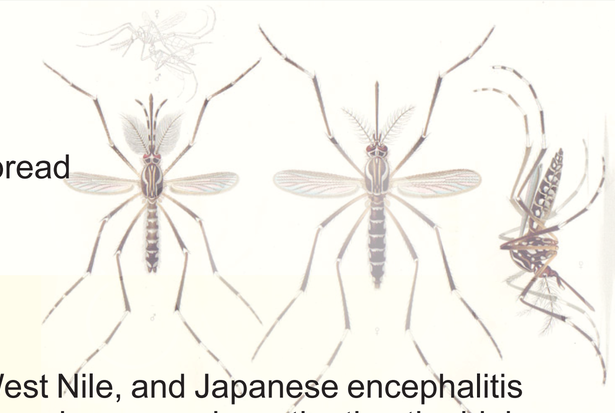
Zika Virus Alert!

Another virus has re-emerged and quickly garnered attention for its association with severe birth defects and its spread across the Americas.



Zika virus (ZIKV) is:

a mosquito-borne ssRNA virus in the family Flaviviridae and genus Flavivirus. It is related to yellow fever, dengue, West Nile, and Japanese encephalitis viruses. Zika virus was first isolated in 1947 from a blood sample taken from a sentinel Rhesus monkey. Initially, researchers were investigating the high incidence of immunity to yellow fever virus among monkeys in Zika forest in Uganda. When one of the monkey developed fever, its blood samples were taken daily and were inoculated into mice. Further isolations of the mice tissues lead to the discovery of the new virus, which then named after the forest. As an arbovirus, ZIKV has been isolated from *Aedes africanus*, *Ae. apicoargenteus*, *Ae. luteocephalus*, *Ae. aegypti*, *Ae. vitattus*, and *Ae. furcifer* mosquitoes.

Epidemiology

Sporadic infections of ZIKV were reported in Africa and Asia. In 1954, ZIKV was isolated from a jaundice patient suspected of having yellow fever in Nigeria, this finding marked the first ZIKV infection in human. Between 1964 and 1970, ZIKV was identified as one of the causative agents in an epidemiological study in Nigeria. In Southeast Asia, several ZIKV infections were reported from Indonesia. The virus was serologically confirmed in acute fever patients in Central Java, Indonesia in 1977. In an arboviral antibodies survey in Lombok 1982, ZIKV was serologically identified in selected samples. Australian citizens were reported of contracting the virus following a brief travel to Jakarta 2013 and Bali 2015.(Fig.1). A sample obtained from a dengue outbreak patient in Jambi 2015 was positively confirmed by RT-PCR for ZIKV. More incidental reports from Cambodia, the Philippines, and Thailand between 2010 and 2014 were later confirmed the sporadic spread of ZIKV in Asia.

Figure 1. Reported zika virus cases and exposure in Indonesia

The first ZIKV outbreak occurred in Yap State, Micronesia in 2007 with 49 confirmed cases. Other outbreaks occurred between 2013 and 2014 in four Pacific countries (French Polynesia, New Caledonia, Cook Islands, and Easter Island). In March 2015, a dengue-like illness outbreak occurred in Bahia, Brazil with 7 out of 24 serum samples from the patients were positively confirmed by RT-PCR for ZIKV. As of 23 January 2016, the US CDC reported active transmission of ZIKV is occurring in 25 countries in the Americas, Oceania/Pacific Islands, and Africa (Fig. 2).

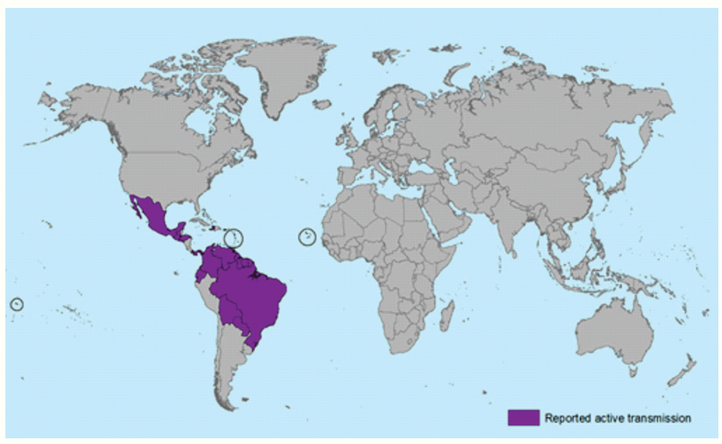


Figure 2. Zika-affected areas as of 23 January 2016 (Source: US CDC, 2016)

Transmission

Mode of transmission is mainly through an infected Aedes mosquito bites. Non-vector routes include mother to child transmission (during pregnancy or birth), blood transfusion, or sexual contact. ZIKV has been detected in breast milk, however transmission through breastfeeding has yet been reported. The incubation period is currently unknown.

Clinical Manifestations

Typically, a ZIKV infection would causes mild symptoms and self-limiting dengue-like illness. An infected patient may experience symptoms for 2-7 days. The symptoms were characterized by low-grade fever, maculopapular rash, conjunctivitis, arthralgia, myalgia, and headache. Hospitalizations or deaths are uncommon. However, possible complications following co-infections of ZIKV with dengue virus may include Guillain-Barré syndrome, other autoimmune diseases, neurological syndrome, as well as ophthalmologic and cardiac complications. In addition, ZIKV infection is likely to be associated with congenital anomaly, such as microcephaly in newborn babies.

The unusual occurrence of microcephaly babies in Brazil and its possible association with ZIKV outbreak in 2015 has generated concerns, since vertical infection during pregnancy resulting in fetal brain abnormality is relatively rare. Microcephaly is a birth defect where a baby's head is smaller than expected when compared to babies of the same sex and age (Fig. 3). In the year 2000, the prevalence of microcephaly in Brazilian newborns was 5.5 cases /100,000 live births. Ten years later, the prevalence was only slightly increased to 5.7 /100,000 live births. As of 30 November 2015, there were twentyfold increase of the prevalence to 99.7 /100,000 live births or 1,248 cases of microcephaly. Brain atrophy and intracranial calcifications are among the prominent abnormalities observed through fetal ultrasound examination. During the outbreak in Brazil, ZIKV RNA has been identified in specimens (brain tissue, placenta, and amniotic fluid) collected from several infants with microcephaly and from fetal losses in women infected with ZIKV during pregnancy. Cerebrospinal fluids from 35 infants with microcephaly from suspected ZIKV-infected mother are currently under investigation.

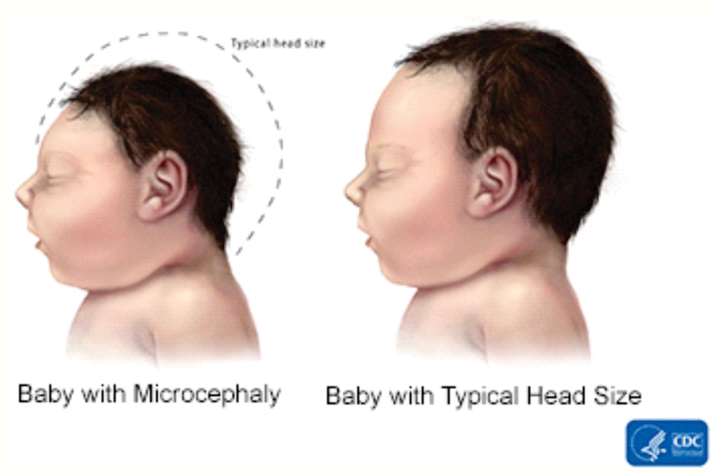


Figure 3. An illustration of a baby with and without microcephaly (Source: US CDC, 2016)

Clinical diagnosis of ZIKV infection based on signs and epidemiological data are sometimes unreliable because of its similarity with dengue or chikungunya virus infection. Variations on complete blood count (CBC) profile in ZIKV patients were reported. Some showed patterns of leukopenia and thrombocytopenia, which are also commonly found in dengue or chikungunya virus infections. Other reports revealed normal CBC results.

Diagnostic tools

Laboratory confirmations for ZIKV infection are made through serological tests for the presence of specific antibodies, molecular assay using reverse-transcription PCR (RT-PCR), or virus isolation (gold standard) for virus detection. Blood samples for serologic tests should be collected approximately 5 days after the onset of symptoms. Note that ZIKV specific IgM and neutralizing antibodies may cross-react with other flaviviruses, such as dengue, West Nile, and yellow fever virus. Cross-reacting antibodies may be differentiated through plaque-reduction neutralization test. For RT-PCR assay or virus isolation, blood samples should be collected during the first 3-5 days after the onset of symptoms. RT-PCR may also be performed with urine or saliva samples. A study demonstrated that ZIKV was detected with RT-PCR at higher titers in urine and stayed positive there for a longer period (>10 days) than in blood. Other study revealed that with RT-PCR, ZIKV was detected in saliva within the same time window as in blood. However, saliva should not be used to replace blood samples since a negative saliva does not necessarily means negative ZIKV.

Treatment

There are no definitive treatment nor vaccine for ZIKV infection yet. Infected people would generally be given supportive or symptomatic treatment. They should get plenty of rest, drink enough fluids, and treat pain and fever with common medicines. Take medicine such as acetaminophen to relieve fever and pain. Do not take aspirin or other non-steroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen and naproxen. Aspirin and NSAIDs should be avoided until the possibility of having dengue infection is excluded. Unfortunately, the performance of diagnostic tools to distinguish the two diseases, especially rapid tests, are still not satisfying. Moreover, there is still much to learn about the signs, symptoms, and pathogenesis ZIKV infection.

Prevention

The patients should also prevent further transmission by protecting themselves from mosquito bites during the first week of illness by using repellent or physical barriers such as clothes, screens, mosquito nets, etc. This prevention methods are applicable as well for those who wish to stay uninfected. Other preventative measures to reduce mosquito breeding sites as suggested for dengue vector control are also recommended. During an outbreak, health authorities may conduct insecticides spray. Pregnant women and women trying to become pregnant are advised not to travel to Zika-affected areas. Some countries even advised women to delay pregnancy up to two years following the outbreaks.

Selected references

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