CURRENT TOPICS

NEW FROM ASM

Genetics May Constrain Chikungunya, but Other Controls Deemed Crucial

Shannon Weiman

Chikungunya virus (CHIKV) outbreaks in the Americas may be limited because of the apparent inability of the currently circulating virus to adapt to particular mosquito species, namely those that might otherwise drive viral outbreaks into more temperate climate zones, according to researchers at the 2015 ICAAC, held in San Diego last September. However, other measures are very much needed to contend with outbreaks already occurring in Central America and the Caribbean region.

Chikungunya is typically transmitted by *Aedes aegypti* mosquitoes, which ordinarily reside in tropical areas, where they preferentially feed on humans. However, when the virus has adapted to another mosquito host, *A. albopictus*, it caused widespread outbreaks across Africa, India, Southeast Asia, and Europe during the past decade, says Scott Weaver of the University of Texas Medical Branch, Galveston. This species endures colder climates, spreading disease into temperate regions.

These *A. albopictus*-adapted CHIKV strains carry point mutations in the genes encoding their E1 and E2 envelope glycoproteins, which mediate fusion to enter host cells. These mutations enhance viral fitness so profoundly that they arose independently many times, according to Weaver. "Phylogenetic and epidemiologic studies indicate that E1-A226V was selected convergently by at least four different CHIKV lineages in different geographic locations," he says. In vitro testing confirms that this mutation increases viral fitness 40- to 100-fold, while the E2-L210Q mutation leads to additional 4- to 6-fold increases in fitness. This enhanced infectivity and replication in the *A. albopictus* midgut leads to higher transmission of the virus to humans.

However, the Asian lineage viruses do not develop comparable mutations, Weaver continues. A specific amino acid at one site prevents them from acquiring that crucial E1–226V mutation, and conformational changes that mediate these enhanced fitness effects cannot occur. "The introduction of the Asian rather than the Indian Ocean lineage may have been stochastic, but these Caribbean strains have a limited ability to adapt to *A. albopictus*, which may limit their spread into temperate regions of the Americas," he says.

While vector transmission is well understood in Africa and Asia, where chikungunya has circulated for decades, the recent jump to the Americas introduces many unknowns, cautions Ann Powers of the Centers for Disease Control and Prevention in Atlanta, Ga. Native mosquito species and animal reservoirs in the Americas may yet do something unexpected.

With chikungunya cases already reaching 1.6 million in tropical regions of the Americas, better prevention and treatment measures are desperately needed, Powers and others say. Although vector control is a mainstay of public health efforts, novel vector-targeted approaches include introducing male mosquitoes that are genetically
engineered to produce inviable offspring or introducing mosquitoes infected with *Wolbachia* bacteria, which interfere with the capacity of the insects to produce and transmit CHIKV.

Ongoing phase 1 vaccine trials could lead eventually to preventive vaccine campaigns across the region. Infusion of anti-CHIKV immunoglobulins for those at risk to develop severe disease is another potential option, and a clinical trial is under way, according to Marc Lecuit of the Institut Pasteur in Paris, France. Moreover, because type I interferon deficiency is linked to high viremia and severe disease in mice and humans, bolstering this host immune response may also be helpful for some such patients.

*Shannon Weiman is a freelance writer in San Francisco, Calif.*

**NEW FROM ASM**

**Chikungunya, Enterovirus D68 Cause Neurologic Symptoms in Children**

**Shannon Weiman**

Recent outbreaks involving the chikungunya virus (CHIKV) and enterovirus D68 in the Americas led to rare but severe neurologic symptoms in infected children that, in some cases, gave rise to long-term neurologic deficits, according to several researchers who spoke during the 2015 International Congress of Chemotherapy and convened in San Diego last September. Researchers continue to probe those rare neurotropisms, for which there are no treatment options, with an aim to develop deficit-sparing interventions.

CHIKV infections are known mainly for causing rheumatic symptoms. However, when transmitted from mother to infant at birth, severe neurologic manifestations afflict 50% of those newborns, while fatalities occur in nearly 17% of such patients, according to Marc Lecuit of the Institut Pasteur in Paris, France, who spoke in the session “Chikungunya: a Global Threat.” With chikungunya’s recent jump to the Americas, and outbreak numbers reaching 1.6 million within two years of its arrival, these severe cases are of growing concern.

“CHIKV infection acquired in the perinatal period can cause lifelong disability,” says Patrick Gerardin of the French National Institute of Health and Medical Research (INSERM). “The neurological outcome of chikungunya encephalopathy... ranges from mild ocular, behavioral, or postural deficiency to severe cerebral palsy with

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**MINITOPIC**

**Microbiology Policy Bulletin Board**

Recent developments involving microbiology and related science policy matters include:

- California Governor Edmund Brown, Jr., signed legislation in October that, beginning in 2018, will sharply limit antibiotic use in livestock—outright prohibiting use of medically important antimicrobial drugs for promoting weight gain in animals, while also restricting their use for treating sick animals to only those cases approved by licensed veterinarians.
- Federal regulations affecting scientific research at universities should be streamlined and made to be consistent across different agencies that fund such research, according to a report released in September by the National Academies of Sciences, Engineering, and Medicine in Washington, D.C. The report, “Optimizing the Nation’s Investment in Academic Research: A New Regulatory Framework for the 21st Century: Part One” is available at http://www.nap.edu.
- Officials of the U.S. Food and Drug Administration (FDA) in October approved the marketing of the first cerebrospinal fluid nucleic acid-based test for simultaneous detecting multiple pathogens that can cause central nervous system infections. The test battery, called the FilmArray Meningitis/Encephalitis Panel, is manufactured by BioFire Diagnostics of Salt Lake City, Utah.
- During the past 20 years, the number of drugs qualifying for expedited development and approval programs grew significantly at FDA, raising the question whether “this trend is being driven by drugs that are not first in class and thus potentially less innovative,” according to Aaron S. Kesselheim of Harvard Medical School in Boston, Mass., and his collaborators. Details appeared 23 September 2015 in BMJ (doi.org/10.1136/bmj.h4633).
- Between 2008 and 2014, the United States invested approximately $820 million in synthetic biology research, with the Defense Department becoming a key funder and the Defense Advanced Research Projects Agency now outspending the National Science Foundation by threefold in this sector, according to a September 2015 report, “U.S. Trends in Synthetic Biology Research Funding,” from the Woodrow Wilson International Center for Scholars in Washington, D.C. For details, see: http://www.synbioproject.org/.
- People who decide not to vaccinate themselves or their children fall into four main categories: complacency, inconvenience, a lack of confidence, and a rational calculation of pros and cons, according to Cornelia Betsch at the University of Erfurt in Erfurt, Germany, and collaborators in Germany and the United States. Details appeared in the October 2015 *Policy Insights from the Behavioral and Brain Sciences* (doi:10.1177/2372732215600716).