PUBLIC HEALTH DIVISION, DEFENSE HEALTH AGENCY
Armed Forces Health Surveillance Branch (AFHSB)

Detecting & Reporting DoD Cases of Acute Zika Virus Disease
Guidance as of 17 MAY 2016

1. **Case Diagnosis**:

- Preliminary diagnosis of acute Zika virus (ZIKV) disease is based on the patient's clinical presentation and epidemiologic factors.
- Clinical criteria, 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.
- Illness is usually mild with symptoms lasting for several days to a week. Severe disease requiring hospitalization is uncommon and fatalities, if they occur, are rare. Only about one in five people infected with ZIKV become symptomatic. There is no vaccine or specific treatment.
- CDC has determined that a causal relationship between ZIKV infection and neurological birth defects, particularly microcephaly, exists. Due to the risk of microcephaly associated with maternal Zika virus infection, fetuses and infants of women infected with Zika virus during pregnancy should be evaluated for possible congenital infection and/or neurologic abnormalities. CDC has issued 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).

2. **Case Definitions:**

Interim case definitions (as of 12 MAY 2016) specifically for ZIKV disease are available from CDC.

- **Suspect**
  - Meets clinical and epidemiological criteria above, **AND**
  - Negative on Zika IgM and/or RT-PCR, or no testing conducted.
- **Probable**
  - Meets clinical and epidemiological criteria above, **AND**
    - Positive IgM without confirmatory 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
  - No evidence of infection with other flaviviruses, such as dengue and yellow fever.
- **Confirmed**
  - Meets clinical and epidemiological criteria above, **AND**
    - Positive RT-PCR in serum or other samples (e.g. saliva, tissues, urine, whole blood), **OR**
    - Positive IgM with a positive confirmatory PRNT.

3. Clinical Diagnostic Testing:

- Diagnosis of ZIKV infection based on clinical presentation alone is not reliable; confirmation requires appropriate laboratory testing.
- FDA has issued Emergency Use Authorizations for two diagnostic assays: Trioplex Real Time RT-PCR Assay for Zika, dengue, and chikungunya viruses in human sera and cerebrospinal fluid, and the ZIKA MAC_ELISA IgM assay for sera and cerebrospinal fluid that is submitted alongside a patient-matched serum specimen.
- CDC recommends that ZIKAV 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 Zika virus 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.
  - The IgM assay is expected to be available at six DoD Laboratory Response Network (LRN)-participating laboratories: NHRC, NMRC/NIDDL, USAFSAM, Brooke AMC, Tripler-AMC, and NAMRU-6. Currently, NIDDL, BAMC, and USAFSAM can conduct patient testing.
  - All Army medical centers, WRNMMC, USAMRIID, USAFSAM, NIDDL, and NHRC are expected to receive the RT-PCR assay, as well as NAMRU-3 and NAMRU-6.
  - NAMRU-6, in Lima, Peru, has a LDT RT-PCR diagnostic assay available.
  - 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.
- Immunoglobulin M 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.
  - Plaque reduction neutralization testing (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.

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

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Navy LRN Laboratories–Service POC

LCDR Dustin J Harrison, PhD, MT(ASCP)
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4. Reporting:

- Zika virus disease is not currently a reportable medical event (RME) in DoD, but it is a disease of concern. Both laboratory confirmed and probable Zika 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.
    - As of 29 JAN 2016, CDC has added Zika virus disease to the National Notifiable Diseases Surveillance System (NNDSS) with the event code 11726.
    - Report Zika virus disease 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.
- 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

5. 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.

6. 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 Zika 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 will include Zika virus 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.

  - Dr. Will Reeves
    Entomologist, U.S. Air Force School of Aerospace Medicine (USAFSAM)
    Epidemiology Consult Services Division
    will.reeves@us.af.mil
    937-938-3071 (DSN 798-3071)

- 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

7. 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 health care 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 health care 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.

8. Risk communication and preparation considerations:

- 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.
- Military health care beneficiaries participating in or attending the 2016 Summer Olympics or Paralympics in Rio de Janeiro should consult the CDC travel notice specific to the games before traveling.
- 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 a man to his sex partners (male and female), before, during, and after the man is symptomatic. The virus persists longer in semen than in blood. However, the duration of virus in semen is unknown.
- 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.

9. AFHSB POCs:

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

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