DEFENSE HEALTH AGENCY
Armed Forces Health Surveillance Branch (AFHSB)

Detecting & Reporting DoD Cases of Zika Virus Disease and Zika Virus Congenital Infection Guidance as of 21 SEP 2016

BACKGROUND

This detecting and reporting guidance provides information to assist with the identification, diagnosis, and reporting of both Zika virus (ZIKV) disease and ZIKV congenital infection. CDC has detailed clinical and laboratory guidance available for healthcare providers.

ZIKV disease is usually a mild illness with symptoms lasting for several days to a week. Severe disease requiring hospitalization is uncommon and fatalities are rare. Only about one in five people infected with ZIKV become symptomatic. There is no vaccine or specific treatment.

CDC has determined that there is a causal relationship between ZIKV congenital infections and neurological birth defects. These birth defects can include microcephaly, intracranial calcifications, and/or other central nervous system abnormalities.

Due to the risk of ZIKV microcephaly associated with maternal ZIKV infection, fetuses and infants of women infected with ZIKV during pregnancy should be evaluated for possible congenital infection and/or neurologic abnormalities. CDC has issued updated guidance for advising and caring for pregnant women, and for evaluating and testing infants with possible ZIKV infection. A significant increase in reported microcephaly cases followed the discovery of ZIKV circulation in French Polynesia in 2013-2015 and Brazil in 2015.

ZIKV infection may increase the risk of developing Guillain-Barré syndrome (GBS). Several countries of the Pacific region and the Americas have reported an increased incidence of GBS in association with an increase in ZIKV infection.

Consider dengue and chikungunya infection, including co-infections. Dengue, chikungunya, and ZIKV are all transmitted by the same mosquitoes (*Aedes* species) and can have similar clinical features. These viruses often circulate in the same area and can occasionally cause co-infections in the same patient.

Differential diagnoses may also include malaria, leptospirosis, rickettsia, group A streptococcus, rubella, measles, parvovirus, enterovirus, adenovirus, other flaviviruses, and alphavirus infections (e.g. Mayaro, Ross River, Barmah Forest, O'nyong-nyong, and Sindbis viruses).

ZIKA VIRUS DISEASE

Case Diagnosis

- Preliminary diagnosis of acute ZIKV disease is based on the patient's clinical presentation and epidemiologic factors.
- Clinical criteria for ZIKV disease includes a person with one or more of the following:
    - Acute onset of fever (measured or reported)
    - Maculopapular rash
    - Arthralgia
    - Conjuncitvitis
    - Complication of pregnancy
        - fetal loss in a mother with compatible illness and/or epidemiologic risk factors, **OR**
        - in utero findings of microcephaly and/or intracranial calcifications with maternal risk factors
    - Guillain-Barré syndrome not known to be associated with another diagnosed etiology.
- Epidemiological criteria:

- Travel to a country or region with known ZIKV transmission, **OR**
- Sexual contact with a laboratory confirmed case of ZIKV infection, **OR**
- Receipt of blood or blood products within 30 days of symptom onset, **OR**
- Organ transplant recipient within 30 days of symptom onset, **OR**
- Association in time and place with a confirmed or probable case.

Case Definitions

Case definitions for ZIKV disease are available from CDC.

- **Suspect**
  - Meets clinical and epidemiological criteria above, **AND**
  - Negative on Zika immunoglobulin M (IgM) and/or RT-PCR, or no testing conducted.
- **Probable**
  - Meets clinical and epidemiological criteria above, **AND**
  - positive ZIKV-specific IgM antibodies in serum or cerebrospinal fluid (CSF), **AND**
  - negative dengue virus-specific IgM antibodies, **AND**
    - No neutralizing antibody testing performed (PRNT), **OR**
    - Less than four-fold difference in neutralizing antibody titers between ZIKV and dengue or other flaviviruses endemic to the region where exposure occurred as determined by a confirmatory plaque reduction neutralization testing (PRNT).
- **Confirmed**
  - Meets clinical and epidemiological criteria above and has laboratory evidence of recent ZIKV infection, **AND**
  - Detection of ZIKV by culture, viral antigen or viral ribonucleic acid (RNA) in serum, CSF, tissue, or other specimen (e.g. amniotic fluid, urine, semen, saliva), **OR**
  - ZIKV IgM antibodies in serum or CSF with ZIKV neutralizing antibody titers 4-fold or greater than neutralizing antibody titers against dengue or other flaviviruses endemic to the region where exposure occurred as determined by a confirmatory PRNT.

Clinical Diagnostic Testing

- Diagnosis of ZIKV infection based on clinical presentation alone is not reliable; confirmation requires appropriate laboratory testing. CDC has issued a "when to test for ZIKV" infographic and guidance for interpretation of ZIKV antibody test results to aid healthcare providers in deciding when to test and what the test results mean.
- FDA has issued Emergency Use Authorizations for ten diagnostic assays, three of which are currently available at DoD laboratories: Trioplex Real Time RT-PCR Assay for Zika, dengue, and chikungunya viruses in human sera and cerebrospinal fluid; the ZIKA MAC_ELISA IgM assay for sera and cerebrospinal fluid that is submitted alongside a patient-matched serum specimen; and the ZIKV Detect IgM Capture ELISA for the presumptive detection of Zika virus IgM antibodies in human sera collected from individuals meeting the CDC ZIKV clinical criteria.
- CDC recommends that ZIKV rRT-PCR be performed on urine collected <14 days after onset of symptoms in patients with suspected ZIKV disease. ZIKV rRT-PCR testing of urine should be performed in conjunction with serum testing. A positive result in either specimen type provides evidence of a confirmed ZIKV infection.
- These assays are being deployed to DoD laboratories, which will need to complete training and the qualification panel before they are authorized to begin testing:
  - IgM assays are currently available at four DoD Laboratory Response Network (LRN)-participating laboratories: NIDDL, BAMC, EAMC, and USAFSAM
  - The NIDDL can perform the confirmatory PRNT

- The Trioplex EUA assay is available at BAMC, CRDAMC, EAMC, LRMC, USAMRIID, WBAMC, MAMC, Brian Allgood ACH, NHRC, USAFSAM, WAMC, NAMRU-3, TAMC, WRNMMC, NIDDL, and NAMRU-6
- Testing should be coordinated with state or local health departments

- RT-PCR can be performed on serum specimens collected within the first week after illness onset.
- IgM and neutralizing antibody testing should be performed on specimens collected ≥4 days after onset of illness. Both acute and convalescent sera should be submitted.
  - ZIKV IgM antibody assays can be positive due to cross reactivity to recent infection by related flaviviruses (e.g., dengue and yellow fever viruses)
  - Virus-specific neutralization testing provides added specificity, but might not discriminate between cross-reacting antibodies in people who have been previously infected with or vaccinated against a related flavivirus
  - PRNT can be performed to measure virus-specific neutralizing antibodies and discriminate between cross-reacting antibodies in primary flavivirus infections
- Consult the CDC's Zika Diagnostic Testing webpage, and CDC's updated diagnostic testing for Zika, chikungunya, and dengue viruses in U.S. Public Health Laboratories for more information.

ZIKA VIRUS CONGENITAL INFECTION

Case Definitions

Case definitions for ZIKV congenital infections are available from CDC.

- **Probable**
  - An infant with microcephaly or intracranial calcifications or central nervous system abnormalities **AND**:
    - Mother lived in or traveled to a country or area with ongoing ZIKV transmission during the pregnancy; **OR**
    - Mother has laboratory evidence of ZIKV or unspecified flavivirus infection during pregnancy, **AND**
  - The infant meets the following laboratory criteria:
    - ZIKV IgM antibodies detected in serum or CSF, **AND**
    - Tests negative for dengue or other endemic flavivirus-specific IgM antibodies, **AND**
      - No neutralizing antibody testing performed (PRNT), **OR**
      - Less than four-fold difference in neutralizing antibody titers between ZIKV and dengue or other flaviviruses endemic to the region where exposure occurred.
- **Confirmed**
  - An infant with microcephaly or intracranial calcifications or central nervous system abnormalities, **AND** meets one of the following laboratory criteria:
    - ZIKV detection by culture, antigen test, or polymerase chain reaction (PCR) in serum, CSF, amniotic fluid, urine, placenta, umbilical cord, or fetal tissue, **OR**
    - ZIKV IgM antibodies present in serum or CSF with ZIKV neutralizing antibody titers 4-fold or greater than neutralizing antibodies against dengue or other flaviviruses endemic to the region where exposure occurred as determined by a confirmatory PRNT.

Clinical Diagnostic Testing

- Consult with your State Health Department or CDC for specific guidance
- Information is available for the CDC web site: Collecting & Submitting Specimens At Time of Birth for Zika Virus Testing

REPORTING AND SURVEILLANCE

Reporting

- ZIKV disease and congenital infection are not currently reportable medical events (RME) in DoD, but are conditions of concern. As of 29 JAN 2016, CDC added ZIKV disease and ZIKV congenital infections to the National Notifiable Diseases Surveillance System (NNDSS).
- Report ZIKV disease and congenital infections to state and local health departments per local civilian reporting requirements to improve cross-communication, mitigate the risk of local transmission, and enhance reporting through ArboNET.
- **ZIKV Disease:** Both laboratory confirmed and probable Zika virus disease cases should be reported in DRSi as "Any Other Unusual Condition Not Listed," with "Zika" entered in the comment field along with a pertinent travel history and, in the absence of a pertinent travel history, recent travel by their sexual partners. For female patients, pregnancy status should be recorded.
- **ZIKV Congenital Infection:** Infants with confirmed or probable laboratory evidence of congenital Zika virus infection should be reported in DRSi as "Any Other Unusual Condition Not Listed," with "Zika Virus Congenital Infection" entered in the comment field.
- **Pregnancy Registries:** Follow local or Service-specific guidance for reporting pregnant women in the United States with laboratory evidence of Zika virus infection and infants with laboratory evidence of congenital Zika virus infection to the U.S. Zika Pregnancy Registry or, in Puerto Rico, the Zika Active Pregnancy Surveillance System (PASS).
- Direct questions on reporting to the appropriate Service-specific public health POCs:
    - Navy - Contact your relevant Navy Environmental and Preventive Medicine Unit (NEPMU) or the DRSi helpdesk:
        - Navy Environmental and Preventive Medicine Unit Two
          Naval Station Norfolk, VA
          COMM: (757) 953-6600; DSN: (312) 377-6600
        - Navy Environmental and Preventive Medicine Unit Five
          Naval Base San Diego, CA
          COMM: (619) 556-7070; DSN: (312) 526-7070
        - Navy Environmental and Preventive Medicine Unit Six
          Joint Base Pearl Harbor-Hickam, HI
          COMM: (808) 471-0237; DSN: (315) 471-0237
        - Navy Environmental and Preventive Medicine Unit Seven
          Naval Station, Rota, Spain
          COMM (international): 011-34-956-82-2230 (local: 727-2230); DSN: 94-314-727-2230
        - Navy and Marine Corps Public Health Center DRSi Helpdesk
          usn.hampton-roads.navmcpubhlthcenpors.list.nmcphc-ndrs@mail.mil
          COMM: (757) 953-0700; DSN: (312) 377-0700
    - U.S. Air Force School of Aerospace Medicine (USAFSAM)
      Epidemiology Consult Service Division
      usafsam.phrepiservic@us.af.mil
      COMM: 937-938-3207; DSN: 798-3207
    - Army Public Health Center (APHC)
      Disease Epidemiology Program

usarmy.apg.medcom-phc.mbx.disease-epidemiologyprogram13@mail.mil
COMM: 410-417-2377; DSN: 867-2377

Surveillance

- Use the Electronic Surveillance System for the Early Notification of Community-based Epidemics (ESSENCE) or Medical Situational Awareness in Theater (MSAT) to monitor febrile illnesses and rash in the population for any increases. An ESSENCE account can be created here. Create an ESSENCE or MSAT syndrome group with the appropriate ICD-10 code, A92.8 (Other specified mosquito-borne viral fevers), and investigate upticks for potential Zika risk factors.
- Since ESSENCE captures only outpatient data, evaluate hospitalized individuals with acute febrile disease and travel to endemic areas. For theater medical data, MSAT can be used to monitor both outpatient and inpatient populations.

ADDITIONAL INFORMATION

Clinical Diagnostic Testing-POCs

The following POCs can be consulted for information on clinical diagnostic testing for ZIKA infection in the DoD. DoD medical personnel requiring clinical diagnostic laboratory testing for suspected ZIKV infections should follow service-specific requirements for coordinating with their state or local laboratories.

Army LRN Laboratories – Service POC
Dr. Bill Nauschuetz, PhD
Program Manager for US Army Lab Response Network, and
Clinical Laboratory Coordinator for Biopreparedness
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LTC Robert Nace
Laboratory Program Manager
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Navy LRN Laboratories–Service POC
LCDR Dustin J Harrison, PhD, MT(ASCP)
Navy Laboratory Response Network Gatekeeper
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U.S. Air Force School of Aerospace Medicine (USAFSAM)
Wright-Patterson AFB, Dayton, OH
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Naval Health Research Center (NHRC)
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Naval Infectious Disease Diagnostic Laboratory (NIDDL)
Naval Medical Research Center, Silver Spring, MD

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Walter Reed National Military Medical Center (WRNMMC)
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Mosquito Surveillance, Entomology, and Environmental Lab Support Points of Contact:

- The Armed Forces Pest Management Board (AFPMB) develops guidance and policy and coordinates pest management activities throughout the DoD. It maintains professional and technical liaison in the area of entomology and integrated pest management with appropriate DoD components, Federal agencies, and others. AFPMB approves all pest management products for use in the DoD. Guidance and information on ZIKV vector control and surveillance are available at the AFPMB's web site.

    - COL Jamie A. Blow
      Director, Armed Forces Pest Management Board
      Jamie.A.Blow.mil@mail.mil
      301-295-8307/8315

- The Army Medical Command has four regional commands, all of which have Entomological Sciences Divisions that perform mosquito-borne disease surveillance. In total, six Army public health laboratories have arboviral testing capability that includes ZIKV testing.

    - For environmental laboratory support:
      LTC Robert Richards
      robert.s.richards.mil@mail.mil
      410-436-5060 (DSN 584-5060)

Thomas Burroughs
Manager, Entomological Sciences Program
thomas.m.burroughs.civ@mail.mil
410-436-3613 (DSN 584-3613)

- The U.S. Air Force School of Aerospace Medicine identifies and tests mosquitoes worldwide for many arboviruses, including Zika and dengue. In addition, USAFSAM provides expertise for operational disease vector surveillance, control, and training.

    - U.S. Air Force School of Aerospace Medicine (USAFSAM)
      Epidemiology Consult Service Division
      usafsam.phrepiservic@us.af.mil
      COMM: 937-938-3207; DSN: 798-3207

- Navy and Marine Corps Public Health Center has the above four regional NEPMUs which provide operational services in entomology. Additionally, the Navy Entomology Center of Excellence provides expertise for operational disease vector surveillance, control, and training.

    - CDR Jeffrey Stancil
      Officer in Charge, Navy Entomology Center of Excellence
      jeffrey.d.stancil.mil@mail.mil
      904-542-4626

Other Resources

- Publicly-shareable Surveillance Summaries for Zika virus disease are available on the AFHSB website. FOUO versions are available to USG e-mail addresses via a distribution list.
- DoD-specific documents and guidance, including a Zika Toolkit, are available from the Military Health System website.
- Zika virus disease and its possible complications are emerging threats, and clinical, laboratory, and public health guidance is evolving. Health professionals should monitor the CDC's healthcare provider website for the most up-to-date information. CDC also has a general interest Zika page.
- The World Health Organization and Pan-American Health Organization have Zika websites with links to information for healthcare providers, public health professionals, and the general public.
- CDC, with OSHA and NIOSH, has issued interim guidance for protecting workers from occupational exposure to ZIKV.

Risk communication and preparation considerations

- CDC has prepared a response plan that focuses on activities that occur when locally acquired ZIKA transmission is identified in the continental United States and Hawaii.
- CDC has issued Alert, Level 2 – Practice Enhanced Precautions travel notices for countries and territories with ongoing ZIKV transmission. Travelers should consult these before visiting tropical or subtropical areas of the Americas, Africa, and Asia. Guidelines for travelers visiting friends and family in areas with chikungunya, dengue, or Zika and for U.S. citizens and residents living in areas with ongoing ZIKV transmission are available from the CDC.
- Beneficiaries living in or traveling to higher risk areas should practice prevention methods for ZIKV, which is transmitted by *Aedes* mosquitoes. See CDC prevention guidelines.
- Pregnant beneficiaries or those planning to become pregnant while living or traveling in an area of ongoing transmission should be made aware of the possible increased risk of congenital neurologic malformations in newborns of women exposed to the virus during pregnancy.

- ZIKV can be spread by sex from an infected person (male and female) to his or her sex partners. It can be passed before, during, and after the person has symptoms. The virus may be passed from a person who never developed symptoms to his or her sex partners. The virus persists longer in semen than in blood. However, the duration of virus in semen is unknown. WHO recommends that both women and men who are returning from Zika-affected areas abstain or practice safe sex for six months, an increase from the previously recommended eight weeks. Information on the risk and prevention of sexual transmission of ZIKV is available from the CDC.
- Spread of ZIKV through blood transfusion is possible and the American Association of Blood Banks recommends donor self-deferral for 28 days after return from an area with ongoing ZIKV transmission.
- There is no antiviral treatment or vaccine currently available for ZIKV infection. Prevention relies on effective mosquito control and avoidance of vectors. Use insect repellent containing EPA-registered repellents, such as DEET or picaridin; wear long sleeves and long pants treated with permethrin for added protection; and limit outdoor activities in order to prevent mosquito bites, decreasing the risk of ZIKV and other mosquito-borne infections.
- Installations should be prepared to carry out necessary mosquito surveillance programs and to execute appropriate mosquito control operations to reduce the size of vector populations and prevent spread of ZIKV. The AFPMB issued updated vector control guidance for *Aedes* mosquitoes.

AFHSB POCs:

For further information, contact the AFHSB's Integrated Biosurveillance (IB) section or the Global Emerging Infections Surveillance (GEIS) section:

Email: dha.ncr.health-surv.list.afhs-ib-alert-response@mail.mil
Phone:
Dr. Stic Harris, Chief, Alert & Response Operations (IB): 301-319-3297; BB: 202-834-1327
Dr. Brett Forshey, Lead, Febrile and Vector-borne Diseases Program (GEIS): 301-319-3284