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Nature's Games: Will the Global Medical Community Triumph Over Zika Virus?

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“Medicine is a science of uncertainty and an art of probability,” maintained William Osler, one of the four founding physicians of the hospital at Johns Hopkins School of Medicine (74). Presently, that uncertainty is exemplified by the escalation of Zika virus from a relatively unknown illness in the heart of Africa to an increasingly troublesome scourge afflicting the Americas (57). A study of Zika virus is particularly intriguing due to the continually developing nature of the epidemic – verging on pandemic, as it spreads around the world – and the resultant ever-changing confirmations of symptoms and connections between the illness and other conditions (84). Furthermore, there is an absence of hindsight bias in evaluating the response of global health authorities to the infection, with the exception of perceiving similarities to past disease outbreaks (63). The attentiveness towards Zika virus and how this devotion to the illness has altered over the course of its history among humans (52) speaks to the broader attitudes of the Centers for Disease Control (CDC), World Health Organization (WHO), government agencies, and additional purported experts towards infections. Specifically, it provides acumen on the question of what incites them to take decisive action in preventing and treating microbial and viral ailments (89). Moreover, the explosion of Zika virus highlights the ability of diseases to expose and exacerbate weaknesses in societies already fraught with economic, political, and social turbulence (8).

This analysis provides an in-depth account of the development and expansion of Zika virus, addressing its origins, spread, modes of transmission, symptomatology, diagnosis, link to and role in causing other illnesses, current treatment, prevention, and aspiring eradication. Throughout an examination of the above themes, this paper presents a comparison of the manner in which the global health community has responded to Zika virus to the way they handled and are currently approaching, respectively, two other infections: acquired immune deficiency

syndrome (AIDS) stemming from the human immunodeficiency virus (HIV), and Lyme disease. Finally, this report explores similarities between contemporary Brazil and previous societies that collapsed over the course of history, offering insights into the role of disease not just on an individual or communal level but also as a dire threat to an established nation. To achieve these objectives, sources are drawn from guidelines presented by health organizations, reports from medical journals, and literature covering previous epidemics and civilization failures with the aim of presenting the most comprehensive investigation currently possible. For the remainder of the paper, Zika virus is referred to as ZIKV.

Origins and Historical Spread

As a prelude to the 2016 outbreak of ZIKV, it is necessary to look back through the sixty-nine-year history of the infection to when it first came to the attention of scientists, as well as and how and why its geographic impact has shifted yet also lingered in its original site of isolation (39). Accordingly, ZIKV was first isolated from a rhesus monkey in Uganda in 1947 during a study of yellow fever virus (YFV) given the known prevalence of immunity to YFV exhibited by these monkeys (21). Blood taken from Rhesus 766, febrile – displaying a fever – at the time, was injected into a group of mice, where a transmissible agent was removed after they, too, fell ill (21). The agent, duly named after this dense belt of forest along Lake Victoria running next to the Entebbe-Karpala road where the study was carried out, was subsequently isolated in 1948 in the same location from *Aedes africanus* mosquitos (21). In 1952, preliminary evidence was ascertained of ZIKV in humans living in East Africa, followed by isolations from three patients at the University College Hospital, Ibadan in Nigeria in 1975 (27). A more extensive study carried out in four Oyo State communities within Nigeria found that 40% of those tested possessed neutralizing antibodies conferring immunity yet also implying recent infection by the

virus (27). Meanwhile, in 1966 ZIKV was discovered for the first time in Southeast Asia and, also significantly, from a mosquito that was not *Ae. africanus* (58). The isolation of a ZIKV strain from *Aedes aegypti* mosquitoes in Bentong, Malaysia reinforced allegations of neutralizing antibodies in residents of the country as well as the presence of the disease in wild monkeys (58). A defining moment came in 2007 when ZIKV infected 75% of the population of Yap island of the Federated States of Micronesia in what was deemed to be an acute outbreak rather than a product of previous clandestine circulation on the island (23). Believed to be carried by *Aedes hensilli* given the role of this vector in communicating dengue virus (DENV), ZIKV was hypothesized to have been initially introduced to the territory by human travelers from the Philippines, prompting what would become valid concerns of the potential spread of the virus to other nations in Oceania and the Americas (23). Having been found up to this point in Uganda, the Central African Republic, Egypt, Gabon, India, Indonesia, Malaysia, Micronesia, Nigeria, Pakistan, the Philippines, Sierra Leone, Tanzania, Thailand, and Vietnam, ZIKV thereafter continued its spread to the Cook Islands, French Polynesia, New Caledonia, the Solomon Islands, and Vanuatu (57).

Portentously, in 2014 ZIKV was introduced to Easter Island, Chile, and in early 2015 patients with symptoms bearing a resemblance to those of the illness were registered in northeastern Brazil around the city of São Paulo (73). The detection of ZIKV corresponding to a strain of the Asian clade in the sera of eight of the patients represented the first report of the disease in Brazil as well as the earliest incidence of within-country (autochthonous) transmission of the infection (85). Numerous theories have been put forth regarding how the virus entered and successively swept across Brazil (25). Among the strongest are the 2014 World Canoeing Championships in Rio de Janeiro that featured a substantial contingent of Pacific Islanders (84)

or the 2014 Fédération Internationale de Football Association World Cup in which high numbers of Asian tourists arrived, also keeping in mind the proximity of Brazil to stricken Chile (25). Following in the path paved by chikungunya virus (CHIKV) and DENV, ZIKV was reported in Colombia in October of 2015 with others to follow almost immediately (84). The CDC currently acknowledges active transmission of the virus in South America – Bolivia, Brazil, Colombia, Ecuador, French Guiana, Guyana, Paraguay, Suriname, and Venezuela – in Central America – Costa Rica, El Salvador, Guatemala, Honduras, Nicaragua, and Panama – in the Caribbean – Aruba, Barbados, Bonaire, Curacao, Dominican Republic, Guadeloupe, Haiti, Jamaica, Martinique, Puerto Rico, Saint Martin, and the US Virgin Islands – in addition to American Samoa, Samoa, and Tonga in the Pacific and Cabo Verde off the western coast of Africa (2).

However, analogous to Lyme disease, substantial evidence exists that indicates ZIKV has a presence that is more inclusive than the CDC admits (1). In 2007, epidemic activity of ZIKV was confirmed in Libreville, Gabon with additional outbreaks in 2010; moreover, the virus was detected for the first time here in the *Aedes albopictus* mosquito (39). As will be discussed in future sections, there are numerous reasons why ZIKV may subsist unreported, yet evidence abounds that the geographic range of ZIKV encompasses not just Central and West African nations such as Burkina Faso, Cameroon, Gabon, Ivory Coast, Senegal, and Sierra Leone but also Eastern African countries – Ethiopia, Kenya, Somalia, Tanzania – and Egypt (39). Furthermore, in 2010 a boy was found to be infected with ZIKV in a Cambodian health clinic, a nation not previously indicted as a locale of the illness (44). The report of a fifty-two-year-old traveler from Australia diagnosed with ZIKV after returning from Jakarta, Indonesia in 2013 in concurrence with a higher prevalence of antibodies to the virus in the sera of inhabitants of both Africa and Asia indicates that ZIKV continues to be actively transmitted in regions outside the

focus of the mainstream medical establishment (50). Reporting on Lyme disease by the CDC confirms the sagacity of the above assertion: the CDC maintains that 96% of Lyme disease cases in the United States occur in fourteen states occupying territory in the northeast and upper Midwest and that it is not a nationwide issue (16). On the contrary, Lyme disease does, in fact, exist throughout the United States – enabled by the presence of black-legged ticks on the West Coast – as well as in upwards of sixty other countries (1).

Transmission

As has been discussed at length, the history of ZIKV has important implications for the continued diffusion of the infection around the world, with an examination of its modes of transmission necessary to fully understand the threat posed by the virus (86). To begin with, mosquitoes are emphasized by the CDC as the predominant vector of ZIKV transmission. During early stages of isolation in Africa, ZIKV was found in *Ae. africanus*, with further insulates acquired from *Aedes luteocephalus* and the belief that due to the high levels of immunity to ZIKV among urban communities, species such as *Ae. aegypti* were and still are liable to factor into the spread of the virus as well (27). *Ae. aegypti* and *Ae. albopictus* are the probable principal vectors in Asia, although as was the case on Yap island, geographically distinct mosquitoes may also be responsible for passing the disease (on Yap, *Ae. hensilli* is prevalent and was indicted in the 2007 epidemic) (42). In French Polynesia, both *Ae. aegypti* and *Ae. polynesiensis* are conjectured to account for transmission in the territory, particularly during the 2013-2014 crisis (65). Despite the pervasiveness of the *Ae. aegypti* mosquito and its typical link to the infection, in the survey in Gabon, only *Ae. albopictus* pools tested positive for ZIKV, with the suburbs in which these mosquitoes were the majority exhibiting human incidences of the illness (39). Both in concurrence and in contrast to the above examples, *Ae. aegypti* is regarded

as the most common route of transmission, particularly in the Brazilian ZIKV epidemic, although concerns persist about *Ae. albopictus* as well (86).

Notably, the CDC recently updated their guidelines to incorporate other methods of communication, specifically to warn of potential sexual transmission of ZIKV following a case or partner-to-partner infection in Texas (51). One of the individuals had recently returned from Venezuela (51). The aptitude of ZIKV to be passed as an STD was formerly construed in Colorado in 2008 when two scientists who had been working in Bandafassi, Senegal displayed symptoms once arriving back in the United States (35). After the wife of one of the patients also became ill and reported having sexual intercourse with her husband yet not having left the country, they were found to have identical results in ensuing serologic analyses (35).

Furthermore, in the midst of the ZIKV epidemic in French Polynesia, blood donors were tested for the virus in an effort to prevent transmission through blood transfusion (64). Although all prospective donors were asymptomatic at the time, 3% were found to be positive for the infection (64). In spite of this evidence and the acknowledgement of CDC Director Dr. Frieden that “there have been isolated cases of spread through blood transfusion or sexual contact,” he affirmed that “the bottom line is mosquitoes are the real culprit here” (51). The CDC maintains it is rare yet conceivable for mothers to pass ZIKV to their child during the delivery process or over the course of the pregnancy itself (91). Accounts of perinatal (the period directly preceding and succeeding birth) transmission of CHIKV, DENV, West Nile virus (WNV), and YFV provide a defense for the same to be true of ZIKV, particularly when viewed in conjunction with the two ostensible incidents of this type in French Polynesia (4). Two mothers tested positive within two days of delivery and their newborns within four days, indicating either trans placental transmission or contagion during delivery may have been the reason (4). Pertaining to the

Brazilian ZIKV outbreak, ZIKV RNA has been observed in the amniotic fluid, brain tissue, and/or placental specimens of infants as well as the fetal discharge of mothers (77).

At present, the CDC and akin global health authorities may definitively confirm these additional methods of transmission as they did with the AIDS epidemic, or they may continue to emphasize one outside vector as in regards to Lyme disease (54). At the conclusion of 1982, the CDC had recognized each component of the epidemiology of AIDS – with the exception of the specific culpable microbe (37). Important aspects included that it was, first and foremost, transmissible, and that these channels consisted of sexual intercourse, blood transfusions, mothers to their children, and sharing needles (generally amongst drug users) (37). Conversely, the CDC upholds that the *Borrelia burgdorferi* bacterium responsible for the preponderance of Lyme disease is passed only through the bite of ticks infected with the microbe (54). As per their report, sexual transmission is not a means of communication between individuals (54). Nevertheless, in a study published in the *Journal of Investigative Medicine* in 2014, researchers discovered the bacterium in the vaginal secretions of all women afflicted by Lyme disease and in the semen of half of the men with Lyme disease (72). Dr. Raphael Stricker summarized the findings by noting that, “There is always some risk of getting Lyme disease from a tick bite in the woods... But there may be a bigger risk of getting Lyme disease in the bedroom” (72).

Symptomatology and Diagnosis

The symptoms of ZIKV and related ailments have been referenced in brief up to this point, and a more extensive discussion of these facets of the circumstances along with a scrutiny of relevant diagnostic procedures serve to illuminate several of the fundamental challenges presented by the illness (43). ZIKV is a member of the biological family *Flaviviridae* and subsequently the genus *Flavivirus* (49). Taken as a whole, the *Flavivirus* genus constitutes more

than seventy viruses, among them dengue (DENV), Japanese encephalitis (JEV), St. Louis encephalitis (SLEV), and yellow fever (YFV) (49). ZIKV and Spondweni (SPOV) specifically belong to clade X situated in the domain of the mosquito-borne cluster; there are also tick-borne and non-vector clusters within the genus (49). On the species level, two lineages of ZIKV have been discovered: an African lineage, responsible for cases including those in Gabon, Nigeria, Senegal, and Uganda, and an Asian lineage, culpable in Cambodia, Malaysia, Micronesia, and, currently, in Brazil (39). Reports of the first ZIKV patients in Brazil cited key symptoms of arthralgia (joint pain), digestive disturbance, fever, headaches, maculopapular rash (a red area of the skin overlaid with bumps), myalgia (muscle pain), oedema (fluid retention, or swelling) of the extremities, retroorbital (eye) pain, and vertigo (85). An advisory printed in Spanish at the beginning of the outbreak forewarned of the above indications in addition to anorexia, stomach pain, and weakness (73). The CDC summarizes the signs of ZIKV as conjunctivitis (red eyes), fever, headache, joint pain, muscle pain, and rash, overall mild and passing within the span of a week (80). The WHO further simplifies the primary portents to slight fever and a rash, noting that the symptoms are comparable to those of CHIKV (an alphavirus) and DENV (88). Specifically, as with ZIKV, DENV also leads to fever, headache, pain in the joints and muscles, and rash (17), yet it is distinguished from ZIKV by a higher fever and more intense muscle pain (88). CHIKV, on the other hand, is marked by more disabling joint pain (11).

Not only is there the potential for attributing one virus to another – for instance, potentially accrediting ZIKV to DENV as may have transpired during WWII in the Pacific theater (42) – multiple infections may persist simultaneously in a patient. A premonition of the above was in the coinfection of thirty-seven patients in central Africa between 2007 and 2010 with both CHIKV and DENV (9). Furthermore, in 2010, from the pool of patients with an acute

fever, twenty-eight were stricken by the two infections (9). Accordingly, the ZIKV epidemic in French Polynesia yielded a teenage boy with both ZIKV and DENV as well as a thirty-eight-year-old-woman in New Caledonia (24). Besides similarities to (and dual infections with) these mosquito-borne viruses – and particularly in developing nations such as Nigeria, a resemblance with the febrile illness-inducing malaria (27) (56) – University of Lancaster virologist Dr. Derek Gatherer explained there is limited knowledge and records of ZIKV because the presentation of the disease is mild in the sense of having a low rate of mortality (84). However, as will be examined in the following section, ZIKV is acutely worrisome due to its suspected role in triggering autoimmune and neurological disorders, rendering an inaccurate or missed diagnosis much more grievous (89).

Accordingly, the CDC asserts that the only testing for ZIKV is performed at their laboratory in Atlanta (19), yet there are, in fact, commercially available analytical methods as well (90). The CDC explains that ZIKV may be diagnosed through reverse transcriptase-polymerase chain reaction in the first week succeeding initial symptoms (19), referred to as acute-phase serum samples (43). In addition, at the completion of one week of sickness, an individual acquires immunoglobulin specific to ZIKV (IgM) alongside neutralizing antibodies (19) that may be detected using an ELISA (enzyme-linked immunosorbent assay) exam (43). In late 2015, a company by the name of Biocan Diagnostics created a test suggested for use in doctor's offices, field settings, and mobile clinics that advertises the delivery of results within ten minutes based on the presence of these IgG/IgM antibodies (90). Furthermore, a similar process utilizing an ELISA analysis to detect ZIKV IgM in samples is exploited by MyBioSource in their product currently selling for \$435 in the free market (92).

Numerous problems impede the effectiveness of these prevailing diagnostic procedures (43). During the outbreak on Yap Island, the sera of patients who had experienced past infections by other flaviviruses expressed greater cross-reactivity, or reactions to the antibodies of chiefly DENV but also those developed against JEV, West Nile virus (WNV), and YFV (43). Although the sensitivity (true positive rate; those properly recognized as having the disease) and specificity (true negative rate; those accurately distinguished as not being infected) have thus been called into question, citing an inadequate number of samples, these values have not been quantified (43). Moreover, around twelve weeks after contracting ZIKV, antibody levels may be too low to register on an ELISA test (31). Similar issues surrounded testing for AIDS notably in African nations in the 1980s (37). Prior to the Bangui meeting sponsored by the CDC and WHO, Robert Biggar and his team found 80% of hospital patients in the Kivu District of eastern Zaire from whom blood samples were taken had antibodies to malaria (37). Significantly, it was the individuals with the most pronounced reaction to malaria who also acted in response to one or all of the human T-lymphotropic virus (HTLV) forms tested, including HTLV-III (HIV) (37). People chronically afflicted by malaria or related parasites generated “sticky sera”, their infected blood causing antibodies and viruses to stick to the surface of the test and be detected following the rinsings in a manner indistinguishable from HIV (37). Consequently, high numbers of false positives were attained in sub-Saharan Africa (37). Whereas tests for ZIKV may, in contrast, underreport the disease, both hamper the abilities of communities to gauge the true scope of an outbreak and respond with appropriate measures (86).

From symptoms – or lack thereof – to coinfections and diagnostic confounds, Lyme disease accords a quintessential comparison to ZIKV (29). For one, the CDC and the Mayo Clinic cite a bulls-eye shaped rash known as “erythema migrans” as a fundamental hallmark of

B. burgdorferi (the causative microbe of the Lyme disease), expounding that this rash may be found on various regions of the body (79). While the CDC testifies the rash occurs in 70-80% of those infected (76), only 39.3% of patients in a 2014 peer-reviewed study actually observed a rash after contracting the illness (46). Because a crucial factor in recognizing and reporting a case of Lyme disease is the presence of a rash, a substantial number of instances consequently go undocumented (46). Likewise, in the confirmed incident of ZIKV in Cambodia, the infected three-year-old boy did not exhibit the typical maculopapular rash (44). He was only diagnosed due to inclusion in an established clinic-based surveillance project to determine the causes of acute fever in the region (44). Additionally, in the study of Lyme disease patients, 23.5% were inflicted with at least one coinfection and 29.8% with two or more; these coinfections included *Anaplasma*, *Babesia*, *Bartonella*, *Ehrlichia*, *Mycoplasma*, and Rocky Mountain Spotted Fever (46). Just as ZIKV exists concurrently with ailments such as CHIKV and DENV and presents approximately analogous symptoms, Lyme disease often occurs alongside these other tick-borne illnesses (46). In addition, the condition produces cognitive deficiencies, fatigue, joint and muscle pain, and mood disorders also characterizing diseases including Alzheimer's, chronic fatigue, depression, fibromyalgia, multiple sclerosis, and Parkinson's (53). Finally, in regards to diagnostic procedures, there is no collectively accepted criteria as to what comprises a positive Western blot test with the test largely held to be unreliable by all but the CDC (29). An ELISA exam is held to be 30-60% accurate, and there is debate as to whether the presence of any of the IgG bands in a Western blot rather than the CDC-specific five (22) is believed are sufficient indicators of Lyme disease infection (29). What these similar discrepancies reveal is that a more open-minded, comprehensive analysis is necessary for the identification of illnesses such as ZIKV and Lyme disease rather than current adherence to one or a few markers that may overlap

with other ailments (29). Weaknesses in testing must be acknowledged and results viewed with a critical eye, for instance, to prevent incidents such as the inaccurate survey of AIDS cases in sub-Saharan Africa (37).

Link to Other Illnesses

Misdiagnosis of an illness such as AIDS or Lyme disease puts the lives of patients and their close companions at risk (46), whereas the consequences for ZIKV may not initially appear to be as severe (80). However, as has come to light in recent years and particularly within the last few months, ZIKV has taken a sinister turn in the conditions it is under investigation for inciting: Guillain-Barre syndrome (GBS) (65) and microcephaly (61). GBS arises when an individual's immune system attacks a portion of their peripheral nervous system, resulting in tingling and weakness that may progress into paralysis and become life-threatening if interfering with breathing, blood pressure, and/or heart rate (40). While the disorder may affect persons of any age and background, GBS often results from a gastrointestinal or respiratory viral infection, surgery, or potentially a vaccine (40). The persistence of symptoms may range from weeks to years, with residual weakness occurring in approximately 30% of patients three years after the initial attack (40). The earliest documented case of GBS following ZIKV infection occurred during the ZIKV epidemic in French Polynesia (65). A woman in her early forties was hospitalized for thirteen days during which time she experienced paresthesia ("pins and needles") progressing into muscle weakness, chest pain, facial palsy, orthostatic hypotension (low blood pressure when standing), and ventricular tachycardia (rapid heartbeat) (65). The presence of a diffuse demyelinating disorder – damage to the sheaths surrounding the nerves – was confirmed, yet the patient developed favorably following intravenous administration of immunoglobulin (65). Partial paralysis, explicitly limited voluntary motor capabilities of her lower limbs,

persisted until day forty (65). Previously, DENV had been correlated with GBS, with three examples of such cases recorded by a hospital in the district of Trivandrum located in the southern state of Kerala, India during the 2002 DENV epidemic (78). At present, the WHO has reported an upsurge in incidents of GBS in Brazil, Colombia, El Salvador, Suriname, and Venezuela yet cautions that the causal factor in the increase cannot be definitely ascertained given the simultaneous existence of CHIKV and DENV in the region (68). Although the WHO concedes that there was an abrupt 19% escalation of the incidence of GBS in the Brazilian state of Bahia in 2015 – one of the territories hardest hit by ZIKV at this same time – and despite the aforementioned studies, they contend there is “no scientific evidence” that corroborates a relationship between ZIKV and GBS, or ZIKV and microcephaly (68). Moreover, the CDC insists that it is challenging to decide if any germ of pathogen triggers GBS (41).

Likewise, ZIKV has been connected to microcephaly, a condition of growing concern that impacts fetuses born to mothers who were stricken with the virus during pregnancy (61). Microcephaly leads a child to have a smaller head than average, either because their brain has not developed correctly over the course of the pregnancy and/or because it ceases to mature after birth (26). Depending on the severity of the condition, an infant may present with other problems including developmental delays (in speech, standing, walking, etc.), feeding difficulties (trouble swallowing), hearing loss, intellectual disabilities (lower capacity to learn), seizures, or vision problems that may persist for life (26). During the pregnancy, it is possible to diagnose a child using ultrasound technology, but the borderline regarding what constitutes abnormal head size is arbitrary and fluctuates across regions (18). Furthermore, it is not feasible to know if the baby will be impacted in any of the additional areas described above, hampering prenatal decision-making regarding a potential abortion or preparations for caring for the newborn (18).

As a possible solution, Ganeshwaran Mochida of Boston Children's Hospital recommends a fetal MRI in an effort to acquire further details about any conceivable brain defects (18). An account of a pregnant twenty-five-year-old European woman who had worked as a volunteer in Natal, Brazil found evidence of fetal brain abnormalities accompanying ZIKV infection in her unborn child (61). Overall, in 2015 the Ministry of Health in Brazil reported an increase in microcephaly by a factor of 20% in babies born in the northeast region of the nation, substantiating two additional recent findings indicating intrauterine transmission of ZIKV from mother to child and resulting microcephaly (61).

The threat of microcephaly has spread to the United States, with two pregnant women afflicted by ZIKV opting for abortions as confirmed by the CDC while two others have endured miscarriages, one has delivered a child with serious defects, and two others have given birth to healthy babies, with two women still in the midst of their pregnancies (18). All of these women visited one or more countries where ZIKV is actively transmitted, yet the timing of the infection appears to be significant provided it was of the six who showed signs of ZIKV during the first trimester of pregnancy who experienced abortions, miscarriages, and the birth of a baby with severe microcephaly (one is still pregnant) (18). Conversely, of the three diagnosed during the second and third trimesters, one remains pregnant while the other two delivered healthy children (18). The CDC states that they are confident there is an association between ZIKV and microcephaly; accordingly, surveys are ongoing in regions where ZIKV is rampant (12), with the virus acknowledged to have been found in four deceased Brazilian babies also exhibiting signs of microcephaly (86).

Looking back into history, the contemporary presentation of ZIKV bears similarities to the emergence of AIDS in the United States (37). One of the preliminary red flags of the latter

materializing health threat was observed by Dr. Michael Gottlieb of UCLA Medical Center who discovered overgrowth of *Pneumocystis carinii* pneumonia (PCP) in the lungs of a young man who otherwise had no prior record of illness, in other words, no apparent signs of a weakened immune system of the type that often facilitates infection by PCP (37). The incident was tied to the proliferation of Kaposi's sarcoma and additional PCP cases recognized by the CDC, ultimately culminating in efforts to identify the source of the compromised immunity of the patients (37). Comparably, while establishing causation for GBS has been circumvented, ZIKV has garnered international attention and extensive investment by global health organizations in recent months in particular because of its ostensible connection to microcephaly exemplified in the outbreak in the Americas (61).

As a point of contrast, the acknowledgment of a prospective link between the conditions described here and other ailments differs remarkably from the treatment of Lyme disease and maladies of which it is potentially a cause (60). For one, cystic structures (fluid-filled sacs) have been documented in patients diagnosed with multiple sclerosis (MS), suggesting that they are chronically infected with a spirochete such as *B. burgdorferi*, the causative agent of Lyme disease, that subsists in these cystic forms to hide from the immune system (7). Cystic structures resembling those of characteristic of long-term Lyme disease were isolated from the cerebrospinal fluid (CSF) of all ten Norwegian MS patients and none of the five controls in a 2001 study, with these cysts reacting positively to antispirochetal antiserum (7). Following culturing of two of the samples of CSF, spirochete-shaped bacteria appeared, consistent with the relapse-remitting nature of MS where an acute attack results from the conversion of these cystic Lister (L) forms back to *B. burgdorferi* (36). Furthermore, spirochetes were found in the blood, brain, and CSF of fourteen Alzheimer's disease (AD) patients, and in three cases genetic and

molecular exams revealed the agent to be *B. burgdorferi* (60). The research suggests that Lyme disease may thereby be connected to the proliferation of amyloid plaques characteristic of AD (60). However, none of these connections are recognized by the prominent medical authorities (33) (76), with an examination later in the paper theorizing why Lyme disease may continue to garner a dissimilar response than those pertaining to ZIKV and AIDS.

Treatment

Endeavoring to consider treatment and prevention for ZIKV yields the sobering truth that there is currently no vaccination available, yet there are agreed-upon measures to alleviate the illness (69). Because ZIKV was previously viewed as relatively asymptomatic, no incentive existed to manufacture a vaccine (52). Consequently, a reliable countermeasure of this type is believed to be at minimum three years away, notwithstanding hastened research following the ZIKV vaccine initiative commenced by the National Institutes of Health (NIH) near the end of 2015 (52). The CDC recommends conventional methods comprising of drinking fluids, resting, and taking acetaminophen (such as Tylenol) to assuage fever and pain as a means of addressing the symptoms (79), with the WHO adding that individuals should only pursue additional medical care if they find their condition deteriorating (87).

Correspondingly, in 1983 those afflicted with AIDS also faced challenges in an initial absence of interest in their well-being, with the NIH overall showing no enthusiasm for dissecting the condition and neither the Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA) nor the National Institute on Drug Abuse (NIDA) assuming any responsibility for research on its transmission and preclusion (37). In addition, a fundamental disagreement spanning medicine, public policy, and science exists concerning the measures necessary to effectively treat Lyme disease (55). For example, the Infectious Diseases Society of America

(IDSA) maintains that Lyme disease is straightforward to cure through a brief course of antibiotics and that chronic Lyme disease does not exist at all (55). In opposition, the International Lyme and Associated Diseases Society sustains that the illness is difficult to diagnose (on one hand, because of the aforementioned attitude) and that it may persist for years in conjunction with additional coinfections, rendering it necessary for patients to develop an individualized and multifaceted treatment approach with a Lyme-literate healthcare provider (55). In contrast to both the CDC and NIH that agree Lyme disease cannot endure after a few weeks of antibiotics and that longer use is, in fact, dangerous, the IDSA and LymeDisease.org advocate treatment until the symptoms have been eliminated, with no formula of antibiotics in itself proving sufficient for completely eradicating the bacteria (55). Neither for AIDS, Lyme disease, nor ZIKV is a vaccination available, proving that effective and inclusive protective measures to avoid infection remain vital for their suppression (29).

Prevention and Eradication

Recalling the various ways ZIKV may be transmitted, the CDC and WHO Regional Office for the Americas (PAHO) have nonetheless predominantly focused on mosquito vectors in regards to prevention and eradication (69). The CDC references remaining in areas with door and window screens, sleeping under mosquito nets, and wearing long-sleeved shirts, pants, and insect repellent to avoid mosquito bites (69). Moreover, they affirm it is imperative to evade being bitten even after contracting the illness due to its circulation in the blood for a week and thus the potential to transmit the virus to those in the vicinity if the mosquito is to subsequently bite these individuals (69). Particularly for pregnant women and those planning on becoming pregnant in the near future, travel to areas where ZIKV is actively proliferating (remembering that these regions may be more numerous than disclosed) is highly discouraged (70).

Furthermore, updated guidelines explain that even asymptomatic pregnant women who may have been endangered are recommended to receive IgM antibody testing between two and twelve weeks post-exposure; in the case of a negative result, the CDC maintains that infection was unlikely (71). For women who live in regions where ZIKV is endemic, recommendations espouse counseling for those of reproductive age as well as management and screening of those currently carrying a child (71).

Brazil was proclaimed free of the *A. aegypti* mosquito in 1958 in the wake of an aggressive campaign involving fumigation and house calls to confirm there was no standing water where mosquitos could breed, yet the key player in the ZIKV epidemic has since returned with a vengeance (86). The WHO explains control relies on not just limiting interaction between mosquitos and people but also on slashing the quantity of mosquitos by eliminating these breeding sites that can also harbor CHIKV and DENV (87). As the CDC elaborates, female mosquitos lay hundreds of eggs on the sides of water filled vessels, and when the water rises over the eggs, they hatch and mature into adults in the span of a week (45). Therefore, brochures aimed at residents of affected areas direct them to empty and scrub or throw out receptacles of liquids including birdbaths, buckets, flowerpots, planters, pools, tires, and trash containers while covering other storage mechanisms such as cisterns and rain barrels (45). Using air conditioning when possible in addition to ensuring screens are functional and shielding open plumbing or vents with narrow wire mesh are measures that are also endorsed (45).

The WHO has congruently pointed to the use of insecticides – particularly larvicides – on sizeable containers of water to aid in mosquito eradication (87). Conversely and controversially, the Argentine-based group Physicians in the Crop-Sprayed Villages has implicated the larvicide known as pyriproxyfen as the source of the soaring rate of microcephaly in Brazil rather than

ZIKV itself (83). The report states that by quickly connecting microcephaly in newborns to the spread of ZIKV, the Brazilian Ministry of Health, PAHO, and WHO have put the commercial interests of the chemical industry above the well-being of the environment and the people, failing to identify that the areas where this larvicide has been introduced into drinking water are the same regions where microcephaly has exploded (81). The group supports their claims by affirming that no birth defects were found to be associated with previous ZIKV epidemics, and that in countries such as Colombia, there have been thousands of ZIKV cases but no documented instances of babies born with microcephaly (81). Based on previous examples of negligence in identifying the causes and scope of illnesses described in this analysis (AIDS and Lyme disease), there are evident hazards in allowing the supposed experts to dispose of a claim rather than investigating additional possibilities (55). However, in this situation, while it is still imperative to retain an open mind and not reject any factors that may play a role in the disorder – particularly when business and chemicals are involved – empirical findings suggest that ZIKV is likely the primary culprit in the upswing in microcephaly (83). In the state of Pernambuco commonly referred to as the “epicenter of microcephaly”, pyriproxyfen is not used in the three cities with the majority of cases – Jaboatao, Paulista, and Recife (5). Moreover, as examined earlier in the paper, ZIKV has been found in the amniotic fluid, blood, and tissues of afflicted babies, and the hormonal system targeted by pyriproxyfen in insects does not exist in mammals (83). Dr. Ian Musgrave of the University of Adelaide in Australia affirms that a human would have to consume a thousand liters of water each day over an extended period of time to reach the toxic threshold, yet pregnant travelers subsequently giving birth to children with microcephaly have not fulfilled this presumed – accepted with caution – requirement (83).

Finally, besides preventing mosquito bites, eliminating sources of water, and theoretically utilizing insecticide, the possibility of employing genetically modified mosquitos has been gaining traction as an insect control strategy, for example, by releasing mosquitos with a dominant lethal gene (OX513A) activated in the absence of laboratory-provided tetracycline that subsequently kills offspring born with the gene in the larvae or pupae stage (3). The strategy itself is genetically feasible, and mathematical models suggest that ultimately the specified population would be suppressed or even eliminated (3). However, a 2011 study found that the OX513A males inseminated approximately half the number of females as did the wild type males, with a higher energy cost of mating (3). Because the number of females inseminated was nearly identical over the first three days, the study concluded that under the condition of frequent releases of the GM males, they may have potential as a facet of a control program (3). Oxitec, a United Kingdom-based firm, launched a pilot program of releasing GM mosquitos in the city of Piracicaba in the state of São Paulo, Brazil in 2014, with the number of DENV cases subsequently plummeting from one hundred and thirty-three to one after ten months (30). However, the project is expensive, and funds are lacking to systematically counter the mosquito using such methods (30).

Easter Island provides an example of a success story where a permanent sanitation plan paired with education about breeding grounds and constant communication surrounding the risks posed by tourism resulted in the eradication of ZIKV (62). Accordingly, in an attempt to duplicate this accomplishment, the PAHO has produced an extensive series of guidelines pertaining to engaging and instructing the public in an accurate and timely manner about steps they may take to control the vector in addition to detailing the procedures being undertaken by healthcare authorities in presently impacted regions (89). Specifically, they pledge “to maintain

credibility and public trust by disseminating accurate science-based material”, “to respond rapidly to concerns and specific needs as quickly as possible”, and “to share information on the first occurrence of the disease to maximize public awareness and ensure the interinstitutional consistency of messages on ZIKV” (89). Risk management in this form is markedly improved from the widespread confusion and fear exemplifying the AIDS epidemic in the United States, where police officers desired gloves to handle “potentially dangerous” individuals and citizens overwhelmed the New York City Health Department with calls inquiring if they would become infected with AIDS by sharing laundry facilities with gay men or touching the handrails of the subway (37).

Modern Threats of Spread

Beyond the dissemination of information lies the greater concern of the spread of ZIKV itself due to the prominence of the responsible vectors in other regions and the escalating calamity of global warming (47). A public health warning was issued in 2009 during the Yap epidemic concerning the conceivable threat of ZIKV spreading through commerce and travel across significant distances, especially pertinent because the outbreak of ZIKV on Yap Island in Micronesia was the first outside of Africa and mainland Asia (43). The CDC went as far as to consider ZIKV an emerging pathogen at this time, a harbinger of what was to come with their hypothesis that mosquitos of the Americas could be capable of proliferating ZIKV (43). Moreover, the report on the epidemic on Yap Island published in the *New England Journal of Medicine* implored the medical community and prominent laboratories to be increasingly vigilant in their epidemiological and surveillance infrastructure to identify the expansion of infectious diseases (23). At present, Dr. Derek Gatherer of the University of Lancaster points to the possibility of ZIKV widening its scope to Europe, particularly the southern region including

France, Greece, Italy, and Spain (84), with the *A. albopictus* (albeit not the tropically-oriented *A. aegypti*) mosquito also found to the northernmost extent of the major American cities of Chicago and New York (86).

Despite these natural ecological conditions, the pervasiveness of air conditioning, mosquito control – minimal standing water – and window screens (86) in combination with lower levels of poverty and an elevated degree of urban development is believed to render chances slim that significant outbreaks will materialize in Europe or North America (84). That said, the narrative of the proliferation of CHIKV demonstrates that ongoing climate change and human patterns of behavior are central factors in the proliferation of a virus such as CHIKV, DENV, and YFV, and thereby theoretically ZIKV as well (63). From animal reservoirs and a potentially enzootic – endemic among animals – state, CHIKV was able to exploit the drying and warming of North Africa to move amongst human water sources, with the African slave trade subsequently carrying the disease around the world and leading to a pandemic entangling the Western Hemisphere in the nineteenth century (63). The spread of CHIKV illustrates the capacity for arboviruses of the likes of CHIKV, DENV, and ZIKV to threaten both developing and developed populaces (39). Unpromisingly, the report on ZIKV infection of humans in Gabon exemplified the adaptive cycle of the infection in utilizing *A. albopictus* and transpiring in an urban setting (39). Furthermore, an association may be drawn to allegations regarding the prospective expansion of Lyme disease (47). Whereas some sources affirm that these tickborne ailments are not directly impacted by climate change (47), a model using the example of Canada found that the topographical range of the vector *Ixodes scapularis* (prominent in the central and eastern regions of the country) will continue to expand as it did from Ontario to twelve additional locations over the course of the last decade as a consequence of global warming (66). Paired

with atmospheric impacts on the habitats of non-mammalian hosts, the appearance of conditions such as Lyme disease may increase in frequency as a result (66).

Summary of Health Organization Responses

Throughout this analysis, ZIKV and the response of global medical authorities to various aspects of the infection have been compared to their reaction to equivalent facets of AIDS and Lyme disease. Across certain areas, attitudes towards and management of the conditions have been or were similar, yet in others, they were or continue to be remarkably different. The key question becomes: why these disparities? Evidence indicates the prevalence of both ZIKV (80) and Lyme disease (76) have been downplayed and their symptoms reduced to a limited number of what are regarded as the most emblematic signs despite variation in individual reactions to foreign substances (44) (46). The CDC has been hesitant to acknowledge all means of transmission of ZIKV (51) and adamantly refutes all conduits but ticks as a vector for Lyme disease (54), whereas by the mid-1980s the four key channels of transmission of AIDS were notorious (37). Testing for Lyme disease is particularly ineffective (29), yet diagnostic methods for ZIKV (43) and AIDS (37) have been problematic as well, with vaccinations nonexistent for any of the three maladies (69). Moreover, connections between ZIKV (86) and AIDS (37) and their corresponding related infections and syndromes have been illuminated and at times garnered more attention than these debilities themselves in contrast to the notable absence of publicized investigations into the link between Lyme disease and other neurological and retention disorders (36). Likewise, government and health organizations present transparent mitigation methods for ZIKV (80) and AIDS (67) to recover from or lessen the severity of the illnesses, respectively, as opposed to the disputed shortsighted treatment procedures for Lyme disease (55) espoused by these same groups. Whereas extensive efforts have been taken to

provide rapid dissemination of accurate information related to the latest developments concerning ZIKV (89), AIDS information was delayed and encountered resistance (37), and knowledge regarding Lyme disease, despite being an active pathogen since 1975, continues to be extremely curt and limited (53).

Notably, at a given point in time, all three illnesses have been the subject of conspiracy theories (81) (37) (10). Conjectures pertaining AIDS included a consignment of polio vaccines concocted on the kidney cells of African green monkeys, the worldwide campaign to eradicate smallpox, and the outcome of genetic engineering sponsored by the US Army at Fort Detrick amidst experiments in biological warfare (37). Dr. John Seale declared that HIV – the precursor to AIDS – resembles a recombinant virus of the type crafted in a laboratory; specifically, he contended it is a mix of bovine leukemia virus (BLV, from cattle), maedi-visna virus (MVV, from sheep), two additional lentiviruses from goats and horses, and adult T-cell leukemia (HTLV-1) (37). Closely related is the most widespread hypothesis concerning Lyme disease: in his book *Lab 257*, Michael Carroll correlates the epidemic of Lyme disease initially appearing, aptly, in Old Lyme, Connecticut, with the Plum Island Animal Disease Center located off of the coast of Long Island (10). The research facility was plagued by safety violations and outbreaks of diseases such as foot-and-mouth (HFMD), with *Lab 257* further revealing hazards posed to people by the studies conducted in the building (located in close proximity to the aforementioned Fort Detrick) (82). Third of all, as was previously described, the association between ZIKV and microcephaly was contended, with the notion that microcephaly is actually triggered by the use of larvicide in drinking water (81). However, ZIKV itself was also the subject of scrutiny for being the hypothetical fallout of the earliest release of GM mosquitos in 2012 (15).

Differences in the geographic origins as well as the economic and political circumstances surrounding the emergence of these illnesses may thereby provide greater insights into their incongruent assessments (2) (37) (10). ZIKV is not recognized as being actively transmitted in Western nations (2), the AIDS epidemic received increasing attention in the form of the first International Conference on AIDS organized by the CDC once it was discovered in Africa rather than when it began displaying heterosexual transmission in the United States (37), and Lyme disease that indiscriminately afflicts a high percentage of the American and European populace (10) persists as a stigmatized chronic illness (55). Democratic Congressman Harry Waxman noted in regards to the AIDS epidemic that “there is no doubt in my mind that if the disease had appeared among Americans of Norwegian descent, rather than gay men, the response of the government and medical community would be different” (37). Bearing this in mind, these results therefore appear to be the opposite of what he anticipated; rather, clarity may emerge when they are viewed in aggregation with the lack of infallible cures for the infections and the aforesaid theories correlated with the origins of the illnesses (21). The CDC is based in Atlanta, Georgia, United States, and the WHO in Geneva, Switzerland. When a challenging health crisis is “over there” – Africa and the professed developing nations of the Americas – it may be less distressing to acknowledge (10), with foreign medical authorities subsequently prepared to enter as the heroes of the day in search of a solution (37). In opposition, when an ailment threatens the alleged superiority of Western society, using the examples of AIDS and Lyme disease, instinct may be to downplay and virtually ignore the complaint for as long as possible (37). An even greater influence is exerted by insurance companies and prescription drug firms (14). While there are extensive regimes of antiretroviral medications that must be taken each day for the rest of one’s life to stave off the progression of HIV to AIDS (67) as well as for MS and other

conditions (59), there are no expensive pharmaceuticals that may be purchased to the profit of these groups to fight off Lyme disease (29). Furthermore, insurance companies do not cover treatment of Lyme disease beyond a short-term course of antibiotics that, as formerly explained, is habitually inadequate for eliminating the pathogen (14).

Finally, whereas ZIKV is apparent within two to five days (88), resultant microcephaly is evident both prenatally and expressly after birth (26), and AIDS symptoms arise within an average span of five to ten years – at which point death is soon to follow (37) – Lyme disease is minimally recognized while alive and rarely accepted as a cause of death (48). An analysis of death certificates records from 1999-2003 yielded Lyme disease as a multiple (contributing to) or underlying cause of mortality in only one hundred and fourteen cases (48), yet on a single Thursday in December of 2013 alone, NBC News reported on three individuals ages twenty-six to thirty-eight who collapsed and passed away with little warning (34). During preparations for tissue donation, all three were found to be infected with *B. burgdorferi*, fatally in what is referred to as Lyme carditis in their hearts (34). The moral of this segment is that no one, irrespective of class, gender, ethnicity, race, sexual orientation, and other personal characteristics, is immune to nature. Whether a microbe or virus acts with efficiency or initiates a period of prolonged suffering, silently or with sudden outcry, it may be no less dangerous (46). As the former analysis demonstrates, though, global health authorities have yet to fully act on this reality.

Science and Society

To bring the topic to a close, ZIKV and the disaster it has become for the country of Brazil in particular provides an appropriate paradigm of the cultural, economic, political, and social impacts of a disease in the sense of how these aspects of society interact with the science and epidemiology of an epidemic (8). More significantly, ZIKV demonstrates how an infectious

agent may intensify weaknesses in the fabric of a nation (8). The literary work *Collapse* by Jared Diamond describes five factors that have been instrumental in the downfall of historic societies (20), and by looking at these in concurrence with the effects of ZIKV, it is intriguing to analyze whether or not Brazil is heading down the same path. Specifically, Diamond cites the influences of destruction imposed by humans on their environment, natural variations in climate, hostile neighbors, diminished backing by affable neighbors, and the responses of society as a whole with a critical emphasis on the reactions of individuals and groups in power (20).

Accordingly, ZIKV has built on existing economic and political instability in Brazil (8) while clashing with cultural values (13) and resulting in strained tensions with other countries (73). Ongoing accusations of corrupt deals between the government and contractors – chiefly with Petrobras, an oil and gas firm – accompanied by allegations of concealing the true scope of the budget deficit have led to calls for the impeachment of President Dilma Rousseff (8). Likewise, the recently appointed head of the Department of Health is a career politician chosen to gain the support of the Brazilian Democratic Movement Party to prevent such impeachment charges rather than a professional in the public health field (8). The debt status of Brazil has been relegated to junk status by two of three prominent credit-rating bureaus with their economy projected to contract by 2.5-3% in 2016 (6). Infrastructure is in a state of disrepair, with severe deficiencies in access to drinking water, the sewage and waste systems, and urban development allowing for the intensified propagation of the *A. aegypti* mosquito and thereby ZIKV (8).

In addition to the aforementioned vector expansion resulting from changing ecologies and warming temperatures ignited by global warming, Brazil continues to witness deforestation in the Amazon (28). The government subsidized agriculture, beef, and mining beginning in the 1970s that incentivized settlement up to the edges of the rainforest, with continued halfhearted

enforcement of property rights further aggravating the felling of old-growth forests (28). The expansion of international commerce facilitated by free trade agreements implemented in the 1990s has also driven excessive exploitation of the region's resources; Brazil is the largest exporter of beef, with one-third of these products coming from Amazon territory, as well as one of the highest exporters of soybeans and a direct contributor to the world market for timber (28).

With the outbreak of ZIKV, an urgent materializing risk facing Brazil is the ensuing breakdown of more positive migration, tourism, and overall relations with other nations (73). Business travelers have expressed anxiety about required trips to infected countries, and a travel agency based in Miami has reported the cancellation of 20% of planned trips to Central and South America out of the fear of infection (75). In this way, the ZIKV threat comes at an inopportune moment, just months away from the scheduled start of the 2016 Olympic Games intended to be hosted by the city of Rio de Janeiro (32). The United States Olympic Committee (USOC) has employed two disease experts to advise them on the situation and particularly to offer recommendations to female athletes of childbearing age (32). U.S. soccer goalkeeper Hope Solo of the defending World Cup Championship team has announced she will not attend if the situation remains in its present condition; in contrast, U.S. marathoner Shalane Flanagan has pronounced her faith in Brazil's ability to guarantee the safety of the athletes (32).

On the topic of pregnancy concerns, ZIKV has challenged beliefs surrounding contraception and abortion as a result of its association with microcephaly (13). Leaders of the Roman Catholic Church, an entrenched tradition in Latin American communities, have maintained that these methods of avoiding pregnancy remain unacceptable even amidst appeals by health officials in countries including Brazil, Colombia, Ecuador, El Salvador, and Jamaica for individuals to refrain from becoming pregnant for the next year (13). Nations of the region

embrace abortion laws ranking among the most stringent in the world, and despite the concession by Pope Francis that contraceptives may be “morally acceptable” in this emergency situation, he has upheld that abortion is a crime (18). Rather, the Catholic Church has encouraged chastity and/or the notoriously unreliable natural family planning method – tracking one’s cycle and withholding from sex when fertile (38). In short, the use of contraceptives and abortion are a taboo stemming from religion that further compromise the stability of Brazil and its ability to mitigate the cost of ZIKV (32).

Taken together, all of the above considerations are inherent to nations on the brink of collapse. Years ago, the indigenous civilization on Easter Island disappeared in the wake of complete extinction of the native trees preceding dwindling crop yields and the loss of wild food sources (20). No longer able to deliver prosperity, the chiefs and priests were overthrown and their society disintegrated into civil war representing a failure of both a political ideology and religious practice (20). Furthermore, the cessation of trade between the Old Norse in Greenland and Norway due to altered climate conditions, specifically the inception of the Little Ice Age in the early 1400s that caused the obstruction of previous sea lanes with ice, deprived them of lumber, tar, and luxury goods for the church (20). Unfriendly relations with the Inuit, the other occupants of the island, and the resistance to adopting their hunting techniques due to strict adherence to a European identity additionally contributed to their demise (20). Neither of these societies, though, are described as experiencing a disease epidemic that contributed to their downfall (20). Perhaps that provides an advantage incurred by Brazil.

Conclusion

ZIKV has illuminated the gravity of the problems facing Brazil (8) and drawn international attention to their plight (31), hypothetically delivering a spark for a transformation

in governing procedures (6) and cultural attitudes (38) to more sustainable strategies for the contemporary world. The challenges ZIKV has posed for the global medical community have also exemplified enduring areas of weakness in responding to disease epidemics, yet as have been discussed throughout this paper, there are numerous ways in which these organizations have impressed in their superior efforts compared to outbreaks of the past. In this regard, too, the CDC, WHO and government agencies can stand to gain from ZIKV in how they may adopt a more genuine and open-minded approach to other illnesses of the present and future. New insights regarding ZIKV appear on the news almost daily, and these revelations will continue to illustrate how quickly and to what extent pertinent aspects of the disease are recognized and addressed. At this time, it is an unknown if the Olympic Games will be able to proceed in Rio de Janeiro (32). Contrariwise, it is undeniable that the perilous games with nature against bacteria and viruses will continue. In the battle against ZIKV, it remains to be seen if the medical establishment or the natural world will emerge the winner.

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