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**Zika Virus Disease:
Diagnosis, Management, and Prevention**

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Overview: Zika virus belongs to Flaviviridae family (includes West Nile and dengue viruses); transmitted by *Aedes* mosquito; documented intrauterine and transfusion-related infections; identified in breast milk (but no infections linked to breastfeeding) and semen; as of February 2016, active cases in 30 countries; not commonly seen outside of Africa and Asia; current spread secondary to invasion by *Aedes* mosquito; in 1970, *Aedes* restricted to Caribbean and South America; by 2002, *Aedes* population had spread significantly; primary vectors *Aedes aegypti* (most common) and *Aedes albopictus* (tiger mosquito)

Zika virus: incubation ≤ 2 wk (similar to dengue); 80% of infected individuals asymptomatic; *symptoms*—fever, rash, joint pain, eye redness, muscle pain, headache, retro-orbital pain, and vomiting; *course of infection*—mild, with symptoms lasting few days to 1 wk; severe disease requiring hospitalization uncommon; cases of Guillain-Barré observed in Brazil thought to be related to Zika virus; rarely fatal; *microcephaly*—complication of Zika virus infection; 147 cases reported in 2014 in Brazil; increased to >4000 cases in 2015; defined as head circumference (HC) >3 standard deviations below mean HC; associated with periventricular calcifications; infection worse in first 12 wk of pregnancy; *other symptoms*—hearing and vision loss; swallowing difficulties

History of Zika virus: *April 1947*—novel virus isolated from macaque monkey during routine surveillance; Zika virus named for forest in Uganda where it was identified; *September 1956*—researcher unable to identify transmission of Zika virus from himself to mice or monkeys via mosquitoes; *1968*—Zika virus responsible for human infections in Nigeria; *1971*—first children identified with Zika virus in Nigeria; *1981*—7 cases identified in Indonesia; *2007*—large outbreak on Yap Island in South Pacific; *2013*—health advisory issued by Centers for Disease Control and Prevention (CDC) for French Polynesia where >20,000 cases of Zika virus reported; *2014*—World Cup in Brazil possibly linked to appearance of Zika virus in Western Hemisphere; first case of Zika virus confirmed in Brazil 1 yr later; *November 28, 2015*—increase in

microcephaly cases linked to Zika virus in Brazil; *December 16, 2015*—Brazilian minister of health warns women to not become pregnant; similar statements made by officials in Ecuador, Columbia, El Salvador, and Jamaica

2016 statements: *January 16*—Hawaiian baby with brain damage first case linked to Zika virus; mother spent most of pregnancy in Brazil; *January 26*—CDC issues travel warning (alert level 2 “enhanced precautions”) for regions with Zika virus; *January 29*—concerns about Zika virus and Olympic Games in Rio de Janeiro, Brazil, including potential for spread to Northern Hemisphere after event; *February 1*—World Health Organization (WHO) declares public health emergency of international concern; predicted >4 million cases of Zika virus in 2016; *February 3*—CDC confirms sexual transmission from man returning from Venezuela to his female partner in Texas; no documented female-to-male or male-to-male transmission; *February 5*—5 confirmed cases and 265 suspected cases in Tonga; CDC releases guidelines on sexual transmission; men in Zika-endemic regions who have pregnant partners should abstain from all sexual contact or use condom correctly throughout entire pregnancy; men in Zika-endemic regions with nonpregnant partners should consider abstaining from intercourse; no current recommendations for testing men returning from Zika-endemic areas before sexual activity; *February 8*—President Obama asks for \$1.8 billion in emergency funding to combat Zika virus (mosquito control, vaccine development); *February 10*—CDC confirms 2 stillbirths and 2 neonatal deaths in Brazil

Management: fetuses and infants of women with Zika virus infection require evaluation for congenital infection; report suspicion of Zika virus infection to local health departments; obtain maternal history of exposure to Zika-endemic regions

Infants with possible congenital Zika virus infection: measure HC, height, and weight; look for neurologic abnormalities; order cranial ultrasonography to identify periventricular calcifications; assess hearing; consider ophthalmologic examination

Infants with microcephaly and/or intracranial calcifications: consult with genetic specialist and pediatric neurologist; screen for other congenital infections; obtain complete blood count with differential and liver function tests; *labs for Zika virus*—infant serology (polymerase chain reaction [PCR] for Zika virus RNA, Zika virus immunoglobulin [Ig] M, and neutralizing antibodies); infant cerebrospinal fluid

AUDIO DIGEST PEDIATRICS

(PCR for Zika virus RNA, IgM, and dengue); placenta (Zika virus on fixed tissue, PCR for Zika virus on fixed or frozen tissue); maternal serology (Zika virus IgM and neutralizing antibodies)

Algorithm for possible exposure and no microcephaly: if maternal history positive for Zika virus infection, proceed with testing assuming infant also infected; if no maternal history, test mother and treat accordingly; if maternal testing negative, provide routine care to infant

Treatment: supportive; no effective antiviral therapy; no vaccine available; emphasize anticipatory guidance; report case; conduct hearing screen; measure HC and follow developmental milestones; refer to appropriate specialists as needed

Prevention: use insect repellent; wear long sleeves and pretreated clothing; review list of effective insect

repellents (*eg*, DEET, picaridin, ethyl butylacetylaminopropionate [IR3535], lemon and eucalyptus oils) issued by CDC

Suggested Reading

CDC Zika Response: Vital signs: preparing for local mosquito-borne transmission of Zika virus—United States 2016. *MMWR Morb Mortal Wkly Rep*, 2016 Apr;65(13):352; **Citil-Dogan et al:** The Zika virus and pregnancy: evidence, management, and prevention. *J Matern Fetal Neonatal Med*, 2016 Apr;1-41; **Flores MS et al:** Zika virus: a primer for clinicians. *Cleve Clin J Med*, 2016 Apr;83(4):261-70; **Hammond A et al:** A CRISPR-Cas9 gene drive system targeting female reproduction in the malaria mosquito vector *Anopheles gambiae*. *Nat Biotechnol*, 2016 Jan;34(1):78-83; **Mlakar J et al:** Zika virus associated with microcephaly. *N Engl J Med*, 2016 Mar;374(10):951-8.