Zika virus infection: An overview

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INTRODUCTION — Zika virus is an arthropod-borne flavivirus transmitted by mosquitoes [1-4]. The virus is related to other flaviviruses including dengue virus, yellow fever virus, and West Nile virus. Clinical manifestations of Zika virus infection occur in approximately 20 percent of patients and include acute onset of low-grade fever with maculopapular pruritic rash, arthralgia (notably small joints of hands and feet), or conjunctivitis (nonpurulent).

Neuropathogenesis of Zika virus has been demonstrated in vivo and in vitro [5-9]. Zika virus infection has been associated with neurologic complications; these include congenital microcephaly (in addition to other developmental problems among babies born to women infected during pregnancy), Guillain-Barré syndrome, myelitis, and meningoencephalitis [10-12]. (See 'Complications' below.)

Currently, there is an ongoing Zika virus outbreak in the Americas, the Caribbean, and the Pacific; the World Health Organization (WHO) has stated that the virus is "spreading explosively" [13] and has declared Zika virus and its associated complications a Public Health Emergency of International Concern [14].

Online updates regarding Zika virus infection may be viewed at the following websites:

- Pan American Health Organization (PAHO)/WHO website
- United States Centers for Disease Control and Prevention (CDC) website
- European Centre for Disease Prevention and Control (ECDC) website

General issues related to Zika virus epidemiology and prevention are reviewed here. Issues related to Zika virus infection in pregnant women and infants with congenital exposure are discussed separately. (See "Zika virus infection: Pregnancy and congenital infection".)

EPIDEMIOLOGY

Geographic distribution — Outbreaks of Zika virus infection have occurred in Africa, Southeast Asia, and the Pacific Islands; currently, there is an ongoing Zika virus outbreak in the Americas, the Caribbean, and the Pacific [15-17]. Updates regarding the geographic distribution of Zika virus may be viewed at the United States Centers for Disease Control and Prevention website and the Pan American Health Organization/World Health Organization website.

Zika virus is named after the Ugandan forest where it was first isolated from a rhesus monkey in 1947 [19]. The first human cases were detected in 1952 in Uganda and Tanzania. The virus subsequently spread across equatorial Africa and Asia, where it was associated with sporadic infections. The first major recognized outbreak occurred in the Yap Islands of Micronesia in 2007; more than 70 percent of the population ≥3 years of age was infected, resulting in an estimated 5000 infections among the total population of 6700 [19-21]. Another larger outbreak occurred in French Polynesia in 2013 to 2014, which affected about two-thirds of the population, resulting in approximately 32,000 infections [22,23]. During the outbreak in French Polynesia, 3 percent of donated blood samples tested positive for Zika virus by polymerase chain reaction [24].

Zika virus infections were first detected in the Western hemisphere in February 2014 on Chile’s Easter Island [25]. Zika virus infections were subsequently detected in Brazil in May 2015 [25]. Molecular analyses have suggested that the virus may have been introduced earlier, in late 2013 or early 2014 [26]. Regions with mosquito-borne transmission of Zika virus are summarized below. (See 'Travel advisories for pregnant women' below.)

In the United States, mosquito-borne transmission has occurred in Florida, and imported Zika infection has been reported in travelers [27-29]. In one report from New York City including 3605 individuals with travel-associated exposure who underwent Zika virus laboratory testing between January and June 2016, positive results were observed in 182 patients (5 percent of cases), including 20 pregnant women [30]. The first case of Zika-related congenital microcephaly in the United States was reported in January 2016 in Hawaii, in a baby born to a woman who had resided in Brazil during her pregnancy [31]. The first case of sexually transmitted Zika virus infection in the United States was reported in Texas in February 2016 [32].
Travel advisories for pregnant women — Given an association between Zika virus exposure during pregnancy and congenital microcephaly, a number of authorities have advised that pregnant women avoid or consider postponing travel to areas below 6500 feet (2000 meters) where mosquito transmission of Zika virus is ongoing; these areas are summarized below [33-38]. Regions above 6500 feet (2000 meters) are excluded from travel precautions, since the mosquitoes that transmit Zika virus are rare in these locations and the risk for mosquito-borne transmission of Zika virus is minimal [38].

Countries and territories with local mosquito-borne transmission of Zika virus include Anguilla, Antigua, Argentina, Aruba, The Bahamas, Barbados, Barbuda, Belize, Bolivia, Bonaire, Brazil, the British Virgin Islands, Cape Verde, Cayman Islands, Colombia, Costa Rica, Cuba, Curacao, Dominica, Dominican Republic, Ecuador, El Salvador, Fiji, French Guiana, Grenada, Guadeloupe, Guatemala, Guyana, Haiti, Honduras, Jamaica, Kosrae (Federated States of Micronesia), Marshall Islands, Martinique, Mexico, New Caledonia, Nicaragua, Panama, Papua New Guinea, Paraguay, Peru, Saba, Samoa, Saint Barthélemy, Saint Lucia, Saint Martin, Saint Vincent and the Grenadines, Singapore, Sint Eustatius, Sint Maarten, Suriname, Tonga, Trinidad and Tobago, Turks and Caicos, the United States, and Venezuela [34,39,40].

Within the United States, mosquito-borne transmission of Zika virus infection has occurred in Florida; pregnant women have been advised to avoid travel to the Wynwood neighborhood of Miami and an area of Miami Beach [41-45]. In addition, mosquito-borne Zika virus transmission in Puerto Rico has been extensive [46,47]. There is also mosquito-borne transmission of Zika virus in the United States territories of the Virgin Islands and American Samoa.

Transmission — Zika virus may be transmitted to humans via the following [24,32,48-53]:

- Bite of an infected mosquito
- Maternal-fetal transmission
- Sex (including vaginal, anal, and oral sex)
- Blood transfusion
- Organ transplantation
- Laboratory exposure

Preventive measures based on the various modes of transmission are discussed below. (See ‘Prevention’ below.)

The primary mode of transmission is via mosquito bites. Zika virus is carried by the Aedes aegypti mosquito, which lives in tropical regions; however, the Aedes albopictus mosquito, which lives in temperate regions, is also capable of carrying it (figure 1 and figure 2) [54-57]. Aedes mosquitoes can also transmit dengue and chikungunya viruses. (See ‘Mosquito protection’ below.)

Zika virus RNA has been detected in blood, urine, semen, saliva, female genital tract secretions, cerebrospinal fluid, amniotic fluid, and breast milk [24,54,58-64]:

- Blood – In nonpregnant individuals with Zika virus infection, Zika virus RNA is detectable in the serum for a few days to a week; Zika virus RNA is detectable in whole blood as late as 58 days following onset of illness [65]. In pregnancy, Zika virus RNA has been detected in the serum as late as 10 weeks after onset of illness [66].
- Urine – Zika virus RNA has been detected in urine up to 91 days after onset of illness [59,62,63,67-69]. Replicating virus has been detected in urine at the time of symptomatic illness [70].
- Semen – Zika virus RNA has been detected in semen up to 188 days after onset of illness; it can be detected in semen when no longer detectable in blood [63,69,71-73]. Replicating virus has been detected in semen 7 days after onset of illness [74]. Sexual transmission of Zika virus as late as 41 days after onset of a partner’s symptoms has been described [50,75]. The viral load in semen may be high; in one report, the viral load in semen more than two weeks after onset of symptoms was roughly 100,000 times that of blood or urine [76]. A probable case of male to female sexual transmission involving an asymptomatic male has also been reported [77].
- Saliva – Zika virus RNA has been detected in saliva up to 91 days after onset of illness [60,63,69]. Replicating virus has been detected in saliva at the time of symptomatic illness [70].
- Female genital tract secretions – Zika virus RNA has been detected in female genital tract secretions (via genital, endocervical swabs, and cervical mucus) during symptomatic illness [64]. Zika virus RNA has also been detected in cervical mucus 11 days after onset of illness, when it was no longer detectable in blood or urine [64].
Issues related to maternal-fetal transmission and breastfeeding are discussed separately. (See "Zika virus infection: Pregnancy and congenital infection", section on 'Congenital infection'.)

The World Health Organization has issued recommendations for prevention of Zika virus infection for individuals planning to travel to Brazil for the Olympic Games in August 2016 [78].

**CLINICAL MANIFESTATIONS** — The incubation period between mosquito bite and onset of clinical manifestations is typically 2 to 14 days. The illness is usually mild; symptoms resolve within two to seven days. Immunity to reinfeciton occurs following primary infection [79]. Severe disease requiring hospitalization is uncommon, and case-fatality rates are low [80-84].

**Symptoms and signs**

**Adults** — Symptoms and signs of Zika virus infection typically include acute onset of low-grade fever (37.8 to 38.5°C), maculopapular pruritic rash, arthralgia (notably the small joints of hands and feet), and conjunctivitis (nonpurulent). clinical illness is consistent with Zika virus disease if two or more of these symptoms are present [33,85-87]. Other commonly reported clinical manifestations include myalgia, headache, retro-orbital pain, and asthenia [80]. Less commonly observed symptoms and signs include abdominal pain, nausea, diarrhea, and mucous membrane ulcerations [88]. Thrombocytopenia, palatal petechiae, and uveitis have been described in case reports [89-93].

Clinical manifestations of Zika virus infection occur in 20 to 25 percent of individuals who become infected with Zika virus. Outside areas with mosquito transmission, the likelihood of Zika virus infection among asymptomatic individuals is low [94].

**Children** — The range of Zika virus infection in children includes intrauterine infection (vertical transmission during pregnancy), intrapartum infection (vertical transmission at the time of delivery), and postnatal infection (transmission via mosquito bites). Issues related to intrauterine and intrapartum infection are discussed separately. (See "Zika virus infection: Pregnancy and congenital infection".)

Clinical manifestations in infants and children with postnatal infection are similar to the findings seen in adults with Zika virus infection [20,95]. Arthralgia is difficult to detect in infants and young children and may manifest as irritability, walking with a limp, difficulty moving or refusing to move an extremity, pain on palpation, or pain with active or passive movement of the affected joint [95]. Thus far, no developmental complications have been observed in otherwise healthy children with postnatal Zika virus infection [96,97]. (See "Evaluation of the child with joint pain and/or swelling".)

**Complications** — Zika virus infection has been associated with complications including congenital microcephaly and fetal losses among women infected during pregnancy, as well as neurologic complications. Issues related to congenital infection are discussed separately. (See "Zika virus infection: Pregnancy and congenital infection".)

**Guillain-Barré syndrome** — Several countries in the Americas have reported unusual increases in cases of Guillain-Barré syndrome (GBS) in parallel with the ongoing Zika virus outbreak [98-101]. An increase in the rate of GBS in association with Zika virus infection has also been observed in other reports [58,102-107].

A case-control study in French Polynesia evaluated the association between GBS and Zika virus infection during the 2013 to 2014 outbreak [106]. Cases included 42 patients diagnosed with GBS; one control group included 98 patients with nonfebrile illnesses (matched for age, sex, and residence), and a second control group included 70 patients with Zika virus infection in the absence of neurological complications. Zika immunoglobulin (Ig)M was positive in 93 percent of GBS cases (versus 17 percent of patients in the first control group); serologic evidence of past dengue infection was similar among all three groups. Anti-glycolipid IgG antibodies were detected in fewer than 50 percent of GBS cases, raising the possibility of direct viral neurotoxicity. Results of nerve conduction studies were consistent with the acute motor axonal neuropathy type of GBS; clinical improvement during follow-up suggested reversible conduction failure. Symptoms of Zika virus infection occurred in 88 percent of patients with GBS; the median interval between viral syndrome and onset of neurological symptoms was six days. All GBS cases received intravenous immune globulin, 38 percent required intensive care, and 29 percent needed respiratory care; all survived. The incidence of GBS during the outbreak was estimated to be 2.4 cases per 10,000 Zika virus infections.

Issues related to diagnosis, evaluation, and management of Guillain-Barré syndrome are discussed further separately. (See "Clinical features and diagnosis of Guillain-Barré syndrome in adults" and "Treatment and prognosis of Guillain-Barré syndrome in adults".)

**Other neurologic complications** — Zika virus has been associated with other neurologic complications including brain ischemia [82], myelitis [108], and meningoencephalitis [109,110]. These entities are discussed further separately.
DIFFERENTIAL DIAGNOSIS — The differential diagnosis of Zika virus infection includes:

- Other viral causes of arthritis:
  - Dengue fever – Dengue virus and Zika virus infections have similar clinical manifestations and are transmitted by the same mosquito vector. However, dengue infection usually presents with high fever, severe muscle pain, and headache and may also be associated with hemorrhage; unlike Zika infection, dengue is typically not associated with conjunctivitis (table 1). Coinfection with Zika, chikungunya, and dengue viruses has been described [111]. The diagnosis of dengue virus infection is established via serology. (See "Clinical manifestations and diagnosis of dengue virus infection").
  - Chikungunya – Chikungunya virus and Zika virus cause similar symptoms and signs and are transmitted by the same mosquito vector. However, chikungunya usually presents with high fever and intense joint pain affecting the hands, feet, knees, and back; unlike Zika infection, chikungunya is typically not associated with conjunctivitis (table 1). Chikungunya infection can be disabling, causing patients to bend over such that they cannot walk, and infected individuals may be unable to perform simple manual tasks. Coinfection with Zika, chikungunya, and dengue viruses has been described [111]. The diagnosis of chikungunya virus infection is established via serology. (See "Chikungunya fever").
  - Parvovirus – Parvovirus infection can present with acute and symmetric arthritis or arthralgia, most frequently involving the small joints of the hands, wrists, knees, and feet. Rash may or may not be present. The diagnosis is established via serology. (See "Clinical manifestations and diagnosis of parvovirus B19 infection").
  - Rubella – Clinical manifestations of rubella include low-grade fever and coryza. Macular rash begins on the face and spreads to the trunk, and arthritis and lymphadenopathy may be present. The diagnosis is established via serology. (See "Rubella").
  - A number of other viruses including enterovirus, adenovirus, and alphaviruses may also cause arthritis; these are discussed further separately. (See "Specific viruses that cause arthritis").
- Measles – Clinical manifestations of measles include fever, cough, sore throat, coryza, conjunctivitis, and lymphadenitis. Koplik spots may precede the generalized rash. The diagnosis is established via serology. (See "Clinical manifestations and diagnosis of measles").
- Leptospirosis – Leptospirosis is characterized by fever, rigors, myalgia, conjunctival suffusion, and headache. Less common symptoms and signs include cough, nausea, vomiting, diarrhea, abdominal pain, and arthralgia. It may be distinguished from Zika virus infection by the presence of jaundice. The diagnosis is established via serology. (See "Epidemiology, microbiology, clinical manifestations, and diagnosis of leptospirosis").
- Malaria – Malaria is characterized by fever, malaise, nausea, vomiting, abdominal pain, diarrhea, myalgia, and anemia. The diagnosis of malaria is established by visualization of parasites on peripheral smear. (See "Clinical manifestations of malaria in nonpregnant adults and children").
- Rickettsial infection – Rickettsial infections with similar manifestations as Zika virus infection include African tick bite fever and relapsing fever. African tick bite fever is observed among travelers to Africa and the Caribbean and is characterized by headache, fever, myalgia, solitary or multiple eschars with regional lymphadenopathy, and generalized rash; the diagnosis is established via serology. Relapsing fever is characterized by fever, headache, neck stiffness, arthralgia, myalgia, and nausea; diagnostic tools include direct smear and polymerase chain reaction. (See "Other spotted fever group rickettsial infections" and "Clinical features, diagnosis, and management of relapsing fever").
- Group A Streptococcus – Clinical manifestations of group A Streptococcus infection include fever, myalgia, cutaneous manifestations (cellulitis, fasciitis), pharyngitis, and shock. The diagnosis established by positive cultures from the blood or other tissues. (See "Group A streptococcal (Streptococcus pyogenes) bacteremia in adults").

DIAGNOSIS — The approach to Zika virus infection may vary depending on available resources; the approach outlined in the following sections may need to be tailored to local circumstances.

The diagnosis of Zika virus infection should be suspected in individuals with typical clinical manifestations and relevant epidemiologic exposure (residence in or travel to an area where mosquito-borne transmission of Zika virus infection has
been reported, or unprotected sexual contact with a person who meets these criteria).

Issues related to diagnosis of Zika virus infection in symptomatic adults (pregnant and nonpregnant) and children with postnatal infection are discussed below.

Issues related to diagnosis of Zika virus infection in asymptomatic pregnant women and infants with possible congenital Zika virus exposure are discussed separately. (See "Zika virus infection: Pregnancy and congenital infection".)

Case definitions — The following interim case definitions have been issued by the World Health Organization (WHO) to provide global standardization for classification and reporting of Zika virus cases [112].

- A suspected case is a person with a rash (maculopapular) and/or fever (37.8 to 38.5°C) with at least one of the following symptoms (not explained by other medical conditions): arthralgia, arthritis, or conjunctivitis (nonpurulent/hyperemic). A suspected case should also have relevant epidemiologic exposure (residence in or travel to an area where mosquito-borne transmission of Zika virus infection has been reported, or unprotected sexual contact with a person who meets these criteria), even though epidemiologic exposure is not included in the WHO categorization of a suspected case.

- A probable case is a suspected case with immunoglobulin (Ig)M antibody against Zika virus (with no evidence of infection with other flaviviruses) and relevant epidemiologic exposure (as described above).

- A confirmed case is a person with laboratory confirmation of Zika virus infection, either by detection of viral RNA or antigen in serum or other samples or by detection of Zika IgM antibody and a positive Zika virus plaque-reduction neutralization test (PRNT). PRNT is needed to determine whether a positive IgM antibody result against Zika virus reflects recent Zika virus infection or a false-positive result.

Guidance issued by the United States Centers for Disease Control and Prevention (CDC) indicates a PRNT titer greater than 10 should be interpreted as evidence of infection with a specific flavivirus when the PRNT to the other flaviviruses tested is less than 10 (table 2) [113]. This guidance reflects a more conservative approach to interpreting PRNT than previously provided by the WHO (PRNT titer ≥20 and PRNT titer ≥4 compared with other flaviviruses) [112], since a fourfold higher titer by PRNT may not reliably discriminate between Zika virus antibodies and cross-reacting antibodies in all individuals who have prior infection or vaccination against a related flavivirus.

For nonpregnant patients residing in areas where mosquito transmission has been established, the diagnosis of Zika virus infection may be suggested based on symptoms and signs and may not necessarily warrant laboratory testing, although differentiation from other illnesses with similar clinical manifestations (eg, dengue, chikungunya) may be difficult [114,115].

For nonpregnant patients residing in areas where mosquito transmission has not been established and laboratory testing is available, diagnostic testing is warranted for individuals with characteristic symptoms and signs and relevant epidemiologic exposure. (See 'Symptomatic adults' below.)

The approach to diagnostic evaluation of pregnant women and infants with intrauterine or intrapartum infection is discussed separately. (See "Zika virus infection: Pregnancy and congenital infection".)

Patient groups — Issues related to diagnosis of Zika virus infection in symptomatic adults (pregnant and nonpregnant) and symptomatic children with postnatal infection are discussed below. There is no role for Zika virus testing in asymptomatic patients who are not pregnant.

Issues related to diagnosis of Zika virus infection in asymptomatic pregnant women and infants with possible congenital Zika virus exposure are discussed separately. (See "Zika virus infection: Pregnancy and congenital infection".)

Symptomatic adults — The diagnosis of Zika virus infection is definitively established via real-time reverse-transcription polymerase chain reaction (rRT-PCR) for Zika viral RNA (in serum or urine) or Zika virus serology [33,85,113,116-119]:

- For individuals presenting ≤7 days after onset of symptoms, diagnostic testing for Zika virus infection should include rRT-PCR of serum and urine for detection of Zika virus RNA. rRT-PCR testing for dengue virus and chikungunya virus should also be pursued.
Serum rRT-PCR is positive only for a brief window (three to seven days) when the infected person has viremia; therefore, negative results cannot exclude infection. Urine rRT-PCR may be positive for up to 14 days following onset of symptoms.

- For individuals presenting 4 to 7 days after onset of symptoms with negative Zika virus rRT-PCR, Zika virus serologic testing should be performed. If Zika virus IgM tests results are positive, equivocal, or inconclusive, testing for neutralization antibodies via PRNT should be performed to determine whether the Zika virus IgM reflects recent Zika virus infection or a false-positive result. A PRNT titer greater than 10 should be interpreted as evidence of infection with a specific flavivirus when the PRNT to the other viruses tested is less than 10 (table 2) [113]. (See 'Case definitions' above.)

Testing for dengue virus infection and chikungunya virus infection should also be pursued. A single laboratory PCR test is available through the CDC and other qualified laboratories to evaluate for presence of Zika, chikungunya, or dengue infection [120].

All serologic results should be interpreted with caution since there can be cross-reactivity with other flaviviruses (including dengue virus and West Nile virus). Cross-reactivity may also be observed in individuals who have been vaccinated against yellow fever or Japanese encephalitis [121]. Issues related to diagnosis of dengue virus and chikungunya virus are discussed separately. (See "Clinical manifestations and diagnosis of dengue virus infection" and "Chikungunya fever", section on 'Diagnosis'.)

- For individuals presenting 8 to 14 days after the onset of symptoms, diagnostic testing for Zika virus infection should include urine rRT-PCR for detection of Zika virus RNA as well as Zika virus serologic testing (Zika virus IgM and PRNT).

- For individuals presenting 15 days to 12 weeks after onset of symptoms, diagnostic testing for Zika virus infection should consist of Zika virus serologic testing (Zika virus IgM and PRNT).

- For individuals presenting more than 12 weeks after onset of symptoms, there is no role for Zika virus serologic testing.

Laboratory testing for Zika virus infection is performed by the Pan American Health Organization/WHO, the CDC Arboviral Diagnostic Laboratory, and some state health departments. In the United States, state health departments should be contacted to facilitate diagnostic testing for Zika virus infection. Laboratory specimens may also be sent to the CDC Arboviral Diagnostic Laboratory; instructions are available online. Communication should be initiated with the laboratory via telephone (1-970-221-6400) prior to shipment of specimens.

The United States Food and Drug Administration has also authorized use of commercial Zika virus serum PCR testing and serologic testing by qualified laboratories [122,123]. As of August 2016, commercial laboratories performing rRT-PCR do not perform Zika IgM enzyme-linked immunosorbent assay (ELISA) or confirmatory serologic testing (PRNT) [124]. Therefore, if possible, providers should store a serum aliquot in a refrigerator (2 to 8°C) for subsequent Zika IgM ELISA testing if the rRT-PCR assay is negative; otherwise, collection of an additional serum sample may be necessary.

Symptomatic children with postnatal infection — Postnatal Zika virus infection (eg, transmitted via mosquito bites) should be suspected in an infant or child <18 years with relevant epidemiologic exposure in the last two weeks and ≥2 of the following manifestations: fever, rash, conjunctivitis, or arthralgia [95]. (See 'Children' above.)

The diagnostic approach for these children is the same as for adults, as described above. (See 'Symptomatic adults' above.)

MANAGEMENT — There is no specific treatment for Zika virus infection. Management consists of rest and symptomatic treatment, including drinking fluids to prevent dehydration and administration of acetaminophen to relieve fever and pain [125].

Aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDS) should be avoided until dengue infection has been ruled out, to reduce the risk of hemorrhage. Aspirin should not be used in children with acute viral illness because of its association with Reye syndrome. (See "Acute toxic-metabolic encephalopathy in children", section on 'Reye syndrome'.)

The World Health Organization has issued initial guidance on psychosocial support for patients and families affected by Zika virus infection and associated complications [126].
PREVENTION — There is no vaccine for prevention of Zika virus infection. Modes of transmission are described above. (See ‘Transmission’ above.) Preventive measures for pregnant and lactating women and women of childbearing potential are discussed separately. (See “Zika virus infection: Pregnancy and congenital infection”, section on ‘Prevention’.)

Mosquito protection — Individuals in areas with risk for transmission should take measures to avoid mosquito bites, including personal protection as well as environmental control measures. Aedes mosquitoes bite during the daytime as well as at twilight; they breed in standing water (particularly manmade containers). Personal protective measures include:

- Preventing mosquito bites by wearing long sleeves and long pants, using insect repellent, and staying indoors as feasible (with air conditioning, window/door screens, and/or mosquito nets to minimize contact between mosquitoes and people). (See “Prevention of arthropod and insect bites: Repellents and other measures”.)
- Individuals with Zika virus infection may reduce spread of infection to others by following the same precautions to avoid mosquito bites during the first week of illness (the likely window of viremia).
- Asymptomatic individuals who have traveled to an area with Zika virus mosquito transmission and then return to an area with no Zika virus mosquito transmission should avoid mosquito bites for three weeks after return (the period during which they could become viremic).

Environmental control measures include identification and elimination of potential mosquito breeding sites. Mosquito larvae breed in standing water; therefore, residents should be instructed to avoid allowing standing water to collect outdoors (such as in flower pots, buckets, bottles, jars, and other similar containers near houses). Domestic water tanks should be covered so that mosquitoes cannot enter, and drains that allow stagnant or standing water should be eliminated. Local and district health departments can help facilitate mitigation of transmission risk. (See “Malaria in endemic areas: Epidemiology, prevention, and control”, section on ‘Mosquito control’.)

Sexual transmission — Sexual transmission has been described; the duration of viral persistence in semen and in female genital tract secretions may be prolonged. (See ‘Transmission’ above.)

In all areas, men or women with Zika virus infection or exposure (via travel to mosquito transmission areas or sexual contact) who have a pregnant partner should abstain from unprotected sex for the duration of the pregnancy. (See “Male condoms” and “Female condoms”.)

Outside areas of Zika virus transmission, we are in agreement with guidance issued by the United States Centers for Disease Control and Prevention (CDC) for couples in which one or both partners have Zika virus infection or exposure, which include the following:

- Men with symptomatic Zika virus infection (confirmed or suspected) should wait at least six months after onset of illness before unprotected sex.
- Women with symptomatic Zika virus infection (confirmed or suspected) should wait at least eight weeks after onset of illness before unprotected sex.
- Asymptomatic men and women with Zika virus exposure should wait at least eight weeks after Zika virus exposure before unprotected sex.

Within areas of Zika virus mosquito transmission, it is prudent for individuals to abstain from sexual activity (vaginal, anal, and oral sex) or use barrier protection while active transmission persists.

Issues related to prevention of Zika virus during pregnancy are discussed further separately. (See “Zika virus infection: Pregnancy and congenital infection”, section on ‘Prevention’.)

Blood/tissue donation — Zika virus is transmissible via blood products and organ or tissue transplantation. Issues related to donor screening are discussed further separately. (See “Blood donor screening: Medical history”, section on ‘Zika virus’, and “Blood donor screening: Laboratory testing”.)

The US Food and Drug Administration (FDA) has issued donor deferral recommendations for hematopoietic stem cells, tissues, and donor gametes; the recommendations do not apply to solid organs. Living donors with Zika virus infection or relevant epidemiologic exposure (residence in or travel to an area where mosquito-borne transmission of Zika virus infection has been reported, or unprotected sexual contact with a person who meets these criteria) should be
considered ineligible for donation for six months. Deceased donors with Zika virus infection in the preceding six months should be also be considered ineligible.

**Nosocomial transmission** — Transmission of Zika virus via occupational exposure in a healthcare setting has not been described. Standard precautions are appropriate for protection of healthcare personnel and patients from Zika virus infection in these settings [132,134]. (See "General principles of infection control", section on 'Standard precautions'.)

**INFORMATION FOR PATIENTS** — UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient education: Zika virus infection (The Basics)" and "Patient education: Guillain-Barré syndrome (The Basics)"

**SUMMARY**

- Outbreaks of Zika virus infection, caused by an emerging mosquito-borne flavivirus, have occurred in Africa, Southeast Asia, and the Pacific Islands; currently, there is an ongoing Zika virus outbreak in the Americas. Zika virus is transmitted to humans via the bite of an infected Aedes mosquito. This type of mosquito usually bites during the daytime and breeds in standing water (particularly manmade containers). (See 'Epidemiology' above.)

- Clinical manifestations of Zika virus infection include acute onset of low-grade fever with maculopapular pruritic rash, arthralgia (notably small joints of hands and feet), or conjunctivitis (nonpurulent); clinical illness is consistent with Zika virus disease if two or more of these symptoms are present. Zika virus infection has also been associated with congenital microcephaly, fetal loss, and Guillain-Barré syndrome. (See 'Clinical manifestations' above.)

- The incubation period between mosquito bite and onset of clinical manifestations is typically 2 to 14 days. The illness is usually mild; clinical manifestations usually resolve within two to seven days. Asymptomatic infection is common; symptoms develop in 20 to 25 percent of individuals who become infected with Zika virus. Once a person has been infected, he or she is likely to be protected from future infections. (See 'Symptoms and signs' above.)

- The diagnosis of Zika virus infection should be suspected in individuals with typical clinical manifestations and relevant epidemiologic exposure (residence in or travel to an area where mosquito-borne transmission of Zika virus infection has been reported, or unprotected sexual contact with a person who meets these criteria). (See 'Diagnosis' above.)

- The diagnosis of Zika virus infection is established via real-time reverse-transcription polymerase chain reaction (rRT-PCR) testing for Zika viral RNA (in serum or urine) or serology. The approach to diagnostic testing depends on the timing of presentation after onset of symptoms. (See 'Patient groups' above.)

- There is no specific treatment for Zika virus infection and there is no vaccine for prevention. Management consists of symptomatic treatment. Preventive measures include personal protective measures to prevent mosquito bites and institution of measures to eliminate and control mosquito breeding sites. (See 'Management' above and 'Mosquito protection' above.)

- Sexual transmission of Zika virus has been described. In all areas, men or women with Zika virus infection or exposure (via travel to mosquito transmission areas or sexual contact) who have a pregnant partner should abstain from unprotected sex for the duration of the pregnancy. Within areas of Zika virus mosquito transmission, it is prudent for individuals to abstain from sexual activity (vaginal, anal, and oral sex) or use barrier protection while active transmission persists. (See 'Sexual transmission' above.)

- Outside areas of Zika virus mosquito transmission, guidance for couples in which one or both partners have Zika virus infection or exposure include the following (see 'Sexual transmission' above):
• Men with symptomatic Zika virus infection (confirmed or suspected) should wait at least six months after onset of illness before unprotected sex.

• Women with symptomatic Zika virus infection (confirmed or suspected) should wait at least eight weeks after onset of illness before unprotected sex.

• Asymptomatic men and women with Zika virus exposure should wait at least eight weeks after Zika virus exposure before unprotected sex.

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Topic 106169 Version 103.0
GRAPHICS

Estimated range of *Aedes aegypti* and *Aedes albopictus* in the United States

These maps show areas where mosquitoes are or have been previously found (based on a variety of sources) and reflect estimates of the potential range of *Aedes aegypti* and *Aedes albopictus* in the United States. These maps do not show exact locations or numbers of mosquitoes living in an area nor do they represent risk for spread of disease.

Graphic 106382 Version 3.0
Global distribution of *Aedes aegypti* and *Aedes albopictus*


Graphic 107582 Version 1.0
## Clinical features: Zika virus compared with dengue and chikungunya

<table>
<thead>
<tr>
<th>Features</th>
<th>Zika</th>
<th>Dengue</th>
<th>Chikungunya</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Rash</td>
<td>+++</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>++</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>++</td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td>Myalgia</td>
<td>+</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Headache</td>
<td>+</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>-</td>
<td>++</td>
<td>-</td>
</tr>
<tr>
<td>Shock</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
</tbody>
</table>


Graphic 106512 Version 1.0
### Interpretation of results of antibody testing for suspected Zika virus infection* — United States, 2016

<table>
<thead>
<tr>
<th>Zika virus and dengue virus IgM ELISA</th>
<th>Zika virus PRNT</th>
<th>Dengue virus PRNT</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive or equivocal (either assay)</td>
<td>≥10</td>
<td>&lt;10</td>
<td>Recent Zika virus infection</td>
</tr>
<tr>
<td>Positive or equivocal (either assay)</td>
<td>&lt;10</td>
<td>≥10</td>
<td>Recent dengue virus infection</td>
</tr>
<tr>
<td>Positive or equivocal (either assay)</td>
<td>≥10</td>
<td>≥10</td>
<td>Recent flavivirus infection; specific virus cannot be identified</td>
</tr>
<tr>
<td>Inconclusive in one assay AND inconclusive or negative in the other</td>
<td>≥10</td>
<td>&lt;10</td>
<td>Evidence of Zika virus infection; timing cannot be determined</td>
</tr>
<tr>
<td>Inconclusive in one assay AND inconclusive or negative in the other</td>
<td>&lt;10</td>
<td>≥10</td>
<td>Evidence of dengue virus infection; timing cannot be determined</td>
</tr>
<tr>
<td>Inconclusive in one assay AND inconclusive or negative in the other</td>
<td>≥10</td>
<td>≥10</td>
<td>Evidence of flavivirus infection; specific virus and timing cannot be determined</td>
</tr>
<tr>
<td>Any result (either or both assays)</td>
<td>&lt;10</td>
<td>&lt;10</td>
<td>No evidence of Zika virus or dengue virus infection</td>
</tr>
<tr>
<td>Positive for Zika virus AND negative for dengue virus</td>
<td>Not yet performed</td>
<td>Not yet performed</td>
<td>Presumptive recent Zika virus infection</td>
</tr>
<tr>
<td>Positive for dengue virus AND negative for Zika virus</td>
<td>Not yet performed</td>
<td>Not yet performed</td>
<td>Presumptive recent dengue virus infection</td>
</tr>
<tr>
<td>Positive for Zika virus AND positive for dengue virus</td>
<td>Not yet performed</td>
<td>Not yet performed</td>
<td>Presumptive recent flavivirus virus infection</td>
</tr>
<tr>
<td>Equivocal (either or both assays)</td>
<td>Not yet performed</td>
<td>Not yet performed</td>
<td>Equivocal results</td>
</tr>
<tr>
<td>Inconclusive in one assay AND inconclusive or negative in the other</td>
<td>Not yet performed</td>
<td>Not yet performed</td>
<td>Inconclusive results</td>
</tr>
<tr>
<td>Negative for Zika virus AND negative for dengue virus</td>
<td>Not indicated</td>
<td>Not indicated</td>
<td>No evidence of recent Zika virus or dengue virus infection</td>
</tr>
</tbody>
</table>

ELISA: enzyme-linked immunosorbent assay; IgM: immunoglobulin M antibodies; PRNT: plaque reduction neutralization test.

* For persons with suspected Zika virus disease, Zika virus real-time reverse transcription–polymerase chain reaction (rRT-PCR) should be performed on serum specimens collected <7 days after onset of symptoms and on urine specimens collected <14 days after onset of symptoms.

† In the absence of rRT-PCR testing, negative IgM or neutralizing antibody testing in specimens collected <7 days after illness onset might reflect collection before development of detectable antibodies and does not rule out recent flavivirus virus infection.
out infection with the virus for which testing was conducted.

Δ Zika IgM positive result is reported as "presumptive positive" to denote the need to perform confirmatory PRNT.

◊ Report any positive or equivocal IgM Zika or dengue results to state or local health department.

§ To resolve false-positive results that might be caused by cross-reactivity or nonspecific reactivity, presumptive positive Zika IgM results should be confirmed with PRNT titers against Zika, dengue, and other flaviviruses to which the person might have been exposed. In addition, equivocal and inconclusive results that are not resolved by retesting also should have PRNT titers performed to rule out a false-positive result.


Graphic 108362 Version 1.0