difference at this time. Compare Robert Knowles and Biraj M. Das Gupta, "A Study of Monkey-Malaria, and Its Experimental Transmission to Man," *Indian Med.*

As a longtime supporter of antimalarial policies centered broadly on economic and environmental improvement, such a development could not have come at a better time for James. The malariological appeal of strategies associated with this approach, including adding mosquito nets to houses, irrigating land to improve productivity, and establishing large-scale quinine administration programs, had begun to fade in the face of Hackett and the Rockefeller Foundation's successful (and seemingly cheaper and self-sustaining) programs centered solely on the eradication of mosquitoes.[98] As the following section demonstrates, the development of explicitly ecological conceptualizations of malarial transmission within the then-emergent malariotherapeutic institutional network helped renew justifications for pluralism in antimalarial practice, in the process recasting eradication as one legitimate strategy among many for those malariologists (James included) who had previously staunchly opposed it.

Malariotherapeutic Malariology Beyond the Limits of Empire

By the second half of the 1930s, the Horton scientists' international collaborations had begun to feed into then-emerging efforts to systematically distinguish mosquito types. Famously, Hackett and Missiroli drew entomological attention at this time to mosquito eggs as a means of differentiating between otherwise physiologically similar *maculipennis* varieties. At Horton Shute also paid particular attention to the differentiation of *maculipennis.* His responsibility for mosquito care and the development of breeding technique there placed him

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Gazette 67, no. 6 (1932): 301–20; "Monkey Malaria in G.P.I.," *British. Med. J.* 2, no. 3901 (October 12, 1935): 672–73; and William D. Nicol, "Correspondence: Monkey Malaria in G.P.I.," *British Med. J.* 2, no. 3902 (October 19, 1935): 760.

[98] Evans, "European Malaria Policy" (n. 18), 44–45.

in an ideal position to contribute to contemporary classificatory shifts. However, whereas Hackett adopted an egg-centered taxonomic strategy at least in part in an attempt to divert malariological interest away from the prevention of symptoms in sufferers and onto attempts to eradicate mosquito "vectors," Shute initially remained primarily concerned with the propagation of mosquito life.[99] Nevertheless, Hackett's entomological program and that of the Horton malariologists converged in a mutual interest in categorization in terms of whole life cycles—an approach critical to the redefinition of *maculipennis* as an ecological "complex" rather than a single "species."

The circulation of a geographically diverse range of malariologists into and out of Horton had expanded the range of research opportunities available to James and Shute. By the mid-1930s James hardly depended on his Horton contacts of course. It is notable however that Shute became increasingly active in international malariology from this time. It is also significant that Shute's principal collaborators also utilized mosquito-borne malariotherapeutic techniques. The establishment of a network of institutions devoted to the practice influenced the pair's approach to epidemiological collaboration, in the process helping transform malariology from an endeavor primarily enacted through formal League of Nations–organized meetings to one in which particular laboratories and field stations became linked through their adoption of common approaches to research and prevention.

The constitution of this network also facilitated an ecological redefinition of relations between mosquitoes, plasmodia, and human populations. Notably, field researchers also involved in malariotherapeutic practice incorporated James and Shute's observations regarding the variability of individual mosquitoes into their studies. In the first place, strains

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[99] Percy G. Shute, "A Study of Laboratory-Bred *Anopheles maculipennis* var. *Atroparvus*, with Special Reference to Egg-Laying," *Ann. Trop. Med. Parasit.* 30, no. 1 (1936): 11–16.

that it had proven difficult to infect Horton's original *maculipennis* with proved readily transmissible when mosquitoes were sourced from elsewhere. As James noted, he and Shute had been "inclined to think that our own *maculipennis* of England . . . a race refractory to *P. falciparum*, until, by taking a batch to Italy, we found that 50 per cent. of [mosquito] individuals readily became infected."[100] Studies conducted at Socola produced similar results.[101] Like people who had developed a resistance to particular kinds of plasmodia, mosquitoes that had been exposed to one particular malaria strain appeared less able to transmit that strain a second time. It was thereby necessary to consider the "life histories" not only of exposed human populations, but of mosquitoes too.

Again, the malariologists increasingly emphasized interactions between insect, human, and animal populations rather than environmental conditions or physiological differences. Shute's collaboration with a group of Romanian researchers led by Professor Mihai Ciucă of Iaşi University became particularly significant in this regard. Ciucă had visited Horton in 1930 in his capacity of secretary of the Malaria Commission. He also arranged for one of his research staff, Dr. Maria Chelarescu-Vieru, to train at the hospital. Other colleagues of his, notably parasitologist Ernest Ungureanu, followed during the subsequent decade.[102] As the 1930s progressed, Shute's malariological interests became ever more entangled with the concerns of these visitors. His informal advice in support of the Romanian malariotherapy

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[100] James, "Some General Results" (n. 47), 488.

[101] Mihai Ciucă, L. Ballif, and Maria Chelarescu-Vieru, "Immunity in Malaria," *Trans. Roy. Soc. Trop. Med. Hyg.* 27, no. 6 (1934): 619–22.

[102] Shute, "Report on a Third Visit" (n. 55). See also S. P. James and M. Ciuca, "Species and Races of Human Malaria Parasites and a Note on Immunity," in *Acta Conventus Tertii de Tropicis Atque Malariae Morbis*, vol. 2 (Amsterdam: Societas Neerlandica Medicinae Tropicae, 1938), 269–81.

program helped foster the connection. Having spent a year at Horton, Chelarescu-Vieru had taken on responsibility for introducing the mosquito-based therapeutic approach at Socola. Yet she had had great difficulty adapting Shute's mosquito-breeding technique, finding that her insects suffered unfathomably high morbidity rates. Failure to resolve the problem via correspondence in 1934 drew Shute on a research trip to Iași with batches of his own mosquitoes in tow.[103] Testing whether Horton mosquitoes could survive in the Romanian context threw the extent to which longevity varied between different varieties of *maculipennis* into sharp relief. Shute's *maculipennis* "*atroparvus*," it turned out, lived far longer than the mixture of "*typicus*" and "*messeae*" varieties bred by Chelarescu-Vieru.[104]

This concern with the cultivation of mosquitoes for use in Romanian malariotherapy quickly broadened out into a more strictly malariological interest in Iași itself. Ungureanu became a particularly close collaborator after Ciucă instructed him to "devote himself to ecological studies."[105] Shute would return numerous times to collaborate with Ungureanu on malariological investigations in the nearby villages of Tomeşti and Osoi.[106] These field studies were initially justified in terms of their capacity to inform malariotherapeutic practice: in 1937 Shute reported to the commission that because "most of the villages around Jassy [*sic*] are malarious," Socola patients offered "a good opportunity for studying immunological

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[103] London School of Hygiene and Tropical Medicine (LSHTM) GB 0809 Shute/05: Percy G. Shute, "A Note on the Habits of *A. maculipennis* as Observed during a Recent Tour of Roumania and Bessarabia. Report to the Malaria Commission, League of Nations. Geneva. June 1935."

[104] Shute and Ungureanu, "Preliminary Report" (n. 50), ii.

[105] Ibid.

[106] Shute, "Report on a Third Visit" (n. 55).

effects and other problems" connected with GPI.[107] Yet the pair were becoming ever more fascinated with the conditions of malarial transmission itself. The same report laid the groundwork for a new, explicitly field-centered project. As he noted to his sponsors, though he had not "see[n] very much field work" on his trip, there was similarly "much to be done in ecological studies" there.[108]

Shute and Ungureanu's collaborative investigations centered on Osoi. Significantly, they were primarily concerned with establishing the relative longevity of the three *maculipennis* types endemic to the area (also *typicus*, *atroparvus*, and *messae*) under the "natural" conditions of a typical "peasant" house. The local dispensary was commandeered as a makeshift laboratory, within which similar conditions to these dwellings would be re-created. Horton served as a model for this space. Each night, batches of recently reared mosquitoes of each variety would be allowed to feed on either rabbits or, if they refused these, a local pony.[109] Some mosquitoes were deliberately infected with malaria to test whether or not carrying the disease shortened their lives. At the same time, almost identical conditions would be created for the same mosquito types at Horton (with the insectary pig serving in place of the pony).[110] The researchers presumed that by supplying each type with sufficient blood and recording the humidity and temperature in their respective artificial habitats, it would be possible to estimate their typical "natural" life spans.

These experiments are especially notable for the extent to which they identified the artificial conditions necessary for malariotherapeutic mosquito breeding and the deliberate

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[107] Ibid.

[108] Ibid.

[109] Shute, "Note on the Habits" (n. 103).

[110] Shute and Ungureanu, "Preliminary Report" (n. 50).

exchange of pathogens between bodies with actual conditions in villages throughout Romania. Shute and Ungureanu drew a direct parallel between malaria transmission "in the wild" and that which prevailed at Horton. It was thus suggested (in direct opposition to Roubaud) that *maculipennis* were "quite indifferent as to their source of food supply, whether . . . oxen, horses, pigs, or man."[111] Instead, mosquito carrying power was primarily affected by the relative longevity of each type.[112] This gave their research a different inflection to ecological studies grounded more firmly in entomological classification. In contrast to Hackett's concern with distinguishing between infective and non-infective *maculipennis* varieties, Shute contended that all might act as carriers were they to live long enough. Thus, when reputedly harmless, short-lived types such as *messeae* were present in "enormous numbers," some might succeed in transmitting the disease.[113] The typical village, with its mixture of cow sheds, pony stables, chicken coops, and human housing, constituted a complex set of relations that could be highly misleading to the untrained eye. Merely finding specimens in a chicken coop, for example, by no means implied that chickens sustained that kind of mosquito: tests on blood samples from such places indicated that the insects were often simply resting after feeding on a mammal.[114] Transmission and propagation had to be

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[111] Shute, "Note on the Habits" (n. 103).

[112] Shute and Ungureanu, "Preliminary Report" (n. 50).

[113] LSHTM GB 0809 Shute/05: Percy G. Shute, "A Review of Malaria Conditions at Osiou with Some Suggestions for Future Malaria Control Work." For a bibliographical overview of contemporary biological control efforts in malariology, see John B. Gerberich and Marshall Laird, *An Annotated Bibliography of Papers Relating to the Control of Mosquitos by the Use of Fish (Revised and Enlarged to 1965)*, World Health Organization, document WHO/Mal/66.562, https://apps.who.int/iris/handle/10665/65337.

[114] Shute, "A Review of Malaria Conditions" (n. 113).

understood in relation to the total living population (animal and human) of a particular locale and the specific life histories of all beings within it.

Shute and Ungureanu's explicitly ecological malariology thereby helped maintain interest in control strategies in which malariologists, increasingly inured to climatological etiology, had begun to lose faith. Instead of replacing approaches such as drainage, housing improvement, segregation of communities, or pharmaceutical "prophylaxis" with a singular focus on mosquito control, the emphasis that their studies put on local context shifted attention to situations in which *each* technique might constitute an appropriate response. Rather than argue about ideal overall solutions, it was incumbent upon properly trained malariologists to select the most effective available given the local situation and resources at hand. Mosquito destruction remained very much on the agenda: at Osio, the primary breeding ground was a "shallow, narrow and semi-stagnant" stream two kilometers from the village center, which made it an ideal eradication target.[115] In other situations however, more environmentally oriented strategies such as the redesign of buildings or relocation of animal accommodation would offer greater protection.[116] Such methodological pluralism encouraged devolution of control policy, and it is in this latter respect that Shute and Ungureanu's studies most obviously overlapped with Hackett's 1937 *Malaria in Europe* (subtitled *An Ecological Study* but containing little explicit discussion of ecology per se). Regarding malarial management, Hackett stated authoritatively that "governments can trust to no formulas . . . but must . . . define and resolve their own problems, locality by locality."[117]

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[115] Ibid.

[116] Shute, "Note on the Habits" (n. 103).

[117] Lewis W. Hackett, *Malaria in Europe: An Ecological Study* (London: Oxford University Press, 1937), 274.

Hence Shute and Ungureanu's investigations contributed to a growing sense among malariologists that disease management should be the responsibility of local rather than supranational authorities. In 1937 the League of Nations' Inter-Governmental Conference of Far-Eastern Countries on Rural Hygiene, held in Bandoeng (Indonesia), both called for "responsibility for malaria control" to "rest squarely on . . . the public health policy of a country" and highlighted a "serious lack of information as to the bionomics [ecological relations] even of . . . dangerous malaria carriers."[118] The same year, the league's Health Organization called for attention to be paid to a technique of malariological control that would place even more emphasis on the significance of organic relations in particular locales: "biological" methods including "the stocking of rivers and stagnant pools with [larvae-eating] fish" and "the destruction of mosquito larva by parasites" appeared to raise the prospect of popularizing truly "naturalistic" control approaches.[119] Again, such beliefs depended on a renewed interest in the management of specific sites rather than singular, overarching solutions.

Ecological malariological strategies thus overlapped with calls for international public health to become more sensitive to the particular concerns of new and emerging nations. Historians have justifiably read calls to devolve responsibility for malaria control to local authorities as both an indication of the increasing unworkability of the Malaria Commission in the face of the rising Western nationalisms of this time, and an implicit endorsement of the

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[118] *League of Nations Health Organization: Report of the Intergovernmental Conference of Far-Eastern Countries on Rural Hygiene* (Geneva: League of Nations, 1937), 90 and 96.
[119] *League of Nations Health Organization: Report to the Council on the Work of the Twenty-Fifth Session of the Health Committee* (Geneva: League of Nations, 1937), 5.

reluctance of colonial authorities to administer to the health of subject populations.[120] Nevertheless, calls for devolution also reflected a growing sense that prescribing interventions without a thorough awareness of how humans, mosquitoes, and other animals interacted in the specific contexts concerned could be highly problematic. As the lingering (if diffuse) presence of racial categories and climatological assumptions in early ecological malariology indicates, the "new liberal" ideals of interstate conduct that had emerged over the previous three decades implied not abandonment of colonial authority but rather a diffraction of it into new areas: in the case of malariology, it should now (ideologues believed) be the responsibility of metropole-trained tropical medical experts to guide appropriately "local" policies and practices. Though the league's commission would be disbanded just as these ideals were beginning to find traction, the malariological vision that it helped foster raised the prospect of a new, biologically oriented rearticulation of epidemiological authority on "ecological" rather than either "environmental" or "entomological" grounds.

Conclusion

This article has shown how some malariologists came to adopt ecologically rather than environmentally or entomologically oriented conceptions of disease transmission and control during the 1930s. In so doing, it has reaffirmed the historical entanglement of ecological concepts regarding the circulation of organic material through networks of exchange and the development of "new liberal" approaches to imperial management noted by historians of biology.[121] Far from being fostered solely among academic biologists, this association also

[120] See esp. Amrith, *Decolonizing International Health* (n. 18), chap. 1.

[121] Anker, *Imperial Ecology* (n. 4).

emerged in connection with colonially oriented approaches to tropical medical practice. Indeed, the articulation of a strand of ecological tropical medicine that emphasized the biological histories of and relations between diverse kinds of macroscopic and microscopic being stemmed at least in part from attempts to adopt prior, more explicitly colonialist environmental modes of thought to changing metropolitan institutional contexts. The establishment of laboratories devoted to clinically oriented insect breeding prompted tropical medical researchers who had hitherto shown little sustained interest in entomology-focused control approaches to attend more closely to insect life. Yet the purposes for which they did this gave their studies a different inflection to those centered principally on entomological physiology or classification. The malariotherapeutic need to take account of the responses of human as well as diverse animal bodies encouraged articulation of a broader conception of ecological interaction, in which the life histories and biological relations of local human populations had to be considered alongside those of plasmodia, insects, and other mammals.

Further, this article indicates that the development of at least some strands of ecological malarial thought depended as much on the construction of networks of similarly oriented institutions as it did on either activities of individual malariologists or work within particular research projects. The transformation of environmentally or climatologically determinist assumptions within malariotherapy-oriented networks of collaboration highlights that emerging conceptions of tropical disease causation were always embedded within broader structural changes in the organization of medicine (and thus, by implication, of states and empires too). While the significance at this time of studies conducted by representatives of colonially subjugated territories for the formation of ecological medical thought should in no way be diminished, it is also necessary to recall the often implicit presence within it of older colonial ideologies. In Britain at the very least, ecological tropical medicine emerged both

from experimental and survey work conducted in colonial settings and from imperial metropolitan clinics and laboratories. Indeed it might even be said to have initially been characterized by attempts to negotiate tensions between these locales, rather than activities centered on one or another of them.

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TOM QUICK obtained his Ph.D. from UCL Centre for the History of Medicine in 2011 and has since worked as a television presenter, developed a digital platform for writing collaboration and source analysis, and published widely. His current work concerns intersections between biomedical and logistical science and practice.

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