Zika poses serious challenges to development of new diagnostics

Ongoing efforts to develop clinically useful diagnostics for Zika virus infection have faced a number of roadblocks, including substantial variation between patients’ immune responses, difficulty identifying asymptomatic cases and incomplete data concerning the optimal patient samples for testing, according to presenters at the American Association for Clinical Chemistry’s Annual Scientific Meeting and Clinical Lab Expo.

“I would say that, by far, Zika has been the most challenging emergency that we’ve had to date, even more than Ebola,” Stephen J. Lovell, PhD, branch chief in the FDA’s Division of Microbiology Devices, said during a late-breaking symposium. “In the case of Zika, 80% of patients could be asymptomatic, whereas for Ebola it was very clear who was symptomatic and who wasn’t. The symptoms paired very closely with the presence of RNA.”

‘Considerable constraints’ on testing availability

Among the 44 tests to which the FDA has given its emergency use authorization (EUA), Lovell said only seven are Zika virus diagnostics. The majority of these are molecular or PCR assays, he said, and the only serologic assay, the MAC-ELISA test, is exclusively used in CDC labs.

This scarcity of platforms has led to difficulties confirming cases of suspected Zika virus infection, according to Randall L. Kincaid, PhD, senior scientific officer in the division of microbiology and infectious diseases at the National Institute of Allergy and Infectious Diseases, and could present further issues for health care providers as Zika spreads into the continental United States.

“There are considerable constraints on the availability of molecular tests,” Kincaid said. “Until recently, almost all testing was done through the offices of public health labs that are administered by the CDC, and only recently have there been tests that have been approved under the EUA for use in clinical labs. While there do exist so-called ‘home-brew’ options that can be carried out in an unauthorized lab environment, there really, at this point, are no simple point-of-care types of options.”

These diagnostics are of increased importance with a disease such as Zika, Kincaid said, as a physician may be unable to make a diagnosis because the “vast majority” of infected individuals are either asymptomatic or show symptoms similar to other neurologic, mosquito-borne viruses.

“Normally, diagnosis is not simply a test,” Kincaid said. “It is a physician’s assessment of condition, which involves symptomology [and] epidemiology, and laboratory epidemiology plays into that.”

Numerous hurdles slow development

For now, the pursuit of simpler diagnostics has been hamstrung by a number of disease-specific factors, Lovell and Kincaid explained. Among them is the dearth of information as to whether serum, saliva, urine or whole Zika tests continues on page 58.

Patients with contact lens-related corneal infections report modifiable risk factors

Over the past decade, contact lens wearers with corneal infections reported modifiable risk factors such as overuse and poor contact lens hygiene, according to a review of FDA records.

“Continued efforts to educate contact lens wearers about prevention of contact lens-related eye infections are needed,” Jennifer R. Cope, MD, MPH, medical epidemiologist in the Division of Foodborne, Waterborne, and Environmental Diseases at the CDC, and colleagues wrote in MMWR.

Cope and colleagues searched the FDA’s Medical Device Report (MDR) database for contact lens-related reports that contained the terms “ulcer” or “keratitis” — words that reliably identify accounts of apparent microbial keratitis.

Among 1,075 MDRs between 2005 and 2015 that contained those terms — 86% of which were filed by contact lens manufacturers — 23.1% (n = 270) described modifiable risk factors known to be associated with contact lens-related corneal infections, including keratitis.

The remainder of the reports did not provide details about risk factors, which was indicative of the passive surveillance system of MDRs — one of several issues linked to eye infection.

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“Continued efforts to educate contact lens wearers about prevention of contact lens-related eye infections are needed.”

— JENNIFER R. COPE, MD, MPH, AND COLLEAGUES

References:

Disclosures: The researchers report no relevant financial disclosures.
Zika tests

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blood would provide the best results.

“While PCR-based and other nucleic acid-based tests can be very definitive, we’re still not clear on exactly which samples we should be testing,” Kincaid said. “But quite recently, a report came out showing that whole blood actually might be a preferred sample type for diagnosis.

“I think this is very important because it could obviate many of the concerns surrounding serologic testing, which is used when a person is concerned that they may have been infected, but have no direct evidence of that.”

While clinicians looking to confirm asymptomatic recent exposures would normally rely on serologic testing, Kincaid said developing these tests, in particular, has been hampered by muddled immune responses. Flaviviruses, he explained, evoke a very similar type of response to other flaviviruses, making reliance on early immunoglobulin M activity difficult.

“To make this even more complicated, there is increasing evidence that prior exposure to another flavivirus will complicate the immune response,” Kincaid said. “So, it’s important to consider the distinctions between people who come from naive environments, such as the continental United States … as opposed to people who are in areas where you have prevalent forms of flavivirus infection. Their immune responses differ considerably.”

Kincaid said some serologic assays have been developed and approved for use in Europe, but that U.S. government agencies believed these tests lacked the sensitivity and specificity required for use in a clinical setting. Further, he noted that because Zika virus infection
involves “very personal and private decisions,” work toward development of new rapid point-of-care diagnostics for use outside of clinics would be of “great interest” and could improve detection among those who would not otherwise present for testing.

**‘Foundational knowledge’ key to success against Zika**

During the session, Kincaid also described several of the ongoing Zika efforts being conducted by NIAID and other government agencies. Although protecting the blood and blood product supply, reducing further transmission and informing pregnant women of Zika risks were among the agencies’ top priorities, he also spoke of research concerning flavivirus-specific immune responses, development of new reagents, and support of clinical trials to clarify the risks for Zika virus and other flaviviruses to pregnant women.

Kincaid and Lovell stressed that each of these approaches — as well as collaboration between researchers, diagnostic manufacturers and government regulators — will play an important role in developing functional Zika assays and limiting the disease’s impact.

“Zika virus is unlikely to be solved in a simple way,” Kincaid said. “It will require the development of foundational knowledge and development of a variety of prototype diagnostic devices which can be vetted, validated and used in different clinical settings.” – by Dave Muoio

**Reference:**

Late-breaking session: Zika virus — global impact and the role of diagnostic testing. Presented at: AACC Annual Scientific Meeting and Clinical Lab Expo; July 31-Aug. 4, 2016; Philadelphia.

**Disclosure:** The researchers report no relevant financial disclosures.
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