The influence of vector-borne disease on human history: socio-ecological mechanisms

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Abstract

Vector-borne diseases (VBDs) are embedded within complex socio-ecological systems. While research has traditionally focused on direct effects of VBDs on morbidity and mortality, it is increasingly clear that VBD impacts are much more pervasive, dynamically linked to feedbacks between environmental conditions, vector ecology, disease burden, and societal responses that drive transmission. VBDs have had profound influence on human history via mechanisms that include: (1) killing or debilitating large numbers of people, with direct demographic and population-level impacts; (2) differentially affecting populations based on prior history of disease exposure, immunity, and resistance; (3) being weaponized to promote or justify existing hierarchies of power, colonialism, racism, classism, and sexism; (4) catalyzing changes in ideas, institutions, infrastructure, technologies, and social practices in efforts to control disease outbreaks; and (5) changing human relationships with the land and environment. We use historical and archaeological evidence interpreted through an ecological lens to illustrate how four major VBDs have shaped society and culture: plague, malaria, yellow fever, and trypanosomiasis. By comparing across diseases, time periods, and geographies, this review highlights the enormous scope and variety of mechanisms by which VBDs have influenced human history from the age of early *Homo sapiens* to the modern context.

Introduction

Vector-borne diseases (VBDs)—illnesses caused by pathogens transmitted by biting arthropods—have played a major role in human history. Today, VBDs account for more than one billion cases, one million deaths, and one-sixth of worldwide disability and illness annually (World Health Organization 2014), disproportionately impacting communities left impoverished and recovering from colonialism. While research in disease ecology predominantly focuses on the direct morbidity and mortality of VBDs, their true effects are much more pervasive. Understanding the full arc of VBD impacts on human history requires both knowledge of how those diseases and their vectors interact with the environment, and placing those dynamics within a societal and cultural context. Here, we aim to synthesize the extent and mechanisms of this influence, emphasizing connections between disease ecology and the societal, geographical, and environmental setting of historical places and times.

VBDs have affected human history via multiple socio-ecological mechanisms: (1) killing or debilitating large numbers of people, with direct demographic and population-level impacts; (2) differentially affecting populations based on prior history of disease exposure, immunity, and resistance; (3) being weaponized to promote or justify existing hierarchies of power, colonialism, racism, classism, and sexism; (4) catalyzing changes in ideas, institutions, infrastructure, technologies, and social practices in efforts to control disease outbreaks; and (5) changing human relationships with the land and environment. Because the impacts of VBDs include both direct demographic effects and indirect societal effects that are intimately linked to human-modified environments and social structures, we cannot understand their full impact without first considering feedbacks within underlying socio-ecological systems (Fig. 1).

151

152 The complex effects of VBDs on society and the environment requires recognizing the
153 prominent role that racism (i.e., a system of advantage based on race) has played in many aspects
154 of VBD ecology and social responses to disease. Of Roberts and Rizzo's psychological factors
155 that contribute to American racism (Roberts & Rizzo 2020), three have been particularly
156 important in the global context of VBDs. *Hierarchy* perpetuates the notion that high-status
157 groups are (and should be) more valuable than low-status groups. *Power* codifies racism through
158 the establishment of social norms, allocation of resources, and formation of policy. *Segregation*
159 ensures that habitable surroundings are accessible to some and inaccessible to others. By
160 emerging from and perpetuating social hierarchy, power, and segregation, VBDs have been
161 intimately linked to maintaining and reinforcing racism throughout history. Further, VBDs'
162 direct and indirect effects on population health are often mediated by racism, along with sexism,
163 classism, and colonialism, across geography and time periods.

164

165 To understand the complex interplay between social and ecological mechanisms driving the
166 impact of VBDs on humans throughout history, we synthesize historical and archaeological
167 evidence within an ecological context (see Box 1 for a discussion of the narrative style and
168 interdisciplinarity of this review). We present case studies from four major diseases—plague,
169 malaria, yellow fever, and trypanosomiasis— selected for their profound and multimodal
170 influence from the age of early humans to the present day, though the underlying mechanisms
171 apply more broadly across all VBDs with high burdens (Fig. 2; Table 1). Each disease has a
172 unique ecology determined by the habitat, breeding, and biting preferences of its vector, which

interacts with human social structures and geography to shape VBD effects (Box 2). While there are a few well-known consequences of VBDs on human history, such as malaria selecting for sickle cell and hemoglobin-related traits, and yellow fever and malaria contributing to the failed French attempt to build the Panama Canal, these are often framed as anomalous events. Here, we highlight examples that illustrate lesser-known mechanisms and historical impacts to argue for the generality and pervasiveness of the socio-environmental consequences of VBDs.

Plague

Disease Ecology

Plague, caused by the bacterium *Yersinia pestis*, is one of just a few VBDs (also including murine typhus) that is maintained in enzootic cycles with rodents and fleas (see Box 3 for disease ecology terms). While *Y. pestis* typically causes low mortality in rodent hosts, it occasionally causes massive die-offs, putting humans at higher exposure risk as rodent fleas seek alternative hosts (Gage & Kosoy 2005). Plague causes three major forms of human disease: bubonic (lymph nodes), septicemic (blood), and pneumonic (lungs), the latter of which can be transmitted among people via airborne droplets. All forms have high fatality rates without antibiotic treatment. Plague is endemic to Africa, the Americas, and Asia; the disease is typically found in semi-arid forests and grasslands (Stenseth *et al.* 2008), but can also exist in densely-populated urban environments. While current rates of human morbidity and mortality due to plague are low, it has exhibited a persistent influence.

(i) Neolithic Revolution in Eurasia

196 Evidence suggests that plague outbreaks emerged from the sanitation and public health
197 shortcomings of early urban hubs, contributing to the downfall of the Cucuteni-Trypillian society
198 and other agricultural settlements more than 5,000 years ago (Rascovan *et al.* 2019). From
199 around 5500 BCE in Eastern Europe, the Cucuteni-Trypillian culture inhabited mega-settlements
200 of tens of thousands of people living in compact arrangements of houses with poor sanitation,
201 high densities of animals, and accumulated food storage: ideal conditions for rodents and plague
202 (Barrett *et al.* 1998). Around 3400 BCE, many buildings were abandoned and burned, residents
203 perished or moved, and mega-settlements collapsed. Phylogenetic and genomic analyses from
204 prehistoric human remains revealed that multiple independent lineages of *Y. pestis* spread across
205 Eurasia during this decline, likely through early trade routes and wheeled transport (Rascovan *et*
206 *al.* 2019). This is one of the earliest known examples of the built environment leading to a major
207 VBD epidemic, which in turn wiped out the human settlement and with it the population density
208 needed to sustain disease transmission (Table 2).
209
210 **(ii) Middle Ages in Europe**
211 The Plague of Justinian (541–544 CE), one of the world's deadliest pandemics, was part of an
212 emerging pattern of trade and urbanization fueling plague pandemics of a magnitude that
213 upended empires and economic systems. As large settlements and transcontinental empires
214 emerged in Medieval Europe, the Plague of Justinian facilitated changing agricultural practices
215 and socio-politics around Constantinople, the capital of the Byzantine Empire. The outbreak was
216 initiated by plague-infected rat fleas found aboard merchant grain ships from Egypt (Haensch *et*
217 *al.* 2010). Plague-infected farmers were unable to tend their crops, inflating grain prices,
218 decreasing tax revenues, and causing famine (Sabbatani *et al.* 2012). Human mobility between

ports spread the plague, critically weakening the Byzantine Empire and ushering in the invasion of the Kingdom of the Lombards (Evans 2005).

The Black Death in the mid-1300s CE, the most well-known plague pandemic, caused large-scale demographic changes that helped to topple the European feudal system by altering the distribution of power among social classes, and in turn facilitating forest regrowth. The Black Death killed tens of millions of people—an estimated 30% of Europe's population (McEvedy 1988; Raoult *et al.* 2013). Even before the arrival of plague in medieval Europe, population growth and rising demand for labor threatened the feudal system (Moore 2002). The subsequent labor shortage following the Black Death increased serf wages and power (Clark 2016), expanding economic freedom for the surviving serfs and making the feudal system unprofitable (Gelman 1979; Blockmans 1980). This demographic and economic transition led to large-scale land abandonment, reduced agricultural activity and grazing, prompted woodland regrowth, and altered human-environment interactions (Williams 2000; Yeloff & Van Geel 2007). Arable land decreased and forest area increased in Southern England from 1307–1377 (Poos 1991), while in France and Denmark pollen cover increased beginning in 1375 due to agricultural decline and reforestation (Stebich *et al.* 2005). The Black Death transformed not just the economy but also the ecological landscape, which in turn would reduce opportunities for plague transmission in urban areas.

(iii) Modern Plague Epidemics in Asia

Society-disrupting plague pandemics in Asia, occurring alongside underlying societal unrest, caused large-scale mortality. In the Yunnan Province of China, a major 19th century plague

pandemic arose from rodent reservoirs in a society undergoing demographic and economic change and volatility from ethnic conflict. Tension culminated in the Panthay (Du Wenxiu) Rebellion (1856–1873), in which Muslim Hui miners rebelled against the Qing following several decades of ethnic and class disputes. Plague killed many Imperial soldiers and was disseminated via mass refugee and troop displacement, resulting in the depopulation of Yunnan Province during the conflict (Peckham 2016). Villages were rapidly deserted following successive epidemic years of plague and other infectious diseases (Benedict 1988); in a single county, 70–80% of the population perished likely due to the plague (Rocher 1879; Benedict 1988). The outbreak, which spiraled into the Third Plague Pandemic, had huge death tolls across Asia.

Although plague epidemics have become more rare since the advent of modern antibiotics, one recent outlier illustrates the continued influence of feedbacks among urbanization, mobility, plague, and social change that can occur within inequitable societal structures. The Indian city of Surat, formerly a key port for the British East India Company, was reshaped by the legacy of exploitative colonial mercantilism, mismanagement, and a pervasive caste hierarchy promoted by the British administration (Wisner *et al.* 2004; Barnes 2014). Surat's resulting poverty and corruption, rapid influx of migrant laborers, and segregation among classes led to unsanitary conditions and under-developed infrastructure (Jacobsen 1996; Dutt *et al.* 2006). This set the stage for an outbreak of over one thousand cases of plague in Surat in 1994, with deaths primarily occurring among lower castes and socioeconomic groups (Barnes 2014), similar to the previous Third Plague Pandemic (Klein 1988). Over half a million people (one-fourth of the population) emigrated from Surat within two days, leading to mass shutdown of businesses and declines in tourism (Dutt *et al.* 2006). In response, the city bolstered its infrastructure, sanitation,

and food hygiene standards (Chatterjee 2015), ultimately becoming a nation-wide model for sanitation and reducing potential for plague transmission.

Malaria

Disease Ecology

Like many of humanity's highest-burden VBDs (Table 1), malaria is transmitted by mosquitoes. Malaria is caused by protozoan *Plasmodium* parasites (primarily *P. falciparum, P. malariae, P. vivax,* and *P. ovale*) and transmitted to humans by *Anopheles* mosquitoes (Dutta & Dutt 1978). Infection with malaria manifests as recurring fever and flu-like symptoms, but severe cases can progress to organ dysfunction, anemia, and death (Bartoloni and Zammarchi 2012). *P. malariae* existed hundreds of thousands of years before human origins and was the only species found among pre-agrarian hunter-gatherer populations of Eurasia and Africa (Carter & Mendis 2002). The other *Plasmodium* species emerged from African non-human primates into humans and migrated out of Africa with humans: *P. vivax* spread to Arabia and Eurasia between 30,000 and 10,000 years ago; *P. ovale* spread to tropical areas like New Guinea approximately 4,000 years ago (Carter & Mendis 2002); *P. falciparum* emerged around the same time in Africa, and over several millennia expanded into Europe, Asia, and eventually to the Americas during the transatlantic slave trade (Rodrigues *et al.* 2018). Unlike the other VBDs described here, the life cycle of the four predominant human malaria parasites occurs almost exclusively within humans and mosquitoes, with no important non-human hosts (although spillover of human malaria into primates and primate malaria into humans does occur) (Faust & Dobson 2015; Grigg & Snounou 2017).

Human movement, malaria control, and climate are key drivers of malaria dynamics, with moderate temperatures required for parasite transmission and sufficient rainfall needed for larval mosquito habitat (Thomson *et al.* 2006; Béguin *et al.* 2011; Mordecai *et al.* 2013; Yamana & Eltahir 2013). Malaria historically occurred in environments ranging from irrigated rice, cotton, and sugarcane plantations in the swampy lowcountry of North America to the Amazon's forest fringes. Although historically distributed throughout temperate and tropical zones in 140 countries, control efforts have restricted malaria to 88 countries in the tropics and subtropics, often centered on agricultural areas undergoing land conversion (Martens *et al.* 1995; Hay *et al.* 2004; Zahouli *et al.* 2017). Today, the vast majority (over 90%) of the 228 million global malaria cases and 405,000 deaths (estimated for 2018) are concentrated in sub-Saharan Africa (World Health Organization 2019, 2020). Malaria has had such a profound influence throughout human history that genetic mutations associated with malaria resistance, such as sickle cell and Duffy-negative alleles, remain widespread in human populations historically exposed to high malaria burdens, especially in Africa and Southeast Asia; this evidence has been reviewed extensively elsewhere (Allison 2009).

(i) Ancient Rome to Modern Italy

Malaria transmission has been associated with, and has shaped, human agricultural and settlement activities throughout history. During the Roman Empire, malaria depressed the agrarian economy and affected demography across the Italian Peninsula, starting in the Imperial period (ca. 100 CE) if not earlier. Archaeological and historical evidence includes biomarkers of the disease detected within Roman-era human skeletal remains from Apulia, Umbria, and

311 Campania; a Late Antique child cemetery linked to a malaria epidemic; and Roman author
312 Cicero's letters to his friend Atticus detailing quartan fevers between 50–49 BCE (Sallares 2002;
313 Soren 2003; Marciniak *et al.* 2016). Romans recognized its major symptom (recurrent fever), and
314 understood that it was tied to environments like marshlands (Sallares 2002). Malaria in Roman
315 Italy likely resulted from the interplay of pan-Mediterannean trade, which promoted the spread
316 of the parasite and its vector from the South and East, and villa estate agriculture, which
317 increased the availability of suitable vector breeding habitat (Sallares *et al.* 2004; Yasuoka &
318 Levins 2007; Harper 2017). Hotspots of malaria probably occurred near coastal marshes, low-
319 lying flood plains, and within the city of Rome, due to wet and warm conditions (Di Luca *et al.*
320 2009).
321
322 Malaria likely reinforced class and gender inequities in Roman Italy, as it often does today
323 (Heggenhougen *et al.* 2003; Shah 2010; WHO 2018). Many enslaved and poor men were forced
324 to live and work in low-lying agricultural fields and unsanitary housing during peak malaria
325 seasons, exposing them to vector bites (Joshel 2010). They lacked access to the high-altitude
326 (non-malarious) rural estates to which wealthy elite Romans retreated in the summer and fall
327 (Sallares 2002). Women in the ancient Roman world were mostly confined indoors and away
328 from swampy, countryside environments (Knapp 2011); malaria's capacity to cause miscarriage
329 and fetal abnormalities and its increased severity in pregant women and children (Saito *et al.*
330 2020) may have contributed to the enforcement of this oppressive social structure.
331
332 Malaria-suitable habitat, land use, settlement patterns, and cultural practices were tightly
333 intertwined in early civilizations in Italy. As early as the Bronze Age, the Nuragic civilization

(1700–238 BCE) on the island of Sardinia adapted their housing and agricultural practices to malaria (Brown 1986; Setzer 2010). While most pastoralist cultures reside in lowlands near the most productive grazing grounds, Sardinian pastoralists established summer settlements in high-elevation areas and grazed lowlands only during winter months with lower malaria risk (Brown 1981, 1986). Like the Romans, Sardinians restricted women (especially pregnant women) to the home and away from the more malarious countryside (Brown 1986).

The ecology of malaria in Italy was tied to inequitable economic systems and human movement, which in turn promoted malaria transmission. The malaria burden increased after the unification of Italy in 1861, as deforestation in the Apennines mountains caused erosion that flooded rivers and created coastal lagoons that increased mosquito breeding habitat (Snowden 2008). In turn, this high burden of malaria discouraged investment in agriculture, left vast tracts of land minimally cultivated, and maintained high mosquito populations via accumulated water. Agriculture in the formerly-Roman South was still dominated by villa estate agriculture, which required an influx of hundreds of thousands of migrant laborers to harvest wheat during peak malaria season (Snowden 2008). These impoverished workers slept in open huts and had poor nutrition, increasing their exposure and susceptibility to malaria. Southern Italy's high malaria burden was a major factor contributing to the Italian diaspora, in which millions emigrated to the Western hemisphere in the late 19th and early 20th centuries (Snowden 2008).

The Italian government's recognition that social and ecological systems together perpetuated malaria prompted the establishment of new social infrastructure to combat the disease. By 1900, Italy had learned that malaria was transmitted by mosquitoes and could be treated with quinine.

Recognizing that the population most at risk was impoverished, illiterate, and did not trust physicians or quinine pills, national malariologists viewed malaria as a social disease and aimed to transform society by empowering the rural poor and earning their trust (Snowden 2008). Rural schools and health centers were developed to teach the population about mosquitoes and to distribute quinine, which together drastically reduced malaria incidence, illiteracy, and overall morbidity and mortality (Snowden 2008). By the beginning of World War I, the geographic area affected by malaria had contracted and deaths had been reduced to one-eighth of their previous levels (Snowden 2008). In this instance, response to malaria led to solutions that enhanced health and wellbeing.

(ii) American Revolution, Civil War, and Reconstruction

The convergence of favorable ecological conditions and differential histories of exposure and resistance to severe disease allowed malaria to play a decisive role in the American Revolution (1775–1783). The humid, swampy Chesapeake and Carolina lowcountry and irrigated rice plantations created ideal environments for *Anopheles* mosquitoes (McCandless 2007). While many Continental Army militiamen had acquired malaria resistance through repeated exposure growing up in the South, most British troops had not previously been exposed (McNeill 2010). After besieging Charleston early in 1780, British general Charles Cornwallis found his troops in a hostile, unfamiliar environment (McNeill 2010). Malaria infection (along with typhoid) incapacitated British forces, with less than half of Cornwallis' troops healthy and able to fight (Humphreys 2001; McNeill 2010). This ultimately led to the British defeat and surrender at Yorktown, which tipped the scales of the Revolutionary War in favor of the Americans (McNeill 2010).

In contrast to its asymmetric effects on the American Revolution, malaria, and more specifically a failure to understand the habitat and climatic drivers of malaria ecology, negatively impacted both sides of the American Civil War (1861–1865). Malaria was responsible for a significant portion of the disease-related casualties and burden, forcing campaigns to be abandoned and prolonging the war (Bell 2010; Lockwood 2012). During the campaign to take Vicksburg in 1862, Union General Winfield Scott encouraged waiting until November, after the "return of frosts," which would reduce fevers in latitudes below Memphis (Lockwood 2009). When his advice was ignored and the campaign began in the summer, malaria decimated Union regiments, and the campaign failed. Confederate troops attempted to recapture Baton Rouge in August 1862 following the Union retreat from Vicksburg, but unexpectedly lost two-thirds of their troops while en-route, largely to malaria, allowing Union troops to narrowly escape defeat (Steiner 1968). The impact of malaria thus postponed campaigns, stretched the duration of the war, and increased the human death toll (Sartin 1993).

Landowners weaponized malaria from the post-war period into the 20th century to justify racial hierarchy, maintain social power, and segregate themselves from at-risk environments, which reinforced exploitation of Black people. Black sharecroppers on rice and sugarcane plantations inhabited porous housing, were overworked and malnourished, and were not allowed access to adequate medical care (Humphreys 2001), contributing to the period of Reconstruction considered the "nadir of Black health status" in America (Byrd & Clayton 1992). White landowners created and perpetuated environments where Black workers were constantly exposed to mosquito bites and suffered a high burden of malaria and other diseases (see Box 1 for a note

403 on capitalization of racial groups). Racist landowners and proponents of eugenics asserted that
404 the higher burden of disease in Black people was due to underlying biological and moral
405 weaknesses associated with race, and used such arguments to justify refusing to improve Black
406 sharecroppers' living conditions and to legitimize Jim Crow laws (Hoffman 1896; Humphreys
407 2001). In this way, malaria interacted with landowner-imposed living conditions and the status
408 quo hierarchy to entrench the social position of Black people in the American South. By contrast,
409 malaria was less of a burden in Louisiana and Arkansas plantations, where Black farmhands
410 lived in towns instead of "bedraggled huts" and conditions, though still terrible, were
411 comparatively better for reducing malaria exposure (Barber 1946; Humphreys 2001).
412
413 **(iii) Modern Global Conflict**
414 Combatants in both World Wars weaponized the ecology of European malaria, in some cases
415 intentionally, to inflict maximum military and civilian damage, leaving behind a devastated
416 socio-ecological landscape that reversed decades of malaria control efforts. In Southern Europe,
417 trenches and artillery craters became prime mosquito breeding habitats, and troop movement
418 brought malaria to areas where it had been eradicated (Snowden 2008). The wars interrupted
419 Italy's anti-malaria campaigns by disrupting the quinine supply, shutting down clinics, and
420 requisitioning livestock such that their role in zooprophylaxis (diverting mosquito bites from
421 humans) was eliminated (Snowden 2008). After World War I, it took six years to reduce malaria
422 back to pre-war levels. In World War II, Nazis used malaria as a barrier to Allied troops'
423 advance and arguably as biological warfare against Italian civilians, whom they viewed as
424 disloyal for switching allegiance (Snowden 2008). The Nazis demolished over 2,000 mosquito-
425 proofed homes and reversed pumps to flood 98,000 acres of former marshland near Rome with

426 seawater, promoting habitat for the most competent local malaria vector, *An. lambranchiae*
427 (Snowden 2008). In the worst-affected places, *An. lambranchiae* became the dominant mosquito
428 species, rising from 30% to 100% of all mosquitoes and causing over 90% of civilians to become
429 infected with malaria (Snowden 2008). Despite this staggering human cost, malaria had little
430 effect on the outcome of either war due to its nearly equal effect on both sides of the conflicts.
431
432 Malaria also played a substantial role in modern conflicts in Asia, lengthening the Pacific
433 Theater of World War II and the Vietnam War by causing significant mortality on both sides of
434 these conflicts. Malaria in WWII contributed to the largest number of military and civilian
435 casualties for any war in human history, debilitating Allied and Axis Powers. U.S. Army General
436 Douglas MacArthur summarized the impact: “This will be a long war if for every division I have
437 facing the enemy I must count on a second division in hospital with malaria and a third division
438 convalescing from this debilitating disease” (MacLeod 1999). Malaria in the Pacific forced the
439 surrender of U.S. troops in Bataan, Philippines and the evacuation of Japanese forces from
440 Guadalcanal (Joy 1999). Malaria also prolonged the Vietnam War (1955–1975): U.S. troops
441 reported over 24,000 cases and nearly 400,000 sick-days due to the disease (Beadle & Hoffman
442 1993). Malaria prevalence among Viet Cong troops was 50–75%, and soldiers may have raided
443 plantations and dispensaries for drugs to treat symptoms (Bruce-Chwatt 1985).
444
445 The massive death toll and weaponization of malaria during modern global conflicts sparked
446 major public health efforts to manage the socio-ecology of disease transmission, as governments
447 recognized it as a national security threat. The Malaria Control in War Areas (MCWA) program
448 was established during World War II to manage malaria around military bases in the Southern

U.S. and minimize lost productivity. MCWA trained local and state health department officials on control techniques. This led to the creation, in 1946, of what became the Centers for Disease Control and Prevention (CDC), with the primary mission of preventing malaria spread across the nation (Parascandola 1996). The CDC's scope has since expanded to become the premier U.S. government agency responsible for disease prevention and surveillance.

Yellow Fever

Disease Ecology

Like malaria, yellow fever is transmitted by mosquitoes. The primary vector of yellow fever, *Aedes aegypti*, also transmits other flaviviruses like dengue, Zika, and Japanese encephalitis as well as alphaviruses like chikungunya and Ross River. Yellow fever is an acute disease caused by an RNA virus (Barnett 2007), with symptoms including hemorrhaging, jaundice, vomiting, muscle pain, and often death (McGuinness *et al.* 2017). The disease is endemic in tropical regions of the Americas and Africa and is maintained in a sylvatic cycle of transmission between non-human primates and tree-hole breeding mosquitoes (Barrett & Monath 2003). Spillover from the sylvatic cycle can result in urban outbreaks of yellow fever with transmission primarily between humans and *Ae. aegypti* mosquitoes (Miller *et al.* 1989). In Africa, an intermediate or savannah cycle has been identified with mixed transmission between mosquitoes, humans, and non-human primates (Barrett & Monath 2003). Historically, *Ae. aegypti* thrived in sugar and other monoculture plantations that provided ample storage containers for mosquito breeding and had fewer insectivorous birds compared to forests (Fig. 1) (McNeill 2010).

Children are more likely than adults to survive yellow fever infection, which confers long-term immunity. Differential immunity between groups varying in previous yellow fever exposure and immunity played a central role in determining the outcomes of conflict, particularly before the discovery of the mosquito transmission cycle and a highly effective vaccine in the early 20th century (McNeill 2010). Related to true differential immunity is *immunocapital*: socially-acknowledged and often socially-constructed differences in disease susceptibility that reinforce the power and privilege of White men, particularly prevalent in the American South (Olivarius 2019).

(i) Colonization and Empire in the Americas

The institutionalization of Black slavery—one of the most exploitative social and economic systems in history—was driven by profiteering and rationalized by racism that intersected with vector-borne disease. In Barbados, English settlers arriving in 1627 initially relied on indigenous captives and White indentured servant labor (Gragg *et al.* 2003; Beckles 2016), until a 1642 treaty allowed access to Portuguese slave dungeons on the African coast (Great Britain & Chalmers 1790). Slave vessels, along with *Ae. aegypti* mosquitoes, soon arrived and caused a major yellow fever epidemic by 1647 (Cray 2015). The immensely profitable system of chattel slavery, in which slaveowners could generate profits from enslaved people until their deaths, was made even more profitable by the fact that African people died of yellow fever at about half the rate of other people in Barbados, likely due to previous exposure and immunity. With this system of unprecedented exploitation in place, slavery became ingrained as the island's primary labor system and rendered Barbados the first full-fledged slave society—and richest American colony—in the British Empire (Berlin 2009; Beckles 2016). The Barbados Slave Code of 1661

provided the legal framework for slavery that extended to other British colonies including Jamaica, Virginia, and South Carolina (Thomas 1930; Nicholson 1994; Dunn 2012; Beckles 2016). Yellow fever spread to other Caribbean islands through commerce. The introduction of *Ae. aegypti* and yellow fever into the Americas and the establishment of plantation ecology were thus intimately linked to the establishment of slavery in the Americas.

Throughout colonial conflicts in the Americas, yellow fever ecology combined with differential immunity to create geographical strategic advantages for those inhabiting and defending colonies against invaders (McNeill 2010). For example, differential immunity aided native Haitians in their fight for independence from France in the turn of the 19th century. The economy of the French colony of Saint-Domingue (now Haiti) was based on sugar and coffee plantations that depended on African slave labor, making it the richest colony in the world and an ecologically suitable environment for yellow fever transmission (Perry 2008). Toussaint L'ouverture, freed from slavery and governing in the name of the French Republic, led enslaved people in revolts between 1791 and 1804, drawing French troops into guerrilla battles away from coastal enclaves and resupply ships, where they were vulnerable to yellow fever (Bell 2009). Yellow fever killed many of the 23,000 immunologically naïve troops Emperor Napoleon Bonaparte deployed to Haiti in 1801 (Bollet & Jay 2004), as well as 10,000 replacement soldiers by 1803. Following these losses, Haiti gained independence in 1804, becoming the first successful slave uprising that led to the establishment of a new country ruled by formerly enslaved people (Maingot 1996). The victory was followed by the massacre of the remaining White colonizers (Girard 2011), creating a "terrified consciousness" among plantation owners in the Americas that led to heightened cruelty against enslaved people in an attempt to suppress revolts (Maingot 1996;

Michael Byrd & Clayton 2000). Realizing major defeat in the Americas and fearing further losses, Napoleon sold the Louisiana territory to the United States and withdrew from the continent.

Just five years later Napoleon would use other VBDs as biological weapons against the largest British force ever assembled in the invasion of Walcheren, Netherlands. Recalling a disastrous French expedition to the swampy island years earlier, Napoleon breached dikes on the Dutch countryside, flooding the area with brackish water to create mosquito habitat, and declared: "We must oppose the English with nothing but fever, which will soon devour them all" (Winegard 2019). Within months, 40% of the British force were debilitated with malaria, typhus, and other diseases, while the French declared victory with minimal combat engagement (Howard 1999).

(ii) Industrial Revolution and Racism in North America

The crowded urban environments of early America, ripe for yellow fever outbreaks, became the catalyst for public health and infrastructure development that effectively reduced transmission, despite the mosquito transmission pathway of the disease remaining unknown. In 1793, Philadelphia had high population density (50,000 residents) and few safeguards to handle a deadly yellow fever outbreak, which originated from French colonizers fleeing Haiti and killed over 5,000 (Foster *et al.* 1998). Seeking a solution to its dirty well water, which citizens believed caused yellow fever (Levine 2010), the city government's Watering Committee commissioned Philadelphia's first municipal water system in 1800 to provide potable drinking water, ended unhygienic water collection, and constructed storm sewers and sewage pipes (Donaldson 1987). The yellow fever epidemic also prompted the creation of the Board of Health—a foundation for

the modern U.S. healthcare system—which implemented sanitary and housing inspection, enforced vaccination of children against diseases like smallpox, chlorinated the water supply, and produced diphtheria antitoxin (Higgins 2016).

Concurrently, false claims of immunity were weaponized during the 1793 Philadelphia yellow fever epidemic to exploit Black labor and entrench social hierarchies in a population that was 94% White and 6% Black (Hogarth 2019). Based on medical treatises that falsely stated that Black people were more resistant to yellow fever, Dr. Benjamin Rush, a prominent White physician, put out a call in the public papers and mobilized leaders in the Black community to urge Black people to volunteer to assist the sick, who were primarily White (Jones & Allen 1794; Hogarth 2019). Many free Black people, believing Dr. Rush's claims that they were immune, nursed sick White people, removed corpses, and connected orphaned children to care, while nearly one-third of White residents fled the city (Jones & Allen 1794; Hogarth 2019). As hundreds of Black people died performing these services, White doctors perpetuated the myth of Black immunity by falsifying and downplaying deaths of Black volunteers from yellow fever (Jones & Allen 1794). Despite risking their lives for little to no compensation, Black people were then publicly accused, in a pamphlet written by a respected Irish-American publisher, of profiteering and plundering sick White people during the outbreak—a profound example of racist beliefs and practices combined with medical gaslighting (Jones & Allen 1794; Hogarth 2019).

Social constructions around purported yellow fever immunity reinforced social hierarchies in New Orleans during the 19th century. During this period, roughly half of all individuals who

564 contracted yellow fever died. As a result, the racially-inconsistent concept of immunocapital took
565 hold, in which White men with demonstrable immunity were deemed worthy of investment and
566 granted expanded economic, political, and social power (Olivarius 2019). Doctors incorrectly
567 reported lower death rates and falsely alleged that Black people were more "naturally resistant"
568 to yellow fever than White people (Olivarius 2016), which racists perverted to argue that Black
569 people had a duty to be enslaved into strenuous labor, impeding their upward social mobility.
570 Immunity therefore translated into immunocapital for White, but not Black, individuals.
571
572 The climatic and environmental suitability of the Southern U.S. for yellow fever interacted with
573 social and economic responses to stifle Southern economic development and entrench racism
574 from the antebellum period into the 20th century (1840-1905). Yellow fever was a substantial
575 burden on economic development in the American South (Humphreys 1999). A large proportion
576 of the South's foreign commerce consisted of agricultural products (e.g., fruit, coffee) grown in
577 tropical regions with high yellow fever rates (Sterns 1900). Mirroring debates around COVID-
578 19, policy debates pitted the protective public health effects of quarantining arriving ships
579 against the negative economic effects of halting trade. Fluctuating public anxiety and the
580 resulting quarantine restrictions rendered business investment in the South risky, limiting
581 Northern investment, port productivity, and the distribution of goods into rural regions
582 (Humphreys 1999). Further, an 1878 yellow fever epidemic caused mass emigration from urban
583 centers like Memphis, Tennessee, halting economic activity almost entirely (Evans 2012).
584 Yellow fever therefore profoundly affected the history of the Americas, from the colonial period
585 to the advent of modern medicine, swaying wars, reinforcing racism, stifling economies, and
586 prompting new technologies and infrastructure.

Trypanosomiasis

Disease Ecology

African trypanosomiasis is distinct from plague, malaria, yellow fever, and all of the highest-burden VBDs (Table 1) in that the ecology of its tsetse fly vector (*Glossina palpalis* and *G. morsitans*) restricts the parasitic disease (caused by three subspecies of *Trypanosoma brucei*) entirely to the African continent. Trypanosomiasis is also unique in that, although African sleeping sickness affects humans (caused by *T. b. rhodesiense* in East Africa and *T. b. gambiense* in coastal West Africa and drainages of the Congo and Niger Rivers), some of its primary historical effects have been mediated by "nagana" (animal trypanosomiasis caused by *T. b. brucei*), which increases livestock mortality and lowers productivity. In humans, symptoms include fever and joint pain, which can progress to behavioral changes, poor coordination, and death. The trypanosomes responsible for nagana and African sleeping sickness evolved around 380 million years ago, and mammals were infected as early as 35 million years ago when the tsetse fly vector evolved. Due to this long shared evolutionary history, many native African wildlife are trypanotolerant (i.e., can be infected without showing signs of disease) and serve as reservoir hosts that can infect domesticated cattle (Lambrecht 1985; Steverding 2008). Further, the tsetse fly's relatively low reproduction rate and breeding site preference for loose soil prevented it from migrating out of Africa—unlike many disease-vectoring mosquitoes—resulting in historical impacts constrained to Africa (Alsan 2015).

(i) Pre-Colonial Africa

The effects of tsetse-transmitted trypanosomes on agriculture and society shaped the pre-colonial history of Africa, causing settlement patterns, agricultural practices, and socioeconomic systems to mirror the geography of the disease. Because nagana limited the use of domesticated animals for draft power in tsetse-suitable land, groups who inhabited these regions were less likely to use plows and harnesses (Alsan 2015), which precluded intensive farming, large agricultural surpluses, and long-range transportation of goods over land (Nash 1969; Diamond 1999). Together, these factors influenced human settlement structure, altered labor specialization, and decreased fiscal capacity in tsetse-endemic regions of Africa (Alsan 2015). Without surplus crops and a tax base to support a ruling class, populations in tsetse-suitable areas with higher burdens of trypanosomiasis were less likely to form politically centralized states (Alsan 2015). Studies have argued that trypanosomiasis was a major obstacle to urbanization and economic development (Connor 1994; Alsan 2015), which are positively correlated with pre-colonial political centralization (Gennaioli & Rainer 2007; Michalopoulos & Papaioannou 2013).

Trypanosomiasis may have impeded the expansion of early Arabic colonizers in Africa by making travel, cultivation, and settlement difficult within the tsetse fly-belt. Documents from 1373–1374 reveal that King Mari Djata II of the Mali Empire was overtaken by “illat an-nawm,” or sleeping sickness (Lambrecht 1964). Trypanosomiasis also determined the geographic range of the Great Zimbabwe civilization (1000–1400 CE). Located on a plateau between the Limpopo and Zambezi rivers, the settlement was described as a “peninsula in a sea of tsetse” (Connah 1987), which archaeologists have suggested climatically aligns with the boundaries of the pastoral civilization (Garlake 1978; Rogers & Randolph 1988).

The unique ecology of African trypanosomiasis altered the routes of migrating pastoralists throughout the 1500s CE, affecting societal practices before the arrival of European colonizers. In the Rift Valley, the main route of travel was on either side of the valley along the high ridge (Lambrecht 1964), likely because it was tsetse-free and preferred by livestock-owning pastoralists. Resting places and watering-holes along migration routes became permanent settlements and marketplaces. Similarly, migratory patterns of pastoral groups in South Africa and the Sahel edge were heavily affected by seasonal shifts of tsetse fly-belts (Fuller 1923; Dicke 1932; Ingold 1987). Archaeological evidence highlights stalled diffusion of domestic animals as compared to ceramics, probably due to trypanosomiasis (Gifford-Gonzalez 2000). The survival advantage of wild game over domesticated animals might have encouraged hunting and gathering over food production reliant on animal husbandry.

(ii) Early Imperial and Colonial Africa

The distinct ecology of trypanosomiasis repelled early European imperialism while promoting political violence throughout Africa by causing widespread mortality of horses and camels. In the 15th and 16th centuries, Portuguese explorers launched expeditions into East Africa's interior. Trypanosomiasis, in conjunction with existing barriers to colonization including deaths of horses and camels from disease, difficulty navigating the landscape, and vulnerability of colonizers away from the coasts, halted further Portuguese incursion into the continental interior (Lambrecht 1964).

Equine mortality from trypanosomiasis reinforced exploitative cycles of economic trade and political violence, limiting conquest and expansion. Within the Malian and Jolof empires of

North Africa and the western Sahara, trypanosomiasis prompted crossbreeding of disease-resistant horses (Webb 1993). These new breeds of horses were directly exchanged for enslaved people along the desert edge, and were used in state warfare in which prisoners of war were sold into the Atlantic and North African slave trades (Webb 1993). In Northern Nigeria, the effects of trypanosomiasis on the Nupe Kingdom and Oyo Empire's cavalry limited southward expansion and maintained the autonomy of the rival Kingdom of Dahomey (Law 1977).

The socio-ecological disruptions in tsetse-suitable areas caused by colonization and the slave trade perpetuated the burden of African trypanosomiasis. While signs of human trypanosomiasis were used to select people for enslavement for centuries by Arabic colonizers, this approach was formalized following British physician Thomas Winterbottom's medical reports in 1803. Winterbottom illustrated enlarged glands and nodules on the back of the neck, markers which were subsequently used to avoid selecting slaves from Sierra Leone who were deemed unlikely to survive the Atlantic crossing (Steverding 2008). Slave dealers simultaneously destroyed communities and spread human trypanosomiasis by disintegrating large settlements into smaller, dispersed populations (Fage & Oliver 1970). Additionally, caravans of enslaved people infected with trypanosomiasis were led through coastal markets, introducing the disease to naïve areas (Lambrecht 1964).

Discussion

The morbidity and mortality caused by vector-borne diseases motivate much of the research on their ecology, and are formally quantified through Susceptible–Infected–Recovered (SIR) and

679 other modeling approaches. More recently, disease ecologists have incorporated variation in
680 susceptibility among populations and environments into our understanding of VBD ecology.
681 However, this research still largely overlooks the complex and reciprocal nature of the socio-
682 environmental effects of disease. This review highlights how VBDs have impacted human
683 history, society, and culture through multiple mechanisms: by killing or sickening large numbers
684 of people, often differentially across populations coming into contact and conflict; through
685 development of new infrastructure, technology, and modified human relationships with land; and
686 by magnifying racism, sexism, colonialism, and classism. Throughout history, people in power
687 have used VBDs to perpetuate hierarchies by exacerbating differences and promoting factions
688 between racial or ethnic groups based on falsely perceived differences in susceptibility to
689 disease, and by using such perceptions to justify and expand hierarchies of power, exploitation,
690 and segregation (Olivarius 2019; Roberts & Rizzo 2020). VBD impacts also depend on their
691 unique ecologies that favor disease transmission and vectors: crowded urban environments with
692 poor sanitation for plague, lowland swamps and agricultural lands for malaria, sugar plantations
693 and urbanizing environments for yellow fever, and a climatically suitable belt within sub-
694 Saharan Africa containing animal reservoirs for trypanosomiasis. These socio-ecological drivers
695 are not confined to the past nor to VBDs. The association between infectious disease and
696 hierarchy, power, segregation, and conflict continues to recur in the modern world.

697

698 While malaria likely altered settlement patterns throughout the Americas, particularly in the
699 Amazon basin (Sawyer 1993), recent evidence suggests that it continues to influence human
700 settlement and economic development today. Malaria vectors in the Americas thrive in forest
701 edges and fringes of rural settlements (de Castro *et al.* 2006; Vittor *et al.* 2006, 2009; Sallum *et*

al. 2019). By reducing the health and productivity of subsistence farmers in the Amazon (Sawyer 1986, 1993; Singer & de Castro 2001), malaria may have inhibited the establishment and consolidation of large, permanent settlements in the Amazonian interior during the colonial period. Evidence from 21st century Brazil suggests that malaria transmission is coupled with deforestation and reduces rates of forest clearing where incidence is highest (MacDonald & Mordecai 2019).

In sub-Saharan Africa, where the modern burden of malaria remains concentrated despite decades of work towards malaria control and elimination, zones of violence increase several risk factors for malaria transmission. Armed conflict displaces inhabitants to regions of high malaria endemicity and marginal environments with ample vector breeding habitats, simultaneously creating large refugee populations and placing them at risk of infection (Toole & Waldman 1997). Countries in civil war tend to face limited access to antimalarial drugs and disrupted healthcare infrastructure (Montalvo & Reynal-Querol 2007), which can propagate antimalarial drug resistance (Takala-Harrison & Laufer 2015). Violence decreases safe water provision, usage of protective measures against mosquitoes (e.g., bed nets), and medical supply delivery (Gayer *et al.* 2007; Fürst *et al.* 2009), all of which normally reduce malaria incidence.

The expanding burden of viruses transmitted by *Ae. aegypti* (the primary yellow fever vector), including dengue, chikungunya, and Zika, illustrate the socio-ecological conditions for disease outbreaks that thrive on social inequities. Dengue fever affects an estimated 96 million people per year (Bhatt *et al.* 2013), primarily those living without reliable access to clean, piped water

724 and window and door screens (Stewart-Ibarra *et al.* 2013). The burden of dengue has grown
725 dramatically in the last three decades with the rise of unplanned urbanization in Latin America
726 and Southeast Asia (Lopez-Gatell *et al.* 2015). The 2016 Zika pandemic caused over 200,000
727 confirmed cases (PAHO/WAHO 2017), and thousands of babies were born with Zika congenital
728 syndrome, many to women who lacked access to contraception, reproductive counseling, or
729 adequate housing and sanitation (Marteleto *et al.* 2017; Borges *et al.* 2018; Castro *et al.* 2018;
730 Freitas *et al.* 2019). Zika led, at least temporarily, to policy changes that widely expanded
731 reproductive rights and contraceptive access (e.g., Z-CAN in Puerto Rico) (Lathrop *et al.* 2018;
732 Romero *et al.* 2018), but also decimated tourism and economies in Latin America and the
733 Caribbean (Gallivan *et al.* 2019). Efforts to control *Ae. aegypti* have led to biotechnological
734 developments in genetic modification and *Wolbachia* infection in mosquitoes to prevent virus
735 transmission (Hoffmann *et al.* 2011). Yet these technological approaches often overlook the
736 underlying social inequities that lead to household water storage, accumulation of unwanted
737 plastics that become mosquito breeding habitats, and housing permeable to mosquitoes and pests,
738 driving disease transmission (Stewart-Ibarra *et al.* 2013; Krystosik *et al.* 2020). Breaking the
739 socio-ecological feedback cycles of inequity that promote arbovirus transmission will be critical
740 for controlling these re-emerging diseases.
741
742 Although we have focused specifically on vector-borne diseases here, the themes of hierarchy,
743 power, and segregation apply to almost all human infectious diseases. Influenza risk and adverse
744 outcomes in the U.S. are higher for those with lower socioeconomic status due to decreased
745 access to primary care, and these cases often go unreported in surveillance systems (Scarpino *et*
746 *al.* 2020). When HIV/AIDS initially emerged in the United States in the 1980s in marginalized

communities of homosexual men and Haitian immigrants, the Reagan administration ignored the problem and under-funded research until the epidemic ballooned. This caused thousands of deaths by delaying basic research intended to establish routes of transmission and suggest behavioral changes to save lives (Nelson 1998). In Africa, the AIDS epidemic is linked to and perpetuates poverty, causes income losses for poorer households by incapacitating primary earners, stigmatizes women and subordinates their status, and undermines social institutions and political stability (Whiteside 2002; International Monetary Fund 2004; Price-Smith 2004; Rankin *et al.* 2005). Tuberculosis, once a disease that primarily affected older, rural, White populations, is now a major problem in prisons both in America (Baussano *et al.* 2010), where young Black people are disproportionately incarcerated due to racist criminal justice policies (e.g., the War on Drugs) (Wildeman & Wang 2017), and around the world. COVID-19 continues to perpetuate the inequitable burden of disease along racial and socioeconomic lines: a disproportionately high number of cases and deaths have occurred in communities of color (Adhikari *et al.* 2020), and racial disparities exist throughout the U.S., primarily driven by occupation, economic ability to work from home, housing density, and pre-existing health and healthcare access disparities (Tai *et al.* 2020; Webb Hooper *et al.* 2020).

It is imperative that research in disease ecology explicitly recognize and combat the deep-rooted structural racism, classism, and sexism that continue to perpetuate environmental and health inequities, primarily afflict those living in poverty and people of color, and promote vector-borne disease transmission. Equity must be brought to the center of ecology and global health in order to make meaningful progress for all of humanity.

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Boxes

Box 1. The narrative structure and interdisciplinary approach of this review

Narrative structure and stylistic choices

The history of human vector-borne disease (VBD) combines the movement, activities, decisions, and social structures of people with the lands they inhabit and modify, and the interactions and conflicts that emerge between populations that come into contact. To understand these historical and modern influences, we draw on an interdisciplinary mix of history, archaeology, psychology, and disease ecology to argue that social structures are inextricable from the ecological settings that promote VBD transmission. While we emphasize socio-ecological mechanisms and feedbacks, and their ties to the ecology of VBDs, we present much of the main text in a narrative format that is common in historical scholarship but less common in ecology. We describe human events as a set of lived experiences, in which biases, beliefs, and social practices shaped outbreaks just as concretely as the physical landscapes and ecological environments in which they occurred.

Most ecological research, and other research in natural and physical sciences, is presented through the lens of empiricism—the idea of science as objective, and thus divorced from narrative. Physicist and race and gender scholar Dr. Chandra Prescod-Weinstein introduces the concept of *White empiricism*: "the phenomenon through which only White people (particularly White men) are read as having a fundamental capacity for objectivity and Black people (particularly Black women) are produced as an ontological other" (Prescod-Weinstein 2020). Similarly, research shows that psychologists tend to present White samples as more general and universal than samples from people of color, which reinforces the idea of White experiences as

1208 being more objective (Cheon *et al.* 2020). This work highlights how the concept of objectivity is
1209 applied unequally depending on race and gender, resulting in asymmetrical access to public
1210 recognition and resource allocation. In this review, we present historical narratives of VBD
1211 impacts on societies, as well as narratives reconstructed from archaeological evidence, as central
1212 to the ecology of VBDs. We attempt to represent previously under-recognized narratives, such as
1213 the exploitative story of Dr. Benjamin Rush during the 1793 yellow fever epidemic in
1214 Philadelphia, as recounted by two Black religious leaders whose accounts were widely
1215 suppressed by their contemporary publishers. This case is a prime example in which the narrative
1216 is inextricable from the socio-ecological setting of the disease outbreak and its impacts.
1217
1218 We highlight one additional stylistic note. There is some disagreement among scholars and fields
1219 about the proper capitalization of the racial designations "White" and "Black." Some have
1220 argued that, because Black people who descended from enslaved people in the Americas were
1221 robbed of their ancestral ethnic and cultural identities and share experiences of marginalization
1222 in the United States and other countries, the term "Black" stands in for these identities, serves as
1223 a unifying racial and ethnic identity, and should therefore be capitalized (Appiah 2020). Others
1224 have argued that White people often ascribe to multiple other identities and do not have the
1225 shared history and experience of racial discrimination based on skin color. Yet some argue that
1226 putting "white" in lowercase perpetuates White invisibility and implies that it is the societal
1227 default, which in turn marginalizes minority racial groups (Appiah 2020). The capitalization of
1228 "White" therefore may serve to situate race and invite readers to be cognizant of and to think
1229 critically about racial identities, prejudices, and injustices that persist today. For these reasons,
1230 while many organizations advocate for capitalizing "Black" but not "white," and others advocate

for capitalizing both “Black” and “White” (Appiah 2020; Bauder 2020; Nguyen & Pendleton 2020), we have chosen to capitalize both “Black” and “White” in this paper with the aforementioned considerations in mind, fully recognizing that other styles are also valid and meaningful.

Contributions from multiple disciplines of natural and social sciences

This paper reflects the interdisciplinary contributions of undergraduates, graduate students, postdoctoral scientists, and faculty members representing a range of academic backgrounds and racial, ethnic, and gender identities. This project was conceived by an ecologist and members of her disease ecology research group. The primary research that became the core of this paper was conducted by an interdisciplinary team with varied academic expertises: biology, ecological parasitology, history, archaeology, psychology, medical entomology, political science, and anthropology.

Box 2. Mechanisms of VBD transmission

Transmission of VBDs to humans results from interactions among primarily arthropod vectors, pathogens, human and/or non-human hosts, and the environment. For pathogens to be transmitted, vectors must be abundant, come in contact with infected human or non-human hosts to acquire the pathogen, and bite uninfected human hosts, who either continue the chain of transmission or end the cycle as dead-end hosts (Baum 2008). Vector population size, physiology, behavior, and competence to transmit pathogens are influenced by abiotic and biotic factors, such as habitat type, climate, predation, and competition (Moore *et al.* 2010; Couret *et*

al. 2014; Ferraguti *et al.* 2016; Mordecai *et al.* 2019; Shocket *et al.* 2020). In particular, because of the partially aquatic life cycle of mosquitoes and many other vectors, vector abundance often depends on freshwater availability and water storage practices (Poh *et al.* 2019).

Human behavior interacts with environmental factors to affect disease transmission. For example, human modification of the physical environment can drive vector breeding habitat availability. Some vector species (e.g., *Anopheles* spp. mosquitoes) thrive in agricultural contexts and breed in ditches, canals, irrigated fields, and lowland freshwater swamps, while other species (e.g., *Aedes aegypti* mosquitoes) breed in abandoned containers (e.g., bottles, jugs, toilets, tires) and in contaminated aquatic systems (Zahouli *et al.* 2017; Du *et al.* 2019). Dense human populations in built environments such as urban centers, army barracks, and ships can facilitate contact between vectors and human hosts (Willoughby 2017). In turn, people may respond to real or perceived disease risk in the environment by distancing themselves, emigrating, or abandoning settlements in regions with high burdens of disease ("disease avoidance").

Finally, VBD dynamics depend on human disease susceptibility. Many pathogens induce some degree of immunity or resistance following infection, resulting in periodic epidemic cycles within populations as susceptibility waxes and wanes. When populations with differing disease histories come into contact, differential immunity to shared pathogens may cause asymmetric effects within and between populations (McNeill 2010). Together, these processes—abiotic factors, human behavior, and host susceptibility—combine to determine transmission and VBD burden in a given location (Bayoh & Lindsay 2004; Alto & Bettinardi 2013; Paaijmans *et al.* 2013).

Box 3. Glossary of relevant disease ecology terms

Acquired immunity: Upon exposure to a pathogen, the host starts to develop immunological memory to recognize the pathogen and to activate the immune system; reliant on highly specific antibodies that can prevent reinfection or limit disease symptoms upon reinfection

Built environments: Human-made structures and spaces in which people live, work, and recreate

Differential immunity: State in which particular classes or groups of people are more susceptible to diseases than others

Disease avoidance: Organisms tend to avoid infectious agents (including vectors), when feasible, since the biological benefits of remaining disease-free may outweigh the temporary costs of avoidance

Enzootic cycle: Process by which animals, which serve as long-term reservoirs for pathogens, maintain and pass on infection to a vector; also known as a sylvatic cycle

Host: An organism that harbors a pathogen, often with some energetic or fitness cost; in the context of this paper, hosts may include humans or other animals

Human-environment interactions: Ways in which humans and their social systems, decision-making, and behavioral processes interact with the natural world

Infrastructure: Basic organizational structures, facilities, and programs which are needed for the successful operation of a human society

Innate immunity: Intrinsic resistance possessed by a host prior to exposure to a pathogen; the

general, nonspecific immune response and defense mounted by the host

Land use change: Process of human activities transforming ecological landscapes

Pathogen: A disease-causing agent, including bacteria, viruses, fungi, protozoa, and other infectious organisms

Reservoir host: Non-human organisms that can harbor pathogens and can contribute to pathogen spillover into human transmission cycles

Social and racial hierarchies: Systems of social stratification that arise from the belief that certain social classes or racial groups are superior to others

Vector breeding habitat: Areas that are suitable for vectors to reproduce; stagnant water is often an optimal habitat for mosquito vectors

Vector competence: Ability of vectors to acquire, maintain, and transmit pathogens to hosts

Vector ecology: Study of arthropods that transmit pathogens, the interaction between such arthropods and disease-causing organisms, the impacts of the environment on their physiology and behavior, and their contact with humans

Vector: Organism that functions as a carrier of pathogens between organisms of a different species, including mosquitoes, ticks, fleas, and tsetse flies

Figures

Note: Actual figures are in the attached PDF files. Below are the titles and captions.

Figure 1. Socio-ecological feedbacks of vector-borne diseases (VBDs) throughout human history. Humans have altered natural environments (yellow) in ways that led to outbreaks of diseases (red) such as plague (P), malaria (M), yellow fever (YF), and trypanosomiasis (T) via mechanisms explained by the corresponding vector ecologies (green). In response to these diseases, human societies have improved technologies, institutions, and infrastructure for human well-being, but also inflicted additional pain and suffering by weaponizing diseases in warfare, and perpetuating hierarchies of power, colonialism, racism, classism, and sexism (blue). Some of these social responses fed back into anthropogenic environmental changes (yellow).

Figure 2. Timeline of vector-borne disease impacts across history. Plague, malaria, yellow fever, and trypanosomiasis have affected human history from the Paleolithic era to the modern age through a variety of mechanisms; case studies highlighted for Africa (orange), Asia (yellow), Australia (purple), Europe (green), North America (blue), and South America (red).

Tables

Note: Actual tables are in the attached Word files. Below are the titles and captions.

Table 1. Major vector-borne diseases ranked in order of annual DALY burden, with primary vector, pathogen, geographical range, and categories of influence. The top 10 vector-borne diseases as ranked by annual disability-adjusted life year (DALY) burden, with associated ecogeographical characteristics and influence.

Table 2. Historical time periods, associated ecological characteristics, and VBDs. The unique ecological and human social context of time periods throughout history have set the stage for specific vector-borne diseases to emerge.