**Ethics cases on Zika Virus**

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# **Case 1—Testing for Zika Virus**

Infection with Zika virus (ZIKV) in pregnant women is a major global concern because of its linkage to congenital abnormalities including microcephaly, spontaneous abortion, and intrauterine growth restriction.(1) In addition, ZIKV infection has been associated with severe neurologic disease and Guillain–Barré syndrome, particularly among older adults.

An infected bite from a female *Aedes aegypti* mosquito is believed to be the primary mode of transmission of ZIKV, but infection through sexual transmission has also been reported. Viral persistence in the testes and semen has been described, and the window of sexual transmission remains uncertain, which has led to much uncertainty, particularly for couples trying to get pregnant.

Data supporting vertical infection and a causal role for ZIKV in the development of congenital malformations include the detection of ZIKV RNA or antigen in the amniotic fluid, the placenta, or the brain tissues of fetuses or infants in whom microcephaly was diagnosed after death in utero or soon after birth; and multiple laboratory work with mice showing that ZIKV targets cortical progenitor cells impairing cell development, and inducing dell death. Moreover, a prospective study involving ZIKV-infected pregnant women in Brazil showed that 29% of fetuses had gestational abnormalities including microcephaly and intrauterine growth restriction, which in a subgroup of cases resulted in fetal death.

Testing for ZIKV is surprisingly complex, and may require three tests to confirm a positive result.(2) One test is called a polymerase chain reaction (PCR), designed to detect the active virus in blood and urine. But the PCR test is reliable only if used within 1-2 weeks of exposure. Since most infected people lack symptoms for ZIKV, many cannot pinpoint the date of exposure.

When a PCR test is negative, the next step is to test the blood sample for ZIKV [antibodies](http://health.nytimes.com/health/guides/test/antibody-titer/overview.html?inline=nyt-classifier). A negative antibody test means a person was not exposed to ZIKV. But a positive result may require a third test, since there is cross-reaction with other viruses, such as dengue and chikungunya, both of which cause flu-like symptoms and are present in Central and South American countries.

The third type, the plaque reduction neutralization test (PRNT), determines conclusively whether a person was exposed to ZIKV. In the U.S., this test is done by the [Centers for Disease Control and Prevention](http://www.cdc.gov/zika/symptoms/diagnosis.html) (CDC) and a limited number of local health department laboratories. However, it requires Biosafety level 3 laboratories.

For men, the story is even more complicated. Infected men can carry ZIKV in their semen for a certain period, but there is no approved test for screening semen.

As worries about the spread of the virus in the US continue to mount, public health department labs in Florida and New York City are running at or close to capacity, while private commercial labs have won emergency approval to run ZIKV tests, and have ramped up their testing capacity. Public health officials in Florida face a backlog of tests for pregnant women, some of whom may be waiting to make decisions about whether to have abortions if they test positive.

The CDC has issued restrictive guidelines about who should be tested, giving priority to pregnant women with possible exposure to ZIKV and to people with ZIKV-like symptoms. This testing policy largely ignores a sizable subgroup of women and men who are also at risk — those who are trying to conceive but fear that they have been exposed to ZIKV. The CDC recommends that women contemplating [pregnancy](http://topics.nytimes.com/top/news/health/diseasesconditionsandhealthtopics/pregnancy/index.html?inline=nyt-classifier) avoid travel to areas where ZIKV transmission is occurring and, if they have traveled, recommends that they wait at least eight weeks before trying to conceive. But it currently does not recommend testing.

Both the CDC and the [World Health Organization](http://www.who.int/mediacentre/factsheets/zika/en/) now recommend six months of protected sex if the male traveled to an area with risk of ZIKV, and eight weeks if the woman was exposed.(3) But neither group recommends testing.

These restrictions are aimed at preventing an onslaught of requests for ZIKV tests that could further clog the system and prevent public health officials from identifying new cases expediently. Consider the analogy of the excess number of specimens submitted to government labs following the post 9/11 anthrax scare in the U.S. After 6+ deaths from respiratory anthrax, some connected to inhalation of white powder that may have been weaponized anthrax, specimens of white powder including talcum, powdered sugar and others were submitted to labs across the U.S. for testing in such numbers that labs were overwhelmed.

Testing without adequate counseling could compound the problem. Tests also shape medical practice and influence insurance coverage, making doctors reluctant to order tests and insurers unwilling to cover the costs — between $229 and $800 on the private market — if patients don’t fit the CDC’s testing criteria.

Many public health experts say that the restrictions are necessary to ensure that people most at risk have access to testing. “We aren’t interested in stimulating the testing of simply anxious people,” said Dr. William Schaffner, an [infectious diseases](http://health.nytimes.com/health/guides/specialtopic/travelers-guide-to-avoiding-infectious-diseases/overview.html?inline=nyt-classifier) specialist and the head of [preventive medicine](http://health.nytimes.com/health/guides/specialtopic/preventive-health-care/overview.html?inline=nyt-classifier) at Vanderbilt University Medical Center. “We want health care providers to provide the appropriate counseling and to be selective in the use of this test, as they are in the use of any other test.”(2)

Some medical groups are pushing back against the CDC guidelines. The [American Society of Reproductive Medicine](https://www.asrm.org/?vs=1), a membership organization representing fertility experts, recommended that men and women who may have been exposed to ZIKV consider being tested and embark on fertility treatments only if tests are negative.

## Scenario

Given the reluctance of many government labs to provide testing to whoever comes forward, the following questions have been put forward to the local state lab:

1. Should testing be offered to all who want it regardless of possible risks as defined by travel or symptoms after possible exposure?
2. Should testing be offered to men, with or without a history of symptoms, who have visited areas where ZIKV has been reported? If so, what level of ZIKV incidence defines an area as high risk?
3. Should testing be given to couples who are planning on pregnancy but want to be sure that both partners are ZIKV free, especially as one may have been exposed to the virus through recent travel or residence?
4. Should testing be limited to pregnant women in their first-trimester only because they are thought to be at greater risk of delivering a child with malformations due to congenital ZIKV syndrome?
5. If the state refuses to provide testing for a man or a woman but their physician believes they have a legitimate claim to be tested and they cannot afford the private test, should the state make an exception and perform the test?
6. Who is liable if a child is born with congenital Zika syndrome and despite parental request, testing has not taken place because the physician was following the CDC guidelines?

(1) Mysoekar, I.U. et al. ”Modeling Zika Virus Infection in Pregnancy, N Engl J Med 2016; 375:481-484, [August 4, 2016](http://www.nejm.org/toc/nejm/375/5/).

(2) Rabin, R.C. ”Want a Zika test? It’s Not Easy”, The New York Times, September 19, 2016.

(3) CDC. “Women & Their Partners Trying to Become Pregnant”, <https://www.cdc.gov/zika/pregnancy/women-and-their-partners.html>.