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SUPPLEMENT ARTICLE

Meeting the Challenge of Epidemic Chikungunya

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Humans will perpetually be threatened by an ever-expanding list of emerging and reemerging infectious diseases [1]. The past few decades alone have seen the onslaught of infectious diseases such as human immunodeficiency virus (HIV) infection and AIDS, Ebola, so-called flesh-eating bacterial infection (pathogenic streptococci), avian influenza A(H5N1) and A (H7N9) virus infection, Middle East respiratory syndrome, severe acute respiratory syndrome, and West Nile virus infection. To this list, we must now add chikungunya, an explosively reemerging mosquito-borne disease [2] that, in 2013, travelled from its historic homes, in Africa and Asia/Southeast Asia, to arrive and spread pandemically in the Americas, threatening permanent establishment in this new location [3] and, eventually, all the way around the globe to West Africa, its presumed ancestral home. On this journey, chikungunya virus, an alphavirus, developed a new genetic lineage with the capacity to be transmitted not only by its traditional mosquito vector, *Aedes aegypti*, the vector of dengue virus, yellow fever virus, and, since 2013, Zika virus, but also efficiently by the more widely dispersed mosquito vector, *Aedes albopictus*. Although an older chikungunya viral lineage transmitted only by *A. aegypti* seems to have caused almost all of the epidemic activity in the western hemisphere to date, it is not inconceivable that viral lineages transmitted by *A. albopictus* mosquitoes may evolve or be introduced [4]. This could potentially contribute to local spread within the United States, where *A. albopictus* mosquitoes are present in at least 32 states [3].

More than 1.9 million cases of acute febrile, prostrating, polyarthritic chikungunya have been reported in the Americas so far. Nearly 5000 authochthonous or travel-associated cases have occurred in 49 US states, including local transmission in Puerto Rico, the US Virgin Islands, and Florida (as of April 2016). Fortunately, only a very small percentage of chikungunya cases, on the order of 1 per 3000, have been fatal; however, the disease can be severely debilitating, and nearly half of affected patients report postinfectious arthralgias for months or even longer following initial infection. About 5% of those patients develop chronic inflammatory rheumatic disease, including rheumatoid arthritis–like syndromes [5], that may or may not be caused by chikungunya virus; officials fear that as many as 400 000 or more such chronic inflammatory arthritic cases may already be destined to occur in the Americas. The economic impact of work absences and medical and public health expenses, along with the societal impact of the incapacity of considerable numbers of working adults, have also been substantial. Studies have estimated direct medical costs of 90€ per each outpatient and 2000€ for each inpatient (about $100 and $2220 US dollars, respectively, at June 2016 exchange rates) during the epidemic on La Réunion, and over 73 million US dollars per 106 592 patients during the epidemic in Colombia [6, 7]).

Chikungunya thus represents yet another exotic rapidly reemerging disease that must be confronted at multiple levels, with robust public health responses and with basic and applied research to develop interventions such as diagnostic assays, therapeutic agents, and vaccines. The National Institute of Allergy and Infectious Diseases (NIAID) has for decades been responding to many other emerging diseases, notably the multiple challenges of the HIV/AIDS pandemic and the multiple threats of pandemic influenzas. The NIAID's dual mandate is not only to maintain a robust portfolio of basic and applied research to address endemic infectious and immune-mediated diseases, but, at the same time, to maintain rapid-response approaches to new and unpredictable diseases that inevitably emerge. It is this latter capacity that now must be brought to bear on chikungunya.

Over the past 10 years, the NIAID funded approximately $83 million of chikungunya research. These efforts have helped to establish a strong cadre of chikungunya researchers now conducting innovative studies on diagnostic assays, therapeutic agents, vaccines, public health approaches to controlling the disease, and basic chikungunya virology and immunology.

On 30 June 2015, the NIAID, together with the Pan American Health Organization and the World Health Organization, convened an expert consultation of 136 scientists, administrators, and public health officials, representing 18 countries from the Americas, Africa, Asia/Southeast Asia, and Europe

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to address gaps and opportunities in chikungunya research, with an emphasis on responding to the new epidemic in the Americas. The specific aims of the consultation were to (1) share knowledge about chikungunya, (2) assess epidemic risks in the Americas, (3) identify critical gaps in technology and research infrastructure, and (4) identify opportunities for collaborations in research and control/prevention.

Sixteen publications in this special supplement of *The Journal of Infectious Diseases* represent some of the efforts of those experts, who, together, identified many unique challenges, foremost among which was the realization that chikungunya is likely to remain a difficult disease to prevent or control, even when vaccines and effective treatments become available. This is due to a number of factors, including the probability that chikungunya will become permanently established in the western hemisphere, either in enzootic reservoirs, or as part of a perpetual human-mosquito-human transmission cycle, or both; that rapid deployment and use of vaccines and drugs will be difficult because epidemics have historically been both explosive and unpredictable in their place of occurrence/recurrence; and the reality that we thus far have only limited understanding of the pathogenic mechanisms of and therapeutic opportunities for eliminating persistent viral infections of the joints [8]. Furthermore, we face the possibility that, even as research progresses, the virus may mutate in its adaptation to local vectors or enzootic hosts or that *A. albopictus*–adapted strains will become established and lead to significant geographic extension of the pandemic. These and other daunting challenges are addressed in many of the articles in this supplementary issue.

It is encouraging that we are already seeing progress in areas such as the development of several new vaccine candidates, some of which are in early phases of human testing; passive immunotherapy with monoclonal antibodies; and imaginative new vector control approaches. Over recent decades, we have learned much about how to respond to sudden emergences of new diseases, by fostering innovative research on accelerated timetables. This is best accomplished by forging and supporting partnerships between host country governments and public health officials, clinicians, researchers, national and philanthropic donors, and industry. The emergence of chikungunya in the Americas requires us to join together with partners to quickly and effectively address yet another new disease that is likely to be with us indefinitely. Significant challenges remain; however, as evidenced by the publications in this supplement, many of our best scientists are already hard at work to meet them.

Notes

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References

1. Fauci AS, Morens DM. The perpetual challenge of infectious diseases. N Engl J Med **2012**; 366:454–61.
2. Burt F, Ralph MS, Rulli NE, Mahalingam S, Heise MT. Chikungunya: a re-emerging virus. Lancet **2012**; 379:662–71.
3. Morens DM, Fauci AS. Chikungunya at the door – déjà vu all over again? N Engl J Med **2014**; 371:885–7.
4. Tsetsarkin KA, Chen R, Weaver SC. Interspecies transmission and chikungunya virus emergence. Current Opinion Virol **2016**; 16:143–50.
5. Thiberville S-D, Moyen N, Dupuis-Maguiraga L, et al. Chikungunya fever: epidemiology, clinical syndrome, pathogenesis, and therapy. Antiviral Res **2013**; 99:345–70.
6. Soumahoro MK, Boelle PY, Gaüzere BA, et al. The chikungunya epidemic on La Réunion Island in 2005–2006: a cost-of-illness study. PLoS Negl Trop Dis **2011**; 5:e1197.
7. Cardona-Ospina JA, Villamil-Gómez WE, Jimenez-Canizales CE, Castañeda-Hernández DM, Rodríguez-Morales AJ. Estimating the burden of disease and the economic cost attributable to chikungunya, Colombia, 2014. Trans R Soc Trop Med Hyg **2015**; 109:793–802.
8. Schwartz O, Albert ML. Biology and pathogenesis of chikungunya virus. Nature Rev Microbiol **2010**; 8:491–500.